Research Article

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Following Cancer Prevention Guidelines Reduces Risk of Cancer, Cardiovascular Disease, and All-Cause Mortality

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Abstract

Background: Few studies have evaluated the combined impact of following recommended lifestyle behaviors on cancer, cardiovascular disease (CVD) and all-cause mortality, and most included tobacco avoidance. Because 80% of Americans are never or former smokers, it is important to consider the impact of other recommended behaviors.

Methods: In 1992 and 1993, 111,966 nonsmoking men and women in the Cancer Prevention Study-II Nutrition Cohort completed diet and lifestyle questionnaires. A score ranging from 0 to 8 points was computed to reflect adherence to the American Cancer Society cancer prevention guidelines on body mass index, physical activity, diet, and alcohol consumption, with 8 points representing optimal adherence. Multivariable-adjusted relative risks (RR) of death and 95% CI were computed by Cox proportional hazard regression.

Results: During 14 years of follow-up, 10,369 men and 6,613 women died. The RR of all-cause mortality was lower for participants with high (7, 8) versus low (0–2) scores (men, RR = 0.58, 95% CI: 0.53–0.62; women, RR = 0.58, 95% CI: 0.52–0.64). Inverse associations were found with CVD mortality (men, RR = 0.52, 95% CI: 0.45–0.59; women, RR = 0.42, 95% CI: 0.35–0.51) and cancer mortality (men, RR = 0.70, 95% CI: 0.61–0.80; women, RR = 0.76, 95% CI: 0.65–0.89). Similar associations, albeit not all statistically significant, were observed for never and former smokers.

Conclusion: Adherence to cancer prevention guidelines for obesity, diet, physical activity, and alcohol consumption is associated with lower risk of death from cancer, CVD, and all causes in nonsmokers.

Impact: Beyond tobacco avoidance, following other cancer prevention guidelines may substantially lower risk of premature mortality in older adults. *Cancer Epidemiol Biomarkers Prev; 20(6); 1089–97. ©2011 AACR.*

Introduction

Many health organizations publish guidelines on nutrition, physical activity, and other modifiable behaviors known to affect risk of cancer, cardiovascular disease (CVD), and other major illnesses (1–6). These guidelines seek to summarize and communicate current scientific knowledge about behaviors that can reduce the risk of specific diseases and promote overall health. For example, the American Cancer Society (ACS) guidelines on nutrition and physical activity (1) are targeted specifically for cancer prevention, although they share many features with other organizations' guidelines (3–5).

Few studies have evaluated the relationship between adherence to multiple health recommendations and risk of developing (7) or dying from major chronic diseases (8–12), and only 1 specifically tested cancer prevention recommendations (12). Most studies combined tobacco cessation with other modifiable risk factors and reported all-cause death or disease incidence rates that were 21% to 78% lower among people who reported several healthful behaviors compared with none (7–11). Given the overwhelmingly large detrimental effects of tobacco use, and the fact that 80% of Americans have either stopped smoking or never started (13), the potential impact of recommended behaviors, separate from smoking, on improving health outcomes is of considerable interest.

This study examined whether adherence to the ACS guidelines on body weight, physical activity, diet, and alcohol consumption was associated with risk of death from all causes, CVD, and cancer in never and former smokers in the large Cancer Prevention Study II (CPS-II) Nutrition Cohort (14).

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Materials and Methods

Study population

The CPS-II Nutrition Cohort is a prospective study of cancer incidence and mortality among 86,403 men and 97,786 women (14). At enrollment in 1992 or 1993, participants were ages 50 to 74 years and completed a 10-page confidential self-administered questionnaire that included questions on demographic, medical, lifestyle, and dietary factors. Nutrition cohort participants are a subgroup of the approximately 1.2 million members of the CPS-II cohort, a prospective study of cancer mortality established by the ACS in 1982 (15), who resided in 21 states with population-based cancer registries (14). The Institutional Review Board of Emory University School of Medicine, Atlanta, GA, approves all aspects of the CPS-II Nutrition Cohort.

Outcome ascertainment

The vital status of participants was determined through December 31, 2006 by linkage with the National Death Index (16). The underlying causes of death were coded according to the International Classification of Diseases, 9th and 10th revisions (ICD-9 and ICD-10; refs. 17–18). Cancer deaths included ICD-9 codes 140–195 and 199–208, or ICD-10 codes C00-C76 and C80-C97. CVD deaths were defined as ICD-9 codes 390–459, or ICD-10 codes I00-I99.

ACS guidelines score

To quantify lifestyle behaviors consistent with recommendations from the 2006 ACS guidelines on nutrition and physical activity for cancer prevention (1), an *a priori* score was developed where each of 4 major guidelines was weighted equally from 0 to 2, where 0 represented not meeting the recommendation, 1 represented partial compliance, and 2 represented full compliance. This scoring approach allowed for a more complete examination of adherence than yes/no scoring. The overall adherence score was the sum of the 4 components and ranged from 0 for those who did not adhere to any of the guidelines to 8 for those who were fully compliant.

The first recommendation, to "maintain a healthy weight throughout life", was scored by height and weight reported in 1982 (from the parent CPS-II cohort) and weight in 1992 to take advantage of the fact that information on adult body weight was reported 10 years prior to baseline, thus providing a long-term measure of body mass index (BMI, in kg/m^2) in adulthood. The optimal score (2) was given to participants whose BMI was within the normal range (18.5–<25 kg/m^2) at both time points. A score of zero was given to individuals who were obese (>30 kg/m^2) at both time points, or obese at 1 time point and overweight (25–<30 kg/m^2) at the other time point. A score of 1 was given to all others. Underweight individuals (<18.5 kg/m^2) were excluded.

The second recommendation is to "adopt a physically active lifestyle with 30 minutes or more of moderate to vigorous intentional physical activity at least 5 days/week; 45 to 60 minutes are preferable" (1). Participants reported the average time spent, per week, in 7 recreational activities at baseline in 1992. These were converted to metabolic equivalent (MET) scores (19). The minimum standard of 30 minutes on 5 days (2.5 hours/week) of moderate activity (3.5 METs) is equal to 8.75 MET-hours/week. One hour per day, 5 days a week (5.0 hours/week), of moderate activity (3.5 METs) is equal to 17.5 MET-hours/week. Therefore, MET-hours/week less than 8.75 received a score of 0, 8.75 to <17.5 earned a score of 1, and ≥17.5 MET-hours earned a score of 2 for reaching "preferable" levels.

The 3rd recommendation is to "consume a healthy diet with an emphasis on plant sources" with specific recommendations as described next (1). Diet was assessed at baseline by a validated 68-item food frequency questionnaire (FFQ; refs. 14, 20, 21). To capture the totality of the recommended diet pattern, sex-specific diet quality scores were first created, which ranged from 0 to 9 (0–3 for each of 3 diet recommendations). For the recommendation "eat 5 or more servings of a variety of vegetables and fruits each day," participants received a point if they consumed ≥5 servings/day and an additional 1 or 2 points for being in the 2nd or 3rd tertile of unique fruits and vegetables consumed per month (a measure of "variety"). For the recommendation to "choose whole grains in preference to processed (refined) grains," the percentage of grains consumed as whole grains (daily servings of whole grains/daily servings of whole grains plus refined grains) was assigned a score of 0 to 3 for the quartile distribution (highest quartile = 3). The recommendation to "limit consumption of processed and red meats" was assigned a score of 0 to 3 for the quartile distribution of servings consumed per week (lowest quartile = 3). All diet recommendations were summed and then collapsed to 0 to 2 points: those who scored 0 to 2 on the 9-point diet score were given a score of 0, 3 to 6 were scored as 1, and 7 to 9 were scored as 2.

The ACS recommendation on alcohol states: "if you drink, limit consumption to 1 drink/day for women and 2 drinks/day for men" (1). Because the relationship with alcohol consumption is different for CVD than for cancer (22, 23), 2 approaches were used to score compliance with the alcohol recommendation for cancer. For all outcomes, the lowest score (0) was given to men who consume more than 2 drinks/day and women who consume more than 1 drink per day, nondrinkers were assigned a score of 1, and those who drink only moderately (>0 but ≤1 drink/day for women and ≤2 drinks/day for men) received a score of 2. In the second analysis of cancer mortality, the alcohol score was changed such that moderate drinkers were assigned the score of 1 and nondrinkers were assigned the score of 2.

In the analysis of overall scores, those in the tails of the distribution (0, 1, and 2 for lowest scores; 7 and 8 for highest) were combined because of small numbers.

Analytic cohort

Men and women were excluded from this analysis if at baseline, they reported a history of cancer (except nonmelanoma skin cancer; $n = 23{,}630$), myocardial infarction ($n = 11{,}431$), or stroke ($n = 2{,}483$); an extreme value for height or weight in 1982 or 1992/1993 (top and bottom 0.1%; $n = 4{,}295$), and below-normal weight (BMI < 18.5 kg/m^2) in 1982 or 1992/1993 ($n = 2{,}510$; ref. 6). Current smokers ($n = 11{,}552$) and individuals with missing information on smoking ($n = 1{,}297$), physical activity ($n = 2{,}048$), and alcohol use ($n = 5{,}394$) or who poorly completed the FFQ ($n = 7{,}583$) were excluded. The final analytic cohort included 50,727 men and 61,239 women. After 14 years of follow-up, the total number of deaths was 16,982 (10,369 men, 6,613 women), including 5,628 deaths due to CVD (3,666 men, 1,962 women) and 5,874 deaths due to cancer (3,318 men, 2,556 women).

Statistical analysis

Participants contributed follow-up time from the date of return of the baseline questionnaire in 1992 or 1993 to the date of death or December 31, 2006. Cox proportional hazards regression analysis (24) was used to estimate the relative risk (RR) of death and 95% CI by using the PHREG procedure in SAS, version 9.1 (SAS Institute).

Age adjustment was achieved by stratifying on single year of age within each Cox model. Covariates included education (less than high school graduate, (ref.) high school graduate, some college/trade, and college graduate) and smoking history (never and former (classified by years since quitting $\leq$5, >5–10, >10–15, >15–20, >20–25, >25) (ref.), and unknown years since quitting). Other covariates considered (nonsteroidal anti-inflammatory drug use, multivitamin use, race, menopausal hormone therapy, and energy) did not change the associations. Although tests of the proportional hazards assumption suggested that the relationship of the guidelines score with all-cause and CVD mortality varied quantitatively over time ($P < 0.05$), the associations were qualitatively similar; therefore, we present results including the full follow-up period.

Associations were examined separately in never and former smokers (current smokers were excluded). In addition, associations between the non-BMI–related guidelines (i.e., physical activity, diet, and alcohol consumption) and mortality were examined in individuals whose BMI was consistently heavy, normal, or other. For this analysis, a modified 0 to 6 point score, excluding BMI, was used. The likelihood ratio test was used to test for multiplicative interactions comparing Cox multivariable models with and without cross-product terms where the score was modeled as a continuous variable. All tests of statistical significance were 2-sided.

Results

The mean (SD) age of men and women at baseline was 63.6 (6.0) and 61.9 (6.5) years. Only 3.5% of men and 4.0% of women met the optimal recommendation for each component of the guidelines and were assigned a score of 8. Table 1 shows age-standardized demographic characteristics in relation to the guidelines score in men and women. Those with higher scores were slightly older and more educated. Men with higher scores were more likely to be never smokers, whereas women with higher scores were more likely to be former smokers. The average grams/day of ethanol consumed was at least 3 times higher among drinkers with low versus high scores. The prevalence of diabetes and hypertension was lower among participants with higher scores.

Table 2 illustrates the all-cause and cause-specific mortality risk associated with the guidelines score. Higher scores were strongly inversely associated with lower total mortality and cause-specific mortality in both sexes. Associations for CVD were strongly linear, whereas those for cancer seemed to level off after a score of 4 in men and 5 in women. Results were similar for cancer mortality when nondrinkers received a score of 2 for the alcohol component.

The associations of individual components of the score (mutually adjusted) are provided in Table 3 (men) and Table 4 (women). As compared with participants with consistently high BMI, men and women with a consistently normal BMI were at lowest risk of death, especially from CVD; the "other BMI combinations" group (score = 1) was also at lower risk. Meeting the physical activity guidelines was inversely related to all-cause and CVD mortality, but was not independently related to cancer mortality. Moderate alcohol consumption, compared with consumption above recommended limits, was inversely associated with risk of all outcomes in men, although the confidence limits included 1.0 for CVD mortality. Men who reported no alcohol consumption had a lower risk of dying from cancer than heavier drinkers. In contrast, nondrinking was associated with higher risk of all-cause and CVD mortality, especially in women. The recommended diet pattern was associated with a significantly lower risk for all outcomes, except for CVD in men ($P_{trend} = 0.2$).

As shown in Figure 1, compared with a referent group of never smokers with a low guidelines score, both never and former smokers who reported greater adherence to the guidelines had a lower risk of all-cause, CVD, and cancer mortality. For cancer mortality, although the trend was stronger in never than former smoking women, and in former than never smoking men, associations stratified by smoking status were not statistically significant ($P_{interaction} > 0.1$).

We examined the role of lifestyle behaviors apart from BMI (diet, physical activity, and alcohol) by using 2 approaches. When BMI was removed from the score (new range = 0–6) and instead included as a covariate (BMI in 1982, <25, 25–<30, and >30 kg/m^2), RRs (95% CI) for scores of 5 or 6 vs. 0 or 1 in women were 0.73 (0.66–0.80) for total mortality ($P_{trend} < 0.0001$), 0.60 (0.51–0.71) for CVD mortality ($P_{trend} < 0.0001$), and 0.86 (0.75–1.00) for

Table 1. Age-standardized baseline characteristics according to the ACS guidelines score in men and women[a]

Characteristic	ACS guidelines score					
	Men			Women		
	0–2	5	7 and 8	0–2	5	7 and 8
n	6,127	10,893	6,929	7,075	13,457	8,189
Mean age, y	62.5	63.9	64.4	60.8	62.1	62.3
Mean BMI, kg/m^2, in 1992	29.6	25.9	24.1	30.8	24.7	22.8
BMI > 30 kg/m^2 in 1992 (%)	46.7	7.3	0.1	55.5	6.9	0.2
Mean weight change, lbs, 1982 to 1992	8.7	2.1	−0.5	13.3	6.4	4.1
Mean exercise MET, h/wk[b]	4.0	14.0	28.1	4.1	11.7	26.0
Dietary components						
Fruit and vegetable,servings /d	2.5	3.3	4.0	2.6	3.5	4.1
Variety of fruits and vegetables	8.0	9.8	10.7	8.7	10.3	11.0
Red and processed meat, servings/wk	8.9	5.1	3.5	6.0	3.1	2.2
% of total grains as whole grains	24.3	47.9	59.4	28.6	54.7	63.5
Alcohol intake						
Nondrinker (%)	46.9	31.8	12.2	66.8	47.9	22.7
Drinker (%)	53.1	68.2	87.8	33.2	52.1	77.3
Amount (g/d) among drinkers	32.2	13.1	9.9	17.1	6.9	4.1
Smoking history						
Never smoker (%)	30.1	39.6	42.8	61.9	61.7	56.6
Former smoker (%)	69.9	60.4	57.2	38.1	38.3	43.4
College graduate (%)	34.8	53.2	66.9	22.9	34.6	42.3
Race (% white)	98.0	97.7	97.6	98.1	97.6	97.6
History of diabetes (%)	10.1	6.7	4.1	9.0	4.1	2.0
History of hypertension (%)	44.2	32.7	27.1	44.4	28.0	20.9

[a]All variables except age are standardized to the age distribution of the entire cohort. Values are presented as means unless otherwise noted. Distribution of scores in men and women is as follows: Men: score 0–2 (12.1%), 3 (15.5%), 4 (20.6%), 5 (21.5%), 6 (16.6%), and 7, 8 (13.7%). Women: score 0–2 (11.6%), 3 (15.6%), 4 (20.5%), 5 (22.0%), 6 (17.1%), 7, 8 (13.4%).
[b]METs are defined for each type of exercise-related physical activity as a multiple of MET of sitting quietly for 1 hour.

cancer mortality ($P_{trend} = 0.02$). For men, estimates were 0.70 (0.65–0.75) for total mortality ($P_{trend} < 0.0001$), 0.72 (0.63–0.81) for CVD mortality ($P_{trend} < 0.0001$), and 0.80 (0.70–0.90) for cancer mortality ($P_{trend} < 0.0001$). In addition, adherence to the diet, physical activity, and alcohol guidelines was associated with reduced risk within each BMI score category ($P_{interaction} > 0.10$ for all endpoints, data not shown).

Sensitivity analyses found similar results after excluding participants with previously diagnosed diabetes (data not shown).

Discussion

After tobacco avoidance and cessation, weight control, physical activity, dietary choices, and moderation of alcohol intake are the primary lifestyle strategies to prevent cancer (1–2). However, few Americans realize the potential of these other lifestyle modifications for cancer prevention (25). Guidelines for cancer prevention largely overlap with those for prevention of diabetes (4) and CVD (3, 26), but some differences, for example, in dietary recommendations, exist. In this large cohort study of never and former smokers, men and women whose behaviors were most consistent with cancer prevention guidelines (1) had a 42% lower risk of death from any cause during the 14-year follow-up period than individuals whose behaviors were least consistent. The risk of death from cancer or CVD was also significantly lower among those reporting behaviors consistent with the guidelines. Maintenance of a healthy BMI seemed to be the component most strongly associated with lower mortality, but all lifestyle behaviors significantly contributed to mortality risk reduction.

The most important strategy to reduce the risk of cancer (27) and many other chronic diseases is tobacco avoidance. Most other studies of all-cause mortality or chronic disease incidence in relation to lifestyle behaviors included tobacco smoking in the risk score (7–11). In these studies, tobacco was often the strongest predictor of risk

Table 2. Association between ACS guidelines score and mortality from all causes, CVD, or cancer

ACS guidelines score	Men				Women			
	Deaths (*n*)	Person-years	RR (95% CI)[a]	P_{trend}[b]	Deaths (*n*)	Person-years	RR (95% CI)[a]	P_{trend}[b]
All-cause mortality								
0–2, referent	1,524	76,693	1.00 (-)		930	93,077	1.00 (-)	
3	1,736	100,148	0.83 (0.78–0.89)		1,216	125,427	0.92 (0.85–1.00)	
4	2,161	134,236	0.75 (0.70–0.80)		1,373	166,235	0.76 (0.69–0.82)	
5	2,156	139,949	0.70 (0.65–0.74)		1,373	179,268	0.68 (0.62–0.74)	
6	1,613	108,962	0.66 (0.61–0.71)		1,001	139,505	0.63 (0.58–0.69)	
7, 8	1,179	90,392	0.58 (0.53–0.62)	<0.0001	720	109,594	0.58 (0.52–0.64)	<0.0001
CVD mortality								
0–2, referent	533	-	1.00 (-)		294	-	1.00 (-)	
3	634	-	0.86 (0.76–0.96)		394	-	0.92 (0.79–1.07)	
4	780	-	0.74 (0.67–0.83)		399	-	0.66 (0.57–0.77)	
5	785	-	0.69 (0.62–0.77)		410	-	0.60 (0.52–0.70)	
6	540	-	0.60 (0.53–0.67)		287	-	0.54 (0.45–0.63)	
7, 8	394	-	0.52 (0.45–0.59)	<0.0001	178	-	0.42 (0.35–0.51)	<0.0001
Cancer mortality								
0–2, referent	496	-	1.00 (-)		340	-	1.00 (-)	
3	555	-	0.85 (0.75–0.96)		421	-	0.90 (0.78–1.04)	
4	649	-	0.73 (0.65–0.83)		540	-	0.85 (0.74–0.98)	
5	673	-	0.73 (0.65–0.82)		501	-	0.72 (0.63–0.83)	
6	529	-	0.73 (0.65–0.83)		429	-	0.79 (0.68–0.91)	
7, 8	416	-	0.70 (0.61–0.80)	<0.0001	325	-	0.76 (0.65–0.89)	<0.0001
Cancer mortality, alternate scoring for alcohol consumption component[c]								
0–2 (referent)	539	87,061	1.00 (-)		277	75,214	1.00 (-)	
3	599	111,549	0.86 (0.76–0.96)		403	118,971	0.90 (0.77–1.05)	
4	724	144,021	0.80 (0.71–0.89)		537	178,206	0.80 (0.69–0.93)	
5	668	140,843	0.75 (0.67–0.84)		581	186,722	0.81 (0.70–0.93)	
6	493	105,029	0.73 (0.65–0.83)		442	149,821	0.76 (0.65–0.88)	
7, 8	295	61,877	0.75 (0.65–0.87)	<0.0001	316	104,172	0.78 (0.67–0.92)	0.0004

[a]Relative risk and 95% CI. Multivariate model adjusted for age, smoking status [never, years since quitting (≤5, >5–10, >10–15, >15–20, >20–25, >25, unknown] and education (less than high school/high school graduate/some college or trade school/college graduate).

[b]*P* value for trend calculated by assigning an ordinal value to each category and modeling as a continuous variable.

[c]Alcohol consumption component scored as: heavy drinkers = 0, moderate drinkers = 1, and nondrinkers = 2.

(8, 9); however, other lifestyle behaviors also reduced risk in never smoking women (10, 12) or men and women combined (7). In the current study, the largest of its type, and the first to examine associations separately in never and former smoking men and women, we confirmed that following healthy lifestyle recommendations for cancer prevention reduce the risk of premature death in these groups. For cancer mortality, inverse associations, albeit not consistently dose related, were observed in all groups.

On the basis of extensive evidence relating excess adiposity to increased incidence and death rates from cancer (28, 29) and CVD (30, 31), the ACS highlights maintenance of a healthy body weight as the first in its list of guidelines on nutrition and physical activity (1). In the current study, maintenance of a healthy body weight for 10 years prior to and including baseline was strongly associated with lower mortality risk than individuals who were consistently heavy. The importance of this issue cannot be overstated as 68% of American adults are overweight or obese (32). In addition, this study found that the inverse associations with healthy patterns of diet, physical activity, and alcohol consumption were observed among those who were consistently lean or consistently heavy. Individuals who are normal weight or overweight might also have metabolic (33) or other risk factors for cancer that may be modified by these behaviors. Ultimately, the current study highlights the benefits of following these recommendations among all individuals.

Table 3. Association between components of the ACS guidelines score and mortality in men

	All-cause mortality			CVD mortality			Cancer mortality		
	n	RR (95% CI)[a]	P_{trend}[b]	*n*	RR (95% CI)[a]	P_{trend}[b]	*n*	RR (95% CI)[a]	P_{trend}[b]
BMI, kg/m^2									
(0) ≥30 at 1 or both time points (referent)	1,934	1.00 (-)		758	1.00 (-)		602	1.00 (-)	
(1) Other combinations	5,587	0.74 (0.70–0.78)		2010	0.66 (0.61–0.72)		1824	0.81 (0.74–0.89)	
(2) 18.5–24.9 in 1982 and 1992	2,848	0.70 (0.66–0.74)	<0.0001	898	0.52 (0.47–0.58)	<0.0001	892	0.77 (0.69–0.85)	<0.0001
Recreational physical activity, MET-h/wk									
(0) <8.75 (referent)	5,383	1.00 (-)		1937	1.00 (-)		1631	1.00 (-)	
(1) 8.75–<17.5	2,099	0.89 (0.85–0.94)		720	0.85 (0.78–0.93)		703	1.00 (0.91–1.09)	
(2) 17.5+	2,887	0.87 (0.83–0.91)	<0.0001	1009	0.84 (0.78–0.91)	<0.0001	984	1.00 (0.92–1.08)	0.9
Alcohol intake, drinks/d									
(0) >2 (referent)	1,452	1.00 (-)		463	1.00 (-)		536	1.00 (-)	
(1) Nondrinker	3,974	1.07 (1.00–1.13)		1481	1.17 (1.05–1.30)		1083	0.85 (0.76–0.94)	
(2) Drinker of ≤2	4,943	0.86 (0.81–0.92)	<0.0001	1722	0.92 (0.83–1.02)	<0.0001	1699	0.83 (0.75–0.91)	0.0008
Healthy diet score									
(0) <3 (referent)	2,544	1.00 (-)		859	1.00 (-)		859	1.00 (-)	
(1) 3–<6	3,327	0.90 (0.86–0.95)		1173	0.93 (0.85–1.02)		1072	0.89 (0.81–0.98)	
(2) 6+	4,498	0.89 (0.84–0.93)	<0.0001	1634	0.93 (0.86–1.02)	0.2	1387	0.86 (0.78–0.94)	0.001

[a]Relative risk and 95% CI. Multivariate model adjusted for age, smoking status [never, years since quitting (≤5, >5–10, >10–15, >15–20, >20–25, >25, unknown], education (less than high school/high school graduate/some college or trade school/college graduate), and all other risk factors included in the table.

[b]*P* value for trend calculated by assigning an ordinal value to each category and modeling as a continuous variable.

In this study, adherence to the multiple dietary recommendations was assessed by a single dietary pattern variable. This approach aggregates the influence of individual dietary factors and captures additive and interactive effects of nutritional constituents (34). A diet low in red and processed meat, with a greater proportion of whole versus refined grains, and high in a variety of vegetables and fruits, was independently associated with lower mortality from all-cause, cancer, and CVD mortality than participants with less optimal diet patterns; however, the association was not statistically significant for CVD in men. Results of other studies examining various diet patterns and cancer outcomes have been inconsistent (8–11, 35–40), possibly due to "dilution" of associations by the inclusion of dietary components (e.g., *trans* fats), as yet not shown to be cancer-related, in the scores. Few other studies specifically tested cancer prevention guidelines (12). Cerhan and colleagues (12) reported a 35% to 43% higher risk of total cancer incidence and death among postmenopausal women with the worst (0, 1) versus the best (6–9) scores on the basis of diet, body weight, and physical activity recommendations from the 1997 World Cancer Research Fund/American Institute for Cancer Research (41).

Physical activity was not independently associated with cancer mortality in our study, but was associated with lower CVD and all-cause mortality. Most physical activity in this older largely retired population involved walking rather than more vigorous activities. Even though relatively low levels of physical activity are known to be associated with lower risk of colon cancer in this (42) and other (29) cohorts, higher levels of physical activity may be necessary for overall cancer prevention (2).

Heavy alcohol consumption is associated with an elevated risk of several cancers (2, 43), injuries, cirrhosis, and possibly hemorrhagic stroke, but moderate consumption is associated with lower risk of coronary heart disease (23). The scoring of "optimal" alcohol consumption in other studies of healthy lifestyle scores and total and cause-specific mortality has varied. For example, 2 studies considered moderate consumption to be optimal (versus none or excessive consumption; refs. 8, 10), 2 other studies considered moderate or none to be optimal (versus excessive; refs. 11–12), whereas a 5th considered any consumption as optimal (versus none; ref. 9). Other studies did not include alcohol in the score (7, 44). In the current analysis, the benefits of moderate drinking (versus heavy or nondrinking) for CVD and total mortality were clear. For cancer mortality, benefits of either nondrinking or moderate alcohol consumption, compared with heavy drinking, were observed in men. Overall, these findings support cancer

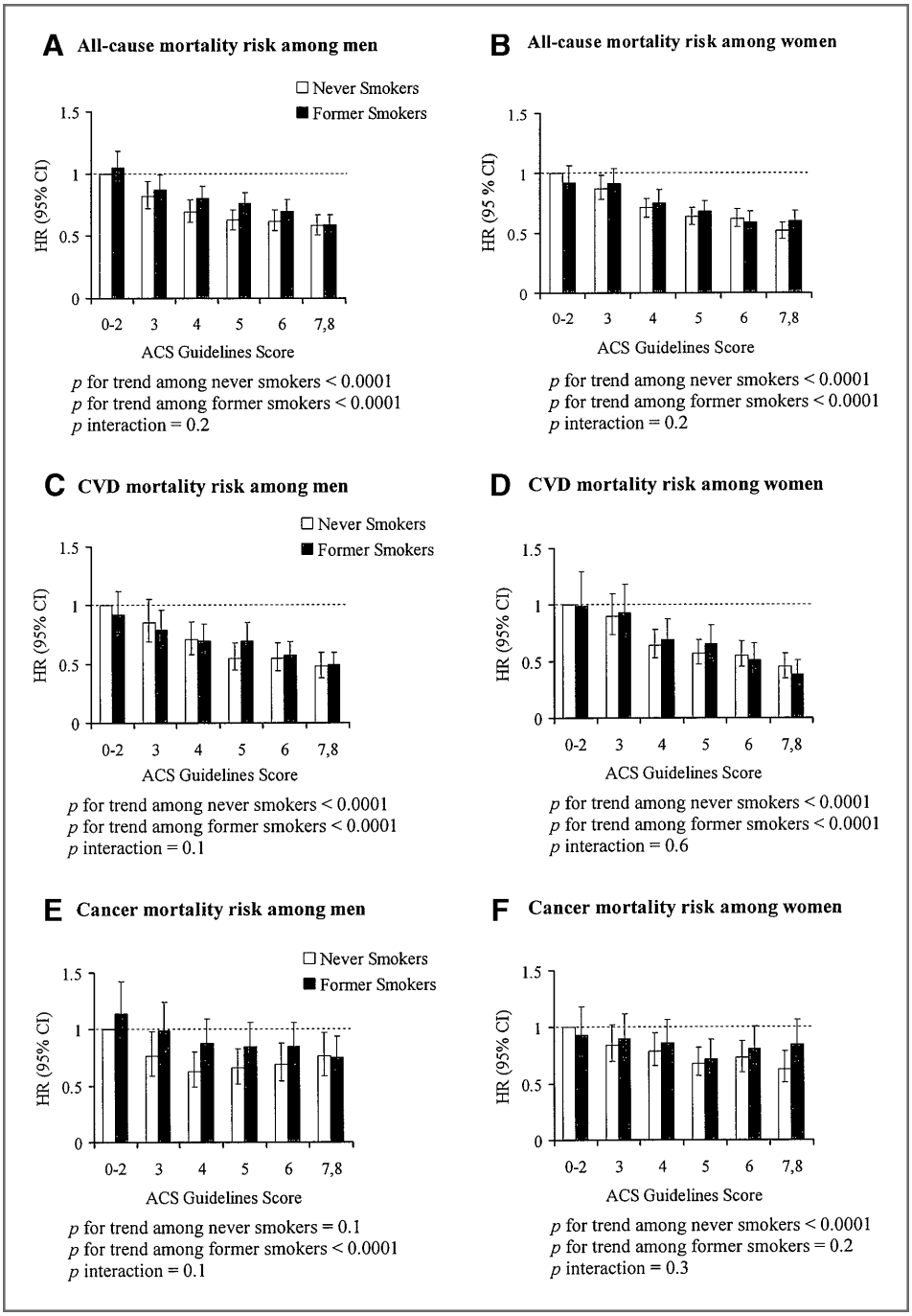

Figure 1. RRs and 95% CI for mortality from all causes, CVD, or cancer by ACS guidelines score in never and former smokers by sex. Common referent group consists of never smokers with low scores. Models of never smokers are adjusted for education (less than high school graduate, high school graduate, some college/trade, and college graduate). Models of former smokers are additionally adjusted for years since quitting (≤5, >5–10, >10–15, >15–20, >20–25, >25, unknown).

prevention recommendations to limit alcohol consumption among those who drink.

Strengths of this study include its large size, prospective design, and detailed assessment of lifestyle factors and smoking history. A limitation is that BMI may be a less useful indicator of adiposity among older individuals who redistribute excess weight centrally—which is also a risk factor for several chronic diseases, independent of BMI (45). The dietary assessment instrument included only 68 line items, but was validated for the food groups used in this analysis (21). Nevertheless, the range of unique fruits and vegetables regularly consumed (0–15) might have underestimated the range of "variety." Furthermore, assessment of physical activity and diet are subject to considerable measurement error (46), so our risk estimates likely underestimate these associations. Participants in the CPS-II Nutrition Cohort are a relatively health-conscious

Table 4. Association between components of the ACS guidelines score and mortality in women

	All-cause mortality			CVD mortality			Cancer mortality		
	n	RR (95% CI)[a]	P_{trend}[b]	*n*	RR (95% CI)[a]	P_{trend}[b]	*n*	RR (95% CI)[a]	P_{trend}[b]
BMI, kg/m^2									
(0) ≥30 at 1 or both time points (referent)	1,360	1.00 (-)		463	1.00 (-)		469	1.00 (-)	
(1) Other combinations	2,387	0.74 (0.69–0.79)		698	0.62 (0.55–0.70)		937	0.86 (0.77–0.96)	
(2) 18.5–24.9 in 1982 and 1992	2,866	0.66 (0.62–0.71)	<0.0001	801	0.53 (0.48–0.60)	<0.0001	1150	0.78 (0.70–0.87)	<0.0001
Recreational physical activity, MET-h/wk									
(0) <8.75 (referent)	3,849	1.00 (-)		1209	1.00 (-)		1393	1.00 (-)	
(1) 8.75–<17.5	1,283	0.83 (0.78–0.89)		348	0.72 (0.64–0.81)		547	0.97 (0.88–1.08)	
(2) 17.5+	1,481	0.88 (0.82–0.93)	<0.0001	405	0.78 (0.69–0.87)	<0.0001	616	0.99 (0.89–1.09)	0.7
Alcohol intake, drinks/d									
(0) >1 (referent)	703	1.00 (-)		177	1.00 (-)		329	1.00 (-)	
(1) Nondrinker	3,621	1.27 (1.17–1.39)		1170	1.44 (1.22–1.70)		1224	1.01 (0.89–1.15)	
(2) Drinker of ≤1	2,289	0.99 (0.91–1.08)	<0.0001	615	0.99 (0.84–1.17)	0.0003	1003	0.97 (0.86–1.11)	0.5
Healthy diet score									
(0) <3 (referent)	1,398	1.00 (-)		410	1.00 (-)		555	1.00 (-)	
(1) 3–<6	2,171	0.91 (0.85–0.98)		634	0.88 (0.78–1.00)		798	0.86 (0.77–0.96)	
(2) 6+	3,044	0.85 (0.79–0.90)	<0.0001	918	0.84 (0.74–0.95)	0.005	1203	0.87 (0.79–0.97)	0.03

[a]Relative risk and 95%CI. Multivariate model adjusted for age, smoking status [never, years since quitting (≤5, >5–10, >10–15, >15–20, >20–25, >25, unknown], education (less than high school/high school graduate/some college or trade school/college graduate), and all other risk factors included in the table.
[b]*P* value for trend calculated by assigning an ordinal value to each category and modeling as a continuous variable.

sample of primarily older Caucasian U.S. adults, and the impact of following these recommendations at younger ages or in other racial/ethnic groups is not known.

In conclusion, these findings provide evidence that adhering to cancer prevention guidelines for body weight, diet, physical activity, and alcohol intake, individually and in aggregate, improve survival among older nonsmoking adults.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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References

1. Kushi LH, Byers T, Doyle C, Bandera EV, McCullough M, McTiernan A, et al. American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention: reducing the risk of cancer with healthy food choices and physical activity. CA Cancer J Clin 2006;56:254–81.
2. World Cancer Research Fund/American Institute for Cancer Research. Food, nutrition, and the prevention of cancer: a global perspective. Washington, DC: AICR; 2007.
3. Lichtenstein AH, Appel LJ, Brands M, Carnethon M, Daniels S, Franch HA, et al. Diet and lifestyle recommendations revision 2006: a scientific statement from the American Heart Association Nutrition Committee. Circulation 2006;114:82–96.
4. American Diabetes Association. Nutrition recommendations and interventions for diabetes. Diabetes Care 2008;31:S61–S78.
5. U.S. Department of Health and Human Services, U.S. Department of Agriculture. Dietary Guidelines for Americans, 2005. 6th ed.Washington, DC: U.S. Government Printing Office; 2005.
6. World Health Organization. Physical status: the use and interpretation of anthropometry: report of a WHO expert committee. Geneva, Switzerland: World Health Organization; 1995.
7. Ford ES, Bergmann MM, Kroger J, Schienkiewitz A, Weikert C, Boeing H. Healthy living is the best revenge: findings from the European Prospective Investigation into Cancer and Nutrition-Potsdam study. Arch Intern Med 2009;169:1355–62.
8. Khaw KT, Wareham N, Bingham S, Welch A, Luben R, Day N. Combined impact of health behaviours and mortality in men and women: the EPIC-Norfolk prospective population study. PLoS Med 2008;5:e12.
9. Knoops KT, de Groot LC, Kromhout D, Perrin AE, Moreiras-Varela O, Menotti A, et al. Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women: the HALE project. JAMA 2004;292:1433–9.
10. van Dam RM, Li T, Spiegelman D, Franco OH, Hu FB. Combined impact of lifestyle factors on mortality: prospective cohort study in US women. BMJ 2008;337:a1440.

11. Kvaavik E, Batty GD, Ursin G, Huxley R, Gale CR. Influence of individual and combined health behaviors on total and cause-specific mortality in men and women: the United Kingdom health and lifestyle survey. Arch Intern Med 2010;170:711–8.
12. Cerhan JR, Potter JD, Gilmore JM, Janney CA, Kushi LH, Lazovich D, et al. Adherence to the AICR cancer prevention recommendations and subsequent morbidity and mortality in the Iowa Women's Health Study cohort. Cancer Epidemiol Biomarkers Prev 2004; 13:1114–20.
13. Center for Disease Control and Prevention.State-specific prevalence and trends in adult cigarette smoking United States, 1998–2007. JAMA 2009;302:250–2.
14. Calle EE, Rodriguez C, Jacobs EJ, Almon ML, Chao A, McCullough ML, et al. The American Cancer Society Cancer Prevention Study II Nutrition Cohort—rationale, study design, and baseline characteristics. Cancer 2002;94:2490–501.
15. Thun MJ, Calle EE, Rodriguez C, Wingo PA. Epidemiological research at the American Cancer Society. Cancer Epidemiol Biomarkers Prev 2000;9:861–8.
16. Calle EE, Terrell DD. Utility of the National Death Index for ascertainment of mortality among Cancer Prevention Study II participants. Am J Epidemiol 1993;137:235–41.
17. World Health Organization. International classification of diseases, Ninth Revision (ICD-9). Geneva, Switzerland: World Health Organization; 1977.
18. World Health Organization. International statistical classification of diseases and related health problems, tenth revision. Geneva, Switzerland: World Health Organization; 1992.
19. Ainsworth BE, Haskell WL, Leon AS, Jacobs DR, Montoye HJ, Sallis JF, et al. Compendium of physical activities: classification of energy costs of human physical activities. Med Sci Sports Exerc 1993;25:71–80.
20. Block G, Hartman AM, Naughton D. A reduced dietary questionnaire: development and validation. Epidemiol 1990;1:58–64.
21. Flagg EW, Coates RJ, Calle EE, Potischman N, Thun MJ. Validation of the American Cancer Society Cancer Prevention Study II Nutrition Survey Cohort food frequency questionnaire. Epidemiology 2000;11: 462–8.
22. Camargo CAJ, Hennekens CH, Gaziano JM, Glynn RJ, Manson JE, Stampfer MJ. Prospective study of moderate alcohol consumption and mortality in US male physicians. Arch Intern Med 1997;157: 79–85.
23. Thun MJ, Peto R, Lopez AD, Monaco JH, Henley SJ, Heath CW, et al. Alcohol consumption and mortality among middle-aged and elderly U. S. adults. New Engl J Med 1997;337:1705–14.
24. Cox DR. Regression models and life-tables. J R Stat Soc [B] 1972; 34:187–220.
25. Behavioral Research Program. Health Information National Trends Survey (HINTs). Bethesda, MD: DCCPS, National Cancer Institute; 2004.
26. National Heart Lung and Blood Institute. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Washington, DC: U.S. Department of Health and Human Services, NIH Publication No. 04-5230; 2004.
27. Gapstur SM, Thun MJ. Progress in the war on cancer. JAMA 2010;303:1084–5.
28. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity and mortality from cancer in a prospectively studied cohort of U.S. adults. N Engl J Med 2003;348:1625–38.
29. IARC. IARC handbooks on cancer prevention: weight control and physical activity. International Agency for Research on Cancer. Vol. 6. Lyon, France: IARC Press; 2002.
30. Kurth T, Gaziano JM, Berger K, Kase CS, Rexrode KM, Cook NR, et al. Body mass index and the risk of stroke in men. Arch Intern Med 2002;162:2557–62.
31. Rexrode KM, Buring JE, Manson JE. Abdominal and total adiposity and risk of coronary heart disease in men. Int J Obes Relat Metab Disord 2001;25:1047–56.
32. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999–2008. JAMA 2010;303:235–41.
33. Stattin P, Björ O, Ferrari P, Lukanova A, Lenner P, Lindahl B, et al. Prospective study of hyperglycemia and cancer risk. Diabetes Care 2007;30:561–7.
34. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. Curr Opin Lipidol 2002;13:3–9.
35. Harnack L, Nicodemus K, Jacobs DR, Folsom AR. An evaluation of the Dietary Guidelines for Americans in relation to cancer occurrence. Am J Clin Nutr 2002;76:889–96.
36. Michels KB, Wolk A. A prospective study of variety of healthy foods and mortality in women. Int J Epidemiol 2002;31:847–54.
37. McCullough ML, Feskanich D, Stampfer MJ, Giovannucci EL, Rimm EB, Hu FB, et al. Diet quality and major chronic disease risk in men and women: moving toward improved dietary guidance. Am J Clin Nutr 2002;76:1261–71.
38. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a mediterranean diet and survival in a Greek population. N Engl J Med 2003;348:2599–608.
39. Kant AK, Leitzmann MF, Park Y, Hollenbeck A, Schatzkin A. Patterns of recommended dietary behaviors predict subsequent risk of mortality in a large cohort of men and women in the United States. J Nutr 2009;139:1374–80.
40. Kant AK. Dietary patterns: biomarkers and chronic disease risk. Appl Physiol Nutr Metab 2010;35:199–206.
41. World Cancer Research Fund, American Institute for Cancer Research. Food, nutrition, and the prevention of cancer: a global perspective. Washington, DC: American Institute for Cancer Research; 1997.
42. Chao A, Connell CJ, Jacobs EC, McCullough ML, Patel AV, Calle EE, Cokkinides VE, et al. Amount, type, and timing of recreational physical activity in relation to colon and rectal cancer in older adults—the Cancer Prevention Study II Nutrition Cohort. Cancer Epidemiol Biomarkers Prev 2004;13:2187–95.
43. Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, Bouvard V, et al. Carcinogenicity of alcoholic beverages. Lancet Oncol 2007;8:292–3.
44. King DE, Mainous AG III, Geesey ME. Turning back the clock: adopting a healthy lifestyle in middle age. Am J Med 2007;120:598–603.
45. Borkan GA, Hults DE, Gerzof SG, Robbins AH, Silbert CK. Age changes in body composition revealed by computed tomography. J Gerontol 1983;38:673–7.
46. Willett WC. Nutritional epidemiology. 2nd ed. New York: Oxford University Press; 1998.