

# Family history of type 2 diabetes: A population-based screening tool for prevention?

Susan Hariri, PhD<sup>1,2</sup>, Paula W. Yoon, ScD<sup>2</sup>, Nadeem Qureshi, MBBS<sup>2</sup>, Rodolfo Valdez, PhD<sup>3</sup>, Maren T. Scheuner, MD<sup>2,4</sup>, and Muin J. Khoury, MD, PhD<sup>2</sup>

**Purpose:** To evaluate the use of self-reported family medical history as a potential screening tool to identify people at-risk for diabetes. **Methods:** The *HealthStyles* 2004 mail survey comprises 4345 US adults who completed a questionnaire to ascertain personal and family history of diabetes, perceived risk of diabetes, and practice of risk-reducing behaviors. Using number and type of affected relatives, respondents were ranked into three familial risk levels. Adjusted odds ratios (AORs) were obtained to evaluate associations between familial risk and prevalent diabetes, perceived risk of disease, and risk-reducing behaviors. Validity of family history as a screening tool was examined by calculating sensitivity, specificity, and positive and negative predictive values. **Results:** Compared to those of average risk, people with moderate and high familial risk of diabetes were more likely to report a diagnosis of diabetes (AOR: 3.6, 95% CI: 2.8, 4.7; OR: 7.6, 95% CI: 5.9, 9.8, respectively), a higher perceived risk of diabetes (AOR: 4.6, 95% CI: 3.7, 5.7; OR: 8.5, 95% CI: 6.6, 17.7, respectively), and making lifestyle changes to prevent diabetes (AOR: 2.2, 95% CI: 1.8, 2.7; OR: 4.5, 95% CI: 3.6, 5.6, respectively). A positive familial risk of diabetes identified 73% of all respondents with diabetes and correctly predicted prevalent diabetes in 21.5% of respondents. **Conclusion:** Family history of diabetes is not only a risk factor for the disease but is also positively associated with risk awareness and risk-reducing behaviors. It may provide a useful screening tool for detection and prevention of diabetes. **Genet Med 2006;8(2):102–108.**

**Key Words:** family history, type 2 diabetes, screening, risk factor, prevention

Type 2 diabetes accounts for 90%–95% of all cases of diabetes<sup>1</sup> and is a classic example of a multifactorial disease involving the complex interplay of modifiable and nonmodifiable risk factors, including family history, obesity, ethnicity, and age.<sup>1–5</sup> In recent years, the prevalence of type 2 diabetes (T2DM) has been steadily increasing in the US, especially among adolescents and African Americans.<sup>6–13</sup>

Given that the onset of and complications from T2DM can be delayed or prevented,<sup>14–18</sup> understanding the separate and joint contribution of genetics and environment in the development of T2DM remains an important challenge toward its prevention and control. Family history of a disease reflects shared environmental and behavioral risk factors and their interactions with genes as shown by the strong familial aggregation of many complex disorders.<sup>19–23</sup> In fact, family history is an independent risk factor for most common chronic diseases

including cardiovascular disease, cancer, and T2DM.<sup>2,3,6,19–24</sup> Recent surveys indicate that the majority of US adults are aware of and can report T2DM among first-degree relatives (88%–95%, depending on type of relative) and, to a lesser extent, second-degree relatives (70%–77%, depending on type of relative).<sup>25</sup> Given such family history knowledge and the public health importance of this chronic condition, family history may provide a useful screening tool for detection and prevention of T2DM and its sequelae.

This study was designed to evaluate the use of self-reported family history of T2DM as a potential screening tool to identify people at increased risk of T2DM and the proportion of persons with undiagnosed T2DM. The specific aims were to assess: 1) family history of T2DM as an independent risk factor for T2DM; 2) possible modification of the association between familial risk and T2DM by other risk factors; and 3) relationship between family history of T2DM and perceived risk of the disease and the presence of risk-reducing behaviors.

## MATERIALS AND METHODS

### Study design

This cross-sectional study is based on the *HealthStyles* 2004, an annual mail survey of health-related attitudes and behaviors among the US adult population aged 18 and older.<sup>26</sup> *HealthStyles* is a subset of a two-part consumer survey designed and

From the <sup>1</sup>Epidemic Intelligence Service Officer, Office of Workforce and Career Development, Centers for Disease Control and Prevention, Atlanta, Georgia; <sup>2</sup>Office of Genomics and Disease Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia; <sup>3</sup>Division of Diabetes Translation, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia; <sup>4</sup>Department of Health Services, UCLA School of Public Health, California.

Dr. Susan Hariri, 4770 Buford Highway, Mailstop K-89, Atlanta, Georgia 30341.

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conducted by Synovate, Inc., a marketing firm that annually recruits approximately 600,000 potential respondents.

*HealthStyles* is used for health communications planning by organizations, including the Centers for Disease Control and Prevention, who influence design and administration of the questionnaire. The data from the survey are post-stratified and weighted so that the sample distribution by age, race, sex, household size, and household income matches the U.S. general population as reported by the U.S. census.

In 2004, *HealthStyles* surveys were sent to a random sample of 6175 US adults residing in households who participated in the consumer marketing component of the survey; 4345 agreed to participate, yielding a response rate of 70%.

### Variable definitions

The survey included a question about personal history of physician-diagnosed T2DM ("Have you ever been diagnosed by your doctor as having type 2 diabetes?"), as well as questions about current or recent (in the past year) medical conditions such as obesity (defined as "BMI > 30"). Additionally, respondents were asked to identify all first-degree (mother, father, brothers and sisters) and second-degree (maternal and paternal aunts, uncles, and grandparents) biological relatives with T2DM. The survey also assessed whether respondents considered family history "very" or "somewhat" important for their own health, and whether they had ever actively collected health information from their relatives for the purposes of developing a family health history. Attitudes toward and perceived risk of T2DM were examined by the respondents' agreement or disagreement with statements such as "Diabetes is a serious disease," "I believe I am at risk for diabetes," and "I believe my family are at risk for diabetes" ranked on a Likert scale. Respondents' behaviors with respect to diabetes were ascertained through several questions related to risk-reducing behaviors such as obtaining regular testing and lifestyle changes such as diet and exercise to prevent diabetes. Although T2DM is likely to represent the majority of cases in respondents and their families, the term diabetes will be used throughout the manuscript to account for the possibility that some cases of type 1 diabetes may have been misreported. However, any such misreporting would be insignificant and unlikely to affect results of the analysis.

### Statistical analysis

Using number and type of affected relatives, respondents were classified into average, moderate, or high familial risk according to the algorithm below, adapted from Scheuner et al.<sup>27</sup>:

High: At least 1) two first-degree relatives with diabetes from same lineage; 2) one first- and two second-degree relatives with diabetes from same lineage; or 3) three second-degree relatives with diabetes from same lineage.

Moderate: Only 1) one first- and one second-degree relative with diabetes from same lineage; 2) one first-degree relative with diabetes; 3) mother and father with diabetes, or 4) two second-degree relatives from same lineage with diabetes.

Average: Only 1) one second-degree relative with diabetes from one or both sides of family; or no family history of diabetes.

Family history is often considered as a risk factor for diabetes without regard to the variable magnitude of risk based on different familial risk profiles. We used a three-tiered familial risk stratification to more accurately measure the effects of familial history on diabetes risk.

Demographic characteristics, diabetes risk factors, and potential confounders were evaluated individually; then unconditional logistic regression (overall and stratified by potential effect modifiers) was performed to obtain adjusted odds ratios (AOR) for the association between family history of diabetes and self-reported diabetes. Likewise, the association between increasing levels of familial risk and perceived risk of disease and risk-reducing behaviors was evaluated. Although all analyses were performed with and without the sampling weights developed for *HealthStyles 2004*, only unweighted results are presented as they did not differ from those obtained in the weighted analysis.

Finally, in addition to the above risk stratification, familial risk was dichotomized by combining the moderate and high risk categories, and sensitivity and specificity (ability of family history to correctly identify respondents with and without diabetes, respectively), and positive and negative predictive values (probability of an individual having or not having diabetes, respectively, given that he/she has a family history) were calculated. All measures were compared with the ability of self-reported obesity to detect the same risks.

## RESULTS

Based on the familial risk stratification, 711 (16.4%) respondents were classified into high-risk, 843 (19.4%) into moderate-risk, and 2791 (64.2%) into average-risk for diabetes. Of the 452 respondents with self-reported diabetes, 204 (45.1%) were classified as high-risk, 125 (27.7%) as moderate-risk, and 123 (27.2%) as average-risk.

### Demographic characteristics

Table 1 presents the distribution of the characteristics of the study population overall and within familial risk strata. The majority of respondents were 35 years or older (82.1%), female (56.7%), and white (69.8%), with at least some college education (67.1%) and annual incomes greater than \$25,000 (71.4%). In addition, 16.8% of respondents reported being obese. Full details of the prevalence of diabetes by selected demographic characteristics, overall and within familial risk-based strata, are summarized in Table 2. There was a graded increase in diabetes prevalence with increasing family history-based risk: average (4.5%), moderate (15.0%), and high (29.1%), even when stratified by other risk factors such as obesity and race.

**Table 1**  
Distribution of select respondent characteristics overall and classified by familial risk of diabetes, HealthStyles 2004

	Overall (N = 4345) % respondents	Average risk (N = 2791) % respondents	Moderate risk (N = 843) % respondents	High risk (N = 711) % respondents
Age, years				
18–34	17.9	19.3	16.0	14.2
35–54	51.1	50.2	53.5	51.8
≥55	31.0	30.4	30.5	34.0
Sex				
Male	43.3	44.9	42.6	38.1
Female	56.7	55.1	57.4	61.9
Race/ethnicity				
White	69.8	71.9	70.9	59.8
African American	12.2	10.8	11.4	18.7
Latino	11.6	10.3	11.5	16.5
Other	6.5	7.0	6.2	5.1
Education				
High school or less	33.9	30.7	27.5	23.1
Some college	36.8	34.7	35.8	35.4
College or more	30.3	29.8	31.7	36.8
Income				
<\$25,000	29.5	39.0	37.8	27.7
\$25,000–59,999	33.6	33.8	32.3	34.3
>\$59,999	36.9	27.2	29.9	38.0
Self-reported obesity				
Yes	16.8	13.6	19.1	26.7
No	83.2	86.4	80.9	73.3
Current smoker				
Yes	22.6	22.2	22.8	24.1
No	77.4	77.8	77.2	75.9
Met recommended exercise guidelines				
Yes	38.1	38.0	36.7	40.0
No	61.9	62.0	63.3	60.0

### Family history and other risk factors for diabetes

Overall, people with moderate and high familial risk of diabetes were more likely to report a diagnosis of diabetes (AOR: 3.6, 95% CI: 2.8, 4.7; OR: 7.6, 95% CI: 5.9, 9.8, respectively) than those with average risk.

Among risk factors examined, advanced age, non-white race, low income and education, and self-reported obesity were statistically significantly associated with diabetes risk, and were evaluated as potential modifiers (along with gender) for the association between familial risk and diabetes. While the strength of this association increased with increasing familial risk across all categories of risk factors examined, the effect of family history appeared to diminish among females, the elderly, and the obese (Table 3).

### Attitudes and behaviors

Overall, 96% of respondents ranked knowledge of family history of disease as either "very" or "somewhat" important to their personal health; this proportion did not vary when stratified by family history-based risk strata. Likewise, there was over 95% agreement among respondents in all familial risk categories that diabetes is a serious disease. However, among respondents without diabetes, perceived risk of diabetes increased significantly with increasing family history-based risk. While only 14% of respondents in the average risk group believed themselves to be at risk for diabetes, more (36%) respondents in the moderate risk group, and even more (51%) in the high risk group considered themselves at risk. Likewise, 18% of respondents in the average risk group felt their family

**Table 2**  
Prevalence of diabetes in total population and by selected demographics characteristics overall and within familial risk strata, HealthStyles 2004

Prevalence of type 2 diabetes	Prevalence of type 2 diabetes			
	Overall (N = 452)	Average risk (N = 123)	Moderate risk (N = 125)	High risk (N = 204)
Total	10.6	4.5	15.0	29.1
Select characteristics				
Age				
18–34	2.9	0.6	4.4	12.9
35–54	7.9	2.2	13.1	22.6
≥55	19.5	10.5	23.3	44.6
Sex				
Female	10.1	4.4	14.5	24.5
Male	11.2	4.5	15.3	35.4
Race				
White	9.8	4.5	14.2	27.3
Black	13.4	4.7	13.5	31.6
Hispanic	12.9	4.2	16.5	29.9
Education				
College +	7.9	3.6	12.9	22.6
Some college	10.1	4.9	13.2	25.4
HS or less	13.3	4.5	18.0	35.1
Income				
>\$59,999	7.0	3.1	11.9	19.8
\$25,000–59,999	9.2	3.8	12.5	25.4
<\$25,000	16.8	7.0	21.0	38.1
Obesity				
BMI < 30	7.7	3.1	11.0	23.2
BMI > 30	25.0	12.6	31.1	43.7
Current smoker				
Yes	10.3	4.1	16.1	25.3
No	10.7	4.5	14.5	29.7
Met exercise guidelines				
Yes	7.3	2.6	9.8	21.8
No	12.1	5.4	17.8	31.8

members were at risk for diabetes compared to 44% in the moderate risk group and 62% in the high risk group. The associations between perceived risks and familial risk are presented in Table 4.

Association between familial risk and behaviors leading to risk reduction or an awareness of risk followed a similar trend as with risk perception. Respondents without diabetes in high familial risk categories were most likely to engage in behaviors such as collecting information from relatives for the purpose of developing a family history (43%); making lifestyle changes to prevent diabetes (49%); getting tested for diabetes in past two years (69%); and talking with their family about diabetes

(73%); followed by those with moderate familial risk (34%, 32%, 57%, and 54%, respectively), with the average risk group reporting fewest such behaviors (28%, 18%, 47%, and 28%, respectively). The association between familial risk and risk-reducing behavior among moderate- and high-risk groups compared to the average-risk group was statistically significant for all behaviors and increased with increasing familial risk (Table 4).

#### Assessment of familial risk as a screening tool

The ability of familial risk to accurately and reliably identify self-reported diabetes, and the probability that a respondent

**Table 3**  
Association between familial risk and diabetes, overall and stratified by risk factors

	Average AOR <sup>a</sup>	Moderate AOR (95% CI)	HighAOR (95% CI)
Overall	1.0	3.6 (2.8, 4.7)	7.6 (5.9, 9.8)
Race/ethnicity			
White	1.0	3.7 (2.6, 5.2)	7.2 (5.2, 10.2)
African American	1.0	2.6 (1.1, 6.1)	9.1 (4.5, 18.6)
Latino	1.0	4.1 (1.7, 9.8)	9.7 (4.4, 21.4)
Age, years			
18–34	1.0	7.8 (1.4, 44.0)	35.8 (7.6, 168.5)
35–54	1.0	7.0 (4.3, 11.2)	10.4 (6.5, 16.5)
≥55	1.0	2.3 (1.5, 3.4)	6.2 (4.3, 8.8)
Sex			
Male	1.0	4.1 (2.6, 6.4)	11.8 (7.7, 17.8)
Female	1.0	3.5 (2.4, 5.0)	6.2 (4.4, 8.8)
Self-reported obesity			
Yes	1.0	3.5 (2.2, 5.7)	5.7 (3.6, 9.0)
No	1.0	3.8 (2.7, 5.5)	9.5 (6.8, 13.3)

<sup>a</sup>Each model adjusted for all other demographic characteristics.

has undiagnosed diabetes based on familial risk are presented in Table 5. As indicated, a positive (moderate or high) familial risk of diabetes identified 73% of all respondents with diabetes. In contrast, only 40% of respondents with type 2 diabetes were identified by self-reported obesity, while the presence of both obesity and a positive family history of diabetes detected 29%, indicating that family history is a better indicator of diabetes among this population than obesity. Moreover, the value of a positive familial risk of disease to predict diabetes in survey respondents was similar to that of the predictive value of obesity which is considered to be one of the most important determinants of diabetes (21.5% vs. 25.0%, respectively). Predictably, the combination of the two risk factors increased disease prediction to almost 40% (Table 5).

## DISCUSSION

The findings herein quantitatively demonstrate the ability of family history as a screening tool for detecting self-reported diabetes, suggesting the potential benefit of collection and use of family history information to identify at-risk and undiagnosed persons with diabetes. Specifically, the results show that a positive family history is a sensitive indicator of the presence of diabetes with much higher sensitivity than obesity, a well established risk factor. It also helps in the estimation of the probability of having the disease almost as accurately as self-reported obesity. Although comparable, the positive predictive values for both increased familial risk as well as obesity are low, potentially resulting in undue anxiety and financial burden in a

high proportion of individuals that may unnecessarily receive further testing. However, use of family history in combination with obesity almost doubles the positive predictive value of each risk factor alone, representing a substantial reduction in false positive rates for screening. Given the consequences of undiagnosed diabetes to society and to individuals and the absence of more accurate screening tools, family history, in conjunction with obesity, provides a readily available, inexpensive screening tool to identify at-risk groups, as well as persons with undiagnosed diabetes, for evaluation, detection, and risk reducing interventions.

These findings also support previous studies demonstrating that family history is a strong and independent risk factor for diabetes.<sup>2,3,5,6,19</sup> However, familial risk must be evaluated in the context of other known or suspected risk factors. These findings indicate differences in the effect of familial risk on other risk factors, suggesting that a high familial risk may increase diabetes risk in males, the young, and the lean. Finally, this analysis illustrates that increasing familial risk is associated with increases in risk-reducing behaviors, but more important, it shows that over half of those at moderate and high familial risk of diabetes fail to engage in risk reducing behaviors, highlighting the urgent need to improve current prevention programs, especially among those at increased risk for the disease.

This study has some important limitations. First, the familial risk stratification used in this analysis is based on best available clinical knowledge of diabetes inheritance and requires further population-level validation. Second, the cross-sectional design of the survey prohibits establishment of any temporal associations. This is of particular concern since persons with diagnosed diabetes may be more aware of diabetes in their family than those without diabetes, thus biasing the sensitivity analysis. Another potential concern is the validity of self-reported data. For example, obesity is likely to have been under-reported leading to underestimation of its true prevalence in the study population.<sup>28</sup> Also, persons with undiagnosed diabetes may be less aware of their family history, further biasing results. Finally, *HealthStyles* participants are a convenience sample and may not be representative of the general population. However, a study using data from the Behavioral Risk Factor Surveillance System showed that demographic characteristics and diabetes prevalence among the *HealthStyles* population were similar to that of the U.S. population.<sup>26</sup> Nonetheless, the results of this study should be reproduced in larger, population-based studies that utilize relevant clinical measurements to allow for more accurate classification of diabetes.

Despite noted limitations, this analysis provides a unique example of how collecting comprehensive multi-generational family history information can be used to classify individuals according to increasing levels of disease risk based on the number and type of affected relatives. As such, this survey can be used as a model for types of family history questions that can be added to population-based surveys to identify individuals with undiagnosed diabetes as well as those at increased risk of the disease. From a more clinical perspective, because family history in part represents unmeasured genetic determinants of the

**Table 4**

Effect of family history-based risk of type 2 diabetes on perceived risk of diabetes and behaviors to reduce risk or increase risk awareness among respondents without diabetes

	Average (n = 2606) AOR <sup>a</sup> (95% CI)	Moderate (n = 706) AOR (95% CI)	High (n = 497) AOR (95% CI)
Perceived risk of diabetes			
Believed self at risk for diabetes	1.0	4.6 (3.7, 5.7)	8.5 (6.6, 17.7)
Believed family at risk for diabetes	1.0	6.5 (4.9, 8.4)	20.2 (13.8, 29.6)
Risk reducing behaviors			
Collected information for family history	1.0	1.3 (1.1, 1.6)	1.8 (1.5, 2.2)
Made lifestyle changes to prevent DM	1.0	2.2 (1.8, 2.7)	4.5 (3.6, 5.6)
Tested in past 2 years	1.0	1.6 (1.3, 1.9)	2.4 (2.0, 3.0)
Talked about diabetes with family	1.0	3.1 (2.6, 3.7)	6.5 (5.2, 8.2)
Met recommended exercise guidelines	1.0	1.0 (0.9, 1.2)	1.4 (1.1, 1.7)

<sup>a</sup>Adjusted for demographic characteristics age, sex, race, education, and obesity.**Table 5**

Sensitivity, specificity, and positive and negative predictive value of family history of diabetes compared to obesity

Risk factor	Diabetes (N)	No diabetes (N)	Total	Diabetes prevalence (%)	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Increased family history	196	989	1185	16.5	72.8	68.4	21.5	95.5
Obesity	48	328	376	12.8	40.0	85.8	25.0	92.3
Increased family history and obesity	133	214	347	38.3	29.4	94.4	38.3	91.8
Neither	75	2278	2353	3.2	16.6	59.8	3.2	96.8
Total	452	3809	4261	-	-	-	-	-

disease, stratifying populations into different levels of familial risk can help identify populations with high prevalence of genetic risk factors in which the use of genetic testing (as they become available) will achieve the highest predictive power.<sup>28</sup> Moreover, by examining public attitudes and knowledge regarding the importance of family history as a risk factor for disease, and assessing willingness to talk to and systematically collect information from relatives, this survey demonstrates a heightened public awareness of, and interest in familial risk of disease, undoubtedly influenced by the widespread media attention to the genetic basis of disease.

Until technological advances deliver on the expectations of population-based screening of genetic susceptibility to modifiable environmental risk factors, no single approach will be sufficient to combat the rising rates of diabetes and other common diseases related to lifestyle changes. Meanwhile, public health efforts to prevent or delay the onset of diabetes and to effectively minimize its sequelae through early detection and management efforts can be enhanced through creative use of existing and novel epidemiologic tools such as evaluation of family history to identify populations at increased risk for diabetes.<sup>22,23,29,30</sup> Additionally, family history can help in the evaluation and comparison of other risk factors affecting groups with disparate risk levels of diabetes. Family history can

be used not only to assess disease risk but also to examine the awareness of this risk and the motivation to engage in risk-reducing behaviors.

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