Effect of diet on mortality and cancer recurrence among cancer survivors: a systematic review and meta-analysis of cohort studies

Carolina Schwedhelm, Heiner Boeing, Georg Hoffmann, Krasimira Aleksandrova, and Lukas Schwingshackl

Context: *Evidence of an association between dietary patterns and individual foods and the risk of overall mortality among cancer survivors has not been reviewed systematically.* ***Objective:*** *The aim of this meta-analysis of cohort studies was to investigate the association between food intake and dietary patterns and overall mortality among cancer survivors.* ***Data Sources:*** *The PubMed and Embase databases were searched.* ***Study Selection:*** *A total of 117 studies enrolling 209 597 cancer survivors were included.* ***Data Extraction****: The following data were extracted: study location, types of outcome, population characteristics, dietary assessment method, risk estimates, and adjustment factors.* ***Results:*** *Higher intakes of vegetables and fish were inversely associated with overall mortality, and higher alcohol consumption was positively associated with overall mortality (RR, 1.08; 95%CI, 1.02–1.16). Adherence to the highest category of diet quality was inversely associated with overall mortality (RR, 0.78; 95%CI, 0.72–0.85; postdiagnosis RR, 0.79; 95%CI, 0.71–0.89), as was adherence to the highest category of a prudent/healthy dietary pattern (RR, 0.81; 95%CI, 0.67–0.98; postdiagnosis RR, 0.77; 95%CI, 0.60–0.99). The Western dietary pattern was associated with increased risk of overall mortality (RR, 1.46; 95%CI, 1.27–1.68; postdiagnosis RR, 1.51; 95%CI, 1.24–1.85).* ***Conclusion:*** *Adherence to a high-quality diet and a prudent/healthy dietary pattern is inversely associated with overall mortality among cancer survivors, whereas a Western dietary pattern is positively associated with overall mortality in this population.*

INTRODUCTION

The number of cancer survivors in the United States and Europe is growing rapidly.[1,2] The needs and metabolic functions of this group, who have experienced a malignant process and its corresponding treatment, might differ from those of healthy populations. To date, however, the evidence to formulate specific dietary recommendations for this group has been considered insufficient,[3] despite the widely held conviction that better insight into both the role of diet after cancer and the relation of diet to survival might offer further opportunities to

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improve long-term treatment options for this growing population. Whereas recent meta-analyses of observational studies clearly demonstrate reduced risks of different types of cancer among healthy populations that follow specific dietary regimens,[4–7] a comparable synthesis of empirical data for cancer survivors, such as a systematic review and meta-analysis, is available only for breast cancer survivors, and even then, the literature is sparse.[8] Furthermore, prospective cohort studies that have investigated the association between composition of diet and overall mortality among cancer survivors show contradicting results.[9] A further complicating factor is that some studies evaluated the relationship between mortality and nutrients instead of between mortality and food patterns,[9,10] the latter being more easily understood and reflecting more accurately the lifestyles of the targeted population. Therefore, the current dietary advice for cancer survivors is to receive personalized nutritional care from a trained professional and to follow current recommendations for cancer prevention, if not otherwise advised.[3]

Most of the single cohort studies on cancer survivors have focused on associations between prediagnosis dietary intake, especially alcohol intake, and overall mortality and/or cancer recurrence, while only a few studies have assessed associations with postdiagnosis dietary intake[11−13] Clinical trials enrolling subjects with existing cancer have the advantage of possessing data on the postdiagnosis diet; however, such studies often focus on nutrients rather than dietary patterns or food groups and are weakly suited for studying long-term successful dietary interventions.

A better understanding of the effect of food intake and food-based dietary patterns on overall mortality and recurrence among cancer survivors can inform the development of tailored prevention strategies in the important area of modifiable lifestyle factors such as diet.

Therefore, the aim of this study was to conduct a meta-analysis of all cohort studies that investigated the effects of adherence to diet-quality indices, dietary patterns, and food and beverage consumption on overall mortality and cancer recurrence among cancer survivors.

METHODS

The review protocol has been registered in the PROSPERO International Prospective Register of Systematic Reviews (no. CRD42015023684).

Data sources and searches

The literature search was performed using the electronic databases PubMed (until May 17, 2016) and Embase (until May 17, 2016), with no restrictions on calendar date, using the following search terms: (“diet” OR “dietary” OR “food” OR “foods” OR “alcohol”) AND (“cancer”) AND (“survivors” OR “survivor” OR “recurrence”) AND (“prospective” OR “cohort” OR “longitudinal” OR “follow up”). The search strategy had no language restrictions. Moreover, the reference lists of reviews and retrieved articles were checked as well. The literature search was conducted by 2 authors (C.S. and L.S.); disagreements were resolved by discussion. MOOSE guidelines[14] were followed when planning, conducting, and reporting the meta-analysis.

Study selection

Studies were included in the systematic review and meta-analyses if they met the following criteria (Table 1): (1) cohort study design (prospective and retrospective); (2) exposure to individual food components such as fruits, vegetables, dairy, meat, fish, cereals, and bread; (3) exposure to beverages such as alcohol, coffee, and tea; (4) use of diet-quality indices (Mediterranean diet, DASH [Dietary Approaches to Stop Hypertension], Healthy Eating Index, WCRF/AIRC [World Cancer Research Fund/American Institute for Cancer Research] dietary guidelines adherence score) that were determined a priori; (5) examination of data-driven dietary patterns (healthy/prudent, unhealthy/Western); (6) overall mortality and/or cancer recurrence included in reported outcomes; and (7) study participants limited to adult populations ($\geq$18 years old) of survivors of various

Table 1 **PICOS criteria for inclusion and exclusion of studies**

Criteria	Description
Participants	Survivors of various types of cancer, adult populations (aged $>$18 y) only. The definition of “cancer survivor” here does not include survivors of cervical lesions or adenomas in the colon
Interventions/exposure	Intake of individual foods: fruits, vegetables, dairy, meat, fish, cereals, and bread Intake of beverages: alcohol, coffee, tea A priori–based diet-quality indices (Mediterranean diet, DASH, Healthy Eating Index, WCRF/AIRC dietary guidelines adherence score) Adherence to data-driven dietary patterns (healthy/prudent, unhealthy/Western)
Comparison	Highest vs lowest categories of exposure
Outcome	Overall mortality and/or cancer recurrence
Study design	Cohort studies (prospective and retrospective)

Abbreviations: DASH, Dietary Approaches to Stop Hypertension; WCRF/AIRC, World Cancer Research Fund/American Institute for Cancer Research.

cancer types (the definition of "cancer survivor" does not include survivors of cervical lesions or adenomas in the colon). When a study seemed to have been published in duplicate, the article containing the most comprehensive information (longest follow-up period) was selected. Finally, studies reporting cancer-specific mortality (but no overall mortality) were excluded.

Data extraction

The following data were extracted from each study: (1) author's last name; (2) country of origin and name of the study; (3) types of outcome (overall mortality, cancer recurrence); (4) sample size of the population and length of the study (mean follow-up duration in years); (5) age of participants at entry; (6) sex of participants; (7) tumor characteristics; (8) assessment of recurrence; (9) exposure assessment, including timeframe; (10) components of diet-quality indices/dietary patterns (including score range); (11) adjustment factors; and (12) multivariate-adjusted risk estimates (risk ratio [RR] or hazard ratio for the highest vs the lowest category) along with their corresponding 95%CIs. If only separate risk estimates were available for specific foods (ie, processed meat and unprocessed meat) or beverages within a food/beverages category (ie, meat), the risk estimates were pooled (using a fixed-effects model) and were treated as 1 study. Moreover, if different categories of alcohol consumption (ie, current and ex-drinkers) were combined (the lowest intake category was considered the reference category), these estimates were pooled (using a fixed-effects model). When a study provided several risk estimates, the multivariate-adjusted model was chosen. Risk estimates were pooled if at least 3 studies reported data for the same exposures (eg, diet-quality indices, dietary patterns, and intakes of fruit, vegetables, dairy, meat, fish, cereals and bread, and beverages [alcohol, tea, coffee]) for overall mortality and cancer recurrence.

Statistical analysis

The meta-analysis was performed by combining the multivariable-adjusted RRs or hazard ratios of the highest dietary categories compared with the lowest dietary categories using a random-effects model (using the Der Simonian-Laird method[15]), which incorporated both within- and between-study variability. This model was chosen because exposures were not rare, and the heterogeneity modeling was deemed important. For clarity, studies of each exposure were grouped by type of cancer (analyzed jointly and separately) when calculating overall mortality and cancer recurrence. As an initial approach, the prediagnosis and the postdiagnosis assessments of exposure were combined and then stratified.

Main analyses assessed food categories before and after diagnosis for all types of cancer. Separate subgroup analyses were performed for studies that assessed postdiagnosis diet and for all studies grouped by type of cancer.

Heterogeneity was estimated by the Cochrane Q test, together with the I^2 test. An I^2 of $>50\%$ was considered an indicator of substantial heterogeneity across studies, as previously reported.[16,17] The heterogi command in Stata software (Stata Corp; College Station, TX, USA) was used to calculate the 95%CI for the heterogeneity estimates. Funnel plots were used to assess small-study effects if at least 10 studies were available, as recommended by the Cochrane Collaboration.[18] Moreover, Egger's test was performed to test for small-study effects.[19] The presence of publication bias was assessed by the symmetry of contour-enhanced funnel plots by plotting risk estimates against their corresponding standard error; shaded areas indicate whether studies with significant or nonsignificant effects seem to be missing.[20]

All analyses were conducted using Review Manager version 5.3 (Nordic Cochrane Collection; Copenhagen, Denmark) and Stata 13.0.

RESULTS

Literature search and study characteristics

The detailed steps of the systematic search and selection process are shown as an adapted PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram in Figure 1. Table S1 in the Supporting Information online provides a list of full-text articles that were excluded, with reasons.

Overall, 117 cohort studies extracted from 1658 studies (excluding duplicates) were identified and included in the qualitative synthesis (112 included in the quantitative synthesis) (Table S2 in the Supporting Information online).

General study characteristics are summarized in Table S2 in the Supporting Information online. Overall, there were 60 134 mortality cases and 9297 recurrence cases. This information was not available for 14 studies, which provided survival or disease-/recurrence-free survival rates (11 provided no information on explicit cases of mortality, and 6 provided no information on cases of cancer recurrence). The total number of participants in the included studies was 209 597. The breakdown of studies according to cancer type is as follows: 41 studies on breast cancer survivors, 18 studies on colorectal cancer survivors, 16 studies on head and neck cancer

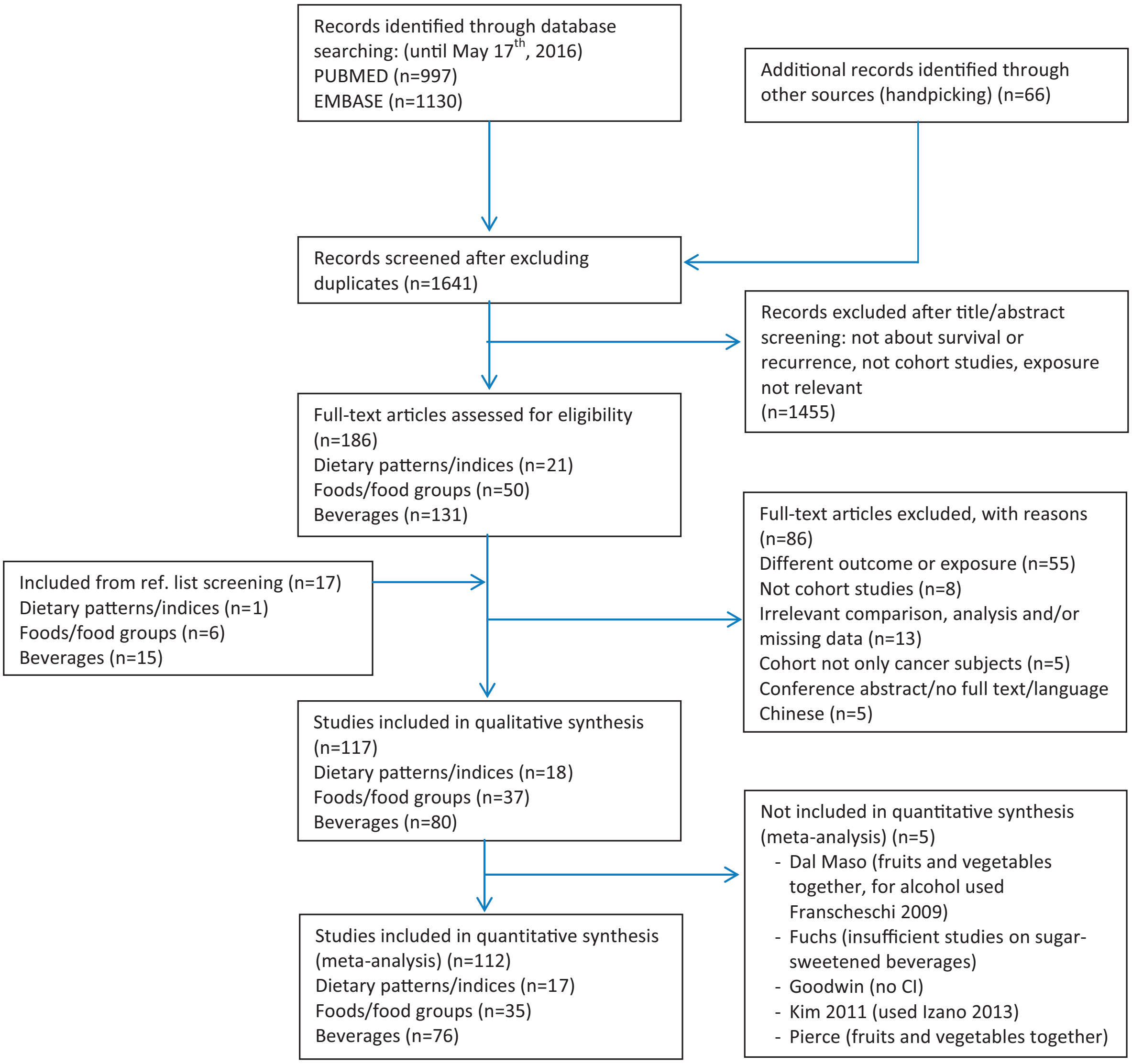

Figure 1 **Flow diagram of the literature search process.** Number of records by dietary pattern/indices, foods/food groups, and beverages may not add up because some studies were listed for multiple exposures (dietary patterns, foods, beverages).

survivors, and 13 studies on gastroesophageal cancer survivors. The sample sizes varied between 57 in a study of head and neck cancer patients from a single institution in Switzerland to 22 890 in a large breast cancer cohort from the United States. The follow-up periods varied from 1.2 to 16 years.

Nine of the included studies used diet-quality scores defined a priori as the exposure measure. Seven of these studies used the Healthy Eating Index (2010 or 2005) or an adapted version of it.[21] A Mediterranean diet score was used in 3 studies and the DASH diet as a score in 2 studies. A WCRF/AIRC dietary guidelines adherence score was used in 1 study, assigning a point to every dietary recommendation met. Furthermore, another study used 2 healthy-diet scores (the Diet Quality Index Revised [DQIR][22] and the Recommended Food Score[23]) that had been developed and used in previous studies. Similar to the other scores mentioned, these indices assign points to a diet high in whole grains, fruit, and vegetable consumption and lower in fat consumption. The DQIR additionally awards points for diet diversity. For the quantitative synthesis, the following diet-quality indices were combined: the alternate Healthy Eating Index (2010),[21] the Healthy Eating Index (2005),[24] the WCRF/AIRC (dietary) guidelines adherence score,[25] the alternate Mediterranean diet,[26,27] the DASH diet,[28] the DQIR,[22] and the Recommended Food Score.[23] All indices for dietary quality focus on high intake of fruit and vegetables, the inclusion of whole grains, legumes and nuts, and low intake of meat (mainly red and processed meat). Eight of these 9 studies were included in the meta-analysis. The ninth study was not included because another study on the same cancer cohort provided a longer follow-up period.

Nine studies assessed the effects of dietary patterns on overall mortality or cancer recurrence. All of these studies used principal component analysis to derive the patterns, which, in most cases, were termed *whole-foods*, *prudent*, or *healthy* if they described a pattern of intake high in fruit and vegetables and whole grains but low in red and processed meat, refined grains, and high-fat foods. Otherwise, patterns describing a diet perceived as unhealthy were mostly labeled as *Western*, *high-fat* or *high-sugar*, *snacks*, or *unhealthy*. For the purpose of this study, patterns were grouped into prudent/healthy and Western/unhealthy dietary patterns. The prudent/healthy food pattern includes high intakes of fruit and vegetables, whole grains, poultry, and low-fat dairy products, whereas the Western/unhealthy dietary pattern is based on high intakes of red and processed meat, refined grains, sweets and desserts, and high-fat dairy products (Table S2 in the Supporting Information online).

Enumerative data for food groups and beverages are shown in Tables 2 and 3.

Main outcomes

The different clinical outcomes documented in the extracted studies were distributed as follows: overall mortality was evaluated in 117 studies (112 included in the meta-analysis) and cancer recurrence in 28 studies (27 included in the meta-analysis) (see Figures S1–S28 in the Supporting Information online).

Overall mortality

When food groups were combined, an inverse association for risk of mortality could be observed for the

Table 2 **Risk of overall mortality comparing the highest vs the lowest category of pre-/post diagnosis dietary exposure (random effects analyses data only)**

Exposure	No. of studies	Risk ratio (95%CI)	I^2 (95%CI)
Diet-quality indices	8	0.78 (0.72–0.85)	0% (0–68%)
Breast cancer	3	0.74 (0.60–0.90)	6% (0–90%)
Postdiagnosis	5	0.79 (0.71–0.89)	0% (0–79%)
Prudent/healthy dietary pattern	8	0.81 (0.67–0.98)	44% (0–75%)
Breast cancer	3	0.76 (0.60–0.95)	4% (0–90%)
Colorectal cancer	3	1.06 (0.83–1.36)	0% (0–90%)
Postdiagnosis	6	0.77 (0.60–0.99)	56% (0–82%)
Western dietary pattern	8	1.46 (1.27–1.68)	0% (0–68%)
Breast cancer	3	1.44 (1.17–1.77)	0% (0–90%)
Colorectal cancer	3	1.55 (1.13–2.13)	35% (0–79%)
Postdiagnosis	6	1.51 (1.24–1.85)	17% (0–62%)
Fruit consumption	19	0.94 (0.87–1.01)	5% (0–52%)
Breast cancer	5	0.93 (0.75–1.17)	33% (0–75%)
Non-Hodgkin lymphoma	3	1.00 (0.88–1.14)	0% (0–90%)
Postdiagnosis	3	0.96 (0.64–1.45)	49% (0–88%)
Vegetable consumption	21	0.86 (0.79–0.94)	43% (5–66%)
Breast cancer	7	0.97 (0.84–1.13)	37% (0–73%)
Postdiagnosis	4	0.88 (0.59–1.30)	78% (39–92%)
Dairy consumption	13	1.08 (0.94–1.23)	66% (38–81%)
Breast cancer	3	1.06 (0.74–1.53)	78% (27–93%)
Colorectal cancer	3	0.93 (0.70–1.26)	76% (22–93%)
Postdiagnosis	6	1.02 (0.75–1.37)	80% (56–91%)
Meat consumption	17	0.91 (0.83–1.01)	53% (18–73%)
Breast cancer	4	0.97 (0.73–1.28)	48% (0–83%)
Colorectal cancer	4	1.10 (0.84–1.43)	54% (0–85%)
Postdiagnosis	4	0.93 (0.75–1.17)	35% (0–77%)
Fish consumption	7	0.85 (0.78–0.93)	0% (0–71%)
Cereals and bread consumption	6	1.03 (0.87–1.22)	0% (0–75%)
Egg consumption	4	1.10 (0.84–1.44)	0% (0–85%)
Alcohol consumption	63	1.08 (1.02–1.16)	70% (61–77%)
Breast cancer	21	0.94 (0.85–1.04)	59% (34–75%)
Colorectal cancer	5	0.95 (0.86–1.06)	5% (0–80%)
Hepatocellular carcinoma	3	1.21 (1.07–1.36)	0% (0–90%)
Non-Hodgkin lymphoma	4	1.33 (1.10–1.63)	46% (0–82%)
Laryngeal and pharyngeal cancer	7	1.48 (1.08–2.02)	49% (0–78%)
Head and neck cancer	5	1.39 (1.10–1.76)	53% (0–83%)
Gastric and esophageal cancer	12	1.14 (0.98–1.34)	69% (44–83%)
Postdiagnosis	15	0.94 (0.81–1.11)	63% (36–79%)
Tea consumption	4	0.78 (0.52–1.19)	33% (0–76%)

Table 3 **Risk of cancer recurrence comparing the highest vs lowest category of pre-/postdiagnosis dietary exposure (random effects analyses data only)**

Exposure	No. of studies	Risk ratio (95%CI)	I^2 (95%CI)
Prudent/healthy dietary pattern	4	0.87 (0.68–1.11)	24% (0–88%)
Postdiagnosis	3	0.94 (0.71–1.24)	19% (0–92%)
Western dietary pattern	4	1.21 (0.69–2.13)	81% (51–93%)
Postdiagnosis	3	1.34 (0.61–2.92)	85% (54–95%)
Vegetable consumption	3	0.99 (0.74–1.33)	69% (0–91%)
Alcohol consumption	17	1.17 (1.05–1.31)	38% (0–65%)
Breast cancer	7	1.21 (1.06–1.39)	23% (0–66%)
Hepatocellular carcinoma	4	1.34 (0.73–2.46)	73% (25–90%)
Postdiagnosis	4	1.31 (1.04–1.66)	54% (0–85%)
Tea consumption	3	0.76 (0.58–1.01)	0% (0–90%)

highest intakes of vegetables (RR, 0.86, 95%CI, 0.79–0.94; $I^2 = 43\%$) and fish (RR, 0.85, 95%CI, 0.78–0.93; $I^2 = 0\%$). Alcohol consumption was associated with increased risk of overall mortality (RR, 1.08; 95%CI, 1.02–1.16; $I^2 = 70\%$). With respect to the remaining food groups, no significant associations could be observed for intakes of dairy, meat, cereals and bread, eggs, tea, red meat, or processed meat. When only studies providing data on postdiagnosis food intakes were retained in the analysis, the results showed no statistically significant associations (Table 2).

Adherence to a high-quality diet was inversely associated with overall mortality (RR, 0.78; 95%CI, 0.72–0.85, $I^2 = 0\%$) (Figure 2[27,29–34] and Table 2). These effects remained consistent following analysis of only the postdiagnosis diet-quality indices (RR, 0.79; 95%CI, 0.71–0.89; $I^2 = 0\%$). The highest category of prudent healthy dietary pattern was inversely associated with overall mortality, both in the main analysis (RR, 0.81; 95%CI, 0.67–0.98; $I^2 = 44\%$) and when taking only postdiagnosis diet into account (RR, 0.77; 95%CI, 0.60–0.99; $I^2 = 56\%$). Conversely, the highest category of adherence to a Western dietary pattern was associated with increased risk of overall mortality (RR, 1.46; 95%CI, 1.27–1.68; $I^2 = 0\%$), which could also be found when synthesizing data of postdiagnosis Western dietary pattern only (RR, 1.51; 95%CI, 1.24–1.85; $I^2 = 17\%$) (Figure 3[27,35–41] and Table 2).

Cancer recurrence

When data for pre- and postdiagnosis levels of alcohol consumption were combined, an increased risk of cancer recurrence was found (RR, 1.17; 95%CI, 1.05–1.31; $I^2 = 38\%$). When only data for postdiagnosis alcohol intake were retained in the analysis, the results remained unchanged (RR, 1.31; 95%CI, 1.04–1.66; $I^2 = 54\%$). No significant associations between cancer recurrence and vegetable or tea intake could be observed. The intake of other food groups such as fruit, dairy, and coffee could not be meta-analyzed because of the limited number of eligible studies (minimum of 3) (Table 3).

The highest category of adherence to a prudent/healthy dietary pattern was not associated with cancer recurrence when compared with the lowest category of adherence (RR, 0.87; 95%CI, 0.68–1.11; $I^2 = 24\%$). These results were confirmed when the postdiagnosis pattern was analyzed (RR, 0.94; 95%CI, 0.71–1.24; $I^2 = 19\%$). Moreover, the Western dietary patterns were not associated with any significant effects on cancer recurrence data (RR, 1.21; 95%CI, 0.69–2.13; $I^2 = 81\%$) (postdiagnosis: RR, 1.34; 95%CI, 0.61–2.92; $I^2 = 85\%$) (Table 3).

Subgroup analyses for types of cancer

Breast cancer. No evidence of an association with overall mortality was observed for individual foods, including fruits, vegetables, dairy, meat, and alcohol. Adherence to high diet-quality indices and a prudent/healthy dietary pattern was associated with a reduced risk of overall mortality ([diet-quality indices: RR, 0.74; 95%CI, 0.60–0.90; $I^2 = 6\%$] [prudent/healthy dietary pattern: RR, 0.76; 95%CI, 0.60–0.95; $I^2 = 4\%$]) among breast cancer survivors. In contrast, high adherence to a Western dietary pattern was associated with an increased overall mortality risk among breast cancer survivors (RR, 1.44; 95%CI, 1.17–1.77; $I^2 = 0\%$). Moreover, alcohol intake was associated with increased risk of breast cancer recurrence (RR, 1.21; 95%CI, 1.06–1.39; $I^2 = 23\%$).

Other cancers. A Western dietary pattern (RR, 1.55; 95%CI, 1.13–2.13; $I^2 = 35\%$) was associated with an increased risk of overall mortality among colorectal cancer survivors. Higher intakes of alcohol were associated with increased mortality rates among survivors of hepatocellular carcinoma (RR, 1.21; 95%CI, 1.07–1.36;

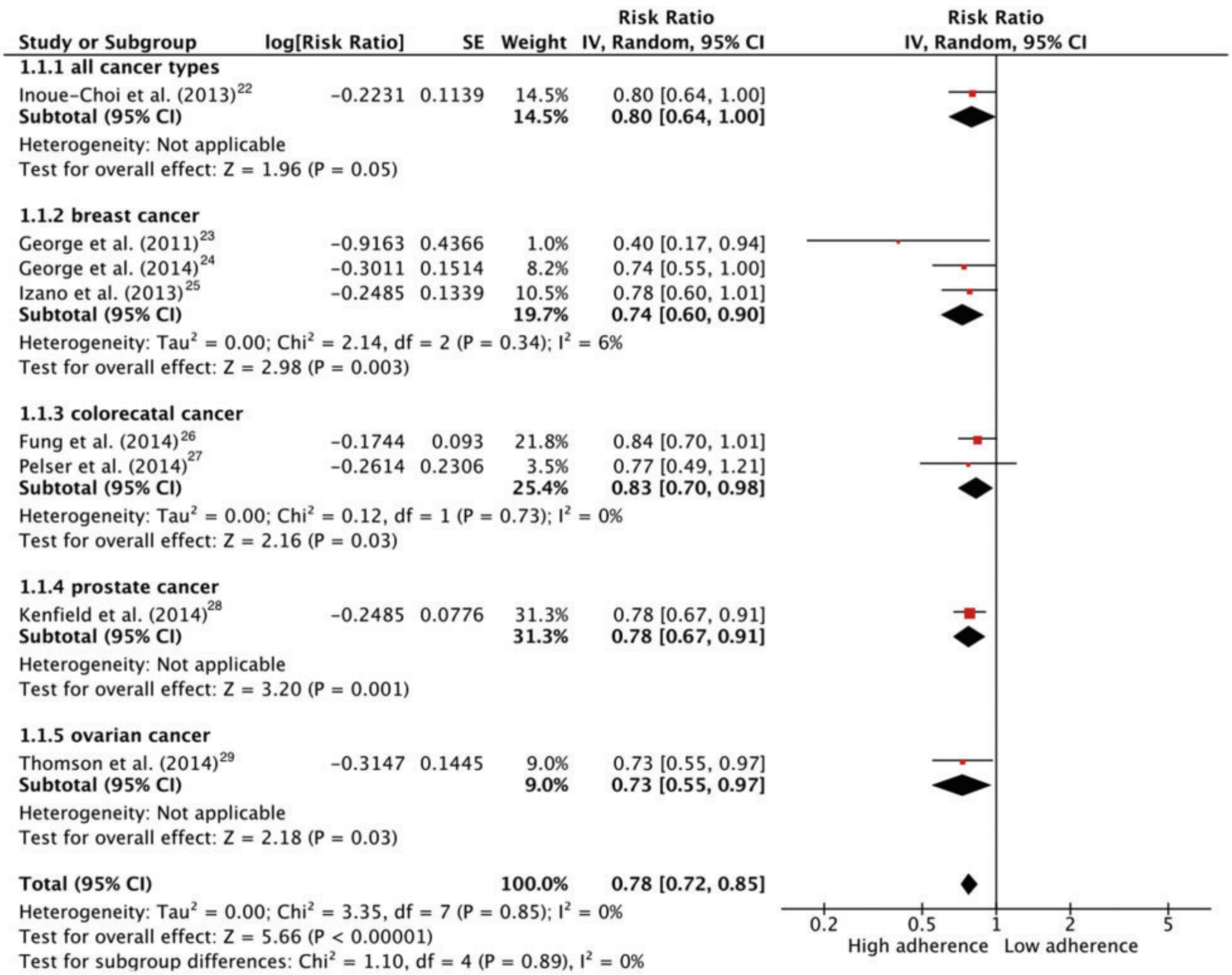

Figure 2 **Forest plot showing pooled risk ratios (RRs) with 95%CIs for overall risk of mortality when comparing the highest vs the lowest category of adherence to diet-quality indices.** *Abbreviations*: I^2, inconsistency; SE, standard error; tau, estimate between study variance.

$I^2 = 0\%$), non-Hodgkin lymphoma (RR, 1.33; 95%CI, 1.10–1.63; $I^2 = 46\%$), laryngeal and pharyngeal cancer (RR, 1.48; 95%CI, 1.08–2.02; $I^2 = 49\%$), and head and neck cancer (RR, 1.39; 95%CI, 1.10–1.76; $I^2 = 53\%$).

Subgroup analyses for adjustment factors and effect measures

Overall, 71% (for diet-quality indices/dietary patterns), 29% (for foods), and 32% (for beverages) of the included studies were adjusted for cancer stage and treatment. A subgroup analysis of only these studies confirmed the primary results that showed associations of diet-quality indices and dietary patterns with overall mortality and cancer recurrence as well as the association between alcohol intake and cancer recurrence. On the other hand, the significant associations between vegetable and alcohol intake and overall mortality shown in the main analysis could not be confirmed (data not shown). Additionally, a subgroup analysis that included only studies that reported hazard ratios as effect estimates (96 of 112 studies) was performed. All results of the main analysis could be confirmed except the significant inverse association between adherence to a prudent/healthy dietary pattern and overall mortality (data not shown).

Small-study effects and publication bias

The Egger's linear regression test was performed for overall mortality as well as for the following exposures: pre- and postdiagnosis intakes of fruits, vegetables, meat, and alcohol. There was no evidence of small-study effects of alcohol intake ($P = 0.716$) on risk of cancer recurrence or of fruit intake ($P = 0.112$), vegetable intake ($P = 0.266$), dairy intake ($P = 0.961$), or

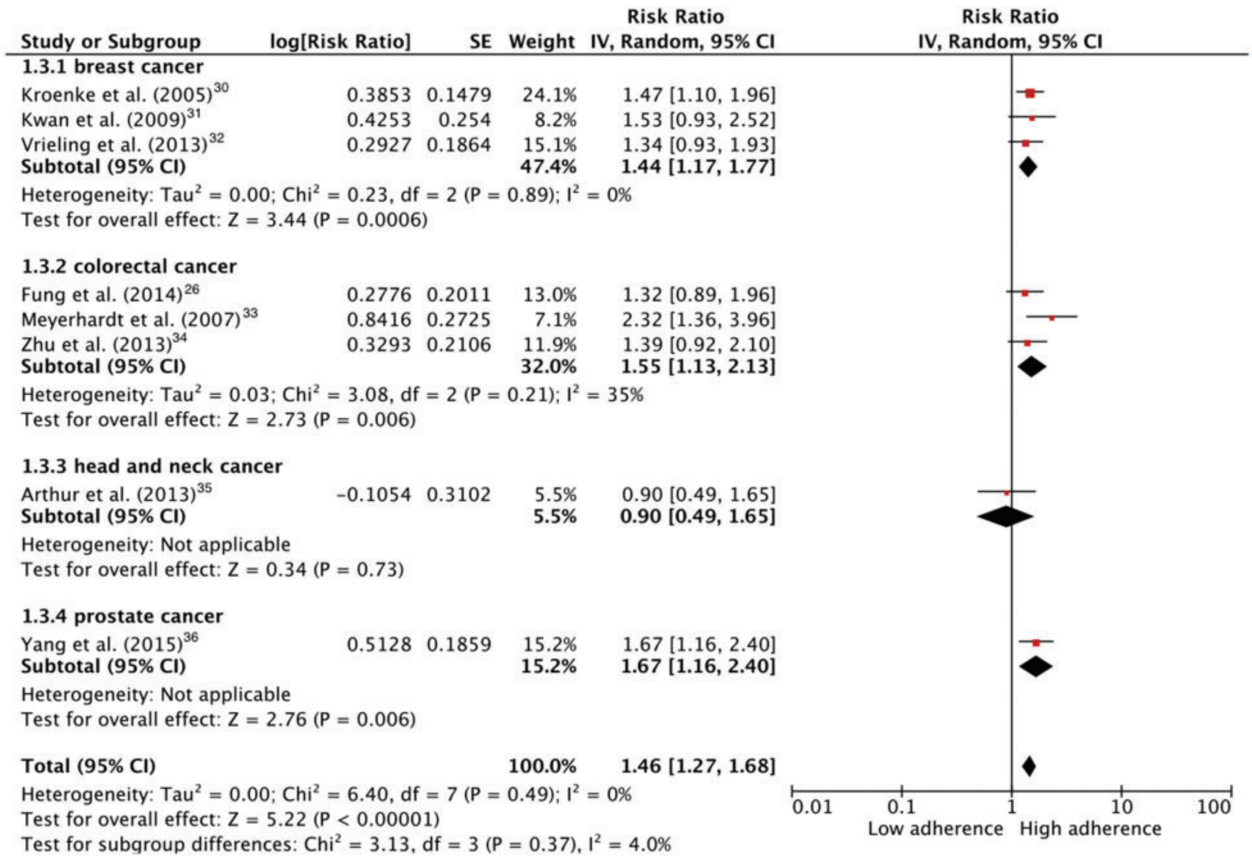

Figure 3 **Forest plot showing pooled risk ratios (RRs) with 95%CIs for overall risk of mortality when comparing the highest vs the lowest category of adherence to a Western dietary pattern.** *Abbreviations*: I^2, inconsistency; SE, standard error; tau, estimate between study variance.

meat intake ($P = 0.520$) on overall mortality. However, a potential risk of bias for alcohol consumption ($P = 0.002$) and overall mortality was observed.

The funnel plots for associations between risk of overall mortality and intakes of fruit, vegetable, dairy, and meat indicate little asymmetry, and the plot for alcohol intake indicates moderate asymmetry, suggesting that small-study effects cannot be completely excluded as a factor of influence in the present meta-analysis (see Figures S29–S34 in the Supporting Information online). Assessment of the contour-enhanced funnel plots suggests that the asymmetry observed is more likely caused by factors other than publication bias (Figures S35–S40 in the Supporting Information online).

DISCUSSION

In summary, higher diet-quality indices and prudent/healthy dietary patterns were associated with a decreased risk of mortality in cancer survivors, whereas Western dietary patterns resulted in the opposite outcome. The food groups of vegetables and fish were associated with lower mortality, while alcohol consumption was associated with higher mortality. In breast cancer survivors, higher adherence to diet-quality indices and prudent/healthy dietary patterns were associated with a decreased risk of overall mortality, but higher fruit and vegetable intakes were not. Similarly, Western dietary patterns were associated with increased risk of mortality in breast cancer and colorectal cancer survivors, but meat consumption was not. The number of studies assessing cancer recurrence was low, but 1 study suggests that a Western dietary pattern is associated with an increased risk of cancer recurrence among colorectal cancer survivors.[38] Finally, consumption of alcoholic beverages was associated with an increased risk of cancer recurrence. This association was also seen among breast cancer survivors and in postdiagnosis alcohol intake.

With increasing numbers of cancer patients, a growing willingness of patients to participate in check-up screenings, and technical improvements in diagnostic and therapeutic tools, it is reasonable to speculate that the number of cancer survivors will increase.[1,2,42] In this context, lifestyle measures will gain importance because they represent an option for patients to make self-controlled decisions. In addition, a switch to a healthier lifestyle can be expected to have benefits even if the lifestyle change takes place after the onset of disease. It is thus critical to provide evidence-based recommendations for cancer patients to prevent unsuitable or even deleterious lifestyle practices in this population.

Classification of the various dietary indices and patterns into their respective components results in a number of food groups. The constituents of these food groups might, at least in part, explain the biochemical mechanisms by which the dietary matrices affect tumor pathogenesis. For example, dietary patterns associated with beneficial effects are regularly high in antioxidants (eg, a prudent or healthy pattern high in olive oil, fruits and vegetables, and fish contains phenolic compounds, flavonoids, and n-3 fatty acids) or dietary fiber. On the other hand, a Western diet is high in food groups with potentially detrimental ingredients, eg, red and processed meats, which contain nitrite and nitrate or proinflammatory fatty acids.[43] High consumption of fruit, vegetables, fish, and whole-grain products has usually been associated with a reduced risk of chronic diseases,[44–47] while abundant consumption of red meat was associated with poor outcomes of colorectal cancer.[48] Inconsistent results have been reported for dairy product consumption and risk of prostate cancer, presumably due to differences in the type of product and source of calcium.[49] Consumption of alcoholic beverages has been reported to be associated with increased incidence rates of cancers of the mouth, larynx, pharynx, esophagus, liver, and colon/rectum as well as with pre- and postmenopausal breast cancer.[50]

Another distinctive feature of this systematic review is the separate evaluation of postdiagnosis subgroups whenever a sufficient amount of data was available. With respect to overall mortality, subgroup analyses confirmed the main results (pre- and postdiagnosis results combined) obtained for diet-quality indices, prudent/healthy dietary patterns, and Western dietary patterns. This shows that the overall results (pre-and postcancer exposures combined) can be used to support lifestyle changes after a diagnosis of cancer.

This review has several strengths (inclusion of a large number of studies and patients, focus on cancer survivors, analyses of postdiagnosis data and cancer recurrence), as well some limitations. The present analyses are based exclusively on cohort studies. Cohort study designs have disadvantages such as unproven across-group gradients in intake because of bias in dietary estimates and confounding caused by other risk factors.[51,52] Sometimes, the number of studies was rather small (especially for studies of cancer recurrence, specific cancer sites, and postdiagnosis dietary assessment). Independent of the power of individual studies, there was – to some extent – high heterogeneity between the different studies (see I^2 values in Tables 1 and 2). This can be explained by several reasons, such as differences in sex and age of participants; time point of diagnosis; types of cancer; and diet-quality indices.

The fact that different diet-quality indices were summarized into one category might pose a problem, particularly since some of these indices are not assessed by standardized methods (eg, different scores for adherence to a Mediterranean diet). However, all of these indices rely on a combination of potentially protective food groups. It is therefore unlikely that the benefit indicated by the resulting effect estimate is attenuated by a single detrimental index. Special attention might be required for the Mediterranean diet, which was shown to exert favorable effects on tumor incidence and mortality in a number of studies.[7] Usually, however, the highest scores for adherence to this type of diet can only be obtained with moderate alcohol consumption. Given the inconsistent results of studies investigating the effects of moderate alcohol intake on cancer,[53,54] recommending alcohol consumption even in small quantities might not be sensible.

An important distinction of the studies is the point during the course of disease at which diet was measured. Most of the included studies analyzed the prediagnosis diet. However, the potential of the postdiagnosis diet to improve survival is of particular interest to cancer survivors.

The development of tumors on different locations is a highly heterogeneous process, and even the pathogenesis of cancer at the same site can vary considerably. Heterogeneity in study design and participant characteristics made it especially difficult to identify clinical factors with an important impact on survival and cancer recurrence when various studies were synthesized. The stage of cancer diagnosis has been recognized as an important factor of disease progression. Patients with tumors diagnosed at an earlier stage show higher survival rates.[55,56] The treatment method and type of hospital can also greatly influence the outcome.[57] Similarly, age and comorbidity could also be relevant predictors of survival in some types of cancer.[58] Nevertheless, most studies included in the present analyses adjusted at least for age, tumor stage, and treatment method.

Despite the advantages offered by a large number of studies and cancer occurrences, different populations are exposed to different potential risks and/or protective factors. Likewise, dietary habits and dietary patterns differ between populations. In the present analysis, most of the data summarized are from studies of US populations (55 studies), followed by studies of European populations (33 studies) and Asian populations (21 studies), with the remaining 9 studies conducted in populations in Canada, Australia, or other countries). With a higher proportion of US populations and an underrepresentation of other populations, such as those from South America and Africa, the results of this review were weighted more heavily toward the US population. Furthermore, sociopolitical factors might have an effect on outcome, too. For instance, the health insurance system can be a predicting factor for the stage at which cancer is diagnosed and the treatment options available.[59]

CONCLUSION

This systematic review and meta-analysis of cohort studies suggests that adherence to a healthy dietary pattern (assessed predominantly prior to cancer diagnosis) is inversely associated with overall mortality, whereas an unhealthy Western dietary pattern is positively associated with risk of overall mortality among cancer survivors. More research is warranted to assess the role of postdiagnosis diet in cancer survival and site-specific cancer recurrence.

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SUPPORTING INFORMATION

The following Supporting Information is available through the online version of this article at the publisher's website.

Table S1 **Full-text articles excluded, with reasons**

Table S2 **Characteristics of the cohort studies included in the present meta-analysis by type of exposure (dietary patterns, food groups, beverages)**

Figure S1 **Forest plot showing pooled risk ratios (RRs) with 95%CIs for overall mortality risk comparing the highest vs lowest adherence to prudent/healthy dietary pattern category.**

Figures S2–S12 **Forest plots showing pooled risk ratios (RRs) with 95%CIs for overall mortality risk comparing the highest vs lowest intake category of different food and beverage groups**.

Figures S13–S14 **Forest plots showing pooled risk ratios (RRs) with 95%CIs for cancer recurrence comparing the highest vs lowest adherence to dietary patterns**.

Figures S15–S17 **Forest plots showing pooled risk ratios (RRs) with 95%CIs for cancer recurrence comparing the highest vs lowest intake category of different food and beverage groups**.

Figures S18–S20 **Forest plots showing pooled risk ratios (RRs) with 95%CIs for overall mortality comparing the highest vs lowest postdiagnosis adherence to diet-quality indices and dietary patterns**.

Figures S21–S25 **Forest plots showing pooled risk ratios (RRs) with 95%CIs for overall mortality comparing the highest vs lowest postdiagnosis intake category of different food and beverage groups**.

Figures S26–S27 **Forest plots showing pooled risk ratios (RRs) with 95%CIs for cancer recurrence comparing the highest vs lowest postdiagnosis adherence to dietary patterns**.

Figure S28 **Forest plot showing pooled risk ratios (RRs) with 95%CIs for cancer recurrence comparing the highest vs lowest postdiagnosis alcohol intake category**.

Figures S29–S33 **Funnel plots showing study precision against the relative risk with 95%CIs for intake of different food and beverage groups and overall mortality**.

Figure S34 **Funnel plot showing study precision against the relative risk with 95%CIs for alcohol intake and cancer recurrence**.

Figures S35–S39 **Contour-funnel plots showing study precision against the relative risk with 95%CIs for**

intake of different food and beverage groups and overall mortality.

Figure S40 **Contour-funnel plot showing study precision against the relative risk with 95%CIs for alcohol intake and cancer recurrence**.

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