Long- and Short-term Weight Change and Incident Coronary Heart Disease and Ischemic Stroke

The Atherosclerosis Risk in Communities Study

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Weight gain increases the prevalence of obesity, a risk factor for cardiovascular disease. Nevertheless, unintentional weight loss can be a harbinger of health problems. The Atherosclerosis Risk in Communities Study (1987–2009) included 15,792 US adults aged 45–64 years at baseline and was used to compare associations of long-term (30 years) and short-term (3 years) weight change with the risks of coronary heart disease (CHD) and ischemic stroke. Age-, gender-, and race-standardized incidence rates were 4.9 (95% confidence interval (CI): 4.6, 5.2) per 1,000 person-years for CHD and 2.5 (95% CI: 2.3, 2.8) per 1,000 person-years for stroke. After controlling for baseline body mass index and other covariates, long-term weight gain (since age 25 years) of more than 2.7% was associated with elevated CHD risk, and any long-term weight gain was associated with increased stroke risk. Among middle-aged adults, short-term (3-year) weight loss of more than 3% was associated with elevated immediate CHD risk (hazard ratio = 1.46, 95% CI: 1.18, 1.81) and stroke risk (hazard ratio = 1.45, 95% CI: 1.10, 1.92). Risk tended to be larger in adults whose weight loss did not occur through dieting. Avoidance of weight gain between early and middle adulthood can reduce risks of CHD and stroke, but short-term, unintentional weight loss in middle adulthood may be an indicator of immediate elevated risk that has not previously been well recognized.

body mass index; body weight changes; coronary heart disease; ischemic stroke

Abbreviations: BMI, body mass index; CHD, coronary heart disease; CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; NHANES II, Second National Health and Nutrition Examination Survey; SD, standard deviation.

Cardiovascular disease (CVD) caused 823,746 deaths in the United States in 2006, with coronary heart disease (CHD) accounting for 68% of CVD deaths and stroke for 17% (1, 2). The association between body mass index (BMI) in adulthood and risks of CHD and ischemic stroke is well established (3–5); however, the role of weight change is less clear. Studies have usually (6–10), but not always (11), found weight gain over a period of 12 or more years to be associated with increased CHD risk. Results on weight loss and CHD are more mixed, with 2 studies finding an association with increased risk (9, 10) and 3 others reporting no association (6–8). One study examining ischemic stroke found increased incidence associated with long-term weight gain but not with weight loss (12).

Diverse findings could be due to differences in study populations, lengths of the weight-change intervals, and the time periods between weight changes and events. Galanis et al. (8) provided insight into this issue by examining CHD risk in relation to 2 weight-change intervals among 6,176 Japanese-American men: 1) the “early interval” from age 25 years to the first study examination (mean = 29 years) and 2) the “late interval” between the first and third examinations (mean = 6 years). Follow-up for incident CHD began at the end of this later interval for both weight-change variables. Compared with weight maintenance (±2.5 kg), the investigators found that the relative risk of CHD was increased with weight gain (>5 kg) in the “early interval” but increased with weight loss (>2.5 kg) in the “late interval.” These
findings may be due to a greater influence of illness on weight change in the “late interval.” To our knowledge, this study of Japanese-American men is the only study to have examined CHD risk associated with early, long-term weight change and later, short-term weight change in the same cohort.

This work, together with the inconsistencies in the literature, led us to hypothesize that risks of CHD and ischemic stroke could differ in adults experiencing earlier, long-term weight change compared with adults experiencing later, short-term weight change. Specifically, we hypothesized that earlier, long-term weight gain experienced over a period of 20 or more years would be associated with increased CHD and stroke risk over a long follow-up period. In contrast, we expected later, short-term weight loss to be associated with increased risk during the years immediately following the weight change. We also explored the impact of BMI and dieting on these relations.

MATERIALS AND METHODS

Study population

We used data from the Atherosclerosis Risk in Communities Study, a study of 15,792 white and black US men and women aged 45–64 years at baseline (examination 1: 1987–1989) (13). Participants were invited to undergo 3 additional examinations at approximate 3-year intervals. This study was approved by the institutional review boards at each field center, and all subjects gave written consent. This secondary analysis was approved by the University of North Carolina at Chapel Hill Non-Biomedical Institutional Review Board.

Study design

We aimed to contrast the association between earlier, long-term weight change from early to middle adulthood and CVD risk during a long follow-up period with the association between later, short-term weight change during mid-adulthood and immediate risk (Figure 1). Earlier, long-term weight change occurred between age 25 years and examination 1 (panel A in Figure 1). Data on events of interest were collected from examination 1 to December 31, 2009; however, we excluded events that occurred within 3 years after examination 1 to avoid including events due to underlying disease and to clearly distinguish the 2 time periods of interest. Throughout this article, we describe results derived from this study design as “long-term.”

Later, short-term weight changes were studied over each of the 3 intervals between the 4 examinations (panel B in Figure 1). After ascertaining an event, we defined short-term weight change as the change between 2 consecutive examinations immediately prior to that event. Follow-up was censored at 3 years after the last examination so that all events occurred within 3 years after weight change. Results from this design will be referred to as “short-term.”

Obesity measures

During examination 1, participants recalled their weight at age 25 years using time-associated events (13), and height was measured to the nearest centimeter with participants wearing no shoes. Body weight was measured at all 4 examinations. These measurements were used to calculate BMI (weight (kg)/height (m)²) at age 25 years and at each of the 4 examinations. Customary BMI categories were used (14): underweight (<18.5), normal-weight (18.5–25.0), overweight (25.0–30.0), and obese (≥30.0). Long-term weight change between age 25 years and examination 1 was categorized as weight gain (≥10%), maintenance (±3%), and weight loss (<10%). Short-term weight change between 2 examinations was categorized as weight gain (<3%), moderate gain (10–<30%), and large gain (≥30%). Short-term weight change was categorized as weight loss (<3%), maintenance (±3%), small gain (3–<10%), and moderate-to-large gain (≥10%). Weight maintenance was defined as weight change of ±3%, since this cutpoint has been shown to indicate an amount of weight change that is less than clinically relevant but more than would be expected from measurement error or diurnal fluctuations in fluid balance under normal conditions (15).

Baseline and follow-up assessments

Interviewer-administered questionnaires (13) assessed education (examination 1), smoking (all examinations), alcohol consumption (all examinations), physical activity (examinations 1 and 3) (by means of the Baecke leisure-time physical activity questionnaire (16)), and dieting to lose weight (examinations 1 and 3). Participants who responded being on a weight-loss diet either at examination 1 and/or at examination 3 were considered to have a propensity for being on a weight-loss diet. In this paper, we will refer to participants with or without a propensity for being on a weight-loss diet as “dieters” and “non-dieters,” respectively.

Ascertainment of incident CHD and ischemic stroke

Incident CHD was defined as definite or probable nonfatal myocardial infarction or definite cardiac death. Inclusion of silent myocardial infarctions and coronary procedures yielded similar results; therefore, we present only the estimates for cardiac death and myocardial infarction. To ascertain cases of incident CHD and ischemic stroke, we used cohort and community surveillance, including discharge lists from local hospitals and local obituaries and annual vital statistics review tapes (13, 17). CHD and ischemic stroke were classified according to the International Classification of Diseases, Ninth Revision.

Exclusions

It was standard in this cohort study to exclude blacks from Washington County, Maryland, or Minneapolis, Minnesota (n = 55), and persons of ethnic groups other than black or white (n = 48) because of small sample sizes. Participants with prevalent or missing information on CHD (n = 1,102) or stroke (n = 325) at examination 1 were also excluded. For the long-term CHD analysis, we excluded participants who had missing covariate data at examination 1 (n = 164) or at age 25 years (n = 194) or had a CHD event within 3 years after examination 1 (n = 176). The corresponding exclusions for the stroke analysis were 185, 201, and 62, respectively.
Data from 14,053 adults were available for our long-term studies of CHD, and data from 14,916 adults were available for stroke. For the short-term CHD analysis, we excluded persons with missing covariate data at examination 1 ($n = 157$) and those who were lost to follow-up or deceased or had an early event within 3 years after examination 1 ($n = 1,081$), as well as those who were missing data on BMI and weight change ($n = 213$). The corresponding exclusions for the stroke analysis were 177, 1,079, and 217, respectively. Sample sizes for the short-term analyses were 13,136 for CHD and 13,891 for stroke.

**Statistical analysis**

Poisson regression was used to calculate incidence rates standardized for age, education, physical activity, and height at examination 1, smoking status at age 25 years and examination 1, and race/field center, gender, and long-term weight change. Cox regression models (18) were used to estimate hazard ratios and 95% confidence intervals. BMI and weight change were analyzed in categorical and continuous forms. Weight change in pounds and weight change in percent yielded similar conclusions; thus, we present only the results from the analyses using percent weight change. We used likelihood ratio tests to fit a parsimonious model characterizing the relationship between weight change and incident CHD and stroke. We first evaluated 9-knot quadratic spline regression models (19) using time since examination 1 as the time scale. Testing of successively simplified models showed that linear models were sufficient for all analyses, except for the analysis of the association of long-term weight change with CHD risk, for which a 3-knot model (5th, 50th, and 95th percentiles) was used. All models were adjusted for race/field center, age, gender, education, and height at examination 1. The long-term analyses were additionally adjusted for smoking at age 25 years and alcohol consumption, physical activity, and smoking at examination 1. For the short-term analyses, smoking, alcohol consumption, and physical activity were used as time-dependent covariates. All models were analyzed for the entire cohort combined and by race/gender group. The interaction terms for interaction between BMI and race/gender groups and between weight change and race/gender groups were not significant; therefore, we present only the findings for all race/gender groups combined. All statistical analyses were performed using SAS, version 9.2 (SAS Institute, Inc., Cary, North Carolina).

**RESULTS**

The examination 1 descriptive characteristics shown in Table 1 are from the data set used for the long-term analyses. The covariate values were almost identical in the short-term subsets and are not shown. Approximately half of the participants were female, and one-quarter were black. The mean BMI at examination 1 was in the overweight range, but the mean BMI at age 25 years was within the normal range.

Long-term weight change (from age 25 years to examination 1) averaged 28 kg (a 21% increase in body weight) over a mean period of 30 years (range, 20–39 years). The mean BMI at examination 1 was in the overweight range, but the mean BMI at age 25 years was within the normal range.

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Standardizing covariates slightly attenuated both rates to 4.1 per 1,000 person-years for CHD and ischemic stroke, respectively. per 1,000 person-years and 3.0 (95% CI: 2.7, 3.2) per 1,000 follow-up were 5.3 (95% confidence interval: 5.0, 5.6) per 1,000 person-years and 3.0 (95% CI: 2.7, 3.2) per 1,000 person-years for CHD and ischemic stroke, respectively. Additionally controlling for long-term weight change did not alter these rates considerably.

BMI at age 25 years and during middle adulthood were both positively associated with incident CHD and stroke (Table 2). A BMI of ≥30 at age 25 years doubled CHD and stroke risk, while a BMI of ≥30 during middle adulthood elevated CHD risk by more than 50%. Additional adjustment for long-term weight change did not substantially change these results (data not shown).

Short-term weight loss, but not long-term weight loss, elevated CHD risk in comparison with weight maintenance (Table 3). Large long-term weight gain was also positively associated with increased CHD risk, and this association was strengthened after additional adjustment for BMI at age 25 years; however, short-term weight gain was not associated with CHD risk. Results for stroke were very similar.

To explore whether the elevated CHD and stroke risks associated with short-term weight loss were related to intentional weight loss or unintentional weight loss, we examined the associations for weight change stratified by dieting status (data not shown). For the CHD analysis, there were 888 dieters, and for the stroke analysis, there were 936 dieters. The average BMI and short-term weight change tended to be higher in dieters (BMI 30.3, a 2.2% gain in weight) than in nondieters (BMI 27.3, a 1.2% gain in weight), and over the short term, 19% of dieters and 18% of nondieters lost more than 3% of their weight for both outcomes. Compared with weight maintainers, the estimate for the association between short-term weight loss and CHD was null and smaller in dieters (hazard ratio (HR) = 1.14, 95% CI: 0.49, 2.68) than in nondieters (HR = 1.45, 95% CI: 1.09, 1.94). This was evidence that dieters who lost weight over a 3-year period did not have elevated CHD risk, but evidence for differences between dieters and nondieters regarding stroke was weak.

Our analyses using continuous weight change elaborated on the categorical analyses. The association between CHD and long-term weight change was U-shaped, with increases in risk leveling off at very high levels (at a weight gain of approximately 65%, representing 91% and 52% increases in CHD risk with and without adjustment for BMI at age 25 years, respectively; Figure 2). The lowest CHD risks were seen in participants who gained 8.5% (95% CI: 5.2, 11.9) without adjustment for BMI at age 25 years and participants who gained 2.7% (95% CI: −4.5, 10.0) with adjustment for BMI at age 25 years. A long-term weight change of ≥16% was associated with a significant increase in CHD (after adjustment for BMI at age 25 years). Although admittedly it is from only 1 study, this result may be useful to policymakers seeking to provide long-term weight-gain cutpoints. In addition, CHD risk was elevated by 50% (95% CI: 1.28, 1.74) at a weight gain of 36%, while a weight gain of 50% elevated CHD risk by 73% (95% CI: 1.46, 2.05) after adjustment for BMI at age 25 years.


<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Coronary Heart Disease Data Set (n = 14,053)</th>
<th>Ischemic Stroke Data Set (n = 14,916)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD) %</td>
<td>Mean (SD) %</td>
</tr>
<tr>
<td>Age, years</td>
<td>54.0 (5.7) 54.1 (5.8)</td>
<td>54.1 (5.8) 55.1 (6.0)</td>
</tr>
<tr>
<td>Female gender</td>
<td>57 55</td>
<td>56 55</td>
</tr>
<tr>
<td>African-American race</td>
<td>26 25</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than high school</td>
<td>22 23</td>
<td>22 23</td>
</tr>
<tr>
<td>High school graduation or equivalent</td>
<td>41 41</td>
<td>41 41</td>
</tr>
<tr>
<td>At least some college</td>
<td>37 36</td>
<td></td>
</tr>
<tr>
<td>BMI³</td>
<td>27.6 (5.4) 27.6 (5.4)</td>
<td>27.6 (5.4) 27.6 (5.4)</td>
</tr>
<tr>
<td>BMI at age 25 years²</td>
<td>23.0 (3.7) 23.0 (3.7)</td>
<td>23.0 (3.7) 23.0 (3.7)</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>43 42</td>
<td></td>
</tr>
<tr>
<td>Former smoker</td>
<td>31 32</td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>26 26</td>
<td></td>
</tr>
<tr>
<td>% who smoked at age 25 years⁴</td>
<td>50 51</td>
<td></td>
</tr>
<tr>
<td>Alcohol drinking status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never/rare drinker</td>
<td>43 42</td>
<td></td>
</tr>
<tr>
<td>Former drinker</td>
<td>18 19</td>
<td></td>
</tr>
<tr>
<td>Light drinker</td>
<td>9 9</td>
<td></td>
</tr>
<tr>
<td>Moderate drinker</td>
<td>16 16</td>
<td></td>
</tr>
<tr>
<td>Heavy drinker</td>
<td>13 14</td>
<td></td>
</tr>
<tr>
<td>Level of physical activity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low (tertile 1)</td>
<td>41 41</td>
<td>41 41</td>
</tr>
<tr>
<td>Medium (tertile 2)</td>
<td>30 30</td>
<td>30 30</td>
</tr>
<tr>
<td>High (tertile 3)</td>
<td>28 28</td>
<td>28 28</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; SD, standard deviation.

* Values shown are from the data sets used for the long-term weight-change analyses examining coronary heart disease and ischemic stroke as outcomes.

* Weight (kg)/height (m)².

* Calculated using weight at age 25 years as recalled at examination 1 and height as measured at examination 1.

* Self-reported smoking at age 25 years from recall at examination 1.

The crude incidence rates over an average of 20 years of follow-up were 5.3 (95% confidence interval (CI): 5.0, 5.6) per 1,000 person-years and 3.0 (95% CI: 2.7, 3.2) per 1,000 person-years for CHD and ischemic stroke, respectively. Standardizing covariates slightly attenuated both rates to 4.1 (95% CI: 3.8, 4.4) per 1,000 person-years and 2.3 (95% CI: 2.1, 2.6) per 1,000 person-years, respectively. Additionally controlling for long-term weight change did not alter these rates considerably.
The negative log-linear relation of short-term weight change with CHD risk indicated that short-term weight losses were associated with elevated immediate risk and weight gains with lowered risk. A short-term weight gain of 5% lowered CHD risk by 8% (95% CI: 0.86, 1.00); this association was slightly attenuated after additional adjustment for BMI at the beginning of the weight-change interval. For stroke, a 5% long-term weight gain elevated risk by 3% (95% CI: 1.01, 1.04), but a 5% short-term weight gain reduced risk by 16% (95% CI: 0.76, 0.93). These estimates changed only slightly after additional adjustment for BMI (Figure 3).

**DISCUSSION**

Our results generally confirmed our hypotheses that compared with weight maintenance, earlier weight gain over a long interval was associated with increased risks of CHD and ischemic stroke, whereas later, weight loss over a shorter interval was associated with increased immediate CHD and stroke risk. Although our analyses of weight change in categories versus a continuous form generally supported each other, there were some differences. Given the reliance of categories on arbitrary cutpoints, the greater power of continuous analyses, and our extensive work to define the shapes of the continuous associations, we are more confident in conclusions drawn from the continuous analyses. We found increased risk with any long-term weight gain for stroke and with weight gain above 2.7% for CHD. The majority of persons in our sample (83%) gained more than 2.7% of their weight at age 25 years and were therefore at elevated CHD risk.

Our estimates of the positive association between long-term large weight gain and CVD agree with previous studies showing that a weight gain of >19 kg since young adulthood (18–21 years) more than doubled the risks of CHD (6) and ischemic stroke (12) in women and the risks of CHD and coronary procedures in men (7), compared with maintaining one’s weight. Associations of short-term weight change with immediate risk have been less well studied. We found that middle-aged adults who lost weight over a 3-year interval without intentionally dieting were more likely to have

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**Table 2.** Associations of BMI<sup>a</sup> at Age 25 Years (Long-term Analysis) and BMI During Middle Adulthood (Short-term Analysis) With Incident Coronary Heart Disease and Ischemic Stroke in the Atherosclerosis Risk in Communities Study, 1987–2009

<table>
<thead>
<tr>
<th>BMI Measure</th>
<th>BMI at Age 25 Years&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Time-dependent BMI During Middle Adulthood&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Events</td>
<td>Person-Years</td>
</tr>
<tr>
<td><strong>Coronary Heart Disease</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Categorical BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight (&lt;18.5)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>67</td>
<td>15,585</td>
</tr>
<tr>
<td>Normal-weight (18.5—&lt;25.0)</td>
<td>885</td>
<td>187,520</td>
</tr>
<tr>
<td>Overweight (25.0—&lt;30.0)</td>
<td>322</td>
<td>47,079</td>
</tr>
<tr>
<td>Obese (≥30.0)</td>
<td>111</td>
<td>10,873</td>
</tr>
<tr>
<td>Linear, continuous BMI (per 5-unit increase)</td>
<td>1,385</td>
<td>261,057</td>
</tr>
<tr>
<td><strong>Ischemic Stroke</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Categorical BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight (&lt;18.5)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>52</td>
<td>16,098</td>
</tr>
<tr>
<td>Normal-weight (18.5—&lt;25.0)</td>
<td>543</td>
<td>198,446</td>
</tr>
<tr>
<td>Overweight (25.0—&lt;30.0)</td>
<td>163</td>
<td>51,382</td>
</tr>
<tr>
<td>Obese (≥30.0)</td>
<td>62</td>
<td>12,002</td>
</tr>
<tr>
<td>Linear, continuous BMI (per 5-unit increase)</td>
<td>820</td>
<td>277,928</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio.

<sup>a</sup> Weight (kg)/height (m)<sup>2</sup>.

<sup>b</sup> Adjusted for smoking status at age 25 years, as well as for race/field center, age, gender, education, smoking status, alcohol consumption, physical activity, and height at examination 1.

<sup>c</sup> Adjusted for race/field center, age, gender, education, and height at examination 1 and for time-dependent smoking status, alcohol consumption, and physical activity.

<sup>d</sup> The hazard ratio for the short-term analysis of BMI is not presented because of a small sample size.
CHD or stroke in the next few years than were adults who maintained their weight or gained weight. Weight loss due to underlying disease and/or sarcopenia has been discussed as part of the obesity paradox, and weight loss in the elderly and in patients suffering heart failure has been found to predict mortality (20–22). Previous studies have also shown involuntary weight loss to be associated with higher mortality (23, 24), while voluntary, controlled weight loss lowered mortality (24, 25).

Table 3. Associations of Long- and Short-term Weight Change With Incident Coronary Heart Disease and Ischemic Stroke in the Atherosclerosis Risk in Communities Study, 1987–2009

<table>
<thead>
<tr>
<th>% Weight Changea</th>
<th>No. of Events</th>
<th>Person-Years</th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Coronary heart disease</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 1b</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight loss</td>
<td>147</td>
<td>19,680</td>
<td>1.22</td>
<td>0.96, 1.56</td>
</tr>
<tr>
<td>Weight maintenance</td>
<td>116</td>
<td>22,693</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Small weight gain</td>
<td>169</td>
<td>39,899</td>
<td>0.84</td>
<td>0.66, 1.06</td>
</tr>
<tr>
<td>Moderate weight gain</td>
<td>543</td>
<td>106,288</td>
<td>1.05</td>
<td>0.86, 1.29</td>
</tr>
<tr>
<td>Large weight gain</td>
<td>410</td>
<td>72,496</td>
<td>1.26</td>
<td>1.02, 1.56</td>
</tr>
<tr>
<td>Model 2c</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight loss</td>
<td>147</td>
<td>19,680</td>
<td>1.06</td>
<td>0.82, 1.35</td>
</tr>
<tr>
<td>Weight maintenance</td>
<td>116</td>
<td>22,693</td>
<td>1.00</td>
<td></td>
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<tr>
<td>Small weight gain</td>
<td>169</td>
<td>39,899</td>
<td>0.88</td>
<td>0.69, 1.11</td>
</tr>
<tr>
<td>Moderate weight gain</td>
<td>543</td>
<td>106,288</td>
<td>1.16</td>
<td>0.95, 1.43</td>
</tr>
<tr>
<td>Large weight gain</td>
<td>410</td>
<td>72,496</td>
<td>1.52</td>
<td>1.22, 1.89</td>
</tr>
<tr>
<td><strong>Ischemic stroke</strong></td>
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<td></td>
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<tr>
<td>Model 1b</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight loss</td>
<td>65</td>
<td>21,218</td>
<td>1.04</td>
<td>0.73, 1.48</td>
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<tr>
<td>Weight maintenance</td>
<td>61</td>
<td>24,484</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Small weight gain</td>
<td>100</td>
<td>42,577</td>
<td>0.98</td>
<td>0.71, 1.34</td>
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<tr>
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<td>312</td>
<td>112,936</td>
<td>1.12</td>
<td>0.85, 1.48</td>
</tr>
<tr>
<td>Large weight gain</td>
<td>282</td>
<td>76,713</td>
<td>1.38</td>
<td>1.04, 1.84</td>
</tr>
<tr>
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<td></td>
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Table 3. Continued

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<th>% Weight Changea</th>
<th>No. of Events</th>
<th>Person-Years</th>
<th>HR</th>
<th>95% CI</th>
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<tr>
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<tr>
<td><strong>Coronary heart disease</strong></td>
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<td></td>
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<tr>
<td>Model 1b</td>
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<td></td>
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</tr>
<tr>
<td>Weight loss</td>
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<td>18,534</td>
<td>1.46</td>
<td>1.18, 1.81</td>
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<tr>
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<td>227</td>
<td>48,637</td>
<td>1.00</td>
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<tr>
<td>Small weight gain</td>
<td>135</td>
<td>29,693</td>
<td>1.09</td>
<td>0.88, 1.35</td>
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<tr>
<td>Moderate-to-large weight gain</td>
<td>25</td>
<td>5,894</td>
<td>1.06</td>
<td>0.70, 1.61</td>
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<tr>
<td>Model 2c</td>
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<td></td>
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</tr>
<tr>
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<td>1.42</td>
<td>1.14, 1.76</td>
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<tr>
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<td>48,637</td>
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<td>29,693</td>
<td>1.10</td>
<td>0.89, 1.36</td>
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<td>1.09</td>
<td>0.72, 1.66</td>
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<td><strong>Ischemic stroke</strong></td>
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<tr>
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<td>80</td>
<td>19,775</td>
<td>1.45</td>
<td>1.10, 1.92</td>
</tr>
<tr>
<td>Weight maintenance</td>
<td>131</td>
<td>51,697</td>
<td>1.00</td>
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<tr>
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<td>31,332</td>
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<td>0.69, 1.25</td>
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<td>Moderate-to-large weight gain</td>
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</tr>
<tr>
<td>Weight loss</td>
<td>80</td>
<td>19,775</td>
<td>1.43</td>
<td>1.08, 1.89</td>
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<tr>
<td>Weight maintenance</td>
<td>131</td>
<td>51,697</td>
<td>1.00</td>
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<tr>
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<td>65</td>
<td>31,332</td>
<td>0.94</td>
<td>0.70, 1.26</td>
</tr>
<tr>
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<td>10</td>
<td>6,269</td>
<td>0.77</td>
<td>0.40, 1.47</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; HR, hazard ratio.

a Weight loss (<−3%), weight maintenance (±3%), small weight gain (3–<10%), moderate weight gain (≥10–<30%), or large weight gain (≥30%).

b The long-term analysis adjusted for smoking status at age 25 years, as well as for race/field center, age, gender, education, smoking status, alcohol consumption, physical activity, and height at examination 1; the short-term analysis adjusted for race/field center, age, gender, education, and height at examination 1 and for time-dependent alcohol consumption, physical activity, and smoking status.

c Model 2 included the model 1 covariates plus body mass index at age 25 years for the long-term analysis and time-dependent body mass index for the short-term analysis.
To our knowledge, no previous study has investigated the association between short-term weight loss and immediate CVD risk. In fact, the literature on weight change over a brief time period (e.g., 3–6 years) and incident CVD is limited in general. Hamm et al. (26) used self-reported weights at several time points between the ages of 20 and 40 years to examine patterns of 25-year fatal CHD risk over segments of weight change averaging 5 years in duration. Compared with men who maintained their weight, those who consistently gained weight did not experience elevated risk; conversely, weight gain followed by weight loss doubled the risk. Two additional studies did not find associations between weight loss over 3–10 years and CHD, possibly because the investigators did not restrict cases to those that occurred immediately after the weight change but included all cases arising during 16–17 years of follow-up (8, 27). These findings illustrate the complex nature of the relationship between timing of weight changes during adulthood and CVD risk.

Our study used serial measurements of body weight during mid-adulthood to examine associations between short-term weight change and CVD risk. Nevertheless, our examination of long-term weight change used recall of weight at age 25 years by participants who were middle-aged. We have shown that bias in recall of past weight is smaller than that seen in recall of current weight and that recalled weight from the remote past (28 years prior) is highly correlated with weight measured at that time ($r > 0.8$) (28–30). In addition, we are aware that end-digit preference and rounding tends to occur with recall. In our sample, 77% of participants reported a weight at age 25 years ending in 0 or 5. However, a study using data from the Second National Health and Nutrition Examination Survey (NHANES II; 1976–1980) showed that the reporting error between people with end-digit preference and those without end-digit preference was not statistically significantly different, indicating that rounding was random in all gender and BMI subgroups, except that severely overweight (BMI ≥ 32.3) women who...
recalled their weight with a 5 or 0 digit preference seemed to be rounding down (31). Nonetheless, severely overweight women with end-digit preference comprised only 1% of our study sample. In our study, the average recalled weight at age 25 years was 165.3 pounds (75.0 kg) (standard deviation (SD), 26.5 (12.0)) in men and 128.1 pounds (58.2 kg) (SD, 21.8 (9.9)) in women, which is comparable to the average weight reported in NHANES II for the age groups 18–24 years (162.7 pounds (73.9 kg) [SD, 28.0 (12.7)] in men and 133.6 pounds (60.7 kg) [SD, 26.3 (11.9)] in women) and 25–34 years (173.4 pounds (78.7 kg) [SD, 30.1 (13.7)] in men and 141.6 pounds (64.3 kg) [SD, 33.0 (15.0)] in women) (32). Nevertheless, measured weights are preferred. Another limitation was that information on dieting was self-reported and only available at 2 examinations. Furthermore, the potential of residual confounding through smoking and comorbid conditions needs to be considered. However, we carefully adjusted our long-term models for smoking status at age 25 years and at examination 1 and adjusted our short-term models for time-dependent smoking status. In addition, we excluded events that occurred within 3 years after examination 1 in the long-term weight-change analysis to avoid inclusion of events due to preexisting illness (33).

Strengths of our study include the use of carefully adjudicated assessments of CHD and ischemic stroke. We adjusted our analyses for BMI because it has been shown that weight change is related to initial weight (27, 34). Further, we attempted to distinguish intentional weight loss from unintentional weight loss over the short term.

Our results support the avoidance of weight gains greater than 2.7% between early and middle adulthood, since such gains are associated with increased risks of CHD and stroke. Because the majority of adults in the United States gain more than 10% of their body weight during this period (35), there is an urgent need for effective interventions to prevent weight gain during this high-risk period. Additional clinical implications from this work point to a need for increased

Figure 3. Hazard ratios for incident ischemic stroke according to long- and short-term weight change in the Atherosclerosis Risk in Communities Study, 1987–2009. Long-term weight change was analyzed using linear models with adjustment for smoking status at age 25 years and for race/field center, age, gender, education, smoking status, alcohol consumption, physical activity, and height at examination 1, as well as with and without adjustment for body mass index (BMI; weight (kg)/height (m)^2) at age 25 years. Short-term weight change was analyzed using linear models with adjustment for race/field center, age, gender, education, and height at examination 1 and for time-dependent alcohol consumption, physical activity, and smoking status, as well as with and without adjustment for BMI at the beginning of the weight-change interval.
attention to unexplained, short-term weight loss. In middle-aged adults, this weight loss could be a warning sign of an impending cardiovascular event. Studies confirming these estimates and elucidating potential mechanisms are needed.

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All authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Conflict of interest: none declared.

REFERENCES


33. Stevens J, Juhaeri, Cai J. Changes in body mass index prior to baseline among participants who are ill or who die during the early years of follow-up. *Am J Epidemiol.* 2001;153(10):946–953.