The role of country of birth, and genetic and self-identified ancestry, in obesity susceptibility among African and Hispanic Americans

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ABSTRACT

Background: African Americans (AAs) and Hispanic/Latinos (HLs) have higher risk of obesity than European Americans, possibly due to differences in environment and lifestyle, but also reflecting differences in genetic background.

Objective: To gain insight into factors contributing to BMI (in kg/m^2) and obesity risk (BMI $\geq$ 30) among ancestry groups, we investigate the role of self-reported ancestry, proportion of genetic African ancestry, and country of birth in 6368 self-identified AA and 7569 HL participants of the New York–based Bio*Me* Biobank.

Methods: AAs and HLs are admixed populations that trace their genetic ancestry to the Americas, Africa, and Europe. The proportion of African ancestry (PAA), quantified using ADMIXTURE, was higher among self-reported AA (median: 87%; IQR: 79–92%) than among HL (26%; 15–41%) participants. Approximately 18% of AA and 59% of HL participants were non–US-born.

Results: Because of significant differences between sexes ($P_{\text{PAA}*\text{sex interaction}} = 4.8 \times 10^{-22}$), we considered women and men separately. Among women, country of birth and genetic ancestry contributed independently to BMI. US-born women had a BMI 1.99 higher than those born abroad ($P = 7.7 \times 10^{-25}$). Every 10% increase in PAA was associated with a BMI 0.29 higher ($P = 7.1 \times 10^{-10}$). After accounting for PAA and country of birth, the contribution of self-reported ancestry was small ($P = 0.046$). The contribution of PAA to higher BMI was significantly more pronounced among US-born (0.35/10%PAA, $P = 0.003$) than among non–US-born (0.26/10%PAA, $P = 0.01$) women ($P_{\text{PAA}*\text{sex interaction}} = 0.004$). In contrast, among men, only US-born status influenced BMI. US-born men had a BMI 1.33 higher than non–US-born men, whereas PAA and self-reported ancestry were not associated with BMI. Associations with obesity risk were similar to those observed for BMI.

Conclusions: Being US-born is associated with a substantially higher BMI and risk of obesity in both men and women. Genetic ancestry, but not self-reported ancestry, is associated with obesity susceptibility, but only among US-born women in this New York–based population. *Am J Clin Nutr* 2019;110:16–23.

Keywords: genetic ancestry, self-reported ancestry, country of birth, BMI, obesity, admixture

Introduction

Obesity is a major risk factor for common diseases, such as diabetes, cardiovascular disease, hypertension, and some cancers (1). More than 35% of adults in the United States are obese [BMI (in kg/m^2) $\geq$ 30], but the prevalence differs between populations of different ancestry (2, 3). Nearly half of all African-American adults (AAs; age-adjusted: 48.4%) and >40% of Hispanic/Latinos (HLs; 42.6%) are obese, as compared with 36.4% of European Americans (EAs), and differences across

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Supplemental Figure 1 is available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/ajcn/.

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Abbreviations used: AA, African American; ARIC, Atherosclerosis Risk in Communities; EA, European American; EHR, electronic health record; HL, Hispanic/Latino; MEGA, Multi Ethnic Genotyping array; OMNI, OmniExpress array; PAA, proportion of African ancestry; SNP, single nucleotide polymorphism.

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ancestries are more pronounced in women than in men (3). Although differences in environment including lifestyle, cultural, and social practices may explain—at least in part—the disparity across ancestries (4), differences in genetic ancestry may also predispose certain populations to obesity more than others (5, 6).

Traditionally, in large-scale epidemiological studies, ancestry is determined by self-report, even though ancestry may be ambiguous for some individuals. People's self-reported ancestry is based on their self-identification with a certain ancestral group, but it may or may not exactly correspond to their genetic ancestry. For example, individuals from Mexico and Puerto Rico may both self-report (or be classified) as HL in the United States, but have a vastly different genetic ancestry (7). Self-reported ancestry also represents a group's lifestyle, cultural norms and habits, health care access, etc., whereas genetic ancestry represents a population's innate biological features. Self-reported and genetic ancestry are both well-known contributors to disparities in disease burden in the United States (8–14). However, this disproportionate disease burden persists even after accounting for differences in relevant environmental factors, such as population-specific lifestyle, cultural norms, health care access, and socioeconomic status (9, 11–13, 15), indicative of genetic factors influencing the population-specific disease susceptibility.

The US population is a "melting pot" of nationalities, cultures, and ethnicities, as migrants have arrived from all over the world since the seventeenth century. These migrant populations have undergone recent genetic admixture, e.g., AAs exhibit up to 20% European ancestry and HLs in New York City exhibit up to 50% African ancestry (16). The European/African admixture in AA and HL populations allows for the disentanglement of the contributions of genetic and self-reported ancestry to disease susceptibility. For example, previous studies have shown that, among individuals who self-identify as AA, a higher proportion of West African ancestry is associated with higher BMI, in particular for women (17–19). So far, contribution of genetic ancestry to common diseases has been mostly studied in one admixed population at a time (17, 18, 20–22). Including multiple admixed populations, e.g., AAs and HLs, allows us to assess not only the role of genetic ancestry, but also the role of self-reported ancestry.

In this study, we aim to assess the extent to which genetic ancestry, self-reported ancestry, and country of birth contribute to variation in BMI and obesity risk among participants who self-identify as AA and HL and who show predominantly African and European admixture.

Methods

Population

The Mount Sinai Bio*Me* Biobank, founded in September, 2007, is an ongoing, broadly consented electronic health record (EHR)-linked bio- and data repository that enrolls participants nonselectively from the Mount Sinai Hospital patient population. The Mount Sinai Hospital is a large teaching and health care center located at the Upper East Side, near East and Central Harlem in Manhattan, New York. The hospital provides services to patients of neighboring areas, known to be of diverse ancestry, and serves as a referral center for primary care providers in and around New York City. Currently, the Bio*Me* Biobank has enrolled >45,000 participants. Bio*Me* participants represent a broad racial, ethnic, and socioeconomic diversity, with a distinct and population-specific disease burden, characteristic of the communities served by Mount Sinai Hospital. Participants are predominantly of AA (24%), HL (35%), EA (32%), and other ancestry (10%). Participants who self-identify as HL further report to be of Puerto Rican (39%), Dominican (23%), Central/South American (17%), Mexican (5%), or other Hispanic (16%) ancestry.

At the time of enrollment, participants consent to link their Biobank record and EHR, which captures a full spectrum of biomedical phenotypes, including clinical outcomes, covariates, and exposures. BMI is calculated as weight (kg) divided over height squared (m^2), using data from the EHR at the time of enrollment. Obesity is defined, using the WHO criteria, as BMI $\geq$ 30. Demographic information on ancestry, country of birth, lifestyle, and family history of disease is collected through an interviewer-administered questionnaire. Specifically, to assess people's self-reported ancestry, we asked the following 4 questions on their race and ethnicity: *1*) Are you Hispanic/Latino? [yes/no]; *2*) Which of the following best describes your heritage? [American Indian, Native American, or Alaskan Native/African American or African/Caucasian or white/Mediterranean/East or Southeast Asian/South Asian/Indian/Jewish/Native Hawaiian or other Pacific Islander/other]; *3*) Which of the following best describes your Hispanic/Latino heritage? [Dominican or Dominican descent/Central American or Central-American descent/Cuban or Cuban descent/Mexican or Mexican descent/Puerto Rican or Puerto-Rican descent/South American or South-American descent/other]; *4*) In addition to being of Hispanic/Latino heritage, which of the following categories would you use to describe yourself? [American Indian or Alaskan Native/Asian/Native Hawaiian or other Pacific Islander/black or African American/white/unknown or not reported]. We refer to non–US-born individuals as those born outside the 50 states and Washington DC. Lastly, as part of enrollment, participants' blood is drawn and their plasma and DNA are extracted. All procedures are in accordance with the ethical standards of the Mount Sinai Institutional Review Board Committee.

Genotyping data

Participants were genotyped using the Illumina Infinium Multi Ethnic Genotyping Array (MEGA) and Illumina OmniExpress (OMNI) array. Briefly, Bio*Me* participants (n = 12,749) of multiple ancestries were genotyped on the Illumina Infinium OmniExpress plus HumanExome array, with 11,212 participants and 866,864 single-nucleotide polymorphisms (SNPs) available for downstream analysis after quality control steps such as call rate <95%, plate failure, and deviance in heterozygosity levels (23). A further 12,686 Bio*Me* samples, genotyped on the MEGA (1,402,653 variants after quality control), were also available for analysis (23).

To merge data ascertained across different platforms we used the PLINK1.9 software to remove all individuals who were duplicated across the OMNI and MEGA data (n = 273 individuals included as intentional duplicates on MEGA, and an additional 2,215 individuals who had been genotyped on

both platforms). Then, we obtained the intersection of autosomal sites on both platforms (n = 461,677 SNPs; n = 21,692 individuals), while simultaneously merging with samples from the Human Genome Diversity Project (http://www.hagsc.org/hgdp/, n = 986), and with other reference samples that were also genotyped on MEGA, namely, n = 303 individuals from the Peruvian Andes, n = 66 indigenous Central-American individuals from Honduras and Colombia, n = 45 Khonami/Nama samples from South Africa, n = 84 from Oaxaca, Mexico, and n = 24 Bari, n = 22 Warao, and n = 24 Yukpa from Venezuela. We intersected our data with sites extracted from the 1000 Genomes Project Phase 3 data (n = 395,531 sites were recovered) and merged the 1000 Genomes Project samples with our data (n = 2504). Finally, we removed palindromic sites (n = 7215 SNPs) and sites with a missingness rate > 1% (n = 517), leaving a total of 377,799 SNPs and 25,750 individuals.

Global ancestry estimation

For global ancestry estimation, genetic data were first filtered to a minor allele frequency >1% (n = 281,666 sites) using PLINK1.9. We also removed all sites that fell within genomic regions known to confound ancestry analysis in humans. This consisted of sites that fell within the human leukocyte antigens region (chr6:27,000,000–35,000,000; hg19), lactase (*LCT*) (chr2:135,000,000–137,000,000), ectodysplasin A receptor (*EDAR*) (chr2:109,000,000–110,000,000), T cell receptor β variable 9 (*TRBV9*) (chr7:142,000,000–145,000,000), a common inversion on chromosome 8 (chr8:6,000,000–16,000,000), Solute Carrier Family 25 (*SLCA25*) (chr15:48,000,000–49,000,000), and a region of long linkage disequilibrium in admixed populations on chromosome 17 (chr17:40,000,000–45,000,000). This resulted in the exclusion of a total of 5911 sites to leave a total of 275,755 SNPs. We also removed individuals inferred to be directly related (removed 1 individual of each pair) (direct relation being defined here as having a Pi hat > 0.2, as calculated via the "–genome" flag in PLINK1.9), and offspring from parent–offspring trios within our Andean reference panel (n = 100), leaving a total of 23,414 individuals.

We used these data as input for ADMIXTURE. To capture Bio*Me* population structure that was not represented in the reference panels, we ran ADMIXTURE across all unrelated Bio*Me* samples and on reference panels combined, unsupervised for up to k = 16 with 5-fold cross-validation.

Our study aimed to assess the contribution of genetic African ancestry to variation in BMI. Thus, we used admixture analysis results from calculations done using k = 2 putative populations which principally distinguish African from non-African ancestry. Furthermore, although the majority of individuals who self-identified as HL in our population sample showed African–European admixture, we used admixture results from k = 3 putative populations (identifying the Native-American ancestral proportion in addition to the African-European) to exclude individuals with significant Native-American ancestry (>30%; n = 1275) (**Supplemental Figure 1**). Analyses were performed among a total of 13,937 genotyped AA (6368; 45.7%) and HL (7569; 54.3%) participants of the Bio *Me* Biobank.

Statistical analyses

Participant descriptive characteristics were compared between groups using t-tests for continuous and chi-square tests for categorical variables. Multiple linear regression was performed to test the association between BMI and proportion of African ancestry (PAA), ancestry, age, and US-born status. PAA × sex, PAA × self-reported ancestry, PAA × US-born status, and self-reported ancestry × US-born status interactions were examined in separate models, and analyses were stratified based on significance of interaction results. Models were subsequently stratified by sex, ancestry, and US-born status. A similar strategy was used for obesity as a dichotomous variable (defined as BMI ≥ 30 compared with BMI < 30), using logistic regression with the aforementioned covariates in the model. Statistical significance was determined with $P < 0.05$. All statistical analyses were performed in R statistical software version 3.3.2 (R Development Core Team).

Results

A total of 13,937 adults (age ≥ 18 y), 6398 of whom self-reported as AA and 7569 as HL, were included in our analyses. All individuals were enrolled in the New York City–based Bio*Me* Biobank, an ongoing EHR-linked bio- and-data repository that enrolls participants nonselectively from the Mount Sinai Medical Center patient population. The mean ± SD age was 51.3 ± 15.7 y, with HLs being ∼2–3 y older than AAs ($P_{t\text{-test}} < 1 \times 10^{-9}$). Overall, mean ± SD BMI of AAs (30.3 ± 7.8) was higher than that of HLs (29.5 ± 6.6) ($P_{t\text{-test}} = 1.9 \times 10^{-12}$), driven by the difference in women ($P_{t\text{-test}} = 8.0 \times 10^{-24}$) (**Table 1**). Correspondingly, obesity prevalence is higher among AA women (50.8%) than HL women (42.7%) ($P_{\text{chi-sq}} = 6.2 \times 10^{-14}$), with no significant difference among men (32.6% compared with 33.4%, $P_{\text{chi-sq}} = 0.54$).

AAs (82%) were twice as likely to be US-born as HLs were (41%). Of the 1144 non–US-born participants who self-reported as AAs, 24.6% were born in Jamaica, ∼10% each in Haiti and Trinidad and Tobago, and the others were born in other African and Caribbean countries. Of the 4483 non–US-born participants who self-reported as HLs, most were born in Puerto Rico (49.8%) or the Dominican Republic (36.9%).

We estimated proportions of continental genetic ancestry using ADMIXTURE and showed that both our AA and HL participants are predominantly African and European admixed. The PAA was significantly higher among those who self-reported as AAs (median 87%; IQR 79–92%) than among those who self-reported as HLs (25%; 15–41%) ($P_{\text{wilcoxon}} < 1 \times 10^{-300}$), with a wide range within each population (Table 1).

Using multiple linear regression analyses, we found that higher PAA, HL ancestry, US-born status, age, and sex were all independently associated with higher BMI (**Table 2**). Because the contribution of PAA to BMI was significantly different in women than men ($P_{\text{interaction}} = 4.8 \times 10^{-22}$), all subsequent analyses were stratified by sex.

Among women, genetic and self-reported ancestry, US-born status, and age were all independently associated with BMI (**Table 3**). Specifically, US-born women had a BMI 1.99 higher ($P = 7.7 \times 10^{-25}$, ∼5.1 kg) than non–US-born women; for every 10% higher PAA, BMI increased by 0.29 ($P = 7.1 \times 10^{-10}$,

TABLE 1 Descriptive characteristics of participants, by self-reported ancestry and sex[1]

	African-American women (n = 3924)	African-American men (n = 2444)	Hispanic women (n = 4671)	Hispanic men (n = 2898)	All (n = 13,937)
Age, y	50.2 ± 15.5	49.9 ± 14.2	52.3 ± 16.4	52.6 ± 15.6	51.3 ± 15.7
BMI, kg/m^2	31.6 ± 8.3	28.4 ± 6.5	29.9 ± 6.9	28.9 ± 6.0	29.9 ± 7.2
Weight, kg	84.9 ± 23.3	89.7 ± 22.3	76.2 ± 18.6	85.7 ± 19.3	83.0 ± 21.4
Height, cm	163.9 ± 7.2	177.7 ± 8.2	159.6 ± 7.1	172.5 ± 8.0	166.7 ± 10.2
Obesity (BMI ≥ 30 kg/m^2), %	50.8	32.6	42.7	33.4	41.3
PAA, %	87 (79, 92)	87 (79, 92)	27 (16, 42)	24 (14, 39)	57 (24, 86)
US-born, %	82.3	81.6	39.9	42.1	59.6

[1] Values are means ± SDs, medians (IQRs), or percentages. PAA, proportion of African ancestry.

equivalent to 0.74 kg for a 1.6-m–tall woman); self-reported HL ancestry was associated with a BMI 0.61 higher (P = 0.046, ∼1.56 kg) than for AA ancestry; and with every 10-y increase in age, BMI increased by 0.30 ($P < 3.8 \times 10^{-7}$, ∼0.77 kg/10 y). The contributions of country of birth, PAA, and age were most pronounced, whereas self-reported ancestry only reached nominal significance. Interaction analyses showed that the association between PAA and BMI was stronger in US-born than in non–US-born women ($P_{interaction}$ = 0.004). Specifically, for every 10% higher PAA, BMI increased by 0.35 (P = 0.003; ∼0.90 kg) in US-born women and by 0.26 (P = 0.10; ∼0.67 kg) in non–US-born women, whereas the contribution of self-reported ancestry was no longer significant in either US- or non–US-born women, when accounting for PAA and age (**Table 4**). This suggests that the lower BMI observed in HL than in AA women is likely due to a higher proportion of non–US-born status and a lower PAA among HL than among AA participants (Table 1).

Contributions of PAA, self-reported ancestry, and country of birth to risk of obesity as a dichotomous trait were generally consistent with associations observed for BMI as a continuous trait (**Tables 2–5**). Specifically, the odds of being obese were 1.55 times higher among US-born women than among those not born in the United States (Table 3). Furthermore, among US-born women, every 10% increase in PAA was associated with 1.10-fold higher odds of obesity.

Among men, only country of birth contributed significantly. BMI was 1.33 (∼4.1 kg for a 1.75-m–tall man) and the odds of obesity were 1.47 times higher among US-born men than among non–US-born men. PAA, self-reported race/ethnicity, and age did not contribute independently to BMI or risk of obesity.

Discussion

Consistent with observations from NHANES, Bio*Me* participants who self-identify as AA have a significantly higher BMI and risk of obesity than those who self-identify as HL—particularly among women. To examine which factors associate to the variation in BMI and obesity risk, we assessed the role played by genetic ancestry (PAA), self-reported ancestry (HL compared with AA), and country of birth (US-born compared with non–US-born).

Country of birth was the most significant contributor to variation in BMI and risk of obesity in both men and women; i.e., being born in the United States increased the odds of obesity by ∼1.5 compared with being born outside the United States. Once country of birth was accounted for, self-reported ancestry (HL compared with AA)—which may reflect differences in lifestyle, cultural norms and habits, and access to health care—did not significantly influence BMI or risk of obesity. Furthermore, genetic ancestry, assessed by PAA, showed a

TABLE 2 Contributions of PAA, self-reported ancestry, country of birth, age, and sex to BMI and obesity risk[1]

	BMI (kg/m^2)		Obesity risk	
	β ± SE	P value	OR (95% CI)	P value
Main effects				
PAA (per 10% increase in PAA)	0.14 ± 0.03	2.8×10^{-05}	1.05 (1.03, 1.07)	5.7×10^{-06}
Self-reported ancestry (HL = 1; AA = 0)	0.58 ± 0.23	0.011	1.23 (1.08, 1.41)	0.002
US-born status (US = 1; non-US = 0)	1.77 ± 0.14	2.2×10^{-35}	1.53 (1.41, 1.66)	2.5×10^{-24}
Age, y	0.02 ± 0.00	1.4×10^{-05}	1.00 (1.00, 1.01)	7.0×10^{-05}
Sex (women = 1; men = 0)	2.06 ± 0.12	1.2×10^{-62}	1.76 (1.64, 1.89)	1.70×10^{-54}
Interaction terms				
PAA × self-reported ancestry	−0.01 ± 0.08	0.88	1.00 (0.95, 1.04)	0.94
PAA × country of birth	0.07 ± 0.04	0.092	1.01 (0.99, 1.04)	0.25
Country of birth × self-reported ancestry	−0.39 ± 0.29	0.18	0.89 (0.75, 1.05)	0.18
PAA × sex	0.37 ± 0.04	4.8×10^{-22}	1.07 (1.05, 1.09)	3.6×10^{-09}

[1] n = 13,937. Statistics were obtained through multiple linear (BMI) and logistic (obesity) regression analyses. AA, African American; HL, Hispanic/Latino; PAA, proportion of African ancestry.

TABLE 3 Contributions of PAA, self-reported ancestry, country of birth, and age to BMI and obesity risk in men and women separately[1]

	BMI (kg/m^2)				Obesity risk			
	Women (n = 8595)		Men (n = 5342)		Women (n = 8595)		Men (n = 5342)	
	$\beta \pm$ SE	P value	$\beta \pm$ SE	P value	OR (95% CI)	P value	OR (95% CI)	P value
Main effects								
PAA (per 10% increase in PAA)	0.29 ± 0.05	7.1×10^{-10}	−0.06 ± 0.05	0.20	1.07 (1.05, 1.10)	1.2×10^{-8}	1.00 (0.97, 1.04)	0.83
Self-reported ancestry (HL = 1; AA = 0)	0.61 ± 0.31	0.046	0.61 ± 0.33	0.065	1.24 (1.06, 1.46)	0.009	1.23 (0.98, 1.54)	0.067
US-born status (US = 1; non-US = 0)	1.99 ± 0.19	7.7×10^{-25}	1.33 ± 0.2	2.9×10^{-11}	1.55 (1.40, 1.72)	3.2×10^{-17}	1.47 (1.28, 1.68)	4.4×10^{-8}
Age, y	0.03 ± 0.01	3.8×10^{-7}	−0.001 ± 0.006	0.86	1.01 (1.00, 1.01)	3.7×10^{-7}	1.00 (1.00, 1.00)	0.68
Interaction effects								
PAA × self-reported ancestry	−0.04 ± 0.11	0.72	0.04 ± 0.11	0.70	0.98 (0.93, 1.04)	0.63	1.02 (0.95, 1.10)	0.55
PAA × country of birth	0.17 ± 0.06	0.004	−0.07 ± 0.06	0.21	1.04 (1.01, 1.07)	0.019	0.98 (0.94, 1.02)	0.33
Country of birth × self-reported ancestry	−0.78 ± 0.40	0.49	0.23 ± 0.41	0.58	0.80 (0.65, 0.99)	0.04	1.05 (0.79, 1.39)	0.76

[1]Statistics were obtained through multiple linear (BMI) and logistic (obesity) regression analyses. AA, African American; HL, Hispanic/Latino; PAA, proportion of African ancestry.

TABLE 4 Contributions of PAA, self-reported ancestry, and age to BMI by sex and country of birth[1]

	Women				Men			
	US-born (n = 5095)		Non–US-born (n = 3500)		US-born (n = 3215)		Non–US-born (n = 2127)	
	$\beta \pm$ SE	P value	$\beta \pm$ SE	P value	$\beta \pm$ SE	P value	$\beta \pm$ SE	P value
PAA (per 10% increase in PAA)	0.35 ± 0.12	0.003	0.26 ± 0.16	0.096	−0.13 ± 0.12	0.27	0.001 ± 0.15	1.00
Self-reported ancestry (HL = 1; AA = 0)	0.47 ± 1.07	0.66	1.23 ± 1.38	0.37	0.30 ± 1.06	0.78	0.87 ± 1.37	0.53
Age, y	0.02 ± 0.01	0.002	0.03 ± 0.01	0.0005	0.00 ± 0.01	0.61	−0.01 ± 0.01	0.33

[1]Statistics were obtained through multiple linear (BMI) and logistic (obesity) regression analyses. AA, African American; HL, Hispanic/Latino; PAA, proportion of African ancestry.

TABLE 5 Contributions of PAA, self-reported ancestry, and age to obesity risk by sex and country of birth[1]

	Women				Men			
	US-born (n = 5095)		Non–US-born (n = 3500)		US-born (n = 3215)		Non–US-born (n = 2127)	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
PAA (per 10% increase in PAA)	1.10 (1.04, 1.16)	0.001	1.07 (0.96, 1.18)	0.21	0.99 (0.92, 1.06)	0.69	0.99 (0.86, 1.12)	0.83
Self-reported ancestry (HL = 1; AA = 0)	1.36 (0.81, 2.28)	0.25	1.46 (0.59, 3.61)	0.41	1.15 (0.61, 2.18)	0.67	0.98 (0.30, 3.17)	0.97
Age, y	1.01 (1.00, 1.01)	1.9×10^{-5}	1.00 (1.00, 1.01)	0.072	1.00 (1.00, 1.01)	0.43	0.99 (0.99, 1.00)	0.11

[1]Statistics were obtained through multiple linear (BMI) and logistic (obesity) regression analyses. AA, African American; HL, Hispanic/Latino; PAA, proportion of African ancestry.

significant association with BMI and risk of obesity, but only among women. Every 10% increase in PAA was associated with a higher risk of obesity, independent of the women's self-reported ancestry, and this association was more pronounced in US-born (OR: 1.10) than in non–US-born (OR: 1.07) women. Genetic ancestry did not influence BMI or obesity risk in men. Thus, the lower BMI and obesity risk observed among HL women than among AA women in the Bio*Me* Biobank appear to be driven by the fact that HL women are more often born abroad and have a lower PAA. Self-reported ancestry does not affect risk of obesity when country of birth and genetic ancestry are accounted for.

The role of country of birth in obesity risk corroborates findings of previous reports that have consistently shown that non–US-born individuals who have immigrated to the United States have a lower BMI and lower prevalence of obesity than do individuals born in the United States (24–32). Furthermore, previous studies have shown that the longer non–US-born individuals spend in the United States, the smaller the difference in BMI and obesity prevalence between non–US-born and US-born individuals becomes. After spending a decade in the United States, the average BMI of foreign-born and native-born individuals is the same (26, 29–31). These data support the notion that exposure to an American lifestyle, characterized by an abundance of highly palatable calorie-dense foods and low physical activity levels, increases the risk of obesity.

Besides country of birth, we found that genetic ancestry, assessed as PAA, associated significantly to BMI and obesity risk, but only among women. This observation is consistent with previous studies (17, 21, 33). For example, among self-reported AAs of the Atherosclerosis Risk in Communities (ARIC) study (n = 3531), the PAA was significantly ($P < 0.0001$) higher among obese individuals (85.7%) than among overweight (84.4%) and normal-weight (83.6%) individuals, and the correlation between PAA and BMI was +0.075 ($P = 8.7 \times 10^{-5}$) (21). No differences between men and women were reported (21). A more recent study, which combined a subset of the ARIC ($n = 1{,}611$) and Multi-Ethnic Study of Atherosclerosis (n = 2814) AA population, also found that higher African ancestry was associated with higher BMI, especially among women ($P_{\text{sex-interaction}} = 0.0005$), but this association only reached significance in ARIC ($P = 0.004$) (17). The Women's Health Initiative, which—like our study—included AA and HL women, found that a higher genetic African ancestry was associated with higher BMI among AA ($n = 11{,}712$, $P < 10^{-4}$) as well as HL (n = 5088, $P = 0.017$) women (33). Two smaller studies, however, found that higher PAA was associated with lower BMI in 145 AA women (18), whereas no association was observed in 64 Puerto Rican women (22). This inconsistency may be due to the fact that both studies used only a very small set of ancestry informative markers to access ancestry. Overall, our results, together with results from previous studies, provide evidence that genetic ancestry contributes to the variation in BMI and obesity risk, particularly among women.

In the Bio*Me* Biobank, BMI and the prevalence of obesity were substantially higher among women who self-identified as AA than among those who self-identified as HL, which is consistent with observations reported in other large-scale studies (3, 33–35). Interestingly, however, once genetic ancestry and country of birth were accounted for, self-reported ancestry did not contribute to the difference in BMI or obesity prevalence between these

2 populations. The lower BMI and prevalence of obesity in HL women were due to a lower PAA and higher frequency of being born abroad. A limitation to our study is the lack of data on socioeconomic status (income, education), which is known to influence obesity risk, and more so in women than in men (36). Because socioeconomic status may correlate with PAA, it may confound the relation between genetic ancestry and BMI. Further analyses are needed to indeed confirm or refute this.

Previous reports have shown that higher PAA is associated with lower waist-to-hip ratio and waist circumference among AA men, but not women (17). The lack of waist circumference measurements in the Bio*Me* Biobank precludes us from examining this relation. However, these findings confirm a sexual dimorphism of genetic ancestry on anthropometric outcomes. The differences observed for waist circumference and BMI suggest that the role of genetic ancestry is different between overall body size and body fat distribution.

By leveraging data of our large-scale, admixed, New York–based Bio*Me* Biobank, we show that the country of birth, representing level of acculturation and possibly adoption of an American lifestyle, is an important contributor to variation in BMI and obesity susceptibility. In women, genetic ancestry, representing an innate, genetic susceptibility, also contributes to the differences observed in BMI and obesity between AA and HL participants. Finally, we did not observe an independent contribution of self-reported ancestry, which represents a combination of genetic and environmental factors, which were likely accounted for by PAA and country of birth. We note that in our sample, we restricted our HL sample to those with a predominant European/African admixture, such that our observation may not be generalizable to other HL populations with more Native-American ancestry.

The authors' responsibilities were as follows—AV and RJFL: drafted the manuscript and had primary responsibility for the final content; RJFL: designed the study; EPB: designed, established, and coordinated the Bio*Me* Biobank; GMB, GLW, CRG, and EEK: implemented methods to derive the genetic ancestry information; AV and GMB: performed the statistical analyses; and all authors: read and approved the final manuscript. None of the authors reported a conflict of interest related to the study.

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