

Development and Validation of a Patient Self-assessment Score for Diabetes Risk

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Background: National guidelines disagree on who should be screened for undiagnosed diabetes. No existing diabetes risk score is highly generalizable or widely followed.

Objective: To develop a new diabetes screening score and compare it with other available screening instruments (Centers for Disease Control and Prevention, American Diabetes Association, and U.S. Preventive Services Task Force guidelines; 2 American Diabetes Association risk questionnaires; and the Rotterdam model).

Design: Cross-sectional data.

Setting: NHANES (National Health and Nutrition Examination Survey) 1999 to 2004 for model development and 2005 to 2006, plus a combined cohort of 2 community studies, ARIC (Atherosclerosis Risk in Communities) Study and CHS (Cardiovascular Health Study), for validation.

Participants: U.S. adults aged 20 years or older.

Measurements: A risk-scoring algorithm for undiagnosed diabetes, defined as fasting plasma glucose level of 7.0 mmol/L (126 mg/dL) or greater without known diabetes, was developed in the development data set. Logistic regression was used to determine which participant characteristics were independently associated with un-

diagnosed diabetes. The new algorithm and other methods were evaluated by standard diagnostic and feasibility measures.

Results: Age, sex, family history of diabetes, history of hypertension, obesity, and physical activity were associated with undiagnosed diabetes. In NHANES (ARIC/CHS), the cut-point of 5 or more points selected 35% (40%) of persons for diabetes screening and yielded a sensitivity of 79% (72%), specificity of 67% (62%), positive predictive value of 10% (10%), and positive likelihood ratio of 2.39 (1.89). In contrast, the comparison scores yielded a sensitivity of 44% to 100%, specificity of 10% to 73%, positive predictive value of 5% to 8%, and positive likelihood ratio of 1.11 to 1.98.

Limitation: Data during pregnancy were not available.

Conclusion: This easy-to-implement diabetes screening score seems to demonstrate improvements over existing methods. Studies are needed to evaluate it in diverse populations in real-world settings.

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Diabetes and its complications are major causes of morbidity and mortality worldwide. More than 60 million U.S. adults are estimated to have diagnosed diabetes, undiagnosed diabetes, or prediabetes, and approximately 30% of diabetes cases are estimated to be undiagnosed. With the steadily increasing prevalence of diabetes, prevention of diabetes has become a major health priority (1–5). Recent clinical trials demonstrate that lifestyle (6–8) and pharmaceutical (6, 9, 10) interventions in persons with impaired glucose tolerance can prevent or delay diabetes, providing a rationale for the identification of high-risk persons who may benefit from early lifestyle interventions.

National guidelines for diabetes screening are available to help detect undiagnosed disease, and various risk assessment tools for prevalent or incident diabetes have been developed to identify persons most in need of screening. Yet, many of these risk assessment tools were developed from specific cohorts, which often have restricted age ranges or racial or ethnic groups, limiting generalizability to the entire population. In the United States, 3 national guidelines for diabetes screening are those of the Centers for Disease Control and Prevention (11), the American Diabetes Association (ADA) (12), and the U.S. Preventive Services Task Force (13). In addition, 2 risk-scoring algorithms for undiagnosed diabetes have been derived from nationally representative samples: Herman and colleagues'

(14) model from the NHANES (National Health and Nutrition Examination Survey) II (conducted from 1976 to 1980) and Heikes and colleagues' (4) model from the NHANES III (conducted from 1988 to 1994). These 2 algorithms are also known as the "ADA diabetes questionnaires."

We developed a new screening score for undiagnosed diabetes in multiethnic U.S. adults by using readily available health information. Our aim was to improve existing algorithms for diabetes-risk scoring by using a more contemporary NHANES (1999 to 2006) and formulating an easy scoring system that enables laypersons to assess their own risk for undiagnosed diabetes.

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Appendix Tables
Appendix Figure
Conversion of graphics into slides

Context

Guidelines disagree about who should receive screening for diabetes. Screening all adults would be expensive and lead to many false-positive results.

Contribution

The authors created a tool that allows people to estimate their own diabetes risk with questions they can easily answer (age, sex, family history of diabetes, personal history of high blood pressure, obesity, and physical activity). This tool performs better than other available methods.

Implication

People can use this tool to help decide whether their risk for diabetes is high enough to warrant seeing a doctor to have blood glucose measured.

—The Editors

METHODS**Study Design and Participants**

The NHANES is a cross-sectional study conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention. To represent the U.S. population, NHANES used complex, multistage probability sampling of the civilian, noninstitutionalized population. To produce reliable statistics, NHANES oversampled elderly persons and some racial and ethnic minorities. We used deidentified data from multiple years of NHANES (1999 to 2006) that are publicly available.

We included participants aged 20 years or older who had fasting plasma glucose (FPG) results. We excluded pregnant women. We used NHANES 1999 to 2004 for prediction modeling and screening score development and NHANES 2005 to 2006 for validation. We conducted further validation by combining the baseline data from 2 biracial cohort studies: the ARIC (Atherosclerosis Risk in Communities) Study (15) and the CHS (Cardiovascular Health Study) (16). Detailed descriptions of these studies are published elsewhere (15, 16). In brief, ARIC enrolled 15 732 participants aged 45 to 64 years between 1987 and 1989 from 4 communities, and CHS recruited 5201 participants aged 65 years or older between 1989 and 1990 from 4 communities. Between 1992 and 1993, CHS enrolled an additional 687 black persons to increase minority participation.

Participant Data

For each participant, we retrieved data that were collected through interviews, physical examinations, and laboratory tests. Specifically, we used data on participants' demographic and socioeconomic characteristics, health care use, personal and family medical histories, health habits, physical examinations (including anthropometric findings), and laboratory test results. For the obesity measure, we combined body mass index and waist circumference.

For variable categorization, we used conventional cutoffs or well-accepted clinical guidelines when available. If information was missing or unknown in categorical variables, we defined the condition as absent, a convention commonly adopted in the risk-questionnaire setting. In our questionnaire, we instructed users, "Enter your score (but if you don't know the answer, enter 0)."

We stratified the participants into 4 groups by diabetes status: known diabetes, normal glucose metabolism (FPG level <5.5 mmol/L [<100 mg/dL]), impaired fasting glucose or prediabetes (FPG level of 5.6 to 6.9 mmol/L [100 to 125 mg/dL]), and undiagnosed diabetes (FPG level ≥ 7.0 mmol/L [≥ 126 mg/dL]) (4, 17, 18). Specifically, we classified participants as having known diabetes if they answered "yes" to the question, "Other than during pregnancy, have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes?" or reported use of insulin or other diabetes medications.

For medical history variables, we considered data from multiple sources. For example, we classified participants as having hypertension if they reported a history of hypertension, reported using prescribed medication for hypertension, had a systolic blood pressure of 140 mm Hg or higher, or had a diastolic blood pressure of 90 mm Hg or higher. We defined hyperlipidemia as a total cholesterol level of 5.17 mmol/L (200 mg/dL) or greater or a triglyceride level of 1.69 mmol/L (150 mg/dL) or greater (19), and high cholesterol level as history of high cholesterol, use of cholesterol-lowering medication, or a fasting low-density lipoprotein cholesterol level of 2.59 mmol/L (100 mg/dL) or greater with a history of cardiovascular disease (20). We defined cardiovascular disease as myocardial infarction or stroke.

When definitions of variables were not identical across the different studies (for example, physical activity), we tried to use the best available variables to achieve reasonable consistency across databases. For example, in NHANES, we classified participants as "physically active" if they answered "more active" to the question, "Compare your activity with others of the same age." Otherwise, we classified participants as "not physically active." In ARIC, physical activity was assessed in a question with a response of "yes" or "no," whereas in CHS, we dichotomized the physical activity question into "no" or "low" versus "moderate" or "high." None of the databases we used collected data during pregnancy. Finally, some ARIC participants ($n = 521$) did not fast. For these persons, we used a random blood glucose level of 11.1 mmol/L (200 mg/dL) as the cut-point to define diabetes (12, 18, 21). We did not include non-fasting participants in the model development (using NHANES) but did include them in the external validation to reflect a realistic scenario.

Statistical Analysis

We used descriptive statistics to characterize the 4 groups according to diabetes status: we used means (SEs)

for continuous variables and percentages for categorical variables. For model fitting, we used multiple logistic regression with cases of undiagnosed diabetes as the end point, excluding cases of diagnosed diabetes. Because of small proportions of missing data, we used all nonmissing observations available in the relevant analyses. The only exception is that we imputed “family history of diabetes” by using a statistical technique (missing data imputation procedure, Proc MI, in SAS, SAS Institute, Cary, North Carolina) to handle missing data in CHS because this information was not collected in CHS (22, 23).

Development of a New Screening Score

Using the development data set (NHANES 1999 to 2004), we included a comprehensive list of predictors known to be potentially associated with undiagnosed diabetes in an initial model. Specifically, we included the main effects of all variables listed in **Appendix Table 1** (available at www.annals.org) and their interaction effects with age. Because the number of covariates was large, we started with continuous variables and later categorized them in the final model. We used backward elimination (deleting the covariate with the largest *P* value, 1 at a time) from the initial model until we reached a final model with statistically significant covariates. We were guided by statistical significance for the model building but also used scientific and qualitative judgments as well. For example, although income and health insurance status were statistically significant, we did not keep these variables in the final model because we deemed them less appropriate or less user-friendly in risk assessment questionnaires. Physical activity showed borderline significance ($P = 0.064$) in the development data set but was kept because this is an underlying protective factor that often does not reach statistical significance for various reasons (for example, difficult to quantify, misclassification, or insufficient statistical power). Moreover, physical activity is highly modifiable compared with demographic and health history variables (24).

In the final model, we double-checked that any important covariates were not erroneously omitted in this sequential process. We intentionally used only categorized variables that captured easy but relevant and validated health information in the prediction model, to develop a user-friendly and educational screening score. We created a weighted scoring system by rounding up all regression coefficients in the final model to the nearest integer (when strong monotonicity was observed, we broke the tie accordingly).

Validation and Comparison With Other Methods

We evaluated our scoring system in NHANES 2005 to 2006. We computed standard validation measures: the proportion of high-risk persons, sensitivity, specificity, positive predictive value (PPV), negative predictive value

(NPV), Youden index ($1 - \text{false-positive rate} - \text{false-negative rate} = \text{sensitivity} + \text{specificity} - 1$), likelihood ratios for a positive test result ($\text{sensitivity}/[1 - \text{specificity}]$) and for a negative test result ($[1 - \text{sensitivity}]/\text{specificity}$), and the area under the receiver-operating characteristic curve (AUC) as a discrimination statistic (25–27). In addition, we refitted our final model to ARIC/CHS. We estimated the prevalence of undiagnosed diabetes per individual score in NHANES and ARIC/CHS.

In validation samples using the aforementioned evaluation measures, we compared our new classification rule with the U.S. screening guidelines and other assessment algorithms for undiagnosed diabetes: Centers for Disease Control and Prevention (11), ADA (12), and U.S. Preventive Services Task Force (13) guidelines; 2 ADA diabetes-risk questionnaires (4, 14); and the Rotterdam model, which was derived from a European sample (28). We included the last model to evaluate the generalizability and transferability of a validated non-U.S. model to the U.S. population.

Ancillary Analyses

We performed 3 ancillary analyses to check the sensitivity and robustness and to test the utility of the new screening score in broadened practical contexts. We repeated the NHANES analyses using “undiagnosed diabetes and prediabetes” as an expanded end point (with “normal glucose” as the reference group); separately for persons younger than 45 years versus persons aged 45 years or older, because 45 years is the age threshold proposed by the ADA for universal screening; and using an alternative definition of the end point, based on hemoglobin A_{1c} level of 6.5% or greater (12, 29). The first analysis may have particular importance for predicting prediabetes, the condition for which prevention has been shown to be more beneficial compared with undiagnosed yet manifest disease.

For statistical analyses, we used SAS, version 9.1 (SAS, Institute, Cary, North Carolina). For NHANES analyses, we used survey procedures with options of strata, cluster, and weight to account for the complex survey design (23, 25). We adopted 2-sided hypotheses and tests for all statistical inferences.

Role of the Funding Source

The Clinical and Translational Science Center at Weill Cornell Medical College provided partial support for data analyses. The funding source had no role in the design of our analysis, its interpretation, or the decision to submit the manuscript for publication.

RESULTS

Our sample comprised 5258 participants in the development data set. **Appendix Table 1** (available at www.annals.org) summarizes characteristics of participants according to diabetes status. The crude weighted prevalence

of undiagnosed diabetes based on fasting glucose in adults aged 20 years or older was 2.8% (2). Participants with diagnosed or undiagnosed diabetes tended to be older and have less education and lower household income than their counterparts without diabetes. These participants also tended to be hypertensive, to exercise less, and to have a family history of diabetes and a personal history of cardiovascular disease. Of note, participants with undiagnosed diabetes were more likely than participants with diagnosed diabetes to have higher blood pressure, body mass index, waist circumference, total cholesterol level, and dyslipidemia (differences were not formally tested).

Table 1 presents the final regression model derived from the development data set. Age, sex, family history of diabetes, personal history of hypertension, obesity, and physical activity were statistically significant predictors of undiagnosed diabetes. Age and obesity status needed multiple categories (with score of 0 to 3 assigned) to capture the risk gradient, whereas other risk factors were binary (with score of 0 or 1 assigned). The 6 risk factors jointly yielded an AUC of 0.79.

Table 1. Risk Factors for Undiagnosed Diabetes*

Risk Factor	Odds Ratio (95% CI)	P Value	Log (Odds Ratio)	Score Assigned
Age				
<40 y	Reference	–	–	0
40–49 y	2.6 (1.3–5.0)	0.004	0.95	1
50–59 y	4.8 (2.2–10.6)	<0.001	1.57	2
≥60 y	8.1 (3.9–16.9)	<0.001	2.09	3
Sex				
Female	Reference	–	–	0
Male	2.6 (1.8–3.7)	<0.001	0.96	1
Family history of diabetes				
No	Reference	–	–	0
Yes	2.0 (1.5–2.6)	<0.001	0.67	1
History of hypertension				
No	Reference	–	–	0
Yes	1.9 (1.2–2.9)	0.004	0.64	1
Obesity†				
Not overweight or obese	Reference	–	–	0
Overweight	1.3 (0.6–2.8)	0.47	0.27	1
Obese	3.1 (1.6–5.8)	<0.001	1.12	2
Extremely obese	7.3 (4.0–13.4)	<0.001	1.99	3
Physically active				
No	Reference	–	–	0
Yes	0.7 (0.5–1.0)	0.06	–0.34	–1

* Based on the final regression model in the development data set, National Health and Nutrition Examination Survey, 1999 to 2004 (n = 5258; area under the receiver-operating characteristic curve, 0.79).

† Extreme obesity was body mass index ≥40 kg/m² (men and women), or waist circumference ≥50 in (men) or ≥49 in (women); obesity was body mass index ≥30 kg/m² but <40 kg/m² (men and women), or waist circumference ≥40 in but <50 in (men) or ≥35 in but <49 in (women); and overweight was body mass index ≥25 kg/m² but <30 kg/m² (men and women), or waist circumference ≥37 in but <40 in (men) or ≥31.5 in but <35 in (women). The Figure shows the questionnaire and a body mass index chart.

We assessed the diagnostic characteristics of different cut-points for total score in the development and validation NHANES data sets. We selected the cut-point of 5 or more points to designate an individual as having a high risk for undiagnosed diabetes. This cut-point defined approximately 35% of the adult population as high risk for undiagnosed diabetes and yielded a sensitivity of 79%, specificity of 67%, PPV of 10%, and NPV of 99%, with an AUC of 0.83 in the validation NHANES data set (Appendix Table 2, available at www.annals.org). On the basis of these results, if we assume that 1000 new persons will go through the risk assessment and use the cut-point of 5, then 350 persons (35%) would undergo diagnostic testing, 31 new cases of diabetes would be identified, and 6 to 7 persons with diabetes would remain untested and undetected (30). If the lower cut-point of 4 is used, then approximately 510 persons (51%) would undergo diagnostic testing, and we can expect 41 cases of diabetes to be newly identified and fewer than 3 cases to go untested and undetected.

When our final prediction model was refitted to ARIC/CHS, we obtained consistent results: All of the risk factors were significant (P ≤ 0.001), and the magnitude of the associations was similar, with an AUC of 0.74 (Appendix Table 3, available at www.annals.org).

The Appendix Figure (available at www.annals.org) shows the prevalence of undiagnosed diabetes for individual total scores in NHANES and ARIC/CHS. A monotonic (quadratic) relationship was clearly observed. Disease prevalence was higher in ARIC/CHS than in NHANES, probably because of older ages in the ARIC/CHS populations (≥45 years). Table 2 summarizes the performance characteristics of the existing guidelines or scores and our own method. Our screening score (cut-point ≥5 points) tended to identify smaller proportions of people being at high risk but resulted in higher overall test accuracy (reflected in the Youden index), PPV, and likelihood ratio for a positive test result, compared with other methods. Negative predictive value was high (≥0.96) for all methods. Among existing methods, the Rotterdam model (developed from a European sample) and the new ADA questionnaire seemed to perform best.

We performed 3 ancillary analyses, described in the Methods section. We again used cut-point scores of 5 and 4. Results below are for a cut-point of 5; values in parentheses are those for a cut-point of 4. In the first ancillary analysis, discrimination ability was somewhat reduced as anticipated when the end point combined undiagnosed diabetes and prediabetes (AUC, 0.72), yielding a sensitivity of 57% (73%), specificity of 74% (57%), PPV of 56% (50%), and NPV of 74% (78%). In the second ancillary analysis, which included only participants aged 45 years or older, a sensitivity was 88% (97%), specificity was 40% (20%), PPV was 9% (8%), and NPV was 98% (99%), with an AUC of 0.73. Using only participants younger than 45 years yielded a sensitivity of 35% (76%), specific-

Table 2. Performance of Diabetes Screening Methods in Validation Data Sets*

Method, by Data Set	High Risk, %	Sensitivity	Specificity	PPV	NPV	Positive LR	Negative LR	Youden Index	Number of Variables†	Requires Clinician's Input?
NHANES 2005 to 2006 (n = 1640)										
CDC‡	90	100	10	5	100	1.11	0	10	1	No
ADA§	82	97	19	5	99	1.20	0.16	16	14 or 15	Yes
USPSTF	28	44	73	7	97	1.63	0.77	17	2	Yes
ADA questionnaire I¶	57	83	44	6	98	1.48	0.39	27	6 or 7	No
ADA questionnaire II**	42	76	59	8	98	1.85	0.41	35	10	No
Rotterdam model††	47	89	55	8	99	1.98	0.20	44	4 or 5	No
New screening score‡‡										
≥5	35	79	67	10	99	2.39	0.31	46	6 or 8	No
≥4	51	97	51	8	100	1.98	0.06	48		
ARIC/CHS (n = 19 728)										
CDC‡	100	100	NA	5	NA	NA	NA	NA	1	No
ADA§	100	100	NA	5	NA	NA	NA	NA	14 or 15	Yes
USPSTF	35	53	66	8	96	1.56	0.71	19	2	Yes
ADA questionnaire I¶	60	80	41	7	97	1.36	0.49	21	6 or 7	No
ADA questionnaire II**	64	86	38	7	98	1.39	0.37	24	10	No
Rotterdam model††	55	81	46	8	98	1.50	0.41	27	4 or 5	No
New screening score‡‡										
≥5	40	72	62	10	98	1.89	0.45	34	6 or 8	No
≥4	64	91	38	8	99	1.47	0.24	29		

ADA = American Diabetes Association; ARIC = Atherosclerosis Risk in Communities; BMI = body mass index; CDC = Centers for Disease Control and Prevention; CHS = Cardiovascular Health Study; LR = likelihood ratio; NA = not available; NHANES = National Health and Nutrition Examination Survey; NPV = negative predictive value; PPV = positive predictive value; USPSTF = U.S. Preventive Services Task Force.

* Data on history of the polycystic ovary syndrome, history of impaired fasting glucose or impaired glucose tolerance, and pregnancy were not collected, so these conditions were omitted for the ADA guideline. Both ARIC and NHANES 2005 to 2006 collected the data on family history of diabetes but not separately for parents and siblings, so we replaced parental history with family history for the ADA questionnaires.

† A smaller number indicates that a person knows their obesity status or BMI.

‡ CDC: All adults aged 25 years or older.

§ ADA: All adults aged 45 years or older and younger adults who are overweight or obese (BMI ≥ 25 kg/m²) and have at least 1 other risk factor, including physical inactivity, family history of diabetes, minority ethnicity, history of gestational diabetes or delivery of a baby weighing >9 lb, hypertension, high-density lipoprotein cholesterol level <0.9 mmol/L (<35 mg/dL) or triglyceride level >2.83 mmol/L (>250 mg/dL), women with the polycystic ovary syndrome, history of impaired fasting glucose or impaired glucose tolerance, other clinical conditions associated with insulin resistance (for example, severe obesity), or history of cardiovascular disease. From reference 12.

|| USPSTF: All adults with sustained blood pressure (either treated or untreated) greater than 135/80 mm Hg. From reference 13.

¶ ADA diabetes questionnaire I: score_Herman ≥ 10 , in which score_Herman = (woman who delivered a baby weighing ≥ 9 lb) $\times 1$ + (parental history of diabetes) $\times 1$ + (sibling's history of diabetes) $\times 1$ + (BMI ≥ 27 kg/m²) $\times 5$ + (age <65 y and not physically active) $\times 5$ + (45 y \leq age <65 y) $\times 5$ + (age ≥ 65 y) $\times 9$. From reference 14.

** ADA diabetes questionnaire II: A function of age, waist, weight, height, gestational diabetes, parental and sibling diabetes history, race, high blood pressure, and exercise. See reference 4 for a graphical presentation of this algorithm.

†† Rotterdam model: score_Rotterdam >6 , in which score_Rotterdam = 2 per 5-y increment from 55 y + (male) $\times 5$ + (use of antihypertensive medications) $\times 4$ + (BMI ≥ 30) $\times 5$. From reference 29.

‡‡ New screening score: score_new ≥ 5 , in which score_new = (40 y \leq age <50 y) $\times 1$ + (50 y \leq age <60 y) $\times 2$ + (age ≥ 60 y) $\times 3$ + (male) $\times 1$ + (family history of diabetes) $\times 1$ + (history of hypertension) $\times 1$ + (overweight) $\times 1$ + (obese) $\times 2$ + (extremely obese) $\times 3$ - (exercise) $\times 1$.

ity of 93% (80%), PPV of 6% (5%), and NPV of 99% (100%), with an AUC of 0.83. This analysis may be limited because the number of patients with diabetes was small. Finally, when we used hemoglobin A_{1c} level instead of FPG for the definition of diabetes, we obtained a sensitivity of 80% (91%), specificity of 63% (47%), PPV of 6% (5%), and NPV of 99% (99%), with an AUC of 0.78. Positive predictive value is directly proportional to the prevalence of the disease or condition (25, 31), which explains why our screening method, as with previous methods, yielded lower PPV for these outcomes.

The Figure provides a sample questionnaire that can be used for community screening for undiagnosed diabetes or prediabetes.

DISCUSSION

Clinical trials demonstrate that high-risk persons can reduce their risk for diabetes by more than half when they

follow a well-structured, intensive lifestyle modification program (6, 8, 18). Therefore, early diagnosis could be crucial to reduce the global burden of diabetes. Widespread blood glucose testing may not be the best way to identify undiagnosed diabetes in a large community or in resource-limited settings. Indeed, existing recommendations for diabetes screening that rely on blood testing are not widely followed, resulting in undiagnosed diabetes in 30% of patients with diabetes (4).

We developed a screening score that can be used in a wide variety of community settings and clinical encounters (including patient waiting rooms or on the Internet) via a simple pencil-and-paper method. Our new diabetes score seemed to perform better than existing methods by quantitative criteria. We believe that it also has good feasibility characteristics: It is simple (with 6 easily answered health-related questions) and efficient (with minimal time needed for survey completion and no need for a calculator, with

Figure. Self-assessment screening score for undiagnosed diabetes or prediabetes.

Question	Answer (Score)	Enter Your Score (Enter 0 If You Don't Know)
1. How old are you?	<40 y (0 point) 40–49 y (1 point) 50–59 y (2 points) ≥60 y (3 points)	
2. Are you a woman or man?	Woman (0 point) Man (1 point)	
3. Do your family members (parent or sibling) have diabetes?	No (0 point) Yes (1 point)	
4. Do you have high blood pressure or are you on medication for high blood pressure?	No (0 point) Yes (1 point)	
5. Are you overweight or obese? (see chart below to answer this question more accurately)	Not overweight or obese (0 point) Overweight (1 point) Obese (2 points) Extremely obese (3 points)	
6. Are you physically active?	No (0 point) Yes (–1 point)	
TOTAL SCORE (add points from questions 1–6)		
If your TOTAL SCORE is ≥4, you are at high risk for undiagnosed diabetes or prediabetes. If your TOTAL SCORE is ≥5, you are at high risk for undiagnosed diabetes. See your doctor for a blood test to look for diabetes if your score is high.		

Obesity definitions

Extreme obesity: BMI ≥40 kg/m² (men and women), or waist circumference ≥50 in (men) or ≥49 in (women)

Obesity: BMI ≥30 kg/m² but <40 kg/m² (men and women), or waist circumference ≥40 in but <50 in (men) or ≥35 in but <49 in (women)

Overweight: BMI ≥25 kg/m² but <30 kg/m² (men and women), or waist circumference ≥37 in but <40 in (men) or ≥31.5 in but <35 in (women)

Body Mass Index (BMI) Chart

Weight	lb	100	105	110	115	120	125	130	135	140	145	150	155	160	165	170	175	180	185	190	195	200	205	210	215
	kg	45.5	47.7	50.0	52.3	54.5	56.8	59.1	61.4	63.6	65.9	68.2	70.5	72.7	75.0	77.3	79.5	81.8	84.1	86.4	88.6	90.9	93.2	95.5	97.7
Height		Underweight				Healthy				Overweight				Obese				Extremely obese							
5'0" (152.4 cm)		19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
5'1" (154.9 cm)		18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	36	37	38	39	40
5'2" (157.4 cm)		18	19	20	21	22	22	23	24	25	26	27	28	29	30	31	32	33	33	34	35	36	37	38	39
5'3" (160.0 cm)		17	18	19	20	21	22	23	24	24	25	26	27	28	29	30	31	32	32	33	34	35	36	37	38
5'4" (162.5 cm)		17	18	18	19	20	21	22	23	24	24	25	26	27	28	29	30	31	31	32	33	34	35	36	37
5'5" (165.1 cm)		16	17	18	19	20	20	21	22	23	24	25	25	26	27	28	29	30	30	31	32	33	34	35	35
5'6" (167.6 cm)		16	17	17	18	19	20	21	21	22	23	24	25	25	26	27	28	29	29	30	31	32	33	34	34
5'7" (170.1 cm)		15	16	17	18	18	19	20	21	22	22	23	24	25	25	26	27	28	29	29	30	31	32	33	33
5'8" (172.7 cm)		15	16	16	17	18	19	19	20	21	22	22	23	24	25	25	26	27	28	28	29	30	31	32	32
5'9" (175.2 cm)		14	15	16	17	17	18	19	20	20	21	22	22	23	24	25	25	26	27	28	28	29	30	31	31
5'10" (177.8 cm)		14	15	16	17	17	18	18	19	20	20	21	22	23	23	24	25	25	26	27	28	28	29	30	30
5'11" (180.3 cm)		14	14	15	16	16	17	18	18	19	20	21	21	22	23	24	25	25	26	27	28	28	29	30	30
6'0" (182.8 cm)		13	14	14	15	16	17	17	18	19	19	20	21	21	22	23	23	24	25	26	26	27	27	28	29
6'1" (185.4 cm)		13	13	14	15	15	16	17	17	18	19	19	20	21	21	22	23	23	24	25	25	26	27	27	28
6'2" (187.9 cm)		12	13	14	14	15	16	16	17	18	18	19	19	20	21	21	22	23	23	24	25	25	26	27	27
6'3" (190.5 cm)		12	13	13	14	15	15	16	16	17	18	18	19	20	20	21	21	22	23	23	24	25	25	26	26
6'4" (193.0 cm)		12	12	13	14	14	15	15	16	17	17	18	18	19	20	20	21	22	22	23	23	24	25	25	26

the maximum score less than 10) screening tool with which patients or health care providers can assess their or their patients' need for formal diabetes testing.

The U.S. guidelines for diabetes screening did not perform well. The 3 diabetes risk assessment scores showed lower overall accuracy and tended to select larger propor-

tions of persons for diabetes screening compared with our score. Low specificities of existing methods have been reported elsewhere (32–34). The screening criteria recommended by different organizations were developed by using different frameworks and for different purposes (for example, to enhance efficiency of screening or to target persons

who could benefit most from screening). So, although they differ in numerical performance characteristics (for example, sensitivity and specificity) based on our analysis, they may be more appropriate for those purposes.

Our primary end point was undiagnosed diabetes rather than the composite outcome of undiagnosed diabetes and prediabetes, but the same questionnaire may be justified for these closely related outcomes (a disease and its precursor) with different cut-points (5 for diabetes and 4 for prediabetes), based on the evidence obtained from our ancillary analyses. In addition, our score is for prediction of currently undiagnosed diabetes and not incident diabetes in the future. However, strong consistency in risk factors for the prediction of prevalent and incident events in diabetes and other chronic diseases has been reported (35–37), and we expect that the same set of risk factors in our model plays an important role in the prediction of future diabetes or prediabetes. Nonetheless, other laboratory or behavioral and lifestyle variables could be useful in predicting future events rather than current events (18, 21, 30, 38–40).

A risk prediction approach that can capture a continuous risk spectrum is a popular tool that has been used to identify important risk factors and to estimate average risk; results can be used in decision making about public health and clinical care. Risk prediction has even been proposed as an alternative to diagnosis for some diseases (41). We believe that ideal risk assessment methods or prediction models should be derived from large representative samples of a target population and consist of fixed and modifiable risk factors together. Simplicity and user-friendliness (including optimal presentation), in addition to accuracy, are key to successful implementation, especially for laypersons (24, 38). To achieve these goals, we adopted a statistical method that yields a systematic scoring system and accounts for design effects of the study appropriately (that is, a logistic regression model suited for complex survey data); carefully selected a parsimonious set of predictors (guided not only by numerical and scientific evidence but also by feasibility perspectives); chose categorized variables in intuitive or well-accepted ways (for example, using deciles for age and obesity definitions); and emphasized an educational purpose of the screening score, highlighting the important risk factors to motivate high-risk persons to be screened or to modify health behaviors (for example, combining body mass index and waist circumference together, rather than using height, weight, and waist circumference separately). This combination of factors may explain the enhanced properties of our new score.

For this study, we tried to identify all existing screening guidelines or risk assessment scores for prevalent undiagnosed diabetes available to the U.S. population and 1 screening score best suited to the non-U.S. population for comparisons. We found 3 national guidelines and 2 scores or questionnaires for diabetes screening in the United States and many prediction models for incident diabetes.

Our search for the best-suited non-U.S. model was guided by recent comparison studies (35, 42). We selected the Rotterdam model because it was developed for prevalent undiagnosed diabetes, has been externally validated in different samples, and requires routinely available demographic or health information in its simple scoring system.

Our study has limitations. First, some variables that are part of existing methods (for example, gestational diabetes) were not available in the databases we used. Therefore, caution should be used in making comparisons between our methods and those of others. Nonetheless, we believe that most key information was available and used, minimizing unfairness in the comparisons. In addition, we could not incorporate oral glucose tolerance test results because these data were not collected in the newer NHANES (1999 to 2006) and in the baseline visits in ARIC and CHS. Thus, we defined the outcome based solely on the FPG. The FPG is a recommended screening test, however, and the lack of oral glucose tolerance test data has not been shown elsewhere to affect the stability of methods of assessing diabetes risk (4, 43). Our results seemed to be robust to different definitions of the end point, based on either FPG or hemoglobin A_{1c} level (for example, AUC of 0.79 vs. 0.78, respectively).

Although the lay population is increasingly aware of the danger of diabetes and its complications, more education is needed in community and clinical settings. In that sense, although further validation of our screening score in other samples is important, this newly developed algorithm could still have immediate applications. In addition to its use in clinical encounters, targeted screenings, and health education programs, the screening score can be applied by health plans to existing databases for case finding. The new algorithm may also help identify optimal populations for enrollment in clinical trials that test new strategies to prevent or manage diabetes.

In conclusion, we see our screening score as a method of identifying persons in need of formal diabetes screening and of calling more attention to prediabetes. A self-assessment method that helps persons decide whether they should seek medical care for diabetes testing may address the lack of interaction with health care facilities and providers, which may underlie the high percentage of the population with undiagnosed diabetes, particularly underserved persons. Although consensus on diabetes screening has not yet been reached (44, 45), we believe that patients who are at high risk should be given priority for formal screening for undiagnosed diabetes. This new diabetes screening score could help identify these high-risk persons while patients and caregivers alike await more definitive evidence-based recommendations (46, 47).

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Appendix Table 1. Characteristics of Participants in NHANES 1999 to 2004, by Diabetes Status*

Characteristic	Normal Glucose (n = 3396)	Impaired Glucose (n = 1652)	Undiagnosed Diabetes (n = 210)	Known Diabetes (n = 482)
Mean age (\pm SE), y	42.4 \pm 0.49	51.8 \pm 0.54	58.3 \pm 1.65	57.6 \pm 0.88
Men, %	44	60	62	51
White, %	72	75	74	61
High school education or beyond, %	83	76	67	70
Annual household income \geq \$25 000, %	65	63	47	49
Married, %	58	64	57	62
Has health insurance, %	81	83	83	92
Mean health care visits in past year (\pm SE), n	1.9 \pm 0.03	2.0 \pm 0.04	2.1 \pm 0.13	3.0 \pm 0.06
History of hypertension, %	28	44	67	69
History of CVD, %	3	7	12	14
Hyperlipidemia, %	52	67	70	64
High cholesterol level, %	34	50	57	78
Family history of diabetes, %	46	48	61	75
Mother or father	20	27	35	47
Brother or sister	7	11	18	31
Family history of CVD, %	40	35	33	49
Smoking status, %				
Current smoker	26	21	20	23
Former smoker	22	32	43	32
Physically active, %	36	36	30	29
Mean systolic BP (\pm SE), mm Hg	120 \pm 0.44	126.7 \pm 0.55	135.1 \pm 2.23	129.6 \pm 1.22
Mean diastolic BP (\pm SE), mm Hg	72.2 \pm 0.26	73.5 \pm 0.43	72.9 \pm 1.37	70.9 \pm 0.86
Mean BMI (\pm SE), kg/m ²	26.9 \pm 0.11	29.5 \pm 0.20	32.3 \pm 0.83	31.6 \pm 0.57
Mean waist circumference (\pm SE), in	36.4 \pm 0.12	39.9 \pm 0.20	43.1 \pm 0.65	42.3 \pm 0.57
Mean total cholesterol level (\pm SE)				
mmol/L	5.14 \pm 0.03	5.36 \pm 0.03	5.41 \pm 0.11	5.16 \pm 0.07
mg/dL	198.6 \pm 1.10	207.1 \pm 1.22	209.2 \pm 4.32	199.6 \pm 2.58
Mean triglyceride level (\pm SE)				
mmol/L	1.45 \pm 0.03	1.91 \pm 0.05	2.82 \pm 0.37	2.22 \pm 0.09
mg/dL	128.9 \pm 2.90	169.0 \pm 4.57	249.4 \pm 33.0	196.6 \pm 8.38
Mean HDL cholesterol level (\pm SE)				
mmol/L	1.39 \pm 0.01	1.27 \pm 0.01	1.18 \pm 0.03	1.22 \pm 0.03
mg/dL	53.7 \pm 0.38	49.1 \pm 0.56	45.6 \pm 1.15	47.0 \pm 0.99
Mean LDL cholesterol level (\pm SE)				
mmol/L	3.09 \pm 0.02	3.25 \pm 0.03	3.10 \pm 0.08	2.98 \pm 0.05
mg/dL	119.5 \pm 0.85	125.7 \pm 1.17	119.8 \pm 3.07	115.1 \pm 1.90
Mean HbA _{1c} level (\pm SE), %	5.20 \pm 0.01	5.27 \pm 0.01	7.06 \pm 0.20	7.16 \pm 0.07

BMI = body mass index; BP = blood pressure; CVD = cardiovascular disease; HbA_{1c} = hemoglobin A_{1c}; HDL = high-density lipoprotein; LDL = low-density lipoprotein; NHANES = National Health and Nutrition Examination Survey.

* Normal glucose is defined as a fasting plasma glucose level <5.5 mmol/L (<100 mg/dL); impaired glucose is defined as a fasting plasma glucose level 5.6 to 6.9 mmol/L (100 to 125 mg/dL); and undiagnosed diabetes is defined as a fasting plasma glucose level \geq 7.0 mmol/L (\geq 126 mg/dL). Sample sizes were unweighted, whereas summary statistics were weighted in fasting subsamples. Actual sample sizes are reduced for some variables; for example, income data are missing for 10% of participants, and other variables had \leq 5% missing data.

Appendix Table 2. Cut-Points for Detecting Undiagnosed Diabetes in NHANES

Total Score, by Data Set	High Risk, %	Sensitivity	Specificity	PPV	NPV	Positive LR	Negative LR
Development data*							
≥6	23	61	79	11	98	2.90	0.49
≥5	39	82	63	8	99	2.22	0.29
≥4	55	93	46	7	99	1.72	0.15
≥3	71	98	30	5	100	1.40	0.07
Validation data†							
≥6	20	62	82	13	98	3.44	0.46
≥5	35	79	67	10	99	2.39	0.31
≥4	51	97	51	8	100	1.98	0.06
≥3	68	99	33	6	100	1.48	0.03

LR = likelihood ratio; NHANES = National Health and Nutrition Examination Survey; NPV = negative predictive value; PPV = positive predictive value.

* NHANES 1999 to 2004 ($n = 5258$; area under the receiver-operating characteristic curve, 0.79).

† NHANES 2005 to 2006 ($n = 1640$; area under the receiver-operating characteristic curve, 0.83).

Appendix Table 3. Final Regression Model Fitted to External Validation Data Sets*

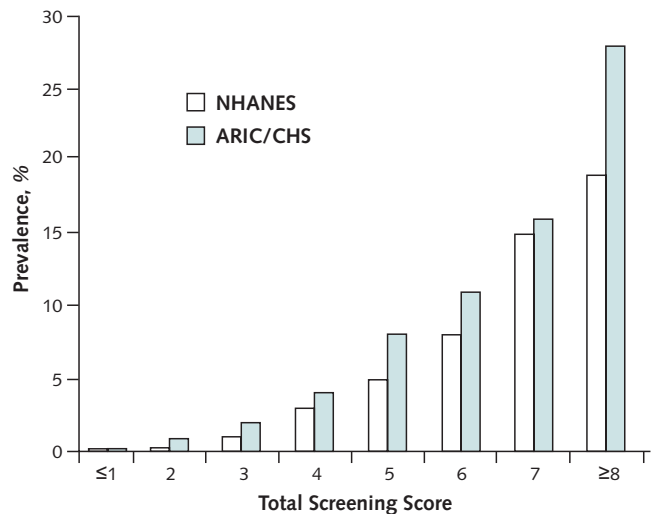
Variable	Odds Ratio (95% CI)	P Value	Log (Odds Ratio)
Age†			
<50 y	Reference	—	—
50–59 y	1.4 (1.1–1.8)	0.001	0.36
≥60 y	2.5 (2.0–3.1)	<0.001	0.91
Sex			
Female	Reference	—	—
Male	1.8 (1.6–2.0)	<0.001	0.57
Family history of diabetes			
No	Reference	—	—
Yes	1.9 (1.7–2.2)	<0.001	0.66
History of hypertension			
No	Reference	—	—
Yes	2.3 (2.0–2.6)	<0.001	0.83
Obesity‡			
Not overweight or obese	Reference	—	—
Overweight	1.8 (1.4–2.3)	<0.001	0.57
Obese	3.6 (2.9–4.5)	<0.001	1.28
Extremely obese	8.8 (6.2–12.4)	<0.001	2.18
Physically active			
No	Reference	—	—
Yes	0.8 (0.7–0.9)	<0.001	–0.23

* Based on Atherosclerosis Risk in Communities/Cardiovascular Health Study ($n = 19\,728$; area under the receiver-operating characteristic curve, 0.74).

† Minimum age in Atherosclerosis Risk in Communities/Cardiovascular Health Study is 45 y.

‡ Extreme obesity was body mass index ≥ 40 kg/m² (men and women), or waist circumference ≥ 50 in (men) or ≥ 49 in (women); obesity was body mass index ≥ 30 kg/m² but < 40 kg/m² (men and women), or waist circumference ≥ 40 in but < 50 in (men) or ≥ 35 in but < 49 in (women); and overweight was body mass index ≥ 25 kg/m² but < 30 kg/m² (men and women), or waist circumference ≥ 37 in but < 40 in (men) or ≥ 31.5 in but < 35 in (women). The Figure shows the questionnaire and a body mass index chart.

Appendix Figure. Estimated prevalence of undiagnosed diabetes, by screening score.



NHANES 1999 to 2006 has 6898 participants, and ARIC/CHS has 19 728 participants. Proportions of persons with scores of $-1, 0, 1, 2, 3, 4, 5, 6, 7, 8,$ or 9 correspond to 1%, 4%, 10%, 14%, 16%, 17%, 16%, 13%, 7%, 2%, and 0.1% in NHANES and 2%, 5%, 11%, 19%, 24%, 22%, 13%, 4%, 0.4%, and 0.01% in ARIC/CHS, respectively. ARIC = Atherosclerosis Risk in Communities; CHS = Cardiovascular Health Study; NHANES = National Health and Nutrition Examination Survey.