Alcohol Consumption, Weight Gain, and Risk of Becoming Overweight in Middle-aged and Older Women

Lu Wang, MD, PhD; I-Min Lee, MBBS, ScD; JoAnn E. Manson, MD, DrPH; Julie E. Buring, ScD; Howard D. Sesso, ScD, MPH

Background: The obesity epidemic is a major health problem in the United States. Alcohol consumption is a source of energy intake that may contribute to body weight gain and development of obesity. However, previous studies of this relationship have been limited, with inconsistent results.

Methods: We conducted a prospective cohort study among 19,220 US women aged 38.9 years or older who were free of cardiovascular disease, cancer, and diabetes mellitus and had a baseline body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) within the normal range of 18.5 to less than 25. Alcoholic beverage consumption was reported on a baseline questionnaire. Body weight was self-reported on baseline and 8 annual follow-up questionnaires.

Results: There was an inverse association between amount of alcohol consumed at baseline and weight gained during 12.9 years of follow-up. A total of 7,942 (41.3%) initially normal-weight women became overweight or obese (BMI ≥25) and 732 (3.8%) became obese (BMI ≥30). After adjusting for age, baseline BMI, smoking status, nonalcohol energy intake, physical activity level, and other lifestyle and dietary factors, the relative risks of becoming overweight or obese across total alcohol intake of 0, more than 0 to less than 5, 5 to less than 15, 15 to less than 30, and 30 g/d or more were 1.00, 0.96, 0.86, 0.70, and 0.73, respectively (P for trend <.001). The corresponding relative risks of becoming obese were 1.00, 0.75, 0.43, 0.39, and 0.29 (P for trend <.001). The associations were similar by subgroups of age, smoking status, physical activity level, and baseline BMI.

Conclusion: Compared with nondrinkers, initially normal-weight women who consumed a light to moderate amount of alcohol gained less weight and had a lower risk of becoming overweight and/or obese during 12.9 years of follow-up.

Arch Intern Med. 2010;170(5):453-461

Obesity is a well-established, modifiable risk factor for many chronic diseases, including hypertension, type 2 diabetes mellitus, cardiovascular disease, and cancer. The increase in prevalence of overweight (defined as a body mass index [BMI; calculated as weight in kilograms divided by height in meters squared] of 25 to <30) and obesity (defined as a BMI of ≥30) in the United States was noted as early as 1960 and continued at least until 1999. A survey conducted from 1999 through 2000 as part of the National Health and Nutrition Examination Survey estimated that nearly two-thirds of US adults have a BMI of 25 or higher, providing evidence of an ongoing obesity epidemic. Balancing energy intake and energy expenditure for the prevention of obesity is of major public health importance in the US population.

More than half of US adults consume alcoholic beverages. Alcohol, with a caloric value of 7.1 kcal/g, represents a nontrivial energy source that may contribute to a positive energy balance and, in the long-term, result in weight gain and the development of obesity. However, epidemiological studies have not provided consistent evidence for alcohol consumption as a risk factor for obesity. Cross-sectional studies have reported associations between alcohol intake and body weight to be positive or null in men and inverse or null in women. Only a few prospective cohort studies have examined alcohol consumption and long-term change in body weight, and the results are conflicting, with positive and null associations found in men and positive, inverse, and null associations found in women. Although overweight and obesity are widely recognized as adverse clinical profiles, to our

Author Affiliations: Divisions of Preventive Medicine (Drs Wang, Lee, Manson, Buring, and Sesso) and Aging (Drs Buring and Sesso), Department of Medicine, Brigham and Women’s Hospital, and Department of Epidemiology, Harvard School of Public Health (Drs Lee, Manson, and Buring), Boston, Massachusetts.
knowledge, no previous studies have specifically investigated the risk of becoming overweight or obese among initially normal-weight individuals. We, therefore, examined the prospective association of alcohol consumption with weight gain and risk of becoming overweight or obese in a large cohort of middle-aged and older US women during 12.9 years of follow-up.

STUDY METHODS

The Women’s Health Study (WHS) was a randomized, clinical trial evaluating the effects of low-dose aspirin and vitamin E in the primary prevention of cardiovascular disease and cancer. A third component, β-carotene, was initially included but was terminated after a median treatment duration of 2.1 years. Blinded treatment with aspirin and vitamin E ended as scheduled on March 31, 2004, and observational follow-up of the WHS cohort continues. Written informed consent was obtained from all participants. The trial was approved by the institutional review board of Brigham and Women’s Hospital. From September 1992 to May 1995, 39,876 female US health care professionals aged 38.9 to 89.0 years and who were free of cardiovascular disease and cancer (except nonmelanoma skin cancer) were randomized into the WHS. Of the 39,876 women randomized, 19,563 (49.1%) who remained for analysis.

STUDY POPULATION

Of the 39,876 women randomized, 19,563 (49.1%) who remained for analysis. We excluded 5 women with missing data on baseline alcohol intake, 128 women with no updated body weight during the entire follow-up period, 194 women with baseline diabetes, and 17 women with prerandomization cardiovascular disease or cancer. As a result of these partially overlapping exclusions, a baseline population of 19,220 women remained for analysis.

ASSESSMENT OF ALCOHOL INTAKE

On a baseline questionnaire, participants were asked how often, on average, they had consumed alcoholic beverages, including beer (1 glass, bottle, or can), red wine (4-oz glass), white wine (4-oz glass), and liquor (1 drink or shot), during the previous year. Nine possible responses ranging from “never or less than once per month” to “6+ per day” were recorded. Alcohol intake was calculated according to the alcohol content in each beverage, assuming ethanol of 13.2 g for 360 mL (12 oz) of beer, 10.8 g for 120 mL (4 oz) of red or white wine, and 15.1 g for 45 mL (1.5 oz) of liquor. Among health care professionals similar to the WHS cohort, the correlation of alcohol intake estimated from dietary records with questionnaire data was 0.90 for total alcohol intake, 0.81 for beer, 0.83 for wine, and 0.80 for liquor intake.

OTHER BASELINE VARIABLES

Women in the WHS reported age, smoking status, physical activity level, menopausal status, postmenopausal hormone use, multivitamin use, and history of diabetes mellitus, hypertension, and hypercholesterolemia on the baseline questionnaire. A total of 39,310 of the 39,876 randomized participants (98.6%) completed a 131-item, validated, semiquantitative food frequency questionnaire. A commonly used unit or portion size was specified for each food item, and participants reported how often they had consumed that amount, on average, during the previous year. Nutrient intake was computed by multiplying the intake frequency of each unit of food by the nutrient content of the specified portion size according to food composition tables from the Harvard School of Public Health. Intake of each nutrient reported in the present study was adjusted for total energy intake using the residual method. The semiquantitative food frequency questionnaire used in the WHS has demonstrated reasonable validity and reproducibility as a measure of long-term average dietary intake.

ASCERTAINMENT OF BODY-WEIGHT CHANGE AND INCIDENCE OF OVERWEIGHT AND/OR OBESITY

The WHS participants reported height and weight on the baseline questionnaire. Information on body weight was updated on the annual follow-up questionnaires during the trial period (referred to as the 2-, 3-, 5-, 6-, and 9-year follow-up questionnaires). After the end of the WHS intervention, 16,322 of the 19,220 women (84.9%) with a normal BMI at baseline agreed to continue in the observational follow-up and updated body weight on the first, second, and third observational follow-up questionnaires (referred to as the 11-, 12-, and 13-year follow-up questionnaires). The BMIs were then calculated using the weight and height self-reported at baseline and at a total of 8 follow-up time points, each classified as normal (18.5 to <25), overweight (25 to <30), or obese (≥30) according to the National Heart, Lung, and Blood Institute and the National Institute of Diabetes and Digestive and Kidney Diseases criteria. Incident cases of becoming overweight or obese were defined as women who had a normal BMI at baseline and subsequently reported a BMI of 25 or higher at any follow-up time point. For each participant who became overweight or obese, the time-of-event was calculated as the estimated time when her BMI crossed the cutoff point (ie, 25) by modeling a regression line from the last reported BMI of less than 25 to the first reported BMI of 25 or higher during follow-up. For women who did not become overweight or obese, the time-of-censoring was calculated as the latest date when a BMI of less than 25 was reported. Incident cases of becoming obese were defined in a similar manner using a BMI of 30 as the cutoff point. Women who developed intermediate diabetes, the management of which typically involves weight control, were censored on the date of the diabetes diagnosis. In similar populations of female health care professionals, self-reported weights were highly correlated with clinic-measured weights (Pearson r = 0.97). Studies in adults across different populations also have found that self-reported overweight and obesity status are accurate.

STATISTICAL ANALYSIS

Statistical analyses were performed using SAS statistical software, version 9.1 (SAS Institute, Cary, North Carolina). Total alcohol intake was divided into predetermined categories of 0, more than 0 to less than 3, 3 to less than 15, 15 to less than 30, and 30 g/d or more. Potential confounders were identified by comparing demographic, lifestyle, clinical, and dietary factors across levels of total alcohol intake. Weight change from baseline to follow-up was calculated at each follow-up time point and compared across categories of baseline alcohol intake using analysis of covariance. Out of concern that body-weight composition and weight-change pattern may be modified by the aging process, we also conducted stratified analyses by baseline age. Cox models were then used to assess the association between alcohol intake and the risk of becoming overweight or obese. The hazard ratios, presented as relative risks (RRs), and 95% confidence intervals (CIs) were estimated across categories of total alcohol intake, with nondrinkers as the reference. The independent associations for each type of alcoholic beverage (beer, red wine, white wine, and liquor) were determined by including the 4 bev-
Among 19 220 middle-aged and older women who reported a baseline BMI of 18.5 to less than 25, 7346 (38.2%) did not consume alcohol, and 568 (3.0%) consumed 30 g/d or more. Compared with nondrinkers, women who consumed a greater amount of alcohol were significantly older, more likely to be white, current smokers, postmenopausal, and hypertensive and had slightly lower baseline BMI (Table 1). Total energy intake significantly increased with increasing alcohol intake, whereas energy intake excluding the calories from alcohol decreased with increasing alcohol intake. Energy expenditure through leisure-time physical activity had a U-shaped relationship with alcohol consumption, with women who consumed intermediate amounts of alcohol having the highest level of physical activity. With regard to the dietary factors, alcohol intake was positively associated with intake of red meats, poultry, and high-fat dairy products; inversely associated with intake of whole grains, refined grains, low-fat dairy products, total and subgroup fats, carbohydrates, and fiber; and unassociated with fruit, vegetable, and protein intake.

During 12.9 years of follow-up, women, on average, gained weight progressively (Table 2). Throughout the
follow-up, the age-adjusted weight gain was the largest for women who did not consume alcohol and then monotonously decreased with increasing total alcohol intake (P for trend <.001 at all time points). This relationship became even stronger after adjusting for race, baseline weight, nonalcohol energy intake, physical activity level, smoking habits, and other lifestyle and dietary factors. The multivariate-adjusted mean weight gain during 12.9 years of follow-up was 3.63 kg (95% CI, 3.45-3.80 kg) for women who did not consume alcohol compared with those consuming 30 g/d or more. However, when women who reported alcohol consumption of 40 g/d or more were compared with those consuming 30 to less than 40 g/d, the weight gains were similar (data not shown). In analyses stratified by baseline age (Figure 1), a trend for decreasing weight gain with increasing total alcohol intake was consistently observed among women younger than 50, 50 to younger than 60, and 60 years or older, although the magnitude of weight gain was smaller in older vs younger women.

Of the 19,220 women with normal weight at baseline, 7,942 (41.3%) became overweight or obese during 12.9 years of follow-up. Compared with nondrinkers, women who consumed more than 0 to less than 5, 5 to less than 15, 15 to less than 30, and 30 g/d or more of alcohol had age-adjusted RRs of 0.96, 0.84, 0.73, and 0.78, respectively, for becoming overweight or obese (Table 3). The risk of becoming overweight or obese was not further reduced for women consuming 40 g/d or more of alcohol (age-adjusted RR, 0.90 [95% CI, 0.71-1.13]). These RRs changed little after multivariate adjustment. An inverse association between alcohol intake and risk of becoming overweight or obese was noted for all 4 types of alcoholic beverages, with the strongest association found for red wine and a weak yet significant association for white wine after multivariate adjustment. Using a BMI of 30 or higher as the cutoff, 7,32 of the 19,220 initially normal-weight women (3.8%) became obese during 12.9 years of follow-up. The multivariate RRs for becoming obese across increasing total alcohol intake of more than 0 to less than 5, 5 to less than 15, 15 to less than 30, and 30 g/d or more were 0.75, 0.43, 0.39, and 0.29, respectively. The inverse associations with risk of becoming obese were also statistically significant for all 4 alcoholic beverage types in a multivariate model.

The inverse association between total alcohol intake and risk of becoming overweight or obese did not substantially differ by subgroups of women (Figure 2). Compared with women who did not consume alcohol and were younger than 50, the RRs of becoming overweight or obese across increasing total alcohol intake decreased from 1 (reference) to 0.68 (95% CI, 0.51-0.90) among women younger than 50, from 0.94 (0.85-1.04) to 0.75 (0.59-0.93) among women aged 50 to younger than 60 years, and from 0.90

<table>
<thead>
<tr>
<th>Follow-up Duration</th>
<th>Total Alcohol Intake, g/d&lt;sup&gt;a&lt;/sup&gt;</th>
<th>No. (%) of Participants</th>
<th>0</th>
<th>&gt;0 to &lt;5</th>
<th>5 to &lt;15</th>
<th>15 to &lt;30</th>
<th>≥30</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 y</td>
<td>Age adjusted</td>
<td>18,998 (98.8)</td>
<td>1.49</td>
<td>1.39</td>
<td>1.22</td>
<td>1.11</td>
<td>0.77</td>
</tr>
<tr>
<td></td>
<td>Multivariate adjusted&lt;sup&gt;b&lt;/sup&gt;</td>
<td>17,955 (93.4)</td>
<td>1.55</td>
<td>1.41</td>
<td>1.14</td>
<td>0.89</td>
<td>0.51</td>
</tr>
<tr>
<td>3 y</td>
<td>Age adjusted</td>
<td>18,096 (94.2)</td>
<td>1.97</td>
<td>1.79</td>
<td>1.64</td>
<td>1.46</td>
<td>1.28</td>
</tr>
<tr>
<td></td>
<td>Multivariate adjusted&lt;sup&gt;b&lt;/sup&gt;</td>
<td>17,118 (89.1)</td>
<td>2.05</td>
<td>1.81</td>
<td>1.53</td>
<td>1.22</td>
<td>0.95</td>
</tr>
<tr>
<td>5 y</td>
<td>Age adjusted</td>
<td>18,065 (94.0)</td>
<td>2.68</td>
<td>2.61</td>
<td>2.26</td>
<td>2.11</td>
<td>1.61</td>
</tr>
<tr>
<td></td>
<td>Multivariate adjusted&lt;sup&gt;b&lt;/sup&gt;</td>
<td>17,195 (89.0)</td>
<td>2.77</td>
<td>2.65</td>
<td>2.16</td>
<td>1.78</td>
<td>1.16</td>
</tr>
<tr>
<td>6 y</td>
<td>Age adjusted</td>
<td>17,775 (92.5)</td>
<td>2.99</td>
<td>2.88</td>
<td>2.54</td>
<td>2.38</td>
<td>1.93</td>
</tr>
<tr>
<td></td>
<td>Multivariate adjusted&lt;sup&gt;b&lt;/sup&gt;</td>
<td>16,820 (87.5)</td>
<td>3.10</td>
<td>2.92</td>
<td>2.42</td>
<td>2.11</td>
<td>1.47</td>
</tr>
<tr>
<td>9 y</td>
<td>Age adjusted</td>
<td>15,341 (79.8)</td>
<td>3.44</td>
<td>3.35</td>
<td>2.94</td>
<td>2.74</td>
<td>2.11</td>
</tr>
<tr>
<td></td>
<td>Multivariate adjusted&lt;sup&gt;b&lt;/sup&gt;</td>
<td>14,576 (75.8)</td>
<td>3.52</td>
<td>3.40</td>
<td>2.83</td>
<td>2.50</td>
<td>1.57</td>
</tr>
<tr>
<td>11 y</td>
<td>Age adjusted</td>
<td>16,322 (84.9)</td>
<td>3.47</td>
<td>3.39</td>
<td>2.91</td>
<td>2.65</td>
<td>2.31</td>
</tr>
<tr>
<td></td>
<td>Multivariate adjusted&lt;sup&gt;b&lt;/sup&gt;</td>
<td>15,481 (80.5)</td>
<td>3.55</td>
<td>3.46</td>
<td>2.81</td>
<td>2.40</td>
<td>1.83</td>
</tr>
<tr>
<td>12 y</td>
<td>Age adjusted</td>
<td>15,992 (83.2)</td>
<td>3.57</td>
<td>3.48</td>
<td>2.97</td>
<td>2.63</td>
<td>2.41</td>
</tr>
<tr>
<td></td>
<td>Multivariate adjusted&lt;sup&gt;b&lt;/sup&gt;</td>
<td>15,178 (79.0)</td>
<td>3.67</td>
<td>3.53</td>
<td>2.86</td>
<td>2.37</td>
<td>2.02</td>
</tr>
<tr>
<td>13 y</td>
<td>Age adjusted</td>
<td>15,634 (81.3)</td>
<td>3.53</td>
<td>3.50</td>
<td>3.05</td>
<td>2.87</td>
<td>2.09</td>
</tr>
<tr>
<td></td>
<td>Multivariate adjusted&lt;sup&gt;b&lt;/sup&gt;</td>
<td>14,849 (77.3)</td>
<td>3.63</td>
<td>3.56</td>
<td>2.95</td>
<td>2.56</td>
<td>1.55</td>
</tr>
</tbody>
</table>

<sup>a</sup>Linear trends were tested using the median value of each alcohol intake category as an ordinal variable. All were P < .001.

<sup>b</sup>Multivariate model was additionally adjusted for race (white or nonwhite), baseline weight (continuous), randomized treatment (vitamin E, aspirin, beta carotene, or placebo), total nonalcohol energy intake (continuous), physical activity level (<200, 200 to <600, 600 to <1500, and ≥1500 kcal/wk), smoking status (never, former, or current), postmenopausal status (yes, no, or uncertain), postmenopausal hormone use (never, former, or current), multivitamin use (never, former, or current), history of hypercholesterolemia (yes or no) and hypertension (yes or no), and intake of fruit and vegetables, whole grains, refined grains, red meats and poultry, low-fat dairy products, high-fat dairy products, energy-adjusted total fat, carbohydrates, and fiber (all in quintiles).

(Reprinted) Arch Intern Med/Vol 170 (No. 5), Mar 8, 2010 www.archinternmed.com 456

©2010 American Medical Association. All rights reserved.
(0.74-1.09) to 0.63 (0.43-0.91) among women aged 60 years or older. The reduction in risk of becoming overweight or obese with increasing total alcohol intake was also similar by stratum of smoking, physical activity level, and baseline BMI (all P for interaction >.05).

Several secondary analyses were performed. First, we additionally adjusted for consumption of other beverages, including varieties of coffee, soft drinks, and tea. Second, we excluded women who smoked or had a history of hypertension or hypercholesterolemia at baseline. Third, we censored women when they developed intermediate chronic diseases, including cardiovascular disease, hypertension, hypercholesterolemia, and cancer, during follow-up. Fourth, we restricted the analyses to 12,132 women who returned all follow-up questionnaires and updated body weight on each questionnaire during the entire follow-up period. Finally, we updated alcohol intake at the 48- and 108-month follow-up points using a time-dependent variable. The overall results did not materially change in any of these secondary analyses and therefore are not presented.

COMMENT

In this large cohort of middle-aged and older women, we found that, compared with consuming no alcohol at all, light to moderate alcohol consumption was associated with less weight gain and a lower risk of becoming overweight and/or obese during 12.9 years of follow-up. These associations remained highly significant after adjustment for multiple lifestyle, clinical, and dietary factors. To our knowledge, this is the first study that examined the association between alcohol consumption and risk of developing clinically defined overweight and obesity among initially normal-weight individuals.

Previous cross-sectional studies of alcohol intake and body weight have shown positive or null associations in men and inverse or null associations in women. Prospective studies that focused on weight change have been equally inconsistent across populations. In the Framingham Heart Study, men and women who increased their alcohol consumption during 20 years of follow-up experienced weight gains larger than the average. A similar association was noted in the Nurses Health Study II: light to moderate alcohol intake and 8-year weight gain was found among 31,940 nonsmoking women. A similar association was noted in the Nurses Health Study I; an inverse association between alcohol intake and 8-year weight gain was found among 31,940 nonsmoking women. A similar association was noted in the Nurses Health Study II: light to moderate alcohol intake and 8-year weight gain was found among 31,940 nonsmoking women. A similar association was noted in the Nurses Health Study II: light to moderate alcohol intake and 8-year weight gain was found among 31,940 nonsmoking women.

![Figure 1. Multivariate adjusted mean body weight change (in kilograms) during 12.9 years of follow-up according to baseline total alcohol intake, stratified by baseline age group. A, Participants younger than 50 years at baseline (n=6430). B, Participants aged 50 to 59 years at baseline (n=6792). C, Participants aged 60 years or older at baseline (n=3998). Model adjusted for age, race, baseline weight, randomized treatment, total nonalcohol energy intake, physical activity level, smoking status, postmenopausal status, postmenopausal hormone use, multivitamin use, history of hypercholesterolemia and hypertension, and intake of fruit and vegetables, whole grains, refined grains, red meats and poultry, low-fat dairy products, high-fat dairy products, energy-adjusted total fat, carbohydrates, and fiber. P value for a linear trend of body weight change across levels of total alcohol intake was tested using the median value of each alcohol intake category as an ordinal variable. P for a linear trend of a smaller weight gain across increasing alcohol intake at the 12.9-y follow-up, <.001 for A and B and .02 for C.](http://www.archinternmed.com/article-pdf/170/5/457/983852/457.pdf)
British men, alcohol consumption of 30 g/d or more significantly increased BMI and the risk of weight gain of 4% or more during a 5-year period (odds ratio, 1.29) compared with nondrinkers/occasional drinkers.17 In contrast to these studies, 2 cohort studies found no significant association between alcohol intake and weight change in men or women.18,34 None of these studies investigated the development of clinically defined overweight or obesity as the endpoint.

The association of alcohol consumption with body weight change and development of obesity seems to differ by sex, which must be considered in the context of energy balance. Male drinkers tend to add alcohol to their daily dietary intake, whereas female drinkers usually substitute alcohol for other foods without increasing total energy intake.11,35 Consistent with previous findings,7,10,11,14 our study showed that women consuming more alcohol had lower energy intake from nonalcohol sources, particularly carbohydrates. On the other hand, there may also be sex differences in the metabolism of alcohol. Compared with male drinkers, female drinkers appear to have less alcohol dehydrogenase activity36 and, thus, are more likely to degrade ethanol through other pathways, such as the hepatic microsomal ethanol oxidizing system, which has low-efficiency energy use.37 Metabolic studies have shown that after drinking alcohol, energy expenditure moderately changed in men,38 but substantially increased beyond the energy content of alcoholic beverages in women,39 suggesting that women are more prone to gain weight through alcohol consumption than men. More research is needed to confirm this finding and further investigate the role of sex in alcohol metabolism.

### Table 3. Relative Risks (RRs) and 95% Confidence Intervals (CIs) of Becoming Overweight and/or Obese Across Alcohol Intake

<table>
<thead>
<tr>
<th>Alcohol Intake</th>
<th>Total No. (% of Participants)</th>
<th>Age-Adjusted</th>
<th>Multivariate-Adjusted</th>
<th>No. (%) of Participants</th>
<th>Age-Adjusted</th>
<th>Multivariate-Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>All alcohol intake, g/d</td>
<td>7346 (38.2)</td>
<td>3150 (39.7)</td>
<td>[Reference]</td>
<td>337 (46.0)</td>
<td>[Reference]</td>
<td>1.00 (1.01-1.00)</td>
</tr>
<tr>
<td>&gt;0 to &lt;5</td>
<td>6312 (32.8)</td>
<td>2721 (34.3)</td>
<td>0.96 (0.91-1.01)</td>
<td>250 (34.2)</td>
<td>0.96 (0.91-1.01)</td>
<td>0.96 (0.91-1.01)</td>
</tr>
<tr>
<td>5 to &lt;15</td>
<td>3865 (20.1)</td>
<td>1500 (18.9)</td>
<td>0.84 (0.79-0.89)</td>
<td>104 (14.2)</td>
<td>0.80 (0.76-0.84)</td>
<td>0.85 (0.80-0.92)</td>
</tr>
<tr>
<td>15 to &lt;30</td>
<td>112 (5.9)</td>
<td>376 (4.7)</td>
<td>0.73 (0.68-0.79)</td>
<td>28 (3.8)</td>
<td>0.62 (0.57-0.68)</td>
<td>0.70 (0.62-0.79)</td>
</tr>
<tr>
<td>≥30</td>
<td>568 (3.0)</td>
<td>195 (2.5)</td>
<td>0.78 (0.74-0.83)</td>
<td>13 (1.8)</td>
<td>0.68 (0.62-0.76)</td>
<td>0.73 (0.62-0.85)</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); ellipses, not applicable.

1 Multivariate model was additionally adjusted for race (white or nonwhite), baseline BMI (continuous), randomized treatment (vitamin E, aspirin, beta carotene, multivitamin use (never, former, or current), history of hypercholesterolemia (yes or no) and hypertension (yes or no), intake of fruit and vegetables, whole grains, refined grains, red meats and poultry, low-fat dairy products, high-fat dairy products, energy-adjusted total fat, carbohydrates, and fiber (all in quintiles).

2 Curvilinear trends were tested by including the quadratic term of continuous alcohol intake in the model.

3 Curvilinear trends were tested using the median value of each alcohol intake category as an ordinal variable.

4 Multivariate model was additionally adjusted for race (white or nonwhite), baseline BMI (continuous), randomized treatment (vitamin E, aspirin, beta carotene, multivitamin use (never, former, or current), postmenopausal status (yes, no, or uncertain), postmenopausal hormone use (never, former, or current), history of hypercholesterolemia (yes or no) and hypertension (yes or no), intake of fruit and vegetables, whole grains, refined grains, red meats and poultry, low-fat dairy products, high-fat dairy products, energy-adjusted total fat, carbohydrates, and fiber (all in quintiles).

5 Curvilinear trends were tested using the median value of each alcohol intake category as an ordinal variable.

©2010 American Medical Association. All rights reserved.
sumed alcohol in women.39 Taken together, regular alcohol consumption would potentially result in a gain of energy balance in men but a net energy loss in women. There have been other mechanisms through which alcohol may modify energy balance and, subsequently, body weight, including effect on nutrient digestion and absorption, interference with lipid oxidation and fat accumulation, increased sympathetic tone and associated thermogenesis, and enhanced adenosine triphosphate breakdown.

Complex interrelationships of alcohol consumption with various lifestyle, clinical, and physiological factors are involved in the effect of alcohol drinking on body weight change and, thus, partially explain the inconsistent findings in previous epidemiological studies. For example, drinking habits may change appetite and the perception of satiety, whereby alcohol drinkers would prefer certain diets.7,9-11,15 Alcohol metabolism appears more efficient among heavy people38; therefore, alcohol intake may be more likely to promote weight gain in overweight women than in lean women.31,42 In our study, higher alcohol consumption was generally associated with more current smoking, more physical activity, slightly lower baseline BMI, and less healthy diet. However, the association of light to moderate alcohol intake with less weight gain and lower risk of becoming overweight or obese remained strong after multivariate adjustment and in subgroup analyses, indicating that alcohol consumption may independently affect body weight beyond its relationship with dietary and lifestyle factors. Because body weight change and body mass composition vary by age, we also specifically stratified our analyses by baseline age. As expected, we found that weight gain gradually diminished with increasing age. Nevertheless, the trend of association between alcohol intake and body weight change was similar across different age groups.

In this study, we cannot separate former drinkers who stopped drinking owing to illness from lifelong abstainers. However, this should not substantially influence our study results because participants with major chronic diseases were excluded from the WHS cohort at baseline. We also excluded women with baseline diabetes from our analyses. In the sensitivity analyses, we further censored women who developed a major illness during follow-up, and the results

Figure 2. Relative risks of becoming overweight or obese according to baseline alcohol intake in subgroups of women. A, Age. B, Smoking status. C, Physical activity level. D, Baseline body mass index (BMI; calculated as weight in kilograms divided by height in meters squared). Model adjusted for age, race, baseline BMI, randomized treatment, nonalcohol energy intake, physical activity level, smoking status, postmenopausal status, postmenopausal hormone use, multivitamin use, history of hypercholesterolemia and hypertension, and intake of fruit and vegetables, whole grains, refined grains, red meats and poultry, low-fat dairy products, high-fat dairy products, energy-adjusted total fat, carbohydrates, and fiber. Models in subgroups of women by smoking status and physical activity level did not adjust for the respective stratifying factors. Interaction was examined using the Wald $\chi^2$ test. Asterisk indicates 1 [Reference].
remained unchanged. Our study results only apply to light to moderate alcohol consumption in association with body weight change. Because very few women in our study reported heavy alcohol intake, we cannot reasonably evaluate the role of heavy alcohol drinking in body weight gain and development of obesity. In our baseline population of women with normal BMI, only 3.0% reported alcohol consumption of 30 g/d or more (corresponding to 2-3 drinks per day or more). In this highest alcohol consumption category, as many as one-third of women were current smokers, suggesting that heavy drinkers may have remarkably different lifestyle patterns compared with those consuming lower amounts of alcohol.

Several limitations of this study deserve comment. First, although previous studies have demonstrated excellent validity of self-reported body weight among health care professionals,23 self-reported weight remains subject to random misclassification, which would tend to bias our results toward the null and underestimate the true effect. Similarly, underreport or underestimation of alcohol intake is possible, and a single baseline assessment did not account for changes over time. However, sensitivity analyses that modeled alcohol intake as a time-dependent variable with updates at 48- and 108-month follow-up have obtained similar results. Second, because the questionnaire used in the WHS did not collect detailed information on drinking patterns, we could not differentiate women who had a small drink most days of the week from those who consumed multiple drinks 1 d/wk. Third, as in all observational studies, residual confounding cannot be completely ruled out. However, the observed associations in our study were robust after adjusting for a variety of dietary, lifestyle, and clinical factors, suggesting that the associations are unlikely to be explained by strong confounding. Finally, WHS participants were predominately white, female health care professionals, which minimizes potential confounding by race/ethnicity and socioeconomic factors but also limits the generalizability of our study results to other populations.

In conclusion, we found that during long-term follow-up of middle-aged and older, initially normal-weight women, light to moderate alcohol consumption was associated with less weight gain and a lower risk of becoming overweight and/or obese compared with abstention. These associations persisted after multivariate adjustment and in subgroup analyses. Our study results suggest that women who have normal body weight and consume a light to moderate amount of alcohol could maintain their drinking habits without gaining excessive weight. However, taking into account the potential medical and psychosocial problems related to drinking alcohol, any recommendation on alcohol use should be made for the individual after carefully evaluating both adverse and beneficial effects of the drinking behavior in a broad context. Further investigations are warranted to elucidate the role of alcohol intake and alcohol metabolism in energy balance and to identify behavioral, physiological, and genetic factors that may modify the alcohol effects.

Accepted for Publication: October 7, 2009.

Correspondence: Lu Wang, MD, PhD, Division of Preventive Medicine, Department of Medicine, Brigham and Women’s Hospital, 900 Commonwealth Ave E, Boston, MA 02215 (luwang@rics.bwh.harvard.edu).

Author Contributions: Drs Wang, Lee, Manson, and Sesso had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Wang, Manson, and Sesso. Acquisition of data: Lee, Buring, and Sesso. Analysis and interpretation of data: Wang, Manson, and Sesso. Drafting of the manuscript: Wang. Critical revision of the manuscript for important intellectual content: Wang, Lee, Manson, Buring, and Sesso. Statistical analysis: Wang. Obtained funding: Sesso. Administrative, technical, and material support: Lee, Manson, and Sesso. Study supervision: Lee, Manson, and Sesso.

Financial Disclosure: None reported.

Funding/Support: This study was supported by research grants DK081141, CA-47988, HL-080467, and HL-43851 from the National Institutes of Health, Bethesda, Maryland. These grants provided funding for study conduct and data collection.

Additional Contributions: We are indebted to the 39,876 participants in the WHS for their dedicated and conscientious collaboration and to the entire staff of the WHS for their assistance in designing and conducting the trial.