

The contribution of family history to the burden of diagnosed diabetes, undiagnosed diabetes, and prediabetes in the United States: analysis of the National Health and Nutrition Examination Survey, 2009–2014

Ramal Moonesinghe, PhD¹, Gloria L.A. Beckles, MD², Tiebin Liu, MSPH³ and Muin J. Khoury, MD, PhD⁴

Purpose: Given the importance of family history in the early detection and prevention of type 2 diabetes, we quantified the public health impact of reported family health history on diagnosed diabetes (DD), undiagnosed diabetes (UD), and prediabetes (PD) in the United States.

Methods: We used population data from the National Health and Nutrition Examination Survey 2009–2014 to measure the association of reported family history of diabetes with DD, UD, and PD.

Results: Using polytomous logistic regression and multivariable adjustment, family history prevalence ratios were 4.27 (confidence interval (CI): 3.57, 5.12) for DD, 2.03 (CI: 1.56, 2.63) for UD, and 1.26 (CI: 1.09, 1.44) for PD. In the United States, we estimate that

10.1 million DD cases, 1.4 million UD cases, and 3.9 million PD cases can be attributed to having a family history of diabetes.

Conclusion: These findings confirm that family history of diabetes has a major public health impact on diabetes in the United States. In spite of the recent interest and focus on genomics and precision medicine, family health history continues to be an integral component of public health campaigns to identify persons at high risk for developing type 2 diabetes and early detection of diabetes to prevent or delay complications.

Genet Med advance online publication 25 January 2017

Key Words: diabetes; family history; prediabetes; public health; undiagnosed diabetes

INTRODUCTION

Type 2 diabetes is a major public health problem in the United States and globally. In 2011–2012, among adults aged 20 years or older in the United States, the prevalence of diagnosed diabetes (DD), undiagnosed diabetes (UD), and prediabetes (PD) based on hemoglobin A_{1C} or fasting plasma glucose (FPG) was 9.2%, 3.1%, and 36.5% respectively.¹ The prevalence of diabetes including UD in the United States has been projected to increase to between one in five and one in three adults by 2050.² Along with overweight, physical inactivity, increasing age, high blood pressure, and minority race/ethnicity groups, family history of diabetes has long been known to be an important risk factor for the occurrence of type 2 diabetes.³ While there are a few genetic disorders associated with the risk of type 2 diabetes,⁴ the cause of most type 2 diabetes is multifactorial, involving the interaction of many genes (polygenic inheritance) and environmental/behavioral risk factors.⁵

In addition to being a risk factor for type 2 diabetes itself, family history of diabetes also seems to be positively associated with risk awareness and behaviors that reduce risk of type 2 diabetes.⁶ There is also evidence that including

family history of diabetes in screening algorithms also improves the detection of previously undiagnosed diabetes.^{7,8} This association may also exist for PD. A study based on a population of European origin conducted in Germany found that having at least one first-degree relative with diabetes was significantly associated with PD (odds ratio (OR) = 1.4; 95% confidence interval (CI) 1.27–1.54) and remained significant after adjusting for sex, age, and body mass index (BMI) (adjusted OR (aOR) = 1.3; 95% CI 1.14–1.40).⁹ In spite of the recent explosion in the discovery of numerous genetic variants associated with type 2 diabetes, most associations have small effect sizes and do not account for the effect of family history as an independent risk factor for type 2 diabetes. Family history of diabetes reflects not only the contribution of genetic factors but also environmental, social, behavioral, nutritional, and other potentially modifiable risk factors that are shared among relatives.^{3,10,11}

The Centers for Disease Control and Prevention and partners have made a concerted effort to educate the general public about the importance of collecting family health history for diabetes and other common chronic diseases using systematic free online tools.^{12,13} After a decade of such efforts,

¹Office of Minority Health and Health Equity, Centers for Disease Control and Prevention, Atlanta, Georgia, USA; ²National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia, USA; ³National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, Georgia, USA; ⁴Office of Public Health Genomics, Centers for Disease Control and Prevention, Atlanta, Georgia, USA. Correspondence: Ramal Moonesinghe (rmoonesinghe@cdc.gov)

Submitted 2 August 2017; accepted 20 November 2017; advance online publication 25 January 2018. doi:10.1038/gim.2017.238

a recent national survey found that most people do not actively collect family health history, even though the vast majority believe it is important for their own health.¹⁴ It is also important to note that information available about the accuracy of such data is sparse. As far as we are aware, only one small study of 10 people with and 10 people without diabetes, conducted in the mid-1980s, has examined accuracy of family history of diabetes. According to this study, family history of diabetes agreed completely with that given by respective relatives in a follow-up interview.¹⁵ Among Hispanics, having a family history of diabetes was associated with increased reported screening, but a similar association was not seen among non-Hispanic whites.¹⁵

Given the importance of family history in the early detection and prevention of diabetes, we sought, using a nationally representative sample of the US population (the National Health and Nutrition Examination Survey (NHANES) 2009–2014) to quantify the national prevalence of reported family health history of diabetes and its contribution not only to DD but as importantly to PD and UD. We were interested in identifying the independent contributions of family history to the burden of DD, UD, and PD in the United States. In addition, we were interested in identifying variations in reported diabetes across subsets of the population (e.g., age, race/ethnicity, sex) and impact of family history on the identification of people at risk for developing type 2 diabetes.

MATERIALS AND METHODS

NHANES is a series of surveys using stratified, multistage probability samples designed to provide assessments on the health and nutrition status of the civilian, noninstitutionalized US population. NHANES is conducted by the Centers for Disease Control and Prevention's National Center for Health Statistics and has continuously collected data based on personal interviews and physical examination of survey participants in 2-year cycles since 1999. The present study included samples of adults aged ≥ 20 years in the cycles 2009–2010, 2011–2012, and 2013–2014. Some population subgroups were oversampled to increase the reliability and precision of estimates of health outcomes for these groups. Sample weights were adjusted to take into account non-response, oversampling, and poststratification. Detailed description of the NHANES sample design is available elsewhere (https://wwwn.cdc.gov/nchs/data/series/sr02_162.pdf). Participants complete an in-home interview for basic demographic and health information along with a scheduled visit to a mobile examination center for physical examination and laboratory testing. Written informed consent was obtained from each participant for both parts of the survey and all protocols were approved by the research ethics review boards of the National Center for Health Statistics. The response rates for the surveys ranged from 68.5% to 77.3%.¹⁶ Pregnant women were excluded due to the effect of pregnancy on glucose measurement.

Definition of DD, UD, PD, and reported family history of diabetes

If a participant reported that they had ever been diagnosed with diabetes by a doctor or other health professional other than during pregnancy, we defined that person as having DD. Participants with a hemoglobin A_{1C} level of $\geq 6.5\%$ or a FPG level of ≥ 126 mg/dl who reported no previous diagnosis of diabetes were defined as having UD.¹ Participants with a hemoglobin A_{1C} level of between 5.7% and 6.4% or a FPG level of between 100 mg/dl and 125 mg/dl who reported no previous diagnosis of diabetes were defined as having PD.¹ To ensure that glucose values we used were consistent with earlier NHANES data, we corrected the measured FPG values using the equation recommended by the National Center for Health Statistics, $0.9835 \times (\text{FPG} - 1.139)$.^{17,18} Participants were asked whether any of their close biological (blood) relatives, including father, mother, sisters, or brothers, were ever told by a health professional that they had diabetes. We defined participants as having a reported family history of diabetes if they responded “yes” to this question. Further information on family history of diabetes is not available in NHANES 2009–2014 to do a more comprehensive analysis.

Statistical analysis

We partitioned the US population into PD, UD, DD, and none of these conditions. We used a polytomous logistic regression model to measure the association between the conditions and reported family history of diabetes by treating those with none of the conditions as the referent group. We included other risk factors in the model: age group (20–39, 40–59, ≥ 60 years), sex, race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, others), BMI (< 25 , 25–30, ≥ 30 kg/m²), hypertension ($\geq 140/90$ / $< 140/90$ mm Hg), and leisure time physical activity (yes/no). We defined participants as physically active if they had met the Healthy People 2010 objective of moderate- or vigorous-intensity physical activity.¹⁹ The risk factors selected were based on the recommendation of the American Diabetes Association.²⁰ We also included income-to-poverty ratio (< 1 / ≥ 1) and education ($< \text{high school}$ / $\geq \text{high school}$) in the model as indicators of socioeconomic status. There were no significant interactions between family history and other risk factors and these terms were excluded from the final model. The interactions were tested by including all the interaction terms in the model and also including one interaction term at a time in the model.

Next, we estimated the weighted prevalence of DD and evaluated the association between DD and family history of diabetes for the US population and for the subgroups of the populations with the risk factors given above using logistic regression models. For example, for the population aged 20–39 years, we estimated the prevalence of DD, 95% CI, and the OR for family history of diabetes adjusted for all the risk factors except for age. We extended this analysis for UD for the populations without DD and for PD for the populations

without DD or UD. We only report significant ($P < 0.05$) ORs.

In case-control and cohort studies, measures of associations are usually reported as ORs and risk ratios. In cross-sectional studies, when prevalent cases are included, the OR may also be mentioned as the prevalence OR; instead of the risk ratio, the prevalence ratio is calculated. For associations between family history of diabetes and DD, UD, or PD having a significant OR, we estimated the population attributable fraction (PAF) for family history of diabetes using the formula, $PAF = \frac{G(R-1)}{G(R-1)+1}$, where G is the prevalence of family history of diabetes in the population and R is the prevalence ratio. For DD and UD, we used OR as an approximate estimate for prevalence ratio. Because the prevalence of PD is relatively large (>10%), the approximate estimate of prevalence ratio was obtained from ORs, using the formula, $prevalence\ ratio = \frac{OR}{(1-p_0)+OR*p_0}$, where p_0 is the prevalence of PD in the population that does not have a family history of diabetes.²¹ Next, we calculated the number of cases impacted by family history of diabetes in the DD, UD, and PD populations by multiplying PAF and the number of cases with each condition. To calculate the total number of cases with each condition by age group, sex, and race/ethnicity categories, we used the distribution of the civilian noninstitutionalized US population obtained from the Census Bureau's Current Population Survey as recommended by the National Center for Health Statistics.¹⁶ We multiplied the average population size for the three survey cycles by the prevalence of each condition. For populations defined by other risk factors, we calculated the product of the average US population size, the prevalence of the risk factor, and the prevalence of each condition. Bonferroni correction was used to determine the significance levels for pairwise comparison tests of prevalence of family history of diabetes between groups.

The survey data were analyzed using SURVEYFREQ and SURVEYLOGISTIC procedures in SAS v. 9.3 (SAS Institute, Cary, NC), taking into account the complex survey design of the NHANES, and the sample weights were adjusted for pooling three cycles of NHANES data.

RESULTS

The study sample consisted of 8,796 nonpregnant adult respondents, which included 2,149 DD cases, 612 UD cases, and 2,719 PD cases. **Table 1** gives the crude prevalence of reported family history of diabetes for the US population, by age group, sex, race/ethnicity, and populations with other risk factors for type 2 diabetes. The prevalence of reported family history of diabetes in the US population age 20 years or over was 36.70% (95% CI: 35.05, 38.26). The prevalence of reported family history of diabetes was significantly higher among females (estimate: 38.72%, (CI: 36.71, 40.73)) compared with males (estimate: 34.47%, (CI: 32.57, 36.36)). By race/ethnicity group, the non-Hispanic black population had the highest prevalence of family history of diabetes, an estimate of 48.92% (CI: 45.92, 51.91). The relative disparities

Table 1 Crude prevalence of reported family history of diabetes by selected characteristics

	Prevalence percentage (95% CI)	P value
US population age 20 years and older		
Total	36.70 (35.05, 38.26)	
Age (years)		
20–39 (1)	31.89 (29.48, 34.29)	
40–59 (2)	40.75 (38.28, 43.23)	
≥ 60 (3)	37.28 (34.75, 39.81)	
Pairwise difference (1,2)		<0.001
Pairwise difference (1,3)		0.001
Pairwise difference (2,3)		0.049
Sex		
Males	34.47 (32.57, 36.36)	<0.001
Females	38.72 (36.71, 40.73)	
Race/ethnicity		
Non-Hispanic white (1)	33.61 (31.82, 35.40)	
Hispanic (2)	41.11 (37.68, 44.54)	
Non-Hispanic black (3)	48.92 (45.92, 51.91)	
Other ^a (4)	36.72 (32.28, 41.15)	
Pairwise difference (1,2)		<0.001
Pairwise difference (1,3)		<0.001
Pairwise difference (1,4)		0.157
Pairwise difference (2,3)		0.002
Pairwise difference (2,4)		0.128
Pairwise difference (3,4)		<0.001
BMI (kg/m²)		
< 25 (1)	28.92 (26.11, 31.74)	
25–30 (2)	35.10 (33.09, 37.12)	
≥ 30 (3)	44.30 (41.68, 46.92)	
Pairwise difference (1,2)		<0.001
Pairwise difference (1,3)		<0.001
Pairwise difference (2,3)		<0.001
Education		
< High school	42.10 (39.0, 45.21)	<0.001
≥ High school	35.51 (33.92, 37.11)	

Table 1 Continued

	Prevalence percentage (95% CI)	P value
Income-to-poverty ratio		
< 1	40.68 (37.53, 43.83)	0.005
≥ 1	35.74 (33.95, 37.53)	
Physical activity		
Not active	37.03 (35.18, 38.87)	0.376
Active	35.50 (32.52, 38.49)	
Hypertension		
Yes (1)	41.76 (38.99, 44.54)	<0.001
No (2)	33.54 (31.57, 35.51)	

BMI, body mass index; CI, confidence interval. ^aNon-Hispanic Asians, non-Hispanic multiracial, and non-Hispanic other race.

in the prevalence of family history of diabetes for the non-Hispanic black and Hispanic populations (estimate: 41.11% (CI: 37.68, 44.54)) compared with the non-Hispanic white population (estimate: 33.61%, (CI: 31.82, 35.40)) were 45.50% and 22.31% respectively. The prevalence of family history of diabetes increased with BMI (estimate: 44.30%, (CI: 41.68, 46.92), in the highest group). Populations with less than high school education (estimate: 42.10%, (CI: 39.0, 45.21)), with hypertension (estimate: 41.76%, (CI: 38.99, 44.54)), and income-to-poverty ratio <1 (estimate: 40.68% (CI: 37.53, 43.83)) had significantly higher prevalence of family history of diabetes than those with more education, without hypertension, and income-to-poverty ratio ≥ 1, respectively.

The results from the polytomous logistic regression model to measure the association between the conditions, PD, UD, and DD, and reported family history of diabetes by treating those with none of these conditions as the referent group are given in **Table 2**. Among the entire US population age ≥ 20 years, after controlling for all the other variables in the model, the prevalence ratios of DD, UD, and PD were 4.27 (CI: 3.57, 5.12), 2.03 (CI: 1.56, 2.63), and 1.26 (CI: 1.09, 1.44) for those with a family history of diabetes compared with those without relative to those with none of these conditions. As expected, out of all the risk factors considered in the model, age group ≥ 60 years compared with age group 20–39 years had by far the highest adjusted prevalence ratios (DD: 26.87, (CI: 19.39, 37.23), UD: 16.33, (CI: 10.38, 25.68), and PD: 5.11, (CI: 4.16, 6.28)). Those with BMI ≥ 30 kg/m² and BMI 25–30 kg/m² had significantly higher prevalence ratios for all three conditions compared with those with BMI < 25 kg/m² ((DD: 6.60, (CI: 5.31, 8.21), UD: 8.19, (CI: 4.65, 14.41), and PD: 2.52, (CI: 1.99, 3.21)) and (DD: 1.93, (CI: 1.55, 2.41), UD: 2.02 (CI: 1.21, 3.37), and PD: 1.40, (CI: 1.13, 1.73)) respectively). Hispanic (DD: 1.89, (CI: 1.55, 2.30), UD: 2.22, (CI: 1.57, 3.15), and PD: 1.23, (CI: 1.03, 1.47)), non-Hispanic black (DD: 1.75, (CI: 1.42, 2.16), UD: 1.98, (CI: 1.36, 2.87), and PD: 1.42, (CI: 1.17, 1.74)), and other race/ethnicity groups (DD: 3.34, (CI: 2.56, 4.34), UD: 4.24, (CI: 2.44, 7.38), PD: 1.47, (CI: 1.18, 1.85)) had significant prevalence ratios for all three conditions compared with the non-Hispanic white population. The adjusted

prevalence ratio for DD was also significant for males, those with hypertension, those with an income-to-poverty ratio < 1, those with less than high school education, and those who were not physically active. Similarly, the prevalence ratio for UD was significant for males, those with hypertension, those with less than high school education, and those who were not physically active, and the prevalence ratio for PD was significant for males, those with hypertension, and those with less than high school education.

Table 3 shows the prevalence of DD, UD, and PD, and aORs and PAFs of reported family history of diabetes in the US population and population subgroups with risk factors considered in this study. Prevalence, aORs, and PAFs of UD are based on the population that does not have DD, and prevalence, aORs, and PAFs of PD are based on the population that does not have DD or UD.

The PAFs for reported family history of diabetes for DD, UD, and PD in the US population were 48.66%, 20.59%, and 4.87% respectively. Among the population subgroups studied, the PAFs for family history of diabetes that were calculated with significant OR ranged from 42.53% (age 20–39 years) to 60.17% (Hispanics) for DD, from 13.95% (age ≥ 60 years) to 46.35% (other race/ethnicity) for UD, and from 3.93% (not physically active) to 7.91% (females) for PD. The aORs between family history of diabetes and PD were not statistically significant for most population subgroups.

During 2009–2014, the average US population ≥ 20 years of age was 224.1 million. Using the prevalence estimates of DD (9.26%), UD (3.45%), and PD (40.55%), we found 20.7 million, 7.0 million, and 79.6 million people had DD, UD, and PD, respectively in the US population. Of these, approximately 10.1 million cases (48.7%) with DD, 1.4 million cases (20.6%) with UD, and 3.9 million cases (4.9%) with PD were attributed to having a family history of diabetes (**Table 3**). Among the non-Hispanic white, non-Hispanic black, and Hispanic cases with DD, 5.6 million, 1.9 million, and 1.8 million, respectively were attributable to having a family history of diabetes (**Table 3**). Similar results are given for population subgroups defined by other risk factor status, and for UD and PD.

DISCUSSION

Our findings confirm the public health importance of family history as a risk factor associated with DD, UD, and PD. Given the high prevalence of reported family history and the high prevalence of diabetes and PD, our findings suggest that millions of people who have DD, UD, and PD in the United States can be identified using family history in first-degree relatives. Among people 20 years and older in the United States, 9.3% had DD, almost half of whom have their diabetes attributable to family history (burden of more than 10 million people). Around 3.4% of adults who were not diagnosed with diabetes had UD with more than 20% PAF for family history of diabetes (burden of more than 1.4 million people). Finally, 40% of the population without diabetes had PD with 5%

Table 2 Estimates of prevalence ratios from polytomous logistic regression when populations having diagnosed diabetes undiagnosed diabetes, and prediabetes were compared with the population not having any of these conditions

	Prevalence ratio estimates (95% CI) by outcome		
	DD	UD	PD
Reported family history			
No ^a			
Yes	4.27 (3.57, 5.12)	2.03 (1.56, 2.63)	1.26 (1.09, 1.44)
Age (years)			
20–39 ^a			
40–59	7.50 (5.56, 10.13)	5.93 (3.76, 9.35)	2.33 (1.97, 2.76)
≥ 60	26.87 (19.39, 37.23)	16.33 (10.38, 25.68)	5.11 (4.16, 6.28)
Sex			
Females ^a			
Males	1.96 (1.64, 2.34)	2.79 (2.06, 3.79)	1.61 (1.38, 1.88)
Race/ethnicity			
Non-Hispanic white ^a			
Hispanic	1.89 (1.55, 2.30)	2.22 (1.57, 3.15)	1.23 (1.03, 1.47)
Non-Hispanic black	1.75 (1.42, 2.16)	1.98 (1.36, 2.87)	1.43 (1.17, 1.74)
Other	3.34 (2.56, 4.34)	4.24 (2.44, 7.38)	1.47 (1.18, 1.85)
BMI (kg/m²)			
< 25 ^a			
25–30	1.93 (1.55, 2.41)	2.02 (1.21, 3.37)	1.40 (1.13, 1.73)
≥ 30	6.60 (5.31, 8.21)	8.19 (4.65, 14.41)	2.52 (1.99, 3.21)
Income-to-poverty ratio			
≥ 1 ^a			
< 1	1.46 (1.14, 1.87)	1.24 ^b (0.86, 1.79)	1.10 ^b (0.91, 1.33)
Education			
≥ High school ^a			
< High school	1.68 (1.40, 2.03)	1.87 (1.44, 2.43)	1.53 (1.25, 1.88)
Physical activity			
Active ^a			
Not active	1.37 (1.05, 1.80)	1.43 (1.01, 2.02)	0.91 ^b (0.78, 1.08)
Hypertension			
No			
Yes	3.53 (2.76, 4.50)	1.99 (1.48, 2.66)	1.51 (1.22, 1.87)

BMI, body mass index; CI, confidence interval; DD, diagnosed diabetes; PD, prediabetes; UD, undiagnosed diabetes.

^aReference group. ^bPrevalence ratios are not significant at 0.05 level.

attributable to family history (burden of nearly 3.9 million people).

These results show the burden of disease for DD, UD, and PD attributable to having a family history of diabetes. More than one third of the US population aged ≥ 20 years has family history of diabetes. In our analyses we found that approximately 13% of the US population in 2009–2014 had both family history of diabetes and PD (data not shown). Even though not everyone with PD will develop diabetes, it is possible, although still not established, that the risk of developing diabetes is higher for those with PD who also have family history of diabetes.

Based on the formula, the PAF declines sharply with the decline in adjusted prevalence ratio. The decline in PAF for DD, UD, and PD (48.7%, 20.6%, and 4.9% respectively) is due to the decline in adjusted OR (3.6, 1.8, and 1.3 respectively). The magnitudes of the association of family history of

diabetes with UD and PD are smaller than that for DD. A possible explanation for this is that people with diagnosed diabetes are more interested in knowing their family history of diabetes than those who are unaware of their disease status.⁷ Similarly, the magnitudes of the significant associations of family history of diabetes with UD and PD were smaller than that for DD for population subgroups for the same reason. The PAFs for DD for most of the population subgroups remain close to the PAF for the overall population. Population subgroups aged 20–39 and non-Hispanic whites have somewhat smaller PAFs (42.5% and 44.5% respectively) whereas the minority populations have relatively larger PAFs (>56%). Lack of significant associations between family history of diabetes and UD in a few population groups could be due to small sample sizes because the prevalence of UD was relatively low. However, there were several population subgroups without significant associations between family

Table 3 Prevalence of diagnosed diabetes, undiagnosed diabetes, prediabetes, adjusted odds ratios, and population attributable fractions of reported family history for population subgroups

	Prevalence (95% CI) by outcome			Adjusted OR			PAF%			No. impacted (in thousands)		
	DD	UD	PD	DD	UD	PD	DD	UD	PD	DD	UD	PD
US population age 20 years and older												
Total	9.26 (8.61, 9.91)	3.45 (3.03, 3.87)	40.55 (38.47, 42.62)	3.59	1.77	1.28	48.66	20.59	4.87	10,098	1,443	3,875
Age (years)												
20–39	1.69 (1.35, 2.03)	1.04 (0.72, 1.35)	24.78 (22.26, 27.31)	3.32	2.27	^a	42.53	28.34	^a	587	236	^a
40–59	9.40 (8.18, 10.62)	4.09 (3.11, 5.07)	44.22 (41.43, 47.02)	3.34	1.90	1.30	48.81	25.21	5.48	3,876	789	1,781
≥ 60	19.49 (17.84, 21.15)	6.45 (5.50, 7.40)	62.40 (58.51, 66.30)	3.88	1.52	1.42	51.78	13.95	3.97	5,834	419	1,078
Sex												
Males	9.49 (8.66, 10.32)	4.40 (3.65, 5.15)	44.90 (42.09, 47.71)	3.89	1.68	^a	49.90	17.60	^a	5,102	755	^a
Females	9.04 (8.28, 9.80)	2.56 (2.06, 3.05)	36.54 (34.08, 38.99)	3.31	1.95	1.41	47.18	25.37	7.91	4,964	686	2,981
Race/ethnicity												
Non-Hispanic white	8.29 (7.48, 9.11)	2.84 (2.29, 3.40)	39.76 (37.09, 42.44)	3.38	1.78	1.29	44.48	19.46	4.70	5,560	765	2,510
Hispanic	9.62 (8.18, 11.07)	4.66 (3.75, 5.56)	41.48 (38.51, 44.45)	4.67	^a	^a	60.17	^a	^a	1,844	^a	^a
Non-Hispanic black	13.27 (12.32, 14.22)	4.56 (3.34, 5.78)	46.59 (43.35, 49.84)	3.63	^a	^a	56.27	^a	^a	1,905	^a	^a
Other	11.18 (8.85, 13.52)	5.09 (3.48, 6.71)	37.08 (32.47, 41.69)	4.58	3.62	^a	56.77	46.35	^a	1,013	335	^a
BMI (kg/m²)												
< 25	3.52 (2.93, 4.11)	1.33 (0.77, 1.90)	28.20 (24.76, 31.64)	4.77	3.29	^a	52.16	38.75	^a	1,257	342	^a
25–30	7.05 (6.21, 7.89)	2.67 (2.08, 3.26)	40.47 (37.09, 43.84)	3.98	2.37	^a	51.08	31.00	^a	2,636	564	^a
≥ 30	15.24 (14.02, 16.46)	6.17 (5.18, 7.16)	52.91 (50.13, 55.68)	3.21	1.43	1.32	49.48	14.81	5.10	6,209	638	1,766
Education												
< High school	13.69 (12.07, 15.31)	5.46 (4.60, 6.32)	51.22 (47.16, 55.27)	3.43	^a	^a	50.52	^a	^a	2,706	^a	^a
≥ High school	8.31 (7.57, 9.06)	3.05 (2.60, 3.50)	38.47 (36.31, 40.63)	3.69	1.91	1.25	48.81	22.86	4.43	7,504	1,182	2,804
Income-to-poverty ratio												
< 1	10.72 (9.22, 12.22)	3.76 (2.92, 4.60)	39.56 (35.44, 43.68)	2.97	1.72	^a	44.42	21.20	^a	1,729	259	^a
≥ 1	8.87 (8.08, 9.66)	3.41 (2.84, 3.99)	40.04 (37.78, 42.30)	3.73	1.78	1.33	49.39	20.35	5.62	8,224	1,189	3,721
Hypertension												
Yes	18.35 (17.04, 19.67)	6.06 (5.36, 6.76)	56.61 (52.84, 60.39)	3.38	1.52	^a	49.89	16.0	^a	7,783	673	^a
No	3.70 (3.13, 4.27)	2.09 (1.60, 2.58)	32.56 (30.46, 34.66)	4.14	2.23	1.30	51.31	28.40	5.80	2,642	797	2,477
Physically active												
Yes	6.04 (5.03, 7.04)	2.44 (1.73, 3.15)	40.63 (36.79, 44.46)	3.63	^a	^a	48.29	^a	^a	1,607	^a	^a
No	10.31 (9.57, 11.05)	3.79 (3.30, 4.29)	40.51 (38.29, 42.74)	3.61	1.81	1.22	49.15	21.17	3.93	8,561	1,217	2,323

Prevalence of UD, adjusted odds ratios, and PAFs are based on the population that does not have DD; prevalence of PD, adjusted odds ratios, and PAFs are based on the population that does not have DD or UD.

BMI, body mass index; CI, confidence interval; DD, diagnosed diabetes; OR, odds ratio; PAF, population attributable fraction; PD, prediabetes; UD, undiagnosed diabetes.

^aNot estimated due to absence of a significant odds ratio.

history of diabetes and PD even in groups with higher prevalence of PD. These findings are consistent with our statement above about the relationship between family history and awareness of disease. Awareness of PD is quite low in the US population (<10% among persons with no family history of diabetes; 10–11% among those with family history of diabetes).²² Furthermore, it has been shown that with lower cutoff points for FPG and A1C levels for PD compared with previously used cutoff points, less than half the population diagnosed with PD is likely to develop diabetes in the next 10 years.²³ There is also some concern that the same cutoff points should not be applied to different race/ethnicity groups.^{23,24} Also, not everyone with PD develop diabetes²³ and a more appropriate comparison group may be people

with a family history of prediabetes. However, this information is not available in current surveys conducted in the United States.

Based on a genome-wide association study, several common genetic variants associated with type 2 diabetes were determined from different ancestral populations.²⁵ However, only 10% of the risk can be explained by these genetic variants.¹¹ A recent study based on large-scale sequencing also did not provide evidence that rare and low-frequency variants increase the risk of type 2 diabetes.²⁶ When considering prevention strategies for type 2 diabetes, it is important to stratify the population into groups by risk of developing type 2 diabetes. Genetic variants so far discovered do not seem to provide much further information in classifying those at

increased risk of developing type 2 diabetes compared with traditional clinical risk factors. Even for genetic variants with higher relative risks in some ethnic groups, it is recommended to consider traditional risk factors in combination with these genetic variants.²⁷

Direct-to-consumer genetic testing companies make genetic tests available to predict risk of type 2 diabetes. Even without considering clinical validity and utility of these tests, these companies provide personalized genetic profiles, claiming that the genetic information received would persuade people at risk to implement healthier behaviors.²⁸ However, based on a parallel group, open, randomized control trial to study the outcome of conveying an estimate of genetic or phenotypic risk of type 2 diabetes, researchers found that knowing a genetic or phenotypic risk estimate did not change behaviors when compared with standard lifestyle advice.²⁸ On the other hand, a study based on a cluster-randomized clinical trial concluded that messages designed to target an individual's familial risk to six common diseases including diabetes moderately increased self-reported physical activity and intake of fruits and vegetables compared with a standard preventive message.²⁹ Another recent study of nondiabetic patients randomized to counseling that included both family health history and genetic tests for type 2 diabetes found that family history was more highly associated with a perception of risk for type 2 diabetes than was genetic risk testing.³⁰ These few studies suggest that knowledge of family history may be more likely to influence lifestyle behaviors than knowledge based on genetic tests.

Study limitations

There are several limitations of our study. NHANES is a cross-sectional survey, and cannot be used to show causal effect of the risk factors on diabetes and PD we used in this study. However, these risk factors are well known in the literature, and thus in calculating impact numbers we assumed the causality of family history of diabetes on diabetes and PD. Also, DD was self-reported in the surveys and there could be differences in reporting bias between population groups. The data that NHANES collects do not allow us to differentiate between type 1 and type 2 diabetes, so our results are for diabetes overall, while interventions are based on evidence of risk reduction of type 2 diabetes. However, type 2 diabetes accounts for about 95% of DD in US adults.³¹ We also did not estimate the sampling errors of the impact numbers because the estimate of impact numbers includes the product of multiple estimates. The total of the impact numbers in demographic groups may not add up to the total for the US population. Moreover, the collection of family health history information is limited in NHANES. Participants were asked whether any of their first-degree relatives were told by a health professional that they had diabetes. Because there is a high prevalence of UD in the population, it is likely that the prevalence of family history is underascertained in the population and its relationship to the burden of diabetes in the population underestimated. There

have been no population-based surveys that examined the accuracy of self-reported family histories of diabetes. However, based on data from the 2004 HealthStyles survey, the respondents' reported awareness of type 2 diabetes status of their first-degree relatives was high, ranging from 87.8 to 94.5% depending on type of relationship.³² However, the differences in prevalence of reported family history between men and women suggest that there may be a recall or knowledge bias.⁷ Further information on family history of diabetes beyond first-degree relatives is not available in NHANES 2009–2014 to do a more comprehensive analysis of family history of diabetes.

In spite of the recent interest and focus on genomics and precision medicine, family health history continues to be an integral component of public health campaigns to identify people at high risk for developing diabetes. Additional national efforts are needed, especially among high-risk groups such as Hispanics, non-Hispanic blacks, and people with BMI ≥ 30 kg/m², to obtain information on family history that may contribute to reduction of incidence of type 2 diabetes, and early diagnosis of diabetes to help prevent or delay complications.

ACKNOWLEDGMENTS

Disclaimer: The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

DISCLOSURE

The authors declare no conflict of interest.

REFERENCES

- Menke A, Casagrande S, Geiss L, Cowie CC. Prevalence of and trends in diabetes among adults in the United States, 1988–2012. *JAMA* 2015;314:1021–1029.
- Boyle JP, Honeycutt AA, Narayan KMV, et al. Projection of diabetes burden through 2050. *Diabetes Care* 2001;24:1936–1940.
- Dorman JS, Valdez R, Liu T, et al. Health beliefs among individuals at increased familial risk for type 2 diabetes: implications for prevention. *Diabetes Res Clin Pract* 2012;96:156–162.
- Flannick J, Johansson S, Njølstad P. Common and rare forms of diabetes mellitus: towards a continuum of diabetes subtypes. *Nat Rev Endocrinol*. 2016;12:394–406.
- Wang X, Strizich G, Hu Y, Wang T, Kaplan RC, Qi Q. Genetic markers of type 2 diabetes: progress in genome-wide association studies and clinical application for risk prediction. *J Diabetes*. 2016;8:24–35.
- Hariri S, Yoon PW, Qureshi N, Valdez R, Scheuner MT, Khoury MJ. Family history of type 2 diabetes: a population-based screening tool for prevention? *Genet Med* 2006;8:102–108.
- Hariri S, Yoon PW, Moonesinghe R, Valdez R, Khoury MJ. Evaluation of family history as a risk factor and screening tool for detecting undiagnosed diabetes in a nationally representative survey population. *Genet Med*. 2006;8:752–759.
- Yang Q, Liu T, Valdez R, Moonesinghe R, Khoury MJ. Improvements in ability to detect undiagnosed diabetes by using information on family history among adults in the United States. *Am J Epidemiol*. 2010;171:1079–1089.
- Wagner R, Thorand B, Osterhoff MA, et al. Family history of diabetes is associated with higher risk for prediabetes: a multicenter analysis from the German Center for Diabetes Research. *Diabetologia* 2013;56:2176–2180.
- Yoon PW, Scheuner MT, Peterson-Oehlke KL, Gwinn M, Faucett A, Khoury MJ. Can family history be used as a tool for public health and preventive medicine? *Genet Med* 2002;4:304–310.

11. Rich SS. Still a geneticist's nightmare. *Nature* 2016;536:37–38.
12. US Department of Health and Human Services. My Family Health Portrait. <https://familyhistory.hhs.gov/FHH/html/index.html>. Accessed 1 August 2017.
13. Centers for Disease Control and Prevention. Family Health History. <https://www.cdc.gov/genomics/famhistory/>. Accessed 1 August 2017.
14. Welch BM, O'Connell N, Schiffman JD. 10 years later: assessing the impact of public health efforts on the collection of family health history. *Am J Med Genet A*. 2015;167A:2026–2033.
15. Kahn LB, Marshall JA, Baxter J, Shetterly SM, Hamman RF. Accuracy of reported family history of diabetes mellitus. Results from San Luis Valley diabetes study. *Diabetes Care* 1990;13:796–798.
16. Centers for Disease Control and Prevention. . National Health and Nutrition Examination Survey: response rates and population totals. https://www.cdc.gov/nchs/nhanes/response_rates_CPS.htm. Accessed 1 August 2017.
17. Centers for Disease Control and Prevention. National Health Nutrition Examination Survey: 2007-2008 data documentation, codebook, and frequencies. https://www.cdc.gov/Nchs/Nhanes/2007-2008/GLU_E.htm. Accessed 1 August 2017.
18. Centers for Disease Control and Prevention. National Health Nutrition Examination Survey: 2005-2006 data documentation, codebook, and frequencies. https://www.cdc.gov/Nchs/Nhanes/2005-2006/GLU_D.htm. Accessed 1 August 2017.
19. Carlson SA, Densmore D, Fulton JE, Yore MM, Kohl HW. Differences in physical activity prevalence and trends from 3 U.S. surveillance systems: NHIS, NHANES, and BRFSS. *J Phys Act Health* 2009;6:S18–27.
20. American Diabetes Association. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* 2003;26: S5–20.
21. Osborn J, Cattaruzza MS. Odds ratio and relative risk for cross sectional data. *Int J Epidemiol* 1995;24:463–64.
22. Centers for Disease Control and Prevention. . Awareness of prediabetes—United States, 2005-2010, MMWR 2013. <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6211a4.htm>. Accessed 14 November 2017.
23. Yudkin JS. The epidemic of pre-diabetes: the medicine and the politics. *BMJ* 2014;349:g4485.
24. Selvin E, Steffes MW, Ballantyne CM, Hoogeveen RC, Coresh J, Brancati FL Racial differences in glycemic marker: a cross sectional analysis of community-based data. *Ann Intern Med*. 2011;154:303–309.
25. Morris AP, Voight BF, Teslovich TM, et al. Large-scale association analysis provides insights into the genetic architecture and pathophysiology of type 2 diabetes. *Nat Genet* 2012;44:981–990.
26. Fuchsberger C, Flannick J, Teslovich TM, et al. The genetic architecture of type 2 diabetes. *Nature* 2016;536:41–47.
27. Florez JC. Leveraging genetics to advance type 2 diabetes prevention. *PLoS Med* 2016;13:e1002102.
28. Godino JG, van Sluijs EMF, Marteau TM, Sutton S, Sharp SJ, Griffin SJ. Lifestyle advice combined with personalized estimates of genetic or phenotypic risk of type 2 diabetes, and objectively measured physical activity: a randomized control trial. *PLoS Med* 2016;13:e1002185.
29. Ruffin 4th MT, Nease Jr DE, Sen A, et al. Effect of preventive messages tailored to family history on health behaviors: the Family Healthware Impact Trial. *Ann Fam Med*. 2011;9:3–11.
30. Wu RR, Myers RA, Hauser ER, et al. Impact of genetic testing and family health history based risk counseling on behavior and cognitive precursors for type 2 diabetes. *J Genet Couns*. 2017;26:133–140.
31. Centers for Disease Control and Prevention. . Diabetes Report Card 2012. <https://www.cdc.gov/diabetes/pubs/pdf/diabetesreportcard.pdf>. Accessed 1 August 2017.
32. Centers for Disease Control and Prevention. . Awareness of family history as a risk factor for disease—United States, MMWR 2004. <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5344a5.htm>. Accessed 1 August 2017.