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Adherence to Diet and Physical Activity Cancer Prevention Guidelines and Cancer Outcomes: A Systematic Review

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Abstract

Many studies have reported that adherence to health promotion guidelines for diet, physical activity, and maintenance of healthy body weight may decrease cancer incidence and mortality. A systematic review was performed to examine associations between adherence to established cancer prevention guidelines for diet and physical activity and overall cancer incidence and mortality. PubMed, Google Scholar, and Cochrane Reviews databases were searched following the current recommendations of Preferred Reporting Items for Systematic Reviews and Meta-analysis Approach (PRISMA). Twelve studies met inclusion criteria for this review. High versus low adherence to established nutrition and physical activity cancer prevention guidelines was consistently and significantly associated with decreases of 10% to 61% in overall cancer colorectal cancer incidence in both men and women (27%-52%). Consistent significant reductions were also shown for breast cancer incidence (19-60%), endometrial cancer incidence (23-60%), and colorectal cancer incidence in both men and women (35-52%). Findings for lung cancer incidence were equivocal and no significant relationships were found between adherence and ovarian or prostate cancers. Adhering to cancer prevention guidelines for diet and physical activity is consistently associated with lower risks of overall cancer incidence and mortality, including for some site-specific cancers.

Keywords

adherence; cancer incidence; cancer prevention guidelines; diet; physical activity

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Introduction

An estimated 1,685,210 new cancer diagnoses and 595,690 cancer deaths are expected in the United States (U.S.) in 2016 (1). Behaviors such as poor diet choices, physical inactivity, excess alcohol consumption and unhealthy body weight could account for more than 20% of cancer cases and therefore be prevented with lifestyle modifications (1). Two-thirds of U.S. cancer deaths can also be attributed to these modifiable behaviors when including exposure to tobacco products (2-6).

To help guide individuals and communities toward healthier lifestyles, nutrition and physical activity guidelines for cancer prevention have been designed by the U.S. Department of Health and Human Services along with leading health organizations such as the American Cancer Society (ACS) (7) and the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) (8). These cancer prevention and health promotion guidelines focus on specific lifestyle recommendations to 1) achieve and maintain a healthy weight throughout life; 2) adopt a physically active lifestyle; 3) consume a healthy diet with an emphasis on plant-based foods; and 4) limit alcohol consumption (2).

Often epidemiological studies attempt to parse out specific, individual risk factors; however, examination of an overall risk pattern also provides key information when considering health-related behaviors which often co-occur (9). For example, a general risk profile pattern can be ascertained by measuring adherence to cancer prevention guidelines. A score can be constructed based on multiple lifestyle aspects including body mass index (BMI), physical activity, alcohol intake, and various aspects of a healthy diet such as intake of fruit and vegetables, whole grains, and red/processed meat. Utilization of such an adherence score would allow for investigation of overall behavior patterns.

The ACS and WCRF/AICR examine the most current, evidence-based research on diet, physical activity, and cancer risk from laboratory experiments, human studies, and comprehensive reviews, and then publish cancer prevention recommendations for individuals and community action. The most recent update from the ACS Nutrition and Physical Activity Guidelines Advisory Committee was published in 2012 (2). The ACS guidelines contain specific strategies to adhere to the aforementioned recommendations. Similarly, WCRF/AICR guidelines focus on improving modifiable risk profiles, with the most recently-published recommendations for healthy lifestyles in 2007 (4). These recommendations also proffer guidelines for remaining as lean as possible within the normal range of body weight, being physically active as a part of everyday life, eating mostly plant foods, limiting intake of red meat and avoiding processed meat, limiting consumption of alcohol, limiting consumption of energy dense foods, avoiding sugary drinks, and limiting salt consumption.

The aim of the systematic review was to synthesize the evidence from prospective cohort studies regarding adherence to the ACS and WCRF/AICR nutrition and physical activity cancer prevention guidelines and the risk of overall cancer incidence and/or cancer mortality.

Methods and Materials

Search Strategy and Identification of Studies

Two independent authors (LNK, DOG) executed the following comprehensive search strategy following the current recommendations of Preferred Reporting Items for Systematic Reviews and Meta-analysis Approach (PRISMA) (10). Key search terms were used to maximize the identification of prospective cohort studies that examined associations between adherence to nutrition and physical activity cancer prevention guidelines and cancer incidence and mortality. Databases were searched in March 2016, using the following search parameters: PubMed key terms “cancer prevention guidelines”, “nutrition,” physical activity,” “adherence,” “cancer incidence and/or cancer mortality”; Google Scholar search “cancer prevention guideline adherence AND nutrition AND physical activity AND cancer incidence” with the exact phrase “cancer prevention guidelines” and at least one of the words “incidence mortality”; and Cochrane reviews strategy “adherence to nutrition physical activity cancer prevention guidelines”. Filters included human studies in English only, articles that had full text available; and papers published within the past ten years. All eligible full-text articles selected for inclusion were examined for citations of relevant studies.

Titles and abstracts were screened by two reviewers; data were extracted by one reviewer (LNK) and double-checked by the second reviewer (DOG) using a pre-designed data extraction form. Data extracted from each study included the author’s first and last names, title, publication year, study population (cohort and sample size), follow-up period, guidelines utilized and how adherence score was generated, covariates, and study outcomes including relative risks (RR) or hazard ratios (HR) and confidence intervals (CI). The Critical Appraisal Skills Programme’s *Making sense of evidence* (11) was the predetermined tool used to assess the risk of bias. The tool was used to assess recruitment procedures, measurement of exposure, confounding variables, study outcomes, and generalizability. A third reviewer (ETJ) resolved any disagreement. The protocol was registered with PROSPERO International Prospective Register of systematic reviews (Ref: CRD42015026614).

Inclusion and exclusion criteria

Only prospective cohort studies were eligible for inclusion as the focus was to ascertain cancer incidence and cancer mortality. Minimally, studies must have collected data for physical activity and diet, generated an adherence score based on either ACS or WCRF/AICR cancer prevention guidelines (2, 12), and reported cancer outcomes of incidence and/or mortality in order to be deemed eligible for this review. Overall cancer incidence and cancer mortality were the primary outcomes of interest. However, site-specific cancer risks were also considered when data were available from at least two studies meeting the eligibility criteria. Commentaries and summary documents were excluded unless they presented additional data.

Results

A total of 2,033 potentially relevant studies were reviewed; after removal of duplicates and exclusion on the basis of title or abstract, 25 full papers on nutrition and physical activity cancer prevention guideline adherence were retained for in-depth consideration. The selection process for the articles is shown in Figure 1. We identified 12 manuscripts that met the *a priori* criteria for inclusion (Table 1). These studies represented analyses of data from 10 cohorts including the Cancer Prevention Study-II (CPS-II) nutrition cohort (13), the Women's Health Initiative (WHI) cohort (14), the National Institutes of Health-American Association of Retired Persons (NIH-AARP) Diet and Health Study cohort (15), the Framingham Offspring (FOS) cohort (16), the Vitamins and Lifestyle (VITAL) Study cohort (17), the Canadian National Breast Screening Study (NBSS) (18), the Swedish Mammography Cohort (SMC) (19), the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort (20, 21), the Southern Community Cohort Study (SCCS) (22), and the Iowa Women's Health Study (IWHS) cohort (23). Adherence scores for these studies were constructed utilizing recommendations from the American Cancer Society (ACS) (Table 2) (7) or the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) (Table 3) (8).

Overall Cancer

Seven studies evaluated the association between guideline adherence for diet, physical activity, healthy body weight, and alcohol consumption and overall cancer incidence and/or mortality. After adjustment for covariates, there were statistically significant effects of guideline adherence on cancer risk. Participants with high adherence to the ACS guidelines were less likely to develop or die from any cancer compared to those participants that had low adherence to the ACS guidelines (24-27). Likewise, meeting or highly adhering to WCRF/AICR recommendations versus low or no adherence to the recommendations also demonstrated statistically significant risk reduction in overall cancer incidence (28) and mortality (29, 30).

The study by McCullough et al. (24) developed an original scoring system to reflect adherence to the ACS guidelines with the goal of evaluating the association between following the recommended guidelines and risk of death from cancer, cardiovascular disease, and all causes. The authors evaluated 111,966 non-smoking men and women in the CPS-II Nutrition cohort, which is a subset of the larger CPS-II (13). Participants were primarily healthy, Caucasian adults aged 50-74 years from 21 states in the U.S. (13). The scoring system weighted each recommendation equally from 0 to 2 possible points, with 0 points representing not meeting the recommendation at all, 1 point for partially meeting the recommendation, and 2 points for fully meeting the recommendation. The overall adherence scores in the study population ranged from 0 for those participants who did not follow any of the guidelines to 8 for those participants that were fully adherent to all four lifestyle factor recommendations (Table 2). High adherence was a score of 7-8 points and low adherence was a score of 0-2 points. McCullough et al. reported a 24% reduction (RR=0.76, 95% CI: 0.65-0.89) and a 30% reduction (RR=0.70, 95% CI: 0.61-0.80) in cancer mortality over 14

years of follow up for men and women, respectively, with high adherence compared to those with low adherence to the ACS guidelines. (24).

Thomson et al. (25) used similar methodology to examine the impact of adherence to the ACS guidelines in 65,838 postmenopausal women aged 50-79 years from the Women's Health Initiative Observational Study (WHI-OS) (14). The WHI-OS was a prospective study of health outcomes in postmenopausal women that were enrolled in 40 U.S. clinical centers from 1993 to 1998 (31). Overall baseline adherence scores were similar to those from the CPS-II cohort, differing only slightly. The recommendation to "maintain a healthy weight throughout life" was assessed from reported weight at 18 years and measured at study baseline. The score for the recommendation to "consume a healthy diet with an emphasis on plant sources" included an extra point or two for diet quality determined by being in the second or third tertile of total carotenoids, respectively (Table 2). Similar to the previous study, the overall adherence scores ranged from 0 for those participants not adherent to any of the guidelines to 8 for fully adherent participants and were collapsed into categories for comparison. The overall cancer incidence or mortality analyses included a comparison of highly adherent participants with a score of 7 or 8 compared to low adherence participants scoring less than 2 points. Cancer-specific mortality analyses further collapsed categories of the score (0-3, 4-5, 6-8) due to smaller numbers of events. In women that had high adherence to the ACS guidelines, Thomson et al. demonstrated a 17% reduction in cancer incidence over the 12.6 years of follow-up (HR=0.83, 95% CI: 0.75-0.92) and 20% reduction in cancer-specific mortality (HR=0.80, 95% CI: 0.71-0.90) compared to women with low adherence to the ACS guidelines (25).

In the third study utilizing the ACS guidelines, nearly half a million men and women aged 50-71 in the NIH-AARP Diet and Health Study (n=476,396) were included from 6 states and 2 metropolitan areas with existing population-based cancer registries from 1995-1996 (15). Adherence scores were modified somewhat from prior ACS-based studies by using only one baseline measurement for BMI, categorizing physical activity by times per week instead of metabolic equivalents of task (MET) hours per week, not including a variety or quality of diet measure, and giving moderate drinkers (1-2 drinks per day for men and 1 drink per day for women) the most adherent score of 2 points for the alcohol consumption recommendation (Table 2). Participants were categorized as most adherent if they scored 8-11 points and least adherent if they scored 0-3 points overall. As shown in Table 1, Kabat et al. reported a statistically significant decrease in cancer incidence over the 10.5 years of follow-up for both highly adherent men (HR=0.90, 95% CI: 0.87-0.93) and women (HR=0.81, 95% CI: 0.77-0.84). A statistically significant reduction in cancer mortality was also reported during the 12.6 years of follow-up for both highly adherent men (HR=0.75, 95% CI: 0.70-0.80) and women (HR=0.76, 95% CI: 0.70-0.83) (27).

Warren Andersen et al. (26) performed the most recent evaluation between adherence to the ACS guidelines and overall cancer incidence utilizing the Southern Community Cohort Study (SCCS) (n=61,098) with a focus on representing low-income Whites and African Americans in the southeastern United States. Adherence scores ranged from 0 to 4 points with 1 point assigned for each recommendation met upon study entry (Table 2). A comparison of the most adherent participants (score=4) versus non-adherent participants

(score=0) demonstrated a nonsignificant 4% reduction in overall cancer incidence (HR=0.96, 95% CI: 0.65-1.42) in the SCCS participants. However, when evaluating only participants free of chronic disease at baseline, a statistically significant 45% reduction in cancer risk (HR=0.55, 95% CI: 0.31-0.99) was found (26).

Romaguera et al. (28) assessed the association between adherence to WCRF/AICR guidelines and overall cancer incidence as well as specific types of cancer incidence in the European Prospective Investigation into Nutrition and Cancer (EPIC) cohort study (n=386,355) (20, 21). The constructed adherence score (Table 3) operationalized the WCRF/AICR recommendations of body fatness, physical activity, intake of food and drinks that promote weight gain, intake of plant foods, intake of animal foods, intake of alcoholic drinks, and breastfeeding. One point was assigned for each recommendation that was fully met, a half point was assigned for partially meeting the recommendation, and all others received zero points for not meeting the recommendation. For women, high adherence to the score was denoted if the score summed to 6-7 points compared to low adherence scoring 0-3 points. For men, high adherence was considered a score of 5-6 compared to low adherence scoring 0-2 points. Romaguera et al. reported a statistically significant decrease in overall cancer incidence over the 11.0 years of follow-up for both highly adherent men (HR=0.84, 95% CI: 0.72-0.99) and women (HR=0.81, 95% CI: 0.72-0.91). In addition, a 1-point increment of the adherence score was associated with a statistically significant 5% reduction in overall cancer incidence (HR=0.95, 95% CI: 0.93-0.97) (28).

Similarly, Vergnaud et al. (30) investigated whether adherence to WCRF/AICR recommendations was associated with risk of death in the EPIC cohort study (n=378,864) after a median follow-up time of 12.8 years (20, 21). The adherence score (Table 3) was modeled after the previous work of Romaguera et al. utilizing the same recommendations and collapsing the score into the same sex-specific high and low adherence categories. A significant reduction in cancer-specific mortality was found among women who were most adherent to WCRF/AICR recommendations (HR=0.76, 95% CI: 0.62-0.93). Statistical significance was not reached in the association for men (HR=0.86, 95% CI: 0.69-1.07); however, an 8-9% reduction in risk per 1-point increase of WCRF/AICR adherence score was statistically significant for both men (HR=0.92, 95% CI: 0.89-0.95) and women (HR=0.91, 95% CI: 0.88-0.94) (30).

Finally, Hastert et al. (2014) also operationalized the WCRF/AICR guidelines (Table 3) to examine the association between meeting guidelines on nutrition and physical activity and cancer mortality in a cohort of men and women (n=57,841) aged 50 to 76 years from the VITAL study (17). Adherence to the WCRF/ AICR guidelines was classified as met or did not meet (DNM) for each of the 6 included recommendations (Table 2). Recommendations to limit salt preserved foods and supplements were not considered as the former was not considered common in the U.S. food supply and the latter because the guidelines did not recommend for or against supplementation for the prevention of cancer. Adherence was measured as follows: BMI by self-reported height and weight, physical activity by minutes per day and intensity, energy density, plant foods, red meat, and alcohol based on responses to the food frequency questionnaire (FFQ). Meeting at least five recommendations compared

to meeting none demonstrated a 61% reduction in cancer-specific mortality over 7.7 years of follow-up (HR=0.39, 95% CI: 0.24-0.62) (29).

Breast Cancer

In addition to overall cancer incidence, eight studies reported results for female breast cancer incidence as an outcome (25, 27, 32-35). Consistent reductions in breast cancer incidence were demonstrated in the WHI, NIH-AARP, and EPIC cohorts for high adherence to nutrition and physical activity cancer prevention guidelines versus low adherence, with HRs (95% CIs) of HR=0.78, 95% CI: 0.67-0.92 (25), HR=0.81, 95% CI: 0.76-0.87 (27), and HR=0.84, 95% CI: 0.78-0.90, respectively (28). Hastert et al. also investigated breast cancer incidence as an outcome using the WCRF/AICR guidelines in a cohort of postmenopausal women aged 50 to 76 years from the VITAL study (n = 30,797). Meeting at least five WCRF/AICR recommendations compared with meeting none was associated with a 60% reduction in breast cancer incidence (HR: 0.40, 95% CI: 0.25-0.65). Furthermore, each additional recommendation met was associated with an 11% reduction in breast cancer risk (HR=0.89, 95% CI: 0.84-0.95). (32). Similarly, Harris et al. demonstrated a 51% reduction in breast cancer incidence (HR: 0.49, 95% CI: 0.35-0.70) (33) for those most adherent (score≥6) compared to least adherent (score ≤2) to the WCRF/AICR guidelines in the primarily post-menopausal women in the Swedish Mammography Cohort (SMC) (n=31,514) that were followed for 15 years (19). Makarem et al. (36) also used the WCRF/AICR guidelines to examine the relationship between meeting the recommendations and obesity-related cancer incidence in a sample of men and women from the Framingham Offspring (FOS) cohort (n=2,983) (16). Cancers were considered obesity-related if clearly or possibly linked to excess adiposity by the ACS. Participants received 1, 0.5, or 0 points for fully meeting, partially meeting or not meeting the WCRF/AICR recommendation, respectively (Table 2). Similar to the VITAL study, hazard ratios for every 1-unit increment in the overall adherence score were computed for obesity-related cancers and site-specific cancers. Conversely, no statistically significant association was found between adherence and breast cancer incidence (HR=0.87, 95% CI: 0.74-1.03) on a per-recommendation basis (36). Catsburg et al. (34) operationalized both ACS and WCRF/AICR guidelines in the Canadian National Breast Screening study (NBSS) (n=47,130 WCRF, n=46,298 ACS)(18). Adherence to all six ACS guidelines compared to at most one guideline was associated with a statistically significant 31% reduction in breast cancer incidence (HR=0.69, 95% CI: 0.49-0.97). Adhering to six or seven WCRF/AICR guidelines compared to at most one guideline was associated with a 21% reduction in risk (HR=0.79, 95% CI: 0.57-1.10) but did not reach statistical significance. Meeting each additional guideline was associated with a 5% (HR=0.95, 95% CI: 0.91-0.98) or 6% (HR=0.94, 95% CI: 0.91-0.98) reduction in breast cancer incidence utilizing the WCRF/AICR and ACS recommendations, respectively (34). Most recently, Nomura et al. (35) evaluated adherence to the WCRF/AICR guidelines and breast cancer incidence among postmenopausal women with and without non-modifiable risk factors in the Iowa Women's Health Study (IWHS) (n=36,626). The eight point adherence score was collapsed into 4 categories: 0-3.5 points (low adherence), 4.0-4.5, 5.0-5.5, 6.0-8.0 (high adherence). High adherence compared to low adherence to WCRF/AICR guidelines was significantly associated with a reduction in breast cancer incidence (HR=0.76, 95% CI: 0.67-0.87) (35).

Colorectal Cancer

A total of four studies reported results for colorectal cancer specifically (25, 27, 28, 36). Significant inverse associations were found between adherence to ACS guidelines and colorectal cancer incidence in the WHI cohort (HR=0.48, 95% CI: 0.32-0.73) (25) as well as the NIH-AARP cohort for women (HR=0.65, 95% CI: 0.54-0.78) and men (HR=0.52, 95% CI: 0.47-0.59) (27). Consistently, a statistically significant reduction in colorectal cancer was associated with higher adherence in the EPIC cohort (HR=0.73, 95% CI: 0.65-0.81) (28). In contrast, the FOS cohort demonstrated no significant association for colorectal cancer incidence and adherence to WCRF/AICR guidelines (HR=0.87, 95% CI: 0.68-1.12) (36).

Lung Cancer

The association between ACS guideline adherence and lung cancer incidence is equivocal. Three studies reported results for the association between nutrition and physical activity guideline adherence and lung cancer incidence (25, 27, 28). In the NIH-AARP cohort, effect modification by sex was demonstrated with a statistically significant inverse association found among highly adherent men (HR=0.85, 95% CI: 0.78-0.93), but not highly adherent women (HR=0.94, 95% CI: 0.84-1.05) (27). Results from the WHI are consistent with these reporting no statistical significance between lung cancer incidence in women and ACS guideline adherence (HR=1.14, 95% CI: 0.81-1.60) (25). The association between high adherence and lung cancer incidence was not statistically significant when evaluated for both sexes combined in the EPIC study (HR=0.86, 95% CI: 0.74-1.00) (28).

Endometrial Cancer

To date, three prospective studies have reported results for the association between nutrition and physical activity guideline adherence and endometrial cancer incidence. The large NIH-AARP and EPIC cohorts both found significant inverse associations demonstrated by higher adherence and lower risk of endometrial cancer (HR=0.40, 95% CI: 0.34-0.46; HR=0.77, 95% CI: 0.62-0.94), respectively (27, 28); while findings from the WHI cohort suggest no significant association (HR=0.73, 95% CI: 0.49-1.09) (25). Although analysis of the adherence score as a categorical variable (high vs. low) in the latter study was not statistically significant for risk of endometrial cancer, the overall trend using ACS score as an ordinal variable (0-8 points) suggested a significant 7% reduction in endometrial cancer incidence (HR=0.93, 95% CI: 0.87-0.98) (25).

Other Cancers

Data were also available from three studies meeting the eligibility criteria for ovarian (25, 27, 28) and prostate (27, 28, 36) cancer incidence. No statistically significant associations were found between ovarian cancer incidence and ACS guideline adherence in the WHI or NIH-AARP cohorts or WCRF/AICR guideline adherence in the EPIC cohort. Likewise, no significant associations were identified for prostate cancer incidence utilizing the ACS guidelines in the NIH-AARP cohort or the WCRF/AICR guidelines in the EPIC or FOS cohorts.

Discussion

This systematic review included 12 studies from 10 different prospective cohorts evaluating the association between adherence to nutrition and physical activity cancer prevention guidelines and cancer outcomes. High versus low adherence to ACS or WCRF/AICR guidelines was consistently and significantly associated with decreases of 10% to 61% in overall cancer colorectal cancer incidence in both men and women (27%-52%). Consistent reductions were also shown for breast cancer incidence (19-60%), endometrial cancer incidence (23-60%), and colorectal cancer incidence in both men and women (35-52%) for those most adherent to the recommendations. Findings from three studies that reported results for adherence and lung cancer incidence were less clear. No significant relationships were found between adherence and ovarian or prostate cancers.

The greatest evidence for an association with the guidelines was significant findings in seven out of eight studies that included breast cancer incidence as an outcome. Regarding the studies specifically related to breast cancer, all eight included women 50 years and older, although WHI, IWHS, and VITAL cohorts included only postmenopausal women, and the SMC cohort consisted of primarily postmenopausal women. ACS guidelines were employed in the WHI, NIH-AARP, NBSS cohorts while the WCRF/AICR guidelines were used in the VITAL, FOS, SMC, EPIC, IWHS, and NBSS cohorts. Unlike the other studies that compared high adherence to low adherence, the FOS adherence score was evaluated and interpreted in 1-point increments (36). Other differences in the FOS cohort include fewer incident cases of breast cancer (n=124) and inclusion of pre- and postmenopausal women, which may contribute to attenuation of findings.

Significant inverse associations were also found between adherence to the guidelines and colorectal cancer incidence in three out of the four studies reviewed. The inconsistency in the FOS cohort could be due to the difference in the set of guidelines used for generation of adherence score, the different analytic approach utilizing the adherence score as a continuous variable versus a dichotomous variable (high versus low), analyzing men and women together unlike other studies, or perhaps the number of incident cases of colorectal cancer (n=63) in the FOS cohort was too small to detect statistically significant associations.

Less clear were the findings from three studies that included lung cancer as an outcome. One study reported a significant reduction in lung cancer for only men who had high adherence compared to men with low adherence, but not for women. Similarly, a second study found no association for women adhering to the guidelines and lung cancer and a third study had null findings when men and women were reported together. Though smoking status is the strongest risk factor associated with lung cancer, broader health-related behaviors such as diet and physical activity may have a significant role in reducing lung cancer risk in men.

Three studies found an inverse relationship between guideline adherence and risk of endometrial cancer; however, only two of those studies showed a statistically significant result for the high versus low adherence comparison. The third study did suggest a significant trend with higher adherence leading to lower risk of endometrial cancer when the adherence score was evaluated as a continuous variable.

To our knowledge, this is the first systematic review of dietary and physical activity cancer prevention guidelines and cancer outcomes. Strengths of this systematic review include strict inclusion criteria to include only prospective studies that constructed adherence scores to the established cancer prevention guidelines by ACS or WCRF/AICR. All of the studies contained sizeable cohorts with multiple years of follow-up leading to sufficient sample sizes, ample power to detect associations, and sufficient number of outcomes, enabling them to evaluate associations for some site-specific cancers. However, there are also some limitations that must be considered. First, all studies generated their own adherence scores based upon recommendations from either the ACS or WCRF/AICR. Most studies assigned points for meeting or partially meeting recommendations while others categorized adherence as “met” or “did not meet” recommendations. Including multiple levels of exposure may better capture the degree of adherence to the guidelines. Although ACS and WCRF/AICR guidelines are very similar, interpretations of how to measure the recommendations varied. Notably, physical activity was assessed several ways including in metabolic equivalents, times per week, and even a physical activity index. Furthermore, studies utilized frequency questionnaires to capture diet and physical activity data. These self-reported measures are well-known sources of measurement error, which may bias findings toward the null, lending to conservative findings in this review. Components of the adherence score were measured singularly at baseline and used to assess cancer risk over time. Repeated measurements of diet and physical activity may have provided an improved exposure assessment of long-term behavior and risk over time. Follow-up times ranged from 7.7-14 years, which may not be sufficient for assessing the protective role of adherence to nutrition and physical activity cancer prevention guidelines. In addition, although the studies evaluated large cohorts, there was limited population heterogeneity with regard to race or ethnicity, with the exception of the WHI and SCCS studies. Furthermore, analyses varied somewhat among the studies. All studies evaluating associations with ACS guideline adherence made comparisons of high versus low adherence. One study used WCRF/AICR guidelines to compare “met” versus “did not meet” recommendations (29), while a single study evaluated adherence to WCRF/AICR guidelines based upon point increments of the overall score (36). Finally, the potential for publication bias is always of concern. Studies with significant findings are more likely to be published than those with null or unimportant findings. Grey literature was included in the search via Google Scholar in an attempt to capture any work that hasn’t been formally published (abstracts, conference proceedings, etc.). Even though the studies differed in some measurements of individual score components, construction of the adherence score, specifics of the set of guidelines used, and analytic methods, it is important to note that studies generally demonstrated agreement in their findings even across countries with varying diet and physical activity patterns.

In conclusion, strong and consistent evidence from ten large prospective cohorts in 12 publications indicates that adherence to ACS and WCRF/AICR cancer prevention guidelines was associated with significant reductions in cancer incidence and cancer mortality for both men and women. Additionally, significant inverse associations were consistently found between guideline adherence and breast, colorectal, and endometrial cancer incidence. Adherence to a pattern of healthy behaviors, as outlined in cancer prevention guidelines from either the ACS or WCRF/AICR, may reduce cancer incidence and mortality.

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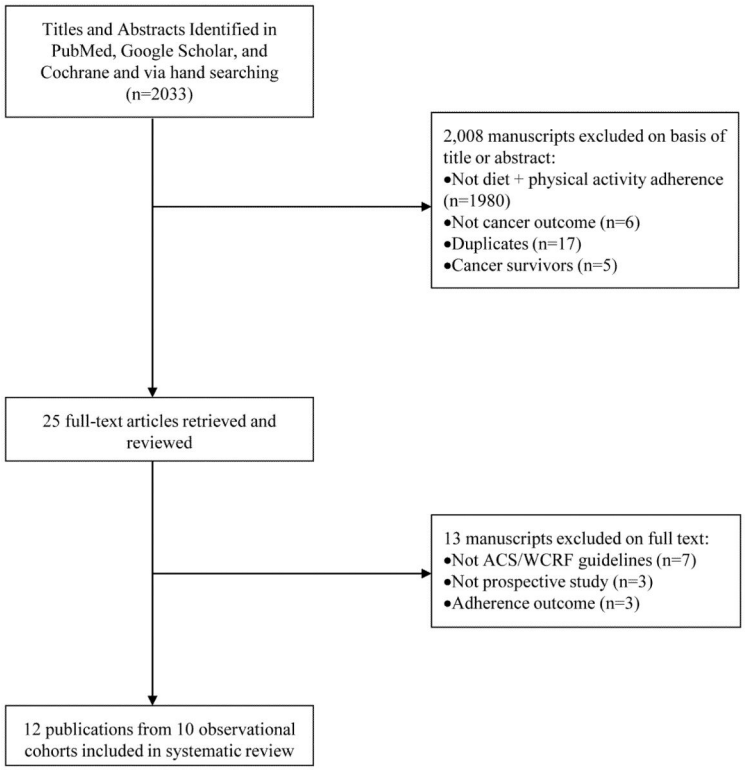

Figure 1. Article selection process

The PRISMA diagram details the search and selection of manuscripts for the review.

Table 1

Characteristics and findings of included prospective studies.

	Author, year	Study name, data collection years, sample size, years follow-up, guidelines	Relevant Outcome(s)	Key Findings
1	McCullough, 2011	CPS-II Nutrition Cohort, 1992-1993, n=111,966, 14 years, ACS[i]-8 point score	All cancer mortality	Men: RR[ii]=0.70, 95% CI[iii]: 0.61-0.80 Women: RR=0.76, 95% CI: 0.65-0.89
2	Thomson, 2014	Women's Health Initiative, 1993-1998, n=65,838, 12.6 years, ACS-8 point score	All cancer incidence, and mortality, site-specific cancer incidence	Cancer incidence: HR[iv]=0.83, 95% CI: 0.75-0.92 Cancer mortality: HR=0.80, 95% CI: 0.71-0.90 Colorectal: HR=0.48, 95% CI: 0.32-0.73 Breast: HR=0.78, 95% CI: 0.67-0.92 Endometrial: HR=0.73, 95% CI: 0.49-1.09 Ovarian: HR=1.13, 95% CI: 0.68-1.87 Lung: HR=1.14, 95% CI: 0.81-1.60
3	Kabat, 2015	NIH-AARP Diet and Health Study, 1995-1996, n=476,396, 10.5-12.6 years, ACS-11 point score	All cancer incidence, site-specific cancer incidence, all cancer mortality	All cancer incidence: Men HR=0.90, 95% CI: 0.87-0.93 Women HR=0.81, 95% CI: 0.77-0.84 All cancer mortality: Men HR=0.75, 95% CI: 0.70-0.80 Women HR=0.76, 95% CI: 0.70-0.83 Colon: Men HR=0.52, 95% CI: 0.47-0.59 Women HR=0.65, 95% CI: 0.54-0.78 Rectal: Men HR=0.60, 95% CI: 0.51-0.72 Women HR=0.64, 95% CI: 0.49-0.83 Lung: Men HR=0.85, 95% CI: 0.78-0.93 Women HR=0.94, 95% CI: 0.84-1.05 Breast: HR=0.81, 95% CI: 0.76-0.87 Endometrial: HR=0.40, 95% CI: 0.34-0.46 Ovarian: HR=0.95, 95% CI: 0.73-1.23
5	Hastert, 2013	VITAL cohort, 2000-2002, n=30,797 post-menopausal women, 7.7 years, WCRF/AICR Met/didn't meet	Breast cancer incidence	HR=0.40, 95% CI 0.25-0.65
4	Hastert, 2014	VITAL cohort, 2000-2002, n=57,841, 7.7 years, WCRF/AICR met/didn't meet	All cancer mortality	HR=0.39, 95% CI 0.24-0.62)
	Makarem, 2015	FOS cohort, 1991, n=2,983, 11.5 years, WCRF/AICR 7 point score	Incidence of obesity-related cancers and site-specific: breast, prostate, and colon	Obesity-related: HR=0.94, CI 0.86-1.02 Breast: HR=0.87, 95% CI: 0.74-1.03 Prostate: HR=1.08, 95% CI: 0.92-1.27 Colorectal: HR=0.87, 95% CI: 0.68-1.12
7	Harris, 2016	SMC, 1987-1990, n=31,514, 15 years, WCRF/AICR 7 point score	Breast cancer incidence	HR=0.49, 95% CI: 0.35-0.70
8	Catsburg, 2014	Canadian NBSS, 1980-1985, n=47,130 WCRF/AICR and n=46,298 ACS, 16.6 years	Breast cancer incidence	ACS: HR=0.69, 95% CI: 0.49-0.97 WCRF/AICR: HR= 0.69, 95% CI: 0.47-1.00

	Author, year	Study name, data collection years, sample size, years follow-up, guidelines	Relevant Outcome(s)	Key Findings
9	Vergnauad, 2013	EPIC Study, 1992-2000, n=378,864, 12.8 years, WCRF/AICR 6 point score for men, 7 point score for women	All cancer mortality	Total: HR=0.80, 95% CI: 0.69-0.93 Men: HR=0.86, 95% CI: 0.69-1.07 Women: HR=0.76, 95% CI: 0.62-0.93
10	Romaguera, 2012	EPIC Study, 1992-2000, n=386,355, 11.0 years, WCRF/AICR 6 point score for men, 7 point score for women	All cancer incidence, site-specific cancer incidence	All cancer incidence: Men HR=0.84, 95% CI: 0.72-0.99 Women HR=0.81, 95% CI: 0.72-0.91 Colorectal: HR=0.73, 95% CI: 0.65-0.81 Lung: HR=0.86, 95% CI: 0.74-1.00 Breast: HR= 0.84, 95% CI: 0.78-0.90 Endometrial: HR= 0.77, 95% CI: 0.62-0.94 Ovarian: HR= 0.99, 95% CI: 0.79-1.25 Prostate: HR=1.02, 95% CI: 0.91-1.14
11	Nomura, 2016	IWHS, 1986, n=36,626 post-menopausal, >23 years, WCRF/AICR 8 point score	Breast cancer incidence	HR=0.76, 95% CI: 0.67-0.87
12	Warren Andersen, 2016	SCCS, 2002-2009, n=61,098 low-income racially diverse adults, 6 years, ACS 4 point score	All cancer incidence	HR=0.96, 95% CI: 0.65-1.42 [v] HR=0.55, 95% CI: 0.31-0.99 [vi]

[i] American Cancer Society

[ii] Relative Risk

[iii] Confidence Interval

[iv] Hazard Ratio

[v] Total analytic population. P-trend 0.09

[vi] Participants without chronic disease at baseline. P-trend 0.003

Table 2

ACS recommendations and adherence score breakdown of selected studies.

American Cancer Society					
Recommendation	**McCullough, 2011 Thomson, 2014**[vii]		**Kabat, 2015**		**Catsburg, 2014**	**Warren Andersen, 2016**
"Maintain a healthy weight throughout life"	0: Obese at both time points or obese at 1 and overweight at the other 1: All others 2: BMI[viii] 18-<25 at both times		0: >35.0 1: 30-34.9 2: 25-29.9 3: 18.5-24.9		18.5 ≤ BMI ≤25	18.5 ≤ BMI ≤25
"Adopt a physically active lifestyle"	0: <8.75 MET[ix] h/wk 1: 8.75-17.5 MET h/wk 2: >17.5 MET h/wk		0: ≤ 3x/mo 1: 1-2x/wk 2: 3-4x/wk 3: ≥5x/wk		≥ 150 min/week	≥ 150 min/wk of moderate, ≥ 75 min/wk of vigorous or ≥ 150 min/wk of moderate + vigorous
"Eat 5 or more servings of a variety of vegetables and fruits each day"	1: ≥5 servings/d fruits +veg +1 or 2 "variety" points for 2nd or 3rd tertile of unique fruits or veg consumed/month		Quartiles		>400g vegetables and fruit per day	≥2.5 cups vegetables + fruits/d
"Choose whole grains instead of refined grains"	Quartiles of the ratio of whole grains to total grains		Quartiles of the ratio of whole grains to total grains		Ratio of whole: refined grains >1	Highest quartile of the ratio of whole grains to total grains
"Limit consumption of processed and red meats"	Quartiles of red + processed meat intake (servings/wk)		Quartiles of red + processed meats		<500g red and processed meat per week	Lowest quartile of red + processed meats
"If you drink, limit consumption to 1 drink/day for women or 2 drink/day for men"	Women: 0: >1 1: >0-≤1 2: Non	Men: 0: >2 1: >0-≤2 2: Non	Women: 0: ≥2 1: Non 2: 1	Men: 0: ≥3 1: Non 2: 1-2	≤1 standard drink/d	Women ≤1 drink/d Men ≤2 drinks/d

[vii] Thomson evaluated BMI as <18.5 excluded 0: BMI >=30 kg/m^2 at age 18 or at baseline, 1: BMI 25-<30 at age 18 or baseline, 2: BMI <25 kg/m^2 at age 18 and baseline; diet score plus 1 or 2 "quality" points for being in the 2nd or 3rd tertile of total carotenoids; alcohol score 2 points for nondrinker at baseline

[viii] Body mass index, kg/m^2

[ix] Metabolic Equivalent of Task

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Table 3

WCRF/AICR recommendations and adherence score breakdown of selected studies.

World Cancer Research Fund/American Institute for Cancer Research						
Recommendation	**Hastert, 2013 & 2014**[x]	**Catsburg, 2014**	**Makarem, 2015**	**Harris, 2016**	**Vergnaud, 2013 Romaguera, 2012**	**Nomura, 2016**
"Be as lean as possible within the normal range of body weight"	18.5 ≤ BMI[xi] <25	18.5 ≤ BMI ≤25	0: <18.5 BMI >30.0 0.5: 25-29.9 1: 18.5-24.9	18.5 ≤ BMI <25	0: <18.5 BMI >30.0 0.5: 25-29.9 1: 18.5-24.9	0: <18.5 BMI ≥30.0 0.5: 25-<30 1: 18.5-<25
"Be physically active as part of everyday life"	≥30 min/d of moderate/fast walking and/or moderate/strenuous activity ≥5 days/wk in ≥7 of the past 10 yrs	≥210 min/wk	0: <30 PAI[xii] 0.5: 30-33 1: >33	≥30 min/d[xiii]	0: <15 min/d[xiv] 0.5: 15-30 min/d[v] 1: Manual/heavy manual job, or >2h/wk vigorous, or >30 min/d[v]	0: all other 0.5: 2-4x/wk moderate or 1x/wk vigorous 1: ≥2x/wk vigorous or ≥5x/wk moderate
"Eat mostly foods of plant origin"	≥5 servings of fruits + veg and ≥1 serving whole grains and/or legumes/d	>400g veg +fruit plus ≥25g whole grains + legumes/d	Fruit + Veg (servings/d) 0: <2.5 0.5: 2.5-<5 1: ≥5 Refined Grains (g/d) Tertiles Vegetables (g/week) 0: S[xv]>503; NS[xvi] <2,471.4 or S>503; NS >2,471.4 0.5: S<503; NS>2,471.4 1: S<503; NS>2,471.4	>400g veg + fruit plus ≥25g whole grains and legumes/d	Fruit + Veg (g/d) 0: <200 0.5: 200 to <400 1: >400 Dietary Fiber (g/d) 0: <12.5 0.5: 12.5 to <25 1: ≥25	Fruit + Veg (servings/d) 0: <3 0.5: 3-<5 1: ≥5 Dietary Fiber (g/d) 0: <12.5 0.5: 12.5 to <25 1: ≥25
"Limit intake of red meat and avoid processed meat"	<18 oz red and/or processed meat per week	<500g red and <25g processed meat per week	0: ≥500 g/wk or ≥50 g/d 0.5: <500 g/wk & 3 to <50 g/d 1: <500 g/wk & <3 g/d	<500g red and <25g processed meat/wk	0: ≥500 g/wk or ≥50 g/d 0.5: <500 g/wk & 3 to <50 g/d 1: <500 g/wk & <3 g/d	0: ≥500 g/wk RP[xvii] or ≥50 g/wk P[xviii] 0.5: <500 g/wk RP & 3 to <50 g/wk P 1: <500 g/wk RP & <3 g/wk P
"Limit alcoholic drinks"	≤1 drink/d for women; ≤2 drink/d for men	≤1 standard drink per day	Women g/day: 0: >21 0.5: 14-	Men g/day: 0: >42 0.5: 28-42	<10g alcohol/d	Women g/d: 0: >20 0.5: >10-20 1: ≤10	Men g/d: 0: >30 0.5: >20-30	0: >20 g/d 0.5: >10-20 1: ≤10

World Cancer Research Fund/American Institute for Cancer Research						
Recommendation	**Hastert, 2013 & 2014[x]**	**Catsburg, 2014**	**Makarem, 2015**	**Harris, 2016**	**Vergnaud, 2013 Romaguera, 2012**	**Nomura, 2016**
			24 1: ≤14 | 1: ≤28		1: ≤20	
"Limit consumption of ED[xix] foods; avoid sugary drinks"	ED of diet <125 kcal/100g or <1 sugary drink/wk	ED of food <125kcal/100g. No soda or drinks with added sugar	ED Foods (servings/wk) Tertiles	<14 servings/wk of ED foods and <2 glasses/d of soda/juice	0: ED: >175[xx] 0.5:>125 to <175 1: ≤125 0: >250 g/d sugary drink 0.5: ≤250 g/d 1: 0 g/d	0: ≥250 g/d sugary drink 0.5: <250 g/d 1: 0 g/d
"Limit consumption of salt"	Not included	<2.4g sodium/d	Salty Foods Tertiles Sodium Intake g/d 0: >3.6 0.5: 2.4-3.6 1: <2.4	Not included	Not included	0: >2400 mg/d 0.5: >1500-2400 mg/d 1: ≤1500 mg/d
"Dietary supplements not recommended for cancer prevention"	Not included	Not included	Not included	Did not report consuming on a regular basis	Not included	Not included
"Mothers to breastfeed"	Not included	Not included	Not included	Not included	0: No BF[xxi] 0.5: >0 to <6 months 1: ≥6 months	Not included

[x] Hastert 2014 evaluated both men and women

[xi] Body Mass Index kg/m^2

[xii] Physical Activity Index

[xiii] Walking/cycling + leisure time exercise

[xiv] Cycling or sports

[xv] Starchy vegetable

[xvi] Non-starchy vegetable

[xvii] Red and processed meat

xviii: Processed meat

[xix] Energy dense/density

[xx] kcal/100g/day

[xxi] Breastfeeding