Is concordance with World Cancer Research Fund/American Institute for Cancer Research guidelines for cancer prevention related to subsequent risk of cancer? Results from the EPIC study[1–4]

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ABSTRACT

Background: In 2007 the World Cancer Research Fund (WCRF) and the American Institute of Cancer Research (AICR) issued 8 recommendations (plus 2 special recommendations) on diet, physical activity, and weight management for cancer prevention on the basis of the most comprehensive collection of available evidence.

Objective: We aimed to investigate whether concordance with the WCRF/AICR recommendations was related to cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC) study.

Design: The present study included 386,355 EPIC participants from 9 European countries. At recruitment, dietary, anthropometric, and lifestyle information was collected. A score was constructed based on the WCRF/AICR recommendations on weight management, physical activity, foods and drinks that promote weight gain, plant foods, animal foods, alcoholic drinks, and breastfeeding for women; the score range was 0–6 for men and 0–7 for women. Higher scores indicated greater concordance with WCRF/AICR recommendations. The association between the score and cancer risk was estimated by using multivariable Cox regression models.

Results: Concordance with the score was significantly associated with decreased risk of cancer. A 1-point increment in the score was associated with a risk reduction of 5% (95% CI: 3%, 7%) for total cancer, 12% (95% CI: 9%, 16%) for colorectal cancer, and 16% (95% CI: 9%, 22%) for stomach cancer. Significant associations were also observed for cancers of the breast, endometrium, lung, kidney, upper aerodigestive tract, liver, and esophagus but not for prostate, ovarian, pancreatic, and bladder cancers.

Conclusion: Adherence to the WCRF/AICR recommendations for cancer prevention may lower the risk of developing most types of cancer. *Am J Clin Nutr* 2012;96:150–63.

INTRODUCTION

Dietary and lifestyle guidelines for the prevention of cardiovascular diseases and health maintenance have been the basis for the development of several index scores. Results from several studies have shown that some of the well-known index scores—such as the Healthy Eating Index, the Diet Quality Index, and the Recommended Food Score, and modifications of these index scores—have little or no association with overall cancer risk and/

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or mortality (1–7). On the other hand, some (8–15), but not all (16–18), studies have shown a stronger association with cancer incidence and mortality for dietary index scores that also incorporate other lifestyle factors such as weight management, physical activity, alcohol consumption, and smoking. Nevertheless, a few studies showed that the association of lifestyle scores with cancer risk was attenuated when the body fatness and physical activity components of the score were excluded, indicating that these 2 components probably explained most of the observed effect of the score on cancer risk (8, 14).

One of the reasons why some indexes failed to show a predictive value for cancer risk and/or mortality could be that most indexes were based on recommendations for prevention of cardiovascular disease or general health. Only 2 previous studies have specifically tested indexes based on cancer prevention recommendations [the 1997 American Institute for Cancer Research Recommendations (14) and the American Cancer Society cancer prevention guidelines (15)]: in both studies, scores based on these recommendations showed significant associations with total cancer incidence (14) and mortality (14, 15); however, neither these nor other studies had enough power to examine the association of health recommendations with specific cancer types that might be more closely related to certain lifestyle factors than others.

In 2007 the World Cancer Research Fund and the American Institute for Cancer Research (WCRF/AICR)[5] issued 8 general and 2 special recommendations on diet, physical activity, and weight management for cancer prevention on the basis of the most comprehensive collection of available evidence (19). Previous research based on the European Prospective Investigation into Cancer and Nutrition (EPIC) has contributed to elucidate the associations between these lifestyle factors individually and cancer risk (20). In the present study, we assessed whether a composite measure of a healthy lifestyle based on the 2007 WCRF/AICR recommendations for cancer prevention is related to the risk of developing total and specific types of cancer in EPIC.

SUBJECTS AND METHODS

Study population

A total of 521,330 men and women, aged 25–70 y, were recruited between 1 January 1992 and 31 December 2000 from 23 centers in 10 European countries: Denmark (Aarhus and Copenhagen), France, Germany (Heidelberg and Potsdam), Greece, Italy (Florence, Naples, Ragusa, Turin, and Varese), the Netherlands (Bilthoven and Utrecht), Norway, Spain (Asturias, Granada, Murcia, Navarra, and San Sebastian), Sweden (Malmö and Umeå), and the United Kingdom (Cambridge and Oxford). The French cohort encompassed members of a health insurance plan for school and university employees. Participants at the Spanish and Italian centers (except Florence) included blood donors, members of several health insurance programs, employees of several enterprises, civil servants, and the general population. In Utrecht and Florence, participants enrolled in mammographic screening programs were recruited for the study. In Oxford, most of the cohort consisted of "health-conscious" subjects from England, Wales, Scotland, and Northern Ireland, many of whom were vegetarians. Participants were recruited from the general population in other centers. The cohorts of France, Norway, Utrecht, and Naples included only women. Approval for this study was obtained from the ethical review boards of the International Agency for Research on Cancer and from all local institutions where subjects had been recruited for the EPIC study. Written informed consent was obtained from all participants before entry into the EPIC study. The details of the study design used in the EPIC study have been described elsewhere (21, 22).

We excluded participants who did not complete the lifestyle (n = 1465) or dietary (n = 5437) questionnaires, participants within the lowest and highest 1% of the cohort distribution of the ratio of reported total energy intake to energy requirements (n = 10,241), participants who were diagnosed with cancer (excluding nonmelanoma skin cancer) before enrollment (n = 22,860), participants with missing date of diagnosis (n = 13), and participants with incomplete follow-up information (n = 4002). For the present study, we also excluded pregnant women (n = 535) and participants with missing data on the following variables: weight or height (n = 4271), physical activity [n = 65,402, including all participants from Umeå (Sweden) and

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[5] Abbreviations used: EPIC, European Prospective Investigation into Cancer and Nutrition; PAF%, population attributable fraction; WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research.

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TABLE 1
WCRF/AICR recommendations for cancer prevention and operationalization of the WCRF/AICR score in the EPIC study[1]

	Personal recommendations	Operationalization[2]	Scoring	Percentage[3]
WCRF/AICR recommendations				
1) Body fatness. Be as lean as possible without becoming underweight.	*1a*) Ensure that body weight throughout childhood and adolescent growth projects toward the lower end of the normal BMI range at age 21 y.	Insufficient data available	NA	
	1b) Maintain body weight within the normal range from age 21 y.	BMI (in kg/m^2): 18.5–24.9	1	48.0
		BMI: 25–29.9	0.5	36.0
		BMI: <18.5 or ≥30	0	16.0
	1c) Avoid weight gain and increases in waist circumference throughout adulthood.	Insufficient data available	NA	
2) Physical activity. Be physically active as part of your everyday life.	*2a*) Be moderately physically active, equivalent to brisk walking, for ≥30 min every day.	Manual/heavy manual job, or >2 h/wk of vigorous PA, or >30 min/d of cycling/sports	1	23.9
		15–30 min/d of cycling/sports	0.5	20.7
		<15 min/d of cycling/sports	0	55.4
	2b) As fitness improves, aim for ≥60 min of moderate or for ≥30 min of vigorous physical activity every day.	Insufficient data available	NA	
	2c) Limit sedentary habits such as watching television.	Insufficient data available	NA	
3) Foods and drinks that promote weight gain. Limit consumption of energy-dense foods; avoid sugary drinks.[4,5]	*3a*) Consume energy-dense foods sparingly.	ED: ≤125 kcal · 100 g^{-1} · d^{-1}	1	23.0
		ED: >125 to <175 kcal · 100 g^{-1} · d^{-1}	0.5	59.1
		ED: >175 kcal · 100 g^{-1} · d^{-1}	0	17.9
	3b) Avoid sugary drinks.	Sugary drink intake: 0 g/d	1	21.2
		Sugary drink intake: ≤250 g/d	0.5	61.4
		Sugary drink intake: >250 g/d	0	17.4
	3c) Consume fast foods sparingly, if at all.	Insufficient data available	NA	
4) Plant foods. Eat mostly foods of plant origin.[4,5]	*4a*) Eat ≥5 portions/servings (≥400 g) of a variety of nonstarchy vegetables and of fruit every day.	F&V intake: ≥400 g/d	1	42.5
		F&V intake: 200 to <400 g/d	0.5	38.4
		F&V intake: <200 g/d	0	19.1
	4b) Eat relatively unprocessed cereals (grains) and/or pulses (legumes) with every meal.	Dietary fiber intake: ≥25 g/d	1	27.3
		Dietary fiber intake: 12.5 to <25 g/d	0.5	60.5
		Dietary fiber intake: <12.5 g/d	0	12.2
	4c) Limit refined starchy foods.	Insufficient data available	NA	
	4d) People who consume starchy roots or tubers as staples should also ensure sufficient intake of nonstarchy vegetables, fruit, and pulses (legumes).	Not applicable to this population	NA	
5) Animal foods. Limit intake of red meat and avoid processed meat.[5]	*5a*) People who eat red meat should consume <500 g/wk and very few, if any, processed meats.	Red and processed meat <500 g/wk and processed meat intake <3 g/d	1	15.0
		Red and processed meat <500 g/wk and processed meat intake 3 to <50 g/d	0.5	35.8
		Red and processed meat ≥500 g/wk or processed meat intake ≥50 g/d	0	49.2

(Continued)

TABLE 1 (*Continued*)

	Personal recommendations	Operationalization[2]	Scoring	Percentage[3]
6) Alcoholic drinks. Limit alcoholic drinks.	*6a*) If alcoholic drinks are consumed, limit consumption to ≤2 drinks/d for men and 1 drink/d for women.	Ethanol intake: ≤20 g/d (men) Ethanol intake: ≤10 g/d (women)	1	66.3
		Ethanol intake: >20–30 g/d (men) Ethanol intake: >10–20 g/d (women)	0.5	16.0
		Ethanol intake: >30 g/d (men) Ethanol intake: >20 g/d (women)	0	17.7
7) Preservation, processing, preparation. Limit consumption of salt. Avoid moldy cereals (grains) or pulses (legumes).	*7a*) Avoid salt-preserved, salted, or salty foods; preserve foods without using salt.	Insufficient data available	NA	
	7b) Limit consumption of processed foods with added salt to ensure an intake of <6 g (2.4 g sodium)/d.	Insufficient data available	NA	
	7c) Do not eat moldy cereals (grains) or pulses (legumes).	Insufficient data available	NA	
8) Dietary supplements. Aim to meet nutritional needs through diet alone.	*8a*) Dietary supplements are not recommended for cancer prevention.	Not applicable to this population	NA	
WCRF/AICR special recommendations				
S1) Breastfeeding. Mothers to breastfeed; children need to be breastfed.	*S1a*) Aim to breastfeed infants exclusively up to 6 mo and continue with complementary feeding thereafter.	Cumulative breastfeeding: ≥6 mo	1	35.3
		Cumulative breastfeeding: >0 to <6 mo	0.5	34.9
		No breastfeeding	0	29.8
S2) Cancer survivors. Follow the recommendations for cancer prevention.	S2a) All cancer survivors should receive nutritional care from an appropriately trained professional.	Not applicable to this population	NA	
	S2b) If able to do so, and unless otherwise advised, aim to follow the recommendations for diet, healthy weight, and physical activity.	Not applicable to this population	NA	

[1] ED, energy density; EPIC, European Prospective Investigation into Cancer and Nutrition; F&V, fruit and vegetables; NA, not available; PA, physical activity; WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research.

[2] ED was calculated as energy (kcal) from foods (solid foods and semi-solid or liquid foods such as soups) divided by the weights (g) of these foods. Drinks (including water, tea, coffee, juice, soft drinks, alcoholic drinks, and milk) were not included in the calculation (27). Sugary drinks included both soft drinks and fruit and vegetable juices. Variables selected to operationalize the recommendation on physical activity are those included in the Cambridge physical activity index (except for vigorous physical activity), which has been validated for use in epidemiologic studies (26).

[3] Percentages show the distribution of the population by each component categorization of the WCRF/AIRC score.

[4] The score for recommendations 3 and 4 was the result of averaging the scores of each subrecommendation.

[5] All dietary variables used for the construction of the WCRF/AIRC score were calibrated by using additive calibration (except for alcohol and ED).

Norway where this information was not collected in sufficient detail], and women with no information on breastfeeding or duration of breastfeeding (n = 20,479, including all female participants from Bilthoven, Netherlands, where this information was not collected). Therefore, 386,355 participants (126,257 men and 260,098 women) were included in the present study.

Data collection and dietary questionnaires

At baseline, participants filled out extensive medical, dietary, and lifestyle questionnaires, including questions on alcohol use, smoking status, physical activity, education, reproductive history, breastfeeding, exogenous hormone use, and previous illnesses. Body weight and height were measured in all centers except for Oxford (health-conscious population) and France where anthropometric measurements were self-reported (23). Usual food intakes were measured by using country-specific validated dietary questionnaires (24), and individual nutrient intakes were derived from foods included in the dietary questionnaires through the standardized EPIC Nutrient Database (25). To correct for any systematic under- or overestimation of dietary intake between the study centers, a dietary calibration study was conducted. A random sample of 36,308 men and women (7.4% of the sample) completed a detailed computerized 24-h dietary recall, and nutrient intake was calculated by using the standardized EPIC Nutrient Database (26). Dietary exposures across centers were scaled by using an additive calibration model (24). Briefly, the differences between the sex- and center-specific means of the values from the dietary questionnaire and the means of the 24-h recall values were calculated and added to the questionnaire values. All dietary variables used in the present study were calibrated by using additive calibration.

WCRF/AICR score construction

An index score reflecting concordance with the WCRF/AICR recommendations for cancer prevention was constructed (WCRF/AICR score). Of 10 recommendations (components), the following 7 in women (and 6 in men) could be used for the construction of the score: body fatness, physical activity, consumption of foods and drinks that promote weight gain, consumption of plant foods, consumption of animal foods, consumption of alcoholic drinks, and breastfeeding in women. The recommendation on preservation, processing, and preparation of foods was not included in this score because sufficient data were not available. The special recommendation related to cancer survivors was excluded because the index was derived from recommendations for cancer prevention. The recommendation "Don't use supplements to protect against cancer" was excluded because it could not be operationalized in terms of cancer prevention without further assumptions about type or dose of supplementation. The score assigned for each component was 1 when the recommendation was met. An intermediate category (0.5 points) was created to appraise a higher proportion of the variability in the population. All other individuals received 0 points. Some recommendations had several subrecommendations: each subrecommendation was scored and the component score was the average of the subrecommendation scores. The score was constructed by using as cutoffs quantitative criteria provided in the WCRF/AICR recommendations. In some cases, arbitrary a priori cutoffs (not based on the distribution of the variable in our sample) were defined for intermediate categories. The scoring system was based in the premise that each major recommendation should contribute equally to the total WCRF/AICR score. The scores obtained for each component were added to calculate a single score for each study participant. The maximum score was 7 points in women and 6 points in men (the recommendation on breastfeeding is applicable only to women). Higher scores indicated greater concordance with the WCRF/AICR recommendations. The score was further categorized into 5 categories according to predefined cutoffs: category 1 (0–2 points in men; 0–3 points in women), category 2 ($>$2 to $<$3 in men; $>$3 to $<$4 in women), category 3 (3 to $<$4 in men; 4 to $<$5 in women), category 4 (4 to $<$5 in men; 5 to $<$6 in women), and category 5 (5–6 in men; 6–7 in women). With this categorization, the minimal score difference between the first and fifth categories was 3 points for both men and women.

Detailed information on the operationalization of the score can be found in **Table 1** (27–29).

Case ascertainment

Cancer cases were identified through population cancer registries in Denmark, Italy, the Netherlands, Spain, Sweden, and the United Kingdom. In France, Germany, and Greece, a combination of methods was used including health insurance records, cancer pathology registries, and active follow-up of study participants and their next of kin. Follow-up began at the date of enrollment and ended at the date of diagnosis of cancer, death, or last complete follow-up. Cancer incidence data were coded according to the 10th revision of the International Statistical Classification of Diseases, Injuries and Causes of Death (30) and the second revision of the International Classification of Diseases for Oncology (31). Only the first primary neoplasm was included in the analysis. Nonmelanoma skin cancer was excluded from the analysis.

Statistical analyses

Descriptive statistics relied on cross-tabulations, showing percentages within groups for categorical variables as well as group means and SDs for continuous variables.

Cox proportional hazards regression was used to estimate the association between the WCRF/AICR score and total cancer risk. Age was used as the primary time variable, with entry time defined as the subject's age at recruitment and exit time as age at diagnosis of cancer, censoring, or death (whichever came first). All analyses were stratified by age at recruitment to control for length of follow-up, by center to control for center effects such as follow-up procedures and questionnaire design, and by sex (except in sex-specific analyses). The WCRF/AICR score was assessed as a continuous variable (1-point increment) and as a categorical variable (using the 5 predefined categories). The WCRF/AICR categorical variable was scored from 1 to 5, and trend tests were calculated on these scores. All models were adjusted for educational level (as a categorical variable: no education, primary school, technical school, secondary school, and university degree), presence of chronic diseases at baseline [including type 2 diabetes, heart disease, and stroke (yes, no)], smoking status and intensity of smoking (never; former: quit smoking $>$20 y ago, quit 11–20 y ago, quit $\leq$10 y ago; smoker:

1–15 cigarettes/d, 16–25 cigarettes/d, >25 cigarettes/d; smoker, pipe or cigar), menopausal status (postmenopausal, perimenopausal, premenopausal, surgical postmenopausal), ever use of hormone replacement therapy (yes, no), ever use of contraception pills (yes, no), age at menarche (<12, 12–15, >15 y), parity (yes, no), age at first full-time pregnancy (<21 y, 21–30 y, >30 y, nulliparous), and total energy intake (continuous). We included participants with missing data for the confounding variables as a separate category for these variables.

We calculated the population attributable fraction (PAF%) and 95% CIs to estimate the proportion of total cancer in this cohort that hypothetically would not have occurred if all participants were in the highest category of the score, with the assumption of a causal relation. We compared participants in the highest category of the score with the rest of the study participants. For these analyses, we estimated HRs from multivariate Cox regression models (32).

The association between the WCRF/AICR score and risk of developing specific cancer types was also calculated by using Cox regression models with the same level of adjustment as specified above. The specific cancer types considered were breast, ovarian, endometrial, prostate, colorectal, lung, bladder, pancreas, kidney, stomach, upper aerodigestive tract, liver, and esophageal cancers. In these models, the WCRF/AICR score was assessed both continuously (per 1-point increment) and categorically (using 4 predefined categories; categories 4 and 5 were combined into a single category because of the low number of cases in the highest category).

Potential effect modifications by baseline BMI category (BMI, in kg/m^2: <25, 25 to <30, and ≥30) and smoking status (former smokers, current smokers, and never smokers) were explored by modeling interaction terms (cross-products) between these variables (categorically) and the WCRF/AICR score (continuous) and by conducting stratified analyses. The effect modification by smoking status was assessed for both smoking-related cancers (lung, bladder, upper aerodigestive tract, kidney, stomach, esophagus, pancreas, liver, and colorectal) and non-smoking-related cancers (ie, cancer risk is not increased by smoking: breast and endometrial cancer in women and prostate cancer in men) (29). Sensitivity analyses were performed after excluding participants with presence of chronic diseases at baseline (type 2 diabetes, heart disease, and stroke) and after excluding the first 2 y of follow-up. Potential heterogeneity between countries in the association between the WCRF/AICR score and total cancer risk was assessed by calculating country-specific estimates and using random-effects meta-analyses (I^2).

We estimated the individual association of each component of the WCRF/AICR score with total cancer risk, after adjustment for all other components of the score. Also, we evaluated the relative importance of each of the components of the WCRF/AICR score on total cancer risk by subtracting alternately one component at a time from the original score and including this component as a covariate in the model. We also assessed the association of the WCRF/AICR score with total cancer risk after excluding simultaneously the body fatness and physical activity components. To be able to compare the risk estimates of the different scores, the total WCRF/AICR score and the alternative scores were assessed as continuous variables by increments of 1 SD.

All statistical analyses were performed with STATA 10.0 (StataCorp) and SAS software (version 9.1; SAS Institute Inc).

RESULTS

After a median follow-up time of 11.0 y (follow-up of 4,243,586 person-years), 36,994 cancer cases were identified in the EPIC cohort (13,838 in men and 23,156 in women). The distribution and characteristics of the study population by the 5 predefined categories of the WCRF/AICR score can be found in **Table 2**. Men and women within the highest categories of the score were more likely to be younger and to have a higher educational level and less likely to be current smokers and to have a chronic disease at baseline. Women within the highest categories of the score were more likely to have ever used contraceptive pills and to be premenopausal and less likely to have ever used hormonal replacement therapy and to be nulliparous.

The results of the association between the WCRF/AICR score and risk of total cancer and specific cancer types are shown in **Table 3** and **Figure 1**. Overall, a 1-point increment in the score was associated with a 5% (95% CI: 3%, 7%) lower risk of developing any cancer. Compared with the first category of the score, the multiple adjusted HRs (95% CI) for total cancer risk observed in the second, third, fourth, and fifth categories of the score were 0.94 (0.89, 0.98), 0.88 (0.84, 0.92), 0.91 (0.85, 0.97), and 0.84 (0.72, 0.99) in men; the corresponding HRs (95% CI) in women were 0.95 (0.92, 0.98), 0.91 (0.88, 0.94), 0.89 (0.85, 0.93), and 0.81 (0.72, 0.91) (P-trend < 0.0001 in both men and women). The risk reduction in participants within the fourth and fifth categories of the score compared with those within the first category was 16% for breast, 27% for colorectal, 14% for lung, 23% for endometrial, 29% for kidney, 38% for stomach, 31% for upper aerodigestive tract, 15% for liver, and 42% for esophageal cancer (P-trend < 0.05). Higher scores were not significantly associated with lower risk of ovarian, prostate, bladder, or pancreas cancer. Overall, 12.6% (95% CI of the PAF%: 3.6%, 21.4%) of all cancers could have been prevented if the whole study population was classified within the fifth category of the score (5–6 points in men and 6–7 points in women; data not shown).

No evidence of effect modification by smoking status (P-interaction = 0.261 in men and 0.692 in women) was observed (**Table 4**); however, among men, no significant association between the WCRF/AICR score and total cancer risk was observed among never smokers. This potential effect modification by smoking status was further assessed for smoking-related and non-smoking-related cancers. In men, the score was significantly associated with a lower risk of smoking-related cancers (lung, bladder, upper aerodigestive tract, kidney, stomach, esophagus, pancreas, liver, and colorectal) in never, former, and current smokers; for non-smoking-related cancers (mainly prostate cancer), no significant association with the score was observed in any of the categories of smoking status. Among women, the score was associated with lower risk of both smoking-related and non-smoking-related (mainly breast and endometrial) cancers in all categories of smoking status, although the association was slightly stronger for smoking-related cancers.

No evidence of effect modification by BMI category was observed (P-interaction = 0.234 in men and 0.596 in women). The HRs for total cancer risk did not change when persons with chronic diseases at baseline were excluded [HR (95% CI) per 1-point increment in the score: 0.95 (0.93, 0.97) in men and 0.96 (0.95, 0.97) in women] or when the first 2 y of follow-up were excluded [HR (95% CI) per 1-point increment in the score: 0.95

TABLE 2
Characteristics of participants in the EPIC study according to categories of the WCRF/AICR score by sex[1]

		WCRF/AICR score categories				
	All	Category 1	Category 2	Category 3	Category 4	Category 5
Men						
Score range	0–6	0–2	>2 to <3	3 to <4	4 to <5	5–6
No. of participants [*n* (%)]	126,257 (100.0)	26,777 (21.2)	36,073 (28.6)	43,727 (34.6)	16,854 (13.4)	2826 (2.2)
Age (y)	53.0 ± 9.8[2]	53.6 ± 8.0	53.6 ± 9.1	53.1 ± 10.1	51.3 ± 11.7	46.7 ± 12.7
Level of education (%)[3]						
None/primary school	34.8	41.2	38.3	33.7	24.4	9.1
Technical/secondary school	35.5	35.3	35.4	36.0	34.5	36.0
University degree	27.4	22.0	24.4	28.0	37.2	48.0
Smoking status (%)[3]						
Never smokers	30.8	21.7	27.4	33.6	41.5	53.3
Former smokers	37.8	37.1	38.2	38.3	37.6	33.0
Current smokers	30.5	40.9	33.6	27.1	19.4	12.1
Baseline chronic diseases (%)[4]						
Yes	7.4	7.6	7.5	7.6	6.8	3.9
Women						
Score range	0–7	0–3	>3 to <4	4 to <5	5 to <6	6–7
No. of participants [*n* (%)]	260,098 (100.0)	57,800 (22.2)	71,922 (27.7)	92,027 (35.4)	34,048 (13.1)	4301 (1.7)
Age (y)	51.7 ± 9.9	51.8 ± 9.2	51.8 ± 9.7	51.8 ± 10.1	51.0 ± 10.6	50.9 ± 10.1
Level of education (%)[3]						
None/primary school	30.4	31.6	33.0	31.2	22.6	15.1
Technical/secondary school	41.7	42.3	41.1	40.9	43.8	43.7
University degree	23.7	21.7	22.0	23.8	28.9	34.7
Smoking status (%)[3]						
Never smokers	59.1	52.6	58.8	62.1	62.5	61.0
Former smokers	21.8	22.0	20.9	21.4	23.8	27.2
Current smokers	17.5	23.9	18.6	15.0	12.2	10.1
Baseline chronic diseases (%)[4]						
Yes	3.6	4.1	3.9	3.5	2.6	2.0
Ever use of contraceptive pills (%)						
Yes	56.7	57.5	55.9	55.6	59.5	62.0
Ever use of HRT (%)						
Yes	24.7	26.2	24.9	24.0	23.6	22.8
Age at first menarche (%)[3]						
<12 y	15.6	17.1	15.9	15.1	14.3	15.1
≥12 to ≤15 y	77.1	75.9	77.1	77.6	77.9	77.5
>15 y	6.2	5.8	6.1	6.4	6.6	6.4
Age at first pregnancy (%)[3]						
Nulliparous	13.5	20.8	14.7	10.6	8.0	0.2
<21 y	11.7	11.3	12.1	12.0	11.0	10.1
≥21 to ≤30 y	63.9	56.5	62.6	67.0	69.5	76.5
>30 y	8.6	7.9	8.1	8.7	10.1	13.0
Menopausal status (%)						
Premenopausal	33.4	31.5	32.5	33.6	36.8	39.9
Postmenopausal	49.9	49.2	50.0	50.8	48.8	46.7
Perimenopausal	16.8	19.3	17.5	15.6	14.5	13.4

[1] EPIC, European Prospective Investigation into Cancer and Nutrition; HRT, hormone replacement therapy; WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research.
[2] Mean ± SD (all such values).
[3] Percentages do not add to 100% because of missing values.
[4] Chronic diseases include type 2 diabetes, heart disease, and stroke.

(0.93, 0.97) in men and 0.96 (0.95, 0.97) in women; data not shown]. No heterogeneity in the association between the WCRF/AICR score and cancer risk among countries was observed in men (*P*-heterogeneity = 0.724) (**Figure 2**A). Among women, *P*-heterogeneity was 0.014 (Figure 2B); however, in all countries inverse associations between the score and cancer risk were observed, indicating that heterogeneity was due to differences in the strength of the association rather than the direction.

The mutually adjusted HRs for total cancer incidence associated with the individual components of the WCRF/AICR score are shown in **Table 5**. In the overall sample (men and women combined), all of the components of the score were significantly associated with cancer risk, except for the component "foods that promote weight gain." In sex-specific analyses, total cancer risk was inversely associated with the components "plant foods," "red and processed meat," and "alcohol intake" in men and with

TABLE 3
HRs (95% CIs) for total cancer and specific cancer types according to categories of the WCRF/AICR score[1]

	WCRF/AICR score category[2]					
	1	2	3	4	5	*P*-trend
Score range (men/women)	0–2/0–3	>2 to <3/>3 to <4	3 to <4/4 to <5	4 to <5/5 to <6	5–6/6–7	
Total cancer						
All (no. of cases)	9224	10,778	12,276	4237	479	
HR (95% CI)	1.00 (reference)	0.94 (0.92, 0.97)	0.90 (0.87, 0.92)	0.89 (0.86, 0.93)	0.82 (0.75, 0.90)	<0.0001
Men (no. of cases)	3431	4272	4497	1473	165	
HR (95% CI)	1.00 (reference)	0.94 (0.89, 0.98)	0.88 (0.84, 0.92)	0.91 (0.85, 0.97)	0.84 (0.72, 0.99)	<0.0001
Women (no. of cases)	5793	6506	7779	2764	314	
HR (95% CI)	1.00 (reference)	0.95 (0.92, 0.98)	0.91 (0.88, 0.94)	0.89 (0.85, 0.93)	0.81 (0.72, 0.91)	<0.0001
Breast cancer						
Women (no. of cases)	2361	2597	3199	1201		
HR (95% CI)	1.00 (reference)	0.93 (0.88, 0.99)	0.92 (0.87, 0.98)	0.84 (0.78, 0.90)		<0.0001
Endometrial cancer						
Women (no. of cases)	306	328	370	144		
HR (95% CI)	1.00 (reference)	0.88 (0.75, 1.04)	0.79 (0.68, 0.93)	0.77 (0.62, 0.94)		0.002
Ovarian cancer						
Women (no. of cases)	212	258	307	129		
HR (95% CI)	1.00 (reference)	1.01 (0.84, 1.21)	0.95 (0.79, 1.14)	0.99 (0.79, 0.25)		0.681
Prostate cancer						
Men (no. of cases)	883	1231	1414	511		
HR (95% CI)	1.00 (reference)	0.99 (0.91, 1.08)	0.99 (0.91, 1.08)	1.02 (0.91, 1.14)		0.841
Colorectal cancer						
All (no. of cases)	1003	1198	1223	456		
HR (95% CI)	1.00 (reference)	0.91 (0.84, 1.00)	0.77 (0.70, 0.84)	0.73 (0.65, 0.81)		<0.0001
Lung cancer						
All (no. of cases)	769	749	703	241		
HR (95% CI)	1.00 (reference)	0.89 (0.80, 0.99)	0.81 (0.73, 0.91)	0.86 (0.74, 1.00)		0.001
Bladder cancer						
All (no. of cases)	380	473	508	153		
HR (95% CI)	1.00 (reference)	1.02 (0.89, 1.17)	0.99 (0.86, 1.13)	0.84 (0.69, 1.02)		0.161
Pancreatic cancer						
All (no. of cases)	192	224	258	109		
HR (95% CI)	1.00 (reference)	0.94 (0.77, 1.14)	0.91 (0.75, 1.10)	1.00 (0.78, 1.28)		0.684
Kidney cancer						
All (no. of cases)	202	210	255	78		
HR (95% CI)	1.00 (reference)	0.83 (0.68, 1.01)	0.87 (0.72, 1.05)	0.71 (0.54, 0.93)		0.030
Stomach cancer						
All (no. of cases)	185	214	229	68		
HR (95% CI)	1.00 (reference)	0.87 (0.72, 1.07)	0.77 (0.63, 0.95)	0.62 (0.46, 0.83)		<0.0001
UADT cancer						
All (no. of cases)	207	195	149	51		
HR (95% CI)	1.00 (reference)	0.88 (0.72, 1.08)	0.67 (0.54, 0.84)	0.69 (0.50, 0.95)		<0.0001
Liver cancer						
All (no. of cases)	130	181	147	64		
HR (95% CI)	1.00 (reference)	1.08 (0.86, 1.36)	0.71 (0.56, 0.91)	0.85 (0.62, 1.16)		0.011
Esophageal cancer						
All (no. of cases)	99	90	94	29		
HR (95% CI)	1.00 (reference)	0.77 (0.57, 1.03)	0.73 (0.54, 0.98)	0.58 (0.38, 0.90)		0.008

[1] Analyses were performed by using a Cox regression model stratified by center, age (1-y increments), and sex in the model of both sexes combined and adjusted for energy intake (kcal), level of education (none, primary school, technical/professional school, secondary school, university degree, unknown/missing), smoking status and intensity of smoking (never; former: quit smoking >20 y ago, quit 11–20 y ago, quit ≤10 y ago; smoker: 1–15 cigarettes/d, 16–25 cigarettes/d, >25 cigarettes/d; smoker, pipe or cigar; missing current or former status; unknown/missing), and presence of chronic diseases at baseline (no, yes, missing). Models for women were further adjusted for ever use of contraceptive pills (no, yes, missing), ever use of hormone replacement therapy (no, yes, missing), age at first menarche (<12 y, ≥12 to ≤15 y, >15 y, missing), age at first pregnancy (<21 y, ≥21 to ≤30 y, >30 y, nulliparous), and menopausal status (premenopausal, postmenopausal, perimenopausal, and surgical postmenopausal). UADT, upper aerodigestive tract; WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research.

[2] WCRF/AICR score category 1: 0–2 in men and 0–3 in women; category 2: >2 to <3 in men and >3 to <4 in women; category 3: 3 to <4 in men and 4 to <5 in women; category 4: 4 to <5 in men and 5 to <6 in women; category 5: 5–6 in men and 6–7 in women. In analyses of specific cancer types, categories 4 and 5 were combined into a single category (score range: 4–6 in men and 5–7 in women) because of the low number of cases in the highest category.

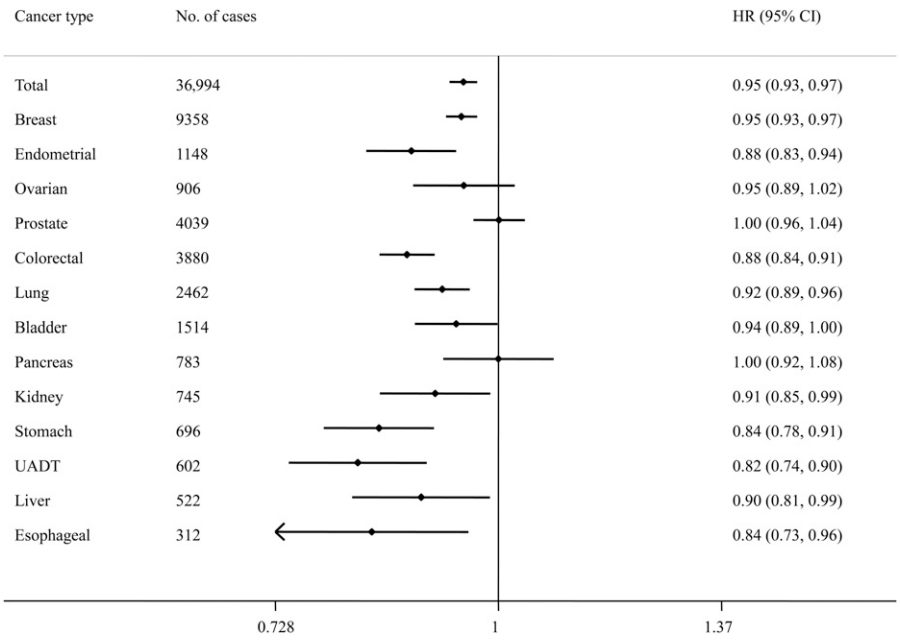

FIGURE 1. HRs (95% CIs) for total cancer and specific cancer types associated with a 1-point increment in WCRF/AICR score (range: 0–6 in men, 0–7 in women). Cox regression models were stratified by center, age (1-y increments), and sex and adjusted for energy intake (kcal), level of education (none, primary school, technical/professional school, secondary school, university degree, unknown/missing), duration of smoking in former smokers (>20 y ago, 11–20 y ago, ≤10 y ago, unknown/missing), number of cigarettes per day among smokers (1–15 cigarettes, 16–25 cigarettes, >25 cigarettes, pipe or cigar, unknown/missing), and presence of chronic diseases at baseline (no, yes, missing). Models for women were further adjusted for ever use of contraceptive pills (no, yes, missing), ever use of hormone replacement therapy (no, yes, missing), age at first menarche (<12 y, ≥12 to ≤15 y, >15 y, missing), age at first pregnancy (<21 y, ≥21 to ≤30 y, >30 y, nulliparous), and menopausal status (premenopausal, postmenopausal, perimenopausal, and surgical postmenopausal). UADT, upper aerodigestive tract; WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research.

the components "body fatness," "physical activity," "plant foods," and "alcohol intake" in women. No change in HRs was observed when individual components of the WCRF/AICR score were excluded alternatively from the overall score or when the "body fatness" and "physical activity" components were simultaneously excluded from the overall score (data not shown in tables).

TABLE 4
HRs (95% CIs) for total cancer and smoking-related and non-smoking-related cancers associated with a 1-point increment in the WCRF/AICR score, by smoking status[1]

	Men			Women		
	No. of cases	HR (95% CI)	*P*-heterogeneity	No. of cases	HR (95% CI)	*P*-heterogeneity
All cancers	13,838	0.95 (0.93, 0.97)	0.261	23,156	0.96 (0.94, 0.97)	0.692
Never smoker	3322	0.99 (0.95, 1.03)		12,662	0.96 (0.94, 0.98)	
Former smoker	5695	0.95 (0.92, 0.98)		5467	0.95 (0.93, 0.98)	
Current smoker	4749	0.93 (0.90, 0.96)		4672	0.95 (0.92, 0.98)	
Smoking-related cancers[2]	6330	0.90 (0.87, 0.93)	0.918	5172	0.91 (0.88, 0.93)	0.170
Never smoker	1010	0.91 (0.84, 0.98)		2365	0.93 (0.89, 0.98)	
Former smoker	2439	0.88 (0.84, 0.93)		1158	0.90 (0.84, 0.95)	
Current smoker	2843	0.91 (0.87, 0.95)		1607	0.89 (0.84, 0.94)	
Non-smoking-related cancers[3]	4039	1.00 (0.97, 1.04)	0.108	10,505	0.94 (0.92, 0.96)	0.845
Never smoker	1312	1.06 (0.99, 1.13)		6088	0.93 (0.91, 0.96)	
Former smoker	1768	1.00 (0.94, 1.05)		2484	0.95 (0.91, 0.99)	
Current smoker	943	0.94 (0.87, 1.01)		1741	0.96 (0.91, 1.01)	

[1] The WCRF/AICR score range was 0–6 in men and 0–7 in women. Analyses were performed by using a Cox regression model stratified by center and age (1-y increments) and adjusted for energy intake (kcal), level of education (none, primary school, technical/professional school, secondary school, university degree, unknown/missing), duration of smoking in former smokers (>20 y ago, 11–20 y ago, ≤10 y ago, unknown/missing), number of cigarettes per day among smokers (1–15 cigarettes/d, 16–25 cigarettes/d, >25 cigarettes/d, pipe or cigar, unknown/missing), and presence of chronic diseases at baseline (no, yes, missing). Models for women were further adjusted for ever use of contraceptive pills (no, yes, missing), ever use of hormone replacement therapy (no, yes, missing), age at first menarche (<12 y, ≥12 to ≤15 y, >15 y, missing), age at first pregnancy (<21 y, ≥21 to ≤30 y, >30 y, nulliparous), and menopausal status (premenopausal, postmenopausal, perimenopausal, and surgical postmenopausal). *P* values for heterogeneity were calculated by modeling interaction terms (cross-products) between smoking status (categorical) and the WCRF/AICR score (continuous). WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research.

[2] Smoking-related cancers included cancers of the lung, bladder, upper aerodigestive tract, kidney, stomach, esophagus, pancreas, liver, and colon (28).

[3] Non-smoking-related cancers included breast and endometrial cancer in women and prostate cancer in men (28).

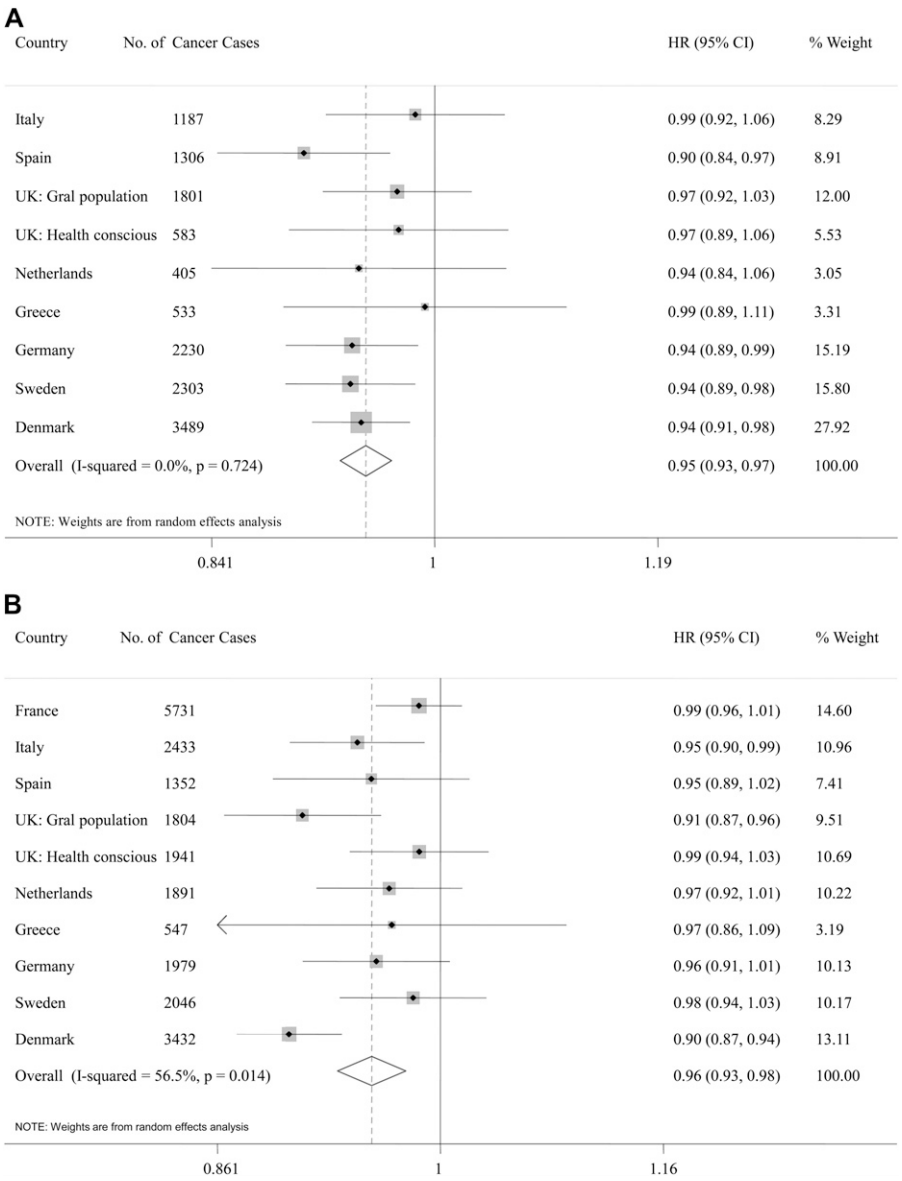

FIGURE 2. HRs (95% CIs) for total cancer associated with a 1-point increment in the WCRF/AICR score (range: 0–6 in men, 0–7 in women) by country in men (A) and women (B). Cox regression models were stratified by center (in countries with more than one center) and age (1-y increments) and adjusted for energy intake (kcal), level of education (none, primary school, technical/professional school, secondary school, university degree, unknown/missing), duration of smoking in former smokers (>20 y ago, 11–20 y ago, ≤10 y ago, unknown/missing), number of cigarettes per day among smokers (1–15 cigarettes, 16–25 cigarettes, >25 cigarettes, pipe or cigar, unknown/missing), and presence of chronic diseases at baseline (no, yes, missing). Models for women were further adjusted for ever use of contraceptive pills (no, yes, missing), ever use of hormone replacement therapy (no, yes, missing), age at first menarche (<12 y, ≥12 to ≤15 y, >15 y, missing), age at first pregnancy (<21 y, ≥21 to ≤30 y, >30 y, nulliparous), and menopausal status (premenopausal, postmenopausal, perimenopausal, and surgical postmenopausal). Gral, general; UK, United Kingdom; WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research.

DISCUSSION

In this European population, individuals with a lifestyle in concordance with the WCRF/AICR recommendations on diet, physical activity, and body fatness for cancer prevention were less likely to develop most types of cancers. Overall, participants within the highest category of the WCRF/AICR score (≥5 points in men and ≥6 points in women) were 18% less likely to develop any cancer compared with those in the first category of the score (≤2 points in men and ≤3 points in women), and there was a significantly lower cancer risk observed even in the second category of the score.

Advantages of the present study include its very large sample size and the large number of incident cancers included, which provided enough power to study the association of the WCRF/AICR score with total cancer as well as specific cancer-type risks and allowed us to perform several sensitivity analyses. Second, we constructed an easily replicable index score that reflected most of the WCRF/AICR recommendations for cancer prevention by using objective cutoffs to operationalize each recommendation and by including intermediate categories to increase the discriminatory power of the score. Participants with higher WCRF/AICR scores were more likely to be nonsmokers,

TABLE 5
Mutually adjusted HRs (95% CIs) for total cancer incidence associated with the components of the WCRF/AICR score[1]

	Men		Women		All	
WCRF/AICR score	HR (95% CI)	*P*-trend	HR (95% CI)	*P*-trend	HR (95% CI)	*P*-trend
Body fatness						
0	1.00 (ref)	0.248	1.00 (ref)	0.002	1.00 (ref)	0.002
0.5	0.92 (0.88, 0.97)		0.95 (0.91, 0.99)		0.94 (0.91, 0.96)	
1	0.95 (0.91, 1.00)		0.93 (0.90, 0.97)		0.94 (0.91, 0.97)	
Physical activity						
0	1.00 (ref)	0.276	1.00 (ref)	0.009	1.00 (ref)	0.004
0.5	0.99 (0.94, 1.03)		0.98 (0.95, 1.01)		0.98 (0.95, 1.01)	
1	0.98 (0.94, 1.02)		0.96 (0.92, 0.99)		0.96 (0.94, 0.99)	
Foods that promote weight gain						
0	1.00 (ref)	0.376	1.00 (ref)	0.829	1.00 (ref)	0.408
0.25	1.02 (0.95, 1.10)		0.98 (0.90, 1.08)		1.00 (0.95, 1.06)	
0.5	1.03 (0.96, 1.11)		1.01 (0.92, 1.11)		1.02 (0.96, 1.08)	
0.75	1.04 (0.96, 1.13)		1.01 (0.91, 1.11)		1.03 (0.96, 1.09)	
1	1.05 (0.92, 1.20)		0.98 (0.87, 1.09)		1.00 (0.93, 1.09)	
Plant foods						
0	1.00 (ref)	<0.0001	1.00 (ref)	0.002	1.00 (ref)	<0.0001
0.25	0.92 (0.85, 1.00)		0.97 (0.92, 1.02)		0.96 (0.92, 1.00)	
0.5	0.91 (0.84, 0.98)		0.96 (0.91, 1.01)		0.94 (0.90, 0.98)	
0.75	0.89 (0.82, 0.96)		0.92 (0.87, 0.97)		0.91 (0.87, 0.95)	
1	0.84 (0.77, 0.92)		0.92 (0.86, 0.98)		0.89 (0.84, 0.94)	
Red and processed meat						
0	1.00 (ref)	0.003	1.00 (ref)	0.458	1.00 (ref)	0.031
0.5	0.98 (0.93, 1.03)		1.00 (0.97, 1.03)		0.99 (0.96, 1.01)	
1	0.85 (0.77, 0.93)		0.98 (0.93, 1.03)		0.94 (0.90, 0.99)	
Alcohol intake						
0	1.00 (ref)	0.009	1.00 (ref)	0.002	1.00 (ref)	<0.0001
0.5	0.94 (0.88, 0.99)		0.94 (0.90, 0.99)		0.94 (0.91, 0.97)	
1	0.94 (0.90, 0.98)		0.94 (0.90, 0.97)		0.94 (0.90, 0.96)	
Breastfeeding						
0			1.00 (ref)	0.145		
0.5			1.02 (0.98, 1.06)			
1			0.98 (0.94, 1.02)			

[1] Analyses were performed by using a Cox regression model stratified by center, age (1-y increments), and sex in the model of both sexes combined and adjusted for energy intake (kcal), level of education (none, primary school, technical/professional school, secondary school, university degree, unknown/missing), smoking status and intensity of smoking (never; former: quit smoking >20 y ago, quit 11–20 y ago, quit ≤10 y ago; smoker: 1–15 cigarettes/d, 16–25 cigarettes/d, >25 cigarettes/d; smoker, pipe or cigar; missing current or former status; unknown/missing), and presence of chronic diseases at baseline (no, yes, missing). Models for women were further adjusted for ever use of contraceptive pills (no, yes, missing), ever use of hormone replacement therapy (no, yes, missing), age at first menarche (<12 y, ≥12 to ≤15 y, >15 y, missing), age at first pregnancy (<21 y, ≥21 to ≤30 y, >30 y, nulliparous), and menopausal status (premenopausal, postmenopausal, perimenopausal, and surgical postmenopausal). All components were mutually adjusted for each other. *P* values for trend were calculated by modeling components of the WCRF/AICR score as continuous variables. ref, reference; WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research.

were more educated, and were generally chronic disease–free, indicating that the score reflected an overall healthy lifestyle. A significant association between the WCRF/AICR score and cancer risk was observed after excluding alternatively each component of the score at a time, even when both physical activity and BMI were excluded, indicating that the combination of all components was responsible of the observed association with cancer risk. In addition, all of the components of the score were significantly associated with cancer risk after mutual adjustment for each other, except for the component "foods that promote weight gain." The lack of association of this component with cancer risk could be explained by the fact that the component "body fatness" was already included in the model, and BMI is likely to be in the etiologic pathway between this recommendation and cancer risk. Finally, an inverse association between the WCRF/AICR score and cancer risk was observed in all countries included in the EPIC study, and for most cancer types.

The main limitation of this study is related to the use of a simple score index based on the sum of several risk factors that are not associated with the risk of developing all cancer types, which may have attenuated the association of the score in cancer-specific analyses. In addition, the inclusion of cancer types that are unrelated to lifestyle factors may dilute the effect of the risk factor–specific analyses. Several other limitations should also be mentioned: EPIC, like many other cohorts, is not a population-based cohort and the consequence of this is that there is a "healthy effect." Therefore, the preventable fraction in the general population is likely to be higher than the one reported here. We could

not include all WCRF/AICR recommendations in our score, because either there were not enough data available or they were not applicable to the objectives of this study; therefore, the WCRF/AICR score constructed by us may underestimate the potential impact of adhering to these recommendations. In addition, some lifestyle factors related to diet, physical activity, and body fatness that have been associated with cancer risk were not included in the score because they were not part of the WCRF/AICR recommendations; for example, abdominal adiposity measurements, such as waist circumference, may be better predictors of some cancer types [eg, colorectal (33) or pancreatic (34)] compared with measurements of general obesity such as BMI. On the other hand, the score incorporates risk factors that are not directly associated with cancer risk, such as "foods that promote weight gain" or "being underweight." Although very standardized and detailed dietary and lifestyle questionnaires were used in the EPIC study, measurement error and misclassification may have biased the estimates toward the null. The multivariate analyses were adjusted for lifestyle factors that were associated with both the score and cancer risk; however, we cannot rule out the possibility of residual confounding associated with exposure measurement errors. No evidence of effect modification by smoking status or BMI was detected, and the association did not change after excluding those with chronic diseases at baseline; nevertheless, a null association between the score and total cancer risk was observed among men who had never smoked. This could either be a chance finding, be due to residual confounding by smoking status, or indicate a stronger protection among those exposed to tobacco smoking, as previously reported (35, 36); nevertheless, we should bear in mind that a large percentage of the cancers among never-smoking men were prostate cancer (a non-smoking-related cancer), which has very weak ties to diet and lifestyle factors, and so could partly explain the lack of association in never smokers with non-smoking-related cancers as well.

In 1981 Doll and Peto (37) estimated that 35% (95% CI: 10%, 70%) of all cancer deaths could be prevented through diet. More recently, the WCRF/AICR estimated that diet, nutrition, physical activity, and body fatness accounted for 26% (95% CI: 6%, 42%) of all cancers (excluding nonmelanoma skin cancer) in the United Kingdom. The corresponding PAF% (95% CI) calculated for the United States, Brazil, and China were 24% (7%, 40%), 19% (3%, 31%), and 20% (5%, 37%) (38). In a previous observational prospective study conducted in women (the Iowa Women's Health Study), it was estimated that the PAF% for not following 6–9 of the 1997 AICR recommendations for cancer prevention was 22% (95% CI: 12%, 30%) (14). Other epidemiologic studies have calculated the PAF% for cancer incidence and/or cancer mortality associated with combinations of several lifestyle factors—ie, diet, physical activity, obesity, and smoking—and observed a PAF% within the 19–60% range (9, 10, 12, 13, 18, 39, 40). In the present study we estimated that lack of adherence to the WCRF/AICR recommendations was associated with a PAF% of 13% (95% CI: 4%, 21%) for total cancer incidence. The corresponding PAF% observed when avoidance of smoking was considered together with the WCRF/AICR recommendations was 23% (95% CI: 14%, 32%; data not shown). These values are somehow lower than previously reported. The main reason for that could be related to the distribution of the exposure in the present population, given that it mostly comprised volunteers participating in the EPIC study and was hence more likely to be healthier than the general population; in addition, the use of an overall score incorporating most WCRF/AICR recommendations for cancer prevention with equal weight given to each recommendation, and the inclusion of all cancer types in the calculation independently of their association with lifestyle factors, may have resulted in a conservative estimate.

The WCRF/AICR score did not predict the risk of cancers of the prostate, ovary, pancreas, and bladder. These null associations are consistent with what was reported in the WCRF/AICR 2007 report (19) as well as what was found in previous studies conducted within EPIC. In EPIC, no clear associations were observed between the risk of prostate cancer and physical activity (41), BMI (42), fiber intake (43), alcohol intake (44), red and processed meat consumption (45), and fruit and vegetable consumption (46). According to the WCRF/AICR 2007 report, there is convincing evidence for an association between body fatness and probably abdominal fatness with pancreatic cancer risk. In EPIC, BMI was not significantly associated with risk of pancreatic cancer, but significant associations were observed for waist circumference and waist-to-hip ratio (34), which are markers of abdominal adiposity that are not directly incorporated as part of the WCRF/AICR score. No significant association between physical activity (34), ethanol intake (47), or fruit and vegetable consumption (48) and pancreatic cancer risk has been observed in EPIC. The WCRF/AICR 2007 report concluded that there is very limited evidence to link any aspect of diet, nutrition, physical activity, and body fatness to risks of either bladder or ovarian cancer. Null results have been mostly reported in EPIC regarding the association of these lifestyle factors and bladder cancer (49, 50) or ovarian cancer risk (51, 52), except for a positive association between obesity (BMI >30) and ovarian cancer risk in postmenopausal women (53).

In conclusion, results of this study suggest that following the WCRF/AICR recommendations on diet, nutrition, physical activity, and weight management for cancer prevention is associated with a lower risk of developing most types of cancer in European populations. More research is needed to elucidate other potential lifestyle risk factors for cancer and how modification of these lifestyle factors could prevent cancer.

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The authors' responsibilities were as follows—TN: is the principal investigator of this project and had primary responsibility for final content; ER: is the overall coordinator of the EPIC study, which was conceptualized, designed, and implemented in collaboration with the main investigators in the collaborating countries; TN and ER: contributed to the study design, subject recruitment, and data collection/acquisition and are also responsible for the ongoing follow-up and management of the EPIC cohort; TN, PHP, CHvG, and ER: conceived the present study; and DR: was responsible of the study design, analyzing the data, interpreting the results, and drafting the manuscript, with close assistance from TN, A-CV, PHP, CHvG, DSMC, PF, and ER, and taking into account the comments and suggestions of the co-authors. All authors contributed to data interpretation and critical reading of the manuscript and have seen and approved the final version of the manuscript. None of the authors declared a conflict of interest.

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