

# Longitudinal Associations Between Body Mass Index During Young Adulthood, Subsequent Weight Change, and Incident Diabetes During Mid- and Older-Adulthood in Non-Hispanic White and African American Populations: The Atherosclerosis Risk in Communities Study

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## Abstract

**Background:** Excess body mass index (BMI) and weight gain are well-known risk factors for diabetes. Nevertheless, the associations of BMI and weight gain in young adulthood with subsequent diabetes in African Americans, and the standardized effects of these weight variables have not been well studied.

**Methods:** We studied 12,672 white and African American men and women 45–64 years of age (*i.e.*, during mid-adulthood) who participated in the Atherosclerosis Risk in Communities Study visit 1 (1987–1989), and were reexamined at three follow-up examinations. Associations between recalled BMI at age 25 (*i.e.*, during young adulthood) and subsequent weight change with incident diabetes at ages 45 and above (*i.e.*, during mid-adulthood to older adulthood) were examined using Cox proportional hazard models.

**Results:** Over the 9-year follow-up, we identified 1,501 cases of incident diabetes. The incidence rates were higher among African Americans (men: 24.5 and women: 26.3 per 1,000 person-years) compared to whites (men: 16.3 and women: 10.5 per 1,000 person years). Compared to normal-weight individuals at age 25, those who were overweight or obese and those who gained more weight after age 25 had a higher risk of developing diabetes later in all four race-sex groups with the highest risk in African Americans. In the race-sex groups combined, the mutually adjusted hazard ratio for BMI at age 25 and percent weight change were 1.97 (1.79–2.17) and 2.89 (2.59–3.11), respectively, comparing the 85th to the 15th percentiles of the exposures.

**Conclusions:** African Americans were at higher risk of diabetes than whites. Both higher BMI at age 25 and subsequent weight gain were independently associated with higher risk for diabetes in all the race-sex groups; however, overall weight gain was more potent than BMI.

**Keywords:** BMI, weight change, diabetes, young adulthood, African American, white

## Introduction

YOUNG ADULTHOOD (ages 20–44) is the period of life in which weight gain is most rapid,<sup>1–4</sup> and more than 35% of U.S. young adults are obese.<sup>5</sup> It is well known that obesity can lead to adverse changes in fasting glucose,<sup>6</sup>

fasting insulin,<sup>7</sup> impaired glucose metabolism,<sup>8</sup> as well as increased risk of type 2 diabetes.<sup>9,10</sup> Perhaps less well recognized is that obesity and weight gain during adolescence and/or young adulthood compared to later in adulthood (*i.e.*, mid- to old-adulthood) are more strongly associated with impaired glucose metabolism<sup>8</sup> and diabetes risk.<sup>11–16</sup>

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These findings are generally from studies that examined diabetes incidence over a contiguous follow-up period of several years in younger versus older adults. Several other studies have shown that obese adolescents and young adults, compared to their normal-weight counterparts, are at an increased risk of developing diabetes decades later when they are in middle or old age.<sup>11,17–22</sup> These studies point to young adulthood as an important time to promote a healthy body weight and weight maintenance to reduce diabetes development. Despite numerous published studies having examined associations of body mass index (BMI) and weight change with diabetes incidence in different age groups, there remain several important issues pertinent to young adults that still need to be clarified.

One area in which further work is needed is in associations of obesity and weight gain with diabetes by race-sex. Findings from a few studies performed in diverse populations and geographic settings suggest that the association between weight status and incident diabetes differs by race/ethnicity<sup>13,23,24</sup> and sex,<sup>25,26</sup> with the risk higher among Asian American, Hispanic/Latin, African American, and Native Hawaiian populations compared to white populations, and among men compared to women. Comparison particularly between whites and African Americans suggests that African Americans have a higher prevalence of diabetes, which has been attributed, in part, to differences in body fat distribution, and obesity.<sup>27–30</sup> Higher diabetes prevalence and incidence may also be driven by ethnic differences in weight gain. Study of weight gain by race and sex supports these findings, showing that over a 15-year period during young to mid-adulthood, African American men and women gained 14 and 16 kg, respectively, while white men and women gained 11 and 10 kg, respectively.<sup>31</sup> Hence further work is needed to evaluate the roles of obesity and weight gain in young adulthood on the development of diabetes, particularly among high-risk groups of African Americans.

Only a few studies have collectively evaluated the long-term associations of both BMI and weight gain during young adulthood on the later development of diabetes. The findings suggest weight gain during young and mid-adulthood period has greater impact when compared to weight gain at older adulthood among populations from Europe,<sup>11</sup> Hawaii,<sup>13</sup> and the United States.<sup>15,18,21,32</sup> Two of these studies are not generalizable to racially diverse U.S. populations<sup>11,13</sup> and two of the U.S. studies were limited to only white adults,<sup>21,32</sup> but nevertheless, these studies underline the importance of maintaining a low body weight throughout the life. Only the two studies<sup>15,18</sup> from the United States collectively evaluated the long-term associations of both BMI and weight change on the development of diabetes in African American adults. One of these<sup>18</sup> studied African American women only, and therefore made no comparison with other ethnic groups or with men. Another study<sup>15</sup> included both African American and white men and women, but did not show separate associations with the amount of weight change by race-sex groups.

In this work, we propose to explore the associations of BMI in young adulthood (*i.e.*, BMI at age 25) and subsequent weight change in younger adults on diabetes development in mid- (45–64 years) to older (65 years and above) African American and white men and women. We use measures of effect that are calculated slightly differently than those currently in the literature in an effort to empha-

size and add to what is known about race-sex differences in diabetes risk and the relative impact of excess weight compared to excess weight gain.

## Methods

### *Study population*

Data were from the Atherosclerosis Risk in Communities (ARIC) Study.<sup>33</sup> In brief, the ARIC study is a prospective study of the natural history and etiology of atherosclerosis and cardiovascular disease in four U.S. communities.<sup>33</sup> The baseline data were collected between 1987 and 1989 on 15,792 predominantly white and African American men and women 45–64 years of age. Participants were invited to three additional examinations, which occurred at ~3-year intervals. The study was approved by institutional boards at each center, and all subjects gave written consent. This secondary data analysis was approved by the University of North Carolina at Chapel Hill Non-Biomedical Institutional Review Board. We analyzed 12,672 individuals who were free of diabetes at the baseline visit and had weight and diabetes information in any of the follow-up visit/s.

### *Measures and covariates*

At the baseline visit 1, participants were asked to recall their body weight at age 25 using time-associated events. Body weight was measured at all study visits (baseline visit 1 through visit 4) using a beam balance scale. Height (without shoes) was measured at visit 1 to the nearest centimeter by using a metal ruler attached to a wall and a standard triangular headboard,<sup>33</sup> and used in all calculations of BMI [weight in kg/height (m)<sup>2</sup>]. Weight changes were calculated as the difference between self-reported weight at age 25 years and measured weight at each study visit (1 through 4), and used to calculate percent weight change.<sup>34</sup>

Diabetes was identified if any of following four conditions was met: (1) fasting glucose  $\geq 126$  mg/dL, (2) non-fasting glucose  $\geq 200$  mg/dL, (3) self-reported physician diagnosis of diabetes, or (4) use of antidiabetes medications, including oral agents and insulin.<sup>35</sup> Participants were followed for a period of ~9 years from visit 1 through visit 4 and diabetes status was ascertained at each study visit. We estimated the date of diabetes diagnosis using a previously published linear interpolation method.<sup>35–37</sup>

Date of birth, race, and sex were self-reported by participants during the recruitment phase and confirmed during visit 1. Other variables were assessed using interviewer-administered questionnaires<sup>33</sup> and included: education (visit 1), cigarette smoking (all visits), alcohol consumption (all visits), diet (visits 1 and 3), and physical activity (visits 1 and 3). Physical activity was assessed using the Baecke leisure time physical activity questionnaire.<sup>38</sup> The ages that smoking was initiated and stopped were collected as well as current smoking status. We used this information to create categories of smoking status as smoker versus nonsmoker at age 25, and current, former, and never smoker at visit 1.

### *Statistical analysis*

We performed descriptive analyses to compare participants' characteristics by race-sex groups and examined Cox proportional hazard models with time to diabetes as the

outcome.<sup>39</sup> Because of our interest in diabetes in African Americans, and because of differences in obesity rates and weight change by sex, we conducted our analyses stratified by race-sex group. We set the reference group for the hazard ratios (HRs) to be white women who were normal weight or weight maintainers (depending on whether primary exposure was BMI level or weight change) because that group had the lowest incidence of diabetes. Covariates in these analyses included education, height, smoking, and alcohol; smoking at age 25; and time-dependent variables such as age and physical activity that changed over study visits.

We also performed hazard models with BMI at age 25 and weight change as continuous variables. In these analyses, we combined the race-sex groups and focused on quantifying the overall risk of diabetes associated with BMI and with weight change by calculating the risk between the 15th and 85th percentile groups for both exposures. This approach provided an estimate of risk associated with BMI and weight change that were equivalent in regard to the relative prevalence of exposures in the community-based sample studied. All analyses were performed using SAS version 9.3 (SAS Institute, Inc., Cary, NC).

## Results

The average age of our study sample at baseline visit 1 ranged from 52.7 to 54.5 years among different race-sex groups (Table 1). Larger proportions of white participants were high school graduates compared to African Americans. Compared to female participants of the same race, larger proportions of male participants reported smoking cigarettes at age 25, and both smoking and alcohol consumption at

visit 1. Males were more active compared to females of similar race.

The average BMI value at age 25 was in the normal range for all race-sex groups (Table 2). The time interval from age 25 to visit 1 (1987–1989) ranged from 19 to 41 years. African American women gained almost twice as much weight as the other race-sex groups during this interval. Overall, participants who were obese at age 25 years gained less weight between age 25 and visit 1 than participants who were normal weight at age 25 (mean weight change: 2.9 vs. 12.8 kg). African American women gained two to three times more weight in all BMI categories compared to other race-sex groups, and women in general gained more weight than men (Table 2). Correlations between BMI at age 25 and subsequent weight change (age 25 to visit 1) were inverse among white and African American men ( $r=-0.33$  and  $-0.36$ , respectively) and stronger than in white and African American women ( $r=-0.04$  and  $-0.14$ , respectively).

During the 9 years of follow-up after visit 1, we observed 1,501 incident diabetes cases. The incidence rates were substantially higher among African American men and women compared to white men and women (Table 3). The HRs (Model 1<sup>a</sup>), calculated using normal-weight white women as the reference group, showed that this group was at the lowest risk when compared to overweight and obese white women, as well as participants of other race-sex combinations who were normal weight, overweight, or obese. Within sex groups, the risk estimates in Model 1<sup>a</sup> were generally higher in African American than in white men or women across every BMI level. Nevertheless, in all the race-sex groups, overweight and obese adults were consistently at higher risk than normal weight, although some confidence intervals overlapped. Additional adjustment for subsequent

TABLE 1. CHARACTERISTICS OF THE STUDY PARTICIPANTS BY RACE-SEX GROUPS, IN THE ATHEROSCLEROSIS RISK IN COMMUNITIES STUDY (ASSESSED AT VISIT 1, 1987–1989)

Characteristics	White women (n=5,269)	African American women (n=1,756)	White men (n=4,585)	African American men (n=1,062)
Age in years at visit 1	53.8 (5.6)	52.7 (5.6)	54.5 (5.7)	53.3 (5.9)
Education at visit 1				
Less than high school	14.6	34.8	16.3	38.9
High school graduation or equivalent	51.2	30.4	39.2	26.7
At least some college	34.1	34.7	44.4	33.9
Cigarette smokers at age 25 (%)	40.8	33.0	65.3	64.9
Smoking status at visit 1 (%)				
Never	50.8	58.3	28.9	28.8
Former	25.2	17.2	47.3	33.3
Current	23.9	24.4	23.8	37.7
Alcohol consumption at visit 1 (%)				
Never/rare	51.9	64.7	25.7	28.1
Former	13.1	18.5	19.1	25.2
Light	11.0	5.6	10.7	6.6
Moderate	11.4	5.3	26.3	23.1
Heavy	12.5	5.3	18.1	16.5
Physical activity at visit 1 (%)				
Low (tertile 1)	39.0	60.5	29.2	50.2
Medium	33.2	25.8	29.9	28.4
High (tertile 3)	27.5	13.5	40.6	20.8

Values are mean (SD) or %. Exclusions from original sample of 15,792: African Americans from Washington county, MD; or Minneapolis, MN ( $n=55$ ); participants of race other than white or African American ( $n=48$ ); prevalent diabetes ( $n=1,863$ ); missing diabetes information ( $n=147$ ) at the visit 1 or missing diabetes information for all three follow-up visits ( $n=879$ ); missing weight at age 25 or at baseline visit 1 ( $n=128$ ).

SD, standard deviation.

TABLE 2. BODY MASS INDEX AT AGE 25 AND SUBSEQUENT WEIGHT CHANGE BETWEEN YOUNG AND MID-ADULTHOOD (45–64 YEARS) PERIOD BY RACE-SEX GROUPS, IN THE ATHEROSCLEROSIS RISK IN COMMUNITIES STUDY (1987–1989)

Characteristics	White women (n=5,269)	African American women (n=1,756)	White men (n=4,585)	African American men (n=1,062)
BMI at age 25 years (kg/m <sup>2</sup> )	21.7 (3.0)	22.2 (3.9)	24.1 (3.2)	23.9 (3.6)
BMI categories at age 25 years (%)				
Underweight	8.1	10.8	1.5	3.6
Normal weight	81.9	72.8	63.5	66.0
Overweight	7.9	12.1	30.1	23.9
Obese	2.2	4.3	4.9	6.5
Weight at age 25 years (kg)	56.9 (8.4)	58.9 (10.3)	74.9 (11.5)	74.4 (12.7)
Weight change between age 25 and visit 1 (kg) <sup>a</sup>	11.7 (11.0)	21.1 (15.1)	9.5 (10.6)	10.8 (13.6)
Weight change between age 25 and visit 1 (%) <sup>b</sup>	20.8 (19.0)	37.0 (26.2)	13.6 (15.0)	15.8 (19.2)
Weight change categories (%) <sup>b</sup>				
Weight losers	6.2	3.5	10.7	14.8
Weight maintainers	24.3	8.1	34.2	25.6
Moderate weight gainers	43.1	33.5	42.2	40.3
Large weight gainers	26.4	54.9	12.9	19.3
Weight change by BMI categories (kg) <sup>a</sup>				
Underweight	12.4 (8.8)	24.6 (15.0)	20.1 (11.6)	22.7 (15.5)
Normal weight	11.6 (10.5)	21.1 (13.7)	11.1 (9.6)	12.4 (11.9)
Overweight	13.7 (14.7)	21.7 (19.1)	6.9 (10.5)	8.3 (13.5)
Obese	3.8 (16.6)	10.4 (19.4)	1.6 (14.2)	-3.1 (17.5)
Weight change by BMI categories (%) <sup>b</sup>				
Underweight	26.8 (19.7)	52.4 (31.8)	36.4 (21.5)	41.7 (30.5)
Normal weight	20.7 (18.5)	37.0 (23.8)	16.4 (14.4)	18.2 (17.3)
Overweight	20.0 (21.1)	31.4 (27.6)	8.4 (12.6)	10.2 (16.2)
Obese	5.2 (18.6)	12.7 (23.2)	1.7 (14.0)	-2.9 (16.5)

Values are mean (SD) or %. Underweight (<18.5 kg/m<sup>2</sup>), normal weight (≥18.5 to <25.0 kg/m<sup>2</sup>), overweight (≥25 to <30 kg/m<sup>2</sup>), obese (≥30 kg/m<sup>2</sup>), weight losers (less than -3%), weight maintainers: included weight maintenance and small weight gain into one category due to small sample size (greater than or equal to -3% to <10%), Moderate weight gainers (≥10% to <30%), large weight gainers (≥30%).

<sup>a</sup>Weight change was calculated as difference between measured weight at visit 1 and self-reported weight at age 25. Hence, positive value represents weight gain during mid- and older adulthood (45–64 years) compared to young adulthood (25 years).

<sup>b</sup>Percent weight change was calculated as [(weight change between visit 1 and age 25) × 100/weight at age 25].  
BMI, body mass index.

weight change (Model 1<sup>b</sup>) slightly attenuated the risk estimates for underweight category of all race-sex groups, but strengthened the risk estimates for the majority of other BMI categories of all race-sex groups. Overall, diabetes risk remained significantly elevated for all race-sex groups who were overweight or obese, and similar trends in race-sex groups identified in Model 1<sup>a</sup> persisted in Model 1<sup>b</sup>. Adjustment for weight change did not extinguish the trend toward lower diabetes risk in white compared to African American men and women.

Within sex groups, the risk of diabetes in model 2<sup>a</sup> tended to be higher in African Americans than in white men and women in every weight change category, except for the weight loser in African American men. In all the race-sex groups, there was increased risk with increased weight gain. Adjustment of weight change model for BMI at age 25 (Model 2<sup>b</sup>) slightly attenuated the HR in several weight change categories among white men and African American men and women. Overall, the risk remained elevated in all weight change categories for all race-sex groups, and associations identified in Model 2<sup>a</sup> generally persisted in Model 2<sup>b</sup>.

Table 4 shows results from a different set of analyses that examined BMI and weight change as continuous variables and included the overall sample with the results adjusted for race and sex, as well as other variables. We showed results

with the race-sex groups combined because the trends were similar when examined using this approach, and confidence intervals in some subgroups were wide. There was an increased risk for incident diabetes associated with higher levels of BMI at age 25 and with higher levels of weight change after age 25. The first column shows the increase in the HR for each one unit increase in BMI and percent weight change, respectively. The last column shows the same HRs standardized for the difference between the BMI or weight change at the 85th compared to the 15th percentile value. Comparison of the 85th to the 15th percentiles, that is, 24.1 versus 19.5 kg/m<sup>2</sup> for BMI and 38.7% versus 1.5% for weight change, showed that the HR associated with weight change after age 25 was higher than that associated with BMI at age 25, and both increased when mutual adjustment was applied.

## Discussion

We showed that diabetes incidence after age 45 (*i.e.*, during mid- to older adulthood) was associated with both higher BMI at age 25 (*i.e.*, BMI at young adulthood) and greater subsequent weight gain between young and mid-adulthood periods in African American and white men and women. Also, among adults who were normal weight, white women had lower risk than white men and African

TABLE 3. INCIDENCE RATES PER 1000 PERSON-YEARS AND ADJUSTED HAZARD RATIOS AND 95% CONFIDENCE INTERVAL FOR ASSOCIATIONS OF BODY MASS INDEX AT AGE 25 AND SUBSEQUENT WEIGHT CHANGE WITH INCIDENT DIABETES BY RACE-SEX GROUPS, IN THE ATHEROSCLEROSIS RISK IN COMMUNITIES STUDY (1987-1998)

	White women (n=5,269)	African American women (n=1,756)	White men (n=4,585)	African American men (n=1,062)	p
Incidence rate (95% CI)	10.5 (9.5-11.5)*	26.3 (23.4-29.2)*	16.3 (14.9-17.6)*	24.5 (20.9-28.1)*	
BMI model (HR and 95% CI)					
Model 1 <sup>a</sup>					
Underweight	0.72 (0.45-1.13)	1.93 (1.18-3.16)*	1.95 (0.95-4.01)	2.11 (0.77-5.76)	0.1445
Normal weight	Ref.	2.46 (2.01-3.01)*	1.50 (1.20-1.87)*	2.13 (1.58-2.88)*	<0.0001
Overweight	2.05 (1.53-2.73)*	2.96 (2.02-4.34)*	2.23 (1.76-2.82)*	2.54 (1.69-3.83)*	<0.0001
Obese	2.62 (1.62-4.23)*	5.05 (3.08-8.29)*	2.64 (1.79-3.91)*	3.52 (1.84-6.73)*	<0.0001
Model 1 <sup>b</sup>					
Underweight	0.59 (0.38-0.94)*	0.60 (0.36-1.01)	1.51 (0.73-3.11)	0.95 (0.35-2.62)	0.9263
Normal weight	Ref.	1.57 (1.27-1.94)*	1.87 (1.50-2.34)*	2.57 (1.91-3.48)*	<0.0001
Overweight	2.13 (1.59-2.84)*	1.86 (1.26-2.75)*	3.51 (2.76-4.47)*	3.59 (2.39-5.41)*	<0.0001
Obese	4.43 (2.73-7.16)*	5.98 (3.63-9.82)*	4.91 (3.30-7.29)*	7.04 (3.66-13.57)*	<0.0001
Weight change model (HR and 95% CI)					
Model 2 <sup>a</sup>					
Weight losers	2.16 (1.12-4.15)*	4.21 (1.46-12.11)*	3.09 (1.75-5.44)*	2.36 (0.89-6.25)	0.0836
Weight maintainers	Ref.	2.99 (1.29-6.91)*	3.82 (2.42-6.03)*	4.66 (2.50-8.71)*	<0.0001
Moderate weight gainers	2.67 (1.74-4.11)*	6.42 (4.02-10.24)*	6.58 (4.25-10.19)*	8.99 (5.48-14.75)*	<0.0001
Large weight gainers	7.23 (4.89-11.28)*	10.60 (6.91-16.26)*	12.43 (7.89-19.58)*	14.01 (8.23-23.84)*	<0.0001
Model 2 <sup>b</sup>					
Weight losers	1.42 (0.73-2.75)	1.89 (0.65-5.52)	1.68 (0.95-2.99)	1.17 (0.44-3.10)	0.7602
Weight maintainers	Ref.	2.40 (1.03-5.56)*	2.56 (1.61-4.06)*	3.40 (1.81-6.36)*	<0.0001
Moderate weight gainers	2.77 (1.80-4.27)*	5.92 (3.71-9.44)*	5.07 (3.27-7.87)*	7.13 (4.34-11.72)*	<0.0001
Large weight gainers	7.73 (5.09-11.74)*	11.08 (7.22-17.00)*	11.39 (7.22-17.95)*	12.72 (7.47-21.65)*	<0.0001

BMI represents BMI at age 25 and included categories underweight (<18.5 kg/m<sup>2</sup>), normal weight (≥18.5 to <25.0 kg/m<sup>2</sup>), overweight (≥25 to <30 kg/m<sup>2</sup>), and obese (≥30 kg/m<sup>2</sup>). Weight change represents subsequent weight change after age 25 (as a percent change) and included categories weight losers (less than -3%), weight maintainers: included weight maintenance and small weight gain into one category due to small sample size (greater than or equal to -3% to <10%), moderate weight gainers (≥10% to <30%), large weight gainers (≥30%). Model 1<sup>a</sup> is adjusted for education, smoking status, alcohol consumption, and height at examination 1, smoking status at age 25 years, and age and physical activity measured from visit 1 through visit 4. Race-sex specific analyses use normal-weight white women as the reference group. Model 1<sup>b</sup> is adjusted for all variables listed in model 1<sup>a</sup>, in addition to percent weight change between visit 1 and age 25. Model 2<sup>a</sup> is adjusted for education, smoking status, alcohol consumption, and height at examination 1, smoking status at age 25 years, and age and physical activity measured from visit 1 through visit 4. Race-sex specific analyses use white women weight maintainers as the reference group. Model 2<sup>b</sup> is adjusted for all variables listed in model 2<sup>a</sup>, in addition to BMI at age 25.

\*Significant values.

CI, confidence interval; HR, hazard ratio.

TABLE 4. ADJUSTED HAZARD RATIO AND 95% CONFIDENCE INTERVALS FOR INCIDENT DIABETES BY BODY MASS INDEX AT AGE 25 AND SUBSEQUENT WEIGHT CHANGE CONTRASTING THE RISK AT THE 85TH VERSUS THE 15TH PERCENTILE OF THE EXPOSURE, IN THE ATHEROSCLEROSIS RISK IN COMMUNITIES STUDY (1987–1998)

	<i>HR (95% CI)<sup>a</sup></i>	<i>15th Percentile</i>	<i>85th Percentile</i>	<i>HR (95% CI)<sup>b</sup></i>
Models <sup>c</sup>				
BMI	1.06 (1.05–1.08)	19.65	26.05	1.47 (1.33–1.62)
Weight change	1.02 (1.02–1.03)	1.54	38.67	2.41 (2.16–2.29)
Model <sup>d</sup>				
BMI	1.11 (1.10–1.13)	19.65	26.05	1.97 (1.79–2.17)
Weight change	1.03 (1.03–1.03)	1.54	38.67	2.89 (2.59–3.11)

<sup>a</sup>HR and corresponding 95% CI for every 1 unit increase in BMI at age 25 or percent weight change and incident type 2 diabetes.

<sup>b</sup>HR and corresponding 95% CI of the comparison between the 15th and 85th percentile for BMI at age 25 or percent weight change and incident type 2 diabetes.

<sup>c</sup>Models are adjusted for education, smoking status, alcohol consumption, and height at examination 1, smoking status at age 25 years, and age and physical activity measured from visit 1 through visit 4, race, and sex.

<sup>d</sup>Model is adjusted for all variables listed in model 1, in addition to mutual adjustments of BMI at age 25 or percent weight change.

American men and women. Similarly, among weight maintainers, white women were at the lowest risk. This difference in risk estimated the impact of factors other than excess BMI and weight gain, and showed that associations of those factors with diabetes incidence varied by race-sex groups. We also showed that, both with and without mutual adjustment, having a relatively large weight gain after age 25 (*i.e.*, weight gain at the 85th percentile of the entire sample) compared to gaining a relatively small amount of weight (at the 15th percentile in this sample) was associated with greater diabetes risk in later adulthood than having a relatively high (85th percentile) versus a relatively low (15th percentile) BMI at age 25. This same type of comparable summary statement could have been made using standardized regression coefficients ( $\beta$ /standard deviation<sup>40</sup>), but we chose to use percentiles because standardized regression coefficients are more susceptible to bias from outliers.

The positive associations we observed between BMI at age 25 and incident diabetes at age 45 or older are consistent with findings from previous studies assessing the impact of young adulthood BMI on later diabetes risk in predominantly white cohorts.<sup>11,17,19,21,22</sup> For instance, studies including mostly U.S. white men<sup>17,21</sup> reported that early adulthood BMI (around 18 or 21 years) was significantly positively associated with risk for diabetes after the midlife period with estimates ranging from 1.1 to 3.3 and 1.4 to 6.0, respectively, in various groups with elevated BMI compared to the reference BM category. Similarly, Schmidt et al. showed that the association of BMI in 22-year-old Danish men with subsequent diabetes development ranged from 3.1 to 8.2 across elevated BMI categories.<sup>19</sup> Another study from Europe modeling BMI at age 25 suggested that the associated risk for diabetes ranged from 1.11 to 1.15 per BMI unit for European women and men.<sup>11</sup>

Several of the studies examined both BMI and subsequent weight change during the young-to-mid-adulthood period.<sup>11–13,17,21,22,32</sup> These studies found that both factors increased the risk, and that a larger weight gain<sup>13,17,21,22</sup> tended to increase risk regardless of whether BMI in young adulthood was in the normal, overweight, or obese range. However, none of the studies used standardized BMI or weight gain to provide comparisons of the relative size of associations with incident diabetes, as we did in this study. Also, few other studies provided estimates in African Americans.<sup>15,18</sup>

Krishnan et al. focused on weight status at age 18 in African American women and examined weight gain and diabetes incidence occurring over an 8-year period that started when the women were between 21 and 69 years of age.<sup>18</sup> They found women with BMI levels of 20 and above at age 18 were at increased risk of diabetes development before, but not after, adjusting for BMI in later life. A weight gain of more than 5 kg was also associated with increased risk of diabetes development, both before and after adjusting for BMI at age 18. Wei et al. studied men and women combined and found that the relative risk associated with 5 U increments of BMI was 1.29 in blacks and 1.37 in whites who were 30–45 years of age at baseline and followed for diabetes development for ~12 years.<sup>15</sup>

Across all these studies, the mathematical form or categories in which BMI and weight change were studied and the comparison or reference category used were defined in a variety of ways. The majority of studies looking at the influence of weight change used absolute weight change, whereas we used percent weight change because we believe that the impact of given amount of weight change on diabetes incidence would not be expected to be equivalent in a person who is small compared to one who is large, and a 5%–10% weight change is frequently cited in the literature to be the amount of change needed to have important health consequences.<sup>41</sup> Covariate sets included in the analytical models also differed between studies as did follow-up time.

It is a strength of this work that we studied BMI at age 25 and a weight change window between young and mid-adulthood, which has been suggested as a critical age of rapid weight gain and influential for risk of diabetes.<sup>8,11</sup> Another strength is that we studied a relatively large cohort of African American and white men and women with regular follow-up data from repeated assessments. Our study is the first to separately study these four race-sex groups and show the separate prospective associations of both BMI in young adulthood and subsequent weight change on incident diabetes. By designating one race-sex group to provide the reference in our analyses, we conveyed the higher risk of diabetes by both race-sex groups and weight-related variables. We do not claim that the use of a single reference group rather than a different, within-group, reference is a better way to conduct this analysis; rather, it is a valid alternative strategy that answers a slightly different question, provides a different perspective, and has public health

relevance. Similarly, we produced a standardized comparison of the diabetes risk associated with two different weight-related exposures using percentiles. This is a well-known approach, but we have not seen it previously applied to this problem. We believe our use of these subtly different types of estimates adds to this literature, and may be useful to policy makers who need a variety of types of information for decision making.

Our study has several limitations. Sample sizes in African Americans were smaller than in whites. Also, we were not able to account for many potentially important covariates at age 25 other than smoking status. Furthermore, we did not have information on several other metabolic risk factors (e.g., total cholesterol, low-density lipoprotein, and fasting plasma glucose) during the young adulthood period, which could contribute to the later development of diabetes.<sup>42</sup> Our study, like several others,<sup>11,17,21,22,32</sup> had to rely on recalled weight at age 25 years. Studies have shown that in adults, current self-reported weight and measured weight are correlated with  $r > 0.9$ ,<sup>43–46</sup> and in the African Americans and whites in the Charleston Heart study, the correlation between 28-year recall of weight with weight measured at that time was 0.82.<sup>43</sup> Nevertheless, we admit that measured weights provide stronger data. Our study had substantial variation in the time elapsed between the weight information assessed at age 25 and the following baseline visit weight assessment to quantify weight change, and this likely introduced error. Finally, our study design dictated exclusion of prevalent diabetes cases at the beginning of the follow-up period. This approach is consistent with previously published studies,<sup>11,17,21,32</sup> but, needs to be considered in the interpretation of results.

This study, along with many others, points to the importance of prevention of excess BMI in early adulthood and subsequent weight gain between early and mid-adulthood to prevent the incidence of diabetes at later ages. Our results highlighted these issues as contributing to, but not totally explaining, racial disparities in diabetes incidence. Comparing the average HRs across our combined racially diverse, community-based sample, weight gain was a more potent risk factor for development of diabetes at middle or older age than was BMI at age 25. We conclude more studies are needed to better understand the role of obesity and weight gain across the lifespan and the development of diabetes in African Americans. Nevertheless, diabetes prevention strategies and guidelines should emphasize on weight gain as one of the key risk factors, and pursue nutritional and physical activity interventions that are effective and help maintain a low body weight throughout the lifespan in this high-risk population.

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## Author Disclosure Statement

No competing financial interests exist.

## Disclaimer

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