

Cardiometabolic Abnormalities Among Normal-Weight Persons From Five Racial/Ethnic Groups in the United States

A Cross-sectional Analysis of Two Cohort Studies

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Background: The relationship between body weight and cardiometabolic disease may vary substantially by race/ethnicity.

Objective: To determine the prevalence and correlates of the phenotype of metabolic abnormality but normal weight (MAN) for 5 racial/ethnic groups.

Design: Cross-sectional analysis.

Setting: 2 community-based cohorts.

Participants: 2622 white, 803 Chinese American, 1893 African American, and 1496 Hispanic persons from MESA (Multi-Ethnic Study of Atherosclerosis) and 803 South Asian participants in the MASALA (Mediators of Atherosclerosis in South Asians Living in America) study.

Measurements: Prevalence of 2 or more cardiometabolic abnormalities (high fasting glucose, low high-density lipoprotein cholesterol, and high triglyceride levels and hypertension) among normal-weight participants was estimated. Correlates of MAN were assessed by using log-binomial models.

Results: Among participants of normal weight ($n = 846$ whites, 323 Chinese Americans, 334 African Americans, 252 Hispanics, and 195 South Asians), the prevalence of MAN was 21.0% (95% CI, 18.4% to 23.9%) in whites, 32.2% (CI, 27.3% to 37.4%) in

Chinese Americans, 31.1% (CI, 26.3% to 36.3%) in African Americans, 38.5% (CI, 32.6% to 44.6%) in Hispanics, and 43.6% (CI, 36.8% to 50.6%) in South Asians. Adjustment for demographic, behavioral, and ectopic body fat measures did not explain racial/ethnic differences. After adjustment for age, sex, and race/ethnicity-body mass index (BMI) interaction, for the equivalent MAN prevalence at a BMI of 25.0 kg/m² in whites, the corresponding BMI values were 22.9 kg/m² (CI, 19.5% to 26.3%) in African Americans, 21.5 kg/m² (CI, 18.5% to 24.5%) in Hispanics, 20.9 kg/m² (CI, 19.7% to 22.1%) in Chinese Americans, and 19.6 kg/m² (CI, 17.2% to 22.0%) in South Asians.

Limitation: Cross-sectional study design and lack of harmonized dietary data between studies.

Conclusion: Compared with whites, all racial/ethnic minority groups had a statistically significantly higher prevalence of MAN, which was not explained by demographic, behavioral, or ectopic fat measures. Using a BMI criterion for overweight to screen for cardiometabolic risk may result in a large proportion of racial/ethnic minority groups being overlooked.

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Overweight and obesity are well-known cardiometabolic risk factors (1–3). However, some persons with normal weight have elevated cardiometabolic risk (4–7), and the relationship between excess adiposity and cardiometabolic abnormality may vary by race/ethnicity (4–7). Although some information is available regarding the prevalence and correlates of metabolic abnormality but normal weight (MAN) in non-Hispanic whites, non-Hispanic African Americans, and Mexican Americans (4, 5), no direct comparisons have been made among East or South Asians who are at high risk for cardiometabolic abnormalities, even at relatively low levels of body mass index (BMI) (8–13).

We therefore compared the prevalence of MAN among members of 5 racial/ethnic groups, including 2 Asian subgroups, by using data from 2 large, well-characterized community-based U.S. cohorts. We also examined the correlates associated with MAN in the 4 racial/ethnic minority groups compared with whites. Lastly, we determined the BMI values in the racial/ethnic minority participants that would yield a MAN prevalence equal to that in whites with a BMI of 25 kg/m².

METHODS

We conducted a cross-sectional analysis of pooled data from MESA (Multi-Ethnic Study of Atherosclerosis) and the MASALA (Mediators of Atherosclerosis in South Asians Living in America) study. To maintain consistency with the lower age limit of MESA participants, we excluded 94 MASALA participants younger than 44 years. Excluded participants differed from those who remained in the study only by age-related clinical outcomes. We compared 803 South Asian participants from MASALA with 2622 white, 803 Chinese American, 1893 African American, and 1496 Hispanic participants from MESA.

MESA Study

The design and conduct of the MESA study have been described elsewhere (14). In brief, study participants included members of 4 racial/ethnic groups

See also:

Summary for Patients 2

(white, Chinese American, African American, and Hispanic) aged 45 to 84 years recruited from the greater New York, New York; Baltimore, Maryland; Chicago, Illinois; Los Angeles, California; Minneapolis-Saint Paul, Minnesota; and Winston-Salem, North Carolina, areas. Baseline data collection and examinations were conducted between July 2000 and July 2002. Questionnaires were used to assess demographic and behavioral characteristics, and seated blood pressure readings, anthropometric measurements, and abdominal and cardiac computed tomography (CT) scans were obtained. Physical activity was assessed by using the Typical Week Physical Activity Questionnaire (15). Fasting serum glucose levels were evaluated by using the glucose oxidase method (Ortho Clinical Diagnostics). Insulin levels were determined by the Access system (Beckman Coulter) and harmonized with an Elecsys assay (Roche Diagnostics). C-reactive protein values were assessed by using a BN II nephelometer (N High-Sensitivity C-reactive protein test, Dade Behring). Total cholesterol and high-density lipoprotein cholesterol (HDL-C) levels were determined by using the cholesterol oxidase method (Roche Diagnostics), and low-density lipoprotein cholesterol concentrations were calculated. Triglyceride levels were measured by using Triglyceride GB reagent (Roche Diagnostics). Usual dietary intake over the past year was assessed by using a 120-item food-frequency questionnaire that was validated in white, African American, and Hispanic populations and modified to include Chinese foods (16).

MASALA Study

The MASALA study involved measures and methods similar to those of MESA to allow for specific cross-racial/ethnic comparisons (17). Its design and objectives also have been described (17). In brief, MASALA studied a community-based sample of South Asian Americans who were aged 40 to 84 years, had no previously known cardiovascular disease, and were living in the greater San Francisco Bay and Chicago areas. To be eligible for the study, participants had to report South Asian ethnicity (defined as having 3 or more grandparents born in India, Pakistan, Nepal, Bangladesh, or Sri Lanka) and be able to speak and read English, Hindi, or Urdu. All other eligibility criteria were identical to those of MESA (17). Recruitment occurred between October 2010 and March 2013. All participants were screened by telephone and invited to either the University of California, San Francisco, or the Northwestern University field center for a baseline clinical examination (17). Bilingual study staff assisted participants in completing the questionnaires, which were the same as those used in MESA. Because dietary intake is distinct in South Asians, the MASALA investigators used the SHARE (Study of Health Assessment and Risk in Ethnic groups) food-frequency questionnaire, which was developed for and validated in South Asians (17). Mean caloric intake was calculated by summing the product of the frequency of consumption, nutrient composition, and portion size of each item across all food items (18).

The protocols used in the MASALA study for seated blood pressure and anthropometry were the same as those used in MESA. After resting in a seated position for 5 minutes, each participant had his or her blood pressure assessed with an automated blood pressure machine (V100 Vital Signs Monitor, GE Healthcare). Seated blood pressure was measured 3 times, and the last 2 readings were averaged to determine systolic and diastolic blood pressure. Participant weight was measured with a standing balance beam or digital scale, height with a stadiometer. Body mass index was calculated as weight in kilograms divided by height in square meters. Waist circumference was determined by using a flexible tape measure at the site of maximum circumference, halfway between the lower ribs and the anterior superior iliac spine. The circumference was measured twice, and the average was used for analysis. Blood samples were collected after a 12-hour overnight fast. Total cholesterol, triglyceride, and HDL-C levels were analyzed by enzymatic methods, and low-density lipoprotein cholesterol concentrations were calculated. Fasting plasma glucose levels were analyzed by using the hexokinase method. Serum insulin was measured by the sandwich immunoassay method (Elecsys 2010, Roche Diagnostics) (19). As in MESA, Luminex adipokine panel A (EMD Millipore) was used to measure adiponectin and resistin levels. The interassay coefficient of variations was 2.34% to 4.12% for adiponectin and 3.25% to 5.03% for resistin (19). Computed tomography scans of the abdomen (Philips Medical Systems, Toshiba Medical Systems, and Siemens Medical Solutions) were used to assess visceral, subcutaneous, and intermuscular fat mass. Noncontrast cardiac CT images were obtained with a cardiac-gated CT scanner (Phillips 16D or Toshiba MSD Aquilion 64 at the University of California, San Francisco, and Siemens Sensation Cardiac 64 at Northwestern University) to assess pericardial fat volume and hepatic fat attenuation. Measurement methods and reading centers were similar to those used in MESA (20).

Classification of Cardiometabolic Abnormalities

We used National Cholesterol Education Program-Adult Treatment Panel III criteria to consider 4 cardiometabolic abnormalities (21). Decreased HDL-C was defined as a level lower than 1.03 mmol/L (<40 mg/dL) in men or 1.29 mmol/L (<50 mg/dL) in women, or any use of lipid-lowering medication (22). Elevated triglyceride was classified as a fasting triglyceride level of 1.7 mmol/L (150 mg/dL) or greater (22). Elevated glucose was classified as a fasting plasma glucose level of 5.6 mmol/L (100 mg/dL) or greater (23) or any use of glucose-lowering medication. High blood pressure was defined as 130/85 mm Hg or greater or any use of antihypertensive medication. The waist circumference criterion was not used because of collinearity with BMI (correlation coefficient, 0.85; $P < 0.0001$). On the basis of previous literature, cardiometabolic abnormality was defined as the presence of 2 or more of the aforementioned components (4, 24-28).

BMI Categories

For white, African American, and Hispanic participants, BMI was classified according to World Health Organization (WHO) standard cut points for normal weight (BMI, 18.5 to 24.9 kg/m²), overweight (BMI, 25.0 to 29.9 kg/m²), and obesity (BMI, ≥30 kg/m²) (27). For South Asian and Chinese American participants, BMI was classified according to WHO Asian cut points for normal weight (BMI, 18.5 to 22.9 kg/m²), overweight (BMI, 23.0 to 27.4 kg/m²), and obesity (BMI, ≥27.5 kg/m²) (28). We also conducted sensitivity analyses by using the standard WHO BMI cut points for all racial/ethnic groups.

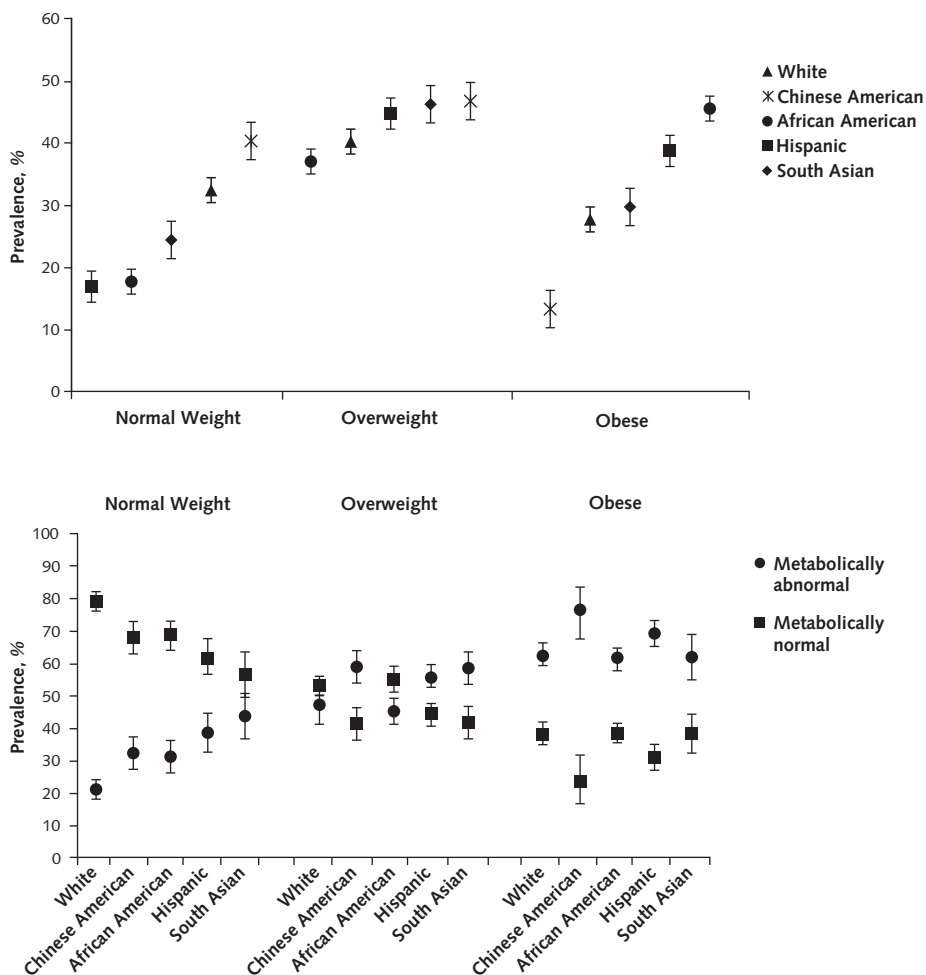
Body size phenotypes were defined on the basis of a combination of BMI category (normal weight) and cardiometabolic health. Combinations of BMI and cardiometabolic status yielded 2 distinct phenotypes (normal weight without cardiometabolic abnormalities

and normal weight with cardiometabolic abnormalities [MAN]). We focused our analysis on the discordant MAN phenotype.

Statistical Analysis

Analyses were conducted by using pooled data from the 2 cohorts. Participant characteristics were described as means, geometric means, and percentages by race/ethnicity. Differences in these characteristics across race/ethnicity were assessed by using chi-square tests or analysis of variance as appropriate. The prevalence of metabolic abnormality was calculated by BMI strata. Prevalence ratios of MAN in Chinese, African American, Hispanic, and South Asian participants compared with whites were estimated by using Poisson models with robust SEs (29). Multivariate models were adjusted for age, sex, education, physical activity, daily caloric intake, alcohol use, smoking status, hepatic fat

Figure 1. Prevalence of BMI categories and metabolic status, by race/ethnicity.



Top. Prevalence of BMI category, by race/ethnicity. Error bars are 95% CIs. Bottom. Prevalence of metabolic normality, by BMI category and race/ethnicity. Metabolically abnormal was defined as the presence of ≥2 of the following components: decreased high-density lipoprotein cholesterol levels (<1.036 mmol/L [<40 mg/dL] in men or <1.295 mmol/L [<50 mg/dL] in women or use of lipid-lowering medication), elevated triglyceride levels (fasting triglyceride levels ≥1.7 mmol/L [≥ 150 mg/dL]), elevated glucose levels (fasting plasma glucose level ≥5.6 mmol/L [≥ 100 mg/dL] or use of glucose-lowering medication), and high blood pressure (≥130/85 mm Hg or use of antihypertensive medication). Error bars are 95% CIs. BMI = body mass index.

Table 1. Characteristics of Participants With MAN Phenotype, by Race/Ethnicity*

| Characteristic | South Asian (n = 85) | White (n = 178) | P Value | Chinese American (n = 104) | P Value | African American (n = 104) | P Value | Hispanic (n = 97) | P Value |
|--|----------------------|-----------------|---------|----------------------------|---------|----------------------------|---------|-------------------|---------|
| Prevalence, % | 43.6 | 21.0 | <0.001 | 32.2 | 0.008 | 31.1 | 0.004 | 38.5 | 0.04 |
| Men, % | 72.9 | 39.3 | <0.001 | 47.1 | <0.001 | 53.4 | 0.007 | 50.5 | 0.02 |
| Mean age (SD), y | 59.6 (8.9) | 68.0 (9.6) | <0.001 | 66.8 (9.0) | <0.001 | 67.0 (9.6) | <0.001 | 64.6 (10.9) | 0.001 |
| Mean systolic blood pressure (SD), mm Hg | 128.4 (15.9) | 132.1 (21.7) | 0.17 | 129.7 (24.3) | 0.68 | 136.1 (19.6) | 0.004 | 134.0 (24.9) | 0.08 |
| Mean diastolic blood pressure (SD), mm Hg | 74.9 (8.8) | 71.6 (10.0) | <0.001 | 71.6 (11.7) | 0.04 | 75.4 (9.9) | 0.67 | 72.8 (10.1) | 0.15 |
| Hypertension, % | 67.1 | 78.1 | 0.57 | 65.4 | 0.81 | 92.3 | 0.002 | 69.1 | 0.09 |
| Mean fasting glucose level (SD) | | | <0.001 | | 0.46 | | 0.36 | | 0.33 |
| mmol/L | 6.3 (1.4) | 5.3 (1.9) | | 6.1 (2.1) | | 6.0 (2.4) | | 6.7 (3.6) | |
| mg/dL | 112.8 (24.6) | 94.9 (34.9) | | 109.3 (37.6) | | 108.0 (43.7) | | 120.2 (65.4) | |
| Diabetes, % | 38.8 | 7.9 | <0.001 | 24.0 | 0.07 | 28.9 | 0.12 | 26.8 | 0.03 |
| Mean total cholesterol level (SD) | | | <0.001 | | 0.008 | | 0.04 | | <0.001 |
| mmol/L | 5.00 (1.04) | 5.11 (1.13) | | 5.00 (0.82) | | 4.91 (1.05) | | 5.21 (0.99) | |
| mg/dL | 177.5 (40.0) | 197.2 (43.5) | | 191.5 (31.7) | | 189.5 (40.6) | | 201.3 (38.3) | |
| Mean LDL-C level (SD) | | | 0.005 | | 0.02 | | 0.02 | | <0.001 |
| mmol/L | 2.62 (0.84) | 2.92 (0.79) | | 2.90 (0.68) | | 2.94 (0.97) | | 3.13 (0.92) | |
| mg/dL | 101.2 (32.4) | 112.8 (30.4) | | 111.6 (26.4) | | 113.7 (37.3) | | 120.8 (35.4) | |
| Mean HDL-C level (SD) | | | 0.58 | | 0.78 | | 0.46 | | 0.07 |
| mmol/L | 1.25 (0.34) | 1.28 (0.40) | | 1.24 (0.32) | | 1.29 (0.41) | | 1.16 (0.36) | |
| mg/dL | 48.3 (13.3) | 49.4 (15.4) | | 47.8 (12.5) | | 49.9 (15.9) | | 44.7 (13.8) | |
| Geometric mean triglyceride level (SD) | | | 0.03 | | 0.07 | | 0.16 | | <0.001 |
| mmol/L | | | | | | | | | |
| mg/dL | 123.5 (2.4) | 143.8 (2.7) | | 141.9 (2.7) | | 110.8 (2.6) | | 161.5 (2.5) | |
| Mean calories (SD), kcal/d | 1719 (477) | 1446 (695) | 0.002 | 1020 (620) | <0.001 | 1473 (710) | 0.009 | 1598 (943) | 0.30 |
| Geometric mean HOMA-IR score (SD) | 2.4 (0.5) | 1.6 (0.2) | <0.001 | 1.9 (0.3) | 0.002 | 2.0 (0.5) | 0.12 | 1.9 (0.4) | 0.02 |
| Geometric mean HOMA- β score (SD) | 70.5 (2.5) | 99.7 (2.9) | <0.001 | 69.9 (2.8) | 0.94 | 82.8 (4.0) | 0.17 | 66.2 (3.8) | 0.60 |
| Geometric mean C-reactive protein level (SD), nmol/L | 8.6 (9.5) | 15.2 (5.7) | <0.001 | 8.6 (9.5) | 0.88 | 18.1 (7.6) | <0.001 | 15.2 (5.7) | <0.001 |
| Geometric mean adiponectin level (SD), ng/mL† | 9.3 (1.3) | 20.4 (1.6) | <0.001 | 14.3 (1.7) | 0.008 | 19.8 (1.9) | <0.001 | 18.8 (1.3) | <0.001 |
| Mean resistin level (SD), ng/mL† | 22.2 (9.5) | 15.8 (4.6) | <0.001 | 13.0 (4.6) | <0.001 | 21.6 (8.7) | 0.99 | 16.7 (7.6) | 0.01 |
| Mean waist circumference (SD), cm | 86.2 (6.0) | 88.9 (7.1) | 0.003 | 82.5 (5.7) | <0.001 | 87.6 (7.2) | 0.15 | 88.1 (6.3) | 0.03 |
| Mean subcutaneous fat area (SD), cm ² † | 155.2 (45.0) | 168.4 (56.5) | 0.16 | 144.8 (48.8) | 0.38 | 182.7 (62.7) | 0.02 | 177.7 (68.8) | 0.04 |
| Mean visceral fat area (SD), cm ² † | 122.4 (44.4) | 121.0 (48.7) | 0.87 | 97.6 (33.6) | 0.03 | 102.4 (47.4) | 0.02 | 120.3 (47.4) | 0.83 |
| Mean hepatic fat attenuation (SD), Hounsfield units | 55.9 (9.5) | 64.0 (10.2) | <0.001 | 64.3 (10.7) | <0.001 | 63.4 (9.5) | <0.001 | 63.7 (12.1) | <0.001 |
| Mean pericardial fat volume (SD), cm ³ | 51.0 (20.4) | 66.4 (30.2) | <0.001 | 64.9 (19.4) | <0.001 | 53.3 (25.6) | 0.49 | 64.3 (25.6) | <0.001 |
| Mean intermuscular fat area (SD), cm ² † | 17.4 (6.4) | 22.9 (8.2) | <0.001 | 18.2 (4.7) | 0.61 | 16.6 (6.9) | 0.57 | 18.2 (6.0) | 0.54 |
| Mean physical activity (SD), metabolic equivalent min/wk | 1057 (7.0) | 1995 (8.0) | <0.001 | 1093 (7.0) | 0.82 | 1791 (8.7) | 0.002 | 1059 (8.0) | 0.99 |
| Never smoker, % | 81.2 | 46.6 | <0.001 | 73.1 | 0.19 | 39.4 | <0.001 | 66.0 | 0.02 |
| Alcohol use, %‡ | 41.1 | 61.0 | 0.003 | 19.4 | 0.001 | 63.5 | 0.002 | 41.2 | 0.99 |

HDL-C = high-density lipoprotein cholesterol; HOMA- β = homeostasis model assessment of β -cell function; HOMA-IR = homeostasis model assessment of insulin resistance; LDL-C = low-density lipoprotein cholesterol; MAN = metabolic abnormality but normal weight.

* P values compare characteristics with those of South Asians.

† Data are from a restricted sample that included only metabolically abnormal participants with measurements of adiponectin and resistin levels, subcutaneous and intermuscular fat area, and visceral fat area (396 South Asian, 281 white, 112 Chinese American, 145 African American, and 202 Hispanic participants).

‡ Defined as consumption of ≥ 1 drink weekly.

attenuation, and pericardial fat volume. Additional, restricted models including only the subset of participants who had measures of visceral fat, adiponectin,

and resistin also were performed. To estimate the BMI values for South Asian, African American, Hispanic, and Chinese American participants that result in metabolic

outcomes equal to those in whites with a BMI of 25 kg/m² or 30 kg/m², we first fit a proportional odds model for the number of cardiometabolic abnormalities, with group-specific 4-knot restricted cubic splines in BMI, adjusting for sex and a 4-knot restricted cubic spline in age, then calculated the marginal expected number of abnormalities among whites, evaluated at a BMI of 25 kg/m² or 30 kg/m². We then used a search algorithm to find the BMI values for each of the other 4 groups that resulted in approximately the same marginal expected number of abnormalities. We also used this procedure to obtain BMI values for South Asian, African American, Hispanic, and Chinese American participants, resulting in an expected MAN prevalence approximately equal to that among whites with a BMI of 25 kg/m², based on a Poisson model for MAN, also adjusting for sex and a 4-knot spline in age. Confidence intervals for the BMI estimates were obtained by using bootstrap resampling. All analyses were performed with SAS, version 9.3 (SAS Institute).

The MESA study protocol was approved by the institutional review boards (IRBs) of the 6 field centers and the National Heart, Lung, and Blood Institute (NHLBI). The IRBs of Northwestern University and the University of California, San Francisco, approved the MASALA study protocol. The analysis was approved by the IRB at Emory University.

Role of the Funding Source

This study was funded by grants from the National Institutes of Health (NIH), National Center for Research Resources (NCRR), and NHLBI. The funders had no role in the design, conduct, or analysis of the study; collection, analysis, or interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

RESULTS

The total sample of 7617 participants comprised 2622 whites, 803 Chinese Americans, 1893 African Americans, and 1496 Hispanic Americans from MESA and 803 South Asians from MASALA. The sample also was made up of 1950 (25.6%) normal-weight, 3163 (41.5%) overweight, and 2504 (32.9%) obese participants. Overall, the South Asian participants were significantly younger than members of all other racial/ethnic groups, and this group had a significantly higher proportion of men compared with all other racial/ethnic groups except for Chinese Americans (Appendix Table 1, available at [Annals.org](#)).

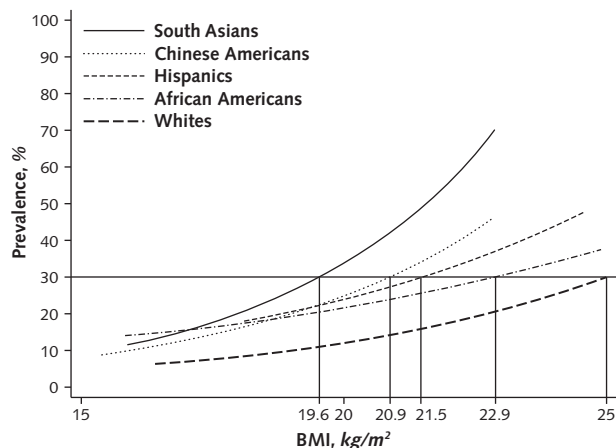
Prevalence of MAN

The overall prevalence of normal weight and obesity varied by race/ethnicity, with white and Chinese American participants having the highest prevalence of normal weight (32.3% and 40.2%, respectively) and African American and Hispanic participants having the highest prevalence of obesity (45.4% and 38.6%, respectively) (Figure 1, top). Overall, 29.1% of the participants with normal weight had the MAN phenotype, whereas 35.8% of those with obesity were metaboli-

Table 2. Unadjusted and Multivariable-Adjusted Prevalence Ratios of the Metabolically Abnormal Phenotype Among Normal-Weight Persons*

| Covariate | Prevalence Ratio (95% CI) | |
|---------------------------------------|---------------------------|-------------------------|
| | Unadjusted | Multivariable-Adjusted† |
| Race/ethnicity | | |
| White | 1.00 (reference) | 1.00 (reference) |
| South Asian | 2.07 (1.69-2.55) | 2.53 (1.99-3.22) |
| Chinese American | 1.53 (1.25-1.88) | 1.27 (1.02-1.59) |
| African American | 1.48 (1.20-1.82) | 1.66 (1.35-2.04) |
| Hispanic | 1.83 (1.49-2.24) | 1.56 (1.26-1.92) |
| Age | | |
| 44-54 y | 1.00 (reference) | 1.00 (reference) |
| 55-64 y | 1.71 (1.36-2.14) | 1.37 (1.10-1.70) |
| 65-74 y | 2.26 (1.82-2.79) | 1.80 (1.45-2.22) |
| 75-84 y | 2.52 (1.99-3.18) | 1.94 (1.51-2.49) |
| Sex | | |
| Male | 1.00 (reference) | 1.00 (reference) |
| Female | 0.79 (0.69-0.90) | 0.94 (0.81-1.10) |
| Highest education level | | |
| High school or less | 1.00 (reference) | 1.00 (reference) |
| Less than a bachelor's degree | 0.70 (0.58-0.83) | 0.87 (0.73-1.05) |
| Bachelor's degree | 0.56 (0.45-0.69) | 0.70 (0.56-0.87) |
| Higher than a bachelor's degree | 0.65 (0.54-0.78) | 0.74 (0.60-0.92) |
| Alcohol use | | |
| ≥1 drink daily | 1.00 (reference) | 1.00 (reference) |
| <1 drink daily | 1.15 (1.00-1.32) | 1.00 (0.86-1.16) |
| Smoking status | | |
| Never | 1.00 (reference) | 1.00 (reference) |
| Former | 0.91 (0.78-1.06) | 0.99 (0.84-1.17) |
| Current | 0.84 (0.66-1.05) | 0.90 (0.72-1.13) |
| Physical activity | | |
| 0-630 metabolic equivalent min/wk | 1.00 (reference) | 1.00 (reference) |
| 631-1470 metabolic equivalent min/wk | 1.00 (0.72-1.40) | 1.15 (0.83-1.59) |
| 1471-3000 metabolic equivalent min/wk | 0.94 (0.68-1.30) | 1.11 (0.80-1.53) |
| >3000 metabolic equivalent min/wk | 0.78 (0.57-1.06) | 1.04 (0.76-1.43) |
| Calories | | |
| <1069 kcal/d | 1.00 (reference) | 1.00 (reference) |
| 1069-1496 kcal/d | 0.94 (0.79-1.12) | 0.90 (0.76-1.07) |
| 1497-2010 kcal/d | 0.93 (0.77-1.12) | 0.89 (0.74-1.07) |
| >2010 kcal/d | 0.76 (0.61-0.94) | 0.75 (0.60-0.93) |
| Pericardial fat volume | | |
| <1.16 cm ³ | 1.00 (reference) | 1.00 (reference) |
| 1.16-1.67 cm ³ | 1.61 (1.35-1.90) | 1.47 (1.23-1.75) |
| 1.68-2.34 cm ³ | 2.21 (1.85-2.64) | 1.93 (1.59-2.34) |
| >2.34 cm ³ | 2.76 (2.20-3.46) | 2.40 (1.88-3.05) |
| Hepatic fat attenuation | | |
| <4.40 Hounsfield units | 1.00 (reference) | 1.00 (reference) |
| 4.40-5.00 Hounsfield units | 0.73 (0.60-0.88) | 0.73 (0.61-0.87) |
| 5.01-5.47 Hounsfield units | 0.54 (0.44-0.66) | 0.59 (0.49-0.71) |
| >5.47 Hounsfield units | 0.50 (0.41-0.61) | 0.54 (0.45-0.65) |

Figure 2. Race/ethnicity-specific BMI values associated with MAN compared with whites with a BMI of 25 kg/m².



MAN was defined as a BMI of 18.5 to 24.9 kg/m² for white, African American, and Hispanic participants or a BMI of 18.5 to 22.9 kg/m² for South Asian and Chinese American participants and ≥ 2 of the following components: decreased high-density lipoprotein cholesterol levels (<1.036 mmol/L [<40 mg/dL] in men or <1.295 mmol/L [<50 mg/dL] in women or use of lipid-lowering medication), elevated triglyceride levels (fasting triglyceride levels ≥ 1.7 mmol/L [≥ 150 mg/dL]), elevated glucose levels (fasting plasma glucose level ≥ 5.6 mmol/L [≥ 100 mg/dL] or use of glucose-lowering medication), and high blood pressure ($\geq 130/85$ mm Hg or use of antihypertensive medication). To obtain BMI values for South Asians, African Americans, Hispanics, and Chinese Americans that would result in an expected MAN prevalence approximately equal to that among whites with a BMI of 25 kg/m², based on a Poisson model for MAN, a proportional odds model was fit for the prevalence of MAN in white participants with a BMI of 25 kg/m², with group-specific 4-knot restricted cubic splines in BMI, adjusting for sex and a 4-knot restricted cubic spline in age. A search algorithm then was used to find the BMI values for each of the other 4 groups that resulted in approximately the same expected prevalence of MAN. BMI = body mass index; MAN = metabolic abnormality but normal weight.

cally normal. The prevalence of MAN varied significantly by race/ethnicity: 21.0% (95% CI, 18.4% to 23.9%) in whites, 32.2% (CI, 27.3% to 37.4%) in Chinese Americans, 31.1% (CI, 26.3% to 36.3%) in African Americans, 38.5% (CI, 32.6% to 44.6%) in Hispanics, and 43.6% (CI, 36.8% to 50.6%) in South Asians (Figure 1, bottom). These patterns were consistent by sex in all racial/ethnic groups except for South Asians, in whom the prevalence of MAN was greater in men (57.4%) than women (26.4%). In sensitivity analyses using the standard BMI criterion for the 2 Asian American subgroups, the prevalence of MAN was 40.4% in Chinese American and 47.9% in South Asian participants.

Among participants with 2 or more cardiometabolic abnormalities, the most common risk factor combination in whites was hypertension and a low HDL-C level (40.0%). In all other racial/ethnic groups, the risk factor combination of high glucose and low HDL-C levels was most common (48.7% in South Asians, 37.3% in Chinese Americans, 36.4% in African Americans, and 37.9% in Hispanics). Appendix Table 2 (available at Annals.org) details the prevalence of risk factor combinations among all racial/ethnic groups.

Among participants with MAN, South Asians were significantly younger than members of all other racial/

ethnic groups (Table 1). A significantly greater proportion of South Asians than whites or Hispanics had diabetes. Mean daily caloric intake was significantly higher in South Asians than members of any other racial/ethnic group except Hispanics. Levels of circulating adiponectin were significantly lower in South Asians than members of all other racial/ethnic groups. South Asians also had less hepatic fat attenuation (more fat in the liver) than all other racial/ethnic groups and less pericardial fat volume than all other groups except African Americans. Appendix Table 3 (available at Annals.org) details the characteristics of participants who were normal weight regardless of metabolic phenotype.

Correlates of the MAN Phenotype

Compared with whites, the prevalence of MAN was approximately 100% greater in South Asians, 50% in Chinese and African Americans, and 80% in Hispanics (Table 2). It was also higher in older participants and those with greater pericardial fat volume and lower in those with higher educational status and greater hepatic fat attenuation (less fat in the liver). In a multivariable-adjusted model, South Asian, Chinese, African American, and Hispanic race/ethnicity remained independently associated with MAN, as did older age, pericardial fat volume, educational status, and hepatic fat attenuation. Adjustment for age, sex, education, smoking status, alcohol use, physical activity, daily caloric intake, hepatic fat attenuation, and pericardial fat volume did not explain the differences in MAN among the study groups.

In restricted models including only normal-weight persons with measured visceral fat mass, adiponectin, and resistin (Appendix Table 4, available at Annals.org), MAN was more prevalent in South Asians, Chinese Americans, African Americans, and Hispanics than whites. In multivariable-adjusted models, the prevalence of MAN remained greater in South Asians and Hispanics, but not in Chinese and African American participants, compared with whites.

Ethnic-Specific BMI Values

We estimated the BMI values at which the expected numbers of metabolic abnormalities among South Asians, Chinese Americans, African Americans, and Hispanics would equal those among whites with a BMI of 25.0 kg/m² or 30.0 kg/m². For the equivalent number of cardiometabolic abnormalities at a BMI of 25.0 kg/m² in white participants, the corresponding BMI values were 22.3 kg/m² (CI, 19.7% to 24.9%) in African Americans, 21.5 kg/m² (CI, 18.5% to 24.5%) in Hispanics, 20.5 kg/m² (CI, 19.6% to 21.4%) in Chinese Americans, and 18.9 kg/m² (CI, 16.7% to 21.1%) in South Asians. For the equivalent number at a BMI of 30.0 kg/m² in whites, the corresponding BMI values were 29.9 kg/m² (CI, 25.6% to 34.2%) in African Americans, 27.0 kg/m² (CI, 26.0% to 28.0%) in Hispanics, 24.5 kg/m² (CI, 23.6% to 25.5%) in Chinese Americans, and 23.3 kg/m² (CI, 22.3% to 24.3%) in South Asians. Figure 2 displays the racial/ethnic BMI values associated with MAN prevalence after adjustment for age, sex, and race-BMI interaction. For the equivalent MAN

prevalence at a BMI of 25.0 kg/m² in whites, the corresponding BMI values were 22.9 kg/m² (CI, 19.5% to 26.3%) in African Americans, 21.5 kg/m² (CI, 18.5% to 24.5%) in Hispanics, 20.9 kg/m² (CI, 19.7% to 22.1%) in Chinese Americans, and 19.6 kg/m² (CI, 17.2% to 22.0%) in South Asians.

DISCUSSION

In this cross-sectional study of 2 large community-based cohorts including participants from several racial/ethnic groups in the United States, we found that nearly a third of those who were normal weight had cardiometabolic abnormalities. Furthermore, MAN prevalence varied by race/ethnicity, with a significantly higher proportion of South Asians and Hispanics, followed by Chinese and African Americans, having this phenotype compared with whites. Adjustment for demographic, behavioral, and ectopic fat variables did not explain these differences. For a MAN prevalence equivalent to that in whites with a BMI of 25 kg/m², the corresponding BMI values were lower in all racial/ethnic minority groups, suggesting that BMI alone is a poor indicator of cardiometabolic risk in most of these populations. A recent, nationally representative study assessing the prevalence and correlates of MAN in whites, African Americans, and Mexican Americans reported that 23.5% of all normal-weight adults had metabolic abnormalities (4). This percentage is lower than our finding of 29%, which partly may be a result of the younger mean age of the prior study's participants. Another difference is that our study included South Asian and Chinese American participants as well as measures of ectopic fat and adipokine levels; a previous study comparing the MESA and MASALA populations found significant differences in ectopic fat distribution and adipokine levels between South Asians and the 4 MESA racial/ethnic groups (30). Although these differences may partially account for the increased predisposition to insulin resistance and type 2 diabetes among South Asians, adjustment for ectopic fat measures and adipokine levels did not explain the difference in MAN among racial/ethnic groups in our study. Our findings also are consistent with those of a larger, longitudinal study, which found that a BMI cut point of 30 kg/m² in whites was equivalent to lower BMI cut points for South Asians, Chinese Americans, and African Americans in terms of diabetes incidence (13). Finally, our results build on those of a study that found elevated glucose and lipid levels at lower BMI values in non-European (South Asian, Chinese, and Aboriginal Canadian) versus European populations (12). Taken together, these findings suggest that established BMI cut points may be practical markers for detecting overweight but may not necessarily correlate with overall cardiometabolic health and that race/ethnicity alone may be a better predictor of cardiometabolic risk in racial/ethnic minority populations.

Our study has several strengths. We investigated cardiometabolic abnormalities in normal-weight persons from 5 U.S. racial/ethnic groups, including the rel-

atively understudied South Asian and Chinese American populations, in whom previous studies showed cardiometabolic abnormalities developing at lower BMI levels than in other racial/ethnic groups (11-13). Furthermore, our study used harmonized data from 2 large cohorts that included several radiographic measures of body composition to assess ectopic fat and adipokine levels.

However, our results also should be interpreted within the context of several limitations. The difference in timing of data collection between studies (2000 to 2002 for MESA and 2010 to 2013 for MASALA) may have resulted in some differences in the prevalence of overweight and obesity between the 2 cohorts. Because the initial enrollment of the MESA cohort began a decade and a half ago, secular changes may have occurred in the adoption of healthier behaviors, such as a decreased prevalence of smoking (31). However, the prevalence of obesity and diabetes has not decreased substantially during the past 2 decades (32-34). Thus, we do not believe that the prevalence of metabolic abnormalities observed in the MESA participants would be much different from that observed in a current sample of middle- to older-aged adults. Furthermore, MESA and MASALA used different food-frequency questionnaires, limiting our ability to assess whether dietary patterns contribute to MAN prevalence. Of note, adjustment for daily caloric intake did not explain differences in MAN prevalence among racial/ethnic groups. Although the MASALA and MESA cohorts are community-based samples, neither is nationally representative; therefore, the results may not be generalizable to younger persons or South Asians and Chinese Americans born in the United States.

In conclusion, our findings suggest a high prevalence of cardiometabolic abnormality among normal-weight persons, particularly those in racial/ethnic minority populations. This disparity cannot be explained by differences in demographic, behavioral, or ectopic fat measures. Therefore, clinicians using overweight and obesity as the main criteria for cardiometabolic screening, as currently recommended by the U.S. Preventive Services Task Force for diabetes testing (35), may fail to identify cardiometabolic abnormalities in many patients from racial/ethnic minority groups. Although the Task Force recommends earlier screening in racial/ethnic minority populations, testing for cardiometabolic abnormalities in normal-weight and underweight members of these groups also may be an important consideration. Future research is needed to identify the prospective associations between MAN and incident diabetes and cardiovascular disease in various racial/ethnic groups.

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Reproducible Research Statement: *Study protocol:* MASALA protocol available from Dr. Kanaya (e-mail, alka.kanaya@ucsf.edu); MESA protocol available at www.mesa-nhlbi.org. *Statistical code:* Available from Dr. Gujral (e-mail, ugujral@emory.edu). *Data set:* Available with steering committee approval from both MESA and MASALA.

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References

1. Da Costa LA, Arora P, Garcia-Bailo B, Karmali M, El-Sohemy A, Badawi A. The association between obesity, cardiometabolic disease biomarkers, and innate immunity-related inflammation in Canadian adults. *Diabetes Metab Syndr Obes*. 2012;5:347-55.
2. Lastra G, Manrique C, Sowers JR. Obesity, cardiometabolic syndrome, and chronic kidney disease: the weight of the evidence. *Adv Chronic Kidney Dis*. 2006;13:365-73. [PMID: 17045222]
3. Holmes MV, Lange LA, Palmer T, Lanktree MB, North KE, Almoquera B, et al. Causal effects of body mass index on cardiometabolic traits and events: a Mendelian randomization analysis. *Am J Hum Genet*. 2014;94:198-208. [PMID: 24462370] doi:10.1016/j.ajhg.2013.12.014
4. Wildman RP, Muntner P, Reynolds K, McGinn AP, Rajpathak S, Wylie-Rosett J, et al. The obese without cardiometabolic risk factor clustering and the normal weight with cardiometabolic risk factor clustering: prevalence and correlates of 2 phenotypes among the US population (NHANES 1999-2004). *Arch Intern Med*. 2008;168:1617-24. [PMID: 18695075] doi:10.1001/archinte.168.15.1617
5. St-Onge MP, Janssen I, Heymsfield SB. Metabolic syndrome in normal-weight Americans: new definition of the metabolically obese, normal-weight individual. *Diabetes Care*. 2004;27:2222-8. [PMID: 15333488]

6. Ruderman N, Chisholm D, Pi-Sunyer X, Schneider S. The metabolically obese, normal-weight individual revisited. *Diabetes*. 1998;47:699-713. [PMID: 9588440]
7. Conus F, Rabasa-Lhoret R, Péronnet F. Characteristics of metabolically obese normal-weight (MONW) subjects. *Appl Physiol Nutr Metab*. 2007;32:4-12. [PMID: 17332780]
8. Misra A, Khurana L. The metabolic syndrome in South Asians: epidemiology, determinants, and prevention. *Metab Syndr Relat Disord*. 2009;7:497-514. [PMID: 19900153] doi:10.1089/met.2009.0024
9. Misra A, Shrivastava U. Obesity and dyslipidemia in South Asians. *Nutrients*. 2013;5:2708-33. [PMID: 23863826] doi:10.3390/nu5072708
10. Ravikiran M, Bhansali A, Ravikumar P, Bhansali S, Dutta P, Thakur JS, et al. Prevalence and risk factors of metabolic syndrome among Asian Indians: a community survey. *Diabetes Res Clin Pract*. 2010;89:181-8. [PMID: 20381187] doi:10.1016/j.diabres.2010.03.010
11. Gordon-Larsen P, Adair LS, Meigs JB, Mayer-Davis E, Herring A, Yan SK, et al. Discordant risk: overweight and cardiometabolic risk in Chinese adults. *Obesity (Silver Spring)*. 2013;21:E166-74. [PMID: 23505200] doi:10.1002/oby.20409
12. Razak F, Anand SS, Shannon H, Vuksan V, Davis B, Jacobs R, et al. Defining obesity cut points in a multiethnic population. *Circulation*. 2007;115:2111-8. [PMID: 17420343]
13. Chiu M, Austin PC, Manuel DG, Shah BR, Tu JV. Deriving ethnic-specific BMI cutoff points for assessing diabetes risk. *Diabetes Care*. 2011;34:1741-8. [PMID: 21680722] doi:10.2337/dc10-2300
14. Bild DE, Bluemke DA, Burke GL, Detrano R, Diez Roux AV, Folsom AR, et al. Multi-Ethnic Study of Atherosclerosis: objectives and design. *Am J Epidemiol*. 2002;156:871-81. [PMID: 12397006]
15. Ainsworth BE, Irwin ML, Addy CL, Whitt MC, Stolarczyk LM. Moderate physical activity patterns of minority women: the Cross-Cultural Activity Participation Study. *J Womens Health Gend Based Med*. 1999;8:805-13. [PMID: 10495261]
16. Nettleton JA, Steffen LM, Mayer-Davis EJ, Jenny NS, Jiang R, Herrington DM, et al. Dietary patterns are associated with biochemical markers of inflammation and endothelial activation in the Multi-Ethnic Study of Atherosclerosis (MESA). *Am J Clin Nutr*. 2006;83:1369-79. [PMID: 16762949]
17. Kanaya AM, Kandula N, Herrington D, Budoff MJ, Hulley S, Vittinghoff E, et al. Mediators of Atherosclerosis in South Asians Living in America (MASALA) study: objectives, methods, and cohort description. *Clin Cardiol*. 2013;36:713-20. [PMID: 24194499] doi:10.1002/clc.22219
18. Wang ET, de Koning L, Kanaya AM. Higher protein intake is associated with diabetes risk in South Asian Indians: the Metabolic Syndrome and Atherosclerosis in South Asians Living in America (MASALA) study. *J Am Coll Nutr*. 2010;29:130-5. [PMID: 20679148]
19. Shah AD, Vittinghoff E, Kandula NR, Srivastava S, Kanaya AM. Correlates of prediabetes and type II diabetes in US South Asians: findings from the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study. *Ann Epidemiol*. 2015;25:77-83. [PMID: 25459085] doi:10.1016/j.annepidem.2014.10.013
20. Tota-Maharaj R, Blaha MJ, Zeb I, Katz R, Blankstein R, Blumenthal RS, et al. Ethnic and sex differences in fatty liver on cardiac computed tomography: the multi-ethnic study of atherosclerosis. *Mayo Clin Proc*. 2014;89:493-503. [PMID: 24613289] doi:10.1016/j.mayocp.2013.12.015
21. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al; American Heart Association. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation*. 2005;112:2735-52. [PMID: 16157765]
22. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome—a new world-wide definition. A consensus statement from the International Diabetes Federation. *Diabet Med*. 2006;23:469-80. [PMID: 16681555]
23. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2010;33 Suppl 1:S62-9. [PMID: 20042775] doi:10.2337/dc10-S062

24. Hinnouho GM, Czernichow S, Dugravot A, Nabi H, Brunner EJ, Kivimaki M, et al. Metabolically healthy obesity and the risk of cardiovascular disease and type 2 diabetes: the Whitehall II cohort study. *Eur Heart J*. 2015;36:551-9. [PMID: 24670711] doi:10.1093/eurheartj/ehu123
25. Aung K, Lorenzo C, Hinojosa MA, Haffner SM. Risk of developing diabetes and cardiovascular disease in metabolically unhealthy normal-weight and metabolically healthy obese individuals. *J Clin Endocrinol Metab*. 2014;99:462-8. [PMID: 24257907] doi:10.1210/jc.2013-2832
26. Appleton SL, Seaborn CJ, Visvanathan R, Hill CL, Gill TK, Taylor AW, et al; North West Adelaide Health Study Team. Diabetes and cardiovascular disease outcomes in the metabolically healthy obese phenotype: a cohort study. *Diabetes Care*. 2013;36:2388-94. [PMID: 23491523] doi:10.2337/dc12-1971
27. WHO Consultation on Obesity. Obesity: Preventing and Managing the Global Epidemic: Report of a WHO Consultation on Obesity, Geneva, 3-5 June 1997. Geneva: World Health Organization; 1998. Accessed at <http://apps.who.int/iris/handle/10665/63854> on 18 March 2016.
28. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet*. 2004;363:157-63. [PMID: 14726171]
29. Zou G. A modified poisson regression approach to prospective studies with binary data. *Am J Epidemiol*. 2004;159:702-6. [PMID: 15033648]
30. Shah AD, Kandula NR, Lin F, Allison MA, Carr J, Herrington D, et al. Less favorable body composition and adipokines in South Asians compared with other US ethnic groups: results from the MASALA and MESA studies. *Int J Obes (Lond)*. 2016;40:639-45. [PMID: 26499444] doi:10.1038/ijo.2015.219
31. Centers for Disease Control and Prevention (CDC). Vital signs: current cigarette smoking among adults aged ≥ 18 years with mental illness—United States, 2009-2011. *MMWR Morb Mortal Wkly Rep*. 2013;62:81-7. [PMID: 23388551]
32. Flegal KM, Carroll MD, Kit BK, Ogden CL. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999-2010. *JAMA*. 2012;307:491-7. [PMID: 22253363] doi:10.1001/jama.2012.39
33. Cowie CC, Rust KF, Ford ES, Eberhardt MS, Byrd-Holt DD, Li C, et al. Full accounting of diabetes and pre-diabetes in the U.S. population in 1988-1994 and 2005-2006. *Diabetes Care*. 2009;32:287-94. [PMID: 19017771] doi:10.2337/dc08-1296
34. Bullard KM, Saydah SH, Imperatore G, Cowie CC, Gregg EW, Geiss LS, et al. Secular changes in U.S. prediabetes prevalence defined by hemoglobin A_{1c} and fasting plasma glucose: National Health and Nutrition Examination Surveys, 1999-2010. *Diabetes Care*. 2013;36:2286-93. [PMID: 23603918] doi:10.2337/dc12-2563
35. Siu AL; U.S. Preventive Services Task Force. Screening for abnormal blood glucose and type 2 diabetes mellitus: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2015; 163:861-8. [PMID: 26501513] doi:10.7326/M15-2345

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Appendix Table 1. Characteristics of Study Participants, by Race/Ethnicity*

| Characteristic | South Asian (n = 803) | White (n = 2622) | P Value | Chinese American (n = 803) | P Value | African American (n = 1893) | P Value | Hispanic (n = 1496) | P Value | Missing, n |
|--|-----------------------|------------------|---------|----------------------------|---------|-----------------------------|---------|---------------------|---------|------------|
| Prevalence, % | 10.5 | 34.4 | <0.001 | 10.5 | 1.0 | 24.9 | <0.001 | 19.6 | <0.001 | 0 |
| Men, % | 52.8 | 48.0 | 0.02 | 48.6 | 0.09 | 44.5 | <0.001 | 48.2 | 0.04 | |
| Mean age (SD), y | 56.9 (8.6) | 62.6 (10.2) | <0.001 | 62.3 (10.3) | <0.001 | 62.1 (10.5) | <0.001 | 62.3 (10.3) | 0.001 | 0 |
| Mean systolic blood pressure (SD), mm Hg | 125.6 (15.9) | 123.5 (20.4) | 0.01 | 124.6 (21.6) | <0.001 | 131.7 (21.6) | <0.001 | 126.7 (21.9) | 0.02 | 3 |
| Mean diastolic blood pressure (SD), mm Hg | 73.3 (9.9) | 70.2 (10.0) | <0.001 | 72.0 (10.3) | 0.007 | 74.5 (10.2) | 0.007 | 71.6 (10.1) | <0.001 | 3 |
| Hypertension, % | 52.8 | 47.4 | 0.007 | 48.1 | 0.06 | 68.3 | <0.001 | 50.7 | 0.34 | 0 |
| Mean fasting glucose level (SD), mg/dL | 104.2 (25.4) | 91.4 (21.5) | <0.001 | 99.0 (28.2) | <0.001 | 100.0 (32.0) | 0.001 | 103.6 (39.1) | 0.72 | 37 |
| Diabetes, % | 21.9 | 6.0 | <0.001 | 13.1 | <0.001 | 17.5 | 0.008 | 17.7 | 0.01 | 0 |
| Mean total cholesterol level (SD), mg/dL | 187.3 (36.7) | 195.7 (35.1) | <0.001 | 192.6 (31.8) | 0.002 | 189.6 (36.2) | 0.12 | 197.9 (37.5) | <0.001 | 27 |
| Mean LDL-C level (SD), mg/dL | 110.6 (32.0) | 117.0 (30.1) | <0.001 | 115.1 (29.0) | 0.004 | 116.5 (33.0) | <0.001 | 119.5 (32.9) | <0.001 | 112 |
| Mean HDL-C level (SD), mg/dL | 50.3 (13.3) | 52.2 (15.7) | <0.001 | 49.5 (12.7) | 0.22 | 52.4 (15.3) | <0.001 | 47.6 (13.1) | <0.001 | 29 |
| Geometric mean triglyceride level (SD), mg/dL | 119.1 (2.1) | 114.4 (2.5) | 0.05 | 124.5 (2.5) | 0.07 | 92.3 (2.2) | <0.001 | 136.7 (2.5) | <0.001 | 26 |
| Mean calories, kcal/d | 1675 (499) | 1688 (761) | 0.66 | 1152 (612) | <0.001 | 1683 (995) | 0.85 | 1696 (930) | 0.56 | 293 |
| Mean geometric mean HOMA-IR score (SD) | 2.6 (0.7) | 1.8 (0.3) | <0.001 | 2.0 (0.4) | <0.001 | 2.2 (0.5) | <0.001 | 2.4 (0.6) | 0.008 | 92 |
| Geometric mean HOMA-β score (SD) | 100.6 (2.9) | 118.0 (2.6) | <0.001 | 96.8 (2.9) | 0.22 | 108.9 (3.2) | 0.01 | 109.9 (3.4) | 0.004 | 92 |
| Geometric mean C-reactive protein level (SD), μg/mL | 1.3 (0.3) | 1.8 (0.7) | <0.001 | 0.9 (0.1) | <0.001 | 1.1 (0.8) | <0.001 | 2.4 (0.9) | <0.001 | 64 |
| Geometric mean adiponectin level (SD), ng/mL† | 10.2 (1.5) | 20.9 (1.7) | <0.001 | 14.1 (1.6) | <0.001 | 15.8 (1.6) | <0.001 | 17.3 (1.5) | <0.001 | 0 |
| Mean resistin level (SD), ng/mL† | 21.9 (12.1) | 16.1 (5.3) | <0.001 | 15.3 (7.5) | <0.001 | 18.0 (13.7) | <0.001 | 16.1 (6.7) | <0.001 | 0 |
| Mean waist circumference (SD), cm | 92.7 (10.0) | 98.0 (14.4) | <0.001 | 87.1 (9.9) | <0.001 | 101.2 (14.7) | <0.001 | 100.6 (13.1) | <0.001 | 1 |
| Mean subcutaneous fat area (SD), cm² | 236.5 (95.2) | 254.5 (115.4) | 0.002 | 179.4 (70.9) | <0.001 | 298.5 (132.2) | <0.001 | 264.0 (108.5) | <0.001 | 0 |
| Mean visceral fat area (SD), cm²† | 136.1 (57.0) | 151.9 (74.9) | <0.001 | 113.9 (47.8) | <0.001 | 119.1 (55.9) | <0.001 | 151.6 (60.7) | <0.001 | 0 |
| Mean hepatic fat attenuation (SD), Hounsfield units | 55.1 (10.6) | 61.4 (12.2) | <0.001 | 61.9 (12.0) | <0.001 | 63.0 (11.7) | <0.001 | 59.4 (14.2) | <0.001 | 80 |
| Mean pericardial fat volume (SD), cm³ | 59.5 (29.6) | 85.2 (46.1) | <0.001 | 73.7 (31.4) | <0.001 | 67.5 (34.7) | 0.49 | 88.3 (43.8) | <0.001 | 30 |
| Mean intermuscular fat area (SD), cm² | 21.7 (8.8) | 26.9 (12.0) | <0.001 | 18.7 (7.5) | <0.001 | 19.9 (12.3) | 0.004 | 23.5 (9.9) | 0.001 | 0 |
| Mean physical activity (SD), metabolic equivalent min/wk | 1048 (6.4) | 1741 (7.7) | <0.001 | 1122 (7.6) | 0.20 | 1574 (8.8) | <0.001 | 1205 (8.7) | 0.009 | 19 |
| Never smoker, % | 82.9 | 44.1 | <0.001 | 75.2 | <0.001 | 44.9 | <0.001 | 53.9 | <0.001 | 22 |
| Alcohol use, %‡ | 32.3 | 64.5 | <0.001 | 21.4 | <0.001 | 51.7 | <0.001 | 46.8 | <0.001 | 84 |

HDL-C = high-density lipoprotein cholesterol; HOMA-β = homeostasis model assessment of β-cell function; HOMA-IR = homeostasis model assessment of insulin resistance; LDL-C = low-density lipoprotein cholesterol.

* This sample includes all participants from the pooled MESA (Multi-Ethnic Study of Atherosclerosis) and MASALA (Mediators of Atherosclerosis in South Asians Living in America) cohorts regardless of weight and metabolic status. P values compare characteristics with those of South Asians. To convert glucose, cholesterol, or triglyceride values to mmol/L, multiply by 0.0555, 0.0259, or 0.0113, respectively.

† Data are from a restricted sample that included only participants with adiponectin, resistin, and visceral fat area measurements (708 South Asian, 645 white, 235 Chinese American, 337 African American, and 382 Hispanic participants).

‡ Defined as consumption of ≥1 drink weekly.

Appendix Table 2. Prevalence of Risk Factor Combinations Among Persons With ≥ 2 Cardiometabolic Risk Factors, by Race/Ethnicity*

| Race/Ethnicity | Elevated Triglycerides/High Blood Pressure | Elevated Triglycerides/Elevated Glucose | Elevated Triglycerides/Low HDL-C | High Blood Pressure/Elevated Glucose | High Blood Pressure/Low HDL-C | Elevated Glucose/Low HDL-C |
|-----------------------|---|--|---|---|--------------------------------------|-----------------------------------|
| White | 104 (9.25) | 11 (0.98) | 172 (15.3) | 106 (9.43) | 449 (39.95) | 282 (25.09) |
| Chinese American | 23 (5.68) | 13 (3.21) | 51 (12.59) | 58 (11.85) | 119 (29.38) | 151 (37.28) |
| African American | 38 (4.00) | 7 (0.74) | 24 (2.53) | 211 (22.23) | 324 (34.14) | 345 (36.35) |
| Hispanic | 57 (6.58) | 19 (2.19) | 137 (15.82) | 112 (12.93) | 213 (24.60) | 328 (37.88) |
| South Asian | 17 (3.79) | 9 (2.01) | 42 (9.38) | 65 (14.51) | 97 (21.65) | 218 (48.66) |

HDL-C = high-density lipoprotein cholesterol.

* Values are numbers (percentages).

Appendix Table 3. Characteristics of Normal-Weight Participants, by Race/Ethnicity*

| Characteristic | South Asian (n = 195) | White (n = 846) | P Value | Chinese American (n = 323) | P Value | African American (n = 334) | P Value | Hispanic (n = 252) | P Value | Missing, n |
|--|-----------------------|-----------------|---------|----------------------------|---------|----------------------------|---------|--------------------|---------|------------|
| Prevalence, % | 24.3 | 32.3 | <0.001 | 40.2 | <0.001 | 17.6 | <0.001 | 16.8 | <0.001 | 0 |
| Men, % | 55.4 | 37.0 | <0.001 | 45.5 | 0.03 | 52.7 | 0.55 | 48.4 | 0.14 | 0 |
| Mean age (SD), y | 57.8 (8.8) | 62.7 (10.7) | <0.001 | 62.8 (10.1) | <0.001 | 63.5 (10.7) | <0.001 | 62.0 (11.2) | <0.001 | 0 |
| Mean systolic blood pressure (SD), mm Hg | 122.9 (16.1) | 118.9 (21.9) | 0.02 | 121.0 (22.8) | 0.31 | 127.6 (21.5) | 0.009 | 123.1 (24.1) | 0.94 | 0 |
| Mean diastolic blood pressure (SD), mm Hg | 72.2 (9.4) | 67.9 (10.1) | <0.001 | 70.3 (10.3) | 0.03 | 74.3 (10.1) | 0.02 | 69.4 (10.1) | 0.004 | 0 |
| Hypertension, % | 42.6 | 36.3 | 0.01 | 37.8 | 0.28 | 59.3 | <0.001 | 42.9 | 0.95 | 0 |
| Mean fasting glucose level (SD), mg/dL | 100.7 (20.3) | 85.7 (18.2) | <0.001 | 95.3 (25.9) | 0.01 | 91.5 (27.3) | <0.001 | 98.9 (44.4) | <0.001 | |
| Diabetes, % | 18.0 | 2.3 | <0.001 | 8.7 | 0.002 | 9.6 | 0.005 | 10.7 | 0.03 | 0 |
| Mean total cholesterol level (SD), mg/dL | 185.3 (35.2) | 196.5 (34.9) | <0.001 | 193.0 (31.3) | 0.01 | 186.6 (36.5) | 0.70 | 197.9 (36.3) | <0.001 | 5 |
| Mean LDL-C level (SD), mg/dL | 108.4 (30.3) | 115.3 (29.6) | 0.004 | 114.6 (27.5) | 0.02 | 108.7 (33.7) | 0.91 | 118.8 (33.0) | <0.001 | 20 |
| Mean HDL-C level (SD), mg/dL | 54.2 (14.8) | 59.8 (17.7) | 0.002 | 54.5 (13.3) | 0.22 | 59.5 (18.9) | <0.001 | 52.8 (16.2) | <0.001 | 7 |
| Geometric mean triglyceride level (SD), mg/dL | 101.2 (2.1) | 92.0 (2.2) | 0.01 | 105.7 (2.3) | 0.32 | 80.1 (2.2) | <0.001 | 115.3 (2.4) | 0.006 | 5 |
| Mean calories (SD), kcal/d | 1648 (494) | 1553 (726) | 0.08 | 1150 (613) | <0.001 | 1617 (911) | 0.66 | 1597 (995) | 0.51 | 55 |
| Geometric mean HOMA-IR score (SD) | 1.7 (0.3) | 1.2 (0.1) | <0.001 | 1.5 (0.2) | <0.001 | 1.3 (0.2) | <0.001 | 1.5 (0.2) | 0.002 | 29 |
| Geometric mean HOMA-β score (SD) | 75.0 (2.3) | 102.5 (2.4) | <0.001 | 83.1 (2.5) | 0.05 | 94.3 (3.0) | <0.001 | 84.5 (3.2) | 0.06 | 29 |
| Geometric mean C-reactive protein level (SD), μg/mL | 0.8 (0.2) | 1.1 (0.1) | <0.001 | 0.7 (0.4) | 0.12 | 1.4 (0.4) | <0.001 | 1.5 (0.5) | <0.001 | 15 |
| Geometric mean adiponectin level (SD), ng/mL† | 11.6 (1.5) | 26.6 (1.8) | <0.001 | 17.2 (1.5) | <0.001 | 18.7 (1.9) | <0.001 | 20.0 (1.4) | <0.001 | 0 |
| Mean resistin level (SD), ng/mL† | 21.6 (9.0) | 15.1 (4.3) | <0.001 | 14.0 (7.5) | 0.008 | 17.9 (10.4) | <0.001 | 15.8 (6.9) | <0.001 | 0 |
| Mean waist circumference (SD), cm | 84.0 (6.3) | 84.6 (8.8) | 0.36 | 79.3 (7.0) | <0.001 | 84.5 (7.7) | 0.43 | 86.2 (7.4) | <0.001 | 0 |
| Mean subcutaneous fat area (SD), cm ² | 162.5 (50.0) | 183.4 (72.0) | 0.001 | 137.2 (49.8) | <0.001 | 188.4 (78.2) | 0.002 | 179.7 (67.2) | 0.02 | 0 |
| Mean visceral fat area (SD), cm ² † | 99.2 (43.9) | 97.3 (44.7) | 0.67 | 82.2 (32.0) | 0.003 | 81.0 (40.3) | 0.003 | 107.9 (46.0) | 0.14 | 0 |
| Mean hepatic fat attenuation (SD), Hounsfield units | 59.6 (9.1) | 65.9 (8.7) | <0.001 | 65.5 (9.2) | <0.001 | 65.8 (9.0) | <0.001 | 65.5 (9.8) | <0.001 | 42 |
| Mean pericardial fat volume (SD), cm ³ | 41.6 (18.9) | 54.0 (24.6) | <0.001 | 57.1 (19.9) | <0.001 | 43.4 (21.7) | 0.03 | 56.7 (25.2) | <0.001 | 8 |
| Mean intermuscular fat area (SD), cm ² | 17.2 (6.1) | 22.1 (8.1) | <0.001 | 16.5 (5.3) | 0.40 | 14.2 (6.0) | <0.001 | 18.5 (6.8) | 0.15 | 0 |
| Mean physical activity (SD), metabolic equivalent min/wk | 1099 (6.7) | 2039 (7.7) | <0.001 | 1072 (7.5) | 0.80 | 1841 (8.8) | <0.001 | 1408 (8.7) | <0.001 | 5 |
| Never smoker, % | 86.2 | 44.6 | <0.001 | 78.0 | 0.02 | 42.5 | <0.001 | 58.7 | <0.001 | 6 |
| Alcohol use, %‡ | 35.4 | 66.3 | <0.001 | 19.7 | <0.001 | 57.7 | <0.001 | 42.9 | 0.10 | 18 |

HDL-C = high-density lipoprotein cholesterol; HOMA-β = homeostasis model assessment of β-cell function; HOMA-IR = homeostasis model assessment of insulin resistance; LDL-C = low-density lipoprotein cholesterol.

* This sample includes both metabolically normal and abnormal participants. P values compare characteristics with those of South Asians. To convert glucose, cholesterol, or triglyceride values to mmol/L, multiply by 0.0555, 0.0259, or 0.0113, respectively.

† Data are from a restricted sample that included only participants with adiponectin, resistin, and visceral fat mass measurements (708 South Asian, 645 white, 235 Chinese American, 337 African American, and 382 Hispanic participants).

‡ Defined as consumption of ≥1 drink weekly.

Appendix Table 4. Unadjusted and Multivariable-Adjusted Prevalence Ratios of the Metabolically Abnormal Phenotype Among Normal-Weight Persons*

| Covariate | Prevalence Ratio (95% CI) | |
|---------------------------------------|---------------------------|-------------------------|
| | Unadjusted | Multivariable-Adjusted† |
| Race/ethnicity | | |
| White | 1.00 (reference) | 1.00 (reference) |
| South Asian | 2.10 (1.55–2.84) | 1.49 (1.10–2.04) |
| Chinese American | 1.20 (0.75–1.91) | 1.10 (0.79–1.53) |
| African American | 1.57 (1.05–2.37) | 1.37 (0.99–1.88) |
| Hispanic | 1.97 (1.38–2.82) | 1.30 (1.00–1.69) |
| Age | | |
| 44–54 y | 1.00 (reference) | 1.00 (reference) |
| 55–64 y | 1.25 (0.90–1.72) | 1.02 (0.82–1.27) |
| 65–74 y | 1.65 (1.21–2.25) | 1.16 (0.93–1.44) |
| 75–84 y | 2.00 (1.40–2.86) | 1.29 (0.93–1.78) |
| Sex | | |
| Men | 1.00 (reference) | 1.00 (reference) |
| Women | 0.61 (0.49–0.77) | 1.07 (0.88–1.29) |
| Education | | |
| Less than a bachelor's degree | 1.00 (reference) | 1.00 (reference) |
| Bachelor's degree or higher | 0.82 (0.67–1.03) | 0.87 (0.74–1.03) |
| Alcohol use | | |
| ≥1 drink daily | 1.00 (reference) | 1.00 (reference) |
| <1 drink daily | 1.05 (0.84–1.32) | 0.97 (0.81–1.16) |
| Smoking status | | |
| Never | 1.00 (reference) | 1.00 (reference) |
| Former | 0.92 (0.71–1.19) | 1.02 (0.84–1.24) |
| Current | 0.82 (0.54–1.26) | 1.08 (0.79–1.48) |
| Exercise | | |
| 0–750 metabolic equivalent min/wk | 1.00 (reference) | 1.00 (reference) |
| 751–1575 metabolic equivalent min/wk | 1.08 (0.84–1.56) | 1.12 (0.90–1.39) |
| 1576–3131 metabolic equivalent min/wk | 0.94 (0.68–1.30) | 1.14 (0.90–1.44) |
| >3131 metabolic equivalent min/wk | 0.91 (0.67–1.30) | 1.14 (0.91–1.43) |
| Calories | | |
| <1033 kcal/d | 1.00 (reference) | 1.00 (reference) |
| 1033–1394 kcal/d | 1.20 (0.87–1.65) | 1.05 (0.82–1.33) |
| 1394–1912 kcal/d | 1.18 (0.89–1.63) | 0.98 (0.76–1.25) |
| >1912 kcal/d | 1.13 (0.81–1.56) | 0.91 (0.71–1.16) |
| Pericardial fat volume | | |
| <0.84 cm ³ | 1.00 (reference) | 1.00 (reference) |
| 0.84–1.12 cm ³ | 1.51 (1.01–2.24) | 1.13 (0.87–1.47) |
| 1.13–1.48 cm ³ | 1.68 (1.14–2.47) | 1.17 (0.88–1.55) |
| >1.48 cm ³ | 2.47 (1.73–3.52) | 1.35 (0.99–1.82) |
| Hepatic fat attenuation | | |
| <4.48 Hounsfield units | 1.00 (reference) | 1.00 (reference) |

Appendix Table 4—Continued

| Covariate | Prevalence Ratio (95% CI) | |
|-------------------------------|---------------------------|-------------------------|
| | Unadjusted | Multivariable-Adjusted† |
| Resistin | | |
| <12.73 ng/mL | 1.00 (reference) | 1.00 (reference) |
| 12.73–16.32 ng/mL | 1.73 (1.19–2.52) | 1.07 (0.98–1.17) |
| 16.32–21.08 ng/mL | 1.58 (1.08–2.33) | 1.04 (0.95–1.14) |
| >21.08 ng/mL | 2.17 (1.52–3.11) | 1.06 (0.98–1.17) |
| Visceral fat area | | |
| <97.38 cm ² | 1.00 (reference) | 1.00 (reference) |
| 97.38–134.78 cm ² | 1.44 (0.89–2.35) | 1.06 (0.80–1.15) |
| 134.79–184.68 cm ² | 2.90 (1.90–4.41) | 1.29 (0.98–1.71) |
| >184.68 cm ² | 3.67 (2.45–5.51) | 1.35 (1.01–1.81) |

* Metabolic abnormality was defined by the presence of ≥2 of the following components: decreased high-density lipoprotein cholesterol (<1.036 mmol/L [<40 mg/dL] in men or <1.295 mmol/L [<50 mg/dL] in women or use of lipid-lowering medication), elevated triglyceride levels (fasting triglyceride levels ≥1.7 mmol/L [≥ 150 mg/dL]), elevated glucose levels (fasting plasma glucose level ≥5.6 mmol/L [≥ 100 mg/dL] or use of glucose-lowering medication), and high blood pressure (≥130/85 mm Hg or use of antihypertensive medication). Data are from a restricted sample that included only metabolically abnormal participants with adiponectin, resistin, subcutaneous fat area, visceral fat area, and intermuscular fat area measurements (396 South Asian, 281 white, 112 Chinese American, 145 African American, and 202 Hispanic participants).

† Each factor was adjusted for every other factor in the table.