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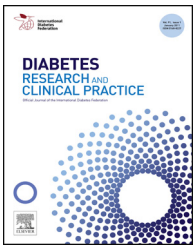

# Finnish Diabetes Risk Score to predict type 2 diabetes in the Isfahan diabetes prevention study

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ABSTRACT

*Aim:* The strong association between the Finnish Diabetes Risk Score (FINDRISC) and risk of diabetes reported in European populations cannot necessarily be generalized to other populations. The aim of this study was to evaluate the ability of FINDRISC to predict progression to diabetes in an Iranian population without diabetes.

*Methods:* A total of 1537 first-degree relatives (FDR) without diabetes of consecutive people with type 2 diabetes 30–70 years old (376 men and 1161 women) were examined and followed for a mean (SD) of 7.8 (1.7) years for diabetes incidence. We examined the incidence of diabetes across quartiles of FINDRISC and plotted a receiver operating characteristic (ROC) curve to assess discrimination. At baseline and through follow-up, participants underwent a standard 75-g 2-h oral glucose tolerance test. Data for the FINDRISC were available from each participant.

*Results:* During 12,046 person-years of follow-up, 41 men and 154 women developed diabetes. The incidence of type 2 diabetes was 14.0 per 1000 person-years in men and 16.9 in women. Those in the top quartile of FINDRISC were 21.7 times more likely to develop diabetes than those in the bottom quartile (relative risk 21.7; 95% CI 9.90, 47.39). The area under the ROC was 75.1% (95% CI 71.3, 78.8).

*Conclusions:* The results of this study show that FINDRISC is a robust predictor of type 2 diabetes in high-risk individuals in Iran.



## 1. Introduction

Type 2 diabetes is an important and growing public health problem worldwide [1]. Its prevalence in low- and middle-income countries, where 80% of people with diabetes and 85% of people with undiagnosed diabetes live [1], is already high and expected to rise more rapidly than elsewhere. Thus, with a strong evidence base for lifestyle interventions to prevent diabetes [2,3], there is great interest in identifying individuals at high risk of developing diabetes. Population screening for diabetes, using blood glucose tests, would not be practicable or cost-effective, especially in low-income countries. A simple, non-invasive, effective tool using readily available clinical information to rapidly identify asymptomatic individuals in whom glucose tolerance tests should be measured to rule out type 2 diabetes would be practical for use by the general public and in primary health care. During the past two decades, many attempts have been made to develop such screening tools to identify persons at high risk for the future development of type 2 diabetes [4–6]. Among these tools, the Finnish Diabetes Risk

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Score (FINDRISC) has been successfully implemented as a practical screening instrument to assess diabetes risk and to detect undiagnosed type 2 diabetes [7–9]. It have been tested in a number of European populations with encouraging results [10–24], but it may not be universally applicable among all ethnic groups and populations [15,17,25,26]. Recent reports [25,26] highlighted the lack of studies on diabetes risk scores for low- and middle-income countries. No study to date has examined diabetes incidence with FINDRISC in Iran.

The objective of this study was to evaluate the ability of FINDRISC to predict incident type 2 diabetes in first-degree relatives (FDR) of people with type 2 diabetes in an Iranian population without diabetes.

## 2. Patients and methods

### 2.1. Data collection

The recruitment methods and examination procedures of the Isfahan Diabetes Prevention Study (IDPS) have been described before [27]. Briefly, IDPS is an ongoing cohort in central Iran to assess the various potential risk factors for diabetes in FDR of people with type 2 diabetes (one of the main risk factors for diabetes). Our study sample comprised 3409 (895 men and 2514 women) FDR of consecutive people with type 2 diabetes. All subjects were attendees at clinics at Isfahan Endocrine and Metabolism Research Center, which is affiliated to Isfahan University of Medical Sciences, Iran. The study was conducted between the years 2003 and 2005. All participants were from Isfahan city and adjoining areas. They completed laboratory tests including a standard 75-g 2-h oral glucose tolerance test (OGTT), a questionnaire on their health status and on various potential risk factors for diabetes, and the FINDRISC questionnaire. Participants received follow-up tests according to Standards of Medical Care in Diabetes [28] to update information on demographic, anthropometric and lifestyle factors and on newly diagnosed diabetes. Accordingly, if the OGTT was normal at baseline, repeat testing was carried out at least at 3-year intervals. Otherwise, repeat testing was usually carried out annually. Tenets of the current version of the Declaration of Helsinki were followed, institutional ethical committee approval was granted, and an informed consent form was signed by each participant.

### 2.2. Follow-up and ascertainment of diabetes

Cases of diabetes were identified from baseline and follow-up OGTT according to American Diabetes Association criteria [29]. Pregnant women and people with type 1 diabetes were excluded. Among 3409 persons who participated at baseline, 308 were excluded because of a diagnosis of diabetes at baseline and 1564 had no follow-up, leaving 1537 participants with a mean age 43.1 (6.6) (range 30–70) years for the present analysis, all of whom had at least one subsequent review during a mean (standard deviation [SD]) follow-up period of 7.8 (1.7) (range 3–10) years. Attendees at the follow-up visit did not differ significantly from non-attendees regarding most baseline characteristics: age, height, weight, body mass index (BMI), waist circumference (WC), hip circumference (HC), waist-hip ratio (WHR) and levels of HbA1c, cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides, systolic and diastolic blood pressure (BP) and obesity. However, non-attendees had slightly lower fasting plasma glucose (FPG) (94.6 mg/dl versus 95.7 mg/dl, $P < 0.05$) and plasma glucose (PG) at 30 min (138.5 mg/dl versus 145.5 mg/dl ($P < 0.001$), 60 min (140.9 mg/dl versus 150.9 mg/dl, $P < 0.001$), 120 min (111.1 mg/dl versus 120.6 mg/dl, $P < 0.001$) and a slightly lower FINDRISC (11.8 versus 12.8, $P < 0.001$), but higher levels of high-density lipoprotein (HDL) cholesterol (46.4 mg/dl versus 45.0 mg/dl, $P < 0.0$).

### 2.3. Procedures

Information on age, gender, body size, HbA1c, cholesterol, LDL cholesterol, HDL cholesterol, triglycerides and BP, family and personal medical history was collected at baseline and through follow-up. The same methodology was used for baseline and follow-up studies. The participants included siblings and children. Participants reported to clinics in the morning after an overnight fast. They were asked to abstain from vigorous exercise in the evening, and in the morning of the investigations. Smokers were encouraged to abstain from smoking in the morning of their visit. First, on arrival at the clinic, the information provided by the participants in the questionnaire on family history was verified. Then, with the subjects in light clothing and without shoes, height, weight, WC and HC were measured using standard apparatus. Weight was measured to the nearest 0.1 kg on a calibrated beam scale. Height, WC and HC were measured to the nearest 0.5 cm with a measuring tape. The waist was measured midway between the lower rib margin and the iliac crest at the end of gentle expiration. Hip circumference was measured over the greater trochanters directly over the underwear. Resting BP was measured after the participant had been seated for 10 min with a mercury sphygmomanometer and appropriately sized cuffs, using standard techniques. FPG was measured with the glucose oxidase method. Participants with FPG $\geq$ 200 mg/dl or pharmacological treatment were considered to have diabetes. If FPG was $\geq$126 mg/dl and <200 mg/dl, a second FPG was measured on another day. If the second FPG was also $\geq$126 mg/dl, participants were considered have diabetes. Those with FPG <126 mg/dl underwent a standard OGTT (75 g glucose, 2 h) at baseline and follow-up visits. Venous blood was sampled 0, 30, 60, and 120 min after oral glucose administration. Plasma samples were centrifuged and analyzed the same day.

Glycated hemoglobin (HbA1c) (measured by ion-exchange chromatography), total cholesterol, triglycerides, HDL, LDL (calculated with the Friedewald equation [30] provided total triglycerides did not exceed 400 mg/dl) were recorded. All blood analysis procedures were performed in the central laboratory of the Isfahan Endocrine and Metabolism Research Center using enzyme-linked method.

### 2.4. Definitions

Based on the OGTT results, participants were categorized as having either normal glucose tolerance (NGT, FPG below 100 mg/dl and the 2-h plasma glucose (2hPG) <140 mg/dl), impaired fasting glucose (IFG, FPG in the range of 100–126 mg/dl and the 2hPG was <140 mg/dl), impaired glucose tolerance

(IGT, FPG < 126 mg/dl, but with 2hPG concentration ≥140 and <200 mg/dl) or diabetes (FPG ≥ 200 mg/dl or pharmacological treatment, FPG ≥ 126 and/or 2hPG of ≥200 mg/dl) [31].

### 2.5. Finnish Diabetes Risk Score

FINDRISC was computed for each participant using clinical and questionnaire data collected at baseline. The FINDRISC comprises eight items [7,9]: age; body mass index [BMI, weight (kg)/height squared ($m^2$)]; WC; physical activity; dietary consumption of fruits, vegetables and berries; use of antihypertensive medication; history of high blood glucose; and family history of diabetes; the maximum achievable score is 26. In the current study, a concise version of the FINDRISC was used. In this shortened version the variables dietary consumption of fruits, vegetables and berries and physical activity were omitted because these items did not add much power for the prediction of diabetes risk in previous studies and as suggested in the original publication [9] and in subsequent studies [17,24,32]. Thus, the maximum achievable score on the modified FINDRISC is 23. High blood glucose was defined as the IFG and/or IGT at baseline.

### 2.6. Determination of diabetes incidence

Incidence was expressed as the number of cases of type 2 diabetes per 1000 person-years of follow-up beginning on the date of completion of the baseline examination in 2003–2005 and continuing until the occurrence of diabetes, the date of the last completed follow-up, death, or end of follow-up on September 31, 2011, whichever came first.

### 2.7. Analysis

Statistical methods included the Student's *t*-test, the chi-squared test and binary logistic regression. Univariate and multivariate binary logistic regression equations were fitted to identify predictors of new-onset diabetes using the SPSS version 18 for Windows (SPSS Inc., Chicago, IL, USA). We calculated the FINDRISC for each participant using baseline age, BMI, WC, use of antihypertensive medication, history of high blood glucose (IFG and/or IGT), and family history of diabetes. We re-coded the FINDRISC into quartiles and compared the risk of developing diabetes in each quartile with the lowest category of risk (reference group). Validity of the FINDRISC was assessed using discrimination and calibration. The ability of FINDRISC, FPG, 2hPG and HbA1c values to predict the incidence of diabetes was examined with receiver operating characteristic (ROC) curves and their respective areas under the curve, in which sensitivity was plotted as a function of 1-specificity. The area under the ROC curve is a global summary statistic of the discriminative value of a model, describing the probability that the score will be higher in an individual developing than in an individual not developing type 2 diabetes. Areas under the ROC curves were compared by the algorithm developed by DeLong et al. [33]. Calibration was evaluated with Hosmer–Lemeshow goodness-of-fit test to determine if the observed incidence rates of diabetes differed significantly from the expected [34]. Calibration assessed the level of correspondence between predicted probabilities and the observed incidence of diabetes per FINDRISC quartile. If the observed incidence of diabetes is close to the predicted probabilities, the FINDRISC is considered to be well calibrated. All tests for statistical significance were two-tailed, and all were done assuming a type I error probability of <0.05.

## 3. Results

Baseline characteristics of the 1342 (87.3%) participants without and the 195 (12.7%) who developed diabetes are shown in Table 1. As expected, those who developed diabetes were older and had higher mean BMI, WC, HC, FPG, and PG at 30, 60 and 120 min, higher HbA1c, triglyceride, cholesterol, systolic BP and FINDRISC at baseline, and a higher proportion of overweight, metabolic syndrome, use of antihypertensive medication, IFG and IGT. The mean (SD) age was 44.5 (7.0) years for those with and 42.9 (6.5.) years for those without diabetes. The mean (SD) FINDRISC was 15.8 (3.2) for those with and 12.3 (4.1.) for those without diabetes. The total score ranged from 5 to 23.

The baseline characteristics of the study participants by FINDRISC quartile are shown in Table 2. Comparing variables at baseline, all variables except HDL were more likely to be higher, and height and follow-up duration more likely to lower across all four subject groups.

During 12,046 (2929 men and 9117 women) person-years of follow-up, 195 (12.7%) (41 men and 154 women) incident cases of type 2 diabetes occurred. The overall incidence of diabetes was 16.2 (95% CI: 13.9, 18.45) per 1000 person-years. Incidence rates were slightly higher in women (16.9%, 95% CI: 14.2, 19.5 per 1000 person-years) than men (14.0%, 95% CI: 10.1, 19.0) but the difference was not statistically significant. The FINDRISC was associated with diabetes incidence. The incidence of diabetes was 38.3 per 1000 person-years (95% CI 31.2, 46.4) for participants in the highest quartile of FINDRISC, and 2.1 per 1000 person-years (95% CI 0.79, 4.33) for the lowest quartile. The risk of type 2 diabetes increased with increasing quartiles of FINDRISC. Compared with participants in the lowest quartile, the risk of diabetes was 18.2 times higher in those in the highest quartile at baseline (rate ratio (RR) 18.2; 95% CI: 8.53, 39.40) and 9.2 times higher in those in the 3rd quartile (RR 9.2; 95% CI: 4.39, 20.80) and 4.2 times higher in those in the 2nd quartile (RR 4.2; 95% CI: 1.85, 9.85) in unadjusted models. Controlling for age and gender did not appreciably alter the RR compared with the unadjusted model (Table 3).

The ROC curves for incident type 2 diabetes for FINDRISC, FPG, 2hPG and HbA1c are shown in Fig. 1. The areas under the ROC curves were 0.751 (95% CI: 0.713, 0.788) for FINDRISC, 0.762 (95% CI: 0.719, 0.805) for FPG, 0.769 (95% CI: 0.728, 0.810) for 2hPG, and 0.659 (95% CI: 0.614, 0.704) for HbA1c. All parameters were significant predictors for future risk of type 2 diabetes ($P < 0.001$). The areas were similar for FINDRISC, FPG and 2hPG. The area for HbA1c was smaller than for FINDRISC. However, it is apparent that in this population of FDR of people with type 2 diabetes, the FINDRISC was similar to FPG and 2hPG in predicting future risk for type 2 diabetes. Calibration of the FINDRISC was good; the observed incidence of diabetes

**Table 1 – Means (SD) and proportional frequencies of selected baseline characteristics in 195 first-degree relatives of people with type 2 diabetes who did and 1342 who did not develop diabetes.**

| Variables | Developed diabetes Mean (SD) | No diabetes Mean (SD) | Difference (95% CI) |
|---|---|---|---|
| Age (years) | 44.5 (7.0) | 42.9 (6.5) | 1.6 (0.61, 2.59)** |
| Height (cm) | 158.4 (7.9) | 159.6 (8.2) | −1.2 (−2.43, 0.03) |
| Weight (kg) | 76.4 (10.9) | 73.1 (11.6) | 3.3 (1.56, 5.04)*** |
| Body mass index (kg/m$^2$) | 30.5 (4.2) | 28.7 (4.1) | 1.8 (1.18, 2.42)*** |
| Waist circumference (cm) | 92.1 (8.6) | 88.4 (9.2) | 3.7 (2.31, 5.09)*** |
| Waist-to-hip ratio | 0.84 (0.06) | 0.82 (0.07) | 0.02 (0.00, 0.03) |
| Hip circumferences (cm) | 110.2 (8.9) | 107.2 (8.7) | 3.0 (1.57, 4.23)*** |
| Follow-up duration (years) | 8.1 (1.7) | 7.8 (1.7) | 0.3 (0.04, 0.56)** |
| Systolic BP (mmHg) | 117.7 (17.7) | 114.9 (16.1) | 2.8 (0.28, 5.32)* |
| Diastolic BP (mmHg) | 76.6 (12.5) | 75.8 (11.9) | 0.8 (−1.04, 2.64) |
| Baseline fasting glucose (mg/dl) | 106.0 (12.0) | 94.1 (11.5) | 11.9 (10.20, 13.60)*** |
| Plasma glucose 30 min (mg/dl) | 170.0 (34.9) | 142.1 (29.6) | 27.9 (23.10, 32.70)*** |
| Plasma glucose 60 min (mg/dl) | 195.8 (40.4) | 144.3 (39.8) | 51.5 (45.40, 57.60)*** |
| Plasma glucose 120 min (mg/dl) | 151.2 (32.1) | 116.1 (32.0) | 35.1 (30.30, 39.90)*** |
| HbA1c (%) | 5.5 (0.9) | 5.0 (0.7) | 0.5 (0.38, 0.62)*** |
| HbA1c (mmol/mol) | 37 (6.1) | 31 (4.3) | 6.0 (5.31, 6.69)*** |
| Triglyceride (mg/dl) | 195.1 (137.8) | 162.5 (91.3) | 32.6 (17.40, 47.80)*** |
| Cholesterol (mg/dl) | 207.1 (48.8) | 194.7 (39.4) | 12.4 (6.12, 18.70)** |
| HDL cholesterol (mg/dl) | 45.1 (12.2) | 45.0 (11.6) | 0.1 (−1.73, 1.93) |
| LDL cholesterol (mg/dl) | 125.4 (41.1) | 118.2 (34.4) | 7.2 (1.51, 12.90)* |
| FINDRISC | 15.8 (3.2) | 12.3 (4.1) | 3.5 (2.9, 4.1)*** |
| **Variables** | **Developed diabetes %** | **No diabetes %** | **Difference (95% CI)** |
| Men | 21.0 | 24.9 | −3.9 (−10.10, 2.29) |
| Overweight (BMI ≥ 25) | 91.2 | 83.5 | 7.7 (3.20, 12.10)** |
| Normal glucose tolerance | 11.8 | 55.4 | −43.6 (−48.8, −38.0)*** |
| Impaired fasting glucose | 17.9 | 20.0 | −2.1 (−7.89, 3.70) |
| Impaired glucose tolerance | 70.3 | 24.6 | 45.7 (38.8, 52.5)*** |
| Metabolic syndrome | 47.2 | 29.5 | 17.7 (10.30, 25.10)*** |
| Use of antihypertensive drug | 24.6 | 17.1 | 7.5 (1.05, 14.10)* |

Differences in mean or percentage values of variables between diabetes and no diabetes. CI – confidence interval.
*$P < 0.05$
**$P < 0.01$
***$P < 0.001$.

was close to the predicted probabilities, with a Hosmer–Lemeshow goodness-of-fit test $p$ value of 0.996.

Test characteristics for various FINDRISC cut-off values are presented in Table 4. At a score of 13 or higher, the sum of sensitivity and specificity was maximized. Accordingly, the optimal cut-point for detecting diabetes was a FINDRISC greater than or equal to 13. Of the total sample, 50.9% had a score of 13.0 or higher. At a FINDRISC greater or equal to 13, sensitivity was 83.6% and specificity was 53.9%. The corresponding positive and negative predictive values were 20.8% and 95.7%, respectively. At a score greater than or equal to 15 (34.0% of the sample), sensitivity was 65.1% and specificity was 70.5%. The corresponding positive predictive value was 24.3%.

## 4. Discussion

In this study, FINDRISC showed a very good ability to predict type 2 diabetes in a cohort of first degree elatives of people with type 2 diabetes, with an area under the ROC of 75%. This was similar to its ability to predict diabetes in other populations tested so far [9,13,15,18–23,35]. Although the FINDRISC tool was developed and validated in European populations [7–9,13–20], it is also valid for Middle Eastern populations, despite the differences in lifestyles compared with the western world. This finding suggests that risk factors for type 2 diabetes are similar in different part of the world. Those in the top quartile of FINDRISC were 21.7 times more likely to progress to diabetes than those in the bottom quartile. FINDRISC, which uses information routinely available in primary care records, is a simple, inexpensive and noninvasive tool. Those with higher fasting PG and 2hPG at baseline had a similar risk of progression to diabetes, further emphasizing the utility of FINDRISC alone in predicting diabetes. This study thus confirms the reliability of FINDRISC for predicting diabetes. Even though FINDRISC, fasting and 2-h glucose values had approximately the same predictive power in our study, FINDRISC is superior in clinical practice because it is noninvasive and does not require blood testing. Thus, FINDRISC may serve as an initial assessment tool to identify those FDR who may need further blood testing.

Several studies in Europe have assessed the risk of diabetes based on the FINDRISC. In a study similar to ours, Alssema et al. examined the incidence of type 2 diabetes in Europid

**Table 2 – Mean number (SD) and proportion of first-degree relatives of people with type 2 diabetes by Finnish Diabetes Risk Score (FINDRISC) quartile in the Isfahan Diabetes Prevention Study.**

| Characteristic | Total | FINDRISC at baseline | | | |
|---|---|---|---|---|---|
| | | 1st quartile (<9.0) | 2nd quartile (9.0–12.99) | 3rd quartile (13.0–15.9) | 4th quartile (16.0–23.0) |
| Number (%) | 1537 (100) | 403 (26.2) | 352 (22.9) | 428 (27.8) | 354 (23.0) |
| FINDRISC | 12.8 (4.2) | 7.4 (1.60) | 11.2 (0.75) | 14.5 (1.10) | 18.3 (1.37)* |
| Age (years) | 43.1 (6.6) | 40.4 (5.5) | 41.9 (6.0) | 44.1 (6.4)† | 46.0 (6.9)* |
| Height (cm) | 159.4 (8.2) | 160.8 (8.3) | 159.7 (8.1) | 159.7 (8.2) | 157.3 (7.5)* |
| Weight (kg) | 73.5 (11.6) | 66.9 (9.3) | 72.7 (12.3) | 74.6 (10.8) | 81.2 (9.9)* |
| Waist circumference (cm) | 88.9 ((9.2) | 82.2 (7.0) | 87.8 (9.4) | 90.1 (7.9) | 95.7 (7.2)* |
| Hip circumference (cm) | 107.6 (8.7) | 102.5 (5.5) | 106.9 (9.4) | 107.7 (7.9) | 113.8 (8.1)* |
| Waist-to-hip ratio | 0.83 (0.07) | 0.80 (0.07) | 0.82 (0.07) | 0.84 (0.07) | 0.84 (0.06)* |
| Body mass index (kg/m$^2$) | 28.9 (4.2) | 25.9 (2.6) | 28.5 (4.2) | 29.2 (3.4) | 32.4 (3.5)* |
| Follow-up duration (years) | 7.8 (1.7) | 8.3 (1.5) | 8.0 (1.6) | 7.7 (1.7)† | 7.3 (1.9)* |
| FPS (mg/dl) | 95.7 (12.2) | 87.0 (7.6) | 92.7 (11.5) | 98.7 (11.4) | 104.8 (10.1)* |
| PG 30 min (mg/dl) | 145.5 (31.6) | 127.9 (26.0) | 143.3 (28.6)† | 150.8 (30.8)† | 161.6 (31.0)* |
| PG 60 min (mg/dl) | 150.9 (43.4) | 121.1 (31.8) | 146.0 (39.9)† | 159.8 (39.4)† | 178.9 (40.8)* |
| PG 120 min (mg/dl) | 120.6 (34.1) | 99.1 (22.0) | 113.9 (31.0) | 128.4 (33.7) | 142.2 (32.5)* |
| HbA1c (%) | 5.1 (0.8) | 4.9 (0.7) | 5.0 (0.7)† | 5.1 (0.8)†‡ | 5.3 (0.8)* |
| HbA1c (mmol/mol) | 32 (5.0) | 30 (4.3) | 31 (4.3) † | 32 (5) †‡ | 34 (5.1)* |
| Cholesterol (mg/dl) | 196.3 (40.9) | 184.7 (37.7) | 191.8 (37.2) | 199.3 (42.2) | 210.3 (41.9)* |
| LDL (mg/dl) | 119.1 (35.3) | 111.7 (36.0) | 115.9 (29.8) | 119.9 (36.2) | 129.6 (36.2)* |
| HDL (mg/dl) | 45.0 (11.7) | 45.0 (11.4) | 44.9 (10.5) | 45.1 (12.6) | 45.1 (12.0) |
| Triglyceride (mg/dl) | 166.5 (98.8) | 145.0 (80.1) | 160.0 (91.5) | 179.1 (118.5) | 182.2 (93.6)* |
| Systolic BP (mm Hg) | 115.2 (16.3) | 108.4 (13.8) | 112.3 (13.5) | 117.0 (15.5)† | 123.6 (18.2)* |
| Diastolic BP (mm Hg) | 75.0 (11.9) | 70.4 (10.7) | 73.1 (10.0) | 76.4 (11.7)† | 80.5 (12.8)* |
| Women, no. (%) | 1161 (75.6) | 279 (69.4) | 262 (74.4) | 317 (74.1) | 303 (85.6)* |
| Overweight, no. (%) | 1286 (84.5) | 260 (65.8) | 271 (78.1) | 404 (94.8) | 351 (99.2)* |

Data are expressed as mean (SD) or number (%). Difference in the mean value of variables compared to the †1st quartile and ‡2nd quartile.
* $P < 0.001$ comparison across all four groups.

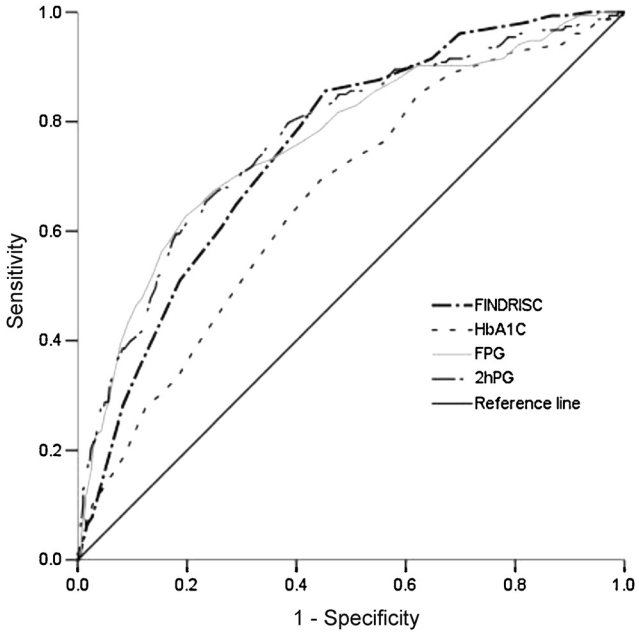
populations, and the 5-year cumulative incidence of diabetes had an area under the ROC of 74.2% [14]. A Greek cross-sectional study found an area under the ROC curve of 72.4% with a shortened version of the FINDRISC [15]. The Italian Impaired Glucose Tolerance and Long-Term Outcomes Observational cohort study showed that undiagnosed diabetes could be predicted with an area under the ROC curve of 72% [23]. As in the present study, a simplified version of the FINDRISC was used to validate FINDRISC in a middle-aged and older German population; the area under the ROC curve was 74.5% [19]. A Bulgarian cross-sectional study obtained an area under the ROC curve of 71.0% [13]. The Whitehall II cohort [22] showed an area under the ROC curve of 67% with the FINDRISC, which was lower than the area originally reported in the FINDRISC surveys [20] and also lower than ours.

Our study has several strengths and limitations. The strengths include use of a sample consisting of both men and women, diagnosis of diabetes based on standard OGTT, and information on potential determinants of glucose intolerance. Selection and information bias were unlikely because of the prospective design. At follow-up, non-attendees in the entire population did not differ from attendees according to major risk factors for progression to diabetes, although a difference too small to explain the high progression rate to diabetes in our study was seen in the mean levels of HDL, PG and FINDRISC. Our database is one of the few that followed

**Table 3 – Incidence rates and rate ratios (RR) of diabetes by Finnish Diabetes Risk Score (FINDRISC) quartile at baseline and OGTT, the Isfahan Diabetes Prevention Study.**

| | FINDRISC at baseline | | | |
|---|---|---|---|---|
| | 1st quartile (<9.0) | 2nd quartile (9.0–12.9) | 3rd quartile (13.0–15.9) | 4th quartile (16.0–23.0) |
| Number of cases (%) | 7 (3.6) | 25 (12.8) | 64 (32.8) | 99 (50.8) |
| Person-years | 3350 | 2806 | 3306 | 2584 |
| Incidence/1000 person-year (95% CI) | 2.1 (0.79, 4.33) | 8.9 (5.80, 13.1) | 19.4 (15.00, 24.60) | 38.3 (31.2, 46.4) |
| Unadjusted RR (95% CI) | 1.00 | 4.2 (1.85, 9.85) | 9.2 (4.39, 20.80) | 18.2 (8.53, 39.40) |
| Gender-adjusted RR (95% CI) | 1.00 | 4.3 (1.85, 10.14) | 9.9 (4.50, 22.00) | 22.1 (10.1, 48.56) |
| Age- and gender adjusted RR (95% CI) | 1.00 | 4.3 (1.86, 10.21) | 9.9 (4.50, 22.00) | 21.7 (9.90, 47.39) |

[a] Unadjusted RR (95% CI) a, Gender-adjusted RR (95% CI) a and Age- and gender adjusted RR (95% CI) a.




Area under the curve (95% CI)

| | |
|---|---|
| Finnish Diabetes Risk Score | 0.751 (0.713, 0.788) |
| Fasting plasma glucose | 0.762 (0.719, 0.805) |
| 2-h plasma glucose | 0.769 (0.728, 0.810) |
| HbA1c | 0.659 (0.614, 0.704) |

**Fig. 1 – Receiver operating characteristic (ROC) curves for Finnish Diabetes Risk Score (FINDRISC), fasting plasma glucose (FPG), HbA1c and 2-h plasma glucose (2hPG) to predict type 2 diabetes in first-degree relatives without diabetes of people with type 2 diabetes. The estimates of the area under the ROC curves and their 95% confidence intervals are shown.**

FDR of people with type 2 diabetes, thereby enabling us to simultaneously control the genetic factors that may predict glucose tolerance status. Our study was limited to a cohort of individuals who are at increased risk of developing type 2 diabetes, because they had a FDR with the disease. This group of individuals will only increase further with time, as the prevalence of diabetes is expected to increase worldwide [36]. The length of follow-up in the IDPS cohort was relatively short. Thus, while the FINDRISC may be good at identifying FDR of people with type 2 diabetes who will progress rapidly to diabetes, it may miss those with a slower disease onset. Alternatively, longer follow-up might increase the RR for the association between the FINDRISC and the incidence of diabetes if more people in the highest risk score category go on to develop diabetes.

We evaluated the concise FINDRISC model instead of the full risk model, which also includes daily consumption of vegetables, fruit or berries and physical activity [9], because our information on these two risk factors was not reliable: only one question asked about diet and physical activity. It is uncertain whether the response to a single isolated question about diet or physical activity is predictive for type 2 diabetes, taking into account that for the development of the original risk model, these items were obtained from an extensive questionnaire. Both factors are considered to be important and were mainly targeted during recent diabetes prevention trials. However, in the Lindstrom and Tuomilehto model both daily intake of vegetables and fruit or berries and physical inactivity were shown not to be statistically significant, but were nonetheless included in the model mainly because prevention studies have demonstrated their importance [2,9,37,38]. It is difficult to apply simple variables for such complex behavioral patterns such as physical activity and diet, and thus in this type of situation they are difficult to use. In term of our definition of incidence diabetes, some selection bias may be present as participants who attended for

**Table 4 – Sensitivity, specificity, positive (PPV) and negative predictive value (NPV) for different FINDRISC cut-off values.**

| Score | Study sample (%) | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | Correctly classified (%) |
|---|---|---|---|---|---|---|
| 5 | 100.0 | 100.0 | 0.0 | 12.7 | – | 12.7 |
| 6 | 94.6 | 100.0 | 6.2 | 13.4 | 100.0 | 18.1 |
| 7 | 90.8 | 99.5 | 10.5 | 13.9 | 99.3 | 21.8 |
| 8 | 88.6 | 99.5 | 13.0 | 14.2 | 99.3 | 23.9 |
| 9 | 83.9 | 98.5 | 18.2 | 14.9 | 98.8 | 28.4 |
| 10 | 73.8 | 96.4 | 29.5 | 16.6 | 98.3 | 38.0 |
| 11 | 68.9 | 91.8 | 34.4 | 16.9 | 96.7 | 41.7 |
| 12 | 59.6 | 86.7 | 44.3 | 18.4 | 95.8 | 49.7 |
| 13 | **50.9** | **83.6** | **53.9** | **20.8** | **95.7** | **57.6** |
| 14 | 45.8 | 77.9 | 58.9 | 21.6 | 94.8 | 61.3 |
| 15 | **34.0** | **65.1** | **70.5** | **24.3** | **93.3** | **69.8** |
| 16 | 31.2 | 61.0 | 73.1 | 24.7 | 92.8 | 71.6 |
| 17 | 23.0 | 50.8 | 81.0 | 27.9 | 91.9 | 77.2 |
| 18 | 13.7 | 31.8 | 89.0 | 29.5 | 90.0 | 81.7 |
| 19 | 10.5 | 26.7 | 91.8 | 32.1 | 89.6 | 83.5 |
| 20 | 3.3 | 7.2 | 97.2 | 27.4 | 87.8 | 85.8 |
| 21 | 2.4 | 5.6 | 98.1 | 29.7 | 87.7 | 86.3 |
| 22 | 0.4 | 0.5 | 99.6 | 16.7 | 87.3 | 87.1 |
| 23 | 0.1 | 0.0 | 99.9 | – | 87.3 | 87.3 |

Values in bold represent best cut-points.

screening may have been more likely to be tested and consequently diagnosed as having diabetes. Thus, participants with diabetes who had low risk score may have been missed through lack of testing.

In conclusion, these data provide further evidence that the FINDRISC is a simple and effective tool to identify FDR of people with type 2 diabetes at increased risk of progression to diabetes in Iran. Fasting glucose and 2hPG showed a similar discriminating ability.

## Conflict of interest

None to declare.

## Authors' contributions

Janghorbani M. conceived and designed the study, analyzed the data and wrote the manuscript, Adineh H.A. contributed to data analysis and revised the manuscript, Amini M. recruited samples and contributed to the discussion and revision of the manuscript and obtained funding for the IDPS.

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