

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Dairy product consumption and development of cancer - An overview of reviews
AUTHORS	Jeyaraman, Maya; Abou-Setta, Ahmed; Grant, Laurel; Farshidfar, Farnaz; Copstein, Leslie; Lys, Justin; Gottschalk, Tania; Desautels, Danielle; Czaykowski, Piotr; Pitz, Marshall; Zarychanski, Ryan

VERSION 1 – REVIEW

REVIEWER	Professor Ian Givens Institute for Food Nutrition and Health University of Reading United Kingdom
REVIEW RETURNED	30-May-2018

GENERAL COMMENTS	<p>Overall, this is a comprehensive piece of work bringing together as far as was possible all the data on the association between dairy foods and risk of cancers. The finding that many identified studies were of too low quality to be included is concerning but not unusual. The methodology and statistical approach appears to be appropriate but I feel it would be wise to have comments from a statistician with expertise in this area. My main concern is that there is no mention or reference to the the reports produced by the World Cancer Research fund/American Institute for Cancer Research (WCRF/AICR) which are regarded by many as the definitive source of evidence on food/diet and cancer risk. For e.g. the continuous update report on diet/nutrition and breast cancer was published in 2017 and updated in 2018. Their third Expert Report on Diet, Nutrition, Physical Activity and Cancer: a Global Perspective has just been published this month. It would be most valuable for the present paper to refer to the WCRF/ACIR reports and discuss agreement or disagreement and other relevant points, perhaps including differences in methodology.</p> <p>A minor point: Lines 40-45 refer to the percentage of primary studies conducted in different parts of the world but the total of studies conducted of Europe, N America, Asia, S America and Oceania is 292%! There may be a simple explanation but it is confusing as given.</p>
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REVIEWER	Jason Tay University of Calgary, Canada
REVIEW RETURNED	11-Jul-2018

GENERAL COMMENTS	<p>I have the following comments:</p> <p>Background</p> <p>1. The authors pose interesting scientific questions: Is there a link between diary consumption and incident cancer, all cause mortality</p>
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	<p>and cancer-related mortality?</p> <p>2. There have been numerous studies and PMASRs with conflicting results</p> <p>3. To further study this question, to assess the current evidence of association of dairy consumption and cancer as well as to evaluate reasons for conflicting PMASRS, the authors conducted a “review of reviews”.</p> <p>4. The language used to convey the message is clear and succinct</p> <p>Methods</p> <p>1. The review protocol was previously registered on PROSPERO</p> <p>2. Thoughtful search criteria were formulated, multiple databases were searched and complemented by hand-searching.</p> <p>3. Standardized review methodology was employed with no gaps identified.</p> <p>4. The primary and secondary outcomes were pertinent</p> <p>Results</p> <p>1. The results of the review were well presented and I enjoyed looking over the Radar Plots.</p> <p>Discussion</p> <p>2. The discussion is thoughtful and in keeping with evidence presented.</p> <p>Suggestions:</p> <p>1. There is a tendency in a review of reviews to indirectly to give equal weight to the identified studies. Would you consider a “subgroup” analysis of higher quality studies using the AMSTAR criteria (moderate and high vs. low) to see if your results might be different?</p> <p>2. Would consider plotting the quality of the studies by year of publication?</p> <p>3. Would there be a way to depict the degree of overlapping primary studies between the PMSARS? This would help the reader appreciate the evolving knowledge base.</p> <p>Taken together and in my opinion, the study is scientifically credible and was conducted in accordance with appropriate reporting guidelines. I would recommend accepting the manuscript for publication with minor changes, rebuttals and/or discussions as noted.</p>
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REVIEWER	Marc Saez University of Girona Spain
REVIEW RETURNED	07-Nov-2018

GENERAL COMMENTS	<p>The authors try to provide a comprehensive systematic overview of current evidence from pooled analyses/meta-analyses and systematic review (PMASRs) pertaining to dairy consumption and incident cancer and/or all-cause or cancer-specific mortality. The authors have been quite successful in achieving their objectives. In fact, I have only one minor comment.</p> <p>- Although the review (and the meta-analysis) has been quite complete, the authors should perhaps include a summary table with their findings.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer 1:

Reviewer Name: Professor Ian Givens

Institution and Country: Institute for Food Nutrition and Health, University of Reading, United Kingdom

Please state any competing interests or state 'None declared': None declared

1. Overall, this is a comprehensive piece of work bringing together as far as was possible all the data on the association between dairy foods and risk of cancers. The finding that many identified studies were of too low quality to be included is concerning but not unusual. The methodology and statistical approach appears to be appropriate but I feel it would be wise to have comments from a statistician with expertise in this area. My main concern is that there is no mention or reference to the reports produced by the World Cancer Research fund/American Institute for Cancer Research (WCRF/AICR) which are regarded by many as the definitive source of evidence on food/diet and cancer risk. For e.g. the continuous update report on diet/nutrition and breast cancer was published in 2017 and updated in 2018. Their third Expert Report on Diet, Nutrition, Physical Activity and Cancer: a Global Perspective has just been published this month. It would be most valuable for the present paper to refer to the WCRF/AICR reports and discuss agreement or disagreement and other relevant points, perhaps including differences in methodology.

Author reply: Thank you.

The 2018 WCRF/AICR reports provide evidence on the association between dairy products and three types of cancers (breast cancer, prostate cancer and colorectal cancer).

As suggested, we have discussed the findings of the WCRF/AICR report in the discussion section of our manuscript (tracked changes provided in the revised manuscript) and added the references to the relevant 2018 WCRF/AICR reports under the references section. We sincerely hope this addresses your comment.

2. A minor point: Lines 40-45 refer to the percentage of primary studies conducted in different parts of the world but the total of studies conducted of Europe, N America, Asia, S America and Oceania is 292%! There may be a simple explanation but it is confusing as given.

Author reply: Thank you. We apologize for the lack of clarity in Lines 40-45. The reason why the total percentage is greater than 100% is because each PMASR had included primary studies that were conducted in many different continents, leading to overlap. For example, 93% of the PMASRs included primary studies conducted in Europe whereas 83% of PMASRs included primary studies conducted in North America. To bring more clarity, we have re-worded/modified the relevant sentence (Lines 40-45) in the manuscript (tracked changes provided in the revised manuscript).

Reviewer 2:

From: Jason Tay, Hematologist, Tom Baker Cancer Centre, University of Calgary, Calgary

I have the following comments:

Background

1. The authors pose interesting scientific questions: Is there a link between dairy consumption and incident cancer, all cause mortality and cancer-related mortality?
2. There have been numerous studies and PMASRs with conflicting results
3. To further study this question, to assess the current evidence of association of dairy consumption and cancer as well as to evaluate reasons for conflicting PMASRS, the authors conducted a “review of reviews”.
4. The language used to convey the message is clear and succinct

Author reply: Thank you.

Methods

1. The review protocol was previously registered on PROSPERO
2. Thoughtful search criteria were formulated, multiple databases were searched and complemented by hand-searching.
3. Standardized review methodology was employed with no gaps identified.
4. The primary and secondary outcomes were pertinent

Author reply: Thank you.

Results

1. The results of the review were well presented and I enjoyed looking over the Radar Plots.

Author reply: Thank you.

Discussion

2. The discussion is thoughtful and in keeping with evidence presented.

Author reply: Thank you.

Suggestions:

1. There is a tendency in a review of reviews to indirectly to give equal weight to the identified studies. Would you consider a “subgroup” analysis of higher quality studies using the AMSTAR criteria (moderate and high vs. low) to see if your results might be different?

Author reply: Thank you. We did consider sorting the summary effect estimates from PMASRs based on study quality and based on whether the PMASR is a systematic review and meta-analysis or just a pooled/meta-analysis. In Supplemental Table 5, we have provided the summary effect estimates only from PMASRs with highest available AMSTAR score/quality for the specific associations between various dairy products and cancer outcomes. In Table 3 & Supplemental Table 6 we have provided the summary effect estimates specifically only from systematic reviews (SRs). These two tables, compared with Supplemental Table 4 (with summary estimates from all studies), provide a comprehensive summary of the evidence based on quality, at a glance. We sincerely hope this addresses your comment.

2. Would consider plotting the quality of the studies by year of publication?

Author reply: Thank you. In our initial manuscript submission, we were only allowed to submit five figures in total and we picked the most important figures for the peer-review process. However, as suggested by you, we have created a line plot (as Supplemental Figure 1) depicting the relationship

between AMSTAR scores (quality) and publication year of the included PMASRs. This brings the total number of figures to 6. The relevant text (with tracked changes) has been included in the revised manuscript under the “Methodological quality of included reviews” section and under the Figure legends.

3. Would there be a way to depict the degree of overlapping primary studies between the PMSARS? This would help the reader appreciate the evolving knowledge base.

Author reply: Thank you. It is possible to depict the degree of overlapping primary studies between PMASRs, but since the primary goal of our overview of reviews as per our *a priori* protocol was only to summarize the evidence from PMASRs (with unit of analysis as PMASRs) we did not extract or analyze the primary studies included in the PMASRs. However, in our future research, which is currently being pursued as a follow-up to this overview of reviews, we will be discussing in detail about the primary studies on this topic (including the quality/risk of bias) to highlight and inform the evolving knowledge base.

Taken together and in my opinion, the study is scientifically credible and was conducted in accordance with appropriate reporting guidelines. I would recommend accepting the manuscript for publication with minor changes, rebuttals and/or discussions as noted. Once again, thank you and the authors for the opportunity review this manuscript.

Author reply: Thank you very much for your feedback and support.

VERSION 2 – REVIEW

REVIEWER	Jason Tay Tom Baker Cancer Centre
REVIEW RETURNED	22-Nov-2018
GENERAL COMMENTS	All my suggestions have addressed. I have no further concerns or suggestions.