Journal of the American Heart Association

ORIGINAL RESEARCH

Quantifying the Sex-Race/Ethnicity-Specific Burden of Obesity on Incident Diabetes Mellitus in the United States, 2001 to 2016: MESA and NHANES

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BACKGROUND: Given the increasing prevalence of diabetes mellitus (DM) in the United States, estimating the effects of population-level increases in obesity on incident DM has substantial implications for public health policy. Therefore, we determined the population attributable fraction, which accounts for the prevalence and excess risk of DM associated with obesity.

METHODS AND RESULTS: We included non-Hispanic White, non-Hispanic Black, and Mexican American participants without DM at baseline from MESA (Multi-Ethnic Study of Atherosclerosis) with available data on body mass index and key covariates from 2000 to 2017 to calculate unadjusted and adjusted (age, study site, physical activity, diet, income, and education level) hazard ratios (HR) for obesity-attributable DM. We calculated national age-adjusted prevalence estimates for obesity using data from NHANES (National Health and Nutrition Examination Survey) in 4 pooled cycles (2001–2016) among adults with similar characteristics to MESA participants. Last, we calculated unadjusted and adjusted population attributable fractions from the race/ethnic and sex-specific HR and prevalence estimates. Of 4200 MESA participants, the median age was 61 years, 46.8% were men, 53.9% were non-Hispanic White, 32.9% were non-Hispanic Black, and 13.3% were Mexican. Among MESA participants, incident DM occurred in 11.6% over a median follow-up of 9.2 years. The adjusted HR for obesity-related DM was 2.7 (95% CI, 2.2–3.3). Adjusted population attributable fractions were 0.35 (95% CI, 0.29–0.40) in 2001 to 2004 and 0.41 (95% CI, 0.36–0.46) in 2013 to 2016, and greatest among non-Hispanic White women.

CONCLUSIONS: The contribution of obesity towards DM in the population remains substantial and varies significantly by race/ethnicity and sex, highlighting the need for tailored public health interventions to reduce obesity.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifiers: NC00005487, NCT00005154.

Key Words: diabetes mellitus ■ obesity ■ population attributable fraction

Diabetes mellitus (DM) is a major public health problem with ≈13% of adults in the United States diagnosed with DM in 2018.[1] DM prevalence nearly doubled between 1990 and 2012,[2] and there has been a recent increase in DM-related complications, including amputations, hyperglycemic crises, hospitalizations, and deaths.[3] The prevalence of DM- and age-adjusted mortality rates for DM are higher among non-Hispanic Black (NHB) and Hispanic individuals compared with non-Hispanic White (NHW) individuals.[4–6] Furthermore, DM incidence continues to rise among NHB and Hispanic individuals, while they have plateaued in NHW individuals.[2]

Given the morbidity and mortality associated with DM, it is important to target factors that contribute to its growth. Obesity is recognized by the American

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For Sources of Funding and Disclosures, see page 9.

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CLINICAL PERSPECTIVE

What Is New?

- Approximately 30% to 53% of incident diabetes mellitus (DM) can be attributed to obesity in the United States.
- The burden of obesity on incident DM has remained elevated over the past 2 decades indicating that obesity continues to be a major driver of DM.
- Obesity-attributable DM varies by sex-race/ethnicity with non-Hispanic White women demonstrating the highest burden of obesity.

What Are the Clinical Implications?

- Current approaches in reducing the burden of DM associated with obesity have not been effective; targeted public health and policy changes are needed to reduce the population burden of obesity and prevent new cases of DM.

Nonstandard Abbreviations and Acronyms

AHA	American Heart Association
DM	diabetes mellitus
MA	Mexican American
MESA	Multi-Ethnic Study of Atherosclerosis
NHANES	National Health and Nutrition Examination Survey
NHB	non-Hispanic Black
NHW	non-Hispanic White
PAF	population attributable fraction

College of Cardiology, American Heart Association, and the American Diabetes Association as an important risk factor for DM.[7,8] Reducing obesity prevalence could have meaningful impacts on DM prevention. The population attributable fraction (PAF) quantifies this potential impact as it accounts for both the prevalence of a risk factor and the excess risk of the disease associated with the risk factor. Specifically, PAF estimates the proportion of an outcome that can be attributed to an exposure assuming complete elimination or prevention of the exposure from the population.[9] While prior studies have reported PAF estimates in various populations,[10–15] contemporary PAF estimates of DM attributable to obesity and their longitudinal trends in the United States are lacking.

Given the increasing prevalence of obesity in the United States and the differential risk for DM associated with obesity among sex and race/ethnicity subgroups, we aimed to determine the population burden of obesity on incident DM, or PAF, from 2001 to 2016 among US adult subgroups. We leveraged the strengths of 2 data sources: (1) MESA (Multi-Ethnic Study of Atherosclerosis), a longitudinal observational cohort study, to quantify the hazards of incident DM associated with obesity; and (2) NHANES (National Health and Nutrition Examination Survey), a nationally representative survey, to obtain population prevalence estimates. Furthermore, given the concerning increases in the prevalence of both obesity and DM in the United States,[2,16] we also investigated whether the population burden has changed over time.

METHODS

Data Set and Analytic Code Availability

A limited MESA data set is publicly available to any researcher through BIOLINCC (https://biolincc.nhlbi.nih.gov/home/); comprehensive data with up-to-date follow-up is available with an approved proposal (https://www.mesa-nhlbi.org/). NHANES data are publicly available through the National Center for Health Statistics at https://wwwn.cdc.gov/nchs/nhanes/Default.aspx. Code will be made freely available to any who request it.

Study Population

MESA

MESA is a longitudinal study of adults aged 45 to 84 years free of clinical cardiovascular disease at recruitment (2000–2002). Data were collected during 5 visits (2000–2017) at 6 centers across the United States. All participants provided written informed consent. Details on the MESA protocol are described in detail elsewhere.[17] S.S.K. had full access to the data and takes responsibility for its integrity and data analysis. The institutional review board of each institution (clinical trial number: NCT00005487) approved the MESA study, and informed consent was obtained before participation. Procedures followed were in accordance with institutional guidelines.

NHW, NHB, or Mexican American (MA) MESA participants aged 45 to 79 years at enrollment were included to ensure comparability with NHANES participants. Participants were required to be free of DM at baseline and to have available follow-up data (N=4200). DM was defined as a fasting glucose level ≥126 mg/dL, self-reported DM, or self-reported use of insulin or hypoglycemic medications (Figure 1).

Incident DM was defined as any observed DM case (untreated or treated) through examination 5 assessed at each follow-up visit. Time to DM was defined as time from examination 1 to the examination where treated

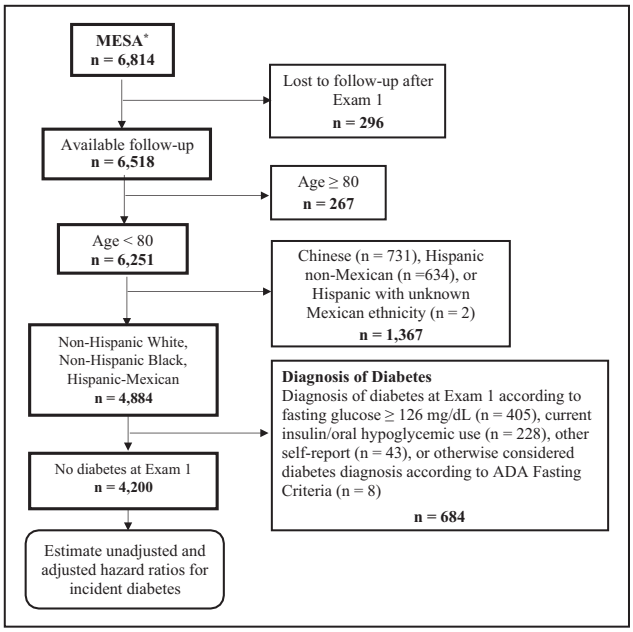

Figure 1. Study population for MESA (Multi-Ethnic Study of Atherosclerosis) utilized.
Participants from MESA were included if they had available follow-up data, were aged <80 years, were non-Hispanic White, non-Hispanic Black, or Hispanic-Mexican, and did not have diabetes mellitus (DM) at examination 1. ADA indicates American Diabetes Association.

or untreated DM was first observed. For patients without incident DM, censoring time was defined as time from examination 1 to the last attended examination or to examination 5 (2010–2011). Height and weight, measured at the first visit, were used to calculate body mass index (BMI).

Covariates of interest included baseline age, MESA site, diet, income, education, and physical activity. Diet was quantified by summing the number of self-reported AHA Healthy Diet Components[18] ranging from 0 to 5. Income was dichotomized as annual family income <$50 000 per year versus ≥$50 000 per year, education as less than high school versus at least a high school education, and physical activity as total moderate and vigorous activity (metabolic equivalent–min per week).[19]

NHANES

NHANES performed cross-sectional, biennial surveys assessing the health of the US population through questionnaires and examination data.[20] Two-year cycles were pooled to create 4 groups of NHANES cycles (2001–2004, 2005–2008, 2009–2012, and 2013–2016). We restricted the analytic sample to participants aged 45 to 79 years with a self-reported race/ethnicity of NHW, NHB or MA, and no cardiovascular disease (Figure 2) to match that of MESA. Although MESA participants with DM at baseline were excluded from the analysis, it was necessary to include NHANES participants with and without DM as required for the calculation of PAF.[9] Measured height and weight were used to calculate BMI; DM was defined as fasting glucose ≥126 mg/dL, use of insulin or other DM medication, or other self-reported DM diagnosis. Fasting glucose measurements were only available for some participants as a result of the study design of NHANES. Participants diagnosed with DM aged <30 years who began insulin treatment within 1 year of that diagnosis were considered to have type 1 DM.[21] All other participants with DM were classified as having type 2 DM. Cardiovascular disease was defined as a self-reported diagnosis of congestive heart failure, coronary heart disease, angina/angina pectoris, heart attack, or stroke.

Statistical Analysis

Incidence of DM in MESA

Baseline characteristics of MESA participants were described using mean (SD) for continuous measures and prevalence for categorical measures. We used Cox proportional hazards models to obtain unadjusted and adjusted hazard ratios (HRs) of obesity on incident DM fit in the overall sample and within each sex-race/ethnicity group. We visually tested and confirmed that the proportionality assumption was met for obesity in the Cox proportional hazards regression models. Reference groups were participants with a BMI <30 kg/m^2. Models fit within sex-race/ethnicity groups were adjusted for age, study site, physical activity, diet, income, and education level, and models fit in the overall study population were further adjusted for race/ethnicity and sex. Missing values for some covariates, physical activity (0.3% missing), diet (4.5% missing), income (4.0% missing), and education (0.4% missing), were imputed 10 times by multivariate fully conditional specification methods using PROC MI (SAS version 9.4, SAS Institute Inc),[22] using predictive mean matching for continuous covariates and the discriminant function method for categorical covariates. All presented adjusted estimates and CI were combined using Rubin rules.[23]

Prevalence of Obesity in NHANES

Weighted prevalence estimates for categorical and weighted means for continuous characteristics of the entire pooled NHANES study population (2001–2016) were calculated. Crude prevalence rates of obesity overall and among participants with DM were estimated in each pooled group of NHANES survey cycles. Four-year and 16-year sample weights were created from examination sampling weights following the NHANES analytic guidelines,[24] to calculate population-level

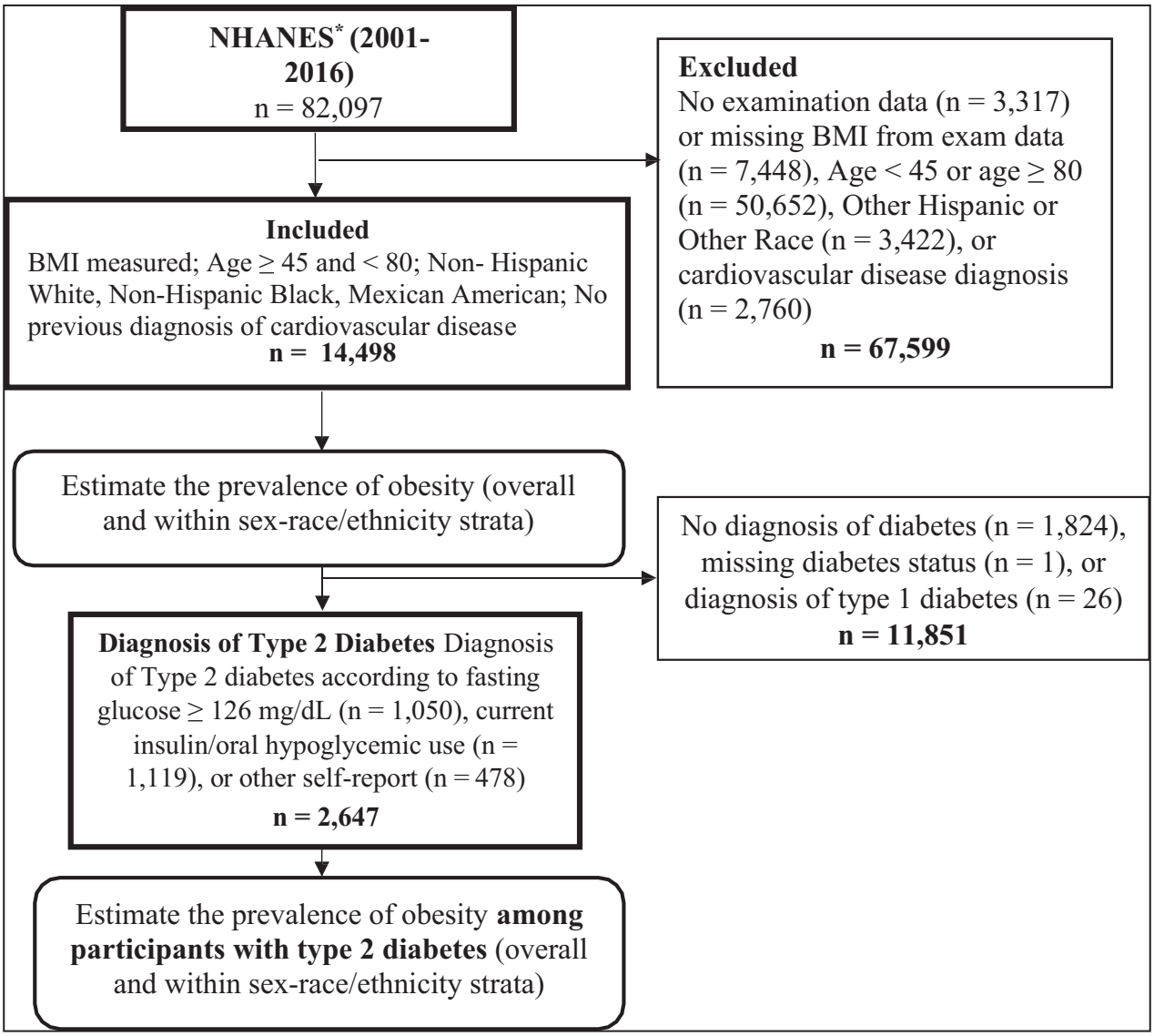

Figure 2. Study population for all continuous cycles of the NHANES (National Health and Nutrition Examination Survey) utilized (2001–2016).
Participants from NHANES were included if they had characteristics similar to those in the Multi-Ethnic Study of Atherosclerosis (aged 45–80 years; non-Hispanic White, non-Hispanic Black, or Mexican American; and no current diagnosis of cardiovascular disease). DM indicates diabetes mellitus.

estimates for each 4- or 16-year period. These weights account for unequal probability of selection resulting from the sample design and planned oversampling of certain subgroups. Taylor series linearization estimated standard errors of all prevalences.

Population Attributable Fractions

Estimates from MESA and NHANES were combined to quantify unadjusted and adjusted PAFs of obesity on DM in NHW, NHB, and MA participants aged 45 to 79 years using equations 1 and 2, respectively. RR_{MESA} and RR^{*}_{MESA} respectively represent the unadjusted and adjusted relative risks of DM. $P(E)_{NHANES}$ and $P(E|D)_{NHANES}$ respectively represent the probability of obesity overall and among participants with DM and, as a result, our sample from NHANES included participants with prevalent DM. HRs from Cox modeling in MESA data were assumed to approximate the relative risk (RR).

$$PAF_{unadj} = \frac{P(E)_{NHANES} * (RR_{MESA} - 1)}{P(E)_{NHANES} * (RR_{MESA} - 1) + 1} \quad (1)$$

$$PAF_{adj} = P(E|D)_{NHANES} * \frac{RR^{*}_{MESA} - 1}{RR^{*}_{MESA}} \quad (2)$$

We used 1000 Monte Carlo simulations to combine uncertainty in estimates to report 95% CIs for PAFs.[9,25,26]

Race/ethnicity and sex were a priori hypothesized to be effect modifiers. Thus, all analyses (in MESA, NHANES, and combined) were tested for effect modification, and stratified results were presented as appropriate. We used linear regression weighted by the inverse of the standard error of the PAF estimates to assess trends in PAF over time overall and within each sex-race/ethnicity subgroup. Analyses were completed using R version 3.6.1[27] or SAS version 9.4.[22]

RESULTS

Demographics

Among 4200 MESA participants, 46.8% were men, 53.9% were NHW, 32.9% were NHB, and 13.3% were MA. The median age was 61.0 years and median BMI was 27.9 kg/m^2. MESA and NHANES participants had a similar distribution by sex and BMI (Table 1). In both groups, a greater proportion of participants with obesity had an annual income <$50 000 and were more likely to be NHB and MA. However, the MESA cohort included a smaller proportion of NHW participants and a lower average fasting glucose than NHANES participants.

Table 1. Baseline Characteristics of Included MESA Participants and Characteristics of Continuous NHANES* Participants From All Cycles Utilized (2001–2016), Stratified by Obesity Status

	MESA		NHANES*	
	BMI <30 kg/m^2	BMI ≥30 kg/m^2	BMI <30 kg/m^2	BMI ≥30 kg/m^2
No.	2788	1412	8635	5863
Age, y†	61.6 (9.7)	59.7 (9.2)	57.74	57.51
Race/ethnicity, %				
NHW	59.9	41.9	85.1	78.7
NHB	28.4	41.6	9.6	14.0
MA	11.6	16.5	5.4	7.3
Sex, %				
Men	49.5	41.5	48.6	44.0
Women	50.5	58.5	51.4	56.0
Site, %				
Winston Salem, NC	21.0	21.0	NA	NA
New York, NY	11.1	11.5	NA	NA
Baltimore, MD	18.8	21.5	NA	NA
Twin Cities, MN	17.3	21.7	NA	NA
Chicago, IL	19.4	12.8	NA	NA
Los Angeles, CA	12.3	11.5	NA	NA
Income, %‡				
Low	48.7	56.9	38.0	42.1
High	51.3	43.1	62.0	57.9
Education, %				
Less than high school	10.9	11.6	14.3	15.6
High school or above	89.1	88.4	85.7	84.4
BMI, kg/m^2‡	25.6 (2.8)	34.5 (4.2)	25.32	35.67
Moderate to vigorous physical activity (MET–min/wk)†	6411 (6327)	6050 (6019)	NA	NA
No. of AHA Healthy Diet Components†	1.5 (1.0)	1.3 (0.9)	NA	NA
Fasting glucose, mg/dL†,§	87.4 (9.8)	91.7 (10.7)	104.05	116.45

AHA indicates American Heart Association; BMI, body mass index; MA, Mexican American; MET, metabolic equivalent; NA, not available; NHB, non-Hispanic Black; and NHW, non-Hispanic White.

*Estimates presented are from NHANES (National Health and Nutrition Examination Survey) participants from 2001 to 2016 (see Figure 2). Estimates are weighted to account for survey design.

†For continuous variables, mean (SD) are reported for MESA (Multi-Ethnic Study of Atherosclerosis) and weighted mean is reported for NHANES.

‡Income is defined differently for MESA and NHANES as a result of differences in income categorization by cohort. Low income is defined as an annual family income <$50 000 for MESA participants and an annual family income <$45 000 for NHANES participants. Likewise, high income is defined as an annual family income of at least $50 000 for MESA participants and at least $45 000 for NHANES participants.

§Fasting glucose is only available for a subset of NHANES participants, so reported means correspond to 4078 participants without obesity and 2721 participants with obesity.

HRs of Incident DM Associated With Obesity From MESA

Overall incidence of DM was 11.6% over a median follow-up of 9.2 years, and was higher among participants with obesity (20.0%) compared with participants without obesity (7.3%). Table 2 presents the unadjusted and adjusted HRs of incident DM in participants with versus without obesity. The overall adjusted HR of incident DM was 2.7 (95% CI, 2.2–3.3). Among men, point values for unadjusted and adjusted HRs were greatest for MA men and, among women, they were greatest for NHW women. For each race/ethnicity-sex group, unadjusted and adjusted HRs were overall similar to each other.

Prevalence of Obesity

Table 3 shows the prevalence estimates from NHANES used to calculate PAFs. Briefly, from the 2001 to 2004 to the 2013 to 2016 survey cycles, the overall prevalence of obesity increased from 34% (95% CI, 32%–37%) to 41% (95% CI, 39%–44%), respectively, and was consistently higher among those with DM. Among women, the prevalence of overall obesity was lower among NHW compared with NHB and MA participants. Overall obesity prevalence among men and obesity prevalence among participants with DM were similar among race/ethnicity subgroups. The greatest difference in obesity prevalence between all participants and those with DM was observed for NHW women.

PAF for Obesity-Related Incident DM

PAFs for obesity-related incident DM in the entire analytic sample ranged from 0.39 (95% CI, 0.37–0.42) to 0.44 (95% CI, 0.41–0.47) (unadjusted) and from 0.35 (95% CI, 0.29–0.40) to 0.41 (95% CI, 0.36–0.46) (adjusted) (Table 4). There were no statistically significant linear trends detected over the study period overall or within sex-race/ethnicity subgroups (data not shown). Nonetheless, within each sex-race/ethnicity group, point estimates of PAF increased over time except for in NHW men, where PAF remained stable. MA men showed the greatest absolute increase in PAF, increasing from 0.22 (95% CI, 0.12–0.33) in 2001 to 2004 to 0.38 (95% CI, 0.25–0.5) (adjusted) in 2013 to 2016.

Risk of DM attributable to obesity differed by sex and race/ethnicity. Point values for unadjusted and adjusted PAFs were greatest among NHW women. Among men, unadjusted PAFs were greatest for MA men. However, this pattern was not consistently observed for adjusted PAFs.

DISCUSSION

The present study leveraged longitudinal data from a well-phenotyped observational cohort (MESA) and serial cross-sectional data from a nationally representative cohort over time (NHANES cycles between 2001 and 2016) to provide robust and contemporary estimates of the population burden of obesity (BMI ≥30 kg/m^2) on incident DM, which ranged from 30% to 53% in the most recent period (2013–2016). Notable differences in DM attributable to obesity existed among sex-race/ethnicity subgroups with NHW women consistently demonstrating the highest PAFs overall, despite this group having the lowest prevalence of obesity. While point estimates for PAF tended to increase over time, no significant trends were noted. Our results emphasize the substantial burden of DM that could potentially be eliminated with optimization of weight and avoidance of obesity across the life course.

Our estimate for excess risk of DM attributable to obesity is in the same range as that obtained from the US Behavioral Risk Factor Surveillance System data in 2017 (37.8%); however, this study relied on

Table 2. Total Patient-Years and Unadjusted and Adjusted* HRs (95% CI) of Incident DM in Participants With Versus Without Obesity From MESA—Overall and Stratified by Sex and Race/Ethnicity

	Total, N	Incident DM, n	Total Follow-Up (Patient-Y)	Unadjusted HRs (95% CI)	Adjusted HRs (95% CI)
Overall	4200	486	32 826	2.9 (2.4–3.4)	2.7 (2.2–3.3)
Men					
NHW	1080	106	8603	2.4 (2.1–2.7)	2.5 (1.7–3.7)
NHB	608	89	4479	2.3 (2.0–2.6)	2.4 (1.6–3.7)
MA	277	52	2043	3.3 (2.8–4.0)	3.4 (1.9–6.3)
Women					
NHW	1182	87	9667	4.1 (3.6–4.7)	3.6 (2.4–5.6)
NHB	773	107	5935	2.2 (1.9–2.5)	2.1 (1.4–3.2)
MA	280	45	2098	2.3 (1.9–2.8)	2.4 (1.3–4.5)

DM indicates diabetes mellitus; HR, hazard ratio; MA, Mexican American; MESA, Multi-Ethnic Study of Atherosclerosis; NHB, non-Hispanic Black; and NHW, non-Hispanic White.

*Adjusted for age, study site, physical activity, diet, annual family income, and education level.

Table 3. Prevalence of Obesity Among NHANES Participants Aged 45 to 79 Years Overall and Among Those With Type 2 DM

	NHANES Pooled Cycle Years			
	2001–2004	2005–2008	2009–2012	2013–2016
Prevalence of obesity				
Overall	0.34 (0.32–0.37)	0.37 (0.34–0.39)	0.39 (0.36–0.42)	0.41 (0.39–0.44)
Men				
NHW	0.32 (0.29–0.35)	0.36 (0.32–0.40)	0.36 (0.32–0.40)	0.37 (0.34–0.41)
NHB	0.31 (0.26–0.36)	0.35 (0.30–0.40)	0.38 (0.35–0.42)	0.40 (0.35–0.46)
MA	0.34 (0.28–0.40)	0.33 (0.27–0.38)	0.41 (0.36–0.46)	0.44 (0.39–0.50)
Women				
NHW	0.34 (0.32–0.37)	0.35 (0.32–0.38)	0.37 (0.32–0.42)	0.41 (0.37–0.46)
NHB	0.50 (0.46–0.54)	0.54 (0.50–0.58)	0.59 (0.55–0.63)	0.59 (0.55–0.64)
MA	0.46 (0.39–0.53)	0.48 (0.42–0.54)	0.57 (0.51–0.63)	0.54 (0.50–0.58)
Prevalence of obesity among those with type 2 DM				
Overall	0.55 (0.49–0.61)	0.64 (0.60–0.69)	0.67 (0.61–0.74)	0.65 (0.60–0.70)
Men				
NHW	0.59 (0.50–0.67)	0.64 (0.55–0.72)	0.65 (0.54–0.76)	0.59 (0.49–0.70)
NHB	0.40 (0.27–0.53)	0.55 (0.45–0.65)	0.55 (0.47–0.63)	0.51 (0.41–0.61)
MA	0.32 (0.18–0.45)	0.44 (0.30–0.58)	0.59 (0.48–0.69)	0.53 (0.42–0.64)
Women				
NHW	0.56 (0.43–0.68)	0.70 (0.61–0.78)	0.74 (0.60–0.87)	0.73 (0.66–0.80)
NHB	0.58 (0.47–0.69)	0.68 (0.58–0.78)	0.75 (0.69–0.81)	0.74 (0.65–0.83)
MA	0.57 (0.43–0.70)	0.64 (0.49–0.78)	0.66 (0.54–0.79)	0.72 (0.61–0.83)

DM indicates diabetes mellitus; MA, Mexican American; NHANES, National Health and Nutrition Examination Survey; NHB, non-Hispanic Black; and NHW, non-Hispanic White. Estimates are presented for the entire population for each pooled cycle group and stratified by race/ethnicity and sex.

cross-sectional data with self-report of obesity and DM, which may introduce bias. In contrast, our study included measured height and weight and laboratory assessment of fasting plasma glucose levels with longitudinal follow-up.[28] Also in line with our findings, several studies conducted in Canada, South America, Asia, the Middle East, and Africa during the 2000s to 2010s demonstrated that the PAF for DM attributable to obesity is greater for women than for men.[11–14] To our knowledge, only 1 US study has previously quantified separate PAFs for incident DM attributable to obesity in distinct racial/ethnic groups. Based on historical NHANES III data from 1988 to 1994 for women alone, PAF was estimated to be greater for NHW (49.9%) compared with NHB (28%) women.[15] Further, no prior studies calculating PAFs have included Latinx participants in spite of the fact that this subgroup bears a disproportionately high burden of obesity and DM in the United States. Our results not only provide contemporary PAF estimates, but also highlight the need to report sex-race/ethnicity-specific obesity and DM statistics, and support future work investigating specific subpopulations at risk.

Differences in the population burden of obesity on incident DM among sex-race/ethnicity subgroups may be related to differences in: (1) the prevalence of obesity; and (2) the risk of incident DM among those with obesity. It is well established that the prevalence of obesity and DM are substantially higher in NHB and Hispanic individuals compared with NHW individuals.[4,29] Even more concerning, DM incidence and mortality are also higher among these groups.[2,5,6] These disparities are likely a result of the complex interplay of social determinants of health, including environmental, psychosocial, and healthcare-related factors.[30] Our study supports the higher prevalence of obesity among NHB and MA individuals compared with NHW individuals. Interestingly, we observed lower PAFs among NHB and MA men and women. These discrepancies may point to the important social determinants of health that contribute to incident DM in NHB and MA individuals in addition to obesity. Prior work has also shown that NHW women tend to accumulate more visceral adiposity, a type of fat specifically associated with insulin resistance,[31] than NHB women.[32–34] This may partially explain observed differences in PAFs among sex-race/ethnicity groups, but should not discount the contribution of individual and population-level socioeconomic factors that contribute to incident DM.

Given the morbidity and mortality associated with DM,[3] and the substantial cost associated with diagnosed DM in the United States ($327 billion in 2017),[35] it is important to identify and quantify the effects of modifiable risk factors that contribute to its population

Table 4. Unadjusted and Adjusted* PAFs of Obesity on Incident DM by Sex and Race/Ethnicity Among Patients Aged 45 to 79 Years for 4 Pooled Groups of NHANES Cycles

	NHANES Pooled Cycle Years			
	2001–2004	2005–2008	2009–2012	2013–2016
Unadjusted PAFs (95% CI)				
Overall	0.39 (0.37–0.42)	0.41 (0.38–0.44)	0.42 (0.39–0.45)	0.44 (0.41–0.47)
Men				
NHW	0.31 (0.29–0.34)	0.34 (0.31–0.36)	0.34 (0.31–0.36)	0.34 (0.32–0.37)
NHB	0.28 (0.25–0.31)	0.31 (0.28–0.34)	0.33 (0.30–0.36)	0.34 (0.30–0.38)
MA	0.44 (0.40–0.49)	0.43 (0.39–0.47)	0.49 (0.45–0.53)	0.51 (0.46–0.55)
Women				
NHW	0.52 (0.49–0.54)	0.52 (0.49–0.54)	0.54 (0.50–0.57)	0.56 (0.53–0.60)
NHB	0.38 (0.34–0.41)	0.40 (0.36–0.44)	0.42 (0.38–0.46)	0.42 (0.38–0.46)
MA	0.37 (0.32–0.43)	0.38 (0.33–0.44)	0.43 (0.37–0.49)	0.41 (0.36–0.47)
Adjusted PAFs (95% CI)				
Overall	0.35 (0.29–0.40)	0.41 (0.36–0.46)	0.42 (0.36–0.49)	0.41 (0.36–0.46)
Men				
NHW	0.35 (0.24–0.46)	0.38 (0.27–0.50)	0.39 (0.26–0.51)	0.36 (0.24–0.47)
NHB	0.23 (0.13–0.34)	0.32 (0.20–0.44)	0.32 (0.21–0.43)	0.30 (0.19–0.40)
MA	0.22 (0.12–0.33)	0.31 (0.19–0.44)	0.41 (0.28–0.55)	0.38 (0.25–0.50)
Women				
NHW	0.40 (0.29–0.52)	0.51 (0.40–0.61)	0.53 (0.40–0.66)	0.53 (0.43–0.63)
NHB	0.31 (0.18–0.43)	0.36 (0.22–0.51)	0.40 (0.25–0.55)	0.39 (0.24–0.55)
MA	0.33 (0.16–0.51)	0.38 (0.18–0.57)	0.39 (0.19–0.59)	0.42 (0.21–0.63)

DM indicates diabetes mellitus; MA, Mexican American; NHANES, National Health and Nutrition Examination Survey; NHB, non-Hispanic Black; and NHW, non-Hispanic White.

*Hazard ratio used in the calculation of the adjusted population attributable fraction (PAF) was adjusted for age, study site, physical activity, diet, annual family income, and education level.

growth. By quantifying the substantial and rising absolute burden of obesity on incident DM among distinct sex-race/ethnicity subgroups using the PAF, we highlight the meaningful impact that reducing obesity at a population level can have on DM prevention in the United States. The lack of a significant relative change in PAF further suggests that obesity continues to be the major driver of incident DM compared with other known risk factors, such as consumption of sugar-sweetened beverages (PAF, 8.7%)[36] and physical inactivity (PAF, 13%–29%),[37] despite current public health efforts. Therefore, reducing obesity in the United States should continue to be a priority. Our data can help inform public health policy and focus resources to enhance and support healthy lifestyles to decrease the population burden of obesity and, therefore, incident DM among all sex-race/ethnicity groups. Currently proposed public health efforts include increasing access to healthy foods, promoting physical activity, and increasing funding for the development of community programs aimed at primary prevention.[38] One successful example is the National Diabetes Prevention Program, now delivered at >1500 sites nationwide.[39] In addition, physicians and other healthcare providers in clinical settings must be better trained in patient-centered obesity care to reverse these unfavorable trends in metabolic health.

Our study is limited by the inclusion of only middle-aged to older adults without cardiovascular disease and, therefore, may not be generalizable to the US population at large. However, rates of DM among adults aged <45 years are extremely low (<5%) and we provide key estimates in sex-race/ethnicity groups that have previously been underrepresented in the literature.[4] In addition, we chose to examine the PAF for DM associated with baseline obesity and, therefore, our HRs may not represent the association of concurrent BMI at the time of onset of DM. Changes in obesity may contribute to DM risk and should be assessed in future studies. Our estimates are also subject to residual confounding, reflect associations, and do not confer causation. However, we reported both unadjusted and adjusted PAFs, with accompanying uncertainty estimates, calculated using appropriate and validated formulas to provide meaningful and interpretable estimates.[26]

A key assumption in our methods is that the relative risk of DM among our derivation cohort (MESA) applies to our target population (NHANES).[26] Therefore, we made rigorous efforts to meet all assumptions

needed for reliable PAF calculations[26] and included NHANES participants with similar demographic characteristics to MESA participants. However, we were unable to specifically match the MESA and NHANES participants by DM status because of the nature of the inputs needed for the PAF calculation. We needed to exclude MESA participants with DM at baseline to calculate incident DM, and had to include NHANES participants with and without DM to calculate the prevalence of obesity in each group.[9] This did lead to some heterogeneity among the populations. Differences were observed in racial/ethnic composition, education and fasting glucose. We accounted for these differences by calculating PAFs for each sex-race/ethnicity subgroup and controlling for education in our adjusted model. While differences in fasting glucose were observed, lower average levels in MESA likely reflects a "healthier" profile of those without DM and of those who participated in a cohort study rather than biologic differences in excess risk for DM attributable to obesity. Although difficult to predict, if truly derived from a healthier profile, the relative risk of DM from MESA might underestimate the risk in NHANES, therefore lowering our estimated PAF compared with the true value.

CONCLUSIONS

Our study provides longitudinal and contemporary estimates of excess risk of DM independently attributed to obesity and highlights the substantial burden of obesity on DM in the United States across time. Furthermore, disparities in obesity-attributable DM exist by sex-race/ethnicity. Public health and policy changes targeting obesity are needed to reduce the morbidity and mortality related to DM.

ARTICLE INFORMATION

Received August 2, 2020; accepted November 25, 2020.

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Acknowledgments

The authors thank the other investigators, the staff, and the participants in MESA for their valuable contributions. A full list of participating MESA investigators and institutions can be found at http://www.mesa-nhlbi.org.

Sources of Funding

Research was supported by grants from the National Institutes of Health (NIH)/National Heart, Lung, and Blood Institute (NHLBI) (KL2TR001424), the American Heart Association (AHA#19TPA34890060), and the NIH's National Center for Advancing Translational Sciences (NCATS) (KL2TR001424). The content is solely the responsibility of the authors and does not represent the official views of the NIH. MESA was supported by contracts 75N92020D00001, HHSN268201500003I, N01-HC-95159, 75N92020D00005, N01-HC-95160, 75N92020D00002, N01-HC-95161, 75N92020D00003, N01-HC-95162, 75N92020D00006, N01-HC-95163, 75N92020D00004, N01-HC-95164, 75N92020D00007, N01-HC-95165, N01-HC-95166, N01-HC-95167, N01-HC-95168, and N01-HC-95169 from the NHLBI, and by grants UL1-TR-000040, UL1-TR-001079, and UL1-TR-001420 from NCATS.

Disclosures

None.

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