



# The 2018 World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) Score and All-Cause, Cancer, and Cardiovascular Disease Mortality Risk: A Longitudinal Analysis in the NIH-AARP Diet and Health Study

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## ABSTRACT

**Background:** The World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) published Cancer Prevention Recommendations in 2018 focused on modifiable lifestyle factors.

**Objectives:** The aim was to examine how adherence to WCRF/AICR recommendations via the 2018 WCRF/AICR score is associated with risk for all-cause, cancer, and cardiovascular disease (CVD) mortality outcomes among older US adults.

**Methods:** Baseline and follow-up questionnaire data ( $n = 177,410$ ) were used to calculate weight, physical activity, and diet components of the 2018 WCRF/AICR score (0–7 total points). Adjusted HRs and 95% CIs were estimated, stratified by sex and smoking status.

**Results:** There were 16,055 deaths during a mean of 14.2 person-years. Each 1-point score increase was associated with a 9–26% reduced mortality risk for all outcomes, except for current male smokers' cancer mortality risk. When the score was categorized comparing highest (5–7 points) with lowest (0–2 points) scores, associations with reduced all-cause mortality risk were strongest in former smokers ( $HR_{\text{males}}: 0.51$ ; 95% CI: 0.43, 0.61;  $HR_{\text{females}}: 0.38$ ; 95% CI: 0.31, 0.46), followed by current smokers ( $HR_{\text{males}}: 0.55$ ; 95% CI: 0.34, 0.89;  $HR_{\text{females}}: 0.44$ ; 95% CI: 0.32, 0.59) and never smokers ( $HR_{\text{males}}: 0.57$ ; 95% CI: 0.47, 0.70;  $HR_{\text{females}}: 0.50$ ; 95% CI: 0.41, 0.60). An association with cancer mortality risk was also seen in former smokers ( $HR_{\text{males}}: 0.59$ ; 95% CI: 0.43, 0.81;  $HR_{\text{females}}: 0.52$ ; 95% CI: 0.37, 0.73) and female current (95% CI: 0.32, 0.96) and never ( $HR_{\text{females}}: 0.57$ ; 95% CI: 0.40, 0.80) smokers; findings were not statistically significant in other strata. For CVD mortality, highest compared with lowest scores were associated with a 49–73% risk reduction, except in male never and current smokers. In exploratory analysis, physical activity, body weight, alcohol, and plant-based foods were found to be predominant components in the score.

**Conclusions:** Greater 2018 WCRF/AICR scores were associated with lower mortality risk among older adults. Future research can explore how smoking modifies these relations, and further examine different populations and other cancer-relevant outcomes. *Curr Dev Nutr* 2022;6:nzac096.

**Keywords:** cancer prevention, diet, nutrition, weight, obesity, older adults, physical activity, dietary guidelines, index score, adherence score

Published by Oxford University Press on behalf of the American Society for Nutrition 2022. This work is written by (a) US Government employee(s) and is in the public domain in the US.

Manuscript received December 22, 2021. Initial review completed May 7, 2022. Revision accepted May 12, 2022. Published online June 2, 2022.

The authors report no funding received for this work.

Author disclosures: The authors report no conflicts of interest.

Supplemental Figures 1 and 2 and Supplemental Tables 1 and 2 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at <https://academic.oup.com/cdn/>.

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Abbreviations used: AICR, American Institute for Cancer Research; CVD, cardiovascular disease; FFQ, food-frequency questionnaire; ICD-9; *International Classification of Diseases, Ninth Revision*; ICD-10; *International Classification of Diseases, Tenth Revision*; MVPA, moderate-to-vigorous physical activity; NCI, National Cancer Institute; UPF, ultra-processed food; WCRF, World Cancer Research Fund.

## Introduction

Cancer is the second leading cause of death in the United States behind cardiovascular disease (CVD), accounting for approximately 600,000 deaths in 2020 alone (1, 2). An estimated 30–50% of cancer cases are preventable (3), highlighting the importance of promoting healthy, modifiable lifestyle factors to reduce cancer risk and mortality.

The World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) published 10 evidence-based Cancer Prevention Recommendations in 2018 focused on modifiable lifestyle behaviors that impact cancer risk in the *Diet, Nutrition, Physical Activity, and Cancer: A Global Perspective, the WCRF/AICR Third Expert Report* (4, 5). The standardized 2018 WCRF/AICR score operationalizes 8 of the 10 recommendations, including those focused on weight, physical activity, diet, and breastfeeding, and allows researchers to examine how

adherence to the recommendations impacts cancer risk and health outcomes (6, 7). Although many studies to date have examined the independent effects of these lifestyle behaviors with cancer and mortality risk, the 2018 WCRF/AICR score is a standardized, integrated approach intended to examine the combined impact of these lifestyle factors on health outcomes, based on the latest evidence for cancer prevention.

A recent meta-analysis of cohort and case-control studies examined adherence to the 2007 WCRF/AICR Cancer Prevention Recommendations from the Second Expert Report and reported a 10% reduction in mortality in healthy populations (8). No standardized scoring system was developed for the 2007 recommendations, so the studies included in this meta-analysis applied varying scoring systems. Consequently, the heterogeneity in scores developed by individual studies may impact the direct comparison of their findings. The standardized 2018 WCRF/AICR score can both assess adherence to updated Cancer Prevention Recommendations from the WCRF/AICR and enable future analyses to address this limitation of comparability.

Most studies utilizing the 2018 WCRF/AICR score primarily focused on cancer risk. Although a recent study found that higher scores were associated with lower risk of mortality due to pancreatic cancer (9), no studies to date have examined the association between adherence to the updated WCRF/AICR recommendations and risk for overall cancer-related mortality. Additionally, cancer-related mortality is an important endpoint, but healthy lifestyle recommendations also influence mortality risk from CVD—the leading cause of death in the United States—and other noncommunicable diseases. Thus, the main objective of this study was to examine how adherence to the 2018 WCRF/AICR Cancer Prevention Recommendations using the standardized 2018 WCRF/AICR score is associated with risk for all-cause, cancer, and CVD mortality among older adults in the NIH-AARP (formerly known as the American Association of Retired Persons) Diet and Health Study. The independent effects of each individual score component were also explored.

## Methods

### Study population

The NIH-AARP Diet and Health Study was a prospective cohort study designed to investigate the relation between diet and health. Details on participant recruitment for the NIH-AARP Diet and Health Study are provided elsewhere (10). Briefly, AARP members aged 50–71 y who were residents of 1 of 6 states (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) or 2 metropolitan areas (Atlanta, GA, and Detroit, MI) were contacted to participate via mailed questionnaires in 1995–1996. These baseline questionnaires completed by respondents ( $n = 566,398$ ) collected data on demographics, diet, and lifestyle. Additional information was collected via a Risk Factor Questionnaire (1996–1997) and Follow-up Questionnaire (2004), including details on lifestyle and reproductive factors and physical activity, respectively. Participants were followed from baseline through December 2011. The NIH-AARP Diet and Health Study was approved by the Special Studies Institutional Review Board of the National Cancer Institute (NCI), and all participants gave written informed consent by virtue of completing and returning the questionnaire.

Study participants were excluded from this secondary analysis if their questionnaires were completed by proxy ( $n = 15,760$ ), they reported a previous history of cancer ( $n = 112,827$ ) or heart disease ( $n = 83,187$ ), their cancer deaths were not registry-confirmed (i.e., not just from the National Death Index;  $n = 4268$ ), or if they reported extreme total energy intakes ( $n = 3109$ ) (Supplemental Figure 1). Respondents were further excluded if they were missing height and/or weight data to estimate BMI or physical activity data from the 2004 Follow-up Questionnaire ( $n = 155,782$ ); if they were missing covariates ( $n = 12,124$ ); or if they had an extreme BMI or total minutes of moderate-to-vigorous physical activity (MVPA;  $n = 1931$ ). Extreme reports of total energy, BMI, and MVPA were defined as more than 2 IQRs above the 75th percentile or below the 25th percentile on the logarithmic scale. The final analytic cohort included 177,410 participants (Supplemental Figure 1).

### The 2018 WCRF/AICR score

The 2018 WCRF/AICR score was developed to estimate adherence to the 2018 WCRF/AICR Cancer Prevention Recommendations from the Third Expert Report (3). Eight of the recommendations are operationalized as components within the standardized scoring system, as detailed by Shams-White et al. (6, 7) and included in Supplemental Table 1. The components addressed by the score are body weight, physical activity, fruit/vegetables and fiber (referred to together herein as plant-based foods), fast foods [defined by the score and referred to herein as ultra-processed foods (UPFs)], red and processed meat, sugar-sweetened drinks, alcohol, and, optionally, breastfeeding. The breastfeeding component was not included in our analyses due to the lack of breastfeeding data in this cohort study and given that our study question was not limited to a subpopulation of females who have children. Thus, total 2018 WCRF/AICR scores ranged from 0 to 7 points in our analyses, with a higher score indicating greater adherence to the recommendations.

### Body composition

The body-weight component of the score is calculated according to BMI ( $\text{kg}/\text{m}^2$ ) and waist circumference as a combined measure. However, waist circumference data were not available for our included participants and thus the score guidance, to double the point value for BMI, was followed (i.e., instead of 0–0.5 points for BMI, the points were doubled to allow the weight subscore to range from 0 to 1) (6). Participants' self-reported weight (pounds) and height (feet and inches) at baseline were converted to kilograms and meters, respectively, and used to calculate BMI.

### Physical activity

Data on participants' MVPA were collected in the 2004 Follow-up Questionnaire. Fifteen activities listed in the survey were estimated as MVPA based on guidance from the 2011 Compendium of Physical Activities (11); participants reported the average time they spent completing each activity per week (none; 5 min; 10 min; 15 min; 30 min; 1 h; 1 h, 30 min; 2–3 h; 4–6 h; 7–10 h; > 10 h). Time value ranges were re-estimated for our calculations as the mean value of the response option (i.e., 2–3, 4–6, and 7–10 h were assumed to be 2.5, 5, and 8.5 h, respectively); > 10 h was interpreted for our calculations as 10.5 h. To calculate the score's physical activity component, hours per week were converted to minutes per week.

## Dietary intake

Study participants completed the NIH-AARP 124-item food-frequency questionnaire (FFQ) at baseline to assess dietary intake over the past 12 mo. Nutrient and energy estimates were calculated using the USDA Survey Nutrient Database associated with the Continuing Survey for Food Intake by Individuals 1994–1996 and the Nutrition Data System for Research database (University of Minnesota Nutrition Coordinating Center, 2004). These data were used to calculate the dietary components of the 2018 WCRF/AICR score: plant-based foods (total fruits/vegetables excluding fruit juice and starchy vegetables and total fiber), UPFs, red and processed meat, sugar-sweetened drinks, and alcohol (7), as well as total energy intake. The approach and food items included to create the adapted UPF variable are described elsewhere (7).

## Outcomes

Vital status of cohort participants was obtained from 1995–1996 to 31 December 2011 via annual linkage with the US Social Security Administration Death Master File, follow-up searches of the National Death Index for those who correspond to the Social Security Administration Death Master File, cancer registry linkage, and responses to mailings. Cancer-specific mortality was defined using groupings created by the NCI Surveillance Epidemiology and End Results coding system (12). CVD-specific mortality was defined using the *International Classification of Diseases, Ninth* (ICD-9), and *Tenth* (ICD-10) *Revisions* (ICD-9 codes 390–398, 401–404, 410–438, and 440–448; ICD-10 codes I00–I13, I20–I51, and I60–I78) and included deaths from heart diseases, cerebrovascular diseases, atherosclerosis, and other CVDs.

## Statistical analysis

Descriptive statistics were used to examine characteristics of the study population, with means, SDs, and ranges reported unless otherwise indicated. Cox proportional HRs and 95% CIs were estimated for the association between 2018 WCRF/AICR scores and all-cause, cancer, and CVD mortality. We tested the proportional hazards assumption by examining both Schoenfeld residuals and exploring interaction of the score by time for all 18 strata and outcomes. No departures were indicated, except for 2 potential violations of the assumption according to the examination of Schoenfeld residuals. However, upon further exploration of time-stratified models, no meaningful differences by time emerged. All models were stratified by sex and smoking status (never, former, or current smoker at baseline) and person-years was used as the underlying time metric. The 2018 WCRF/AICR score was included in models as both a continuous (i.e., examining risk per 1-point increase) and categorical variable. Score categories were categorized a priori [0–2 (reference), >2 to <5, and 5–7]; sensitivity analyses were performed using cohort-based tertiles. Multivariate models adjusted for covariates measured at baseline: age (years, continuous), race/ethnicity (White, other), marital status (married, other), education (less than high school, high school graduate, some college, college graduate), diabetes (yes/no), menopausal hormone therapy status (females only, yes/no) and total energy intake (kilocalories, continuous).

Additional models were run to explore the independent effects of each individual 2018 WCRF/AICR score component on mortality outcomes (i.e., looking at the impact of each 0.25–0.5-point increase, depending on each component's subscore), while adjusting for the other 6 score components (i.e., subtracted the component being examined

from the total score) and aforementioned covariates. SAS statistical software (version 9.4; SAS Institute, Inc.) was used for all analyses. Statistical tests were 2-sided, with a significance level of 0.05.

## Results

### Study participant characteristics

Among the 177,410 participants included in the current analyses, there were 16,055 deaths reported (9665 males, 6390 females) from 1995–2011 during a mean 14.2 person-years of follow-up (males: 14.1 person-years; females: 14.4 person-years). The absolute mortality rate in males and females were 725 of 100,000 and 537 of 100,000 person-years, respectively. Of these deaths, 5080 (32%) were due to cancer (males:  $n = 3042$ ; 228/100,000 person-years; females:  $n = 2038$ ; 171/100,000 person-years) and 4200 (26%) were due to CVD (males:  $n = 2625$ ; 197/100,000 person-years; females:  $n = 1575$ ; 133/100,000 person-years).

Characteristics of study participants are included in [Table 1](#). Fifty-four percent of participants were male, and the mean age was 61 y at baseline for males and females. Most males were former smokers, while most females were never smokers; a small proportion of participants were current smokers. The majority of participants were White and had at least some college education. Although most males were married (87%), less than half of females were married (48%). Additionally, most females reported at baseline that they either currently or never received hormone replacement therapy. The mean BMI of males and females was overweight (in kg/m<sup>2</sup>; 26.8 and 26.3, respectively), and the median MVPA was high among males and females ([Table 1](#)).

[Table 2](#) includes the total mean 2018 WCRF/AICR scores by sex and scoring proportions by component; the score breakdown is further illustrated in [Supplemental Figure 2](#). Males and females had a mean 2018 WCRF/AICR score of 3.3 and 3.5, respectively. Most participants met or partially met the recommendations for body weight and met the recommendation for physical activity. Additionally, most partially met the recommendations for plant-based foods and alcohol and did not meet the recommendation for sugar-sweetened drinks. More females met or partially met the red and processed meat recommendation compared with males ([Table 2](#)).

### 2018 WCRF/AICR score and all-cause, cancer, and CVD mortality

[Tables 3](#) and [4](#) include univariate and adjusted HRs for all-cause, cancer, and CVD mortality by level of adherence to the 2018 WCRF/AICR score for males and females, respectively. In fully adjusted models, each 1-point increase in the 2018 WCRF/AICR score was associated with a 9–26% reduced risk of mortality for all outcomes, except for current male smokers' risk for all cancers.

When the score was analyzed as a categorical variable with all males and females with the highest scores (5–7) compared with the lowest scores (0–2), associations with reduced all-cause mortality risk ranged from 43% to 62%, depending on smoking status. Associations with risk reduction were strongest among former smokers (males, HR: 0.51; 95% CI: 0.43, 0.61; females, HR: 0.38; 95% CI: 0.31, 0.46), followed by current smokers (males, HR: 0.55; 95% CI: 0.34, 0.89; females, HR: 0.44; 95% CI: 0.32, 0.59) and never smokers (males, HR: 0.57; 95% CI: 0.47, 0.70;

**TABLE 1** Distribution of selected baseline characteristics of participants in the NIH-AARP Diet and Health Study<sup>1</sup>

	Males	Females
Sample size, n (%)	94,854 (53.5)	82,556 (46.5)
Age, mean (SD), range, y	61.2 (5.4), 50.3–71.5	61.3 (5.4), 50.3–71.5
Smoking, n (%)		
Never	34,381 (36.3)	40,520 (49.1)
Former	52,642 (55.5)	32,600 (39.5)
Current	7831 (8.3)	9436 (11.4)
Race, n (%)		
White	89,462 (94.3)	76,252 (92.4)
Other	5392 (5.7)	6304 (7.6)
Education, n (%)		
Less than high school	14,963 (15.8)	22,396 (27.1)
High school graduate	8121 (8.6)	8727 (10.6)
Some college	19,950 (21.0)	21,143 (25.6)
College graduate	51,820 (55.6)	30,290 (36.7)
Marital status, n (%)		
Married	82,456 (86.9)	39,319 (47.6)
Other	12,398 (13.1)	43,237 (52.4)
Menopausal hormone therapy, n (%)		
Never	—	35,397 (42.9)
Former	—	7148 (8.7)
Current	—	40,011 (48.5)
History of diabetes, n (%)	5625 (5.9)	3485 (4.2)
BMI, mean (SD), range, kg/m <sup>2</sup>	26.8 (3.7), 17.3–40.8	26.3 (5.1), 13.8–47.8
Total moderate-vigorous physical activity, median, range, min/wk	570.0, 0.0–4920.0	455.0, 0.0–5250.0
Total kcal/d, median, range	1883.1, 428.0–6231.3	1452.3, 319.8–4761.5

<sup>1</sup>n = 177,410.

females, HR: 0.50; 95% CI: 0.41, 0.60). Similarly, the highest WCRF/AICR scores compared with the lowest scores were associated with a reduced risk of cancer mortality for former smokers (males, HR: 0.59; 95% CI: 0.43, 0.81; females, HR: 0.52; 95% CI: 0.37, 0.73), female current smokers (HR: 0.55; 95% CI: 0.32, 0.96), and female never smokers (HR: 0.57; 95% CI: 0.40, 0.80); the association was not seen among male never and current smokers (Tables 3 and 4). For CVD mortality, the highest WCRF/AICR scores compared with the lowest scores were associated with a 49–73% reduction in risk for both males and females depending on smoking status, except for male current smokers (HR: 0.44; 95% CI: 0.16, 1.21).

When the 2018 WCRF/AICR scores were categorized based on cohort-based tertiles (Supplemental Table 2), the highest scores (4–7) were associated with significant reductions in risk compared with the lowest scores (0 to <3) for males and females across smoking statuses (HR range: 0.54–0.86), except for all current smokers' risks for cancer mortality and male current smokers' risk for CVD mortality.

The HRs and 95% CIs for the association between 2018 WCRF/AICR score components and mortality outcomes are included in Table 5. Greater adherence to the physical activity recommendation was associated with the largest reduction in all mortality outcomes except in male former smokers, ranging from a 26% to 70% risk reduction across sex and smoking status groups. Greater adherence to the body-weight recommendation was associated with a 16–48% risk reduction across outcomes and groups except among current smokers. Greater adherence to the alcohol recommendation was also associated with a 14–46% reduced mortality risk for all outcomes in male current

smokers, all-cause and cancer mortality in former male smokers, and cancer mortality in female current smokers. Additionally, greater adherence to the plant-based foods recommendation was significantly associated with an 18–32% reduced risk for all-cause mortality in current smokers and male former smokers, as well as cancer mortality in male former smokers and female current smokers. A few components were associated with increased mortality risk in some strata, including fast foods and sugar-sweetened drinks (Table 5).

## Discussion

The current study examined the association between the 2018 WCRF/AICR score and risk for all-cause, cancer, and CVD mortality among older adults. Every 1-unit increase in the 2018 WCRF/AICR score was associated with a reduced risk for all-cause, cancer, and CVD mortality among males and females across smoking statuses, except for cancer mortality among male current smokers. When the score was categorized and highest (5–7) and lowest scores (0–2) were compared, most associations for all-cause and cancer mortality were strongest in former and current smokers; associations for CVD mortality were strongest in former and never smokers. There were no significant associations with cancer and CVD mortality risk in male current smokers, nor with cancer mortality risk in male never smokers.

The study's findings support the importance of the multiple 2018 WCRF/AICR recommendations together not only for cancer risk but also mortality outcomes. The associations with reduction in risk were



**TABLE 2** Participant adherence to the 2018 WCRF/AICR score: total score and by component<sup>1</sup>

	Males (n = 94,854)	Females (n = 82,556)
Total 2018 WCRF/AICR score, mean (SD), range	3.3 (0.9), 0.0–7.0	3.5 (1.0), 0.0–7.0
By component, n (%)		
Body weight		
Met	30,633 (32.3)	38,106 (46.2)
Partially met	46,957 (49.5)	26,676 (32.3)
Did not meet	17,264 (18.2)	17,774 (21.5)
Physical activity		
Met	85,007 (89.6)	70,808 (85.8)
Partially met	5294 (5.6)	6174 (7.5)
Did not meet	4553 (4.8)	5574 (6.8)
Plant-based foods		
Met	11,275 (11.9)	6571 (8.0)
Partially met	65,656 (69.2)	59,661 (72.3)
Did not meet	17,923 (18.9)	16,324 (19.8)
Fast foods <sup>2</sup>		
Met	32,063 (33.8)	27,073 (32.8)
Partially met	32,270 (34.0)	26,867 (32.5)
Did not meet	30,521 (32.2)	28,616 (34.6)
Red and processed meat		
Met	7036 (7.4)	16,912 (20.5)
Partially met	28,051 (29.6)	37,589 (45.5)
Did not meet	59,767 (63.0)	28,055 (34.0)
Sugar-sweetened drinks		
Met	526 (0.6)	699 (0.9)
Partially met	25,854 (27.3)	30,943 (37.5)
Did not meet	68,474 (72.2)	50,914 (61.7)
Alcohol		
Met	4241 (4.5)	6416 (7.8)
Partially met	69,659 (73.4)	61,488 (74.5)
Did not meet	20,954 (22.1)	14,652 (17.8)

<sup>1</sup>n = 177,410. Met = 1 point; Partially met = 0.5 points; Did not meet = 0 point. AICR, American Institute for Cancer Research, WCRF, World Cancer Research Fund.

<sup>2</sup>Fast-food categories were defined by total participant tertiles as % of total kilocalories from ultra-processed foods. Met: 0.0% to <32.5% total kcal; Partially met: 32.5% to <42.1% total kcal; Did not meet: 42.1–90.9% total kcal.

generally greater among former and current smokers compared with never smokers, although associations were stronger in female never smokers compared with current smokers for CVD mortality. The lack of association for cancer and CVD mortality risk observed in male current smokers when comparing the highest with the lowest scores may reflect the impact of smoking on mortality risk. As the leading preventable cause of death in the United States (13), tobacco smoking is the strongest modifiable risk factor for 17 types of cancers and various chronic disease mortality outcomes (14, 15). However, the associations with reduced CVD mortality risk were statistically significant for male current smokers when scores were examined on a continuous scale. The lack of association may thus also be due to score categorization in this study impacting the statistical power of the analysis, given the limited number of smokers—approximately 8% and 11% of males and females, respectively—and the limited number of participants with scores in the highest category (5–7), 4% of males and less than 9% of females.

To the best of our knowledge, no other studies to date have examined the association between the 2018 WCRF/AICR score and all-cause, cancer, or CVD mortality. One recently published study by Zhang et al. (9) examined the association between adherence to the 2018 WCRF/AICR score and pancreatic cancer mortality in the Prostate, Lung, Cancer, and

Ovarian (PLCO) Cancer Screening Trial (n = 95,962) using all 8 scoring components (i.e., including the breastfeeding component). They reported 307 pancreatic cancer deaths over a mean 13-y follow-up and found that every 1-unit increase in the score was associated with a 12% decrease in mortality risk (HR: 0.88; 95% CI: 0.78, 0.99) (9). Although cancer-specific, this is similar to the score's associations with 9–14% reduced risk in females and the 9–13% reduced risk in male never and former smokers for overall cancer mortality.

Past studies in NIH-AARP also found protective effects of weight, physical activity, and diet in association with mortality outcomes when behaviors were examined individually (16–18) and when some were combined in models (19) or other dietary or lifestyle indices (20–26). Although other dietary and lifestyle scores are utilized in research, each was developed based on different guiding principles and interpretation of the scientific evidence. The 2018 WCRF/AICR score provides a unique approach to study alignment with the 2018 WCRF/AICR Cancer Prevention Recommendations, examining an integrated pattern of behaviors relating to weight, physical activity, diet, and other factors in a standardized way to allow for comparison across other cohorts.

Previous studies examining adherence to 2007 recommendations and mortality outcomes overall found higher scores were similarly

**TABLE 3** HRs (95% CIs) for mortality by level of adherence to the 2018 WCRF/AICR score (0–7 points) in males by smoking status<sup>1</sup>

	Cases/person-years	Model <sup>2</sup>	Continuous	2018 WCRF/AICR score a priori categories		
			HR (95% CI)	0–2 (n = 9385)	> 2 to <5 (n = 81,578)	5–7 (n = 3891)
All-cause						
Never smoker	2449/487,023	Univariate	0.88 (0.84–0.92)	1.00 (Ref)	0.61 (0.54–0.69)	0.64 (0.52–0.78)
		Multivariate	0.85 (0.81–0.89)	1.00 (Ref)	0.58 (0.52–0.66)	0.57 (0.46–0.70)
Former smoker	623/738,947	Univariate	0.84 (0.82–0.87)	1.00 (Ref)	0.68 (0.63–0.73)	0.58 (0.49–0.69)
		Multivariate	0.81 (0.78–0.83)	1.00 (Ref)	0.64 (0.59–0.69)	0.51 (0.43–0.61)
Current smoker	1593/107,224	Univariate	0.92 (0.86–0.97)	1.00 (Ref)	0.79 (0.69–0.90)	0.62 (0.38–1.00)
		Multivariate	0.82 (0.83–0.93)	1.00 (Ref)	0.74 (0.65–0.85)	0.55 (0.34–0.89)
All cancers						
Never smoker	677/487,023	Univariate	0.93 (0.86–1.01)	1.00 (Ref)	0.82 (0.63–1.05)	0.90 (0.62–1.33)
		Multivariate	0.91 (0.84–0.99)	1.00 (Ref)	0.78 (0.60–1.000)	0.84 (0.57–1.24)
Former smoker	1767/107,224	Univariate	0.90 (0.85–0.95)	1.00 (Ref)	0.78 (0.68–0.90)	0.65 (0.47–0.88)
		Multivariate	0.87 (0.82–0.92)	1.00 (Ref)	0.74 (0.64–0.85)	0.59 (0.43–0.81)
Current smoker	598/7831	Univariate	1.05 (0.95–1.16)	1.00 (Ref)	1.07 (0.84–1.36)	0.84 (0.39–1.81)
		Multivariate	1.02 (0.93–1.13)	1.00 (Ref)	1.02 (0.80–1.30)	0.81 (0.37–1.76)
CVD						
Never smoker	745/487,023	Univariate	0.88 (0.81–0.95)	1.00 (Ref)	0.55 (0.45–0.67)	0.59 (0.42–0.84)
		Multivariate	0.84 (0.77–0.91)	1.00 (Ref)	0.51 (0.41–0.63)	0.51 (0.35–0.73)
Former smoker	1500/738,947	Univariate	0.83 (0.79–0.88)	1.00 (Ref)	0.70 (0.61–0.82)	0.56 (0.40–0.79)
		Multivariate	0.79 (0.75–0.84)	1.00 (Ref)	0.66 (0.57–0.76)	0.48 (0.34–0.68)
Current smoker	380/107,224	Univariate	0.86 (0.75–0.97)	1.00 (Ref)	0.71 (0.54–0.93)	0.53 (0.19–1.44)
		Multivariate	0.81 (0.71–0.92)	1.00 (Ref)	0.67 (0.51–0.87)	0.44 (0.16–1.21)

<sup>1</sup>n = 94,854. Attained person-years as the underlying time metric. The total and mean follow-up time for males was 1,333,194 person-years and 14.1 person-years, respectively. AICR, American Institute for Cancer Research, CVD, cardiovascular disease; Ref, reference; WCRF, World Cancer Research Fund.

<sup>2</sup>Multivariate model adjusted for age, race/ethnicity (White, other), marital status (married, other), education (less than high school, high school graduate, some college, college graduate), total energy (continuous), and diabetes (yes/no).

associated with a reduced risk of all-cause mortality in the general population (27–29) and among cancer survivors (30, 31). Findings were mixed for cancer mortality: 4 studies found a significant reduction in cancer mortality (27–29, 31), whereas 1 study among cancer survivors did not find a statistically significant association (30). For those who examined scores in relation to CVD mortality (28–30), only 1 study (29) reported a statistically significant reduction in risk. However, as previously mentioned, the results of adherence scores are not directly comparable given the variations in the scoring approaches that were derived for the 2007 recommendations. Furthermore, the 2007 and 2018 Cancer Prevention Recommendations also slightly differ, which limits comparability of earlier studies with our findings. Future studies are needed in diverse populations to further assess how adherence, assessed by the standardized 2018 WCRF/AICR score, may impact mortality risk.

### By-component analysis

The score is intended to examine the combined impact of adherence to the recommendations on outcomes of interest; however, in an effort to examine the contribution of individual components, we explored the associations between individual components and mortality risk through a by-component analysis. The physical activity component of the 2018 WCRF/AICR score had the strongest inverse associations with mortality risk across all outcomes and smoking statuses except for male former smokers. This aligns with substantial evidence supporting the importance of physical activity in reducing mortality risk (4, 32–34). Body weight was also a significant score compo-

nent for all except current smokers. The lack of association in current smokers may be explained by the association often seen between current smoking status and lower BMI (35, 36). Meeting the alcohol recommendation was associated with reduced risk of mortality in male former and current smokers, and cancer mortality in female current smokers. Some components were counterintuitively associated with an increased mortality risk in males, including adhering to recommendations for (i.e., reducing the intake of) fast foods and sugar-sweetened drinks. However, it is important to keep in mind that this was an exploratory aim and that the score is not intended to be taken apart and examined by component but rather assessed as a whole. It may be that there is synergy or redundancy between components, particularly with body-weight, fast-food, and sugar-sweetened drink components, given that the latter 2 are cancer-prevention recommendations due to their sources of excess calories and contributions to obesity. Additionally, the exploratory associations seen here should not be interpreted as drivers of the score overall, but rather provide context for this specific population. It is valuable to examine whether benefits of adherence are observable in the context of overall high health status as was seen in this older, relatively healthy population. However, different associations may be seen in other populations with different health behavior profiles, age distributions, and/or health conditions. Additionally, the standardized 2018 WCRF/AICR score weights each component equally; the current findings can inform hypotheses for future methodological work examining how weighting the score components may impact associations with mortality risk and provide context for future score revisions.

**TABLE 4** HRs (95% CIs) for mortality by level of adherence to the 2018 WCRF/AICR score (0–7 points) in females by smoking status<sup>1</sup>

	Cases/person-years	Model <sup>2</sup>	Continuous	2018 WCRF/AICR score a priori categories		
			HR (95% CI)	0–2 (n = 6738)	> 2 to <5 (n = 68,569)	5–7 (n = 7249)
All-cause						
Never smoker	2378/588,883	Univariate	0.82 (0.79–0.86)	1.00 (Ref)	0.57 (0.51–0.65)	0.50 (0.42–0.60)
		Multivariate	0.82 (0.79–0.85)	1.00 (Ref)	0.59 (0.52–0.67)	0.50 (0.41–0.60)
Former smoker	2519/467,396	Univariate	0.78 (0.75–0.81)	1.00 (Ref)	0.54 (0.48–0.60)	0.36 (0.30–0.44)
		Multivariate	0.78 (0.75–0.81)	1.00 (Ref)	0.56 (0.50–0.63)	0.38 (0.31–0.46)
Current smoker	1493/132,689	Univariate	0.81 (0.77–0.86)	1.00 (Ref)	0.65 (0.57–0.75)	0.51 (0.38–0.69)
		Multivariate	0.78 (0.74–0.82)	1.00 (Ref)	0.62 (0.54–0.71)	0.44 (0.32–0.59)
All cancers						
Never smoker	723/588,883	Univariate	0.88 (0.82–0.95)	1.00 (Ref)	0.70 (0.55–0.90)	0.61 (0.44–0.86)
		Multivariate	0.86 (0.80–0.93)	1.00 (Ref)	0.70 (0.54–0.789)	0.57 (0.40–0.80)
Former smoker	801/467,396	Univariate	0.85 (0.79–0.91)	1.00 (Ref)	0.64 (0.51–0.79)	0.51 (0.37–0.72)
		Multivariate	0.85 (0.79–0.91)	1.00 (Ref)	0.65 (0.52–0.81)	0.52 (0.37–0.73)
Current smoker	514/132,689	Univariate	0.93 (0.85–1.02)	1.00 (Ref)	0.85 (0.66–1.11)	0.61 (0.36–1.06)
		Multivariate	0.91 (0.83–0.998)	1.00 (Ref)	0.83 (0.64–1.07)	0.55 (0.32–0.96)
CVD						
Never smoker	649/588,883	Univariate	0.79 (0.73–0.85)	1.00 (Ref)	0.50 (0.42–0.61)	0.37 (0.27–0.50)
		Multivariate	0.79 (0.73–0.86)	1.00 (Ref)	0.57 (0.45–0.72)	0.43 (0.30–0.61)
Former smoker	610/467,396	Univariate	0.73 (0.67–0.79)	1.00 (Ref)	0.53 (0.42–0.66)	0.26 (0.17–0.40)
		Multivariate	0.74 (0.68–0.80)	1.00 (Ref)	0.55 (0.44–0.70)	0.27 (0.17–0.42)
Current smoker	316/132,689	Univariate	0.80 (0.71–0.90)	1.00 (Ref)	0.58 (0.44–0.78)	0.59 (0.32–1.07)
		Multivariate	0.76 (0.67–0.85)	1.00 (Ref)	0.54 (0.40–0.73)	0.47 (0.26–0.86)

<sup>1</sup>n = 82,556. Attained person-years as the underlying time metric. The total and mean follow-up time for females was 1,188,968 person-years and 14.4 person-years, respectively. AICR, American Institute for Cancer Research, CVD, cardiovascular disease; Ref, reference; WCRF, World Cancer Research Fund.

<sup>2</sup>Multivariate model adjusted for age, race/ethnicity (White, other), marital status (married, other), education (less than high school, high school graduate, some college, college graduate), total energy (continuous), hormone replacement therapy (never, former, current), and diabetes (yes/no).

### Tertiles

Given that studies that utilize diet-based scores and indexes often create data-driven categories, we also conducted a sensitivity analysis to examine the impact of changing from a priori decisions to subjective tertiles. Overall reductions in mortality risk were similarly observed when comparing the highest scores (4–7) with the lowest scores (0 to <3), although the reductions in risk overall were weaker than the a priori category-based findings. In addition to the known limitations to categorization, including loss of statistical power, this data-driven approach to create categories led to wide highest and lowest score tertile ranges and a very narrow middle tertile range, thereby limiting the interpretability of resulting comparisons (37). Notably, given that tertiles may greatly vary between study populations, we believe it is best to use the continuous WCRF/AICR scores and a priori categories presented; we encourage a similar approach in future studies to aid comparability of findings.

### Strengths and limitations

A key strength of this secondary analysis was that it was conducted in a prospective, longitudinal cohort with a follow-up of over 16 y. We also used the standardized scoring system, providing an opportunity for comparison with findings of future studies utilizing the 2018 WCRF/AICR score. Additionally, we examined mortality outcomes with the score as a continuous variable and a priori categories, as well as with cohort-based tertiles. The former will further aid in comparisons of findings across future studies utilizing the score.

One limitation of our analysis was the use of self-reported data, including self-reported height and weight. Physical activity was estimated

based on a summary of self-reported MVPA/week rather than examining daily bouts, and diet was collected via an FFQ representing diet over a 12-mo period. Key limitations of self-reported data include recall bias and measurement error, both of which may lead to misclassification. Included measures were also each collected at 1 time point and assumed to be consistent over time for this analysis, which may have also led to potential measurement error and misclassification of these variables; for both of these caveats, it is likely that the true effect size would be underestimated. There is also the potential for survivorship bias, given that adults had to be at least 50 y of age to be included in the cohort study (i.e., adults who died before they were 50 were not included) and adults with a previous history of cancer or heart disease were excluded from this analysis. Results may thus not be generalizable to younger adults, cancer survivors, or those with pre-existing cardiovascular conditions. This study also had an unequal distribution of participants by smoking status, with the smallest group being current smokers, and across categories of subscores, with most participants meeting the physical activity recommendation and partially meeting the alcohol recommendation. The cohort's large sample size still provided a relatively large number of participants in smaller categories, but the present distributions highlight the importance of examining the association between the 2018 WCRF/AICR score and mortality outcomes in more diverse populations. Additionally, all components of the standardized scoring system are weighted equally, although there are multiple dietary components in the score and our exploratory findings suggest some components like physical activity and weight may be the predominant components associated with mortality risk in this specific population. How-

**TABLE 5** HRs (95% CIs) for the 7 components of the 2018 WCRF/AICR score (0–7 points) and mortality outcomes by sex and smoking status<sup>1</sup>

	Smoking status					
	Males (n = 94,854)			Females (n = 82,556)		
	Never (n = 34,381)	Former (n = 52,642)	Current (n = 7831)	Never (n = 40,520)	Former (n = 32,600)	Current (n = 9436)
<b>All-cause mortality</b>						
Body weight	0.74 (0.66–0.83)	0.76 (0.70–0.82)	1.06 (0.92–1.22)	0.69 (0.62–0.76)	0.77 (0.69–0.85)	0.91 (0.79–1.04)
Physical activity	0.34 (0.30–0.39)	0.39 (0.36–0.42)	0.43 (0.38–0.49)	0.36 (0.32–0.41)	0.37 (0.33–0.41)	0.37 (0.33–0.42)
Plant-based foods	0.93 (0.80–1.09)	0.78 (0.71–0.87)	0.78 (0.65–0.94)	1.02 (0.87–1.21)	0.87 (0.74–1.02)	0.68 (0.56–0.82)
Fast foods	1.12 (1.01–1.24)	1.03 (0.97–1.10)	1.08 (0.96–1.21)	1.12 (1.01–1.23)	0.98 (0.89–1.08)	1.04 (0.92–1.18)
Red and processed meat	1.15 (1.01–1.32)	0.87 (0.79–0.96)	1.03 (0.84–1.27)	1.01 (0.89–1.15)	0.94 (0.83–1.06)	0.90 (0.76–1.06)
Sugar-sweetened drinks	1.00 (0.83–1.19)	1.22 (1.09–1.36)	1.35 (1.11–1.65)	0.89 (0.75–1.05)	0.93 (0.80–1.09)	1.02 (0.83–1.24)
Alcohol	1.06 (0.88–1.28)	0.86 (0.77–0.96)	0.75 (0.62–0.92)	1.34 (1.12–1.62)	1.12 (0.96–1.32)	0.86 (0.71–1.05)
<b>Cancer mortality</b>						
Body weight	0.72 (0.58–0.90)	0.84 (0.73–0.96)	1.14 (0.90–1.44)	0.68 (0.56–0.82)	0.75 (0.63–0.90)	1.04 (0.82–1.31)
Physical activity	0.74 (0.55–0.99)	0.84 (0.70–1.00)	0.70 (0.54–0.90)	0.66 (0.52–0.85)	0.71 (0.57–0.88)	0.55 (0.44–0.70)
Plant-based foods	0.98 (0.73–1.33)	0.75 (0.63–0.89)	0.79 (0.59–1.06)	0.99 (0.73–1.34)	0.94 (0.71–1.25)	0.62 (0.45–0.87)
Fast foods	1.01 (0.83–1.21)	0.78 (0.65–0.93)	1.26 (0.90–1.75)	0.91 (0.72–1.14)	0.89 (0.72–1.10)	1.32 (1.07–1.63)
Red and processed meat	0.95 (0.74–1.24)	0.83 (0.73–0.94)	1.09 (0.83–1.43)	0.92 (0.76–1.11)	0.90 (0.75–1.07)	0.95 (0.72–1.26)
Sugar-sweetened drinks	1.21 (0.87–1.68)	1.35 (1.11–1.64)	1.65 (1.20–2.26)	0.80 (0.59–1.08)	0.99 (0.75–1.31)	1.09 (0.77–1.54)
Alcohol	0.93 (0.65–1.33)	0.81 (0.66–0.98)	0.72 (0.52–0.996)	1.40 (1.00–1.95)	1.04 (0.79–1.38)	0.72 (0.51–0.997)
<b>CVD mortality</b>						
Body weight	0.56 (0.46–0.69)	0.52 (0.45–0.61)	0.90 (0.67–1.21)	0.71 (0.58–0.87)	0.63 (0.51–0.78)	0.82 (0.61–1.11)
Physical activity	0.32 (0.26–0.39)	0.39 (0.34–0.46)	0.39 (0.30–0.51)	0.34 (0.28–0.42)	0.30 (0.24–0.36)	0.35 (0.26–0.45)
Plant-based foods	1.06 (0.80–1.41)	0.95 (0.79–1.16)	0.72 (0.50–1.05)	0.94 (0.68–1.29)	0.84 (0.61–1.16)	0.82 (0.53–1.27)
Fast foods	1.19 (1.00–1.42)	1.19 (1.05–1.35)	1.30 (1.01–1.67)	1.11 (0.91–1.34)	1.01 (0.83–1.23)	0.98 (0.75–1.29)
Red and processed meat	1.27 (1.00–1.61)	0.90 (0.75–1.08)	1.03 (0.67–1.58)	0.86 (0.68–1.09)	1.13 (0.88–1.45)	0.86 (0.60–1.23)
Sugar-sweetened drinks	0.88 (0.64–1.22)	1.08 (0.88–1.34)	0.93 (0.61–1.42)	1.04 (0.76–1.42)	1.07 (0.77–1.46)	0.94 (0.60–1.46)
Alcohol	1.39 (0.99–1.96)	0.85 (0.69–1.05)	0.54 (0.36–0.82)	1.30 (0.92–1.85)	1.00 (0.72–1.38)	1.02 (0.66–1.56)

<sup>1</sup>n = 177,410. Attained person-years as the underlying time metric; the mean follow-up time for all participants was 14.2 y. Components are examined on a continuous scale (i.e., per 0.25- or 0.5-point increase depending on the component); multivariate models adjusted for age, race/ethnicity (White, other), marital status (married, other), education (less than high school, high school graduate, some college, college graduate), total energy (continuous), hormone replacement therapy (females only: never, former, current), diabetes (yes/no), and the other 6 score components (i.e., subtracting the component being examined from the total score) and aforementioned covariates. AICR, American Institute for Cancer Research; CVD, cardiovascular disease; WCRF, World Cancer Research Fund.



ever, the emphasis of these components may differ by population and not based on a single cohort, and the evidence currently supports the included recommendations for cancer prevention; reweighting the score or removing components cannot be justified at this time. Rather than being a data-driven exercise in each cohort, future studies are needed to examine weighting in multiple cohorts to inform the feasibility of an altered and/or weighted scoring approach. Last, although categorized scores may be more interpretable than continuous score results, they may lead to a loss of power and interpretation. For example, the cut-offs may unfairly penalize or reward those near the cutoff bounds. Our research team is pursuing future methodological work to examine implications of reweighting between and within components, implementing stricter cutoffs, and using discrete versus continuous scoring within the middle category. We encourage researchers to pursue similar exploratory work in other cohorts. It is through continued scientific and methodological research examining the relation between the score and health outcomes that our understanding will evolve on how to optimally assess and integrate these lifestyle behaviors for disease prevention.

## Conclusions

This study found that greater adherence to the 2018 WCRF/AICR Cancer Prevention Recommendations, as operationalized in the 2018 WCRF/AICR score, was associated with a reduced risk of all-cause, cancer-specific, and CVD mortality among older adults. These findings highlight the importance of considering multiple lifestyle factors together in reducing mortality risk. Although there were mixed findings in subgroups such as male current smokers, the sample size of current smokers was limited; further research is needed to further explore how smoking modifies these relations. Future work is also needed to examine the influence of the individual score components and the impact of weighted components, in other populations and with other cancer-relevant outcomes, to inform whether future updates are needed to the score.

## Acknowledgments

The authors' responsibilities were as follows—MMS-W, NTB, PM, and JR: designed the research; MMS-W, LLK, and JR: analyzed data; MMS-W and JR: wrote the manuscript; MMS-W: had primary responsibility for final content; and all authors: read and approved the final manuscript.

## Data Availability

Data described in the manuscript, code book, and analytic code will be made available upon request pending study proposal approval from the NIH-AARP Diet and Health Study Steering Committee. Further details are provided at <https://www.nihaarpstars.com/>.

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