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(Article begins on next page)
Combined impact of lifestyle factors on mortality: prospective cohort study in US women

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ABSTRACT
Objective To evaluate the impact of combinations of lifestyle factors on mortality in middle aged women.
Design Prospective cohort study.
Setting Nurses’ health study, United States.
Participants 77 782 women aged 34 to 59 years and free from cardiovascular disease and cancer in 1980.
Main outcome measure Relative risk of mortality during 24 years of follow-up in relation to five lifestyle factors (cigarette smoking, being overweight, taking little moderate to vigorous physical activity, no light to moderate alcohol intake, and low diet quality score).
Results 8882 deaths were documented, including 1790 from cardiovascular disease and 4527 from cancer. Each lifestyle factor independently and significantly predicted mortality. Relative risks for five compared with zero lifestyle risk factors were 3.26 (95% confidence interval 2.45 to 4.34) for cancer mortality, 8.17 (4.96 to 13.47) for cardiovascular mortality, and 4.31 (3.51 to 5.31) for all cause mortality. A total of 28% (25% to 31%) of deaths during follow-up could be attributed to smoking and 55% (47% to 62%) to the combination of smoking, being overweight, lack of physical activity, and a low diet quality score. Additionally considering alcohol intake did not substantially change this estimate.
Conclusions These results indicate that adherence to lifestyle guidelines is associated with markedly lower mortality in middle aged women. Both efforts to eradicate cigarette smoking and those to stimulate regular physical activity and a healthy diet should be intensified.

METHODS
Study population
The nurses’ health study is a prospective cohort study that was established in 1976 when 121 700 female registered US nurses, aged 30 to 55 years, completed a mailed questionnaire on known and suspected risk factors for chronic diseases. Since then, participants have been sent biennial follow-up questionnaires to update information on lifestyle and health conditions. For the current analysis, we began follow-up in 1980, because this was the first year when diet was assessed. In 1980, 98 462 women, aged 34 to 59 years, completed the questionnaire. We excluded women with previously diagnosed cancer (except non-melanoma skin cancer) or cardiovascular disease (n=8527). We also excluded alcohol abstainers who reported on the 1980 questionnaire a great decrease in alcohol consumption during the previous decade (n=2797), because this
could be subsequent to alcoholism or disease. Similarly, we excluded women with a body mass index below 18.5 (n=1848), because this may be due to weight loss secondary to preclinical diseases. Finally, we excluded participants who left 10 or more items blank on the 1980 diet questionnaire, those with implausibly high or low reported energy intakes (below 2.09 or above 14.63 MJ/day), those with ages outside the eligible range, and those with missing information for smoking or body mass index (n=7562). After exclusions, a total of 77,782 women remained for the current analysis. Completion of the questionnaire was considered to imply informed consent.

### Assessment of risk factors

Diet was assessed with a 61 item food frequency questionnaire in 1980. An expanded questionnaire including approximately 120 food items was used to update information about diet every two to four years. Participants were asked how often, on average, during the previous year they had consumed a specified common unit or portion size of a specific type of food.

The seven included items were vegetables (recommended: at least five servings a day), fruit (at least four servings a day), nuts and soya (at least one serving a day), ratio of fish and poultry to red meat (ratio at least 1:4 and <15 g/day), ratio of polyunsaturated to saturated fatty acid ratio (ratio at least 1:4), and cereal fibre (≥15 g/day). For alcohol consumption, we defined low risk as light to moderate consumption (≥1 and <15 g/day)—that is, up to approximately one drink a day.

To quantify the healthiness of the diet, we used the previously designed alternative healthy eating score. For this analysis, we decided a priori to use only seven of the nine original items: we did not include multi-vitamin intake, because this has become less relevant as a folate source as a result of widespread fortification of foods, and we did not include alcohol intake, because we wanted to present results on alcohol intake separately. For each of the remaining seven items, we assigned a score between 0 (least healthy) and 10 (recommended intake). We then added the scores for the individual items, resulting in a minimum healthy diet score of 0 and a maximum healthy diet score of 70.

### Classification of low risk categories

or adiposity, we defined low risk as a body mass index between 18.5 and 25.0. For physical activity, we defined low risk as an average of at least 30 minutes a day of activity of at least moderate intensity (requiring ≥3 metabolic equivalents an hour, including brisk walking), consistent with existing guidelines. For cigarette smoking, we defined low risk as never smoking. For alcohol consumption, we defined low risk as light to moderate consumption (≥1 and <15 g/day)—that is, up to approximately one drink a day.

To quantify the healthiness of the diet, we used the previously designed alternative healthy eating score. For this analysis, we decided a priori to use only seven of the nine original items: we did not include multi-vitamin intake, because this has become less relevant as a folate source as a result of widespread fortification of foods, and we did not include alcohol intake, because we wanted to present results on alcohol intake separately. For each of the remaining seven items, we assigned a score between 0 (least healthy) and 10 (recommended intake). We then added the scores for the individual items, resulting in a minimum healthy diet score of 0 and a maximum healthy diet score of 70.

The seven included items were vegetables (recommended: at least five servings a day), fruit (at least four servings a day), nuts and soya (at least one serving a day), ratio of fish and poultry to red meat (ratio at least 1:4 and <15 g/day), ratio of polyunsaturated to saturated fatty acid ratio (ratio at least 1:4). We considered participants with a healthy diet score in the upper two fifths (highest 40%) to be in the low risk category for diet.

### Ascertainment of mortality

Deaths were reported by next of kin, the postal authorities, or both or were ascertained through searching for non-responders in the National Death Index. Follow-up for deaths in the National Death Index has been estimated to be 98% complete for this cohort. Information on the cause of death was obtained from the next of kin (for external deaths such as those due to traffic accidents), death certificates, or medical records. We requested permission from the next of kin to review medical records for suspected deaths due to cancer or cardiovascular diseases if we did not yet have these records for follow-up of disease incidence. The cause of death was determined after our validation study, the correlation between self reported and technician measured weight was 0.97. Father’s occupation when the participant was 16 years of age was assessed on the 1976 questionnaire. In 1992, we also asked about the degrees the participant had received (registered nurse, bachelors, masters, doctorate) and, for women who were married or widowed, the highest level of education that their husband completed (less than high school, some high school, high school graduate, college graduate, graduate school).
review by physicians and primarily based on medical records if both medical records and death certificates were available. We used ICD-8 (international classification of diseases, 8th revision) codes to distinguish deaths due to cancer (140-207) and cardiovascular diseases (390-439 and 795).

Statistical analysis
Women contributed follow-up time from the date of return of the baseline questionnaire to the date of death or 1 June 2004, whichever came first. We used pooled logistic regression analysis stratified by two year calendar time periods to estimate multivariate relative risks and corresponding 95% confidence intervals. We chose this method because it obtains all information needed for the calculation of partially adjusted population attributable risk estimates, including estimation of the relative risks for age.21 Pooled logistic regression analysis is asymptotically equivalent to Cox proportional hazards regression if time intervals are relatively short and the probability of the outcome in the intervals is small,22 conditions that were satisfied for this analysis.

We calculated population attributable risks, which are estimates of the percentage of deaths during follow-up that would not have occurred if all women had been in the low risk category for lifestyle factors, assuming that the observed associations represent causal effects. For these analyses, we compared women in the low risk category for each of the component risk factors with all other women.23 We calculated population attributable risks by using previously described formulas that were elaborated for this specific study design and are appropriate for use with multivariate adjusted relative risks (SAS macro: www.hsph.harvard.edu/faculty/spiegelman/software.html).21 24 25 Because of the large computational computer capacity needed for this calculation, we reduced the number of categories for the covariable calendar time by combining 12 two year time periods into four periods. We estimated prevalence of exposures for 1990, because this year is

Table 1  Multivariate relative risk of death from any cause, cardiovascular disease, and cancer during 24 years of follow-up according to body mass index, cigarette smoking, alcohol consumption, physical activity, and diet

<table>
<thead>
<tr>
<th>Body mass index (kg/m²)</th>
<th>Person years</th>
<th>Deaths from any cause</th>
<th>Cardiovascular deaths</th>
<th>Cancer deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Relative risk (95% CI)</td>
<td>Cases</td>
<td>Relative risk (95% CI)</td>
</tr>
<tr>
<td>18.5-24.9</td>
<td>1 174 514</td>
<td>5095</td>
<td>1.00 (1.00 to 1.00)</td>
<td>855</td>
</tr>
<tr>
<td>25-29.9</td>
<td>404 856</td>
<td>2359</td>
<td>1.18 (1.12 to 1.24)</td>
<td>511</td>
</tr>
<tr>
<td>≥30.0</td>
<td>180 039</td>
<td>1428</td>
<td>1.67 (1.57 to 1.78)</td>
<td>424</td>
</tr>
</tbody>
</table>

Cigarette smoking
Never: 787 104 cases, 2998 person years, 1.00 (1.00 to 1.00); Past: 667 250 cases, 4076 person years, 1.18 (1.12 to 1.24); Current ≤15/day: 404 039 cases, 609 person years, 1.46 (1.31 to 1.63); Current >15/day: 200 626 cases, 145 person years, 2.81 (2.49 to 3.17).

Alcohol consumption†† (g/day)
0: 386 395 cases, 2044 person years, 1.00 (1.00 to 1.00); 1-4: 745 039 cases, 3589 person years, 0.81 (0.76 to 0.85); 5-14: 405 344 cases, 1861 person years, 0.80 (0.75 to 0.86); 15-29: 155 024 cases, 900 person years, 0.90 (0.83 to 0.98); ≥30: 67 369 cases, 485 person years, 1.11 (1.00 to 1.23).

Physical activity‡‡ (hours/week)
0-0.4: 116 915 cases, 1143 person years, 1.00 (1.00 to 1.00); 0.5-1.9: 745 039 cases, 3589 person years, 0.81 (0.76 to 0.85); 2.0-3.4: 405 344 cases, 1861 person years, 0.80 (0.75 to 0.86); 3.5-5.4: 201 459 cases, 768 person years, 0.72 (0.65 to 0.79); ≥5.5: 248 639 cases, 636 person years, 0.63 (0.57 to 0.69).

Healthy diet score§
Fifth 1: 337 747 cases, 2122 person years, 1.00 (1.00 to 1.00); Fifth 2: 348 559 cases, 1848 person years, 0.85 (0.79 to 0.90); Fifth 3: 355 705 cases, 1766 person years, 0.80 (0.75 to 0.85); Fifth 4: 359 442 cases, 1701 person years, 0.76 (0.71 to 0.81); Fifth 5: 357 955 cases, 1445 person years, 0.65 (0.61 to 0.70).

*Relative risks adjusted for age (5 year categories), time period (12 periods), and other risk factors included in table.
†Three deaths and 239 person years not included because of missing values.
‡Of moderate to vigorous intensity; 1279 deaths and 224 893 person years not included because of missing values.
§In 1990 healthy diet score was <22.61 (median 18.65) for fifth 1, 22.61-28.85 (median 25.89) for fifth 2, 28.86-34.57 (median 31.68) for fifth 3, 34.58-41.38 (median 37.72) for fifth 4, and >41.39 (median 46.34) for fifth 5.
midway during follow-up and approximates average exposure during follow-up.

To estimate relative risks for cigarette smoking and diet, we updated information during follow-up by using the most recently available information. For physical activity and alcohol intake, we used the cumulative average from all available questionnaires up to the start of each two year follow-up. To minimise bias owing to the effects of poor health before death leading to weight loss, we used the baseline (1980) body mass index in our analysis. In a sensitivity analysis, we examined potential confounding by measures of socioeconomic status by adding father’s occupation, education degree received by the participant, and education level of the husband to the multivariate model. Because education level was only assessed in 1992, we did this analysis for follow-up from 1992 until 2004.

We considered two tailed P values lower than 0.05 to be statistically significant. We used SAS software, version 9.1 for all analyses.

RESULTS

During 1 759 408 person years of follow-up we documented 8882 deaths, including 1790 from cardiovascular disease and 4527 from cancer. Table 1 shows the multivariate adjusted relative risks for lifestyle factors and death during follow-up. Cigarette smoking, higher body mass index, less physical activity, and a lower healthy diet score were all associated with increased cardiovascular, cancer, and all cause mortality. Alcohol consumption was associated with a lower risk of cardiovascular mortality than alcohol abstinence. However, heavy alcohol consumption was associated with an increased risk of cancer mortality. As a result, light to moderate alcohol consumption was associated with the lowest all cause mortality.

Table 2 shows the multivariate adjusted relative risks and population attributable risks of mortality for the high risk compared with the low risk category of lifestyle factors. The estimated population attributable risks were 28% for cigarette smoking, 14% for being overweight, 17% for lack of physical activity, 13% for low diet quality, and 7% for not having light to moderate alcohol consumption. Population attributable risks were higher for cardiovascular mortality than for cancer mortality. Among never smokers, the relative risk of mortality for being overweight was higher than that for the whole study population (1.55, 95% confidence interval 1.44 to 1.66), resulting in a higher population attributable risk (22%, 18% to 27%).

We also evaluated combinations of lifestyle risk factors in relation to mortality. As shown in the figure, cardiovascular, cancer, and all cause mortality increased with an increasing number of risk factors. The relative risk for combining cigarette smoking, being overweight, lack of physical activity, and a low healthy diet score compared with none of the risk factors was 6.91 (4.50 to 10.63) for cardiovascular mortality, 2.65 (2.14 to 3.28) for cancer mortality, and 3.41 (2.90 to 4.00) for all cause mortality (table 3). The population attributable risk for having any of these four risk factors was 72% for cardiovascular mortality, 44% for cancer mortality, and 55% for all cause mortality. When we also considered alcohol consumption, the population attributable risks for having any of the five lifestyle risk factors were modestly greater than for the four risk factors (table 3).

Results among never smokers were consistent with those for the whole study population (table 4). We also examined whether results differed for younger (<60 years) and older (≥60 years) participants by recalculating the relative risks for these subgroups and using the prevalence of risk factor specific for these subgroups. The population attributable risk for all cause mortality for the five risk factors combined (smoking, diet, physical activity, overweight, alcohol consumption) was 51% (30% to 67%) for younger women and 63% (52% to 72%) for older women. Finally, we examined potential confounding by measures of socioeconomic status (father’s occupation, education level of participant and husband). Adjustment for these variables did not materially alter the association between any of the lifestyle factors and mortality during follow-up (data not shown).

DISCUSSION

In this study of 77 782 middle aged US women, never smoking, engaging in regular physical activity, eating a

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Table 2 | Relative risk and population attributable risk (PAR) (95% confidence intervals) of all cause, cardiovascular, and cancer mortality during 24 years of follow-up*  

<table>
<thead>
<tr>
<th>Variable</th>
<th>Women in high risk category (%)</th>
<th>Death from any cause</th>
<th>Cardiovascular death</th>
<th>Cancer death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Relative risk</td>
<td>PAR (%)</td>
<td>Relative risk</td>
<td>PAR (%)</td>
</tr>
<tr>
<td>Ever v never smoking</td>
<td>56</td>
<td>1.66 (1.59 to 1.74)</td>
<td>27.9 (24.6 to 31.2)</td>
<td>1.83 (1.65 to 2.02)</td>
</tr>
<tr>
<td>Body mass index ≥25 v 18.5-24.9</td>
<td>48</td>
<td>1.32 (1.27 to 1.38)</td>
<td>14.2 (11.6 to 16.9)</td>
<td>1.85 (1.68 to 2.04)</td>
</tr>
<tr>
<td>Physical activity ≥30 min/day v &lt;30 min/day</td>
<td>75</td>
<td>1.25 (1.17 to 1.32)</td>
<td>16.5 (11.7 to 21.1)</td>
<td>1.47 (1.27 to 1.69)</td>
</tr>
<tr>
<td>Healthy diet score in lower three fifths v upper two fifths</td>
<td>59</td>
<td>1.25 (1.19 to 1.30)</td>
<td>12.9 (9.6 to 16.2)</td>
<td>1.35 (1.22 to 1.50)</td>
</tr>
<tr>
<td>Heavier drinking or abstaining v light to moderate alcohol intake</td>
<td>34</td>
<td>1.18 (1.13 to 1.24)</td>
<td>7.4 (4.6 to 10.2)</td>
<td>1.31 (1.19 to 1.44)</td>
</tr>
</tbody>
</table>

*Relative risks and population attributable risks adjusted for age (5 year categories), time period (four periods), and other risk factors included in table.
†Based on prevalence in 1990.
Not all of these risk factors have been avoided by adherence to these four lifestyle guidelines. Light to moderate alcohol consumption (up to one drink a day) was also associated with a lower risk of all cause mortality during follow-up. Participants who smoked, were physically inactive, were non-moderate alcohol consumers, and had low fruit and vegetable intakes (measured by plasma vitamin C concentrations) had a relative risk of all cause mortality during follow-up of 4.04 (2.95 to 5.54) compared with participants who met none of these criteria. Few previous studies have examined combinations of lifestyle factors in relation to mortality. In the EPIC-Norfolk study, lifestyle factors were studied in relation to mortality in men and women aged 45 to 79 years during an average of 11 years of follow-up. Participants who smoked, were physically inactive, were non-moderate alcohol consumers, and had low fruit and vegetable intakes (measured by plasma vitamin C concentrations) had a relative risk of all cause mortality during follow-up of 4.04 (2.95 to 5.54) compared with participants who met none of these criteria. In another British prospective study, the estimated probability of surviving 15 years free of cardiovascular events and diabetes for a man aged 50 years ranged from 89% in a moderately physically active man with a body mass index between 20 and 24 who had never smoked to 42% in an inactive smoker with a body mass index of 30 or higher. In a cohort of elderly Europeans aged 70 to 90 years, the combination of non-smoking, a Mediterranean-style diet, regular physical activity, and moderate alcohol consumption was associated with a relative risk of 10 year all cause mortality of 0.35 (0.28 to 0.44) compared with adherence to only one or fewer of these lifestyle factors. The estimated population attributable risk for the combination of lifestyle factors was 60% for all cause mortality, 61% for cardiovascular mortality, and 60% for cancer mortality. For women in high income countries in the global burden of disease study, the estimated population attributable risk for mortality was 14% for smoking, 8% for overweight, 5% for physical

### Results in relation to other studies

Smoking, overweight, physical activity, and quality of diet have consistently been associated with risk of chronic diseases and mortality in prospective cohort studies. Not all of these risk factors have been studied in randomised controlled trials with disease incidence or mortality end points, and this may never be done for feasibility or ethical reasons. However, findings from randomised controlled trials support the protective effect of a prudent Mediterranean-style diet and substitution of polyunsaturated for saturated fat for coronary heart disease; of the combination of physical activity, a healthy diet, and moderate weight loss for type 2 diabetes; and of smoking cessation for premature mortality. In addition, randomised controlled trials have shown beneficial effects of moderate alcohol consumption, reduced trans fat intake, high fruit and vegetable intake, and whole grain intake on biological markers of cardiovascular risk.

#### Table 3 | Risk of mortality during 24 years of follow-up according to combinations of lifestyle risk factors

<table>
<thead>
<tr>
<th>Four risk factors: smoking, overweight, low diet quality, low physical activity</th>
<th>Death from any cause</th>
<th>Cardiovascular death</th>
<th>Cancer death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative risk (95% CI):</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>No risk factors (3.4%):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One risk factor (16%):</td>
<td>1.30 (1.10 to 1.53)</td>
<td>1.43 (0.91 to 2.24)</td>
<td>1.32 (1.06 to 1.63)</td>
</tr>
<tr>
<td>Two risk factors (33%):</td>
<td>1.75 (1.49 to 2.05)</td>
<td>2.42 (1.58 to 3.71)</td>
<td>1.61 (1.23 to 1.98)</td>
</tr>
<tr>
<td>Three risk factors (34%):</td>
<td>2.52 (2.15 to 2.95)</td>
<td>3.98 (2.60 to 6.08)</td>
<td>2.12 (1.73 to 2.60)</td>
</tr>
<tr>
<td>Four risk factors (13%):</td>
<td>3.41 (2.90 to 4.00)</td>
<td>6.91 (4.50 to 10.63)</td>
<td>2.65 (2.14 to 3.28)</td>
</tr>
<tr>
<td>Population attributable risk (%) for having any of the four risk factors (95% CI):</td>
<td>54.8 (46.7 to 61.9)</td>
<td>72.0 (58.6 to 81.6)</td>
<td>44.3 (31.2 to 55.8)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Five risk factors: above four and alcohol abstinence or heavy drinking</th>
<th>Death from any cause</th>
<th>Cardiovascular death</th>
<th>Cancer death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative risk (95% CI):</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>No risk factors (2.4%):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One risk factor (12%):</td>
<td>1.34 (1.09 to 1.64)</td>
<td>1.13 (0.67 to 1.89)</td>
<td>1.55 (1.18 to 2.02)</td>
</tr>
<tr>
<td>Two risk factors (27%):</td>
<td>1.70 (1.40 to 2.07)</td>
<td>1.88 (1.15 to 3.05)</td>
<td>1.71 (1.32 to 2.22)</td>
</tr>
<tr>
<td>Three risk factors (34%):</td>
<td>2.25 (1.85 to 2.72)</td>
<td>2.80 (1.73 to 4.54)</td>
<td>2.07 (1.60 to 2.68)</td>
</tr>
<tr>
<td>Four risk factors (21%):</td>
<td>3.27 (2.70 to 3.97)</td>
<td>4.77 (2.94 to 7.72)</td>
<td>2.79 (2.15 to 3.62)</td>
</tr>
<tr>
<td>Five risk factors (4.2%):</td>
<td>4.31 (3.51 to 5.31)</td>
<td>8.17 (4.96 to 13.47)</td>
<td>3.26 (2.45 to 4.34)</td>
</tr>
<tr>
<td>Population attributable risk (%) for having any of the five risk factors (95% CI):</td>
<td>58.1 (49.3 to 65.7)</td>
<td>75.2 (60.9 to 84.7)</td>
<td>46.0 (31.7 to 58.3)</td>
</tr>
</tbody>
</table>

*Relative risks and population attributable risks adjusted for age (5 year age categories) and time period (four periods); additionally adjusted for alcohol consumption (0, 1-4, 5-14, 15-29, ≥30 g/d) for “four risk factor” model.
†Overweight: body mass index ≥25; low diet quality: healthy diet score in lower three fifths; low physical activity: <30 min/day.
‡Prevalence in 1990.
§0 or ≥15 g/day alcohol.
inactivity, 4% for low fruit and vegetable intake, and ~3% for alcohol use. Mokdad and colleagues estimated that the population attributable risks for US mortality in 2000 was 18% for tobacco, 15% for poor diet and physical inactivity, and 3.5% for excess alcohol consumption. Thus, our results are consistent with those from previous cohort studies that included European and male participants and suggest that the population attributable risk estimates from studies using an indirect approach may be conservative for the demographic group that we studied.

Heavy alcohol consumption was associated with higher cancer mortality in our study and has been associated with an increased risk of various cancers, liver cirrhosis, hypertension, psychiatric disorders, injuries, and violence in other studies. Consistent with previous studies, we found that light to moderate alcohol consumption was associated with lower cardiovascular mortality. However, even moderate alcohol consumption has been associated with a higher risk of breast cancer and traffic accidents. In addition, people with moderate alcohol consumption may be more likely to transition to heavy consumption, and a greater average alcohol consumption may facilitate heavy consumption in communities. For individual people, the balance of risks and benefits of moderate alcohol consumption may depend on other characteristics; possible benefits may exist for older women with cardiovascular risk factors, and a greater likelihood of adverse effects may exist for women with a personal or family history of alcoholism, alcohol related cancers, or risk factors for these conditions. Given the complexity of the effects of alcohol consumption on personal health, women could usefully discuss these risks and benefits with their physician.

### Strengths and limitations

Strengths of our study include the large sample size, the prospective design with 24 years of follow-up and high response rates, and the repeated collection of detailed information on lifestyle. Some measurement error is inevitable, particularly in the assessment of diet and physical activity, and is likely to have weakened the associations seen. We would probably have seen a lower mortality if we had used more restrictive criteria for the low risk group (for example, healthy diet score in the highest fifth). However, our results indicate that even modest differences in lifestyle can have a substantial impact on reducing mortality. Although residual confounding can never be excluded in non-randomised studies, evidence from prospective studies in other populations and randomised controlled trials supports our findings. Because incomplete adjustment for smoking habits can weaken the association between overweight and mortality, our estimates for the association between overweight and mortality in never smokers may be more accurate than those for the total study population. Variation in socioeconomic status in our study of registered nurses was more limited than in the general population. Consistent with results from a British study, adjustment for various measures of socioeconomic status did not appreciably affect associations between lifestyle factors and mortality during follow-up. In analyses with mortality as an end point, confounding by poor health that precedes

| Table 4 | Risk of mortality during 24 years of follow-up according to number of lifestyle risk factors in never smokers* |
|-------------------|-------------------|-------------------|
| **Death from any cause** | **Cardiovascular death** | **Cancer death** |
| Three risk factors: low diet quality, low physical activity, overweight‡ | | |
| Relative risk (95% CI): | 1.00 | 1.00 | 1.00 |
| No risk factor (7.7%)‡‡ | 1.00 | 1.00 | 1.00 |
| One risk factor (27%) | 1.20 (1.02 to 1.43) | 1.44 (0.91 to 2.27) | 1.19 (0.95 to 1.49) |
| Two risk factors (41%) | 1.54 (1.31 to 1.81) | 2.24 (1.44 to 3.46) | 1.37 (1.11 to 1.70) |
| Three risk factors (25%) | 2.17 (1.83 to 2.57) | 3.58 (2.30 to 5.58) | 1.75 (1.39 to 2.19) |
| Population attributable risk (%) for having any of the three risk factors (95% CI) | 34.3 (18.9 to 48.0) | 56.1 (27.7 to 75.5) | 22.8 (−0.01 to 44.3) |
| Four risk factors: above three and alcohol abstinence or heavy drinking§ | | |
| Relative risk (95% CI): | 1.00 | 1.00 | 1.00 |
| No risk factor (5.4%)‡‡ | 1.00 | 1.00 | 1.00 |
| One risk factor (20%) | 1.25 (1.01 to 1.53) | 1.18 (0.70 to 1.99) | 1.39 (1.05 to 1.83) |
| Two risk factors (34%) | 1.48 (1.22 to 1.81) | 1.78 (1.08 to 2.92) | 1.42 (1.08 to 1.85) |
| Three risk factors (30%) | 1.95 (1.60 to 2.38) | 2.64 (1.61 to 4.33) | 1.70 (1.30 to 2.22) |
| Four risk factors (10%) | 2.64 (2.13 to 3.26) | 3.94 (2.35 to 6.60) | 2.11 (1.57 to 2.83) |
| Population attributable risk (%) for having any of the four risk factors (95% CI) | 41.5 (24.3 to 56.2) | 60.9 (28.3 to 80.9) | 25.7 (−1.4 to 49.3) |

*Relative risks and population attributable risks adjusted for age (5 year age categories) and time period (four periods); additionally adjusted for alcohol consumption (0, 1-4, 5-14, 15-29, ≥30.0 g/d) for the “three risk factor” model.
‡Low diet quality: healthy diet score in lower three fifths; low physical activity: ≤30 min/day; overweight: body mass index ≥25.
§Prevalence in 1990.
80 or ≥315 g/day alcohol.
These findings underscore the importance of intensifying both efforts to eradicate cigarette smoking and those aimed at improving diet and physical activity.

Conclusions
Avoiding cigarette smoking is of pivotal importance for the prevention of premature death. In our study of middle aged women, adherence to lifestyle guidelines involving a healthy diet, regular physical activity, and weight management was also associated with markedly lower mortality. Of note, our results indicate that a healthy diet and regular physical activity have important health benefits independent of reducing adiposity. These findings underscore the importance of intensifying both efforts to eradicate cigarette smoking and those aimed at improving diet and physical activity.

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