

Assessing Risk for Development of Diabetes in Young Adults

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ABSTRACT

PURPOSE The prevalence of diabetes is increasing to epidemic levels. A multivariable risk score for the development of diabetes has been shown to be predictive for middle-aged adults; however, it is unclear how well it performs in a younger adult population. The purpose of this study was to evaluate a preexisting multivariable risk score for the development of diabetes in a young adult cohort.

METHODS We analyzed the Coronary Artery Risk Development in Young Adults (CARDIA), a population-based observational study of participants aged 18 to 30 years recruited in 1985-1986. We observed individuals without diabetes at baseline for 10 years for the development of diabetes ($n = 2,543$). We computed receiver operating characteristic (ROC) curves for a diabetes risk score composed of the following 6 variables: elevated blood pressure, low high-density lipoprotein cholesterol levels, high triglyceride levels, body mass index, large waist circumference, and hyperglycemia.

RESULTS The area under the ROC curve was .70 in this population, which was less than the .78 previously found among middle-aged adults. BMI alone (.67) was not significantly different from the risk score. Blacks (.72; 95% CI, .69-.74) and whites (.68; 95% CI, .66-.71) do not significantly differ in the area under the ROC curve for the risk score; however, the area under the ROC curve for BMI is significantly larger for blacks (.69; 95% CI, .66-.72) than for whites (.63; 95% CI, .60-.65).

CONCLUSION An established risk score for the development of diabetes among middle-aged persons has limited utility in a younger population. Future research needs to focus on identifying novel factors that may improve the risk stratification for diabetes development among young adults.

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INTRODUCTION

Considerable evidence has been presented on the increased prevalence of diabetes in the United States.¹ This prevalence has become so large that diabetes has been termed an epidemic.^{1,2} In particular, diabetes is increasingly diagnosed among adolescents and younger adults.^{3,4} One factor thought to be driving the diabetes epidemic is the increase in obesity.⁵⁻⁷

Prediction of chronic conditions that have a definable onset in adults can help to guide interventions and health policy development. Prediction is an important issue, given that diabetes leads to considerable morbidity and mortality, which can be mitigated through early recognition and treatment.⁸ Major risk factors for diabetes have been identified and are currently used by the American Diabetes Association to guide screening strategies. Risk scores for diabetes fall into 2 primary categories that are conceptually distinct. Although risk scores are usually thought to quantify an individual's risk of developing disease, as with the Framingham Risk Score for coronary heart disease, most self-identified diabetes risk scores do not assess the risk of developing disease; rather, they assess the likeli-

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hood of having undiagnosed diabetes.⁹⁻¹⁴ There are few measures that assess the risk of developing diabetes.^{15,16}

Some risk scores for the likelihood of having undiagnosed diabetes have been tested in populations other than the ones in which they were created and have unfortunately not worked as well.^{17,18} Considering the importance of identifying individuals at risk for developing diabetes, a strategy for assessing risk of developing diabetes in young adults has many benefits, including targeted interventions for young adults at high risk. Thus, the purpose of this study was to evaluate how well a risk score for developing diabetes that was created with a middle-aged population performs in a cohort of young adults.

METHODS

This study is based on an analysis of the Coronary Artery Risk Development in Young Adults (CARDIA), a population-based observational study of participants aged 18 to 30 years recruited in 1985-1986. Participants were recruited in 4 communities: Birmingham, Alabama; Chicago, Illinois; Minneapolis, Minnesota; and Oakland, California. Recruitment was stratified by race (black and white), age (18 to 24 years, and 25 to 30 years), and education (less than high school, and high school or more). Second (1987-1988), third (1990-1991), fourth (1992-1993), fifth (1995-1996), and sixth examinations (2000-2001) have been completed in the cohort. The public use data set used for this study, however, only includes information from the first 5 examinations.

For the progression to diabetes analyses, all individuals had no indication of diabetes at baseline. This cohort was comprised of 2,543 persons. A total of 100 persons out of 2,543 developed diabetes within the 10 years.

Diabetes

Diabetes was defined by self-report in response to the question, "Has a doctor or nurse ever said you had diabetes (high sugar in blood or urine)?" and by a fasting plasma glucose of ≥ 126 mg/dL. Although this biomarker definition deviates from the definition in place at baseline (≥ 140 mg/dL), we believed that it was important to use a current definition of diabetes, whether diagnosed or not. This definition is also consistent with the diabetes risk score used in this study.¹⁵ Development of diabetes was defined as having diabetes at year 10 (examination 5).

Diabetes Risk Score

The risk score used in this study predicts the development of diabetes, not the risk of having undiagnosed diabetes.¹⁵ It was created from an analysis of individu-

als aged 45 to 64 years in Atherosclerosis Risk in Communities (ARIC) study and is based on the metabolic syndrome.¹⁹ Among individuals without diagnosed diabetes or fasting plasma glucose ≥ 126 mg/dL at baseline, a scoring strategy was developed that included large waist circumference (>102 cm in men and >88 cm for women), raised blood pressure ($>130/85$ mm Hg or antihypertensive medications), low high-density lipoprotein cholesterol levels (<40 mg/dL for men and <50 mg/dL for women), high triglyceride levels (>150 mg/dL), body mass index (BMI) of greater than 30 kg/m², and hyperglycemia. Each of the characteristics are worth 1 point except for hyperglycemia, which can be worth 2 points if fasting glucose is ≥ 102 mg/dL or 5 points when fasting glucose ≥ 111 mg/dL. A score of ≥ 4 puts an individual at high risk for development of diabetes, either diagnosed or undiagnosed.

This particular risk score was chosen for several reasons. First, it has moderate sensitivity (68%) and specificity (75%). The area under the receiver operating characteristic (ROC) curve was 0.78. Second, it is computed in a reasonably straightforward manner without having to use coefficients from the ARIC cohort that may be specific to that cohort.

Family History

Family history of diabetes has been shown to be a predictor of development of diabetes.²⁰ We defined family history as either a parent having diagnosed diabetes, or a parent or sibling having diagnosed diabetes.

Data Analysis

We used MedCalc software²¹ to compute ROC curve analyses in an effort to evaluate the ability of the diabetes risk score, as well as other variables, including family history of diabetes and BMI, to predict development of diabetes in 10 years. We specifically examined the usefulness of family history as an alternative to the diabetes risk score, because family history was not included in the risk score. We also examined the predictive ability of BMI by itself, because recent evidence showed that BMI was as predictive of having undiagnosed diabetes as the Cambridge Risk Score.¹⁷ The parsimonious benefit of prediction by means of one easily accessible variable (eg, BMI) instead of a 6-variable measure would be substantial. BMI was evaluated in a continuous manner as well as in a 3-category classification (<25 , 25-29.9, ≥ 30). To compute the benefits of adding family history of diabetes to BMI, we needed to provide a point score for the new variable. Thus, we scored 1 point for BMI <25 , 2 points for BMI 25-29.99, 3 points for BMI ≥ 30 , and 1 point for family history of diabetes.

Finally, we stratified the CARDIA cohort by race to examine the utility of the diabetes risk score within dif-

ferent racial groups, because recent evidence indicated that some risk scores for undiagnosed diabetes do not work equally well in different racial or ethnic groups.¹⁸

RESULTS

Table 1 displays the characteristics of the cohort. Only 2.1% of this young adult cohort was classified at baseline as being at high risk for developing diabetes, whereas 3.9% developed diabetes within 10 years. Further, 32.9% of the cohort was overweight or obese at baseline (BMI ≥ 25). The proportion of individuals with a family history of diabetes had a moderate increase when the definition of family history was changed from parents to parents and siblings.

The area under the ROC curve for the diabetes risk score in this young adult cohort is not optimal at .70 compared with .78 found in the middle-aged cohort in the ARIC study (Table 2). A diabetes risk score of 4 or greater had a sensitivity of 15.0% and a specificity of 98.4% in the CARDIA participants.

The area under the ROC curve does not increase significantly when family history is added to the diabetes risk score. Moreover, the 3-category BMI variable is not significantly different from the multivariable diabetes risk score in the area under the ROC curve, nor is BMI plus family history of diabetes significantly better than BMI alone ($P = .08$).

Table 3 shows the analyses within racial groups. Blacks (.72; 95% CI, .69-.74) and whites (.68; 95% CI, .66-.71) do not significantly differ in the area under the ROC curve for the risk score, as indicated by the overlapping 95% confidence intervals. The area under the ROC curve for BMI is significantly larger for blacks (.69; 95% CI, .66-.72) than for whites (.63; 95% CI, .60-.65). Similarly, the area under the ROC curve for BMI plus family history is significantly larger for blacks (.73; 95% CI, .70-.76) than for whites (.64; 95% CI, .61-.66).

DISCUSSION

As the prevalence of diabetes rises, and more young adults and adolescents develop diabetes, it is crucial from a clinical and public health perspective to be able to identify high-risk populations. The findings of this study indicate that a risk score for the development of diabetes created from a middle-aged population is a less successful predictor of the development of diabetes in a younger population.

We chose to assess the diabetes risk score developed in the ARIC cohort because it is one of the few measures designed to assess the risk of developing diabetes rather than the likelihood of having undiagnosed diabetes (eg, Cambridge Risk Score). An alter-

native measure to the ARIC diabetes risk score was considered for evaluation, but it included in the model "history of high blood glucose," which was defined as "Have you ever been told by a health-care professional that you have diabetes or latent diabetes?"¹⁶ Including

Table 1. Characteristics of the Study Cohort

Characteristic	Value
Development of diabetes, %	3.9
Female, %	55.7
Black, %	41.2
Mean age \pm SD, y	25.0 \pm 3.6
ARIC diabetes risk score ≥ 4 , %	2.1
Body mass index, kg/m ²	
<25, %	67.0
25-29.99, %	22.6
>30, %	10.3
Family history of diabetes	
Parents, %	13.6
Siblings and parents, %	14.4

ARIC = Atherosclerosis Risk in Communities.

Table 2. Area Under ROC Curve Using a Diabetes Risk Score, Family History of Diabetes, and BMI to Predict Development of Diabetes Within 10 Years

Predictors	Area Under ROC Curve
ARIC diabetes risk score	.70
Family history of diabetes	
Parents	.57*
Siblings and parents	.58*
BMI	
Continuous	.65 [†]
3 categories	.67 [†]
3 categories plus family history of diabetes (siblings and parents)	.69 [†]

ARIC = Atherosclerosis Risk in Communities; BMI = body mass index; ROC = receiver operating characteristic.

* Area under the curve significantly different from that of diabetes risk score.
[†] Not significantly different.

Table 3. Area Under ROC Curve to Predict Development of Diabetes Within Groups of White and Black Participants

Predictors	White	Black
ARIC diabetes risk score	.68	.72
BMI, 3 categories	.63*	.69*
BMI, 3 categories plus family history of diabetes (siblings and parents)	.64*	.73*

ARIC = Atherosclerosis Risk in Communities; BMI = body mass index; ROC = receiver operating characteristic.

* Not significantly different.

a previous diagnosis of diabetes as a predictor of the development of diabetes did not seem to be a logical strategy for identifying individuals at high risk for developing diabetes. Thus, we believed that the Lindstrom score was not as useful for evaluation as the ARIC diabetes risk score.

Multivariable risk scores that are diagnostically helpful should be clinically less burdensome in the age of personal digital assistants and electronic health records and should therefore allow the clinician to go beyond assessing risk factors singly for development of disease. In this case, the multivariable diabetes risk score does not predict the development of diabetes any better than simply using the BMI. Because the diabetes risk score includes BMI in addition to 5 other variables, it would be expected to perform better than BMI alone. With an area under the ROC curve of .67, however, BMI as a predictor of the development of diabetes in young adults is not optimal. Further, the addition of family history to either BMI or the diabetes risk score did not significantly improve prediction of the development of diabetes. These findings suggest that more work is needed to create an effective strategy for identifying young adults at high risk for developing diabetes.

Recent evidence has suggested that risk assessment strategies may need to differ depending on which racial or ethnic population is being evaluated.¹⁸ The results reported in this study indicate that although the diabetes risk score did not differ significantly between young black and white adults in the prediction of diabetes, BMI and BMI plus family history did differ between the 2 groups: BMI plus family history was a significantly more predictive strategy for identifying risk for the development of diabetes among blacks than among whites. These racial differences in the relationship of BMI and the development of diabetes may be due to the interaction of race and diet, as Pereira et al²² found that fast-food habits varied by race and sex and were related to insulin resistance in the CARDIA study. This finding indicates the need to be more aware of racial and ethnic differences in diabetes risk and the need to include that awareness in the development of diabetes risk assessment strategies. Further evaluation of the novel factors, including biomarkers, underlying these differences is also necessary.

There are several limitations to this study. First, the biomarker diagnosis of diabetes in the CARDIA data is based on a single fasting glucose test. This strategy, although common in epidemiological studies, could potentially underestimate the prevalence of diabetes associated with isolated postchallenge hyperglycemia, which occurs more commonly in women and lean populations. It could also overestimate diabetes prevalence, because a clinical diagnosis of diabetes

in asymptomatic persons requires 2 abnormal fasting glucose levels. Second, racial differences in the predictive utility of the risk assessment strategies suggest that evaluating the risk score and other markers may be enhanced by having a diverse sample of ethnic groups. The CARDIA study is limited to blacks and whites and thus does not allow for evaluation with other racial or ethnic groups. Third, not only is it inherently difficult to improve on conventional risk factors when developing a scoring system as a prognostic tool, as shown by Wang et al²³ and discussed by Ware,²⁴ it is also difficult to improve on conventional risk factors when developing a prognostic tool. Hence, we compared the ARIC metabolic syndrome (augmented) model with BMI alone and BMI plus family history of diabetes to determine whether multivariate diabetes risk factors performed better than more general risk factors.

In conclusion, an established risk score for the development of diabetes among middle-aged persons had limited utility in a younger population. The diabetes risk score had no advantage compared with BMI alone. Neither BMI nor the risk score, however, had optimal predictive ability, suggesting that future research needs to focus on identifying novel factors that may improve the risk stratification for diabetes development among young adults.

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References

- Engelgau MM, Geiss LS, Saaddine JB, et al. The evolving diabetes burden in the United States. *Ann Intern Med.* 2004;140(11):945-950.
- Steinbrook R. Facing the diabetes epidemic—mandatory reporting of glycosylated hemoglobin values in New York City. *N Engl J Med.* 2006;354(6):545-548.
- Prevalence of diabetes and impaired fasting glucose in adults—United States, 1999-2000. *MMWR Morb Mortal Wkly Rep.* 2003;52(35):833-837.
- Duncan GE. Prevalence of diabetes and impaired fasting glucose levels among US adolescents: National Health and Nutrition Examination Survey, 1999-2002. *Arch Pediatr Adolesc Med.* 2006;160(5):523-528.

5. *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: The Evidence Report*. Bethesda, MD: National Institutes of Health; 1998. NIH Publication No. 98-4083.
6. Sturm R. Increases in clinically severe obesity in the United States, 1986-2000. *Arch Intern Med*. 2003;163(18):2146-2148.
7. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999-2000. *JAMA*. 2002;288(14):1723-1727.
8. Vijan S, Stevens DL, Herman WH, Funnell MM, Standiford CJ. Screening, prevention, counseling, and treatment for the complications of type II diabetes mellitus. Putting evidence into practice. *J Gen Intern Med*. 1997;12(9):567-580.
9. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. *Circulation*. 1998;97(18):1837-1847.
10. Glumer C, Carstensen B, Sandbaek A, Lauritzen T, Jorgensen T, Borch-Johnsen K. A Danish diabetes risk score for targeted screening: the Inter99 study. *Diabetes Care*. 2004;27(3):727-733.
11. Herman WH, Smith PJ, Thompson TJ, Engelgau MM, Aubert RE. A new and simple questionnaire to identify people at increased risk for undiagnosed diabetes. *Diabetes Care*. 1995;18(3):382-387.
12. Baan CA, Ruige JB, Stolk RP, et al. Performance of a predictive model to identify undiagnosed diabetes in a health care setting. *Diabetes Care*. 1999;22(2):213-219.
13. Griffin SJ, Little PS, Hales CN, Kinmonth AL, Wareham NJ. Diabetes risk score: towards earlier detection of type 2 diabetes in general practice. *Diabetes Metab Res Rev*. 2000;16(3):164-171.
14. Franciosi M, De Berardis G, Rossi MC, et al. Use of the diabetes risk score for opportunistic screening of undiagnosed diabetes and impaired glucose tolerance: the IGLOO (Impaired Glucose Tolerance and Long-Term Outcomes Observational) study. *Diabetes Care*. 2005;28(5):1187-1194.
15. Schmidt MI, Duncan BB, Bang H, et al. Identifying individuals at high risk for diabetes: The Atherosclerosis Risk in Communities study. *Diabetes Care*. 2005;28(8):2013-2018.
16. Lindstrom J, Tuomilehto J. The diabetes risk score: a practical tool to predict type 2 diabetes risk. *Diabetes Care*. 2003;26(3):725-731.
17. Thomas C, Hypponen E, Power C. Type 2 diabetes mellitus in midlife estimated from the Cambridge Risk Score and body mass index. *Arch Intern Med*. 2006;166(6):682-688.
18. Glumer C, Vistisen D, Borch-Johnsen K, Colagiuri S. Risk scores for type 2 diabetes can be applied in some populations but not all. *Diabetes Care*. 2006;29(2):410-414.
19. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA*. 2001;285(19):2486-2497.
20. von Eckardstein A, Schulte H, Assmann G. Risk for diabetes mellitus in middle-aged Caucasian male participants of the PROCAM study: implications for the definition of impaired fasting glucose by the American Diabetes Association. Prospective Cardiovascular Munster. *J Clin Endocrinol Metab*. 2000;85(9):3101-3108.
21. *MedCalc for Windows, Statistics for Biomedical Research, Software Manual*. Version 8.1. Mariakerke, Belgium: MedCalc Software.
22. Pereira MA, Kartashov AI, Ebbeling CB, et al. Fast-food habits, weight gain, and insulin resistance (the CARDIA study): 15-year prospective analysis. *Lancet*. 2005;365(9453):36-42.
23. Wang TJ, Gona P, Larson MG, et al. Multiple biomarkers for the prediction of first major cardiovascular events and death. *N Engl J Med*. 2006;355(25):2631-2639.
24. Ware JH. The limitations of risk factors as prognostic tools. *N Engl J Med*. 2006;355(25):2615-2617.