Online Supporting Material Appendix 1: MOOSE Checklist

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Nut consumption and risk of cardiovascular disease: A systematic review and meta-analysis

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Criteria		**Brief description of how the criteria were handled in the meta-analysis**
Reporting of background should include		
√	Problem definition	We systematically review and synthesize the effect of higher vs. lower nut consumption on mortality, fatal CHD/CVD, total CHD/CVD, all stroke, death from stroke, non-fatal myocardial infarction, and sudden cardiac death.
√	Hypothesis statement	In the introduction the following hypothesis is provided: The goal of our study is to systematically review the updated literature on nut intake and CVD and to conduct a meta-analysis to determine if nut consumption is associated with

		lower risk of cardiovascular outcomes such as stroke mortality and sudden cardiac death.
√	Description of study outcomes	All-cause mortality, CVD (fatal and non-fatal MI and stroke), CVD mortality (all heart disease, ICD-9 codes 390-459 including MI and stroke), CHD (non-fatal MI, sudden cardiac death), CHD death (ischemic heart disease including MI), stroke, death from stroke, non-fatal MI (according to WHO's criteria and lab results), sudden cardiac death (death within 1 hour of symptom onset with no other cause).
√	Type of exposure or intervention used	High vs. low exposure to dietary nut consumption, as assessed by dietary instruments.
√	Type of study designs used	We focused on prospective cohort studies. Randomized controlled trials were included in the literature search but there were no eligible studies.
√	Study population	All adults.

Reporting of search strategy should include		
√	Qualifications of searchers	The search strategy was developed by two of the investigators (Alexandra Mayhew and Andrew Mente), with credentials indicated in the author list.
√	Search strategy, including time period included in the synthesis and keywords	All databases were searched through July 8, 2015. The complete search strategy keywords and results can be found in **Online Supplementary Appendix 2.**
√	Databases and registries searched	MEDLINE (from 1946); EMBASE (from 1946); Cochrane Central Registry of Controlled Trials (from 1996), and Evidence Based Medicine Reviews (from 1996). Reference lists of retrieved articles and previous systematic and narrative reviews were reviewed. The complete search strategy keywords and results can be found in **Online Supplementary Appendix 2.**
√	Search software used, name and version, including special features	OvidSP was used to perform the search. RefWorks was used to merge retrieved citations and eliminate duplications
√	Use of hand searching	Reference lists of retrieved articles and previous systematic and narrative reviews were hand-searched.
√	List of citations located and those excluded, including justifications	Details of the literature search process are outlined in Figure 1. The citation list of excluded citations is available upon request
√	Method of addressing articles published in languages other than English	Only English language articles were searched for.
√	Method of handling abstracts and unpublished studies	We included only full-text published articles.
√	Description of any contact with authors	No authors were contacted.

Reporting of methods should include		
√	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	Detailed inclusion criteria were described in the methods section. Quality assessment done using Newcastle-Ottawa scale.
√	Rationale for the selection and coding of data	We extracted all study data relevant to description of study characteristics and outcomes.
√	Assessment of confounding	Primary pooled effects were of most-adjusted estimates only; least-adjusted estimates are presented in tables, for comparison.
√	Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	Two authors (de Souza and Mayhew) assessed the risk of bias (RoB) of included studies using the Newcastle-Ottawa Scale (NOS), and disagreements were resolved by discussion (**Online Supplementary Appendix 3**). We determined *a priori* that studies with a rating of 5 or 6 stars would be considered to be at "moderate" risk of bias, and 7 or more stars would be judged at ''low '' risk of bias. All studies were used for analyses, with sensitivity analyses limiting analyses to include only studies at "low" risk of bias. We used meta-regression to assess the impact of study quality on effect estimates.
√	Assessment of heterogeneity	The presence of statistically significant heterogeneity was assessed using Cochran's Q test (significant at $P<0.10$), and the I^2 statistic (ranging from 0% to 100%).
√	Description of statistical methods in sufficient detail to be replicated	Description of methods and software used to pool risk (and odds) ratios, detect and quantify heterogeneity, subgroup analyses, sensitivity analyses, and publication bias addressed in methods section.
√	Provision of appropriate tables and graphics	Summary forest plots for each of the 9 major exposure-outcome relationships (with at least 2 studies) presented in **Figures 3-9.**

Reporting of results should include		
√	Graph summarizing individual study estimates and overall estimate	**Figures 3-9**
√	Table giving descriptive information for each study included	**Table 1**
√	Results of sensitivity testing	Described within the section reporting results for each exposure-outcome association ("leave-one-out" analysis; limiting studies to those at low risk of bias and presented least-adjusted summary relative risks. Reported on the effect of type of nuts (results and **Supplementary Appendix 5**) and geographic location (results and **Supplementary Appendix 6)**
√	Indication of statistical uncertainty of findings	We present each effect estimate with its 95% CI and heterogeneity tests. We also assess the confidence in each effect estimate using GRADE (**Supplementary Appendix 4).**

Reporting of discussion should include		
√	Quantitative assessment of bias	The possibility of publication bias was not explored because of the limited number of studies.
√	Justification for exclusion	Excluded were animal/*in vitro* studies, those which did not provide a measure of association between exposures and outcome(s) of interest, did not directly measure exposure (e.g. nuts in conjunction with another diet), and those which did not directly measure the endpoints of interest (i.e. we excluded biomarker studies such as lipid profiles, blood pressure, etc.).
√	Assessment of quality of included studies	The median risk of bias rating using the Newcastle-Ottawa scale for studies informing this systematic review was 7.5 (**Supplementary Appendix 3**). The most common threats to validity were failure to completely adjust for known confounders of diet-disease associations (total energy intake and family history of disease [53% of studies] and using study participants which may not be representative of the average person at risk for the outcomes of interest [63%].

Reporting of conclusions should include		
√	Consideration of alternative explanations for observed results	Possibility of residual confounding always must be considered in observational studies. Study limitations included incomplete (or possibly over-) adjustment for confounders, high attrition, and uncertain outcome confirmation.
√	Generalization of the conclusions	Generalizable to people at risk of CVD and mortality
√	Guidelines for future research	Future studies investigating different types of nuts on cardiovascular disease risk would help guide dietary recommendations. Studies outside North America in low and middle income countries in which different types of nuts are consumed are required to determine the effect of nut consumption on cardiovascular disease outcomes in populations with different dietary patterns.
√	Disclosure of funding source	Alexandra Mayhew is the recipient of an Ontario Graduate Scholarship. Russell de Souza is the recipient of a Canadian Institutes of Health Research postdoctoral fellowship, and has received research support from the Canadian Foundation for Dietetic Research, the Calorie Control Council (investigator-initiated, unrestricted), and the Coca-Cola Company (investigator-initiated, unrestricted). Andrew Mente is a recipient of a Research Early Career Award from Hamilton Health Sciences Foundation. Sonia Anand is a recipient of the Heart and Stroke Michael G. DeGroote Chair in Population Health Research and a Canada Research Chair in Ethnicity and Cardiovascular Disease.