Reviewer’s report

Title: Health outcomes of non-nutritive sweeteners: analysis of the research landscape

Version: 0 Date: 05 Mar 2017

Reviewer: Celeste Naude

Reviewer's report:

Thank you for the opportunity to review this manuscript. It is clear that many hours of hard work were spent on this study and the writing of the paper. It contains high-quality and commendable components for which the authors deserve due credit.

The topic of this scoping review has importance for nutrition research and practice, and the most likely readership of the journal.

Comments and revisions are suggested to improve the scientific writing structure of the manuscript, and enhance the reader's understanding of the methods, results and the relevance of the research. Most of the necessary information is presented in the manuscript, however, in its current form and structure, the aim and objectives, methods, results and conclusions are not clearly presented and major revisions are needed.

TITLE:

The inclusion of observational studies in the scoping review means that the word "effects" in the first part of the title does not accurately reflect the content of the manuscript. I suggest rephrasing the title to better reflect the aim of the scoping review, and use of the term health outcomes rather than health effects.

ABSTRACT:

The abstract should be rewritten using the sections: Background, Methods, Results and Conclusions as per the Author Instructions. These sections in the abstract should closely reflect the key content of the corresponding sections of the manuscript. The results presented in the abstract should align with the main aim and key objectives of the study. The abstract is very important and should provide an informative and easy-to-follow summary of what was done and what was found.

Very important: All the comments and edits made for each section below are also relevant to the abstract, and must be included when the abstract is rewritten.
INTRODUCTION:

The term "objective" is used in the abstract and the term "aim" is used in the manuscript - be consistent. Also the aim presented at the end of the introduction is incomplete when compared to the objective presented in the abstract. A different aim is then presented in the Methods (line 48, page 5).

Please rephrase the main aim and objectives of the study. The main aim (overall purpose) should be comprehensively stated at the end of the Introduction, followed by the objectives, formulated as the detailed, feasible steps to accomplish the main aim.

The main aim was "to map the evidence about health outcomes possibly associated with regular NNS consumption by examining the extent, range, and nature of research activity in this area"

The specific objectives for this overall aim should be clearly stated - elaborate on the concepts of health outcomes, extent, range and nature of research activity.

The gap described in the Introduction systematically flows into the motivation for the scoping review on page 5. The main aim and objectives should logically follow from this motivation. The purpose of the study is clear, but the steps that were taken to accomplish this aim (objectives) are not clearly presented.

A slightly more detailed description of the approach to a scoping review, including the process of evidence mapping, should also be included in the Introduction.

The Introduction only mentions non-discretionary intake of NNSs, but the scoping review includes both non-discretionary intake and discretionary use of NNSs by consumers (in tea or coffee for example). Therefore, a brief discussion of current literature on the discretionary use of NNSs should also be included in the Introduction.

Please add references to the first paragraph on page 5.

For ease of reading and to supplement the current information, I suggest capturing details about the different types of NNSs in a table, and also including the information related to where their use is approved in the table - without repeating information in the text and table.

METHODS:

The methods should correspond with the stated objectives ensuring that methods used for each objective are included and documented in way that they are replicable. Certain sections of the Methods are currently vague and require more detail.
Inclusion criteria - include no restriction based on language here; were only the listed As, NNCSs and NNSs included? If yes, make this clear; were any forms or dosages of NNSs eligible for inclusion?

Search strategy - why were there different search dates for AS and NNCS and NNS?

Data extraction and management - line 12 page 7: should no. 6) be the size of the study sample and not the size of the study population? More detail is needed to explain what is meant by the sentence on the use of Bubble charts on page 7. What are bubble charts? How are they used to highlight correlations? Perhaps providing an example of this will be helpful.

Line 8 page 6: write out the abbreviation DC the first time it is used

Line 36 page 7: the word 'analyzed' should be replaced with the word 'summarized'

RESULTS:

The reporting of the results should be improved and should be in accordance with the objectives once they are formulated. There are currently inconsistencies, namely: directions of effects are provided in Table 2 and 3 for primary studies, but are not included in Table 1 for systematic reviews; also health outcomes reported on by systematic reviews are not included in Figure 2; the terms used for the various outcomes and groupings in the text (from line 48 page 8 to end of Results section) are inconsistent with the terms used in Figure 2 - please edit to use consistent terms and groupings in the text and figures.

Please include the headings that are described in lines 33 to 41, page 8 (short-term outcomes, long-terms outcomes in healthy populations and health outcomes in diseased populations) above the relevant categories of outcomes - this makes it easier for the reader to follow. Also include these categories in Figure 2.

Currently, the references to all 372 included studies are not reported. The references for all the included studies should be added when they are reported on in the Results section, as has been done in line 54 on page 8 for eating behaviour and metabolic effects.

It would also be very useful to extract and report on the form and dose (or dose range) of the NNSs intervention or exposure in the included studies, when reported. This is very important for comparisons between studies and would add to the interpretation of the included research. I would suggest extracting and including this data, where possible.

It would also be useful to report the eligible NNSs not addressed by any included studies, if applicable.

Line 51 page 7: delete the word PRISMA please, this is not a systematic review
Line 56 page 7: the following phrase does not make sense: Of those full texts of fifteen papers could not be retrieved

Line 33 page 8: the word discuss should be replaced by the word report

First sentence under Cancer on page 9: what is meant by dedicated systematic review versus broad systematic review? Please clarify - is reference 19 a systematic or narrative review?

Table 3 should be completely revised to reflect each of the 16 studies on dental caries, much like Table 2. In its current form it is confusing and does not add any value in better understanding the nature and extent of the studies reporting on NNSs and dental caries. It is currently not possible to sensibly link the population, interventions, outcomes, study design and effects and thus the information cannot be interpreted in a meaningful way.

Line 12 page 13: should be Obstetric not Obstetrical

DISCUSSION:

The summary of the findings should be about the main aim and objectives of the study, and should not be centred on the directions of effects/associations reported by the 372 studies for selected outcomes. This is particularly important since the strengths of effects/associations (and variation around these effects) are not reported, and these studies have not been critically appraised, which could lead to invalid interpretations of this evidence. The study sought to scope the health outcomes and nature and extent of the research evidence in this area, and not to report generally on some findings of studies on selected outcomes.

Line 19 page 17: should be Strengths and limitations of study

Line 56 page 17: the 'strength of effect' has not been extracted or reported, only the direction of effect - please correct

Line 15 to 20 on page 18: please substantiate or reference this general statement about methodological limitations of existing systematic reviews

Line 38 to 46 on page 18: this eligibility criteria described as 'our primary focus' conflicts with what is reported in the methods section under Inclusion criteria where no mention is made of clear definition of intervention/exposure. The exclusion of studies that defined interventions as diet drink/beverage/soda (line 23 to 46 on page 18) should rather be included in the limitations section as a limitation; remove the etc. in the final sentence.

Line 53 page 18: The Implications of findings section is currently too vague and should be much more specific - I suggest using the EPICOTplus framework to assist with improving this section. Statements should be substantiated and explained in detail.
CONCLUSIONS:

This section is currently focused on generalizations of selected effects reported by the 372 studies, and should be rewritten to report on findings pertaining to the main aim of the study. This is particularly important since the strengths of effects/associations (and variation around these effects) in the studies are not reported in this paper, and these studies have not been critically appraised, which could lead to invalid interpretations of this evidence.

Figure 1:

Please clarify what is meant by "wrong publication format" since there were no limitations on study design.

I suggest including the dates for each of the search yields and the names of the databases searched.

I suggest including a comprehensive list (or sensible groupings) of the health outcomes possibly associated with regular NNS consumption covered by the 372 studies, since this is the main aim of the scoping review (perhaps as a textbox under the last textbox)

Figure 2:

Please add explanations for all abbreviations used in the figure;

Correct spelling errors in the words obstetric and caries;

Add more detail on what is meant by Blood profile (is this lipids?), Tolerance and Other;

It is unclear what is meant by non-As in the figure?

Level of interest
Please indicate how interesting you found the manuscript:

An article of importance in its field

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published
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Please complete a declaration of competing interests, considering the following questions:

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