

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	The impact of dietary patterns and the main food groups on mortality and recurrence in cancer survivors: a systematic review of current epidemiological literature
AUTHORS	Jochems, Sylvia; Van Osch, Frits; Bryan, Richard; Wesselius, Anke; van Schooten, Frederik; Cheng, Kar Keung; Zeegers, Maurice

VERSION 1 – REVIEW

REVIEWER	Marji McCullough, ScD American Cancer Society, USA
REVIEW RETURNED	03-Nov-2016

GENERAL COMMENTS	<p>This is an ambitious review on dietary factors and mortality in cancer survivors, including cancer types with a 50% or greater 5-year survival rate. The results underscore the limited and inconsistent evidence on diet and mortality in cancer survivors, and highlight the need for more research. Methodological diversity across studies precluded meta-analyses. Strengths of this paper are the adherence to protocols for literature reviews, and summaries of the evidence in Tables which will provide a helpful single resource. However, because the analysis focused on foods and data-driven diet pattern analysis (the rationale for this was not clear), and did not include nutrients or a priori diet scores, conclusions drawn do not cover all of "diet". Suggest that the authors consider including these exposures or at least diet scores so that "foods and diet patterns" can be the focus. Alternatively, the authors would need to make clear what is not covered. Recurrence would also be a useful outcome to evaluate; it is not clear whether that is feasible in one paper, but it is of interest to patients and clinicians.</p> <p>Additional minor suggestions: Page 4, line 12: Do the authors mean "aberrations" or "alterations"? Line 21: Should "susceptible" be "responsive"? Line 30: Please check if WCRF made this determination in 2007 (not 2012). Suggest referencing the 2014 WCRF CUP for breast cancer survivors. This also adds to the rationale to conduct this review (no convincing or probable risk factors for mortality from breast cancer or other causes were identified). Line 50: Only data-driven methods are used for diet patterns (except the Mediterranean diet is assessed by diet score). As above, suggest adding diet scores to the list of diet patterns studies reviewed. Methods: Note that nutrients are not reviewed, and clarify what is meant by "red (processed)". Did the authors review red unprocessed meats, as well as processed meats?</p>
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	<p>Page 8, line 32: The number of studies on diet and prostate cancer survival seems low (n=3), given various studies on tomatoes, meat, etc. There was a recent literature review on diet and lifestyle and prostate cancer progression and mortality (2016 World J Urol, online only).</p> <p>Page 19, line 16: suggest “an adverse” or “positive association”</p> <p>Page 22, line 10: with “surgically” treated cancers?</p> <p>Discussion: Page 25, line 16. Why “compelling”?</p> <p>The purpose of the 2nd - 4th paragraph of the discussion is unclear, as the sections starting with 4.1 interpret the findings of the review. The tally of studies would be better in Results.</p> <p>Page 26 line 25: This section can be updated if the review is expanded to include all diet scores. Also, please describe the DietCompLyf study.</p> <p>Page 28, line 5: suggest adding “prostate” ... cancer development. In section 4 in general, there should be more integration of the study findings in this discussion.</p> <p>Page 31, section 4.10: This paragraph provides interesting rationale for the approach of this SLR; consider putting some of this up front.</p> <p>Page 32, line 26: suggest “hundreds or thousands.”</p> <p>Page 33, last paragraph: it is unclear what is meant by making sure that “preliminary” findings of individual studies reach cancer survivors (versus, evidence based guidelines process).</p> <p>In the Summary Table on diet patterns, please make sure to indicate which diet pattern (e.g. Prudent or Mediterranean) RRs are being presented.</p>
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REVIEWER	Allison Hodge Cancer council Victoria, Australia
REVIEW RETURNED	18-Nov-2016

GENERAL COMMENTS	<p>Diet and mortality in cancer survivors</p> <p>This is clearly an important area of research and the authors have covered a wide range of studies in their review. I have not carefully assessed whether the search strategy missed relevant papers but it looks very detailed. Overall I found the manuscript hard to follow and the actual findings were not clearly described. A clear statement summarising the results to underpin future recommendations for cancer survivors is missing.</p> <ol style="list-style-type: none"> 1. In the abstract objective ‘dietary intake’ is too vague, it would be better if the specific aspects of diet to be studied were described. 2. Abstract conclusion – the current review did not find much on which to base recommendations but why review dietary constituents and micronutrients? How does that conclusion arise from current work? 3. The summarized strengths and limitations under abstract are not useful. Is the first one a strength or a limitation? Because the ‘dietary intake’ to be studied has not been defined this point is also unclear. The second point is obviously a limitation but should be explained in a bit more detail by mentioning that RCTs if practical would be better evidence. The last point is also unclear as this is the first time that food groups and dietary patterns have been mentioned. 4. Top of page 4 ‘epigenetic abbreviations’ is not right. 5. Para 2, page 4. ‘Susceptible sounds like being at risk of a disease, maybe receptive to health promotion/education to improve diet.
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	<p>The study suggesting cancer survivors had poorer diets than other individuals could be explained in a bit more depth.</p> <p>6. Given that WCRF/AICR experts could not find enough evidence to make recommendations for cancer survivors it would be relevant to make a comment somewhere about what new evidence you found and reviewed.</p> <p>7. A better explanation of why the dietary exposures were chosen is required. Why data driven dietary patterns rather than indices? Many of the dietary patterns listed on page 6 as being included in the search are unlikely to be found in a posteriori dietary patterns. Also the patterns are not likely to be consistent across studies even if some similar characteristics. Why weren't grains/cereals or legumes included in the list of food groups?</p> <p>8. Did the RCTs use factor analysis to analyse diet?</p> <p>9. Even if you cannot conduct meta-analysis it would be good to summarize at the end of each section. Eg for the breast cancer RCTs the low fat intervention diets did not show any benefit in mortality. For bowel cancer and prudent diet, three studies found no association, that is what we need to know.</p> <p>10. The first paragraph of the discussion should summarise findings. Can you say anything from the studies reviewed? Hard to see what was 'compelling'.</p> <p>11. The discussion is not well organised, either put all studies on similar dietary exposure together or on same cancer. The second para on page 25 goes from alcohol and bowel cancer to fruit and veg and breast cancer.</p> <p>12. The para starting 'Regarding dietary patterns...' at the bottom of page 25 describes a few studies but does not even mention whether the dietary patterns were related to the outcomes.</p> <p>13. Bottom of page 26 'portions' does not seem to be the right word.</p> <p>14. The discussion does not relate to the findings, for example section 4.3 about red meat does not even mention the current findings.</p> <p>15. Table 4 notes that the outcome is overall or cancer specific mortality whereas other tables are not specific. This is probably important because even if diet does not relate to cancer outcomes there is good evidence that diet is related to other causes of mortality, in particular CVD.</p> <p>16. In section 4.7 an association between vitamin D and bowel cancer survival is noted. There are also several studies providing evidence for this in breast cancer survivors, for example Maalmi et al Eur J Cancer 2014 (50)1510-1521 concludes that higher 25(OH)D were associated with reduced mortality in patients with colorectal and breast cancer.</p> <p>17. Section 4.9 does not relate to anything that has been studied. No doubt cancer survivors need better information but that is not part of the current research. Cannot provide better information until more studies are done and more evidence is available.</p> <p>18. Strengths and weaknesses could be better presented. If examining dietary patterns is strength, say that. The sentence about encouraging survivors to adhere to an overall healthy and balanced diet does not fit here. If not using RCTs is a weakness say that. Small changes like increasing amounts of fruit and vegetables and reducing meat and alcohol are not part of the strengths and weaknesses and there is no statement in the results that actually supports this as a recommendation. Then you go on to talk about studies of diet during treatment which does not relate to strengths and weaknesses at all. The use of FFQs in all the reviewed studies is more of a weakness as these are associated with considerable measurement error,</p>
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	<p>despite being the most practical method for many studies. Is the paragraph starting with heterogeneity between studies part of strengths and weaknesses?</p> <p>19. The conclusion doesn't match with the results. Still no clear statement of what was found re diet and mortality for different types of cancer.</p>
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REVIEWER	Minmin, Zhu Shenzhen Nanshan Center for Chronic Disease Control, China
REVIEW RETURNED	15-Mar-2017

GENERAL COMMENTS	<p>This systematic review provides an evaluation of studies addressing the relationship between dietary patterns and food groups intake and mortality among different groups of survivors. The paper provide a clear search strategy and was written in good logical and English language. Some minor reminders:</p> <ol style="list-style-type: none"> 1. In the RISMA Flow Diagram, detailed reasons for records and full-text articles exclusion should be mentioned; 2. The results of dietary patterns was not well showed in the abstract and not well discussed in the discussion section: <ol style="list-style-type: none"> a) For post-diagnosis dietary pattern and mortality: there are two study showed that prudent/Mediterranean diet was associated with decreased overall mortality, i.e. in Kenfield (2014) study HR= 0.78; 95% CI 0.67-0.90, and in study of Yang (2015) RR= 0.64; 95% CI 0.44-0.93 (p for trend = 0.02) (please check, in text it was written as HR=0.64, but in Table S2 it is RR=0.64). b) In the section of discussion for the dietary pattern, only two RCT trails were referred, not contain the observe studies, such as the above two. 3. Is there any study consider the association between "dietary changes" after a successful cancer treatment and mortality, not only just the pre- or post-treatment diet?
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REVIEWER	Lukas Schwingshackl German Institute of Human Nutrition Germany no conflict of interest
REVIEW RETURNED	27-Mar-2017

GENERAL COMMENTS	<p>Thank you very much for the opportunity to review this interesting paper entitled: "The impact of diet on mortality in cancer survivors: A systematic review of current epidemiological literature. "</p> <p>The authors included 58 observational studies and 2 RCTs, and concluded that the evidence is too limited whether dietary behaviour prior to or after diagnosis could influence mortality among cancer survivors.</p> <p>Although the topic is of general interest, I have several comments to improve the quality of the systematic review:</p> <p>Major:</p> <p>The paper is quite long; please consider shortening by approximately 25% (mainly Results section)</p> <p>Please update the search;</p> <p>There are several studies</p>
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	<p>Please consider to perform a meta-analysis if a least 3 studies are available for a dietary pattern within a specific cancer type (ie. Bowel cancer and prudent dietary pattern; similar for breast cancer,...)</p> <p>Minor:</p> <p>Abstract</p> <p>Objectives: be more specific; what does dietary intake mean? Dietary pattern, food groups, foods, nutrients, beverages, dietary supplements?</p> <p>Design: add the name of the tool for the assessment of study quality</p> <p>Introduction</p> <p>Please consider the following references by adding a sentence focusing on dietary pattern/ diet quality indices: PMID: 25680825, 24476641, 26471010</p> <p>There is a recent meta-analysis (27864535) investigating the association between dietary factors and all-cause mortality among cancer survivors, please elaborate the 3rd paragraph of the Introduction</p> <p>Please be more specific: what types of observational studies? (prospective cohort studies, case-control studies, case-cohort studies, nested case-control studies, RCTs can be also analyzed as observational studies)</p> <p>Methods</p> <p>Please add full search strategy</p> <p>Why studies based on a priori dietary pattern (investigator driven methods) were excluded? Why than Mediterranean diet was than included, if diet quality indices were excluded (sorry this makes no sense)</p> <p>Why you did not include the food group: whole grains?</p> <p>What about food records?</p> <p>Please add the study protocol as supplementary file</p> <p>Results</p> <p>You mean clinical or statistical heterogeneity</p> <p>Please add a Table (supplementary material) with the risk of bias for each study. Please explain what tool do you applied for the assessment of study quality among observational studies</p> <p>If you are talking about observational cohort study; please rename: prospective cohort</p> <p>Last sentence for bladder cancer paragraph could be removed</p>
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REVIEWER	Gordon H. Guyatt Department of Health Research Methods, Evidence, and Impact, McMaster University, Canada
REVIEW RETURNED	13-Apr-2017

GENERAL COMMENTS	<p>Major points:</p> <p>1) The reviewers state that they used GRADE methods, but they seem to have done so in a cursory way and do not appear to have followed GRADE guidance. The only relevant statement is “The quality level of the body of evidence of the included studies was rated ‘low’ to ‘moderate’ by two of the authors (SJ and FvO) when applying the grading system developed by the GRADE collaboration.”</p> <p>A) For the two RCTs we see no reason the authors do not pool the results. The authors do not provide a specific rating of quality/certainty of the evidence except as quoted above.</p>
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	<p>Assuming there is no problem with risk of bias, indirectness, or publication bias the result appear to provide moderate quality evidence (consistent results with wide confidence intervals). This should be highlighted, with the conclusion that the impact of fat reduction remains uncertain (confidence intervals will include an appreciable relative risk reduction). These findings, the highest quality evidence in the review, are worth highlighting.</p> <p>B) The authors do not present appropriate ratings of evidence for the observational studies. From what we can gather, all the evidence is of very low quality (observational studies start as low quality and given the authors' statement "The great heterogeneity amongst the included studies let to the decision of conducting a systematic review only and no meta-analysis" it appears that they should be rated down further for inconsistency.</p> <p>C) Providing an evidence profile for each question addressed would be very helpful in sorting out how the authors applied GRADE. Because the level of confidence associated with very low, low, and moderate GRADE certainty ratings differ, doing so will improve the interpretability of the results presented. Additionally, presenting GRADE ratings will make explicit and transparent the authors' reasoning for rating up/down the quality of evidence.</p> <p>D) Ultimately, the quality of evidence for each question should be included in the abstract.</p> <p>2) The authors assessment of risk of bias seems as superficial as their use of GRADE. The only statement they make is "All 58 observational studies had an acceptable risk of bias according to the Cochrane Collaboration risk of bias assessment tool". This would be an extraordinary result – no variability in risk of bias across 58 studies. We recommend the authors consider presenting individual risk of bias assessments for each study in an appendix. Although the table would large and cumbersome to synthesize, this information can be valuable to readers, whose confidence in the results of the studies may differ depending on the domains that were rated down. The authors may choose to present a modified version of the ROBINS-I tool, given its length. For example, they may choose to only focus on domains they consider to be of critical importance to the interpretation of the results. Alternatively, for each comparison, the authors may consider presenting the proportion of studies that were at high/low/unclear risk of bias in each domain of the risk of bias tool. If they end up telling us that all studies were rated identically, we would question the rigor with which they applied the instrument.</p> <p>3) Given the heterogeneity that exists in common cancers, further clinical and molecular characteristics (e.g., ductal or lobular and receptor status for breast cancer) of the cancers studied should be reported, if the information is available from the primary papers.</p> <p>4) The authors' statement in the abstract ("Multivitamin supplement use and fruit and vegetable consumption do not appear to improve breast cancer survivors' mortality. Other studies addressing diet and mortality amongst groups of cancer survivors were too limited or could not be identified") is inconsistent with their statement in the discussion (Nevertheless, small changes like increasing the amounts of fruit and vegetables and reducing the consumption of meat and alcohol in the diet are feasible goals and should be highly considered based on the results identified").</p>
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	<p>Minor points:</p> <p>5) P. 5, line 14: It is unclear whether title and abstract screening was also undertaken in duplicate.</p> <p>6) Given that GRADE considers rating up the evidence when a dose-response relationship is evident in observational studies, were data also abstracted for dose-response analyses or only high vs. low? If data were also abstracted for dose-response analyses, this information could be included in the evidence profiles</p> <p>7) P. 6, line 21 seems to suggest that only processed red meat was studied. This can be corrected to indicate that both processed and unprocessed red meat was studied.</p> <p>8) P. 8 line 14: 'let' should be corrected to 'led.'</p> <p>9) P. 33, line 23-25: The advantages of FFQs are overstated. We recommend the authors to also discuss limitations with this approach of measuring diet.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Marji McCullough, ScD
 Institution and Country: American Cancer Society, USA
 Please state any competing interests: None declared

Please leave your comments for the authors below

See attachment

Note that my "no's" on the score sheet referred to For 9) that the review should be expanded to include other diet patterns and 11) And that the discussion should emphasize more of what was found in the review.

BMJ Open: The impact of diet on mortality in cancer survivors: A systematic review of current epidemiological literature

Comment: This is an ambitious review on dietary factors and mortality in cancer survivors, including cancer types with a 50% or greater 5-year survival rate. The results underscore the limited and inconsistent evidence on diet and mortality in cancer survivors, and highlight the need for more research. Methodological diversity across studies precluded meta-analyses. Strengths of this paper are the adherence to protocols for literature reviews, and summaries of the evidence in Tables which will provide a helpful single resource. However, because the analysis focused on foods and data-driven diet pattern analysis (the rationale for this was not clear), and did not include nutrients or a priori diet scores, conclusions drawn do not cover all of "diet". Suggest that the authors consider including these exposures or at least diet scores so that "foods and diet patterns" can be the focus. Alternatively, the authors would need to make clear what is not covered. Recurrence would also be a useful outcome to evaluate; it is not clear whether that is feasible in one paper, but it is of interest to patients and clinicians.

Response: We thank the Reviewer for her positive and insightful comments.

We have now included cancer recurrence as an outcome and dietary indices as an exposure. The word 'diet' is adjusted throughout the paper to specify dietary patterns/indices, foods and beverages. The rationale for the inclusion whole foods, and not nutrients, is that traditional analyses in nutritional epidemiology typically examine diseases in relation to a single or a few nutrients or foods. Although the role of cancer in relation to a single or a few nutrients has been quite valuable, it has several conceptual and methodological limitations: people do not eat isolated nutrients, they eat a variety of foods with complex combinations of nutrients that are likely to be interactive. Furthermore, the correlation between some nutrients makes it difficult to examine their separate effects; the effect of a single nutrient may be too small to detect, but the cumulative effects of multiple nutrients included in a dietary pattern may be sufficiently large to be detectable [PMID: 11790957].

Additional minor suggestions:

Comment: Page 4, line 12: Do the authors mean "aberrations" or "alterations"?

Response: We changed the word to aberrations

Comment: Line 21: Should "susceptible" be "responsive"?

Response: We changed the word to responsive

Comment; Line 30: Please check if WCRF made this determination in 2007 (not 2012). Indeed, experts from the WCRF made this determination in 2007 and experts of the American Institute for Cancer Research made this determination in 2012. The sentence is removed from the introduction and replaced by a more fitted reference to the CUP report investigating diet among breast cancer survivors, as you suggest in your next comment

Suggest referencing the 2014 WCRF CUP for breast cancer survivors. This also adds to the rationale to conduct this review (no convincing or probable risk factors for mortality from breast cancer or other causes were identified).

Response: See the previous answer

Comment: Line 50: Only data-driven methods are used for diet patterns (except the Mediterranean diet is assessed by diet score). As above, suggest adding diet scores to the list of diet patterns studies reviewed.

Response: Diet scores are added to the review

Comment: Methods: Note that nutrients are not reviewed

Response: Nutrients are not added for the reason given

Comment: And clarify what is meant by "red (processed)". Did the authors review red unprocessed meats, as well as processed meats?

Response: The term 'red (processed)' is adjusted to 'red', and for each study investigating meat intake it is clearly described if it was red and/or processed

Comment: Page 8, line 32: The number of studies on diet and prostate cancer survival seems low (n=3), given various studies on tomatoes, meat, etc. There was a recent literature review on diet and lifestyle and prostate cancer progression and mortality (2016 World J Urol, online only).

Response: I refer to the literature review that you mention. For our initial objective, considering only mortality as an outcome and whole diets and foods and beverages as exposure, there are no more studies summarised in that literature review that we could add. However, now that we have added cancer recurrence to our review, there are additional studies that we have added.

Comment: Page 19, line 16: suggest “an adverse” or “positive association”

Response: We adjusted it to ‘positive association’

Comment: Page 22, line 10: with “surgically” treated cancers?

Response: Yes, the patients in that specific study were ‘surgically’ treated cancers. We added the word ‘surgically’ to the sentence

Comment: Discussion: Page 25, line 16. Why “compelling”?

Response: We used the word compelling to say even though the evidence is sparse, the studies that are conducted are promising. Nevertheless, we have rewritten the first part of the discussion to reduce the length of the review, as asked by other reviewers, and the sentence with the word compelling is removed

The purpose of the 2nd - 4th paragraph of the discussion is unclear, as the sections starting with 4.1 interpret the findings of the review. The tally of studies would be better in Results. The tally of studies has been removed from the discussion to the results section. I agree that summarising the results and then explaining them in detail is perhaps too lengthy. It has been moved to the Results section, as suggested.

Comment: Page 26 line 25: This section can be updated if the review is expanded to include all diet scores.

Response: The review is expanded to include all diet scores, and the section has been updated

Comment: Also, please describe the DietCompLyf study.

Response: We included this study as an example of a study with high potential to examine lifestyle behaviour in breast cancer survivors. The sentence with naming the dietcomplyf study is now deleted in the revised version of the manuscript

Comment: Page 28, line 5: suggest adding “prostate” ... cancer development.

Response: For dairy intake, there are studies from breast, colon and prostate cancer survivors

Comment: In section 4 in general, there should be more integration of the study findings in this discussion.

Response: There is now more integration of the study findings in the discussion

Comment: Page 31, section 4.10: This paragraph provides interesting rationale for the approach of this SLR; consider putting some of this up front.

Response: We moved some sentences from this paragraph to the introduction

Comment: Page 32, line 26: suggest “hundreds or thousands.”

Response: We changed it to ‘hundreds or thousands’

Comment: Page 33, last paragraph: it is unclear what is meant by making sure that “preliminary” findings of individual studies reach cancer survivors (versus, evidence based guidelines process).

Response: We used the word preliminary to say even though the evidence is sparse, the studies that are conducted are promising. Nevertheless, we have rewritten the discussion section to reduce the length of the review, as asked by other reviewers, and the sentence with the word preliminary is removed

Comment: In the Summary Table on diet patterns, please make sure to indicate which diet pattern (e.g. Prudent or Mediterranean) RRs are being presented.

Response: We made a clear indication for which dietary pattern the HR/RRs are presented in the summary table

Reviewer: 2

Reviewer Name: Allison Hodge

Institution and Country: Cancer council Victoria, Australia

Please state any competing interests: None declared

Please leave your comments for the authors below

Diet and mortality in cancer survivors

This is clearly an important area of research and the authors have covered a wide range of studies in their review. I have not carefully assessed whether the search strategy missed relevant papers but it looks very detailed. Overall I found the manuscript hard to follow and the actual findings were not clearly described.

A clear statement summarising the results to underpin future recommendations for cancer survivors is missing.

We thank the Reviewer for their insightful comments.

1. In the abstract objective ‘dietary intake’ is too vague, it would be better if the specific aspects of diet to be studied were described.

Response: We agree and have adjusted the term ‘dietary intake’ to dietary patterns/indices, foods and beverages

2. Abstract conclusion – the current review did not find much on which to base recommendations but why review dietary constituents and micronutrients? How does that conclusion arise from current work?

Response: One finding from our review is that there are only limited studies available to date in cancer survivors. We hope that our review shows the need for more research in this field and that the studies that are conducted until now on both dietary constituents and micronutrients together could be the start of new RCT or cohort studies in populations of cancer survivors.

3. The summarized strengths and limitations under abstract are not useful. Is the first one a strength or a limitation? Because the 'dietary intake' to be studied has not been defined this point is also unclear. The second point is obviously a limitation but should be explained in a bit more detail by mentioning that RCTs if practical would be better evidence. The last point is also unclear as this is the first time that food groups and dietary patterns have been mentioned.

Response: In our revised version, the term 'dietary intake' is described more specifically, and other amendments have been made, as suggested.

4. Top of page 4 'epigenetic abbreviations' is not right.

Response: We changed the word to aberrations

5. Para 2, page 4. 'Susceptible sounds like being at risk of a disease, maybe receptive to health promotion/education to improve diet. The study suggesting cancer survivors had poorer diets that other individuals could be explained in a bit more depth.

Response: We changed the word to responsive

6. Given that WCRF/AICR experts could not find enough evidence to make recommendations for cancer survivors it would be relevant to make a comment somewhere about what new evidence you found and reviewed.

Response: The WCRF/AICR stated that the amount of studies was too limited, but we think it is important that the few published studies regarding this topic are summarized in order to highlight the gaps in evidence and the need for further studies

7. A better explanation of why the dietary exposures were chosen is required. Why data driven dietary patterns rather than indices? Many of the dietary patterns listed on page 6 as being included in the search are unlikely to be found in a posteriori dietary patterns. Also the patterns are not likely to be consistent across studies even if some similar characteristics. Why weren't grains/cereals or legumes included in the list of food groups?

Response: Now we included all possible dietary pattern and diet scores and also grains/cereals and legumes as foods part of the main food groups and why we choose these

8. Did the RCTs use factor analysis to analyse diet?

Response: Yes they did

9. Even if you cannot conduct meta-analysis it would be good to summarize at the end of each section. Eg for the breast cancer RCTs the low fat intervention diets did not show any benefit in mortality. For bowel cancer and prudent diet, three studies found no association, that is what we need to know.

Response: I made summaries at the end of each section and reorganised the section by cancer type

10. The first paragraph of the discussion should summarise findings. Can you say anything from the studies reviewed? Hard to see what was 'compelling'.

Response: We have removed this sentence and have adjusted the first part of the discussion to summarise findings

11. The discussion is not well organised, either put all studies on similar dietary exposure together or on same cancer. The second para on page 25 goes from alcohol and bowel cancer to fruit and veg and breast cancer.

Response: At first we organised the discussion per dietary exposure. Now we reorganised the discussion per cancer type

12. The para starting 'Regarding dietary patterns...' at the bottom of page 25 describes a few studies but does not even mention whether the dietary patterns were related to the outcomes.

Response: We adjusted the section to discuss these studies in more detail

13. Bottom of page 26 'portions' does not seem to be the right word.

Response: We have changed the word to 'intake'

14. The discussion does not relate to the findings, for example section 4.3 about red meat does not even mention the current findings.

Response: Most studies find no association with meat intake, but we still wanted to describe why meat could increase mortality based on studies on cancer risk

15. Table 4 notes that the outcome is overall or cancer specific mortality whereas other tables are not specific. This is probably important because even if diet does not relate to cancer outcomes there is good evidence that diet is related to other causes of mortality, in particular CVD.

Response: All tables have the same outcomes mentioned

16. In section 4.7 an association between vitamin D and bowel cancer survival is noted. There are also several studies providing evidence for this in breast cancer survivors, for example Maalmi et al Eur J Cancer 2014 (50)1510-1521 concludes that higher 25(OH)D were associated with reduced mortality in patients with colorectal and breast cancer.

Response: Thank you for this suggestion, I have added it to the discussion

17. Section 4.9 does not relate to anything that has been studied. No doubt cancer survivors need better information but that is not part of the current research. Cannot provide better information until more studies are done and more evidence is available.

Response: With this section we wanted to stress the importance of more studies among cancer survivors. Nevertheless, it is correct that we cannot provide guidelines for cancer survivors based on this review, and therefore we have removed it

18. Strengths and weaknesses could be better presented. If examining dietary patterns is strength, say that. The sentence about encouraging survivors to adhere to an overall healthy and balanced diet does not fit here. If not using RCTs is a weakness say that. Small changes like increasing amounts of fruit and vegetables and reducing meat and alcohol are not part of the strengths and weaknesses and there is no statement in the results that actually supports this as a recommendation. Then you go on to talk about studies of diet during treatment which does not relate to strengths and weaknesses at all. The use of FFQs in all the reviewed studies is more of a weakness as these are associated with considerable measurement error, despite being the most practical method for many studies. Is the paragraph starting with heterogeneity between studies part of strengths and weaknesses?

Response: We reorganised the strength and weaknesses part of the discussion. We now state that dietary patterns are a strength, but only including two RCTs is a weakness. The statement on small changes in diet has been removed. The section concerning diet during treatment has been removed, the use of FFQs has been named as a weakness, and the section regarding heterogeneity is indeed moved to the strengths and weaknesses section

19. The conclusion doesn't match with the results. Still no clear statement of what was found re diet and mortality for different types of cancer.

Response: We adjusted the conclusion to

Reviewer: 3

Reviewer Name: Minmin, Zhu

Institution and Country: Shenzhen Nanshan Center for Chronic Disease Control, China

Please state any competing interests: None declared

Please leave your comments for the authors below

This systematic review provides an evaluation of studies addressing the relationship between dietary patterns and food groups intake and mortality among different groups of survivors. The paper provides a clear search strategy and was written in good logical and English language.

We thank the Reviewer for their positive and insightful comments.

Some minor reminders:

1. In the PRISMA Flow Diagram, detailed reasons for records and full-text articles exclusion should be mentioned;

Response: I adjusted the PRISMA flow diagram to include detailed reasons for exclusion

2. The results of dietary patterns was not well showed in the abstract and not well discussed in the discussion section:

a) For post-diagnosis dietary pattern and mortality: there are two study showed that prudent/Mediterranean diet was associated with decreased overall mortality, i.e. in Kenfield (2014) study HR= 0.78; 95% CI 0.67-0.90, and in study of Yang (2015) RR= 0.64; 95% CI 0.44-0.93 (p for trend = 0.02) (please check, in text it was written as HR=0.64, but in Table S2 it is RR=0.64).

Response: We adjusted the numbers in the review

b) In the section of discussion for the dietary pattern, only two RCT trails were referred, not contain the observe studies, such as the above two.

Response: We adjusted this part to include more details about the cohort studies as well

3. Is there any study consider the association between "dietary changes" after a successful cancer treatment and mortality, not only just the pre- or post-treatment diet?

Response: Yes, one study investigating the role of meat intake amongst bowel cancer survivors looked at both pre- and post-diagnosis intake and changes. These changes were however small and it is questionable whether any survivors really changed their meat intake.

Reviewer: 4

Reviewer Name: Lukas Schwingshackl

Institution and Country: German Institute of Human Nutrition, Germany

Please state any competing interests: no conflict of interest

Please leave your comments for the authors below

Thank you very much for the opportunity to review this interesting paper entitled: "The impact of diet on mortality in cancer survivors: A systematic review of current epidemiological literature. "

The authors included 58 observational studies and 2 RCTs, and concluded that the evidence is too limited whether dietary behaviour prior to or after diagnosis could influence mortality among cancer survivors.

Although the topic is of general interest, I have several comments to improve the quality of the systematic review:

We thank the Reviewer for their insightful comments.

Major:

Comment: The paper is quite long; please consider shortening by approximately 25% (mainly Results section)

Response: We have shortened the results and discussion sections

Comment: Please update the search; There are several studies

Response: We have updated the search until April 2017 and included more studies

Comment: Please consider to perform a meta-analysis if a least 3 studies are available for a dietary pattern within a specific cancer type (ie. Bowel cancer and prudent dietary pattern; similar for breast cancer,...)

Response: The rationale is that different cancer types have different pathogenesis and tumour biology. Given the heterogeneous nature of cancer, it should be noted that when a diet or food has been evidenced to influence the risk of recurrence and/or mortality for a certain cancer type, this does not necessarily apply for survivors of all cancer types. Therefore, we do not combine these studies in one analysis. Additionally, we believe we should not combine pre- and post-diagnosis dietary intake in one analysis. After cancer diagnosis, it is too late to amend lifestyle factors before diagnosis.

There are only a few studies that correct in their statistical analysis for pre-diagnosis intake when investigating post-diagnosis intake - when no corrections are made for pre-diagnosis intake or dietary change after diagnosis, there is no clear answer if the results are not biased because of dietary changes survivors made after diagnosis. Theoretically, we could conduct a meta-analysis with only 2 studies. However, we decided to take 3 studies as a minimum to include in a meta-analysis. If you look at our summary of findings Tables, you can see that there are hardly any outcomes with the same exposure for each cancer type. Only pre-diagnosis red and processed meat intake with overall mortality and cancer-specific mortality in bowel cancer survivors and pre-diagnosis total vegetable intake with overall mortality remain. Regarding the diet scores, all scores are based on the inclusion of different food items and it is questionable if combining all diet scores would be correct. The focus of our systematic review is on each cancer type individually.

Minor:

Abstract

Objectives: be more specific; what does dietary intake mean? Dietary pattern, food groups, foods, nutrients, beverages, dietary supplements?

Response: We have made the term dietary intake more specific

Design: add the name of the tool for the assessment of study quality

Response: We have added the name of the tool for the assessment of study quality in the review (RoB 2.0 & ROBINS-I)

Introduction

Please consider the following references by adding a sentence focusing on dietary pattern/ diet quality indices: PMID: 25680825, 24476641, 26471010

Response: We have added a sentence to the review focusing on dietary patterns and diet quality indices

Comment: There is a recent meta-analysis (27864535) investigating the association between dietary factors and all-cause mortality among cancer survivors, please elaborate the 3rd paragraph of the Introduction

Response: We have observed that your meta-analysis has been published whilst this systematic review has been under review at BMJ Open Therefore, we could not have included it in the original manuscript but we have now added it to our introduction in the current revised version.

Comment: Please be more specific: what types of observational studies? (prospective cohort studies, case-control studies, case-cohort studies, nested case-control studies, RCTs can be also analysed as observational studies)

Response: We have been more specific in the review and have changed the word observational study to cohort study

Methods

Please add full search strategy

A full search strategy can be found in box 1

Comment: Why studies based on a priori dietary pattern (investigator driven methods) were excluded? Why than Mediterranean diet was than included, if diet quality indices were excluded

Response: I'm not under the impression that the study did investigate anything other than diet scores. In the new version of the systematic review all principal component analysis derived dietary patterns and diet index based scores are included

Comment: Why you did not include the food group: whole grains?

Response: We have now added the food group of whole grains

Comment: What about food records?

Response: All possible tools of measuring dietary intake were included in the review

Comment: Please add the study protocol as supplementary file

Response: The study protocol is added as a supplementary file

Results

Comment: You mean clinical or statistical heterogeneity

Response: We mean heterogeneity regarding variability in pre- and post-diagnosis intakes and cancer types. We rephrased the text regarding this statement

Comment: Please add a Table (supplementary material) with the risk of bias for each study.

Response: Please explain what tool do you applied, we explained more in detail which tool we applied for the assessment of study quality among the studies and a Table with the risk of bias for each study can be provided on request.

If you are talking about observational cohort study; please rename: prospective cohort

Last sentence for bladder cancer paragraph could be removed

Please see previous response.

Reviewer: 5

Reviewer Name: Gordon H. Guyatt

Institution and Country: Department of Health Research Methods, Evidence, and Impact, McMaster University, Canada

Please state any competing interests: None declared

Please leave your comments for the authors below

The authors undertake a rigorous systematic review of the impact of empirically derived dietary patterns and food groups on mortality in survivors of common cancers. The review is ambitious, but suffers from important methodological limitations.

We thank the Reviewer for their insightful comments.

Major points:

1) The reviewers state that they used GRADE methods, but they seem to have done so in a cursory way and do not appear to have followed GRADE guidance. The only relevant statement is “The quality level of the body of evidence of the included studies was rated ‘low’ to ‘moderate’ by two of the authors (SJ and FvO) when applying the grading system developed by the GRADE collaboration.”

Response: We have elaborated on how we applied the GRADE method in the review.

2) For the two RCTs we see no reason the authors do not pool the results. The authors do not provide a specific rating of quality/certainty of the evidence except as quoted above. Assuming there is no problem with risk of bias, indirectness, or publication bias the result appear to provide moderate quality evidence (consistent results with wide confidence intervals). This should be highlighted, with the conclusion that the impact of fat reduction remains uncertain (confidence intervals will include an appreciable relative risk reduction). These findings, the highest quality evidence in the review, are worth highlighting.

Response: We do rate both RCT together for the GRADE rating. The summary of findings Tables are now included in the supplementary files

3) The authors do not present appropriate ratings of evidence for the observational studies. From what we can gather, all the evidence is of very low quality (observational studies start as low quality and given the authors’ statement “The great heterogeneity amongst the included studies led to the decision of conducting a systematic review only and no meta-analysis” it appears that they should be rated down further for inconsistency.

Response: The evidence is indeed of very low and low quality. Unfortunately, I cannot provide a better explanation for this than that I wrote (very)low and with editing the ‘very’ part disappeared. We wrote it now more specifically down in the review

4) Providing an evidence profile for each question addressed would be very helpful in sorting out how the authors applied GRADE. Because the level of confidence associated with very low, low, and moderate GRADE certainty ratings differ, doing so will improve the interpretability of the results presented. Additionally, presenting GRADE ratings will make explicit and transparent the authors’ reasoning for rating up/down the quality of evidence.

Response: We can add the GRADE ratings to the characteristics table

5) Ultimately, the quality of evidence for each question should be included in the abstract.

Response: A general statement is made in the abstract on the level of quality

6) The authors assessment of risk of bias seems as superficial as their use of GRADE. The only statement they make is “All 58 observational studies had an acceptable risk of bias according to the Cochrane Collaboration risk of bias assessment tool”. This would be an extraordinary result – no variability in risk of bias across 58 studies.

We recommend the authors consider presenting individual risk of bias assessments for each study in an appendix. Although the table would be large and cumbersome to synthesize, this information can be valuable to readers, whose confidence in the results of the studies may differ depending on the domains that were rated down. The authors may choose to present a modified version of the ROBINS-I tool, given its length. For example, they may choose to only focus on domains they consider to be of critical importance to the interpretation of the results. Alternatively, for each comparison, the authors may consider presenting the proportion of studies that were at high/low/unclear risk of bias in each domain of the risk of bias tool. If they end up telling us that all studies were rated identically, we would question the rigor with which they applied the instrument.

Response: We have used a modified version of the ROBINS-I tool. The reason that all studies had an acceptable risk of bias was that some studies were already excluded from the review from the beginning before a risk of bias assessment because of our inclusion and exclusion criteria. Studies that did not adjust for age, sex (if applicable), tumour characteristics, and preferably initial treatment in the statistical analysis were already excluded. Study that included less than 200 survivors in the analysis of their study, had a follow-up period less than 4 years (for most cancer types, the risk of cancer recurrence is the greatest within the first three years)

Key limitations of cohort studies include use of inappropriate controls and failure to adequately adjust for prognostic imbalance. We only included cohort studies with cancer survivors, differences in measurement of exposure were for all cohort studies a questionnaire/FFQ, and failure to adequately control for confounding we already made sure that studies who did not adjust for important confounders including age, sex, and tumour characteristics were excluded. We did include the GRADE summary of findings tables to the supplemental data files. However, the risk of bias assessments for each individual study is very large in size for all size and will therefore be available on request.

7) Given the heterogeneity that exists in common cancers, further clinical and molecular characteristics (e.g., ductal or lobular and receptor status for breast cancer) of the cancers studied should be reported, if the information is available from the primary papers.

Response: Additional information on these characteristics is probably beyond the scope of this review. For that reason, we will not include them in our characteristics table.

8) The authors' statement in the abstract ("Multivitamin supplement use and fruit and vegetable consumption do not appear to improve breast cancer survivors' mortality. Other studies addressing diet and mortality amongst groups of cancer survivors were too limited or could not be identified") is inconsistent with their statement in the discussion (Nevertheless, small changes like increasing the amounts of fruit and vegetables and reducing the consumption of meat and alcohol in the diet are feasible goals and should be highly considered based on the results identified").

Response: The statement in the discussion has been deleted

Minor points:

9) P. 5, line 14: It is unclear whether title and abstract screening was also undertaken in duplicate.

Response: We added a sentence to the abstract on the title and abstract screening

10) Given that GRADE considers rating up the evidence when a dose-response relationship is evident in observational studies, were data also abstracted for dose-response analyses or only high vs. low? If data were also abstracted for dose-response analyses, this information could be included in the evidence profiles

Response: No data were extracted for dose-response analyses, only for high versus low intake

11) P. 6, line 21 seems to suggest that only processed red meat was studied. This can be corrected to indicate that both processed and unprocessed red meat was studied.

Response: We corrected it to both processed and unprocessed red meat

12) P. 8 line 14: 'let' should be corrected to 'led.'

Response: We have made this change

13) P. 33, line 23-25: The advantages of FFQs are overstated. We recommend the authors to also discuss limitations with this approach of measuring diet.

Response: We discuss the limitations of FFQs.

VERSION 2 – REVIEW

REVIEWER	Marjorie L. McCullough Strategic Director, Nutritional Epidemiology American Cancer Society USA
REVIEW RETURNED	26-Jun-2017

GENERAL COMMENTS	<p>The authors did a remarkable job responding to reviewer comments, especially with the addition of diet scores, and are to be commended on the comprehensive nature of this work. The paper is much easier to follow.</p> <p>However, I still have some general, and detailed comments which I think will further improve the paper.</p> <p>General comments:</p> <ol style="list-style-type: none"> 1. Page 11 includes extra detail and could be shortened or moved to Supplemental material. 2. Results for soy foods are provided in the tables for NHL, but is not in the search list. If the authors mention soy, suggest including soy in the search (and reporting findings in the tables for breast, and other cancers if applicable). 3. Please review all tables and data carefully (see detailed comments). 4. It seems that some additional interpretation is needed in the discussion (see detailed comments). For example, interpretation of associations with cancer-specific mortality or recurrence vs. overall mortality.
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	<p>Detailed comments:</p> <ol style="list-style-type: none"> 1. Abstract, line 39: suggest “quality” or “grade” – “level” seemed to vague. 2. Abstract, line 42: I thought that diet scores/diet quality was mostly related to other causes of death in breast cancer survivors, and not as much to breast cancer-specific mortality (Table S2). 3. Page 3, line 57: Suggest adding “Most” (studies investigating) 4. Page 5, line 89: do the authors mean “survivors of individual cancer sites”? or “groups of cancer sites individually”? 5. Page 7, lines 126-130 was unclear. Did the authors mean that “Additionally, studies were excluded when outcomes were combined, such as mortality and cancer progression, or mortality and diagnosed metastasis, or where prostate cancer recurrence ...” 6. Page 7, line 135: suggest “the following “diet scores” or “diet quality indices””, and then on line 141, put a semicolon after refs 25,26 and add “empirical patterns reviewed included ...” 7. Page 7, lines 142 and 143: the HEI and AHEI are different. At the very least, suggest giving each its own sentence. 8. Page 8, lines 150-162: Suggest clarifying why you decided to review less healthy foods (the wording currently sounds as though the foods reviewed are only nutritious, but processed meat is included, for example). 9. Page 9, line 183: “inconsistency of results”: do the authors mean inconsistency within a paper, or strength of association? 10. Page 9, line 185: “all possible sources of confounding”—is this referring to observational studies or RCTs as well? Suggest, for observational, “control for key known risk factors and confounders” or something similar. 11. Page 10, line 206: suggest adding that RRs for each study, by outcome, can be found in Table S2. 12. Page 12, line 260 to page 13, line 263: this study included both men and women (remove “female” from the description). 13. Page 13, line 285: The study by Yang et al (ref. 42) did see a protective association with milk consumption after a colorectal cancer diagnosis (the RRs listed in Table S2 for post-diagnostic milk intake and mortality in colorectal cancer survivors are incorrect; please fix). 14. Page 15, line 312: The WINS trial did see a 24% reduction in relapse, but it is thought that might be due to weight loss. Why only provide results on survival? 15. Page 15, line 335 Please add “breast cancer” before “mortality” on line 335. Note: this study observed an inverse association with the continuous score and other causes of death, and with meat consumption and total mortality and other causes of death (but not breast cancer-specific mortality). 16. Page 17, line 372 (and elsewhere): Suggest using “association” instead of “difference”. 17. Page 20, line 453: Suggest “associated with increased...” vs “non-beneficially associated” 18. Page 21, line 472: Do the authors mean “adverse” instead of “inverse”? 19. Discussion, page 21. It might be good to distinguish cancer-specific from total mortality. For example, higher diet pattern scores, in general, have been associated with lower risk of non-breast cancer causes of mortality. It’s not clear what is meant by a “general assumption”: meaning, confounding due to other lifestyle behaviors, or specifically due to fruits and vegetables? 20. Page 22, line 491: if discussing specific (e.g. “two”) studies, please add references. 21. Page 24, conclusions: the first sentence may fit better at the end.
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REVIEWER	Allison Hodge Cancer Council Victoria Australia
REVIEW RETURNED	30-Jun-2017

GENERAL COMMENTS	<p>This manuscript has been improved by revision according to previous reviewer's comments. A few things to consider: Background in Abstract notes '...review of limited evidence...' You did not know how limited until the review was done so should say '...review of available evidence...' here. Given that the study focuses on cancers where 10-year survival is $\geq 50\%$ the introduction should also point out that many of these people will die of other causes such as CVD so there is logic in looking at dietary patterns/foods that are likely to be associated with reduced CVD mortality. Even if the exposures identified don't help cancer recurrence, given the survivors of these cancers have potential for long-term survival it is desirable for them to follow- a diet that could help reduce other conditions. Line 125. 'Exclusion' should be 'Excluded'. Line 136 WCRF/AICR Line 303 'carefully' is not the best word to use here. Line 312. What was the aim with the dietary intervention in the WINS study? Describe according to what the diet was and then comment on whether that was achieved. Lines 400-402 needs editing. Lines 406-9. Do you mean authors of the paper being reviewed or of the current review? How did you conclude no conclusive evidence for diet and mortality in prostate cancer survivors when there were several significant associations? What criteria were used to decide when there was evidence? Line 509. Comparing vegetarian vs non-vegetarian cannot help elucidate associations of processed meat and mortality specifically. Previous comments re section 4.7 Vit D has disappeared, nothing has been added as suggested in the response.</p>
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VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Marjorie L. McCullough

Institution and Country: Strategic Director, Nutritional Epidemiology, American Cancer Society, USA

Please state any competing interests: None declared

Please leave your comments for the authors below

The authors did a remarkable job responding to reviewer comments, especially with the addition of diet scores, and are to be commended on the comprehensive nature of this work. The paper is much easier to follow.

However, I still have some general, and detailed comments which I think will further improve the paper.

General comments:

1. Page 11 includes extra detail and could be shortened or moved to Supplemental material. Some of the extra details on page 11 has been shortened. However, as other reviewers requested more detailed information in the abstract on the risk of bias and level of quality, not all of the extra detail will be moved.

2. Results for soy foods are provided in the tables for NHL, but is not in the search list. If the authors mention soy, suggest including soy in the search (and reporting findings in the tables for breast, and other cancers if applicable).

You are correct, the result on soy for NHL have been removed.

3. Please review all tables and data carefully (see detailed comments).

All tables are reviewed and adjusted were necessary

4. It seems that some additional interpretation is needed in the discussion (see detailed comments). For example, interpretation of associations with cancer-specific mortality or recurrence vs. overall mortality.

A more clear distinction has been made in the results and discussion on overall mortality, death from other causes, recurrence and cancer-specific mortality for the evidence obtained. We cannot, however, provide an explanation on why certain dietary patterns/indices or foods are association with overall mortality and in other studies with death from other causes. We can only speculate that it can depend on multiple factors such as how mortality was obtained for the individual studies, or how good the quality was of obtaining data on the causes of death.

Detailed comments:

1. Abstract, line 39: suggest “quality” or “grade” – “level” seemed to vague.

Response: We have changed this in the text

2. Abstract, line 42: I thought that diet scores/diet quality was mostly related to other causes of death in breast cancer survivors, and not as much to breast cancer-specific mortality (Table S2).

Response: You are right, we made this more specifically in the abstract

3. Page 3, line 57: Suggest adding “Most” (studies investigating)

Response: We have changed this in the text

4. Page 5, line 89: do the authors mean “survivors of individual cancer sites”? or “groups of cancer sites individually”?

Response: We have changed this in the text

5. Page 7, lines 126-130 was unclear. Did the authors mean that “Additionally, studies were excluded when outcomes were combined, such as mortality and cancer progression, or mortality and diagnosed metastasis, or where prostate cancer recurrence ...”

Response: We have changed this in the text

6. Page 7, line 135: suggest “the following “diet scores” or “diet quality indices””, and then on line 141, put a semicolon after refs 25,26 and add “empirical patterns reviewed included ...”

Response: We have changed this in the text

7. Page 7, lines 142 and 143: the HEI and AHEI are different. At the very least, suggest giving each its own sentence.

Response: Thank you for that remark, we elaborated more on the difference between the HEI and AHEI score

8. Page 8, lines 150-162: Suggest clarifying why you decided to review less healthy foods (the wording currently sounds as though the foods reviewed are only nutritious, but processed meat is included, for example).

Response: We did make the switch to only foods from the main food groups and adherence to dietary patterns/indices to make the review more focussed as was asked by some of the reviewers. The reason processed meats was still included was that some studies make no distinction between red/processed/unprocessed meat. Nevertheless, lean red meat is part of the main food group and can fit in a healthy diet. Now we have now excluded the results on purely processed meats but kept results that included (lean) red meat and sometimes processed meat but described this and interpreted this with great caution.

9. Page 9, line 183: “inconsistency of results”: do the authors mean inconsistency within a paper, or strength of association?

Response: We have changed this in the text

10. Page 9, line 185: “all possible sources of confounding”—is this referring to observational studies or RCTs as well? Suggest, for observational, “control for key known risk factors and confounders” or something similar.

Response: Thank you for this remark, we have changed this in the text

11. Page 10, line 206: suggest adding that RRs for each study, by outcome, can be found in Table S2.

Response: We have changed this in the text

12. Page 12, line 260 to page 13, line 263: this study included both men and women (remove “female” from the description).

Response: We have removed this from the description

13. Page 13, line 285: The study by Yang et al (ref. 42) did see a protective association with milk consumption after a colorectal cancer diagnosis (the RRs listed in Table S2 for post-diagnostic milk intake and mortality in colorectal cancer survivors are incorrect; please fix).

Response: We adjusted this in the text however we did state the correct number in the tables for this study regarding the outcomes we include from this study

14. Page 15, line 312: The WINS trial did see a 24% reduction in relapse, but it is thought that might be due to weight loss. Why only provide results on survival?

Response: We now also included the reduction in relapse for this study

15. Page 15, line 335 Please add “breast cancer” before “mortality” on line 335. Note: this study observed an inverse association with the continuous score and other causes of death, and with meat consumption and total mortality and other causes of death (but not breast cancer-specific mortality).

Response: Thank you, we have changed this in the text

16. Page 17, line 372 (and elsewhere): Suggest using “association” instead of “difference”.

Response: We have changed this in the text

17. Page 20, line 453: Suggest “associated with increased...” vs “non-beneficially associated”

Response: We have changed this in the text

18. Page 21, line 472: Do the authors mean “adverse” instead of “inverse”?

Response: We have changed this in the text

19. Discussion, page 21. It might be good to distinguish cancer-specific from total mortality. For example, higher diet pattern scores, in general, have been associated with lower risk of non-breast cancer causes of mortality. It's not clear what is meant by a “general assumption”: meaning, confounding due to other lifestyle behaviors, or specifically due to fruits and vegetables?

Response: We have adjusted the text so this to be more precisely described

20. Page 22, line 491: if discussing specific (e.g. “two”) studies, please add references.

Response: We have added references on multiple places where necessary.

21. Page 24, conclusions: the first sentence may fit better at the end.

Response: We agree and moved the first sentence to the end

Reviewer: 2

Reviewer Name: Allison Hodge

Institution and Country: Cancer Council Victoria, Australia

Please state any competing interests: None declared

Please leave your comments for the authors below

This manuscript has been improved by revision according to previous reviewer's comments. A few things to consider:

Background in Abstract notes ‘...review of limited evidence...’ You did not know how limited until the review was done so should say ‘...review of available evidence...’ here.

We agree, however, due to the limitation of words in the abstract, we had to remove that sentence. Given that the study focuses on cancers where 10-year survival is $\geq 50\%$ the introduction should also point out that many of these people will die of other causes such as CVD so there is logic in looking at dietary patterns/foods that are likely to be associated with reduced CVD mortality. Even if the exposures identified don't help cancer recurrence, given the survivors of these cancers have potential for long-term survival it is desirable for them to follow- a diet that could help reduce other conditions. Thank you for this insightful remark, we have added it to the introduction

Comment: Line 125. 'Exclusion' should be 'Excluded'.

Response: We changed this in the text

Comment: Line 136 WCRF/AICR

Response: We have written the name in full

Comment: Line 303 'carefully' is not the best word to use here.

Response: We deleted the word carefully in this sentence

Comment: Line 312. What was the aim with the dietary intervention in the WINs study? Describe according to what the diet was and then comment on whether that was achieved.

Response: We agree that the comment is made too early in the text and the aim of the WINs study has been described in the results section before commenting on whether the aim of the intervention was achieved

Comment: Lines 400-402 needs editing.

Response: We agree, and we edited the sentences

Comment: Lines 406-9. Do you mean authors of the paper being reviewed or of the current review? How did you conclude no conclusive evidence for diet and mortality in prostate cancer survivors when there were several significant associations? What criteria were used to decide when there was evidence?

A sentence has been added to the paper explaining that whether evidence is conclusive or not according to the authors of this review – it is based on the level of evidence described in the paper. Line 509. Comparing vegetarian vs non-vegetarian cannot help elucidate associations of processed meat and mortality specifically.

Previous comments re section 4.7 Vit D has disappeared, nothing has been added as suggested in the response.

Response: We agree that comparing those groups cannot elucidate those specific associations and removed it. Nevertheless, as results on processed meats analyses separately were excluded from the review after a comment from another reviewer, there is no conclusive evidence left for a role of meat and therefore this is not applicable anymore.

Reviewer: 4

Reviewer Name: Lukas Schwingshackl

Institution and Country: Department of Epidemiology, German Institute of Human Nutrition, Germany

Please state any competing interests: NA

Please leave your comments for the authors below

The authors have answered my previous comments.

Although I not fully agree to no conduct a meta-analysis (see WCRF CUP), i have only 2 minor points:

1) The added Reference 11 is incorrect; please revise: PMID: 27864535

Response: We changed this in the text

2) please add also the following references in Line 66: PMID: 28446499 and PMID: 26471010;

Response: We added these references in the text

VERSION 3 – REVIEW

REVIEWER	Allison Vodge Cancer Council Victoria Australia
REVIEW RETURNED	29-Aug-2017

GENERAL COMMENTS	The authors have made a lot of changes and the revised manuscript is much improved. I missed a summary of the changes and noted that the new section lines 226-230 needed some editing. Also the conclusion in the abstract is good but the conclusion in the main text is rather vague. Do we need more well conducted studies (I think this is the case given many associations were based on single studies), or do we need to pass the results of current studies to health care providers. Do we need more RCTs given cohort studies were rated as very low-low quality?
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REVIEWER	Lukas Schwingshackl German Institute of Human Nutrition Germany no conflict of interest
REVIEW RETURNED	22-Aug-2017

GENERAL COMMENTS	As already commented in the previous round: Reference 2 is incorrect (please remove and add instead PubMedID: 28446499)
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VERSION 3 – AUTHOR RESPONSE

Reviewer Name: Allison Vodge

Institution and Country: Cancer Council Victoria, Australia

Please state any competing interests: None declared

Please leave your comments for the authors below

Comment: The authors have made a lot of changes and the revised manuscript is much improved. I missed a summary of the changes and noted that the new section lines 226-230 needed some editing.

Response: Again thank you for your comments on the manuscript.

A summary of changes from the second revision are: shortening the methods section, describing the differences between the outcomes (overall mortality, cancer-specific mortality, death from other causes) in more detail, including dietary patterns/indices and foods from the main food groups as an exposure, editing of words throughout the manuscript, adding some references, and pointing out that if the exposures identified don't help cancer recurrence, given the survivors of these cancers have potential for long-term survival it is desirable for them to follow a diet that could help reduce other conditions as you suggested.

Comment: Also the conclusion in the abstract is good but the conclusion in the main text is rather vague. Do we need more well conducted studies (I think this is the case given many associations were based on single studies), or do we need to pass the results of current studies to health care providers. Do we need more RCTs given cohort studies were rated as very low-low quality?

Response: We adjusted the conclusion to saying more large en well conducted studies, preferably RCTs, are needed.

Reviewer Name: Lukas Schwingshackl

Institution and Country: German Institute of Human Nutrition, Germany

Please state any competing interests: no conflict of interest

Please leave your comments for the authors below

Comment: As already commented in the previous round: Reference 2 is incorrect (please remove and add instead PubMedID: 28446499)

Response: Thank you for your comment, it is adjusted correctly now.

VERSION 4 – REVIEW

REVIEWER	Allison Hodge Cancer Council Victoria Australia
REVIEW RETURNED	08-Sep-2017
GENERAL COMMENTS	The authors have fixed the references