Body Mass Index From Early-, Mid-, and Older-Adulthood and Risk of Heart Failure and Atherosclerotic Cardiovascular Disease: MESA

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Background—Obesity contributes significantly to risk of atherosclerotic cardiovascular disease (ASCVD) and especially for heart failure (HF). An elevated body mass index (BMI) in older adults might not carry the same risk as in younger adults, but measured weights at other lifetime points are often not available. We determined the associations of self-reported weights from early- and mid-adulthood, after accounting for measured weight at older age, with incident HF/ASCVD risk.

Methods and Results—We studied 6437 MESA (Multi-Ethnic Study of Atherosclerosis) participants (aged 45–84, free of baseline HF/ASCVD) with self-reported weights at ages 20 and 40 years (by questionnaire), measured weights at up to 5 in-person examinations (2000–2012), and follow-up for adjudicated HF/ASCVD events. Participant mean±SD age at the baseline examination was 62.2±10.2 years. Over median follow-up of 13 years, 290 HF and 828 ASCVD events occurred. After adjustment for cardiovascular risk factors and baseline BMI, higher self-reported weights at ages 20 and 40 years were independently associated with increased risk of incident HF with hazard ratios (95% confidence interval) of 1.27 (1.07–1.50) and 1.36 (1.18–1.57), respectively, per 5-kg/m² higher BMI. For incident ASCVD, only higher BMI at age 20 years was associated after accounting for current BMI (1.13 [1.01–1.26] per 5 kg/m²).

Obesity during follow-up examinations was also associated with incident HF (1.72 [1.21–2.45]) but not ASCVD.

Conclusions—Self-reported lifetime weight is a low-tech tool easily utilized in any clinical encounter. Although subject to recall bias, self-reported weights may provide prognostic information about future HF risk, incremental to current BMI, in a multiethnic cohort of middle-aged to older adults.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00005487. (J Am Heart Assoc. 2018;7:e009599. DOI: 10.1161/JAHA.118.009599.)

Key Words: cardiovascular disease • heart failure • lifetime weights • obesity • prevention
Clinical Perspective

What Is New?

- We determined whether asking individuals about a self-reported weight history from early (age 20 years) or mid-adulthood (age 40 years) added any incremental prognostic information to current assessment of heart failure risk.
- Even after accounting for current measured body mass index and cardiovascular risk factors, we found that self-reported elevated body mass index is associated with future heart failure risk (3-fold risk for obesity at age 20 years and 2-fold risk for obesity at age 40 years).

What Are the Clinical Implications?

- Our study supports that assessment of individuals’ weight throughout decades of adulthood is important in understanding a more comprehensive risk profile and can better inform clinicians and patients about risk for developing incident heart failure.
- Although subject to recall bias, self-reported weights provide prognostic information about future heart failure risk, incremental to current body mass index, in a multi-ethnic cohort of middle-aged to older adults.
- These results may inform future screening protocols, but future work is needed to determine how best to incorporate this into clinical decision making.

“protective” against mortality, although this idea has been contested. Indeed, a recent study found that while a single baseline measurement of body mass index (BMI) had an inverse association with mortality, this obesity paradox was reversed when considering a maximum BMI over long-term follow-up. Thus, considering a patient’s lifetime weight history might be more prognostic of HF or atherosclerotic CVD (ASCVD) risk than a current office visit BMI, especially for older adults.

Despite this, in clinical practice healthcare providers typically counsel patients on their ASCVD/HF risk based only on a single office BMI or from a few office-obtained BMI measures obtained within a relatively short time interval. Measured weights from earlier lifepoints, such as early- and mid-adulthood, are often not available. Consider 2 hypothetical patients, Mr. L and Mr. J, with similar current weights and ASCVD risk profiles (Figure 1). Could asking about their self-reported weights from early- and mid-adulthood offer any additional information to guide their risk assessment for future HF and ASCVD beyond what is known from their current profile?

Using data from a multiethnic community-based cohort of middle-aged and older adults, we evaluated whether assessing BMI in early- and mid-adulthood (based on self-reported weights) added incremental prognostic information about ASCVD/HF risk after considering current measured BMI.

Methods

Data Availability Statement

The MESA (Multi-Ethnic Study of Atherosclerosis) cohort participates in the National Heart, Lung, and Blood Institute's Biologic Specimen and Data Repository (BioLINCC). The MESA data are available upon request through BioLINCC, including data from examinations 1 to 5, used in this analysis.

Study Participants

MESA is an ongoing longitudinal study of 6814 men and women aged 45 to 84 years without clinical ASCVD or HF at baseline. The methodology and data collection for MESA has been extensively documented previously. Between 2000 and 2002, participants of 4 race/ethnicities were recruited from 6 US communities: Baltimore, MD; Chicago, IL; Forsyth County, NC; New York City, NY; Los Angeles County, CA; and St. Paul, MN. Participants in our sample were excluded if they were missing self-reported weight at age 20 or 40 years (N=31), had no follow-up information for ASCVD or HF (N=27), or were missing key covariates (N=319). Our final sample size was 6437 participants (Figure S1).

The MESA protocols were approved by the institutional review boards of the participating universities, with written informed consent obtained from all participants at each study visit.

BMI Assessment

At the MESA baseline examination (2000–2002), participants underwent a health assessment using questionnaires, physical examination, and fasting blood draw following standardized protocols performed by trained staff, as previously described. Participant’s height and weight were measured while they wore minimal clothing and no shoes, with values rounded to the nearest 0.1 cm and 0.5 kg, respectively. BMI was calculated as weight (kg) divided by height squared (m²). Participant’s weights at ages 20 and 40 years were self-reported by questionnaire. BMIs at age 20 and 40 years were calculated using these self-reported weights and measured height from the baseline examination, under the assumption that height is relatively stable during adulthood. After the baseline examination, participants attended up to 4 follow-up examinations: Exam 2 (2002–2004), Exam 3 (2004–2005), Exam 4 (2005–2007), and Exam 5 (2010–2012). BMI was reassessed at each study visit using concomitantly measured weight and height.
Covariates

Demographic and lifestyle factors such as race/ethnicity, smoking status (never, former, or current smoker), educational attainment (<high school, high school/technical school/associate degree, and college/graduate/professional school) were assessed by questionnaires. Physical activity was ascertained using a Typical Week Physical Activity Survey and quantified into the metabolic equivalent task-minutes of intentional moderate or vigorous exercise per week.\(^8\) Diet was assessed by food frequency questionnaire and adherence to a healthy diet was scored, as previously described.\(^9\) Medications were reviewed by inventory.

Blood pressure was measured 3 times 1 minute apart, and the second and third measurements were averaged. Plasma glucose, triglycerides, and total and high-density lipoprotein cholesterol were measured from fasting blood samples as described previously.\(^10\) Diabetes mellitus was defined as a history of diabetes medications, self-reported prior physician diagnosis of diabetes mellitus, or fasting serum glucose of \(\geq 126 \text{ mg/dL}\). Serum creatinine and cystatin C concentrations were used to calculate estimated glomerular filtration rate using the CKD-EPI equation.\(^11\)

Assessment of Outcomes

After the baseline examination, participants received follow-up telephone interviews every 9 to 12 months regarding interim hospital admissions, outpatient cardiovascular diagnoses and procedures, and deaths; family members were contacted if the study participant was deceased. Medical records were requested for those who reported being hospitalized or receiving an outpatient cardiovascular diagnosis. Records were obtained for 98% of cardiovascular events associated with hospitalization. Two physician members of the MESA mortality and morbidity review committee adjudicated and classified events and incidence dates.\(^12\)

Our primary outcome was incident definite or probable HF (hospitalized), which required confirmation of symptoms such as edema or shortness of breath.\(^9\) Probable HF required diagnosis by a physician and medical treatment for HF in addition to the aforementioned symptoms. Definite HF required 1 or more of the following additional criteria: evidence of left ventricular diastolic dysfunction, or poor left ventricular function by ventriculography or echocardiography, ventricular dilation, or pulmonary congestion or edema by...
If ejection fraction was known, HF was further subclassified as either HF with preserved ejection fraction (HFpEF, left ventricular ejection fraction $\geq 45\%$) or with reduced EF (HFrEF, left ventricular ejection fraction $< 45\%$).

Our secondary outcome was incident definite or probable ASCVD, which include coronary heart disease (CHD) events (myocardial infarction, CHD deaths, definite angina, and probable angina if followed by coronary revascularization), stroke, stroke death, and other atherosclerotic deaths. Event follow-up information was obtained from the baseline visit until a study end point, death, or December 31, 2013.

Table 1. Baseline Characteristics of Study Participants by BMI: MESA (2000–2002)

| BMI Based on Measured Weight at MESA Baseline Examination | Overall (n=6437) | BMI <25 (n=2551) | BMI 25 to <30 (n=283) | BMI $\geq$30 (n=2013) | P Value |
|----------------------------------------------------------|-----------------|-----------------|----------------------|----------------------|---------|
| Age, y                                                    | 62.2 (10.2)     | 62.7 (10.7)     | 62.8 (10.2)          | 61.0 (9.7)           | <0.001  |
| Men                                                      | 3049 (47.4)     | 833 (44.4)      | 1384 (54.4)          | 832 (41.3)           | <0.001  |
| BMI at age 20, kg/m²                                      | 22.1 (3.4)      | 20.5 (2.5)      | 21.9 (3.0)           | 23.7 (3.9)           | <0.001  |
| BMI at age 40, kg/m²                                      | 25.2 (4.2)      | 22.1 (2.3)      | 25.0 (2.8)           | 28.5 (4.6)           | <0.001  |
| BMI at baseline                                           | 28.2 (5.4)      | 22.6 (1.8)      | 27.4 (1.4)           | 34.5 (4.2)           | <0.001  |
| Race/ethnicity                                            |                 |                 |                      |                     | <0.001  |
| White                                                    | 2514 (39.1)     | 820 (43.7)      | 1010 (39.7)          | 684 (34.0)           |         |
| Chinese-American                                         | 797 (12.4)      | 517 (27.5)      | 246 (9.7)            | 34 (1.7)             |         |
| Black                                                    | 1711 (26.6)     | 302 (16.1)      | 652 (25.6)           | 757 (37.6)           |         |
| Hispanic                                                 | 1415 (22.0)     | 239 (12.7)      | 638 (25.1)           | 538 (26.7)           |         |
| Education                                                 |                 |                 |                      |                     | <0.001  |
| <High school                                              | 1151 (17.9)     | 289 (15.4)      | 497 (19.5)           | 365 (18.1)           |         |
| High school, technical school, or associate degree        | 2977 (46.2)     | 803 (42.8)      | 1125 (44.2)          | 1049 (52.1)          |         |
| College, graduate or professional school                  | 2309 (35.9)     | 786 (41.9)      | 924 (36.3)           | 599 (29.8)           |         |
| Smoking                                                   |                 |                 |                      |                     | <0.001  |
| Never                                                    | 3257 (50.6)     | 1027 (54.7)     | 1243 (48.8)          | 987 (49.0)           |         |
| Former                                                   | 2376 (36.9)     | 614 (32.7)      | 968 (38.0)           | 794 (39.4)           |         |
| Current                                                  | 804 (12.5)      | 237 (12.6)      | 335 (13.2)           | 232 (11.5)           |         |
| Total intentional exercise, met-min/wk*                  | 3990.0 (1980.0–7425.0) | 3795.0 (1950.0–7050.0) | 4215.0 (2130.0–7740.0) | 3900.0 (1815.0–7402.5) | 0.001   |
| Systolic BP, mm Hg                                        | 126.5 (21.4)    | 121.6 (22.0)    | 127.2 (20.9)         | 130.1 (20.6)         | <0.001  |
| Diastolic BP, mm Hg                                       | 71.9 (10.2)     | 69.8 (10.2)     | 72.8 (9.9)           | 72.7 (10.3)          | <0.001  |
| Total cholesterol, mg/dL†                                 | 194.1 (35.7)    | 194.4 (34.7)    | 194.6 (35.9)         | 193.0 (36.3)         | 0.28    |
| HDL cholesterol, mg/dL†                                   | 51.0 (14.9)     | 56.8 (17.1)     | 49.5 (13.4)          | 47.6 (12.8)          | <0.001  |
| LDL cholesterol, mg/dL†                                   | 117.1 (31.3)    | 114.9 (30.7)    | 118.6 (31.8)         | 117.2 (31.3)         | <0.001  |
| Triglycerides, mg/dL†                                      | 111.0 (78.0–161.0) | 95.0 (68.0–137.0) | 115.0 (81.0–164.0)   | 122.0 (86.0–181.0)   | <0.001  |
| eGFR, ml/min per 1.73 m²                                  | 77.7 (16.2)     | 77.8 (15.3)     | 77.1 (15.9)          | 78.3 (17.2)          | 0.03    |
| Antihypertension medication                               | 2390 (37.1)     | 473 (25.2)      | 949 (37.3)           | 968 (48.1)           | <0.001  |
| Lipid-lowering medication                                 | 1053 (16.4)     | 221 (11.8)      | 459 (18.1)           | 373 (18.6)           | <0.001  |
| Diabetes mellitus                                         | 797 (12.4)      | 127 (6.8)       | 284 (11.2)           | 386 (19.2)           | <0.001  |

Data are mean (SD), n (%). BMI indicates body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MESA, Multi-Ethnic Study of Atherosclerosis; met, metabolic equivalent of task.

*Data are median (interquartile range).
†To convert total cholesterol, HDL-C, and LDL-C to mmol/L from mg/dL, divide by 38.67. To convert triglycerides to mmol/L from mg/dL, divide by 88.57.
Statistical Analysis

Baseline characteristics of participants were examined by BMI groups at the baseline examination (<25, 25 to <30, ≥30 kg/m²) and by self-reported BMIs from ages 20 and 40 years. Means (SDs) were used to present approximately normally distributed continuous variables. Medians (interquartile ranges) were used for skewed continuous variables. Categorical variables were presented as counts with percentages.

The outcomes of interest for this analysis were incident hospitalized HF, HFpEF, HFrEF, and ASCVD. For each age point, BMI was modeled continuously (per 5-kg/m² higher value) and by BMI categories (<25 [reference], 25 to <30, ≥30 kg/m²). The incidence rates per 1000 person-years and their 95% confidence intervals, adjusted for age, sex, race/ethnicity, and center, were reported for each outcome by BMI at each age point. Cox proportional hazards models were used to determine the multivariable-adjusted hazard ratios and 95% confidence intervals for incident HF and ASCVD associated with BMI for each adulthood age. We tested whether the proportional hazards assumption was met using Schoenfeld residuals and confirmed that the hazard was proportional. We also assessed the risk for HF and ASCVD associated with BMI measured during follow-up at older ages (Exam 1 through Exam 5), which was approximately a 10-year interval. For this latter analysis, BMI status was updated at each study visit (time-varying).

Three progressively adjusted models were used. Model 1 (the sociodemographic model) adjusted for age at baseline examination, sex, race/ethnicity, education, and study center site. Model 2 (Model 1 plus CVD risk factors) additionally adjusted for smoking, physical activity, healthy diet score, total cholesterol, high-density lipoprotein cholesterol, use of cholesterol-lowering medications, systolic blood pressure, use of antihypertensive medications, and diabetes mellitus. Model 3 additionally adjusted for measured BMI at the MESA baseline examination.

We evaluated effect modification by age, sex, and race/ethnicity. P values as reported were 2-sided with significance set at 0.05; STATA version 15 was used to perform all analyses (StataCorp LP, College Station, TX).

Results

The study population’s characteristics at the MESA baseline examination, for overall and by BMI categories, are presented in Table 1. Participants had a mean (SD) age of 62.2 (10.2) years and 53% were women. Participants with BMI ≥30 kg/m² at MESA baseline had higher mean self-reported BMIs at both ages 20 and 40 years, compared with those with BMI <25 kg/m² at MESA baseline. Health conditions related to obesity and overweight status—such as diabetes mellitus, use of antihypertension medication, use of lipid-lowering medication, triglyceride

Table 2. Participant Demographic Characteristics at the MESA Baseline Examination Stratified by Self-Reported BMIs at Age 20 Years and Age 40 Years

| BMI Based on Self-Reported Weight at Age 20 Years | Overall (n=6437) | <25 (n=5387) | 25 to <30 (n=909) | ≥30 (n=144) | P Value |
|-----------------------------------|-----------------|-------------|------------------|-------------|---------|
| Age, y                            | 62.2 (10.2)     | 62.3 (10.2) | 62.3 (10.6)      | 60.2 (10.1) | 0.05    |
| Men                               | 3049 (47.4)     | 2388 (44.4) | 584 (64.2)       | 77 (53.5)  | <0.001  |
| Race/ethnicity                    |                 |             |                  |             |         |
| White                             | 2514 (39.1)     | 2120 (39.4) | 350 (38.5)       | 44 (30.6)  |         |
| Chinese-American                  | 797 (12.4)      | 755 (14.0)  | 39 (4.3)         | 3 (2.1)    |         |
| Black                             | 1711 (26.6)     | 1365 (25.4) | 285 (31.4)       | 61 (42.4)  |         |
| Hispanic                          | 1415 (22.0)     | 1144 (21.2) | 235 (25.9)       | 36 (25.0)  |         |

| BMI Based on Self-Reported Weight at Age 40 Years | Overall (n=6437) | <25 (n=3473) | 25 to <30 (n=2248) | ≥30 (n=716) | P Value |
|-----------------------------------|-----------------|-------------|-------------------|-------------|---------|
| Age, y                            | 62.2 (10.2)     | 63.0 (10.1) | 62.1 (10.3)       | 58.6 (9.9)  | <0.001  |
| Men                               | 3049 (47.4)     | 1464 (42.2) | 1250 (53.6)       | 335 (46.8)  | <0.001  |
| Race/ethnicity                    |                 |             |                   |             |         |
| White                             | 2514 (39.1)     | 1505 (43.3) | 792 (35.2)        | 217 (30.3)  |         |
| Chinese-American                  | 797 (12.4)      | 648 (18.7)  | 144 (6.4)         | 5 (0.7)     |         |
| Black                             | 1711 (26.6)     | 791 (22.8)  | 650 (28.9)        | 270 (37.7)  |         |
| Hispanic                          | 1415 (22.0)     | 529 (15.2)  | 662 (29.4)        | 224 (31.3)  |         |

Data are mean (SD), n (%). BMI indicates body mass index; MESA, Multi-Ethnic Study of Atherosclerosis.

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and low-density lipoprotein cholesterol levels—were all predictably higher in the obese/overweight groups compared with the normal-weight group. Table 2 shows the baseline demographics based on self-reported BMI categories for ages 20 and 40 years. Blacks were more likely to have self-reported obesity at age 20 and age 40 years than other race/ethnicity groups. The pairwise correlations of BMIs at each age point are as follows: BMI at age 20 and age 40 years ($r=0.625$), BMI age 20 years and MESA baseline ($r=0.398$), BMI at age 40 years and MESA baseline ($r=0.687$); all $P$ values were $<0.001$. Patterns of weight change throughout adulthood are presented in Figure 2. Those who were overweight or obese at age 20 years were far more likely to stay in those elevated BMI groups at age 40 years and at their age at the MESA baseline examination.

Participants were followed for a median of 13.0 (interquartile range 11.5, 13.7) years for incident HF and 12.9 (10.2, 13.6) years for incident ASCVD events. There were 290 HF and 828 ASCVD events.

Higher BMIs and obesity status at any adult age point (age 20 years, age 40 years, and age at MESA baseline) were strongly associated with incident HF after accounting for demographics and CVD risk factors (Figure 3A and Table 3, Model 2). Obesity later in life during the 10-year period between MESA Exam 1 to 5 was also associated with incident HF (hazard ratio 1.72 [95% confidence intervals, 1.21–2.45]). After further accounting for measured BMI obtained at the MESA baseline examination, higher self-reported BMIs in early adulthood (age 20 years) and mid-adulthood (age 40 years) were
still independently associated with incident HF. The hazard ratios were 1.27 (1.07–1.50) at age 20 years and 1.36 (1.18–1.57) at age 40 years, respectively, per 5-kg/m² higher BMI (Table 3, Model 3). Compared with those with normal weights (BMI <25 kg/m²), participants with self-reported obesity (BMI ≥30) at age 20 years had a 3-fold increased risk for HF (3.20 [1.93–5.32]) and those with self-reported obesity at age 40 years had nearly a 2-fold increased risk of HF (1.92 [1.31–2.83]), even after accounting for measured BMI later in life.

Higher BMIs at age 20 years and age 40 years were associated with increased risk for both HfPfEF (Table 4) and HFrEF (Table 5), after adjusting for CVD risk factors (Model 2). However, after additionally accounting for current BMI (Model 3), self-reported weights at ages 20 and 40 years had qualitatively stronger associations with HFrEF than HfPfEF, although confidence intervals overlapped. On the other hand, when considering current BMI at the MESA baseline examination and time-varying BMI during follow-up (Exam 1 through 5), this appeared to be stronger risk factors for HfPfEF (Table 4) than HFrEF (Table 5), after adjusting for CVD risk factors (Model 2).

In contrast with the findings for HF, the associations of BMI at each age point were less strongly associated with incident ASCVD, as compared with incident HF (Table 6 and Figure 3B). Notably, only higher self-reported BMI at age 20 years (per 5-kg/m²) was statistically significantly associated with ASCVD after accounting for current BMI (1.13 [1.01–1.26]) (Table 6, Model 3).

No meaningful interactions were found by age, sex, or race/ethnic groups for these associations (P>0.1 for all; Table S1). The P value of the interaction by age was 0.60, 0.83, 0.48, and 0.38 for the associations between baseline BMI with HF, HfPfEF, HFrEF, and ASCVD. The associations of BMI at each age point with incident HF were similar when stratified by ages <60 years and ≥60 years at the MESA baseline examination, and presented in Table S2.

Discussion

We found in a multiethnic community-based cohort of middle-aged and older adults that assessment of self-reported weights from early and mid-adulthood was independently associated with future HF risk and, to a lesser extent, ASCVD, even after taking into account measured weight and other traditional CVD risk factors in later life. Asking patients about their weights at ages 20 and 40 years is a low-tech tool that can easily be utilized at any clinical encounter and might provide additional insight into risk beyond considering a single baseline weight measure alone.

The association of obesity with incident CVD risk, and particularly HF risk, is well established. The Framingham Heart Study found that higher BMI at age 50 was associated with increased risk of HF over an average follow-up of 14 years. In the ARIC study (Atherosclerosis Risk in Communities), among middle-aged individuals (age 45–64 years)
Table 3. Incidence Rates and Adjusted Hazard Ratios (95% CI) for Incident Heart Failure Associated With BMI at Each Age Point

| BMI categories | N Events/Person-Year | IR (95% CI)* | Model 1† | Model 2‡ | Model 3§ |
|----------------|----------------------|--------------|----------|----------|----------|
|                 |                      |              |          |          |          |
| BMI at age 20 y |                      |              |          |          |          |
| Normal          | 210/62 708           | 3.7 (3.2, 4.2) | Reference (1) | Reference (1) | Reference (1) |
| Overweight      | 61/10 107            | 5.8 (4.3, 7.3) | 1.56 (1.16, 2.08) | 1.48 (1.10, 1.98) | 1.33 (0.98, 1.79) |
| Obese           | 19/1502              | 16.4 (8.9, 23.9) | 4.44 (2.75, 7.17) | 3.94 (2.42, 6.41) | 3.20 (1.93, 5.32) |
| BMI at age 40 y |                      |              |          |          |          |
| Normal          | 130/40 590           | 3.4 (2.8, 4.0) | Reference (1) | Reference (1) | Reference (1) |
| Overweight      | 97/25 736            | 4.0 (3.2, 4.8) | 1.15 (0.88, 1.50) | 1.06 (0.81, 1.39) | 0.95 (0.72, 1.27) |
| Obese           | 63/7990              | 10.7 (8.0, 13.5) | 3.10 (2.26, 4.26) | 2.43 (1.75, 3.38) | 1.92 (1.31, 2.83) |
| BMI categories baseline | | | | | |
| Normal          | 62/22 009            | 3.1 (2.3, 4.0) | Reference (1) | Reference (1) | Reference (1) |
| Overweight      | 114/29 329           | 3.9 (3.2, 4.6) | 1.24 (0.90, 1.71) | 1.09 (0.79, 1.52) | Reference (1) |
| Obese           | 114/22 979           | 5.9 (4.8, 7.1) | 1.86 (1.34, 2.60) | 1.42 (1.00, 2.03) | Reference (1) |
| Time-varying BMI (v1–v5) | | | | | |
| Normal          | 60/21 843            | 2.7 (2.0, 3.4) | Reference (1) | Reference (1) | Reference (1) |
| Overweight      | 112/28 401           | 3.8 (3.1, 4.5) | 1.39 (1.01, 1.92) | 1.26 (0.91, 1.76) | Reference (1) |
| Obese           | 112/23 399           | 5.9 (4.7, 7.0) | 2.15 (1.54, 3.01) | 1.72 (1.21, 2.45) | Reference (1) |

BMI indicates body mass index; CI, confidence interval; CVD, cardiovascular disease; HDL, high-density lipoprotein; IR, incidence rates; MESA, Multi-Ethnic Study of Atherosclerosis; SES, socioeconomic status.

*IR: incidence rate (95% CI) per 1000 person-y, adjusted for age, sex, race, and center.
†Model 1 (demographics and SES model): adjusted for age at baseline, sex, race/ethnicity, center, and education.
‡Model 2 (+CVD risk factors): additionally adjusted for smoking, physical activity, healthy diet score, total cholesterol, HDL cholesterol, use of cholesterol-lowering medications, systolic blood pressure, use of antihypertensive medications, and diabetes mellitus.
§Model 3 (for analyses of BMIs at age 20 and 40 y): additionally adjusted for BMI at MESA baseline.

Followed for 23 years, severe obesity at baseline (BMI >35 kg/m²) was independently associated with a 2-fold increased risk of incident CHD and a nearly 4-fold increased risk for HF. In contrast, other studies have suggested that, among patients with established HF, those who are overweight or obese had a lower risk of all-cause and CVD mortality when compared with normal-weight counterparts. This is the “obesity paradox,” and its precise mechanism and validity is still debated in the literature.

The association between obesity and CVD risk is further complicated by the fact that patients’ weights can fluctuate over the course of their lives. An older study evaluated self-reported weight at age 20 years and subsequent weight gain for incident ASCVD among white men aged ≥40 years (n=3102). In this study, those with ≥30 pounds of weight gain since age 20 years had an increased age-adjusted incidence of CHD compared with those with <30 pounds. Similarly, an analysis from the ARIC cohort found that greater cumulative weight from young adulthood (ie, greater total “BMI-years”) was associated with increased risk of subclinical myocardial damage as measured by high-sensitivity cardiac troponin.

A recent study combining data from 3 large prospective cohorts (n=225 072) found that when considering a single baseline weight, a paradoxical inverse association of overweight status and all-cause mortality was noted. Conversely, higher maximum BMI over the 16 years of weight history was associated with increased CHD and CVD mortality. This study highlights that long-term weight history is a stronger metric of CVD risk than a single baseline weight. The mean ages in these 3 cohorts ranged from 50 to 68 years. Adding to this evidence, our study now found that asking individuals about their weights at even earlier stages of their life (ie, early- and mid-adulthood) revealed additional information about their HF risk profile beyond considering their single weight at the MESA baseline. Our findings (for the outcomes of HF and ASCVD) are consistent with a study of Japanese
individuals that found that self-reported weight at age 20 years (assessed by questionnaire) was associated with future risk of hypertension incremental to the measured weight at baseline examination (baseline mean age of 50 [9] years).22

In our analyses, we confirmed the phenomenon of obesity “tracking” over the course of patients’ lives—that participants who become obese or overweight at earlier time points in their life are more likely to remain obese throughout adulthood. We found that weight history appeared qualitatively strongly associated with incident HF than for incident ASCVD, although confidence intervals for both outcomes overlapped. The relatively greater strength of the association between obesity and incident HF, as compared with ASCVD (CHD and stroke), has been previously demonstrated in the ARIC study.2 Our study newly shows the incremental risk associated with self-reported obesity status at age 20 and 40 years, even when we controlled for baseline BMI. Finally, we found that current obesity status might be a stronger predictor of HFrEF, while a history of obesity at ages 20 and 40 years (accounting for current BMI) might be a stronger predictor of HFpEF.

In sum, our results might support the potential utility of asking patients about their prior weights throughout their adult lives to more completely evaluate their HF and ASCVD risk, incremental to their current weight and risk profile. While the 2 patients in Figure 1 might appear to be similar based on their current office assessment, asking about their self-reported weight history would identify that Mr. L is likely at higher risk of HF than Mr. J. While both patients should be counseled on lifestyle management to improve their cardiometabolic profile, more resource-intensive preventive efforts might be matched to the higher-risk individual. Additionally, a higher BMI at younger ages, even in the

### Table 4. Incidence Rates and Adjusted Hazard Ratios (95% CI) for Incident Heart Failure With Preserved Ejection Fraction Associated With BMI at Each Age Point

| BMI at age 20 y, per 5 kg/m² higher | N Events/Person-Year | IR (95% CI)* | Model 1† | Model 2‡ | Model 3§ |
|-----------------------------------|---------------------|--------------|----------|----------|----------|
| Normal                            | 115/74 317          | 1.7 (1.4, 2.0) | 1.36 (1.06, 1.75) | 1.35 (1.05, 1.74) | 1.11 (0.84, 1.47) |
| Overweight                        | 115/74 317          | 1.7 (1.4, 2.0) | 1.55 (1.32, 1.80) | 1.47 (1.24, 1.75) | 1.25 (1.00, 1.57) |
| Obese                             | 115/74 317          | 1.7 (1.4, 2.0) | 1.61 (1.36, 1.91) | 1.52 (1.27, 1.82) | 1.25 (1.00, 1.57) |
| Time-varying BMI (v1–v5) per 5 kg/m² higher | 115/74 118        | 1.6 (1.3, 1.9) | 1.67 (1.42, 1.97) | 1.59 (1.34, 1.89) | 1.25 (1.00, 1.57) |

BMI categories at age 20 y:

| Category | N Events/Person-Year | IR (95% CI)* | Model 1† | Model 2‡ | Model 3§ |
|----------|---------------------|--------------|----------|----------|----------|
| Normal   | 89/62 708           | 1.5 (1.2, 1.9) | Reference (1) | Reference (1) | Reference (1) |
| Overweight | 20/10 107          | 2.1 (1.2, 3.1) | 1.37 (0.83, 2.25) | 1.34 (0.81, 2.22) | 1.09 (0.65, 1.82) |
| Obese    | 6/1502              | 5.7 (1.1, 10.3) | 3.71 (1.60, 8.60) | 3.51 (1.50, 8.23) | 2.33 (0.96, 5.65) |

BMI categories at age 40 y:

| Category | N Events/Person-Year | IR (95% CI)* | Model 1† | Model 2‡ | Model 3§ |
|----------|---------------------|--------------|----------|----------|----------|
| Normal   | 53/40 590           | 1.3 (1.0, 1.7) | Reference (1) | Reference (1) | Reference (1) |
| Overweight | 39/25 736          | 1.7 (1.2, 2.2) | 1.29 (0.84, 1.97) | 1.22 (0.79, 1.87) | 0.97 (0.61, 1.52) |
| Obese    | 23/7990             | 4.4 (2.5, 6.3) | 3.31 (1.97, 5.57) | 2.63 (1.53, 4.52) | 1.62 (0.88, 3.02) |

BMI categories baseline:

| Category | N Events/Person-Year | IR (95% CI)* | Model 1† | Model 2‡ | Model 3§ |
|----------|---------------------|--------------|----------|----------|----------|
| Normal   | 26/22 009           | 1.2 (0.7, 1.7) | Reference (1) | Reference (1) | Reference (1) |
| Overweight | 43/29 329          | 1.5 (1.1, 2.0) | 1.27 (0.77, 2.10) | 1.16 (0.69, 1.95) | 0.97 (0.61, 1.52) |
| Obese    | 46/22 979           | 2.5 (1.7, 3.3) | 2.09 (1.24, 3.52) | 1.71 (0.98, 2.99) | 1.25 (0.98, 1.57) |

Time-varying BMI (v1–v5):

| Category | N Events/Person-Year | IR (95% CI)* | Model 1† | Model 2‡ | Model 3§ |
|----------|---------------------|--------------|----------|----------|----------|
| Normal   | 24/21 935           | 1.0 (0.6, 1.4) | Reference (1) | Reference (1) | Reference (1) |
| Overweight | 42/28 610          | 1.4 (1.0, 1.9) | 1.46 (0.87, 2.44) | 1.39 (0.82, 2.36) | 1.25 (0.98, 1.57) |
| Obese    | 49/23 573           | 2.7 (1.9, 3.5) | 2.77 (1.63, 4.70) | 2.38 (1.36, 4.14) | 1.25 (0.98, 1.57) |

BMI indicates body mass index; CI, confidence interval; CVD, cardiovascular disease; HDL, high-density lipoprotein; IR, incidence rates; MESA, Multi-Ethnic Study of Atherosclerosis; SES, socioeconomic status.

*IR: incidence rate (95% confidence intervals) per 1000 person years, adjusted for age, sex, race, and center.
†Model 1 (demographics and SES model): adjusted for age at baseline, sex, race/ethnicity, center, and education.
‡Model 2 (+CVD risk factors): additionally adjusted for smoking, physical activity, healthy diet score, total cholesterol, HDL cholesterol, use of cholesterol-lowering medications, systolic blood pressure, use of antihypertensive medications, and diabetes mellitus.
§Model 3 (for analyses of BMIs at age 20 and 40): additionally adjusted for BMI at MESA baseline.
| Based on self-reported weights.
| Statistically significant (P<0.05).
absence of elevated BMI at older age, might also indicate that an individual is at higher risk for developing clinical HF and might warrant closer surveillance. However, the best strategies of how to mitigate risk in this scenario are uncertain. Future studies are needed to determine how best to incorporate prior weight history into clinical management.

There are many strengths of our study including the use of a well-characterized multi-ethnic community-based cohort with long-term follow-up for adjudicated HF and ASCVD events. However, our study findings should be considered in the context of several limitations. First, our study is observational and although we carefully adjusted for numerous confounding and potentially mediating variables, there might be unmeasured factors linking self-reported weights in early- and midlife with later life HF/ASCVD risk. Second, the BMI estimates for ages 20 and 40 years were calculated using height measured in later life, using the assumption that height is relatively stable across adulthood, but loss of vertebral height in spine and kyphosis can lead to reduced height in older adults. However, this height assumption was uniformly applied across all MESA participants, and the BMIs at baseline and during follow-up examinations were based on concurrently measured heights. Third, MESA participants were all free of clinical HF/ASCVD at entry and there might be survival bias.

Finally, weights at ages 20 and 40 years were collected by retrospective self-report. It is inevitable that the weights reported are prone to both variation in memory and inherent biases. Self-reported weight has been found to be a reasonably valid surrogate in epidemiology studies, but accuracy may vary by race and sex. Several studies have characterized the validity of retrospective-recalled self-reported weight and measured weight in longitudinal cohorts. In the longitudinal Charleston Heart Study, male and female, black and white, adults aged 60

### Table 5. Incidence Rates and Adjusted Hazard Ratios (95% CI) for Incident Heart Failure With Reduced Ejection Fraction Associated With BMI at Each Age Point

| BMI at age 20 y, per 5 kg/m² higher | N Events/Person-Year | IR (95% CI)* | Model 1† | Model 2‡ | Model 3§ |
|-----------------------------------|----------------------|-------------|-----------|-----------|-----------|
| Normal                            | 80/62 708            | 1.5 (1.1, 1.8) | Reference (1) | Reference (1) | Reference (1) |
| Overweight                        | 29/10 107            | 2.4 (1.5, 3.3) | 1.65 (1.07, 2.55) | 1.54 (0.99, 2.38) | 1.56 (0.99, 2.46) |
| Obese                             | 9/1502               | 6.7 (2.2, 11.1) | 4.34 (2.15, 8.76) | 3.67 (1.79, 7.52) | 3.78 (1.79, 8.00) |

BMI categories at age 40 y

| BMI at age 40 y, per 5 kg/m² higher | N Events/Person-Year | IR (95% CI)* | Model 1† | Model 2‡ | Model 3§ |
|-----------------------------------|----------------------|-------------|-----------|-----------|-----------|
| Normal                            | 48/40 590            | 1.4 (1.0, 1.8) | Reference (1) | Reference (1) | Reference (1) |
| Overweight                        | 43/25 736            | 1.6 (1.1, 2.1) | 1.19 (0.78, 1.81) | 1.11 (0.72, 1.69) | 1.17 (0.75, 1.84) |
| Obese                             | 27/7990              | 4.0 (2.4, 5.5) | 2.80 (1.71, 4.56) | 2.20 (1.32, 3.67) | 2.50 (1.36, 4.57) |

BMI categories baseline

| BMI categories baseline | N Events/Person-Year | IR (95% CI)* | Model 1† | Model 2‡ | Model 3§ |
|------------------------|----------------------|-------------|-----------|-----------|-----------|
| Normal                 | 26/22 009            | 1.6 (0.9, 2.2) | Reference (1) | Reference (1) | Reference (1) |
| Overweight             | 46/29 329            | 1.5 (1.1, 1.9) | 0.96 (0.59, 1.57) | 0.84 (0.51, 1.39) |
| Obese                  | 46/22 979            | 2.2 (1.6, 2.9) | 1.39 (0.84, 2.30) | 1.04 (0.61, 1.77) |

Time-varying BMI (v1–v5)

| BMI at age 20 y, per 5 kg/m² higher | N Events/Person-Year | IR (95% CI)* | Model 1† | Model 2‡ | Model 3§ |
|-----------------------------------|----------------------|-------------|-----------|-----------|-----------|
| Normal                            | 28/21 921            | 1.5 (0.9, 2.1) | Reference (1) | Reference (1) |
| Overweight                        | 45/28 512            | 1.5 (1.0, 1.9) | 0.96 (0.60, 1.55) | 0.85 (0.52, 1.40) |
| Obese                             | 40/23 690            | 1.9 (1.3, 2.5) | 1.25 (0.75, 2.07) | 0.96 (0.56, 1.64) |

BMI indicates body mass index; CI, confidence interval; CVD, cardiovascular disease; HDL, high-density lipoprotein; IR, incidence rates; MESA, Multi-Ethnic Study of Atherosclerosis; SES, socioeconomic status.

*IR: (95% CI) per 1000 person-y, adjusted for age, sex, race, and center.
†Model 1 (demographics and SES model): adjusted for age at baseline, sex, race/ethnicity, center, and education.
‡Model 2 (+CVD risk factors): additionally adjusted for smoking, physical activity, healthy diet score, total cholesterol, HDL cholesterol, use of cholesterol-lowering medications, systolic blood pressure, use of antihypertensive medications, and diabetes mellitus.
§Model 3 (for analyses of BMIs at age 20 and 40 y): additionally adjusted for BMI at MESA baseline.
kBased on self-reported weights.
¶Statistically significant (P<0.05).
to 100 years were asked in 1987 to 1989 to recall their weights back in 1960 and 1984. The correlation coefficients comparing recalled weight from 28 and 4 years prior, compared with measured visit weights, were found to be 0.822 and 0.935, respectively. Participants in the lowest BMI quartile overestimated their weight, while participants in the highest quartile underestimated their weight. Of note, as performance on cognitive tests declined, the percent error between recalled and measured weight increased. An analysis from the Swedish Twin Adoption Study cohort found that 82.4% of participants accurately assessed their weight within 10% error after a 20-year recall interval. Another study of Japanese men aged 34 to 61 years recalled their adult weight at age 25 years (12–37 years later) with strong correlation (r=0.849). In sum, the literature regarding the validity of self-reported recalled weight suggests that while individual differences with large variation exist, recalled weight approximates the mean measured weight on the population level with reasonable validity.

More recent evidence suggests that self-reported weights can be used as a valid measure for clinicians, especially as mobile technology and weight tracking methods become more widespread. Healthcare providers often do not have access to their patients’ healthcare records (and measured weights) from 1 or 2 decades earlier or more prior. Our assessment of weight from retrospective self-report would be equivalent to a healthcare provider asking their patients—either via questionnaire or during the clinical encounter—about their weights from earlier time points in their lives. In the clinical setting, healthcare providers frequently rely on a patient’s self-report for many other aspects of their health (diet, physical activity, smoking status, etc), which are similarly prone to recall bias and misclassification.

### Table 6. Incidence Rates and Hazard Ratios (95% CI) for Incident ASCVD Associated With BMI at Each Age Point

| BMI categories at age 20 y | N Events/Person-Year | IR (95% CI)* | Model 1† | Reference (1) | Reference (1) | Reference (1) |
|---------------------------|----------------------|-------------|----------|--------------|--------------|--------------|
| Normal                    | 662/61 003           | 12.0 (11.0, 12.9) | Reference (1) | Reference (1) | Reference (1) |
| Overweight                | 142/9798             | 13.9 (11.5, 16.2) | 1.15 (0.96, 1.38) | 1.10 (0.91, 1.32) | 1.08 (0.89, 1.30) |
| Obese                     | 14/25/02             | 19.2 (11.5, 27.0) | 1.39 (0.92, 2.10) | 1.34 (0.88, 2.05) |
| BMI categories at age 40 y |                      |             |          |              |              |              |
| Normal                    | 407/39 465           | 11.1 (10.0, 12.2) | Reference (1) | Reference (1) | Reference (1) |
| Overweight                | 326/24 929           | 13.5 (12.0, 14.9) | 1.19 (1.02, 1.38) | 1.06 (0.90, 1.24) |
| Obese                     | 95/7927              | 15.6 (12.4, 18.8) | 1.37 (1.09, 1.73) | 1.09 (0.86, 1.38) | 1.03 (0.78, 1.34) |
| BMI categories baseline   |                      |             |          |              |              |              |
| Normal                    | 206/21 430           | 10.6 (9.1, 12.1) | Reference (1) | Reference (1) |
| Overweight                | 341/28 468           | 12.0 (10.7, 13.3) | 1.12 (0.94, 1.35) | 0.93 (0.77, 1.12) |
| Obese                     | 281/22 423           | 14.8 (13.0, 16.6) | 1.36 (1.12, 1.65) | 0.99 (0.80, 1.21) |
| Time-varying BMI (v1–v5)  |                      |             |          |              |              |              |
| Normal                    | 197/21 336           | 9.2 (7.9, 10.6)  | Reference (1) | Reference (1) |
| Overweight                | 335/27 554           | 11.6 (10.4, 12.9) | 1.27 (1.06, 1.52) | 1.09 (0.91, 1.32) |
| Obese                     | 281/22 824           | 14.7 (12.9, 16.5) | 1.56 (1.29, 1.90) | 1.20 (0.98, 1.48) |

ASCVD indicates atherosclerotic cardiovascular disease risk; BMI, body mass index; CI, confidence intervals; CVD, cardiovascular disease; HDL, high-density lipoprotein; IR, incidence rates; MESA, Multi-Ethnic Study of Atherosclerosis; SES, socioeconomic status.

*IR: incidence rate (95% CI) per 1000 person-year, adjusted for age, sex, race, and center.
†Model 1 (demographics and SES model): adjusted for age at baseline, sex, race/ethnicity, center, and education.
‡Model 2 (+CVD risk factors): additionally adjusted for smoking, physical activity, healthy diet score, total cholesterol, HDL cholesterol, use of cholesterol-lowering medications, systolic blood pressure, use of antihypertensive medications, and diabetes mellitus.
§Model 3 (for analyses of BMIs at age 20 and 40 y): additionally adjusted for BMI at MESA baseline.
¶Based on self-reported weights.
*Statistically significant (P<0.05).
Conclusions

In summary, among an ethnically diverse cohort of men and women, we found that while a single baseline measure of BMI in middle-aged to older adulthood does predict incident HF (and to a lesser extent ASCVD) risk, it may not tell the whole story. Even after accounting for lifestyle factors associated with obesity (diet and physical activity) and for other variables that may potentially mediate this association (ie, blood pressure, diabetes mellitus, and lipids), and even after accounting for baseline BMI, a self-reported weight history from age 20 and age 40 years still was independently associated with future HF risk. In a typical clinical practice setting, patients are often counseled about their ASCVD/HF risk based on a single BMI, or perhaps based only on a few office-obtained BMIs obtained over a relatively short period. Our study supports the potential utility of assessing an individual’s weight throughout decades of adulthood to gain a more comprehensive understanding of one’s risk for developing incident HF. Future work is needed to determine how best to incorporate this into clinical decision making. Our findings suggest that control of BMI throughout the lifetime is important for reducing the risk of HF.

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Disclosures

None.

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Table S1. P-interaction for the association between BMI and HF.

|        | BMI at age 20 | BMI at age 40 | BMI at baseline |
|--------|---------------|---------------|-----------------|
| Age    | 0.56          | 0.15          | 0.60            |
| Sex    | 0.45          | 0.32          | 0.64            |
| Race   | 0.51          | 0.45          | 0.60            |

Models adjusted for age at baseline, sex, race/ethnicity, center, education, smoking, physical activity, healthy diet score, total cholesterol, HDL cholesterol, use of cholesterol lowering medications, systolic blood pressure, use of anti-hypertensive medications, and diabetes.
Table S2. Hazard ratio for HF associated with BMI at each age point, stratified by age at the MESA baseline exam (2000-2002).

|                                | Age ≤ 60 (n = 2,914) | Age > 60 (n = 3,523) | p-value for interaction |
|--------------------------------|----------------------|----------------------|-------------------------|
| BMI at age 20, per 5 kg/m² higher | 1.38 (1.03, 1.86)    | 1.40 (1.17, 1.67)    | 0.56                    |
| BMI at age 40, per 5 kg/m² higher | 1.32 (1.03, 1.68)    | 1.48 (1.31, 1.68)    | 0.15                    |
| BMI at baseline, per 5 kg/m² higher | 1.25 (1.01, 1.54)    | 1.34 (1.17, 1.54)    | 0.60                    |

Models adjusted for age, sex, race/ethnicity, center, education, smoking, physical activity, healthy diet score, total cholesterol, HDL cholesterol, use of cholesterol lowering medications, systolic blood pressure, use of anti-hypertensive medications, and diabetes.
Figure S1. Participant Inclusion and Exclusions.

6814 participants at MESA Baseline Exam (2000-2002)

Excluded:
31 with missing self-reported weights
27 with no f/u HF or ASCVD data
319 missing covariates

6,437 participants included