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Adherence to the WCRF/AICR cancer prevention recommendations and cancer-specific mortality: Results from the Vitamins and Lifestyle (VITAL) Study

Theresa A. Hastert[a,b], **Shirley A.A. Beresford**[b,a], **Lianne Sheppard**[c,d], and **Emily White**[a,b]

[a]University of Washington Department of Epidemiology, 1959 NE Pacific Street, Health Sciences Building F-262, Box 357236, Seattle, WA 98195-7236, USA

[b]Fred Hutchinson Cancer Research Center, 1100 Fairview Ave. N., Seattle, WA 98109, USA

[c]University of Washington Department of Environmental and Occupational Health Sciences, 1959 NE Pacific Street, Health Sciences Building, Box 357234, Seattle, WA 98195-7236, USA

[d]University of Washington Department of Biostatistics, 1959 NE Pacific Street, Health Sciences Building F-600, Box 357232, Seattle, WA 98195-7236, USA

Abstract

Purpose—In 2007 the World Cancer Research Fund (WCRF) and American Institute for Cancer Research (AICR) released eight recommendations related to body fatness, physical activity and diet aimed at preventing the most common cancers worldwide. The purpose of this paper is to estimate the association between meeting these recommendations and cancer-specific mortality.

Methods—We operationalized six recommendations (related to body fatness; physical activity; and consumption of foods that promote weight gain, plant foods, red and processed meat, and alcohol) and examined their association with cancer-specific mortality over 7.7 years of follow-up in the VITamins And Lifestyle (VITAL) Study cohort. Participants included 57,841 men and women ages 50–76 in 2000–2002 who had not been diagnosed with cancer prior to baseline. Cancer-specific deaths (n = 1,595) were tracked through the Washington State death file.

Results—Meeting the recommendations related to plant foods and foods that promote weight gain were most strongly associated with lower cancer-specific mortality (hazard ratio (HR): 0.82, 95% confidence interval (CI): 0.67, 1.00 and HR: 0.82, 95% CI: 0.70, 0.96, respectively). Cancer-specific mortality was 61% lower in respondents who met at least five recommendations compared to those who met none (HR: 0.39, 95% CI: 0.24, 0.62). Cancer-specific mortality was 10% lower on average with each additional recommendation met (per-recommendation HR: 0.90, 95% CI: 0.85, 0.94; P_{trend} <0.001). This association did not differ by sex or age but was stronger in non-smokers (HR: 0.84, 95% CI: 0.76, 0.92) than in smokers (HR: 0.93, 95% CI: 0.87, 0.98; $P_{interaction}$ = 0.086)

Corresponding Author (present address): Theresa A. Hastert, PhD MPP, Center for Social Epidemiology and Population Health, University of Michigan School of Public Health, 3622 SPH Tower, Ann Arbor, MI 48109-2029, USA, Phone: +1 (734) 615-9214, Fax: +1 (734) 764-8466, thastert@umich.edu.

Conflict of interest
The authors declare that they have no conflict of interest.

Conclusion—Adherence to the WCRF/AICR cancer prevention recommendations developed to reduce incidence of common cancers could substantially reduce cancer-specific mortality in older adults.

Keywords

alcohol; cancer-specific mortality; cancer prevention; diet; physical activity; recommendations

In 2007 the World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR) issued eight recommendations related to body fatness, diet and physical activity aimed at reducing incidence of the most common cancers worldwide.[1] The goal in developing these recommendations was to interpret the available evidence related to cancer prevention and combine it into one set of lifestyle guidelines aimed at reducing cancer risk.

Indexes that include risk factors such as smoking, body fatness and physical activity in addition to diet have been found to predict both cancer incidence[2,3] and cancer-specific mortality,[4–10,2] but less is known about meeting recommendations specific to cancer prevention and cancer outcomes, including cancer-specific mortality. A previous study reported a 20% decrease in cancer-specific mortality in participants with the highest adherence to the 2007 WCRF/AICR cancer prevention recommendations compared with those with the lowest adherence in the European Prospective Investigation into Nutrition and Cancer (EPIC) cohort.[9] Additionally, adherence to the American Cancer Society cancer prevention guidelines, including recommendations related to obesity, diet, alcohol and physical activity, was associated with cancer-specific mortality that was 30% lower among men and 24% lower among women in the Cancer Prevention Study-II cohort,[11] and 20% lower among women in the Women's Health Initiative.[2] A study of an earlier version of the WCRF/AICR recommendations (released in 1997[12]) found that cancer-specific mortality was 43% higher in women who met the fewest recommendations compared to those who met the most.[13]

The purpose of this study is to assess whether a cancer-specific index of behaviors based on the 2007 WCRF/AICR recommendations is associated with reduced cancer-specific mortality in a cohort based in the United States. Furthermore, we examined which of the recommendations are associated with the greatest reductions in cancer-specific mortality and whether the association between adhering to the recommendations and cancer-specific mortality differed by sex, age and smoking status. This study will help guide individuals as well as organizations that implement cancer prevention programs as to the potential benefit of following the WCRF/AICR guidelines based on their association with total cancer-specific mortality, an important measure of overall cancer burden.

Materials and Methods

Study cohort

VITamins And Lifestyle (VITAL) is a prospective cohort study designed to investigate the associations between use of dietary supplements and cancer risk and has previously been described in detail.[14] Men and women were eligible to join the cohort if they were

between the ages of 50 and 76 and lived in one of the 13 counties included in the Western Washington Surveillance, Epidemiology and End Results cancer registry at baseline.

Using names purchased from a commercial mailing list, baseline questionnaires were mailed to 364,418 men and women between October, 2000 and December, 2002. A total of 79,300 questionnaires were returned, of which 77,719 passed quality control checks. Overall, 57,841 men and women were included in the current analysis after excluding the following: respondents with a history of cancer other than non-melanoma skin cancer (n = 11,259) or whose cancer history was missing (n = 214); those missing data on body mass index (BMI) (n = 2,478) or physical activity (n = 1,093); and those whose food frequency questionnaires (FFQs) had <5 items completed on a single page (n = 4,331) or whose estimated energy intake was <600 calories per day for women or <800 calories for men (n = 2,304) or >4,000 calories per day for women or >5,000 calories for men (n = 547) (exclusions are not mutually exclusive). In order to reduce the possibility for reverse causality (i.e. changes in behavior due to symptoms of undiagnosed cancer) the first year of follow-up (including 47 cancer deaths and 559 other censoring events) was also excluded.

Data collection

Baseline questionnaires included questions on medical history, self-reported height and weight, physical activity over the previous 10 years, cancer screening, and diet as measured by a 126-item FFQ adapted from the questionnaire developed for the Women's Health Initiative and other studies. Measurement properties of earlier versions of the FFQ have been published previously.[15] Energy (in kcal) of each food item was obtained using the Nutrient Data System for Research database from the University of Minnesota's Nutrition Coordinating Center.[16]

Operationalization of the WCRF/AICR recommendations

The main exposures of this study were whether respondents met each individual recommendation and the number of recommendations met. The WCRF/AICR recommendations include 8 broad recommendations, with 1–4 more-specific personal recommendations and several public health goals for each. An expert panel of nutritional epidemiologists with knowledge of VITAL made recommendations on the operationalization of the recommendations. The key components of each recommendation were identified (noted in italics in Table 1) and specific cutoffs were selected based on information provided in the recommendations or from external sources.

The recommendation to be as lean as possible within the normal range of body weight and to avoid weight gain throughout adulthood was operationalized as having a BMI ≥18.5 but <25 kg/m^2 (based on the normal weight range set by the World Health Organization[17] as suggested in the recommendation[1]) at ages 18, 30, 45 and at baseline. For participants missing baseline BMI but reporting BMI at age 45 (n = 922), baseline BMI was imputed by calculating the average annual change in BMI (assuming a linear association between BMI and age) within 36 sex-, age-, and race/ethnicity-specific strata, multiplying that value by the difference between respondents' baseline age and 45 and adding the product to their BMI at age 45. Participants missing BMI at age 45 and at baseline were excluded from the analysis,

while those with missing BMI at earlier ages were assumed to have met the recommendation if it was met at age 45 and at baseline. The recommendation to be physically active as a part of everyday life was operationalized as engaging in moderate or fast walking and/or moderate or strenuous activity for an average of at least 30 minutes/day, on at least 5 days/week, in at least 7 of the past 10 years. Respondents who were missing data for this constructed variable but whose physical activity responses were complete enough to estimate their metabolic equivalent task (MET)-hours per week of walking and/or moderate or strenuous activity (n = 3,604) were categorized as meeting this recommendation if they engaged in an average of at least 10 MET-hours of walking and/or moderate/strenuous activity per week (based on an estimate of 4.0 METs/hour × 0.5 hours/day × 5 days/week) over the previous 10 years.

The recommendation to limit consumption of energy-dense foods and to avoid sugary drinks was operationalized as consuming a diet where the energy density of the foods consumed was less than 125 kcal/100 g on average, and also consuming <1 serving of regular (not diet) soda, fruit drinks and/or cranberry juice per week. Fruit juices which typically do not have added sugar (e.g. orange juice) were not counted as sugary drinks. The energy density cutoff was based on a public health goal included in the WCRF/AICR recommendation that specified that the value did not include drinks; therefore beverages were not included in the energy density calculation.

The recommendation to eat mostly plant foods, specifically the personal recommendations to eat at least 5 servings of non-starchy vegetables and fruits every day and to eat relatively unprocessed grains and/or legumes with every meal, was operationalized as consuming at least 5 servings of fruits and/or vegetables (excluding fruit juices and potatoes) and also at least one serving of whole grains and/or legumes per day. Because the VITAL FFQ only included 5 items relevant to whole grains (covering breads and breakfast cereals) and failed to fully separate whole grains from other grains (e.g., brown rice from white rice), we used a cutoff of one serving per day rather than per meal to represent habitual consumption of whole grains and/or legumes.

The recommendation to limit intake of red meat and avoid processed meat was operationalized as consuming <18 ounces of red or processed meat per week. Meat from mixed dishes was included by assuming that it accounted for one-quarter of their weight.

The recommendation to limit alcoholic drinks was operationalized as consuming ≤1 alcoholic beverage (defined as 12 ounces of beer; 4 ounces of wine; 1.5 ounces of liquor or one mixed drink) per day on average for women and ≤2 per day for men.

The recommendation to limit salt-preserved foods and moldy cereals and legumes was not operationalized because those exposures are not common in the United States food supply and data were not available in VITAL. The recommendation to meet nutritional needs through diet alone and not through use of dietary supplements was not operationalized and not included in the recommendation score. This was because this recommendation, unlike the other recommendations, was not based on evidence that taking supplements would increase one’s risk of cancer, but rather that it would likely have no effect.

Case ascertainment and censoring

Date and cause of death were ascertained by annual linkage with the Washington State death file. In our analyses, cancer deaths included deaths due to any malignant neoplasm, equivalent to International Classification of Disease (ICD-10) codes C00–C97.[18] Linkage is largely automated and based on ranking agreement between items common to both sets of data, such as Social Security number, name, and date of birth. Matches with high concordance were linked automatically whereas visual inspection was used to adjudicate incomplete matches. After excluding the first year of follow-up, 1,595 cancer deaths were identified in an average of 7.7 years of follow-up.

Participants who did not die of cancer in Washington State were right-censored at the earliest of the following: date they requested removal from the study (n = 15), date they moved out of Washington State (n = 2,896), date of death due to other causes (n = 2,498) or December 31, 2010 (n = 50,837). Moves out of Washington State were identified through linkage with the National Change of Address System.

Statistical analyses

Each recommendation was coded as met (1) or not met (0), and the total number of recommendations met was summed across the 6 recommendations operationalized. Hazard ratios (HRs) and 95% confidence intervals (CIs) of death due to cancer associated with meeting (vs. not meeting) each recommendation individually and for the number of recommendations met compared with meeting no recommendations were estimated using Cox proportional hazards models. We used participant age as the time scale, with participants entering the analysis at their age one year after completing the baseline questionnaire and exiting at age at death due to cancer or censoring event. Proportional hazards assumptions were examined using scaled Schoenfeld residuals. No significant ($P < 0.05$) deviations from proportionality were observed. *P*-values for trend were calculated using the Wald test associated with modeling the number of recommendations met as a continuous variable. Multivariate analyses included adjustment for potential confounders selected *a priori*, including known risk factors associated with cancer incidence and mortality, as listed in the footnotes to tables. Analyses of the association between number of recommendations met and cancer-specific mortality were also stratified by sex, age (<65/65+ at baseline) and smoking status (ever/never). Effect modification was assessed by including interaction terms in models estimating the hazard ratios associated with meeting each additional recommendation. All statistical tests were two-sided. All analyses were conducted using Stata 12.1 (StataCorp LP, College Station, TX).

Results

The highest proportion of all respondents and of those who died of cancer during follow-up (85.5% and 83.5%, respectively) met the recommendation to limit alcohol consumption, followed by the recommendation to limit consumption of red and processed meat (55.1% and 49.3%) (Table 1). Fewer participants met the recommendations to maintain normal body weight (22.3% and 18.7%), be physically active (18.6% and 15.6%), limit consumption of

energy dense foods and sugary drinks (19% and 14.2%), and consume mostly plant foods (11.4% and 8.2%).

Table 2 gives baseline characteristics of the overall study population and those who died of cancer during follow-up. The average age at baseline was 60.7 years for the entire study population and 65.5 for those who died of cancer. Both groups were predominantly white and had similar family history of cancer. Compared with the cohort as a whole, a smaller proportion of respondents who subsequently died of cancer were women, college graduates, married, or received cancer screening tests. Respondents who died of cancer reported an average of 28 pack-years of smoking compared to 13.1 in the entire cohort.

The leading cause of cancer-specific mortality was lung cancer (30.6%), followed by hematologic cancers (9.7%), cancers of the pancreas (9.2%), colon or rectum (6.9%), breast (3.0%), and prostate (2.4%) (data not shown).

Table 3 gives hazard ratios and 95% confidence intervals for cancer-specific mortality associated with meeting (vs. not meeting) each of the individual recommendations. All hazard ratio estimates were <1.0. Meeting the recommendations to consume mostly plant foods and to limit the energy density of the diet were associated with lower cancer-specific mortality (HR: 0.75, 95% CI: 0.62, 0.91 and HR: 0.78, 95% CI: 0.67, 0.91, respectively) in covariate-adjusted analyses and remained associated with an 18% lower cancer-specific mortality after also adjusting for whether respondents met each of the other recommendations.

Table 4 gives hazard ratios and 95% confidence intervals for cancer-specific mortality associated with the number of recommendations met. In adjusted analyses each additional recommendation met was associated with 10% lower cancer-specific mortality (HR: 0.90; 95% CI: 0.85, 0.94; P_{trend} <0.001). Meeting 1–2 recommendations is associated with 22–24% lower cancer-specific mortality. Compared with meeting no recommendations, meeting 3 recommendations was associated with a statistically significant 31% lower cancer-specific mortality, and meeting 4 recommendations was associated with 41% lower cancer-specific mortality. Meeting 5–6 recommendations was associated with cancer mortality that was 61% lower than meeting no recommendations (HR: 0.39, 95% CI: 0.24, 0.62). These results were unchanged in a sensitivity analysis in which we included (rather than excluded) the first year of follow up and in another in which we excluded those with missing BMI at baseline, rather than using imputed BMI values (data not shown).

We evaluated effect modification by sex, age and smoking history (data not shown). Results were similar by sex, with each additional recommendation met associated with 10% lower cancer-specific mortality among men (HR: 0.90, 95% CI: 0.84, 0.97) and 11% lower cancer-specific mortality among women (HR: 0.89, 95% CI: 0.82, 0.95; $P_{interaction}$ = 0.35) in covariate-adjusted analyses. The association was also similar in respondents younger than 65 years at baseline (HR: 0.88, 95% CI: 0.81, 0.96) compared with those 65 and older (HR: 0.90, 95% CI: 0.85, 0.97; $P_{interaction}$ = 0.84). Among never-smokers, each additional recommendation met was associated with 16% lower cancer-specific mortality (HR: 0.84, 95% CI: 0.76, 0.92) compared with 7% for current or former smokers (HR: 0.93, 95% CI:

0.87, 0.98; $P_{interaction} = 0.086$). This could be driven by differences in the association between meeting the recommendation related to body fatness and cancer-specific mortality by smoking status (HR for ever-smokers: 1.06, 95% CI: 0.91, 1.24; HR for never-smokers: 0.61, 95% CI: 0.47, 0.78; $P_{interaction} < 0.001$).

Discussion

In this study, each additional WCRF/AICR recommendation met was associated with lower cancer-specific mortality on average, and cancer-specific mortality was lower by more than half among participants who met the most recommendations compared with those who met none. This association was consistent by sex and age, but somewhat stronger in never-smokers than ever-smokers. Meeting the recommendations related to plant foods and energy density were most strongly associated with lower cancer-specific mortality.

Our findings are consistent with the EPIC study of the 2007 WCRF/AICR recommendations and cancer-specific mortality that reported an average of a 9% (95% CI: 7%, 11%) lower cancer-specific mortality for each 1-point increase in WCRF/AICR adherence score;[19] however, in that study, cancer-specific mortality was 20% (95% CI: 7%, 31%) lower in participants with the highest adherence compared to those with the lowest, an association that is substantially weaker than our reported 61% lower cancer-specific mortality in participants meeting the most recommendations.

The WCRF/AICR recommendations were developed with the aim of reducing the incidence of the most common cancers worldwide, but our findings, consistent with previous work,[13,9] suggest that meeting these guidelines could substantially reduce cancer-specific mortality as well. This is likely due to reductions in cancer incidence, consistent with previous research reporting lower total and site-specific cancer incidence associated with meeting the WCRF/AICR and similar cancer prevention recommendations.[3,20,2] However, another recent study reported that cancer mortality was 37% lower in female cancer survivors in the highest quartile of adherence to the 2007 WCRF/AICR recommendations compared to those in the lowest quartile, suggesting that these health behaviors could also improve cancer survival.[21]

Several biological mechanism have been proposed linking the WCRF/AICR recommendations with cancer outcomes.[22] Diets high in plant foods could affect cancer outcomes through the effect of antioxidants, which can reduce lipid oxidation and oxidative stress and resultant DNA damage and may also provide anitproliferative and anti-inflammatory effects.[23] Obesity has been implicated as a probable cause of several cancers, and may influence cancer risk and survival through inflammation, insulin resistance, and its effects on hormone levels.[24] Similarly, physical activity may impact cancer outcomes through its effect on hormones and inflammation, as well as by improving immune function.[25] Alcohol consumption can influence cancer risk by affecting DNA methylation and by producing acetaldehyde, a carcinogen, through ethanol metabolism.[26]

Our results are stronger than two previous studies that reported inverse associations between adherence to other cancer prevention recommendations and cancer-specific mortality.

Cancer-specific mortality was 43% higher in women with the lowest adherence scores to a previous version of AICR recommendations compared with those with the highest adherence in the Iowa Women's Health Study (HR: 1.43, 95% CI: 1.11, 1.85).[13] Similarly, meeting the American Cancer Society cancer prevention guidelines related to BMI, physical activity, diet, and alcohol was inversely associated with cancer-specific mortality (HR for high vs. low adherence: 0.70, 95% CI: 0.61, 0.80 among men; HR: 0.76, 95% CI: 0.65, 0.79 among women).[11]

Differences in our analyses compared to the previous studies could account for the stronger associations presented here. In the previous studies of the WCRF/AICR[13,9] and American Cancer Society cancer prevention recommendations[27,2] and cancer-specific mortality, participants were assigned partial points on the risk score for near-adherence to each recommendation, while our analyses focused on meeting or not meeting each recommendation. In sensitivity analyses using categories similar to those in the EPIC study[9] and giving partial points for near-adherence to the recommendations, cancer-specific mortality was 19% lower in participants in the highest-adherence group (5–6 recommendations) compared to those in the lowest-adherence group (0–2 recommendations) (HR:0.81, 95% CI: 0.59. 1.10), similar to the results of that study.[19] The EPIC study also included the special recommendation related to breastfeeding, which was not available in our study.

The WCRF/AICR recommendations were designed to focus on body fatness, diet and physical activity. Previous studies of health behavior risk scores not based on specific recommendations and cancer-specific mortality have also included smoking. Several reported inverse associations between positive health behavior scores and cancer-specific mortality in European cohorts, with reported hazard ratios of 0.31 (95% CI: 0.19, 0.50) for respondents with the highest (vs. lowest) scores,[4] and hazard ratios of 1.7 (95% CI: 1.1, 2.7),[5] 3.35 (95% CI: 1.67, 6.70)[6] and 3.74 (95% CI: 2.34, 5.98)[7] for those with the lowest (vs. highest) scores. The stronger association between most risk scores including smoking and cancer-specific mortality relative to our results is not surprising given that tobacco use is the single largest cause of cancer in Western countries[28] and smoking has been found to be the most significant predictor of cancer-specific mortality.[4,6]

Our results suggest that the association between meeting the WCRF/AICR cancer prevention recommendations and cancer-specific mortality could be stronger in never-smokers than in ever-smokers. This is consistent with two previous studies of cancer prevention recommendations and cancer-specific mortality, each of which also reported stronger associations among never-smokers compared with current or former smokers, although the interactions were not statistically significant ($P_{\text{interaction}} = 0.1$ for men, 0.3 for women)[11] or not reported.[13] This difference in association by smoking status could be plausible given previous findings that higher BMI is associated with lower incidence and mortality of lung cancer,[29] which accounts for more than 30% of the cancer deaths in our sample.

Limitations of this study should be noted. It is possible that the recommendations as they are operationalized do not represent the most etiologically-relevant time period in which they

could affect risk of death due to cancer. The operationalization of each recommendation was based on self-reported data, which could result in misclassification of whether respondents met each recommendation and measurement error in the total number of recommendations met. Misclassification of whether respondents met individual recommendations would bias associations between those recommendations and cancer-specific mortality toward the null, as would misclassification of the total number of recommendations met.[30] Residual confounding may exist due to missing or misspecified confounders. Additionally, because of its emphasis on recruiting supplement users, VITAL participants may have had more positive health behaviors than the general population; however, selection bias is unlikely to affect results in a prospective study where future cancer outcomes were unknown at baseline. Also, we limited our study to respondents with no history of cancer at baseline to avoid reverse causality (i.e. to avoid a diagnosis of cancer leading to changes in behaviors). This led to deaths from cancers that are rapidly fatal being overrepresented in our results compared with their actual proportion of cancer deaths in the general population. Although lung cancer is the leading cause of cancer death among men and women nationally and accounts for more deaths than any other malignancy in our study, breast, prostate and colorectal cancer deaths are underrepresented here relative to their share of all cancer deaths. [31]

Strengths of this study include its large sample size, prospective design and the detailed information collected at baseline that allowed us to operationalize six of the WCRF/AICR recommendations and control for several potential confounders. Linkage with the Washington State death file provided accurate and near-complete ascertainment of cancer deaths. Excluding the first year of follow-up also reduced the possibility of reverse causality whereby respondents may have changed their behaviors due to symptoms of undiagnosed cancer.

In summary, the results of our U.S.-based study along with those of the EPIC study suggest that cancer-specific mortality may be lower by approximately 10% with each WCRF/AICR recommendation met, or each additional point of an adherence score based on those recommendations. Additionally, we found that the benefit may be even greater for non-smokers, with a 16% lower risk for each recommendation met. Thus, even though these recommendations were developed to reduce cancer incidence, increased adherence to the WCRF/AICR cancer prevention recommendations could substantially reduce mortality from cancer.

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Abbreviations

WCRF World Cancer Research Fund

AICR American Institute for Cancer Research

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Table 1

WCRF/AICR Cancer Prevention Recommendations,[1] and Their Operationalization in the Vitamins And Lifestyle (VITAL) Study, and the Percentage Who Met Each Recommendation, Washington State, 2000–2002

WCRF/AICR Recommendation	Associated Personal Recommendations	Met/Did Not Meet Recommendation in This Study if:	VITAL Cohort (N=57,841)		Cancer Deaths (N=1,595)	
			N	%	N	%
1. Body fatness *Be as lean as possible within the normal range of body weight*	• Ensure that weight through childhood and adolescent growth projects toward the lower end of the normal BMI range at age 21	**Met:** 18.5 kg/m^2 ≤ BMI <25 kg/m^2 at ages 18, 30, 45 and at baseline	12,894	22.3	298	18.7
	• Maintain body weight within the normal range from age 21 • Avoid weight gain and increases in waist circumference throughout adulthood	**Did not meet:** BMI <18.5 kg/m^2 or BMI ≥25 kg/m^2 at age 18, 30, 45 and/or baseline	44,947	77.7	1,297	81.3
2. Physical activity Be physically active as part of everyday life	• Be moderately physically active, equivalent to brisk walking, for at least 30 minutes every day • As fitness improves, aim for 60 minutes or more of moderate, or for 30 minutes or more of vigorous, physical activity every day	**Met:** ≥30 minutes per day of moderate or fast walking and/or moderate or strenuous activity on at least 5 days per week in at least 7 of the past 10 years	10,770	18.6	249	15.6
	• Limit sedentary habits such as watching television	**Did not meet:** <30 minutes per day or <5 days per week or <7 of the previous 10 years of moderate or fast walking and/or moderate or strenuous activity	47,071	81.4	1,346	84.4
3. Energy density Limit consumption of energy dense foods; avoid sugary drinks	• Consume energy-dense foods sparingly • Avoid sugary drinks • Consume ‘fast foods’ sparingly, if at all	**Met:** Energy density of diet <125 kcal per 100 g and <1 sugary drink per week	10,963	19.0	226	14.2
		Did not meet: Energy density of diet ≥125 kcal per 100 g or ≥1 sugary drink per week	46,878	81.1	1,369	85.8
4. Plant foods Eat mostly foods of plant origin	• Eat at least five portions/servings (at least 400 g or 14 oz) of a variety of non-starchy vegetables and of fruits every day • Eat relatively unprocessed cereals (grains) and/or pulses (legumes) with every meal • Limit refined starchy foods • People who consume starchy roots or tubers as staples also to ensure intake of sufficient non-starchy vegetables, fruits, and pulses (legumes)	**Met:** ≥5 servings of fruits and vegetables and ≥1 serving of whole grains and/or legumes per day	6,605	11.4	130	8.2
		Did not meet: <5 servings of fruits and vegetables and/or <1 serving of whole grains and/or legumes per day	51,236	88.6	1,465	91.9

WCRF/AICR Recommendation	Associated Personal Recommendations	Met/Did Not Meet Recommendation in This Study if:	VITAL Cohort (N=57,841)		Cancer Deaths (N=1,595)	
			N	%	N	%
5. Red meat Limit intake of red meat and avoid processed meat	• People who eat red meat to consume less than 500 g (18 oz) a week, very little if any to be processed	**Met:** <18 oz red and/or processed meat per week	31,880	55.1	786	49.3
		Did not meet: ≥18 oz red and/or processed meat per week	25,961	44.9	809	50.7
6. Alcohol Limit alcoholic drinks	• If alcoholic drinks are consumed, limit consumption to no more than two drinks a day for men and one drink a day for women	**Met:** ≤ 1 drink per day for women; ≤2 drinks per day for men	49,475	85.5	1,331	83.5
		Did not meet: >1 drink per day for women; >2 drinks per day for men	8,366	14.5	264	16.6
7. Salt Limit consumption of salt; avoid moldy grains or legumes	• Avoid salt-preserved, salted, or salty foods; preserve foods without using salt • Limit consumption of processed foods with added salt to ensure an intake of less than 6 g (2.4 g sodium) a day • Do not eat moldy cereals (grains) or pulses (legumes)	**Not operationalized**	--	--	--	--
8. Supplements Aim to meet nutritional needs through diet alone	• Dietary supplements are not recommended for cancer prevention	**Not operationalized**	--	--	--	--

Italicized text indicates portions of the WCRF/AICR recommendations operationalized in this study. These represent the key components of the recommendations selected by an expert panel.

Table 2

Baseline Characteristics of the Study Population and of Cancer Deaths in the Vitamins And Lifestyle (VITAL) Study, Washington State, 2000–2002

	VITAL Cohort (N=57,841)		Cancer Deaths (N=1,595)	
Characteristic	**N**	**%**	**N**	**%**
Sex				
Men	29,008	50.2	906	56.8
Women	28,833	49.9	689	43.2
Age (years)				
50–54	14,909	25.8	151	9.5
55–59	13,928	24.1	218	13.7
60–64	10,622	18.4	277	17.4
65–69	8,925	15.4	369	23.1
70 or older	9,457	16.4	580	36.4
Education				
High school graduate/GED or below	10,460	18.1	465	29.2
Some college/technical school	21,907	37.9	632	39.6
College graduate	14,808	25.6	338	21.2
Advanced degree	10,499	18.2	156	9.8
Missing	167	0.3	4	0.3
Race/ethnicity				
White	53,989	93.3	1,503	94.2
Hispanic	491	0.9	13	0.8
African American	615	1.1	13	0.8
American Indian/Alaska Native	838	1.5	26	1.6
Asian/Pacific Islander	1,353	2.3	26	1.6
Other/missing	555	1.0	14	0.9
Marital status				
Married	44,012	76.1	1,141	71.5
Living with partner	1,523	2.6	28	1.8
Never married	1,904	3.3	59	3.7
Separated/divorced	6,556	11.3	195	12.2
Widowed	3,581	6.2	168	10.5
Missing	265	0.5	4	0.3
Smoking status				
Never smoked	27,869	48.2	472	29.6
Former smoker (quit 10+ yrs. Before baseline)	4,663	8.1	293	18.4
Former smoker (quit <10 yrs. Before baseline)	3,731	6.5	191	12.0
Current smoker	21,247	36.7	618	38.8
Missing	331	0.6	21	1.3
Mammogram in 2 years prior to baseline (women only)				
No	2,491	8.6	96	13.9

	VITAL Cohort (N=57,841)		Cancer Deaths (N=1,595)	
Characteristic	**N**	**%**	**N**	**%**
Yes	26,249	91.0	592	85.9
Missing	93	0.3	1	0.2
PSA screening in 2 years prior to baseline (men only)				
No	8,088	27.9	286	31.6
Yes	20,601	71.0	609	67.2
Missing	319	1.1	11	1.2
Colonoscopy or sigmoidoscopy in 2 years prior to baseline				
No	25,580	44.2	721	45.2
Yes	31,860	55.1	855	53.6
Missing	401	0.7	19	1.2
Number of first-degree family members diagnosed with cancer				
None	30,940	53.5	847	53.1
One	18,223	31.5	470	29.5
Two or more	7,571	13.1	240	15.1
Missing	1,107	1.9	38	2.4

Table 3

Hazard Ratios (HRs) and 95% Confidence Intervals (CIs) for Cancer-specific mortality Associated With Meeting (vs. Not Meeting) Each WCRF/AICR Recommendation in the Vitamins And Lifestyle (VITAL) Study, Washington State

	Age- and Sex-Adjusted[a]		Covariate-Adjusted[b]		Fully-Adjusted[c]	
Recommendation	**HR**	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
Body fatness	0.75	0.66, 0.86	0.88	0.77, 1.01	0.89	0.78, 1.02
Physical activity	0.73	0.64, 0.84	0.88	0.76, 1.01	0.91	0.79, 1.04
Energy density	0.69	0.60, 0.80	0.78	0.67, 0.91	0.82	0.70, 0.96
Plant foods	0.67	0.56, 0.80	0.75	0.62, 0.91	0.82	0.67, 1.00
Red meat	0.79	0.71, 0.88	0.92	0.82, 1.04	0.97	0.85, 1.09
Alcohol	0.86	0.76, 0.99	0.93	0.81, 1.07	0.93	0.81, 1.07

[a] Age is used as the timeline in the Cox proportional hazards model. Model includes 57,841 respondents, of whom 1,595 died from cancer.

[b] Adjusted for age (as the timeline in the Cox model), sex, education (high school graduate/GED or below, some college/technical school, college graduate, advanced degree), race/ethnicity (white, Hispanic, African-American, American Indian/Alaska Native, Asian/Pacific Islander, other/missing), marital status (married, living with partner, never married, separated/divorced, widowed), mammography in previous 2 years (yes/no, women only), PSA screening in previous 2 years (yes/no, men only), colonoscopy or sigmoidoscopy in previous 10 years (yes/no), cancers diagnosed in first-degree relatives (0, 1, 2+), non-steroidal anti-inflammatory medication and regular or low-dose aspirin use (each categorized as none, <4 days/week or in <4 of past 10 years, 4+ days/week in at least 4 of past 10 years), pack-years of smoking (continuous), and kilocalories of average daily energy intake (continuous). Several additional reproductive factors were included for women, including: age at menarche (≤11, 12, 13, 14, 15+), age at birth of first child (≤19, 20–24, 25–29, 30–34, 35+, no children), years of estrogen-only and of combined estrogen plus progestin hormone therapy use (each categorized as none or <1, 1–4, 5–9, 10+), hysterectomy (none, simple, total hysterectomy/oophorectomy), and age at menopause (≤39, 40–44, 45–49, 50–54, 55+, peri-menopausal at baseline). Participants with missing data were treated as their own category for each potential confounder. Model includes 54,370 respondents, of whom 1,479 died of cancer.

[c] Adjusted for the factors in the covariate-adjusted model, as well as for whether respondents met each of the other recommendations. Model includes 54,370 respondents, of whom 1,479 died from cancer.

Table 4

Hazard Ratios (HRs) and 95% Confidence Intervals (CIs) for Cancer-specific mortality Associated With Number of WCRF/AICR Recommendations Met at Baseline in the Vitamins And Lifestyle (VITAL) Study, Washington State

	VITAL Cohort (N = 57,841)		Cancer Deaths (N = 1,595)		Age- and Sex- Adjusted[a]		Covariate-Adjusted[b]	
Recommendations Met	**%**	**N**	**%**	**N**	**HR**	**95% CI**	**HR**	**95% CI**
None	4.5	2,589	7.0	112	1.00		1.00	
1	28.3	16,388	31.7	505	0.72	0.58, 0.88	0.76	0.61, 0.94
2	34.3	19,847	35.9	572	0.64	0.52, 0.78	0.78	0.63, 0.97
3	20.3	11,756	17.6	280	0.51	0.41, 0.64	0.69	0.55, 0.88
4	9.3	5,378	6.4	102	0.40	0.31, 0.53	0.59	0.44, 0.78
5–6	3.3	1,883	1.5	24	0.26	0.17, 0.40	0.39	0.24, 0.62
Per recommendation[c]					0.81	0.78, 0.85	0.90	0.85, 0.94
P_{trend}[c]						<0.001		<0.001

[a] Age is used as the timeline in the Cox proportional hazards model. Model includes 57,841 respondents, of whom 1,595 died from cancer.

[b] Adjusted for age (as the timeline in the Cox model), sex, education (high school graduate/GED or below, some college/technical school, college graduate, advanced degree), race/ethnicity (white, Hispanic, African-American, American Indian/Alaska Native, Asian/Pacific Islander, other/missing), marital status (married, living with partner, never married, separated/divorced, widowed), mammography in previous 2 years (yes/no, women only), PSA screening in previous 2 years (yes/no, men only), colonoscopy or sigmoidoscopy in previous 10 years (yes/no), cancers diagnosed in first-degree relatives (0, 1, 2+), non-steroidal anti-inflammatory medication and regular or low-dose aspirin use (each categorized as none, <4 days/week or in <4 of past 10 years, 4+ days/week in at least 4 of past 10 years), pack-years of smoking (continuous), and kilocalories of average daily energy intake (continuous). Several additional reproductive factors were included for women, including: age at menarche (≤11, 12, 13, 14, 15+), age at birth of first child (≤19, 20–24, 25–29, 30–34, 35+, no children), years of estrogen-only and of combined estrogen plus progestin hormone therapy use (each categorized as none or <1, 1–4, 5–9, 10+), hysterectomy (none, simple, total hysterectomy/oophorectomy), and age at menopause (≤39, 40–44, 45–49, 50–54, 55+, peri-menopausal at baseline). Participants with missing data were treated as their own category for each potential confounder. Model includes 54,370 respondents, of whom 1,479 died of cancer.

[c] Per recommendation HRs, 95% CIs and *P*-values were calculated using a two-sided test for linear trend modeling categories (0–6) as a continuous variable.