ORIGINAL RESEARCH

Racial and Ethnic Differences in Cardio-Metabolic Risk in Individuals with Undiagnosed Diabetes: National Health and Nutrition Examination Survey 1999–2008

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BACKGROUND: Although early recognition and treatment of diabetes may be essential to prevent complications, roughly one-fifth of diabetes remains undiagnosed.

OBJECTIVE: Examine cardio-metabolic risk factors and their control in non-Hispanic white (NHW), non-Hispanic black (NHB) and Mexican American (MA) individuals with undiagnosed diabetes.

DESIGN: Nationally representative cross-sectional study of participants in the National Health and Nutrition Examination Survey (NHANES) continuous cycles conducted 1999 through 2008.

PARTICIPANTS: Of 22,621 non-pregnant individuals aged ≥ 20 years, 2521 had diagnosed diabetes. Of the remaining 20,100 individuals, 17,963 had HbA1c measured, 551 of whom were classified as having undiagnosed diabetes and comprise the study population.

MAIN MEASURES: Undiagnosed diabetes was defined as HbA1c $\geq 6.5\%$ without a self-report of physician diagnosed diabetes. Cardio-metabolic risk factor control was examined using regression methods for complex survey data.

KEY RESULTS: Among individuals with undiagnosed diabetes, mean HbA1c level was 7.7% (95% CI: 7.5, 7.9), 19.3% (95% CI: 14.2, 24.3) smoked, 59.7% (95% CI: 54.5, 64.8%) had hypertension and 96.5% (95% CI: 94.6, 98.4%) had dyslipidemia. Lipid profiles were remarkably different across racial-ethnic groups: NHB had the highest LDL- and HDL-cholesterol, but the lowest triglycerides, while MA had the highest triglycerides and the lowest LDL-cholesterol. After adjusting for age, sex, NHANES examination cycle and use of either blood pressure or lipid medication, the odds of having blood pressure $\geq 130/80$ mmHg was higher in NHB [1.92 (95% CI: 1.09, 3.55)] than NHW, while the odds of having LDL-cholesterol >100 mg/dl was higher in NHW [2.93 (95% CI: 1.37, 6.24)] and NHB [3.34 (95% CI: 1.08, 10.3)] than MA.

CONCLUSIONS: In a nationally representative sample of individuals with undiagnosed diabetes, cardio-metabolic risk factor levels were high across all racial/ethnic groups, but NHB and MA had poorer control compared to NHW. Interventions that target identification of

diabetes and treatment of cardio-metabolic risk factors are needed.

KEY WORDS: undiagnosed diabetes; disparities; cardio-metabolic risk; HbA1c.

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INTRODUCTION

The Veterans Affairs Diabetes Trial (VADT) is one of a series of recent clinical trials which demonstrate that tight control of hyperglycemia does not reduce the risk of cardiovascular events or micro vascular complications in individuals with poorly controlled long-standing diabetes.^{1,2} In contrast, results from the Diabetes Control and Complications Trial indicate that retinopathy and long-term incidence of cardiovascular disease are lowered by tight control of hyperglycemia in individuals with early stage type 1 diabetes.^{3,4} Moreover, in the UKPDS study, which enrolled individuals with newly diagnosed diabetes, HbA1c levels were a strong predictor of both micro and macro vascular complications.⁵ Based on these findings, early recognition and treatment of diabetes may be essential to prevent complications.

Diabetes has an asymptomatic preclinical phase; hence, in the absence of routine screening a significant proportion of individuals with diabetes remain undiagnosed. The American Diabetes Association Clinical Practice Recommendations 2010 added hemoglobin A1c (HbA1c) $\geq 6.5\%$ as criteria for the clinical diagnosis of diabetes.⁶ Using data from the National Health and Nutrition Examination Survey (NHANES) and a HbA1c $\geq 6.5\%$ as diagnostic of diabetes, estimates for undiagnosed diabetes were 2.1% in 1988–1994, 1.6% in 1999–2002 and 1.8% in 2003–2006 in the U. S. adult population age ≥ 20 years.⁷ These translated to a prevalence of undiagnosed diabetes among those with diabetes of 28.9% in 1988–1994, of 20.6% in 1999–2002 and of 21.5% in 2003–2006,⁷ or roughly one-fifth of all diabetes cases in more recent years.⁷ The prevalence of

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undiagnosed diabetes in the general population increases with age, was higher in men than women, and was higher in non-Hispanic blacks (NHB) and Mexican Americans (MA) than in non-Hispanic whites (NHW).^{7–10}

In the general population, racial differences in cardio-metabolic risk factor levels are well documented, with hypertension and diabetes being more common and less controlled in NHB than in NHW, but NHB having more favorable lipid profiles than NHW.^{10–19} Racial differences in cardio-metabolic risk factor levels may explain racial patterns in diabetes complications. Relative to NHW, NHB with diabetes are at higher risk of complications typically related to hypertension including end stage renal disease, lower extremity amputation and blindness.²⁰ In contrast, macro-vascular complications, including coronary heart disease (CHD) and cardiovascular mortality, which are typically related to dyslipidemia, seem to have similar or even lower rates in NHB than NHW individuals with diabetes.^{20,21}

Continuous NHANES data conducted between 1999 and 2008 (i.e., 1999–2000, 2001–2002, 2003–2004, 2005–2006, and 2007–2008) included measurement of HbA1c on all adults; hence, it was possible to identify and characterize a large nationally representative sample of individuals with undiagnosed diabetes. Therefore, our objective was to examine cardio-metabolic risk factor levels and their control in NHW, NHB and Hispanics with undiagnosed diabetes using continuous NHANES between 1999 and 2008. We hypothesized that ethnic minorities (NHB and Hispanics) with undiagnosed diabetes would have poorer control of cardio-metabolic risk factors compared to NHW.

METHODS

Study Population And Data

This study utilized data from five cycles of continuous NHANES conducted between 1999 and 2008 (i.e., 1999–2000, 2001–2002, 2003–2004, 2005–2006, and 2007–2008) by the National Center for Health Statistics (NCHS) within the Center for Disease Control and Prevention (CDC).²² Each continuous NHANES cycle was designed to be representative of the U.S. civilian non-institutionalized population using a complex, multistage probability sample. Participants are interviewed in their homes and subsequently receive a physical and laboratory examination in a mobile examination center. Among eligible subjects 82.0%, 83.9%, 79.3%, 80.5%, and 78.4%, were interviewed and 76.3%, 79.6%, 75.6%, 77.4%, and 75.4%, were examined during continuous NHANES cycles 1999–2000, 2001–2002, 2003–2004, 2005–2006, and 2007–2008, respectively.²²

Between 1999 and 2008, 22,621 non-pregnant NHW, NHB and MA individuals aged ≥ 20 years completed the

household interview. Of these 22,621 individuals, 2521 were classified as having diagnosed diabetes based on responding yes to the question, “Have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes?” Of the remaining 20,100 individuals, 17,963 had HbA1c measured, 551 of whom were classified as having undiagnosed diabetes and serve as the study population. Undiagnosed diabetes was defined based on the American Diabetes Association criteria of having a $\text{HbA1c} \geq 6.5\%$ without a self-reported clinical diagnosis of diabetes.⁶ Reports comparing diagnosis of diabetes based on HbA1c to diagnosis of diabetes based on fasting and 2-hour glucose indicate that HbA1c has high specificity, but low sensitivity, resulting in identification of fewer individuals as having undiagnosed diabetes.^{7,23,24} Moreover, racial-ethnic differences in the identification of individuals with undiagnosed diabetes may be disproportionately greater using HbA1c criteria as compared to glucose criteria.^{7,23,24}

Demographics included being born in the United States and markers of socio-economic status (SES) (i.e., education and income level). Information on access to health care included number of physician visits per year, having a routine place to receive care and having been hospitalized in the past year. Chronic disease was also assessed through self-report of arthritis, cancer (i.e., of any kind including skin), chronic heart failure, CHD (including self-reported CHD, myocardial infarction or angina) and stroke.

Procedures for blood collection and processing are described elsewhere.²² Serum glucose and triglyceride levels were only measured on examinees randomly assigned to the morning fasting sample ($\sim 45.7\%$ of our study population). Smoking was defined as being a current smoker and having smoked ≥ 100 cigarettes during one's lifetime. Hypertension was defined as having systolic ≥ 140 mmHg, diastolic ≥ 90 mmHg, or being prescribed medication to treat high blood pressure. Uncontrolled blood pressure was defined as having systolic/diastolic $\geq 140/90$ mmHg regardless of whether or not an individual was taking medication to control their blood pressure. Meeting blood pressure guidelines for individuals with diabetes was defined as having systolic < 130 mmHg and a diastolic < 80 mmHg.⁶ Dyslipidemia was defined as total cholesterol ≥ 200 mg/dl, LDL-cholesterol ≥ 100 mg/dl, HDL-cholesterol < 45 mg/dl in men or < 55 mg/dl in women, triglycerides ≥ 200 mg/dl, or being prescribed lipid lowering medication. Meeting lipid guidelines for individuals with diabetes was defined as having LDL-cholesterol levels < 100 mg/dl regardless of whether or not an individual was taking lipid lowering medication.⁶ Awareness concerning hypertension and dyslipidemia was defined as self-reported physician diagnoses of hypertension and dyslipidemia, respectively.

Statistical Analysis

Data were analyzed using the SAS System (version 9.3; SAS institute; Cary, NC) and its complex survey-specific procedures. All analyses accounted for the clustered sampling design and oversampling, and were adjusted for differential non-coverage and non-response across the five continuous NHANES cycles included in the analysis.

Means and frequencies of participant characteristics (i.e., demographics, access to care and cardio-metabolic outcomes) were determined in the total population and stratified by race and ethnic group. When looking at blood pressure and LDL-cholesterol levels and their control, results are further stratified by medication use. Linear regression models were used to assess cardio-metabolic risk factor levels and multivariate logistic regression models were used to assess awareness, treatment and control of elevated cardio-metabolic levels. All regression models were properly adjusted for complex sampling and NHANES cycle was modeled as an ordinal variable. Initial regression models were adjusted for demographic and cohort effects (i.e., age, sex and NHANES cycle). Subsequent regression models were additionally adjusted for SES (i.e., income, education level), access to care (i.e., number of physician visits) and common chronic diseases (i.e., arthritis, CHD). Our intent was to determine to what extent were race/ethnic differences in cardio-metabolic outcomes among individuals with undiagnosed diabetes independent of SES, access to care and chronic disease burden. Additionally, in linear regression

models blood pressure and LDL-cholesterol levels were stratified by medication use, while in logistic models medication use was adjusted for. Additionally, because obesity is an early cardio-metabolic risk factor and the mean BMI in our population was high, for continuous outcomes we examined to what extent were race/ethnic differences in cardio-metabolic outcomes independent of BMI. All covariates were identified a priori based on the literature. P-values less than 0.05 were taken as statistically significant. No correction for multiple testing was applied to reported p-values.

RESULTS

During the time period from 1999 through 2008 in adults ≥ 20 years, the overall prevalence of undiagnosed diabetes was 1.5% (95% CI: 1.2, 1.8) in NHW, 3.1% (95% CI: 2.6, 3.5) in NHB, and 2.7% (95% CI: 2.1, 3.3) in MA, while the prevalence of diagnosed diabetes was 6.7% (95% CI: 6.0, 7.3) in NHW, 11.3% (95% CI: 10.3, 12.3) in NHB, and 7.6% (95% CI: 6.8, 8.4) in MA; hence, undiagnosed diabetes accounted for 18.5% (95% CI: 15.4, 21.5), 21.3% (95% CI: 18.1, 24.6), and 26.0% (95% CI: 21.5, 30.4) of diabetes in NHW, NHB and MA respectively.

In individuals with undiagnosed diabetes, MA were the youngest at 49.1 years, followed by NHB at 56.5 years and NHW at 60.7 years (Table 1). MA and NHW were more likely to be male than female, 57.5% and 62.4% male, respectively, while only 38.1% of NHB were male. MA and

Table 1. Sample Demographics (Means, Prevalence and 95% CI) Stratified by Race and Ethnicity

	NHW (n=223)	MA (n=159)	NHB (n=169)	p-value ^a	Total (n=551)
Male (%)	62.4 (55.0, 69.9)	57.5 (47.9, 67.1)	38.1 (30.7, 45.5)	<0.0001	56.9 (51.7, 62.1)
Age (years)	60.7 (58.6, 62.7)	49.1 (47.0, 51.3)	56.5 (53.7, 59.3)	<0.0001	58.4 (57.0, 59.8)
NHANES Cycle					
NH 1999-2000	19.1 (2.7, 25.5)	12.7 (3.8, 21.5)	12.0 (6.4, 17.7)	0.5221	16.9 (12.7, 21.0)
NH 2001-2002	14.2 (10.1, 18.4)	10.3 (5.6, 15.0)	20.7 (14.8, 26.5)		15.0 (12.4, 17.7)
NH 2003-2004	20.3 (11.2, 29.4)	25.9 (10.4, 41.5)	14.4 (8.9, 19.9)		19.8 (14.0, 25.7)
NH 2005-2006	20.5 (12.2, 28.8)	23.6 (13.2, 33.9)	20.5 (14.2, 26.7)		20.9 (15.5, 26.3)
NH 2007-2008	25.9 (15.3, 36.4)	27.5 (17.9, 37.1)	32.4 (24.2, 40.6)		27.4 (20.9, 33.9)
High School Graduate ^b (%)	80.3 (73.9, 86.7)	33.0 (24.0, 42.0)	53.0 (45.6, 60.5)	<0.0001	69.0 (63.6, 74.4)
Household Income					
< \$20,000	19.6 (12.8, 26.3)	31.6 (23.3, 40.0)	30.8 (21.5, 40.2)	0.0241	23.2 (18.2, 28.2)
≥ \$75,000	21.5 (14.0, 28.9)	16.4 (8.3, 24.6)	12.1 (7.3, 17.0)		19.0 (13.6, 24.5)
Born in the U.S.	96.2 (94.0, 98.4)	33.7 (24.7, 42.7)	91.5 (86.5, 96.5)	<0.0001	87.6 (84.5, 90.6)
Physician Visits Past Year					
0 visits	13.1 (7.8, 18.5)	34.1 (25.8, 42.4)	16.2 (10.2, 22.3)	<0.0001	16.3 (12.3, 20.4)
1 visit	16.1 (10.2, 21.1)	28.1 (20.9, 35.3)	17.8 (11.0, 24.6)		18.0 (13.7, 22.2)
2 or more visits	70.7 (63.1, 78.3)	37.8 (30.0, 45.6)	65.9 (59.0, 72.9)		65.7 (60.3, 71.1)
Health Care Home (%)	92.2 (87.6, 96.8)	60.7 (49.6, 71.9)	89.4 (85.2, 93.6)	<0.0001	87.7 (84.2, 91.3)
Hospitalized Past Year ^c	12.1 (8.0, 16.2)	5.0 (1.2, 8.7)	8.2 (2.5, 13.8)	0.1066	10.3 (7.4, 13.3)
Chronic Disease					
Cancer (%)	15.5 (10.7, 20.4)	2.8 (0.7, 4.9)	5.8 (1.8, 9.8)	<0.0001	12.0 (8.3, 15.6)
Arthritis (%)	37.7 (30.8, 44.6)	16.2 (9.7, 22.7)	37.5 (30.1, 45.1)	0.0003	35.0 (29.9, 40.1)
Chronic Heart Failure (%)	5.9 (2.6, 9.2)	1.1 (0.1, 2.1)	7.8 (2.9, 12.2)	0.0748	5.7 (3.2, 8.1)
Coronary Heart Disease (%)	12.8 (7.6, 18.0)	6.1 (2.2, 10.1)	15.3 (10.0, 20.5)	0.1290	12.5 (8.8, 16.1)
Stroke (%)	4.4 (1.4, 7.3)	3.2 (0.2, 6.2)	6.3 (3.0, 9.6)	0.5026	4.6 (2.6, 6.6)

^aP-value for differences across the three race/ethnic groups, either Rao-Scott Chi-square or F tests; ^bHigh school graduate includes individuals who completed a GED; ^cHospitalized in the past year was not available in 1999-2002

NHB were less likely to have graduated from high school and were more likely to have a low household income than NHW. Slightly over a third of MA were born in the U.S. (33.7%) with the vast majority of NHB (91.5%) and NHW (96.2%) being born in the U.S. Only 37.8% of MA report two or more physician visits in the past year, while 65.9% of NHB and 70.7% of NHW report two or more physician visits in the past year. Similarly, roughly 90% of NHW and NHB report having a routine place to receive health care, while only 60.7% of MA report having a routine place to receive health care.

Cardio-metabolic risk factor levels were high in individuals with undiagnosed diabetes, regardless of race or ethnic group (Table 2). Mean HbA1c levels ranged from 7.5% (95% CI: 7.3, 7.8) in NHW to 8.5% (95% CI: 8.0, 8.9) in MA with 75.8% of NHW, 67.0% of NHB and 82.6% of MA having fasting glucose ≥ 126 mg/dl. The prevalence of hypertension ranged from 38.8 (95% CI: 30.1, 47.6) in MA to 63.5% (95% CI: 53.7, 73.3) in NHB with 42.7% of the population using blood pressure medication. Finally, 96.5% (95% CI: 94.6, 98.4) of the population had at least one form of dyslipidemia.

After adjusting for age, sex and NHANES exam cycle, cardio-metabolic risk factor levels varied across race-ethnic

groups among individuals with undiagnosed diabetes (Table 3). Among those not using blood pressure medications, systolic blood pressure was higher in NHB than NHW. Lipid profiles were different across racial-ethnic groups: NHB had the highest LDL- and HDL-cholesterol, but the lowest triglycerides, while MA had the highest triglycerides and the lowest LDL-cholesterol. Further adjusting cardio-metabolic risk factor levels for BMI did not attenuate racial-ethnic differences for cardio-metabolic risk factor levels. Further adjusting cardio-metabolic risk factor levels for education level, household income level, number of physician visits in the past year, arthritis and CHD (but not BMI) attenuated racial-ethnic differences between MA and NHW as well as NHB for some factors, but did not attenuate racial-ethnic differences between NHB and NHW. Specifically, HbA1c levels were no longer significantly different across the three racial-ethnic groups and fasting glucose levels were no longer significantly higher in MA than NHW. Differences in blood pressure and lipid levels across racial-ethnic groups remained.

After adjusting for age, sex and NHANES exam cycle the odds of hypertension [OR=2.07 (95% CI: 1.21, 3.54)]; self-reported hypertension [OR=2.42 (95% CI: 1.48, 3.97)]; or using medication to treat hypertension [OR=2.69 (95%

Table 2. Cardio-Metabolic Outcomes (Means, Prevalence and 95% CI) Stratified by Race and Ethnicity

	NHW (n=223)	MA (n=159)	NHB (n=169)	p-value ^a	Total (n=551)
HbA1c (%)	7.5 (7.3, 7.8)	8.5 (8.0, 8.9)	7.8 (7.4, 8.1)	0.0024	7.7 (7.5, 7.9)
Fasting glucose ^a (mg/dL)	170 (155, 185)	183 (165, 201)	165 (152, 178)	<.0001	170 (159, 181)
Fasting glucose ≥ 126 mg/dl ^b (%)	75.8 (66.7, 84.9)	82.6 (73.6, 91.5)	67.0 (56.2, 77.7)		74.5 (67.8, 81.3)
BMI (kg/m ²)	33.3 (32.2, 34.3)	33.3 (32.0, 34.6)	35.0 (33.6, 36.3)	0.1202	33.6 (32.8, 34.4)
Waist Circumference (cm)	113 (111, 115)	108 (106, 110)	111 (108, 114)	0.0045	112 (110, 114)
Current Smoker (%)	16.3 (10.7, 24.2)	22.3 (15.3, 31.3)	21.2 (15.0, 29.1)	0.0835	19.3 (14.2, 24.3)
Blood Pressure					
Hypertension (%)	62.1 (55.2, 69.1)	38.8 (30.1, 47.6)	63.5 (53.7, 73.3)	0.0017	59.7 (54.5, 64.8)
Self-Reported Hypertension (%)	53.4 (45.7, 61.0)	32.4 (23.8, 40.9)	59.8 (50.5, 69.0)	0.0012	52.1 (46.5, 57.7)
Blood Pressure Medication (%)	36.0 (38.5, 52.5)	20.2 (13.2, 27.1)	46.7 (37.7, 55.7)	0.0001	42.7 (37.6, 47.8)
Blood Pressure Among Those Not on Medication					
Systolic (mm Hg)	128 (123, 132)	127 (123, 132)	133 (128, 138)	0.2126	129 (125, 132)
Diastolic (mm Hg)	71 (68, 74)	74 (71, 76)	76 (72, 79)	0.1273	72 (70, 75)
SBP/DBP $\geq 140/90$ mm Hg (%)	27.9 (18.6, 37.2)	21.9 (13.7, 30.1)	28.7 (16.3, 41.2)	0.6675	27.1 (20.6, 33.5)
SBP/DBP $\geq 130/80$ mm Hg (%)	50.9 (39.2, 62.5)	49.0 (35.9, 62.0)	56.1 (51.5, 78.6)	0.1822	53.2 (44.5, 61.9)
Blood Pressure Among Those on Medication					
Systolic (mm Hg)	136 (131, 141)	139 (133, 146)	141 (137, 145)	0.4213	137 (133, 141)
Diastolic (mm Hg)	71 (67, 75)	65 (60, 71)	72 (67, 76)	0.1486	71 (68, 74)
SBP/DBP $\geq 140/90$ mm Hg (%)	35.1 (24.7, 45.6)	45.5 (27.5, 63.4)	50.9 (40.7, 61.2)	0.0615	39.1 (31.3, 46.8)
SBP/DBP $\geq 130/80$ mm Hg (%)	60.4 (48.0, 72.8)	78.5 (64.6, 92.4)	73.3 (63.0, 83.7)	0.0873	64.1 (54.9, 73.3)
Lipids					
Total cholesterol (mg/dL)	206 (200, 212)	211 (201, 221)	213 (205, 221)	0.4033	208 (204, 212)
HDL cholesterol (mg/dL)	43 (41, 44)	43 (41, 45)	50 (47, 53)	0.0005	44 (43, 45)
Triglycerides ^{b,c} (mg/dL)	186 (160, 217)	226 (194, 263)	122 (106, 141)	<.0001	173 (155, 193)
Dyslipidemia (%)	97.0 (94.9, 99.1)	95.8 (89.8, 100)	96.3 (93.4, 99.3)	0.8744	96.5 (94.6, 98.4)
Self-Report Hyperlipidemia (%)	40.7 (33.9, 47.5)	26.9 (19.3, 34.5)	39.0 (30.2, 47.8)	0.0764	38.7 (33.8, 43.5)
Lipid Medication (%)	28.8 (22.1, 35.4)	9.4 (3.8, 15.0)	21.2 (13.3, 29.2)	0.0016	24.9 (20.0, 29.7)
LDL Among Those Not on Medication					
LDL cholesterol ^b (mg/dL)	121 (117, 126)	115 (114, 116)	140 (139, 140)	<.0001	125 (123, 128)
LDL > 100 mg/dl (%)	79.3 (70.2, 88.4)	72.7 (62.4, 82.9)	79.0 (67.6, 90.4)	0.7267	78.4 (72.3, 84.5)
LDL Among Those on Medication					
LDL cholesterol ^b (mg/dL)	107 (105, 108)	77 (72, 81)	123 (121, 124)	<.0001	110 (108, 111)
LDL > 100 mg/dl (%)	42.2 (25.6, 58.8)	21.7 (0.2, 43.2)	73.0 (55.4, 90.5)	0.0036	48.6 (35.1, 62.0)

^aP-value for differences across the three race/ethnic groups, either Rao-Scott Chi-square or F tests; ^bMeasured only on participants examined during a morning session (i.e., fasting): fasting glucose (n=251), triglycerides (n=252) and LDL from Friedewald calculation (n=229); ^cgeometric mean

Table 3. Adjusted Mean Levels of Cardio-Metabolic Risk Factors among Individuals with Undiagnosed Diabetes Stratified by Race and Ethnicity

Cardio-metabolic Outcomes	NHW	MA	NHB
Adjusted for age, sex and NHANES exam cycle.			
HbA1c (%)	7.5 (7.2, 7.7)	8.3 (7.9, 8.7)*	7.8 (7.4, 8.1)
Fasting glucose (mg/dL)	167 (157, 177)	188 (180, 196)*	168 (165, 170) [†]
BMI (kg/m ²)	33.3 (32.2, 34.4)	31.2 (29.9, 32.6)	33.6 (32.2, 35.0) [†]
Waist Circumference (cm)	113 (111, 115)	105 (102, 108)*	110 (107, 113) [†]
Total cholesterol (mg/dL)	206 (200, 212)	208 (197, 220)	212 (203, 221)
HDL cholesterol (mg/dL)	43 (41, 45)	45 (42, 47)	50 (47, 52)* [†]
Triglycerides [‡] (mg/dL)	183 (176, 190)	257 (245, 269)*	131 (126, 136)* [†]
Among Those Not on Medication			
Systolic blood pressure ^a (mm Hg)	128 (123, 132)	132 (127, 136)	135 (130, 140)*
Diastolic blood pressure ^a (mm Hg)	71 (68, 74)	71 (67, 74)	74 (71, 78)
LDL cholesterol (mg/dL) ^b	121 (117, 125)	112 (108, 116)*	138 (136, 139)* [†]
Among Those on Medication			
Systolic blood pressure ^a (mm Hg)	136 (132, 141)	141 (135, 147)	142 (137, 146)
Diastolic blood pressure ^a (mm Hg)	69 (66, 72)	62 (56, 68)*	71 (67, 75) [†]
LDL cholesterol (mg/dL) ^b	109 (109, 109)	71 (67, 75)*	117 (114, 119)* [†]
Adjusted for age, sex, NHANES exam cycle and BMI.			
HbA1c (%)	7.5 (7.3, 7.8)	8.3 (7.8, 8.7)*	7.8 (7.5, 8.1)
Fasting glucose (mg/dL)	169 (159, 180)	187 (179, 194)*	169 (166, 171) [†]
Total cholesterol (mg/dL)	206 (200, 213)	209 (197, 220)	213 (204, 222)
HDL cholesterol (mg/dL)	43 (41, 45)	44 (42, 47)	50 (47, 53)* [†]
Triglycerides [‡] (mg/dL)	184 (177, 191)	253 (242, 265)*	129 (124, 135)* [†]
Among Those Not on Medication			
Systolic blood pressure ^a (mm Hg)	128 (124, 133)	132 (127, 136)	135 (130, 140)*
Diastolic blood pressure ^a (mm Hg)	71 (68, 74)	71 (67, 74)	74 (71, 78)
LDL cholesterol (mg/dL) ^b	122 (117, 126)	114 (110, 118)*	140 (138, 141)* [†]
Among Those on Medication			
Systolic blood pressure ^a (mm Hg)	136 (131, 141)	141 (134, 147)	141 (137, 146)
Diastolic blood pressure ^a (mm Hg)	69 (66, 72)	62 (56, 69)	71 (67, 76) [†]
LDL cholesterol (mg/dL) ^b	109 (109, 110)	71 (67, 75)*	117 (114, 120)* [†]
Adjusted for age, sex, NHANES exam cycle, education level, household income level, number of physician visits in the past year, self-reported arthritis and self-reported coronary heart disease.			
HbA1c (%)	7.6 (7.3, 7.9)	8.0 (7.6, 8.4)	7.8 (7.5, 8.1)
Fasting glucose (mg/dL)	175 (168, 182)	174 (173, 174)	171 (170, 171) [†]
BMI (kg/m ²)	33.1 (32.0, 34.3)	31.8 (30.2, 33.4)	33.7 (32.3, 35.1)
Waist Circumference (cm)	113 (111, 115)	106 (103, 109)*	110 (107, 114)
Total cholesterol (mg/dL)	207 (200, 214)	206 (195, 217)	213 (204, 221)
HDL cholesterol (mg/dL)	43 (42, 45)	44 (41, 47)	49 (46, 51)* [†]
Triglycerides [‡] (mg/dL)	191 (178, 205)	249 (240, 259)*	134 (131, 136)* [†]
Among Those Not on Medication			
Systolic blood pressure ^a (mm Hg)	128 (123, 132)	132 (128, 137)	136 (131, 141)*
Diastolic blood pressure ^a (mm Hg)	70 (66, 73)	72 (68, 75)	75 (71, 78)
LDL cholesterol (mg/dL) ^b	122 (121, 123)	111 (111, 111)*	135 (135, 136)* [†]
Among Those on Medication			
Systolic blood pressure ^a (mm Hg)	136 (132, 140)	140 (131, 149)	143 (138, 147)*
Diastolic blood pressure ^a (mm Hg)	69 (66, 72)	62 (54, 70)*	71 (66, 75) [†]
LDL cholesterol (mg/dL) ^b	110 (108, 112)	81 (70, 92)*	117 (116, 119)* [†]

^aBlood pressure levels are stratified based on whether or not individuals are taking blood pressure medication; ^bLDL cholesterol values are stratified based on whether or not individuals are taking lipid lowering medication; *P-value < 0.05 for comparison with NHW; [†] P-value < 0.05 for comparison with MA; [‡]geometric mean

CI: 1.64, 4.40)] were over two times higher in NHB than MA with undiagnosed diabetes (Table 4). The odds of self-reported hypertension [OR=1.72 (95% CI: 1.01, 2.95)] and using medication to treat hypertension [OR=2.24 (95% CI: 1.32, 3.82)] were also higher in NHW than MA with undiagnosed diabetes (Table 3). However, after additionally adjusting for use of blood pressure medication, the odds of having uncontrolled blood pressure defined as systolic/diastolic $\geq 130/80$ mmHg was similar in MA and NHW, but higher in NHB than NHW [OR=1.97 (95% CI: 1.09, 3.55)]. Use of lipid lowering medications followed a similar pattern to that of blood pressure lowering medications; namely, NHB [OR=2.19 (95% CI: 1.00, 4.77)] and NHW [OR=2.85 (95%

CI: 1.40, 5.78)] with undiagnosed diabetes were more likely to use lipid lowering medication than MA. Moreover, after further adjusting for use of lipid lowering medication the odds of having LDL > 100 mg/dl was higher in NHW [OR=2.93 (95% CI: 1.37, 6.24)] and NHB [OR=3.34 (95% CI: 1.08, 10.3)] than MA. Further adjusting odds ratios for education level, household income level, number of physician visits in the past year, arthritis and CHD attenuated some odds ratios; however, the odds of self-reported hypertension [OR=2.06 (95% CI: 1.22, 3.49)] remained higher in NHB than MA and the odds of using medication to treat hypertension remained higher in NHB [OR=2.11 (95% CI: 1.20, 3.69)] and NHW [OR=1.74 (95% CI: 1.02, 2.99)] than

Table 4. Odds Ratios (and 95% Confidence Intervals) Predicting Prevalent Cardio-Metabolic Outcomes Comparing the Three Race and Ethnicity Categories

Cardio-metabolic Outcomes	Odds Ratios (95 % confidence intervals)		
	NHW vs. MA	NHB vs. MA	NHB vs. NHW
Adjusted for age, sex and NHANES exam cycle.			
Current Smoker	0.68 (0.32, 1.43)	0.94 (0.55, 1.61)	1.38 (0.71, 2.70)
Blood Pressure			
Hypertension	1.65 (0.99, 2.72)	2.07 (1.21, 3.54)	1.26 (0.69, 2.27)
Self-Reported Hypertension	1.72 (1.01, 2.95)	2.42 (1.48, 3.97)	1.41 (0.81, 2.45)
High Blood Pressure Medication	2.24 (1.32, 3.82)	2.69 (1.64, 4.40)	1.20 (0.71, 2.02)
SBP/DBP $\geq$ 140/90 mm Hg ^a	0.86 (0.48, 1.54)	1.33 (0.71, 2.50)	1.55 (0.94, 2.54)
SBP/DBP $\geq$ 130/80 mm Hg ^a	0.80 (0.44, 1.45)	1.58 (0.80, 3.10)	1.97 (1.09, 3.55)
Lipids			
Dyslipidemia	2.79 (0.49, 15.9)	1.76 (0.19, 16.4)	0.63 (0.15, 2.60)
Self-Report Hyperlipidemia	1.35 (0.78, 2.31)	1.47 (0.84, 2.57)	1.10 (0.67, 1.79)
Lipid Medication	2.85 (1.40, 5.78)	2.19 (1.00, 4.77)	0.77 (0.43, 1.39)
LDL $>$ 100 mg/dl ^b	2.93 (1.37, 6.24)	3.34 (1.08, 10.3)	1.14 (0.41, 3.15)
Adjusted for age, sex, NHANES exam cycle, education level, household income level, number of physician visits in the past year, self-reported arthritis and self-reported coronary heart disease.			
Current Smoker	0.94 (0.44, 1.98)	1.11 (0.59, 2.07)	1.15 (0.66, 2.00)
Blood Pressure			
Hypertension	1.28 (0.76, 2.16)	1.53 (0.84, 2.77)	1.19 (0.66, 2.15)
Self-Reported Hypertension	1.32 (0.83, 2.11)	2.06 (1.22, 3.49)	1.55 (0.86, 2.82)
High Blood Pressure Medication	1.74 (1.02, 2.99)	2.11 (1.20, 3.69)	1.21 (0.68, 2.15)
SBP/DBP $\geq$ 140/90 mm Hg ^a	0.83 (0.46, 1.49)	1.30 (0.66, 2.54)	1.56 (0.95, 2.56)
SBP/DBP $\geq$ 130/80 mm Hg ^a	0.91 (0.45, 1.84)	1.72 (0.81, 3.67)	1.90 (0.99, 3.63)
Lipids			
Dyslipidemia	0.79 (0.40, 1.55)	0.85 (0.44, 1.67)	1.09 (0.63, 1.88)
Self-Report Hyperlipidemia	1.46 (0.63, 3.35)	1.05 (0.42, 2.63)	0.72 (0.34, 1.55)
Lipid Medication	1.71 (0.66, 4.40)	2.26 (0.55, 9.37)	1.33 (0.48, 3.69)

^aAlso adjusted for being on medication for high blood pressure; ^bAlso adjusted for being on lipid lowering medication.

in MA. After further controlling for use of blood pressure medication, the odds of having uncontrolled blood pressure was no longer statistically significantly higher in NHB than NHW [OR=1.90 (95% CI: 0.99, 3.63)].

DISCUSSION

In a population representative of individuals in the United States with undiagnosed diabetes, cardio-metabolic risk factor levels were high across racial/ethnic groups, but NHB and MA had poorer cardio-metabolic risk factor control compared to NHW. The low access to care in MA was striking with over a third of MA reporting having not seen a physician in the past year and only 60.7% reporting a health care home. NHB were more likely to have hypertension than MA. Use of blood pressure and lipid lowering medication was lower in MA than in NHW or NHB and may be a result of low access to care. Interestingly, adjusting for BMI did not attenuate racial-ethnic differences in cardio-metabolic risk factors levels; however, although mean BMI levels were high across all three race-ethnic groups, mean BMI only varied between NHB and MA. In contrast, adjusting for SES, access to care and chronic diseases attenuated racial-ethnic differences in HbA1c, fasting glucose and BMI levels, but not blood pressure or lipid levels. With respect to awareness, treatment and control of hypertension and dyslipidemia, adjusting for SES, access to care and chronic diseases

attenuated racial-ethnic differences somewhat, but in many cases point estimates for odds ratios remained over two. In summary, racial-ethnic differences in blood pressure and lipid subtype appear independent of SES and access to care, while more research is required to determine to what extent racial-ethnic differences in awareness, treatment and control are independent of SES and access to care.

Few prior studies have compared racial/ethnic differences in cardio-metabolic risk factor levels in individuals with undiagnosed diabetes. In a single study which used data from continuous NHANES 1999-2000 and focused on glycemic control, the authors report that Hispanics with undiagnosed diabetes were more likely to have HbA1c levels of 7% or greater than NHB or NHW.²⁵ These results were consistent with our age, sex and NHANES exam cycle adjusted results of higher mean levels of HbA1c in MA than in NHB or NHW. In a recent retrospective cohort study conducted among 1,456 black and 2,624 white veterans with recently diagnosed diabetes who were receiving consistent primary care at VHA facilities, the authors reported that at the time of diagnosis of diabetes and at the time of initiation of glucose lowering medication, glucose and HbA1c levels were higher in blacks than whites.²⁶ Specifically, at the time of diabetes diagnosis, average HbA1c levels were 7.8% in blacks, but only 7.1% in whites (with similar results for glucose: 154 vs. 148 mg/dl). At the time of initiation of glucose lowering medication, average HbA1c levels were 8.5% in blacks, but only 7.8% in whites

(with similar results for glucose, 176 vs. 169 mg/dl).²⁶ In a recent study using NHANES data from 1999-2008, among adults with diagnosed diabetes Ford et al. reported that NHB and MA had poorer glycemic control than NHW and that MA had worse control of LDL-cholesterol than NHW.¹⁹

Few studies have focused on individuals with undiagnosed diabetes; however, several studies have examined chronic complications of diabetes and the economic cost prior to the onset of clinical diabetes. Studies of chronic complications of diabetes indicate that cardiovascular risk factor levels,²⁷⁻³¹ atherosclerosis (as measured by carotid artery intima-media thickness),³² microalbuminuria³³ and cardiovascular events³⁴ are elevated prior to the clinical recognition of diabetes. Similarly, economic studies indicate that cost is elevated prior to the onset of clinical disease.^{35,36} The few studies completed in individuals with unrecognized diabetes indicate elevated levels of chronic complications of diabetes including elevated levels of nephropathy and peripheral neuropathy³⁷ as well as elevated estimated cardiovascular risk relative to those without diabetes.³⁸ Finally, in 2007 in the United States, the economic cost of undiagnosed diabetes was estimated to be \$18 billion, or \$2,864 per person with undiagnosed diabetes.^{39,40} This estimate includes \$11 billion in medical costs and \$7 billion indirect costs.^{39,40}

This study provides essential information regarding cardio-metabolic risk factor profiles of individuals with undiagnosed diabetes, a population of high vulnerability due to their lack of disease awareness, and focuses on racial and ethnic differences. Strengths of the current study include its relatively large population of individuals with undiagnosed diabetes and the population-based study population representative of Hispanic, NHB and NHW individuals in the United States with undiagnosed diabetes. Limitations of the study include its cross-sectional design and the lack of fasting and 2-hour glucose levels from an oral glucose tolerance test across the entire NHANES population. Another potential limitation is the use of a diagnostic parameter (i.e., HbA1c) to identify individuals with undiagnosed disease which was not valid when the sample was selected.

This study fills an important gap in examining cardio-metabolic risk factor level, treatment and control in a population representative of individuals in the United States with undiagnosed diabetes. In summary, cardio-metabolic risk factor levels were high across racial/ethnic groups, but NHB and MA had poorer cardio-metabolic risk factor control compared to Whites. Studies across the continuum of health care, focusing on the patient and the provider as well as the health care system, are required to improve identification and treatment of individuals with undiagnosed diabetes.

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