Influence of Familial Risk on Diabetes Risk–Reducing Behaviors Among U.S. Adults Without Diabetes

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OBJECTIVE—To test the association of family history of diabetes with the adoption of diabetes risk–reducing behaviors and whether this association is strengthened by physician advice or commonly known factors associated with diabetes risk.

RESEARCH DESIGN AND METHODS—We used cross-sectional data from the 2005–2008 National Health and Nutrition Examination Survey (NHANES) to examine the effects of family history of diabetes on the adoption of selected risk-reducing behaviors in 8,598 adults (aged \geq 20 years) without diabetes. We used multiple logistic regression to model three risk reduction behaviors (controlling or losing weight, increasing physical activity, and reducing the amount of dietary fat or calories) with family history of diabetes.

RESULTS—Overall, 36.2% of U.S. adults without diabetes had a family history of diabetes. Among them, ~39.8% reported receiving advice from a physician during the past year regarding any of the three selected behaviors compared with 29.2% of participants with no family history (P < 0.01). In univariate analysis, adults with a family history of diabetes were more likely to perform these risk-reducing behaviors compared with adults without a family history. Physician advice was strongly associated with each of the behavioral changes (P < 0.01), and this did not differ by family history of diabetes.

CONCLUSIONS—Familial risk for diabetes and physician advice both independently influence the adoption of diabetes risk–reducing behaviors. However, fewer than half of participants with familial risk reported receiving physician advice for adopting these behaviors.

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The Centers for Disease Control and Prevention (CDC) recently reported that 25.8 million people in the U.S. (8.3% of the population) have diabetes (1). A total of 1.9 million new cases of diabetes were diagnosed in people aged \geq 20 years in 2010 in the U.S., and 25.6 million (11.3%) people in this age-group have diabetes. Worldwide, it is estimated that 280 million people had diabetes in 2010—a number that is projected to increase to 430 million by 2030 (2). Studies

have reported strong and consistent evidence that lifestyle factors might prevent or delay type 2 diabetes among people at high risk, including those with a family history of the disease (3,4). In 2002, the World Health Report (5) identified risk-reducing behaviors (such as controlling or losing weight, increasing physical activity, and reducing fat or calories) as important lifestyle risk factors for a number of chronic diseases, including diabetes, cardiovascular disease, and cancer.

Many variables, including genetic, environmental, medical, and socioeconomic factors, influence the development of diabetes (6). The association of family history of diabetes with risk for the disease has been well documented (7). Although a 2009 National Institutes of Health State of the Science conference concluded that there was insufficient evidence to support the routine use of family history as a screening tool for risk of common complex conditions in primary care (8), an individual patient's family history remains a critical element in risk assessment for many chronic conditions, including diabetes (9). While accurate and complete family history information needs to be collected to identify high-risk individuals, substantial barriers exist to obtaining this information in primary care practice, though clinicians are trained to do so. These barriers include lack of time to collect the information, lack of proper training to interpret the information, and lack of reimbursement (10).

Evidence also supports the effectiveness of physician advice on lifestyle modifications to prevent or delay the risk of chronic diseases (11). A recent study on diabetes risk reduction behaviors found that the proportion of adults with prediabetes who reported performing risk reduction behaviors was higher among those who received physician advice compared with those who did not receive such advice (12).

In light of the evidence summarized above, we used data from the 2005–2008 National Health and Nutrition Examination Survey (NHANES), a large populationbased and nationally representative survey of the U.S., to test the hypotheses that a family history of diabetes is associated with greater adoption of diabetes risk–reducing behaviors and that the association is strengthened by the receipt of physician advice regarding these behaviors, in addition to other commonly known factors associated with diabetes risk.

RESEARCH DESIGN AND

METHODS—NHANES is a complex, multistage cross-sectional sample survey conducted annually by the National Center

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Familial risk, diabetes risk-reducing behaviors

for Health Statistics of the CDC (13). The survey is designed to provide national statistics on the health and nutritional status of the civilian, noninstitutionalized population of the U.S. This current study includes behavioral, environmental, and clinical information available from the 2005-2006 and 2007-2008 NHANES surveys. Details of the surveys are available online (13). We restricted our analyses to adults (aged ≥ 20 years; n = 10,549) and then excluded those who were pregnant (n = 393) and those who had diagnosed or undiagnosed diabetes (n = 1,558 [definition below]). This resulted in a sample of 8,598 adults, among whom 3,205 had a family history of diabetes, 5,203 had no family history of diabetes, and 190 were missing information on family history.

Definition of diabetes

Participants with self-reported diabetes (those who acknowledged being told by a physician that they have diabetes) or participants with HbA_{1c} levels \geq 6.5% (14) were defined as diabetic and excluded from all analyses.

Definition of family history of diabetes

We classified all participants without diabetes into two distinct groups based on their self-reported family history (FHx) of diabetes: 1) FHx+, \geq 1 biological first-degree relative (parents or siblings) with diabetes and 2) FHx-, no first-degree relatives with diabetes.

Definition of outcomes and covariates

We assessed three risk reduction behaviors from the NHANES diabetes questionnaire file. All participants were asked whether they are now 1) controlling their weight or losing weight, 2) increasing their physical activity or exercise, or 3) reducing the amount of fat or calories in their diet. Participants were also asked whether they had been told by a physician or health professional in the past 12 months to perform each of these behaviors.

Demographic factors included in the analyses were sex, age (\leq 45 or >45 years), race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, other), and education (either less than high school or greater than or equal to high school). Clinical factors were obtained from medical examination and laboratory data. BMI was dichotomized as \geq 25 or <25 kg/m². Participants with systolic blood pressure \geq 140 mmHg or diastolic blood pressure \geq 90 mmHg or currently

taking antihypertension medication were defined as hypertensive. Participants with serum total cholesterol ≥240 mg/dL or currently taking cholesterol-lowering medication were defined as hypercholesterolemic.

Statistical analyses

We used multiple logistic regression to model the likelihood of adopting three diabetes risk-reducing behaviors among adults without diabetes according to the presence of a family history of diabetes (yes or no). Predicted margins and 95% CIs were estimated for the differences across groups (15). The level of statistical significance was set at 0.05. All models included NHANES sample weights for the variables included in the model (sex, age, race/ethnicity, education, BMI, hypertension, hypercholesterolemia, and physician advice). We tested interactions between family history and commonly known factors associated with diabetes risk, including physician advice, to further examine whether the adoption of each of the three behaviors varied by family history of diabetes and whether the included participants received physician advice on these behaviors. We used χ^2 statistics based on the log odds ratio to determine the significance of the selected characteristics of the participants by family history of diabetes. We used the Satterthwaite-adjusted *F* statistic to account for the unequal selection probabilities and nonresponse rates within NHANES. Statistical analyses were conducted using SAS-callable SUDAAN 10.0 (Research Triangle Institute).

RESULTS

Characteristics of adults without diabetes

Selected demographic and clinical characteristics of the included NHANES participants are presented in Table 1. Overall, 36.2% of U.S. adults without diabetes aged ≥ 20 years had a family history of diabetes. In univariate analysis, FHx+ adults were more likely to be female, to have lower educational attainment, to be overweight, or to be hypertensive than FHx- adults. There were no significant differences in the prevalence of a family history of diabetes by

Table 1—Selected characteristics of U.S. adults without diabetes by family history of diabetes (NHANES 2005–2008)

		Family histor	y of diabetes*		
	FHx+(n=3,	205 [36.2%])†	FHx - (n = 5)	5,203 [63.8%])	
	Sample n	Prevalence	Sample n	Prevalence	P‡
Sex					
Male	1,479	45.2 (0.9)	2,740	50.8 (0.8)	< 0.01
Female	1,726	54.8 (0.9)	2,463	49.2 (0.8)	
Age (years)					
≤45	1,624	53.5 (1.6)	2,477	52.6 (1.3)	0.53
>45	1,581	46.5 (1.6)	2,726	47.4 (1.3)	
Race/ethnicity					
Non-Hispanic white	1,431	67.3 (2.5)	2,787	74.4 (2.2)	< 0.01
Non-Hispanic black	763	13.1 (1.6)	963	9.2 (1.1)	
Mexican American	666	9.8 (1.2)	827	6.8 (0.8)	
Other	345	9.8 (1.0)	626	9.6 (1.2)	
Education					
Less than high school	906	19.5 (1.2)	1,388	17.1 (1.1)	< 0.01
Greater than or equal					
to high school	2,297	80.5 (1.2)	3,806	82.9 (1.1)	
BMI (kg/m ²)					
≥25	2,296	71.0 (1.2)	3,299	62.2 (1.0)	< 0.01
<25	870	29.0 (1.2)	1,815	37.8 (1.0)	
Hypertension					
Yes	1,068	31.6 (1.0)	1,717	28.7 (0.9)	0.02
No	2,005	68.4 (1.0)	3,294	71.3 (0.9)	
Hypercholesterolemia					
Yes	853	26.9 (1.2)	1,251	25.1 (1.1)	0.18
No	2,169	73.1 (1.2)	3,657	74.9 (1.1)	

Data are percent (SE) unless otherwise indicated. *Based on first-degree relatives. \ddagger Estimates were calculated using NHANES sample weights. \ddagger P value was calculated using χ^2 statistics based on log odds ratio.

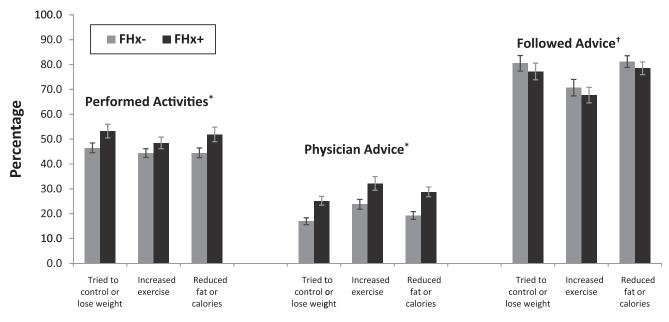
age-group or hypercholesterolemia status. Among FHx+ adults, ~39.8% reported receiving advice from a physician (or other health professional) during the past year regarding at least one of the three selected behavioral changes compared with 29.2% of FHx- adults (P < 0.01 [data not shown]).

Figure 1 displays the unadjusted prevalence of the three risk reduction behaviors among adults without diabetes who, in the past 12 months, reported performing risk-reducing behaviors (regardless of receiving physician advice), reported receiving physician advice, or reported both receiving physician advice and performing the behavioral changes. Compared with FHx- adults, FHx+ adults were more likely (P < 0.01) to have controlled or lost weight, increased exercise, or changed their diet regardless of physician advice (53.2 vs. 46.5%, 48.5 vs. 44.4%, and 51.9 vs. 44.5%, respectively). For each individual risk reduction behavior, FHx+ adults were also more likely (P < 0.01) to have received physician advice about these behavior changes compared with FHx- adults (25.2 vs. 17.0%, 32.2 vs. 23.8%, and 28.8 vs. 19.3%, respectively). However, among adults who received and followed the physician advice, there were no significant differences $(P \ge 0.15)$ between FHx+ and FHx- adults regarding the percentage of individuals performing each of the three risk-reducing behaviors (77.2 vs. 80.5%, 67.7 vs. 70.7%, and 78.5 vs. 81.2%, respectively).

In univariate analyses (Supplementary Table 1), clinical and demographic variables commonly associated with diabetes were strongly associated (P < 0.01) with reports of engaging in any of the three risk reduction behaviors, except for the associations between age and increasing exercise (P = 0.12) and the association between race/ethnicity and reducing fat or calories in the diet (P =0.19). When physician advice was given in the past 12 months, the odds of people engaging in any of the three activities increased 3.8-6.7 times compared with participants who were not given advice (P < 0.01 for each behavior). A family history of diabetes was also strongly associated with each of the behavioral changes (P < 0.01). This association with family history remained significant with controlling or losing weight after adjusting for all the selected demographic and clinical variables (odds ratio 1.13 [95% CI 1.01-1.26], P = 0.03 [data not shown]). However, the associations of family history with increasing exercise (1.05 [0.94– 1.18], P = 0.36) and with reducing fat or

calories in the diet (1.13 [0.98–1.31], P = 0.10) disappeared after multivariate adjustment (data not shown). In multivariate analyses, physician advice was also strongly associated with each of the behavioral changes (4.05 [3.24–5.05] for controlling or losing weight [P < 0.01], 3.39 [2.87–4.01] for increasing exercise [P < 0.01], and 5.40 [4.68–6.23] for reducing fat or calories in the diet [P < 0.01] [data not shown]).

Table 2 displays the adjusted prevalence of the selected risk-reducing behaviors by family history, regardless of physician advice. Overall, there were few significant differences in the performance of the selected behaviors across demographic or clinical variables. Interestingly, FHx+ adults who were not overweight were more likely to be engaged in controlling or losing weight (P < 0.01) or in changing their diet (P = 0.02) than FHx- adults, though the same relationship was not present in overweight adults. Also, hypertensive FHx- adults were more likely to have increased their physical activity than hypertensive FHx+ adults (P = 0.01). In these multivariable analyses, physician advice was associated with a higher prevalence of both FHx+ and FHx – participants engaging in each of the three behavior changes compared



Risk Reduction Behaviors

Figure 1—Behavior risk reduction profile of adults without diabetes by family history of diabetes, NHANES 2005–2008. *P < 0.01 for each comparison of FHx- and FHx+ participants within each behavior category. †Individuals who reported both receiving physician advice and performing the specified activity in the past 12 months; $P \ge 0.15$ for each comparison of FHx- and FHx+ participants within each behavior category.

Familial risk, diabetes risk-reducing behaviors

	Now controlling	Now controlling or losing weight		Now increasing physical activity or exercise	physical activity treise		Now reducing th calorie	Now reducing the amount of fat or calories in diet	
	FHx+	FHx-	P*	FHx+	FHx-	Р	FHx+	FHx-	Р
	44.8 (40.7–48.8)	44.1 (41.9–46.3)	0.17	42.5 (39.4–45.6)	42.7 (40.5–44.8)	0.37	42.7 (38.8–46.6)	40.1 (38.3-41.9)	0.92
	(1.00 –1.46) 1.16	(८.८८ –८.७८) ४.६८		(6.66–6.74) 4.16	(7.75–6.64) (4.64)		(1.66-8.26) 8.06	(0.06-0.16) 8.86	
	(1) (46 7 <u>-</u> 55 4)	46 4 (43 7_40 M)	100	(1 23 U 40 V 40 V 23 U)	46 1 (44 1_48 1)	0.04	47 6 (44 1 <u>-</u> 51 1)	44 6 (41 8-47 4)	C
	51.9 (48.3–55.5)	51.4 (48.9–53.8)	17:0	44.4 (41.3–47.6)	45.7 (42.5–49.0)		51.9 (47.9–55.8)	49.8 (47.4–52.2)	1.0
Non-Hispanic white	50.9 (47.2–54.5)	49.6 (47.3–52.0)	0.38	46.0 (42.3-49.6)	46.1 (43.7-48.6)	0.89	48.9 (45.3–52.6)	47.2 (44.8-49.6)	0.24
Non-Hispanic black	51.1 (45.2–57.1)	51.0 (47.1–54.8)		51.6 (45.8–57.4)	51.5 (47.9–55.2)		46.6 (41.8–51.5)	48.8 (46.2–51.4)	
	47.5 (42.6–52.3)	41.7 (37.5-45.8)		43.5 (38.3-48.8)	42.2 (37.8-46.6)		51.5 (47.0-56.1)	46.5 (43.2-49.8)	
	59.0 (52.9-65.1)	45.3 (40.2–50.3)		53.7 (47.0-60.5)	41.5 (37.2–45.8)		56.3 (49.9–62.7)	44.7 (39.2–50.3)	
Less than high school	46.0 (41.2–50.7)	38.0 (35.1–40.9)	0.05	41.8 (37.7–45.9)	36.1 (32.9–39.3)	0.07	42.4 (38.3–46.6)	35.9 (32.8–39.0)	0.14
Greater than or equal									
	52.5 (49.0–56.1)	51.0 (48.8–53.2)		48.2 (44.9–51.5)	48.0 (45.9–50.1)		51.1 (47.4–54.7)	49.4 (47.4–51.3)	
	54.3 (50.6–58.0)	54.0 (51.8–56.2)	< 0.01	48.7 (45.3–52.0)	49.0 (46.7–51.3)	0.09	52.6 (49.5-55.8)	51.8 (49.4-54.2)	0.02
	47.1 (43.0–51.2)	39.5 (36.9–42.0)		44.7 (40.9–48.5)	40.4 (37.8-43.0)		44.8 (40.6–49.0)	38.6 (36.1–41.2)	
	50.9 (46.9–55.0)	50.4 (46.7–54.1)	0.38	44.2 (40.6–47.8)	48.5 (45.2–51.8)	0.01	50.9 (47.4–54.3)	50.3 (47.7–52.9)	0.35
No	51.7 (48.0–55.4)	48.1 (45.7–50.5)		48.5 (45.1–51.8)	44.9 (42.6-47.3)		49.2 (45.3–53.0)	45.8 (43.6–48.0)	
	53.1 (49.1–57.1)	51.7 (48.2–55.1)	0.50	46.1 (42.4–49.8)	45.0 (41.3-48.8)	0.96	49.7 (46.0–53.3)	47.7 (44.1–51.3)	0.79
	50.9 (47.6–54.2)	47.8 (45.7–49.9)		47.5 (44.1–50.9)	46.3 (44.3-48.2)		49.6 (46.3–52.9)	46.9 (45.1–48.7)	
Told by a doctor to control									
	73.0 (68.7–77.3)	76.6 (72.3–80.8)	0.02	NA	NA		NA	NA	
	46.4 (43.2–49.6)	42.0 (39.7–44.4)		NA	NA		NA	NA	
Told by a doctor to increase									
physical activity or exercise									
	NA	NA		65.8 (62.4–69.3)	68.8 (65.0–72.5)	0.05	NA	NA	
	NA	NA		40.3 (36.8-43.9)	37.5 (35.2–39.7)		NA	NA	
Told by a doctor to reduce the									
amount of fat or calories in diet									
	NA	NA		NA	NA		75.1 (71.6–78.6)	78.1 (75.5–80.6)	0.02
	NA	NA		NA	NA		47 5 (38 9-46 0)	38 1 (36 0-40 3)	

with those who had not received physician advice (Table 2). Overall, physician advice on each of the three behaviors varied by family history of diabetes ($P \le 0.05$), with FHx- participants slightly more likely to perform the risk-reducing behaviors if they received physician advice compared with FHx+ participants.

Among adults who received physician advice, ~70-80% also engaged in each risk-reducing behavior (Supplementary Table 2). However, the adoption of these behaviors after receiving physician advice was not influenced by any of the examined clinical or demographic variables commonly associated with diabetes when stratified by family history of diabetes (P > 0.05 for each variable). When examining the participants who did not receive physician advice (Supplementary Table 3), fewer than half reported performing these risk-reducing behaviors. The performance of one or more of the behaviors in the past year varied by educational attainment, BMI, and hypertension status among those with and those without a family history of diabetes (P < 0.05).

CONCLUSIONS—Our data suggest that slightly more than one-third of U.S. adults without diabetes had a family history of diabetes in 2005-2008 but that fewer than half reported receiving a physician's or health professional's advice during the past year about diabetes risk-reducing behavioral changes. Although there is substantial evidence that diabetes can be prevented by healthy lifestyle changes, our data show that no more than onehalf of U.S. adults without diabetes reported trying to perform these risk-reducing behaviors in the past 12 months. However, when physician advice was received, >70% of U.S. adults without diabetes reported following the advice and engaging in one or more of these behavioral changes. In contrast, a smaller percentage of people who did not receive physician advice acknowledged making these changes.

Consistent with prior studies (11), our study confirms independent associations of physician advice and diabetes risk factors, including familial risk for diabetes, with diabetes risk–reducing behaviors in the general adult U.S. population without diabetes. However, the effect of family history of diabetes on risk-reducing behavior changes was diminished after accounting for all commonly known associated risk factors for diabetes.

Family history is an important risk factor that reflects inherited genetic susceptibility, shared environment, and common behaviors. Valdez et al. (7) reported that approximately one of every three adults in the U.S. population has a moderate or high familial risk of diabetes. People with a family history of diabetes have been found to have two to six times higher risk of having type 2 diabetes (16). Studies have suggested that the use of family history as a screening tool to detect diabetes and cardiovascular diseases is an inexpensive method of extracting genomic information (17). Regardless, a recent study on the impact of a positive family history and genetic risk variants on the incidence of diabetes reported a difference in diabetes incidence according to family history in the early years of intervention but that this difference disappeared upon follow-up (18). Our data suggest that people with a reported family history of diabetes participate more in risk-reducing behavior changes than those with no family history (without accounting for all commonly known associated risk factors, including the reception of physician advice). This could be because FHx+ individuals are more aware of their risk of diabetes than are FHx- individuals (19).

In agreement with other studies (20), our data suggest a strong effect of physician advice on the adoption of risk-reducing behavioral changes in the previous year, which varied by demographic characteristics. However, the prevalence of performing risk-reducing behaviors did not differ by family history of diabetes for those who received and followed physician advice on behavioral changes. Given the high percentage of people performing these behaviors if in receipt of advice, our data suggest that this advice was effective but that the knowledge of a positive family history did not increase the already high percentage of people adopting the preventive behaviors. A prior study on lifestyle modification to improve blood pressure control in individuals with diabetes concluded that physician advice is effective at changing hypertension-related lifestyle factors among people with diabetes, regardless of sex or race/ethnicity (11). Studies also reported that patients with type 2 diabetes might visit their family physicians up to nine times yearly (21), giving physicians and other health care professionals many opportunities to assess and to encourage patients to engage in risk-reducing behaviors. In spite of the influence of family

Chang and Associates

history in risk-reducing behavior changes and the important role of physician advice on lifestyle changes, our data suggest that more than one-half of people at high risk (i.e., with a positive family history of diabetes) had not received physician advice on lifestyle changes in the past 12 months. Using our data and data from a recent CDC diabetes report (1), we estimate that there are >49 million people aged \geq 20 years who do not have diabetes but who are at high risk because of a positive family history who have not received physician advice on lifestyle changes or recommended interventions. These findings indicate a great challenge in diabetes prevention, particularly for high-risk individuals.

Previous studies have reported that numerous factors may influence the routine provision of physician advice on lifestyle changes, for example, lack of time for counseling, physician training and education, limited staff support, reimbursement for preventive services, knowledge of successful strategies, community resources, limited English proficiency, and perceived success rate (11). Despite these barriers, adoption of these risk-reducing behaviors could be substantially promoted if physician advice is provided (22). Therefore, as physicians are increasingly encouraged to offer preventive care, effective strategies need to be developed to promote lifestyle changes and to help physicians overcome barriers to promoting a healthy lifestyle.

Strengths and limitations

This study has several strengths. First, we conducted this study using data from a nationally representative sample of the U.S. population, making our estimates generalizable to the entire population of U.S. adults without diabetes. Second, NHANES provides substantial data on biological and lifestyle factors, all of which were collected using standard laboratory and physical measurements. Finally, our study includes 4 years of data and, thus, a large sample size, powering our statistical ability to detect associations. However, there are several limitations. First, NHANES is cross-sectional, so we could not formally assess the temporal relation between physician advice and family history with behavior changes or assess these factors in relation to diabetes incidence. We were only able to evaluate how risk-reducing behaviors associated with family history and how much of this association is due to physician advice. We accessed the association

Familial risk, diabetes risk-reducing behaviors

of family history on reports of behavioral changes for the preceding 12 months. Nevertheless, it is unclear whether these lifestyle changes would continue long term. Second, there may be substantial social desirability bias introduced by self-reported responses regarding lifestyle changes and the receipt of physician advice. There are no separate methods in NHANES to validate self-reported variables, including family history of diabetes. Third, family history of diabetes could only be defined based on first-degree relatives, since information for other relatives was not asked in the 2005–2008 NHANES. As reported in a previous study (23), differences in the definition of family history between studies may lead to inconsistent findings. Fourth, the terms "physician advice" and "physician counseling" may not be interpreted consistently (11). Therefore, there should be some caution when comparing our estimates of the effect of physician advice on the adoption of diabetes risk reduction behaviors with the findings of other studies. In addition, other factors affect the influence of physician advice, such as the use of effective counseling techniques, the duration of counseling, how often patients have physician visits and get counseled, and the physician's attitude and perceptions (24). These factors were not considered in the current study. Finally, the results of this study may be influenced by the misclassification of diabetes (25). We did not use measures of fasting plasma glucose or results from glucose tolerance tests because these tests were performed in only a subset of NHANES participants, which would have largely reduced our sample size. Therefore, we defined diabetes by self-report and by using the new HbA1c criteria recently recommended by the American Diabetes Association (14).

In conclusion, our data suggest that family history of diabetes and advice from a health professional both influence the adoption of diabetes risk-reducing behaviors. Our data also indicated that people with family history are more likely to have a discussion with their doctors on behavior changes. There is room for improvement regarding the proportion of adults who actually receive such advice. However, once the advice is provided, familial risk does not seem to affect the adoption of these behaviors. It appears likely that the continued development of practical methods and effective strategies to promote behavioral changes is needed to contain, and perhaps reverse, the modern epidemic of diabetes.

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M.-h.C. had full access to and takes responsibility for the integrity of all data in the study and the accuracy of data analyses and contributed to the study concept and design, acquisition of data, research methods, statistical analysis, interpretation of data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content. R.V. contributed to the study concept and design, research methods, statistical analysis, interpretation of data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content. R.M.N. contributed to the drafting of the manuscript, critical revision of the manuscript for important intellectual content, and administrative, technical, and material support of the study. T.L. contributed to the acquisition of data, research methods, statistical analysis, interpretation of data, critical revision of the manuscript for important intellectual content, and administrative, technical, or material support of the study. Q.Y. contributed to the research methods, statistical analysis, interpretation of data, critical revision of the manuscript for important intellectual content, and supervision of the study. A.Y. contributed to the acquisition of data, research methods, statistical analysis, interpretation of data, critical revision of the manuscript for important intellectual content, and administrative, technical, or material support of the study. N.F.D. contributed to the critical revision of the manuscript for important intellectual content; administrative, technical, or material support of the study; and supervision of the study. J.B.M. contributed to the drafting and critical revision of the manuscript for important intellectual content. M.S.B. and M.J.K. contributed to the critical revision of the manuscript for important intellectual content and supervision of the study.

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