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Real-world clinical validation of the Qatar pre-diabetes risk score: a cross-sectional study

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ABSTRACT

Introduction Pre-diabetes stands as a prominent, independent risk factor for the onset of type 2 diabetes (T2D), with 5%–10% of individuals with pre-diabetes progressing to T2D annually. The effectiveness of rigorous lifestyle interventions in averting the transition from pre-diabetes to T2D has been substantiated across multiple investigations and populations. Consequently, the clinical imperative of early pre-diabetes detection becomes unequivocal. This study assessed the validity of the recently developed pre-diabetes risk score in Qatar (PRISQ) in a real-world clinical setting.

Research design and methods We recruited 1021 walk-in participants from 3 different health centres of Qatar's Primary Health Care Corporation. Only adult people without known pre-diabetes or diabetes were included in the study. Along with blood collected for the haemoglobin A1c (HbA_{1c}) test to confirm pre-diabetes, we recorded the age, gender, weight, waist circumference, systolic and diastolic blood pressure, nationality, smoking state and family history of diabetes. Negative predictive value, positive predictive value, sensitivity and specificity of PRISQ were computed.

Results Of the 1021 participants, 797 agreed to provide blood. HbA_{1c} test revealed that 21.9% of the 797 subjects had pre-diabetes (HbA_{1c} between 5.7% and 6.5%) while 3.3% had undiagnosed diabetes ($HbA_{1c} \geq 6.5\%$). Using a PRISQ cut-off of 16, PRISQ sensitivity exceeded 90% in all subgroups of individuals aged 40 years and above, regardless of ethnicity. We did not see any significant improvement in PRISQ sensitivity when we considered the family history of diabetes.

Conclusions We confirmed a good PRISQ diagnostic rate for pre-diabetes from a representative sample of the Qatar population recruited in a real-world clinical setting. PRISQ can potentially play a significant role in curbing the T2D epidemic sweeping Qatar and beyond.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The progression from pre-diabetes to type 2 diabetes (T2D) can be prevented through lifestyle intervention in a significant proportion of individuals. Timely diagnosis and the subsequent appropriate treatment are both needed to reduce the burden of T2D. Current pre-diabetes diagnosis, that is, fasting blood glucose, haemoglobin A1c or oral glucose tolerance test, involves an invasive and potentially expensive blood test, unsuitable for populations screening. Hence, urgent development of non-invasive tools for large-scale screening, especially in high pre-diabetes prevalence countries, is needed.

WHAT THIS STUDY ADDS

⇒ The current study provides evidence that a pre-diabetes risk score in Qatar (PRISQ) we developed recently using clinical data from Qatar biobank, and which uses only non-invasive parameters, can correctly diagnose pre-diabetes in more than 90% of ≥40 years individuals in a real clinical setting.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ PRISQ stands as a powerful solution, providing a rapid and cost-effective pre-diabetes diagnosis through exclusively non-invasive parameters. Tailored for population screening in primary healthcare centres, its applicability transcends Qatar, holding the promise to globally address the T2D crisis. Furthermore, PRISQ could benefit populations living in regions where invasive and potentially expensive blood tests may not be easily accessible. The implementation of PRISQ in primary healthcare centres is not just beneficial; it is imperative for proactive healthcare, offering relief to healthcare systems grappling with the diabetes epidemic.

INTRODUCTION

Pre-diabetes is a metabolic condition characterised by elevated blood glucose concentrations that surpass normal levels but do not meet the definitive diagnostic criteria for diabetes mellitus. Current estimates indicate that approximately 7.5% of the global population is affected by pre-diabetes.[1] Importantly, pre-diabetes confers a substantial increase in the risk of progression to type 2 diabetes (T2D). Longitudinal studies have consistently demonstrated an annual transition rate of 5%–10% among individuals with pre-diabetes progressing to manifest T2D.[2] Projections forecast a rise in the global pre-diabetes

prevalence in the next 20 years,[1] exacerbating the anticipated future incidence of T2D unless effective preventive measures are promptly implemented.

A fundamental quandary encountered when tackling pre-diabetes revolves around its inherent potential for prolonged asymptomatic manifestation, a trait it shares with T2D. Consequently, it can surreptitiously and progressively compromise vital organs, thereby establishing the groundwork for the onset of diabetes-associated microvascular and macrovascular complications.[3]

Epidemiological studies across diverse Middle Eastern nations, particularly within the Gulf Cooperation Council (GCC) countries, have documented a notable prevalence of pre-diabetes akin to T2D.[4 5] Considering the previously mentioned annual transition ratios, these findings evoke heightened apprehension in the region. Encouragingly, a multitude of scientific findings have established that the progression from pre-diabetes to T2D can be averted, or at minimum delayed, in a substantial proportion of pre-diabetes individuals through interventions such as intensive lifestyle modification or pharmacological approaches like metformin.[6–11] This observation highlights the paramount significance of promptly identifying individuals with pre-diabetes. This proactive measure holds substantial promise as a cost-effective intervention in mitigating the prevailing T2D epidemic sweeping the Middle East region.

According to a a secondary data analysis of a cross-sectional survey that included 2497 Qatari nationals aged 18–64 years, the prevalence of pre-diabetes was 11.9%.[12] However, a pilot screening programme (n=3515) involving individuals at risk for T2D (eg, obese, hypertensive, family history of diabetes (FHD)) revealed that about 21% of the screened individuals had pre-diabetes.[13] Other studies from the different nations of the GCC have reported pre-diabetes rates from 19.4% to 40 in Kuwait,[5 14] 25.5% in a cohort of Saudi adult males[4] and 17.02% in adult Emirates.[15] These rates are among the highest in the world.[1] Given the high prevalence of pre-diabetes in Qatar, we have recently developed a pre-diabetes risk score (PRISQ) based on data collected from 6000 Qatari individuals sourced from Qatar Biobank.[16] PRISQ uses only non-invasive parameters, including age, gender, body mass index (BMI), waist circumference (WC) and blood pressure, to generate a score indicative of the risk level of having pre-diabetes. PRISQ has a performance of 80% and a sensitivity of 86%.[16] In pursuit of clinical validation of PRISQ, with the prospect of deploying this tool in primary healthcare clinics, we embarked on a study to ensure the tool's robustness, reliability and accuracy when applied in real-world medical scenarios.

RESEARCH METHODS

Study setting

The study was conducted in Primary Health Care Corporation (PHCC), Qatar's largest primary care provider. Approximately 70% of Qatar's population is registered with PHCC across 31 health centres located in the country's three geographical regions (Central, Western and Northern).

Study population and design

A meticulously designed cross-sectional study was conducted to validate the efficacy of PRISQ within a real-world clinical setting. Individuals aged 18 or above with no previous history of diabetes mellitus and who could communicate in English or Arabic were eligible for inclusion. Exclusion criteria included pregnancy, not being able to consent, having a BMI<18.5 or >60 kg/m^2, and having an existing diagnosis of either T1D or T2D. The recruitment took place from December 2022 to March 2023.

For the recruitment of participants, we used a probability sampling method. One health centre was randomly selected from each geographic region. Every fifth individual was approached to participate in the study at each health centre.

The sample size required for the study was calculated as 176 subjects with pre-diabetes and 528 without pre-diabetes. According to the American Diabetes guidelines,[17] pre-diabetes subjects were defined as those individuals with Haemoglobin A1c (HbA1c) between 39 mmol/mol (5.7%) and 47 mmol/mol (6.4%), whereas controls were those with HbA1c<39 mmol/mol (5.7%). An additional 20 participants in each group were included to factor withdrawals. Therefore, the overall sample required was estimated to be 744. The calculations were performed according to the equations in Flahault *et al*.[18]

Participant recruitment

Trained data collectors approached potential participants as they entered waiting areas of health centres. They established the eligibility of participants, following which they obtained written informed consent before proceeding to data collection.

Study locations and data collection

The study was conducted at one randomly selected PHCC health centre from each of the three geographical regions of Qatar as follows—Central Region (Al Thumama Health Center), Western Region (Muaither Health Center) and Northern Region (Al Gharrafaat Al Rayyan Health Center).

Potential participants were provided with information about the study, and if they agreed to participate, written informed consent was obtained. Data collectors recorded the following information from participants: age, gender, nationality, weight, height, WC, systolic and diastolic blood pressure readings, smoking status, and FHD. BMI (kg/m^2) was calculated by dividing the weight in kilograms by the square of the height in metres. The WC measurement was performed using a flexible measuring tape wrapped around the waist at the midpoint between the iliac crest and subcostal margins. The tape was placed

directly on the skin or a thin layer of clothing without any compression. Additionally, a certified phlebotomist meticulously drew blood to facilitate subsequent HbA1c analysis.

PRISQ model

PRISQ was initially developed in a randomly selected training set (1902 subjects with pre-diabetes and 3912 subjects without pre-diabetes(80% of the total sample)) and internally validated in a testing set (983 without pre-diabetes and 471 with pre-diabetes (20%). The clinical data used to develop PRISQ were obtained from the Qatar Biobank cohort, which enrols people from the general population.[19] PRISQ includes five predictors: age, gender, BMI, WC, and systolic and diastolic blood pressure. The PRISQ score ranges from 0 to 45, and at a cut-off point of 16 yielded sensitivity and specificity of 86.2% (95% CI 82.7% to 89.2%) and 57.9% (95% CI 65.5% to 71.4%), respectively. The area under the curve (AUC) of the score was 80% (95% CI 78% to 83%).

Statistical analysis

All statistical analyses were performed using R V.4.0, RStudio V.1.2.5031 (R Core Team (2021)), and Stata V.16 (StataCorp). Participants were divided into subgroups according to their age in years (all, ≤40 or>40) and nationality's geographical region. The analysis conducted in our study included two distinct risk levels to assess the likelihood of having pre-diabetes, as determined by the PRISQ score. We categorised the participants into two groups: those with a PRISQ score ≤16 are considered to have low risk level of having pre-diabetes, are thus free of pre-diabetes and coded 0 while those with a PRISQ score >16 are considered to have increased risk level of having pre-diabetes and coded 1.

The total score for each participant was calculated by summing the scores attributed to each variable category by multiplying the coefficient by 10 and rounding to the nearest integer following the logistic regression equation in our previous paper.[16] Predicted values, obtained based on the PRISQ score of each participant and observed values, obtained based on the HbA_{1c} value measured from the blood of each participant, were used to generate confusion matrices and calculate the true and false positives (FPs) and negatives, which are defined as fellow[20 21]:

- True positives (TP) are the cases where PRISQ correctly predicted the positive class.
- True negatives are the cases where PRISQ correctly predicted the negative class.
- FPs are the cases where PRISQ incorrectly predicted the positive class when the actual class was negative.
- False negatives are the cases where PRISQ incorrectly predicted the negative class when the actual class was positive.

The positive predictive value (PPV), which measures the probability that a positive test result is truly positive, and the negative predictive value (NPV), which measures the probability that a negative test result is truly negative, were calculated using the following formulas:

$$PPV = \frac{TP}{TP+FP} \times 100$$

$$NPV = \frac{TN}{TN+FN} \times 100$$

The sensitivity, which measures the proportion of actual positive cases that the test correctly identifies as positive, was calculated as follows[20 21]:

$$Sensitivity = \frac{TP}{TP+FN} \times 100$$

The specificity, which measures the proportion of actual negative cases that the test correctly identifies as negative, was calculated as follows:

$$Specificity = \frac{TN}{TN+FP} \times 100$$

We used the χ^2 Test to compare the sensitivities of PRISQ in different subgroups. Statistical significance was considered at $p<0.05$.

To generalise PRISQ across various ethnicities within the Qatari population, we stratified the cohort into distinct subgroups based on participants' citizenship, categorised following established global regional demarcations.[22]

Patient and public involvement

Volunteer participants were not involved in any stage of the research process.

RESULTS

Study population description

The chart of the flow of the study is shown in figure 1. The baseline characteristics of the study population are summarised in table 1. Among the 1021 individuals who initially consented to participate, only 816 agreed to donate blood for the HbA_{1c} test. Following the exclusion of individuals with a BMI>60and BMI<18.5 kg/m^2, 797 participants (65.11% of whom were female and had an average age of 37±10 years) were kept in the final cohort. Consequently, PRISQ validation was evaluated within this subset.

Among the 797 individuals, 541 (67.87%) exhibited overweight or obesity, defined as BMI ≥25 kg/m^2. Within the male subset of 278 participants, 107 possessed waist circumferences (WC) below 94 cm, 93 had WC between 94 and 102 cm and 78 had WC beyond 102 cm. Among the 519 female participants, 134 had WC less than 80 cm, 122 ranged from 80 to 88 cm, and 263 exhibited WC greater than 88 cm. Hypertension, defined as systolic blood pressure (SBP) ≥130 mm Hg or diastolic blood pressure (DBP) ≥80 mm Hg, was observed in 51.7% of males and 37.3% of females. Current smokers represented only 8% of the sample; thus, we did not use this trait in further analysis.

Validation of the diagnostic accuracy of PRISQ

Of the 797 individuals, 596 (74.8%) were without pre-diabetes, 175 (21.9%) had pre-diabetes and 27 (3.3%)

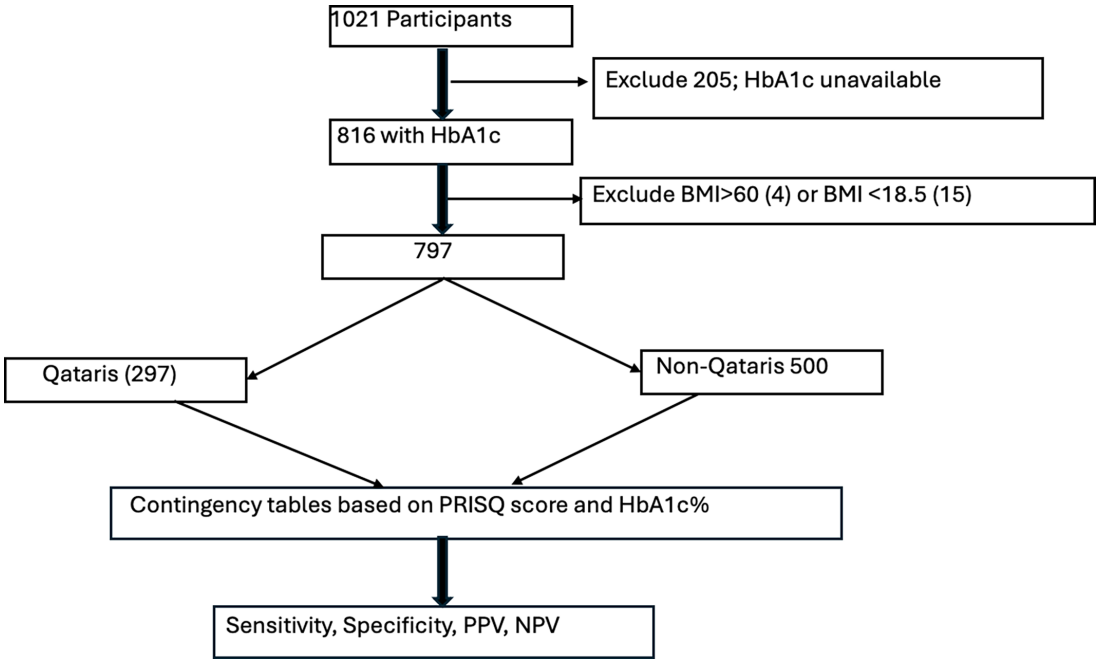

Figure 1 Flow chart of the study design. BMI, body mass index; HbA1c; haemoglobin A1c; NPV, negative predictive value; PPV, positive predictive value; PRISQ, pre-diabetes risk score in Qatar.

had undiagnosed diabetes (figure 2A). Pre-diabetes and diabetes were defined based on HbA_{1c} values.

In the subsequent analysis, we evaluated the discriminative efficacy of PRISQ by calculating standard diagnostic test metrics, specifically sensitivity, specificity, PPV and NPV. To ensure the comprehensive detection of individuals with hyperglycaemia, encompassing pre-diabetes and diabetes, we adopted a threshold criterion. Specifically, individuals were categorised according to their PRISQ scores. Those scoring a score of 16 or below were assigned to the low-risk category while scores ranging from 17 to 27 indicated a moderate risk of harbouring pre-diabetes or diabetes. Individuals with scores exceeding 27 were classified as high-risk individuals. Employing these delineations, we observed that 420 individuals, constituting 53% of the total cohort, possessed PRISQ scores surpassing 16, thereby implicating moderate to high-risk levels of pre-diabetes or diabetes, as depicted in figure 2B.

Table 1 Baseline characteristics of the participants

	Female N=519	Male N=278	P value
Age (years)	36.4 (±9.8)	38 (±10)	0.05
BMI (Kg/m^2)	28 (±6)	28 (±5)	0.70
SBP	117 (±13)	123 (±13)	<0.001
DBP	76 (±8)	79 (±8)	<0.001
WC (in cm)	90 (±15)	97 (±15)	<0.001
HbA1c %	5 (±1)	6 (±1)	<0.001

BMI, body mass index; DBP, diastolic blood pressure; HbA1c, haemoglobin A1c; SBP, systolic blood pressure; WC, waist circumference.

In the initial phase, we assessed the sensitivity of the PRISQ for the entire cohort, yielding a sensitivity of 70.3%. Subsequently, we conducted separate evaluations for the Qatari participants (sensitivity of 70.5%, n=297) and non-Qatari participants (sensitivity of 70.2%, n=500).

Given that age has a major contribution to the final score of PRISQ[16] and considering that T2D typically manifests after the age of 40 years, we examined the prevalence of pre-diabetes in individuals younger than 40 years (40–) and those aged 40 years or older (40+) (figure 2C,D). Our analysis revealed that 35% of individuals in the 40+ cohort exhibit pre-diabetes, compared with only 20% in the 40– cohort.

The contingency tables pertaining to the entire sample population and various subpopulations are illustrated in online supplemental figures S1–S4.

Compared with PRISQ sensitivity in all participants and 40– groups (whole cohort (40–), Qataris (40–) and non-Qataris (40–), the PRISQ sensitivity in all the 40+ subgroups demonstrated a notable improvement, exceeding 90% (table 2). For instance, the PRISQ sensitivities in 40+ Qatari and non-Qatari subjects are, respectively, 93.9% and 96.3% compared with 42.9% and 54% in 40– Qataris and 40– non-Qataris, and 70.5% and 70.2% in all Qataris and all non-Qataris subjects (table 2). These differences in sensitivity were statistically significant (figure 3).

As the initial development of PRISQ was predicated on a cohort composed of 6000 Qatari Citizens, we assessed the generalisability of PRISQ across various ethnicities within the Qatari population. Prominent representation was observed in regions encompassing North Africa, southern Asia, southeastern Asia and Western Asia. The

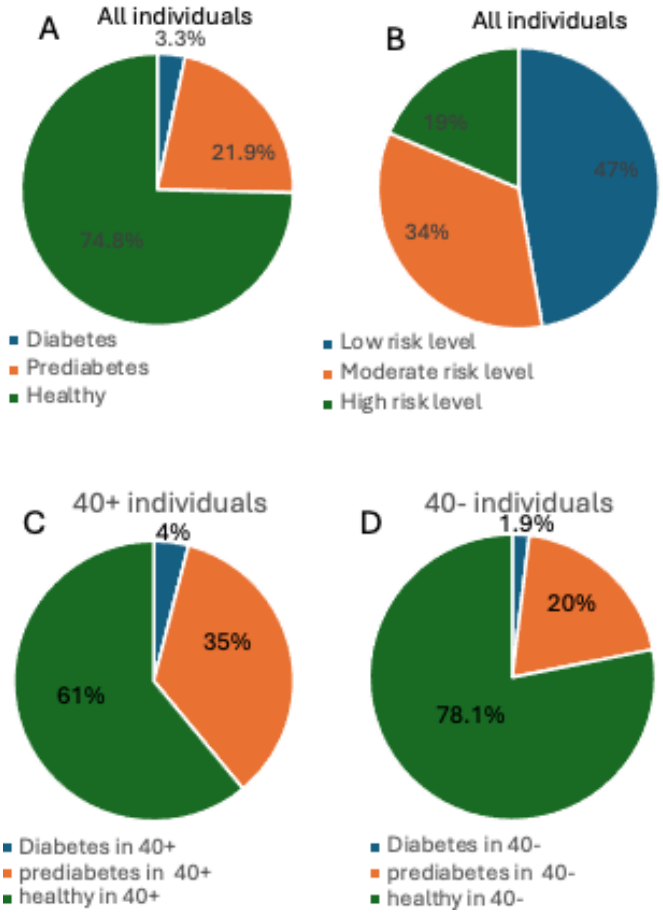

Figure 2 (A) Prevalence of pre-diabetes and diabetes in the whole cohort (n=797). (B) Levels of risk based on PRISQ score in the whole cohort. (C) Prevalence of pre-diabetes and diabetes in the group of individuals younger than 40. (D) Prevalence of diabetes and pre-diabetes and diabetes in individuals gaed 40 and above. Pre-diabetes and diabetes were defined based on $_{HbA1c}$ values according to the American Diabetes Association (ADA) criteria as described in methods. PRISQ, pre-diabetes risk score in Qatar.

enrolment of individuals originating from other regions, such as Europe or North America, fell short of a substantive threshold required to form statistically significant subpopulations. As delineated in table 2 and figure 3, the discerned sensitivity of PRISQ among diverse ethnicities surpasses 90% within the 40+ age group, as compared with their 40– counterparts, where it attains a maximal value of 66.7%, explicitly observed within the North African subgroup. Figure 3 shows that the differences between 40+ and 40– sensitivities are statistically significant in all ethnicities.

The established body of literature affirms the pivotal role of an FHD as a prominent prognostic factor for the onset of diabetes. Consequently, we sought to examine whether the PRISQ sensitivity could be improved if we consider FHD. As delineated in table 2 and illustrated in figure 3, the discerned sensitivity of PRISQ in the 40+ Qatari individuals with an FHD showed a modest increment in comparison to when FHD was not considered (94.4% as opposed to 93.9%, p=0.67). In the 40+ non-Qatari with an FHD, PRISQ sensitivity reached 100%, demonstrating an improvement of nearly four percentage points compared with scenarios where FHD was not considered. However, this improvement is not significant (100% vs 96.3%, p=0.51)

DISCUSSION

As several studies have consistently shown, pre-diabetes can be reversed when met with targeted lifestyle interventions,[6–11] underscoring the substantial potential for averting the progression to full-blown diabetes by timely identification and intervention in individuals with pre-diabetes. By capitalising on the reversibility of pre-diabetes and the cost-effectiveness of lifestyle interventions, a significant reduction in the burdens associated with T2D in terms of healthcare expenditures and immeasurable societal costs could be attained.

Recently, we developed a PRISQ using data from 6000 Qatari adults who participated in the Qatar Biobank cohort. PRISQ uses five non-invasive parameters (age, BMI, SBP, DBP and WC) and yields a score ranging from 0 to 45.[16] A score above 16 indicates a moderate risk level of having pre-diabetes, while a score above 27 indicates a high-risk level.[16] The sensitivity of PRISQ was 86%.[16] In comparison to pre-diabetes risk scores formulated for adult populations in various international contexts, PRISQ exhibited superior discriminative capacity. As assessed by the AUC, PRISQ yielded an AUC of 80%, surpassing several analogous scores developed in disparate locales. Notably, these include risk scores from Indonesia (AUC: 62.3%),[23] China (two distinct scores with AUCs of 74% and 70%)[24 25] and the USA (AUC: 74%).[26] Furthermore, our risk score demonstrated commendable sensitivity, quantified at 86.02%, with a designated cut-off value of 16.

In this study, we evaluated the performance of PRISQ in a real-world clinical setting by recruiting walk-in adult participants in three primary healthcare centres. Contrary to the original cohort, composed exclusively of Qatari citizens, in this investigation, we sought to ascertain the PRISQ performance across a diverse cohort, transcending ethnic boundaries.

Our results unequivocally affirm the outstanding performance of PRISQ, irrespective of participants' ethnicity. PRISQ correctly identified more than 90% of the subjects with pre-diabetes among participants aged 40 years or above. This robust performance underscores the test's reliability in capturing pre-diabetes in a clinical context, thus substantiating its potential as a pivotal tool in healthcare settings in Qatar to fight the T2D epidemic.

In the context of the relentless surge in the global incidence of pre-diabetes and T2D, particularly in the Middle East,[27 28] a compelling imperative emerges to advance and enhance screening tools meticulously designed to enable comprehensive, population-wide screening. This need pertains notably to countries characterised by a heightened prevalence of these conditions,

Table 2 PRISQ metrics in different subgroups

Subgroups (n)	Sensitivity (95% CI)	Specificity (95% CI)	NPV (95% CI)	PPV (95% CI)
All participants (797)	70.3 (63.5 to 76.5)	52.3 (48.2 to 56.3)	83.8 (80 to 87.4)	33.3 (28.9 to 38)
All participants ≤40 (546)	51.3 (41.8 to 60.7)	66.6 (61.9 to 71)	83.7 (79.3 to 87.4)	29.1 (22.9 to 35.8)
All participants >40 (251)	95.4 (88.6 to 98.7)	14.6 (9.61 to 21)	85.7 (67.3 to 96)	37.2 (30.9 to 43.9)
All Qataris (297)	70.5 (57.4 to 81.5)	61 (54.5 to 67.3)	88.9 (83 to 93.3)	32 (24.1 to 40.4)
Qataris ≤40 (190)	42.9 (24.5 to 62.8)	80.2 (73.3 to 86.1)	89 (82.8 to 93.6)	27.3 (15 to 42.8)
Qataris >40 (107)	93.9 (79.8 to 99.3)	18.7 (10.7 to 29.7)	87.5 (61.7 to 98.4)	34.1 (24.5 to 44.7)
All non-Qataris (500)	70.2 (61.9 to 77.6)	46.5 (41.3 to 51.8)	79.7 (73.8 to 85.1)	34 (28.6 to 39.8)
Non-Qataris ≤40 (356)	54 (43 to 64.8)	58.4 (52.2 to 64.3)	79.7 (73.4 to 85.1)	29.6 (22.6 to 37.3)
Non-Qataris >40 (144	96.3 (87.3 to 99.5)	11.1 (5.46 to 19.5)	83.3 (51.6 to 97.9)	39.4 (31 to 48.3)
All participants with FHD (315)	69.7 (59-79)	46.9 (40.3 to 53.6)	79.9 (71.9 to 86.2)	34.1 (27.2 to 41.4)
Participants ≤40 with FHD (215)	52.7 (38.8 to 66.3)	61.9 (53.9 to 69.4)	79.2 (71 to 85.9)	32.2 (22.8 to 42.9)
Participants >40 with FHD (100)	97.1 (84.7 to 99.9)	10.6 (4.37 to 20.6)	87.5 (47.3 to 99.7)	35.9 (26.1 to 46.5)
All Qataris with FHD (122)	75.8 (57.7 to 88.9)	53.9 (43 to 64.6)	85.7 (73.8 to 93.6)	37.9 (26.2 to 50.7)
Qataris ≤40 with FHD (73)	53.3 (26.6 to 78.7)	77.6 (64.7 to 87.5)	86.5 (74.2 to 94.4)	38.1 (18.1 to 61.6)
Qataris >40 with FHD (49)	94.4 (72.7 to 99.9)	9.68 (2.04 to 25.8)	75 (19.4 to 99.4)	37.8 (23.8 to 53.5)
All non-Qataris with FHD (193)	66.1 (52.2 to 78.2)	42.3 (33.9 to 51.1)	75.3 (64.2 to 84.4)	31.9 (23.6 to 41.2)
Non-Qataris ≤40 with FHD (142)	52.5 (36.1 to 68.5)	52.9 (42.8 to 62.9)	74 (62.4 to 83.5)	30.4 (19.9 to 42.7)
Non-Qataris >40 with FHD (51)	100 (79.4 to 100)	11.4 (3.2 to 26.7)	100 (39.8 to 100)	34 (20.9 to 49.3)
All North Africans (83)	75 (47.6 to 92.7)	28.4 (18 to 40.7)	82.6 (61.2 to 95)	20 (10.8 to 32.3)
North Africans ≤40 (53)	66.7 (34.9 to 90.1)	43.9 (28.5 to 60.3)	81.8 (59.7 to 94.8)	25.8 (11.9 to 44.6)
North Africans >40 (30)	100 (39.8 to 100)	3.85 (0.09 to 19.6)	100 (2.5 to 100)	13.8 (3.89 to 31.7)
All Southern Asians (243)	67.9 (56.8 to 77.6)	50.9 (42.9 to 58.9)	75 (65.7 to 82.8)	42.2 (33.8 to 51)
Southern Asians ≤40 (185)	53.7 (39.6 to 67.4)	59.5 (50.6 to 68)	75.7 (66.3 to 83.6)	35.4 (25.1 to 46.7)
Southern Asians >40 (58)	93.3 (77.9 to 99.2)	10.7 (2.27 to 28.2)	60 (14.7 to 94.7)	52.8 (38.6 to 66.7)
All Southeastern Asians (92)	80 (59.3 to 93.2)	56.7 (44 to 68.8)	88.4 (74.9 to 96.1)	40.8 (27 to 55.8)
Southeastern Asians ≤40 (63)	61.5 (31.6 to 86.1)	66 (51.2 to 78.8)	86.8 (71.9 to 95.6)	32 (14.9 to 53.5)
Southeastern Asians >40 (29)	100 (73.5 to 100)	29.4 (10.3 to 56)	100 (47.8 to 100)	50 (29.1 to 70.9)
All Western Asians (358)	70 (57.9 to 80.4)	58.2 (52.2 to 64.1)	88.6 (83.1 to 92.8)	29.5 (22,7 to 37.1)
Western Asians ≤40 (227)	42.4 (25.5 to 60.8)	76.3 (69.7 to 82.1)	88.6 (82.8 to 93)	23.3 (3.4 to 36)
Western Asians >40 (123)	94.6 (81.8 to 99.3)	17.4 (1.0.1 to 27.1)	88.2 (63.6 to 98.5)	33 (24.2 to 42.8)

FHD, family history of diabetes; NPV, negative predictive value; PPV, positive predictive value; PRISQ, pre-diabetes risk score in Qatar.

such as Qatar and other Gulf countries.[28 29] In view of the annual conversion rate from pre-diabetes to T2D (5%–10%[2]), the critical significance of early diagnosis of pre-diabetes, and T2D for that matter, to formulate intervention strategies and the efficacious management of this widespread health challenge is undeniable. At a cut-off of 16, the sensitivity of PRISQ exceeded 90% in the 40+ subgroups regardless of ethnicity/race. This observation aligns with the fact that age significantly contributes to PRISQ score. Indeed, the age scores of 12 and 22 points for individuals between 36 and 55 years and those aged 55 or above, respectively. It is also noteworthy that T2D usually develops after the age of 40 years, and it is, therefore, not surprising that PRISQ performs better in the 40+ groups. We have observed a significant decline in the specificity of PRISQ, decreasing sharply from 66% in the under-40 group to 14% in the 40+ group. This steep decline is likely due to the higher prevalence of pre-diabetes in the 40+ cohort compared with the under-40 cohort (35% vs 20%). Additionally, the small sample size may contribute to this observed reduction in specificity. A wealth of evidence demonstrates the variation in diabetes prevalence among various racial and ethnic groups.[30 31] Still, there is a lack of thorough knowledge of the underlying mechanics. The general view among the scientific and medical communities is that racial genetic variables have a negligible impact on the development of diabetes.[32] Instead, a person's susceptibility to pre-diabetes and T2D is more significantly influenced by non-genetic factors, which include physical characteristics, dietary habits, lifestyle decisions and more general social determinants of health like socioeconomic status,

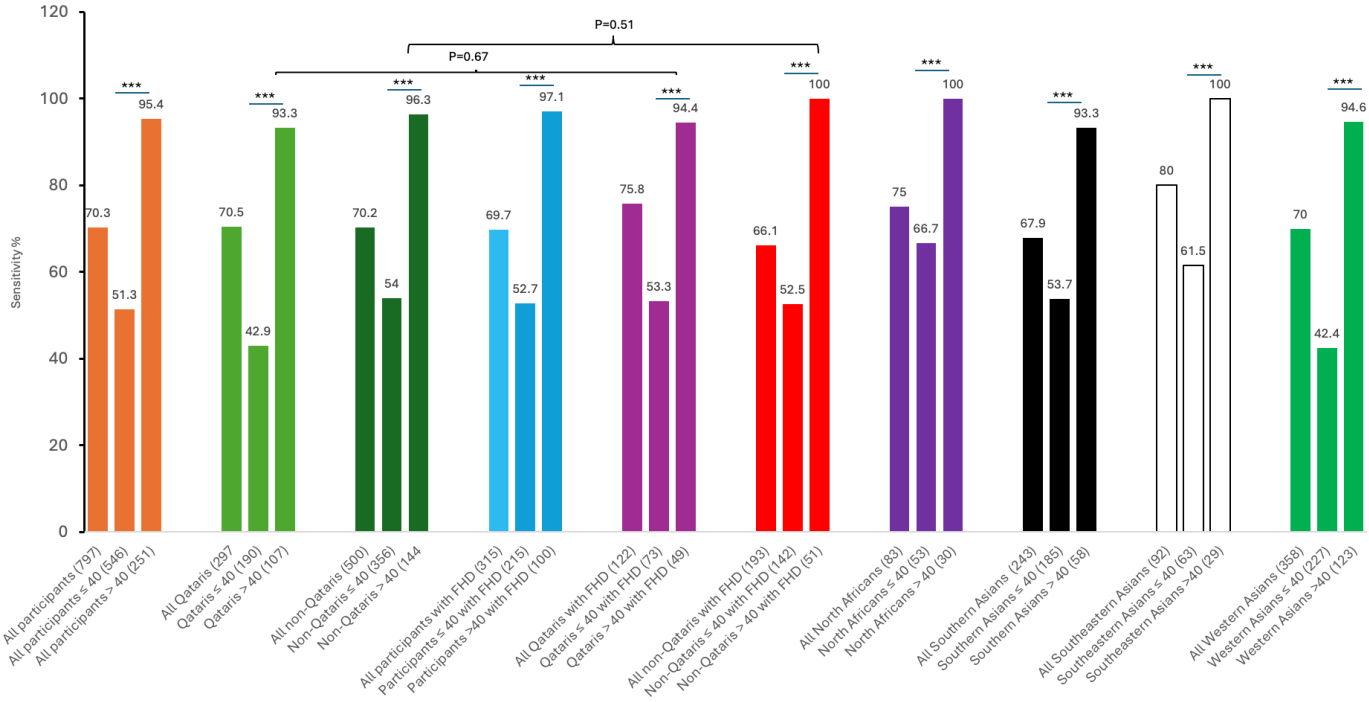

Figure 3 Comparison of PRISQ sensitivities between different subgroups. The values above the bars indicate sensitivity. ***p<0.001. PRISQ, pre-diabetes risk score in Qatar.

level of education, food insecurity and residential environment.[33] Noteworthy is that all these non-genetic risk factors are amenable to cost-effective preventative interventions. Of particular interest is the observation that, aside from age and gender, the remaining predictors (BMI, WC, SBP and DBP) used in the computation of PRISQ could be modified, a characteristic that may elucidate the commendable performance of PRISQ across various ethnic and racial backgrounds.

The FHD exhibits a robust association with the disease's incidence, yet the precise determinants underpinning this relationship remain incompletely elucidated.[34 35] In the initial development of PRISQ, we consciously opted against incorporating FHD as a predictive variable, primarily due to the inherent challenges associated with this aspect. Many individuals may lack accurate knowledge of their family members' medical histories,[36] rendering familial history potentially unreliable.[37] Moreover, situations may arise where individuals' relatives have T2D or pre-diabetes but remain undiagnosed. Our current analysis has revealed that the differences between sensitivities of PRISQ within the 40+ age subgroups with and without FHD fail to attain statistical significance. This observation substantiates the rationale for our initial exclusion of FHD from the PRISQ model. The predictors used for PRISQ computation prove to be comprehensive and objective and can be readily ascertained by a healthcare professional in a primary healthcare setting, such as a nurse in a triage room.

Clinical importance of the study

With lifestyle interventions showing high efficiency in resolving pre-diabetes in many affected individuals, the significance of timely diagnosis of pre-diabetes cannot be overstated in the battle against the T2D epidemic sweeping the world in general and the Middle East region in particular. In this crucial endeavour, the PRISQ emerges as a beacon of hope. By relying solely on non-invasive parameters, the PRISQ tool offers a powerful means of diagnosing pre-diabetes quickly and cost-effectively. Importantly, contrary to blood tests, PRISQ is suitable for population screening in primary healthcare centres as the required parameters can all be quickly and non-invasively obtained by a nurse in the triage room before the encounter with the attending physician who is empowered to exercise discretion regarding the necessity of further recourse to confirmatory blood tests. This pragmatic approach necessitates the recognition that a nominal investment in preemptive measures to address potential FPs is financially judicious, given the far greater economic burden and clinical repercussions incurred by inadvertent oversight of TP cases. The potential of PRISQ impact extends far beyond Qatar's borders, as it holds the potential to mitigate the worsening T2D crisis not only within the nation but also across the broader Middle East region, given the cultural, behavioural and ethnical similarities between the Middle Eastern populations, especially the nations of the GCC. The results we obtained with residents of Qatar originating from outside the Middle East countries could extend the use of PRISQ in other countries, especially from Southern, Southeastern and Western Asia. Embracing PRISQ in primary healthcare centres could be critical in preventive healthcare, promising to safeguard the health and well-being of countless individuals while relieving the

strain on healthcare systems grappling with the diabetes epidemic.

The main limitation of this study was the relatively small number of participants and the lack of validation in populations outside Qatar. There is also the issue of low discordance between HbA_{1c} and OGTT to diagnose pre-diabetes.[38 39] It would have been ideal to use OGTT to confirm pre-diabetes. However, this approach would not be scientifically sound since PRISQ was developped based on HbA_{1c} vlaues. Moreover, while we recognise that our diagnostic test may have low specificity, meaning it might produce some FPs, we are acutely aware of the potential consequences of overlooking TP results. FPs can lead to additional testing, which may incur limited additional costs, but missing TP cases can result in delayed intervention, disease progression and increased healthcare costs in the long term. Therefore, despite the limitations of our test, we prioritise sensitivity to ensure that genuine cases are not overlooked, even at the risk of some FPs. PRISQ can indeed be a starting point for further blood tests, especially OGTT, to confirm or reject the presence of pre-diabetes. We believe, however, that the strength of the study resides in the use of data from individuals from different ethnicities, indicating that PRISQ could potentially be useful in other populations.

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REFERENCES

1 Rooney MR, Fang M, Ogurtsova K, *et al*. Global prevalence of prediabetes. *Diabetes Care* 2023;46:1388–94.
2 Tabák AG, Herder C, Rathmann W, *et al*. Prediabetes: a high-risk state for diabetes development. *Lancet* 2012;379:2279–90.
3 Brannick B, Wynn A, Dagogo-Jack S. Prediabetes as a toxic environment for the initiation of microvascular and macrovascular complications. *Exp Biol Med (Maywood)* 2016;241:1323–31.
4 Aldossari KK, Aldiab A, Al-Zahrani JM, *et al*. Prevalence of prediabetes, diabetes, and its associated risk factors among males in Saudi Arabia: a population-based survey. *J Diabetes Res* 2018;2018:2194604.
5 Alkandari A, Longenecker JC, Barengo NC, *et al*. The prevalence of pre-diabetes and diabetes in the Kuwaiti adult population in 2014. *Diabetes Res Clin Pract* 2018;144:213–23.
6 Jiang L, Johnson A, Pratte K, *et al*. Long-term outcomes of lifestyle intervention to prevent diabetes in American Indian and Alaska native communities: the special diabetes program for Indians diabetes prevention program. *Diabetes Care* 2018;41:1462–70.
7 Knowler WC, Barrett-Connor E, Fowler SE, *et al*. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002;346:393–403.
8 Knowler WC, Fowler SE, Hamman RF, *et al*. 10-year follow-up of diabetes incidence and weight loss in the diabetes prevention program outcomes study. *Lancet* 2009;374:1677–86.
9 Pan XR, Li GW, Hu YH, *et al*. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. *Diabetes Care* 1997;20:537–44.
10 Ramachandran A, Snehalatha C, Mary S, *et al*. The Indian diabetes prevention programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). *Diabetologia* 2006;49:289–97.
11 Tuomilehto J, Lindström J, Eriksson JG, *et al*. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 2001;344:1343–50.
12 Al-Thani MH, Al-Mutawa KA, Alyafei SA, *et al*. Characterizing epidemiology of prediabetes, diabetes, and hypertension in Qataris: a cross-sectional study. *PLoS One* 2021;16:e0259152.
13 Marhaba QsPIG. Patients benefit from HMC amd PHCC diabetes care services. 2018. Available: https://www.marhaba.qa/patients-benefit-hmc-phcc-diabetes-care-services/ [Accessed 28 Apr 2024].
14 Zhang FF, Al Hooti S, Al Zenki S, *et al*. Vitamin D deficiency is associated with high prevalence of diabetes in Kuwaiti adults: results from a national survey. *BMC Public Health* 2016;16:100.
15 Hamoudi R, Saheb Sharif-Askari N, Saheb Sharif-Askari F, *et al*. Prediabetes and diabetes prevalence and risk factors comparison between ethnic groups in the United Arab Emirates. *Sci Rep* 2019;9:17437.
16 Abbas M, Mall R, Errafii K, *et al*. Simple risk score to screen for Prediabetes: a cross-sectional study from the Qatar biobank cohort. *J Diabetes Investig* 2021;12:988–97.
17 American Diabetes Association. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes-2019. *Diabetes Care* 2019;42:S13–28.
18 Flahault A, Cadilhac M, Thomas G. Sample size calculation should be performed for design accuracy in diagnostic test studies. *J Clin Epidemiol* 2005;58:859–62.
19 Al Kuwari H, Al Thani A, Al Marri A, *et al*. The qatar biobank: background and methods. *BMC Public Health* 2015;15:1208.
20 Simon R. Specificity, PPV, and NPV for predictive biomarkers. *J Natl Cancer Inst* 2015;107:djv153.
21 Trevethan R. Specificity, and predictive values: foundations, pliabilities, and pitfalls in research and practice. *Front Public Health* 2017;5:307.
22 MINN M. World regions. 2024. Available: https://michaelminn.net/tutorials/regions-world/index.html [Accessed 24 Mar 2024].
23 Fujiati II, Damanik HA, Bachtiar A, *et al*. Development and validation of prediabetes risk score for predicting prediabetes among Indonesian adults in primary care: cross-sectional diagnostic study. *Interv Med Appl Sci* 2017;9:76–85.
24 Ouyang P, Guo X, Shen Y, *et al*. A simple score model to assess prediabetes risk status based on the medical examination data. *Can J Diabetes* 2016;40:419–23.
25 Wang H, Liu T, Qiu Q, *et al*. A simple risk score for identifying individuals with impaired fasting glucose in the Southern Chinese population. *Int J Environ Res Public Health* 2015;12:1237–52.

26 Koopman RJ, Mainous AG, Everett CJ, *et al*. Tool to assess likelihood of fasting glucose impairment (TAG-IT). *Ann Fam Med* 2008;6:555–61.
27 Saeedi P, Salpea P, Karuranga S, *et al*. Mortality attributable to diabetes in 20-79 years old adults, 2019 estimates: results from the international diabetes federation diabetes atlas. *Diabetes Res Clin Pract* 2020;162:108086.
28 El-Kebbi IM, Bidikian NH, Hneiny L, *et al*. Epidemiology of type 2 diabetes in the Middle East and North Africa: challenges and call for action. *World J Diabetes* 2021;12:1401–25.
29 Abuyassin B, Laher I. Diabetes epidemic sweeping the Arab world. *World J Diabetes* 2016;7:165–74.
30 Cheng YJ, Kanaya AM, Araneta MRG, *et al*. Prevalence of diabetes by race and Ethnicity in the United States, 2011-2016. *JAMA* 2019;322:2389–98.
31 Pham TM, Carpenter JR, Morris TP, *et al*. Ethnic differences in the prevalence of type 2 diabetes diagnoses in the UK: cross-sectional analysis of the health improvement network primary care database. *Clin Epidemiol* 2019;11:1081–8.
32 Rosella LC, Mustard CA, Stukel TA, *et al*. The role of ethnicity in predicting diabetes risk at the population level. *Ethn Health* 2012;17:419–37.
33 Han X, Wei Y, Hu H, *et al*. Genetic risk, a healthy lifestyle, and type 2 diabetes: the Dongfeng-Tongji cohort study. *J Clin Endocrinol Metab* 2020;105:dgz325.
34 Scott RA, Langenberg C, Sharp SJ, *et al*. The link between family history and risk of type 2 diabetes is not explained by anthropometric, lifestyle or genetic risk factors: the EPIC-interact study. *Diabetologia* 2013;56:60–9.
35 Wagner R, Thorand B, Osterhoff MA, *et al*. Family history of diabetes is associated with higher risk for prediabetes: a multicentre analysis from the German center for diabetes research. *Diabetologia* 2013;56:2176–80.
36 Goergen AF, Ashida S, Skapinsky K, *et al*. What you don't know: improving family health history knowledge among multigenerational families of Mexican origin. *Public Health Genomics* 2016;19:93–101.
37 Daelemans S, Vandevoorde J, Vansintejan J, *et al*. The use of family history in primary health care: a qualitative study. *Adv Prev Med* 2013;2013:695763.
38 Chatzianagnostou K, Vigna L, Di Piazza S, *et al*. Low Concordance between Hba1C and OGTT to diagnose prediabetes and diabetes in overweight or obesity. *Clin Endocrinol (Oxf)* 2019;91:411–6.
39 Gosmanov AR, Wan J. Low positive predictive value of hemoglobin A1C for diagnosis of prediabetes in clinical practice. *Am J Med Sci* 2014;348:191–4.