Organic food consumption and the incidence of cancer: a systematic review protocol

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ABSTRACT

Objective: The objective of this review is to evaluate the association between organic food consumption and the incidence of cancer among adults.

Introduction: Organic foods differ from traditional food in the methods in which they are produced. There is literature to suggest that they are associated with better health outcomes, including a lower incidence of some cancers. The association between organic food consumption and the incidence of cancer has not yet been synthesized.

Inclusion criteria: Studies that compared organic food consumption to conventional food consumption, measured the incidence of cancer among adults, and captured disease incidence, such as prospective and retrospective cohort methodologies, will be included.

Methods: A comprehensive search strategy will be implemented to retrieve relevant studies from PubMed, CINAHL, LILACS, Embase, PsycINFO, Science.gov, Web of Science/Web of Knowledge, and Academic Search Premiere, as well as gray literature sources such as Google Scholar, DARE and Dissertation Abstracts International. The search parameters will include studies for which the full text in English is available, and studies dated 2009 or later, as this was the date of a previous systematic review on the association between organic food consumption and health outcomes that did not find any studies with cancer-related outcomes. Study screening, critical appraisal, and data extraction will be performed independently by pairs of reviewers among the authorship team. Data synthesis will include narrative review and meta-analysis if appropriate.

Systematic review registration number: PROSPERO CRD42019126224

Keywords: cancer; carcinogen; conventional food; organic food; traditional food

Introduction

Cancer is a leading cause of death globally, second only to ischemic heart disease.\textsuperscript{1} In 2017, there were 24.5 million new cancer cases and 9.6 million cancer deaths worldwide.\textsuperscript{2} The five-year global prevalence of cancer is about 44 million cases.\textsuperscript{3} Dietary patterns, which are thought to increase cancer risk either directly or through excessive caloric intake leading to overweight and obesity,\textsuperscript{4} are now the number one cause of death in developed nations, ahead of other risk factors such as inadequate physical activity, tobacco, and alcohol use.\textsuperscript{5} The emphasis for nutrition-driven chemoprophylaxis (ie, cancer prevention) has predominantly been on what types of food to consume (ie, less processed meats, red meats, refined carbohydrates, added sugars and fats, and more whole grains, nutrient-rich fruits and vegetables) and on how much food to consume (ie, smaller portions).\textsuperscript{4} However, given the rapidly growing popularity and higher production costs and retail prices of organic foods,\textsuperscript{6} there is a growing need to consider the differences between organic versus non-organic types of food as an additional area of clinical and public health significance for cancer chemoprophylaxis.

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The authors declare no conflict of interest.
DOI: 10.11124/JBIES-20-00115
The regular consumption of organic foods is thought to be associated with better health outcomes than the consumption of traditionally grown foods. Organic foods are defined as when production avoids artificial fertilizers and pesticides, and uses crop rotation and other processes for the maintenance of soil fertility, weed control, and disease avoidance. Conventional food production methods may include the use of artificial fertilizers and pesticides for plant-based products, as well as the use of antibiotics and growth hormones for animal food products. There are claims in the literature that the production of organic foods avoids these potentially risky conventional food production methods, the regular consumption of organic foods may be associated with fewer harmful health effects, such as cancer, and better health outcomes overall.

A number of health-related aspects of organic food consumption have been studied and reviewed extensively in the literature relative to non-organic or traditional/conventional food consumption. For example, a prior systematic review has found that there are differences in the levels of pesticides, heavy metals, and other toxic chemicals between organic and conventionally grown crops, with organic crops having higher concentrations of beneficial antioxidants, lower concentrations of harmful compounds such as cadmium and other heavy metals, and a lower incidence of pesticide residues than the non-organic crops when compared across regions and production seasons. Another systematic review on the nutrient content of these two types of foods found no evidence of a difference in overall nutrient quality between organically and conventionally produced foods (including animal-derived food products), with the exception of non-organic foods having a higher concentration of nitrogen and organic foods having a higher concentration of phosphorus and acidity. This study also concluded that any small differences in nutrient content detected between these two types of foods may be due to differences in production methods.

Lastly, the risk of contamination of foods with pesticides and antibiotic-resistant bacteria has been examined in another systematic review. This review found that although there is a lack of strong evidence that organic foods are significantly more nutritious than conventional foods, the consumption of organic foods does appear to be associated with lower exposure to pesticide residues and antibiotic-resistant bacteria, which might support the notion that they lead to fewer adverse health effects, such as cancer. However, this review found no studies that directly examined the association between organic food consumption and any clinical outcomes, such as the incidence of cancers or other diseases.

While no prior review has specifically examined the association between organic food consumption and the incidence of cancer, a previous review that searched the literature up until the year 2009 did not identify any studies on this topic. Since then, a number of published primary research studies have been identified that suggest an association between organic foods and a decreased incidence of some cancers, but their findings remain conflicted.

A preliminary search of PROSPERO, MEDLINE, the Cochrane Database of Systematic Reviews and the JBI Database of Systematic Reviews and Implementation Reports was conducted and no current or in-progress systematic reviews on the topic were identified. Therefore, there is a need to synthesize the literature on the association between organic food consumption and the incidence of cancer. The objective of this review is to evaluate the association between organic food consumption and the incidence of cancer among adults.

**Review question**

What is the association between organic food consumption and the incidence of cancer among the adult population?

**Inclusion criteria**

**Participants**

Given that the instruments used to measure the exposure of interest are based on self-report, and given that food choices are inherently the purview of adults rather than children, the review will consider studies that include only adults (age 18 or older). This review will consider for inclusion all studies that meet the inclusion criteria regardless of context or setting.

**Exposure of interest**

This review will consider studies that evaluate the exposure of interest, which is the relative level of exposure to organic food consumption and non-organic/traditional/conventional food consumption, captured using any available methods. For the purpose of this review, measurement of the exposure...
may include self-report from the study participants, observed or direct measurement of organic food consumption by the researchers, or proxy-based measurement of organic food consumption, such as the examination of the food purchase records of study participants. In this review, the exposure groups are the “frequent,” “regular,” “high,” “always,” or “usual” users or consumers of organic foods versus the “infrequent,” “irregular,” “low,” “sometimes,” or “never” users or consumers of organic foods, as measured via the aforementioned methods of ascertaining of the exposure of interest. All methods of ascertainment of the exposure of interest must allow discrimination between regular versus irregular or non-consumption of organic foods. For this review, these methods of ascertainment of the exposure must also use either an ordinal or nominal scale of measurement that allows dichotomization of the exposure into at least two distinct, mutually exclusive groups.

Outcomes
The principal outcomes of interest for this review are the overall incidence of cancer and the organ-specific incidence of cancer. All cancers, including lymphoma, leukemia, breast, colon, lung, prostate, pancreatic, liver, genitourinary, gastrointestinal, or brain cancer, whose incidence is measured and reported in the included studies, will be considered. Studies will not be excluded on the basis of the timing and effect measures. The impact of the timing of the measurement of the exposure or outcome, if any, will be examined via meta-regression or subgroup analysis, as appropriate based on the availability of the relevant data. No other outcomes will be explored, given that other health-related outcomes have been explored previously in other relevant systematic reviews.12

Types of studies
This review will only include experimental and epidemiological study designs that can provide incidence data. These studies must therefore measure the outcome of interest at two or more time points, have at least two exposure groups, and follow an identifiable cohort of participants, whether prospectively or retrospectively. The following study designs are eligible for inclusion: natural experimental designs, quasi-experimental studies, before and after studies, pragmatic clinical trials, and prospective or retrospective cohort studies. Case control studies, cross sectional designs, case series, and case reports will be excluded as they do not provide incidence data.

Methods
The proposed systematic review will be conducted in accordance with the JBI methodology for systematic reviews of etiology and risk.14 This protocol has been registered in the PROSPERO database (CRD42019126224).

Search strategy
The search strategy aims to find both published and unpublished studies. A three-step search strategy will be implemented in this review. An initial search of MEDLINE and CINAHL will be performed, followed by an analysis of the text words contained in the title and abstract, and of the index terms used to categorize the articles. A second search using all identified keywords will be done across all included databases to identify all potentially relevant articles. A research librarian familiar with systematic review methodology will be recruited to assist in this process. In the third step of this strategy, citation chasing will be performed, whereby the reference lists of all included articles will be searched for additional relevant articles. Only studies published in the English language will be considered for inclusion in this review. Studies that have an English-language title or abstract will be retrieved in the search but excluded from the review if they lack an available English-language full text version, as the authors do not have access to language translation services. Databases will be searched from 2009 to the present, as this is the year that a previous systematic review on the relationship between organic food consumption and health outcomes concluded its search of the literature.12 This prior review searched the literature from 1966 to 2009 and found no studies with any cancer-related health outcomes. Appendix I shows a sample search strategy for one database.

The databases to be searched include: MEDLINE (Ovid), The Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL (EBSCO), EMBASE (Elsevier), PsycINFO (EBSCO), LILACS, Science.gov, Web of Science/Web of Knowledge, Academic Search Premiere (EBSCO), Dissertation

The search for unpublished studies will include: Google Scholar, ProQuest Dissertation and Theses Database, The US National Library of Medicine and NIH (National Institute of Health) subset and NLM Gateway Proceedings First, Agency for Healthcare Research and Quality (AHRQ), and WHO Library Database (WHOLIS).

Additional search considerations: The research team will contact investigators known to be involved in previous studies to obtain information about unpublished trials or cohort studies, incomplete studies, or other sources of gray literature, and will hand search the journals of a select number of organizations known to publish this type of research, including the American Cancer Society’s journal CA: A Cancer Journal for Clinicians, Journal of the American Medical Association (JAMA), and the British Journal of Cancer. Initial keywords to be used will be: organic, organic food(s), organics, natural food(s), cancer(s).

Study selection
Following the search, all identified citations will be collated and uploaded into the citation management software EndNote version X9.3.3 (Clarivate Analytics, PA, USA) and duplicates removed. Titles and abstracts will then be screened by two independent reviewers for assessment against the inclusion criteria for the review. Potentially relevant studies will be retrieved in full and their citation details imported into the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI; JBI, Adelaide, Australia). The full text of selected citations will be assessed in detail against the inclusion criteria by two independent reviewers among the members of the research team. Reasons for exclusion of full text studies that do not meet the inclusion criteria will be recorded and reported in the systematic review. Any disagreements that arise between the reviewers at each stage of the study selection process will be resolved through discussion or with a third reviewer. The results of the search will be reported in full in the final systematic review and presented in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

Assessment of methodological quality
Papers that meet the inclusion criteria will be assessed by two independent reviewers to determine the methodological validity of studies using standardized critical appraisal tools. The JBI critical appraisal tool that corresponds to each specific study methodology will be used in this review. Authors of papers will be contacted to request missing or additional data for clarification, where required. Any disagreements that arise between any two reviewers will be resolved through discussion or with a third reviewer. The researchers will be trained in the appropriate use of these tools, including piloting each tool between at least two reviewers on the first four studies that meet the inclusion criteria, and defining in advance which critical appraisal criteria are paramount. The risk of bias assessment results will be reported in narrative form and in a table showing each included study as well as the aggregate risk of bias across all studies. All studies, regardless of the results of their methodological quality, will undergo data extraction and synthesis (where possible).

Data extraction
Data will be extracted from studies included in the review using a de novo data extraction tool to be piloted among the reviewers. The data extraction will retrieve specific details relevant to the research question, such as: study methods (specific study design and any variations in methods that deviate from the identified methodology); study population (total number in each group and their baseline comparability, and average age, male to female proportion, prior history of cancer and family history of cancer, basal metabolic index [BMI] and smoking status as confounding variables); exposures (frequent/usual consumers of organic foods vs. infrequent/non-consumers of organic foods, and cutoff levels used to define exposure vs. non-exposure); and outcomes of interest and their results (sample size and number of incident cancers in each exposure group, number of participants lost to follow-up and number included in the final analysis). The researchers of the primary studies will be contacted on an as-
needed basis to retrieve missing data. Appendix II shows the data extraction instrument.

**Data synthesis**

Data from experimental and observational studies will be meta-analyzed separately. The random effects model accounts for the between-study variability and is the preferred meta-analytic approach in this review. The data will be subject to double entry for verification of accuracy. The outcome data for the meta-analysis will be dichotomized based on the 50th percentile for ascertainment of the exposure to organic food consumption: outcome data for groups that fall at or below the 50th percentile will be grouped under “irregular organic food consumption,” and outcome data for groups that fall above the 50th percentile will be grouped under “regular organic food consumption.” If the available outcome data is partitioned based on the same cutoff levels for the ascertainment of exposure to organic food consumption across studies, then a dose-response meta-analysis will be conducted to preserve these cutoffs and produce a more precise estimate of the impact of the exposure on the outcome.

All effect sizes will be expressed as relative risks (RR), and their 95% confidence intervals will be calculated. Odds ratios (OR) will not be used as the review will only include studies that provide true incidence/risk measures. Between-study heterogeneity will be assessed using the Cochran’s Q-test and I² value. Given that the nature of this review’s research question suggests that it is likely that primarily observational and quasi-experimental study designs will be found, which are known to be at greater risk of heterogeneity, the I² value will be calculated and reported but will not influence the decision to explore reasons for any heterogeneity present, unless its value is 0, in which case no exploration of heterogeneity is necessary. The statistical analyses will be performed using the JBI SUMARI or Open Meta[Analyst] (Center for Evidence Synthesis in Health, Brown, RI, USA) software program. The choice of statistical software package will be based on the analytic needs of the review and the capabilities of each of these software programs. Where statistical pooling is not possible the findings will be presented in narrative form, including tables and figures to aid in data presentation where appropriate. Funnel plots and statistical tests for funnel plot asymmetry (Egger test, Begg test, Harbord test) will be performed using the Open-Meta Analyst for Ecology and Evolution (OpenMEE) to assess publication bias if there are 10 or more studies included in the meta-analysis.

Meta-analysis will be of the appropriately adjusted effect estimates reported by the studies. If the adjusted estimates are not reported, the meta-analysis will adjust for the identified confounders via meta-regression. If sufficient data is available from the included studies, subgroup analysis or meta-regression will be used to explore the impact of a variety of study-level confounding variables on the outcome of interest, including all the variables that characterize the population (eg, differential mean age, male to female proportion, smoking status, prior history of cancer, family history of cancer and BMI across the studies), those that may influence the nature of the exposure or outcome of interest (eg, differential timing of the measurement of the exposure or outcome across the studies, differential cutoffs used to define levels of exposure, or differential outcomes between the identified types of cancers), and the impact of variation in study methods (eg, prospective versus retrospective cohort designs). Sensitivity analysis will also be used to evaluate the impact of individual studies and the use of different cutoff levels to ascertain exposure (eg, 50th percentile vs. quartiles vs. quintiles) on the final interpretation of the meta-analysis.

**Assessing certainty in the findings**

The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach for grading the certainty of evidence will be followed and a Summary of Findings will be created using GRADEpro GDT 2015 (McMaster University, ON, Canada). The Summary of Findings will present the following information where appropriate: absolute risks for the treatment and control; estimates of relative risk; and a ranking of the quality of the evidence based on the risk of bias, directness, heterogeneity, precision, and risk of publication bias of the review results. The outcomes reported in the Summary of Findings will be: the overall incidence of cancer and the incidence of organ-specific cancers.

**Funding**

This project is funded through the Health Resources and Services Administration (HRSA), training grant# 1 D33HP31671-01-00. The proposed topic was selected by the authors on the basis of the
funder’s priority areas. The funder has no role in the conduct or reporting of the systematic review.

References


### Appendix I: Search strategy

**MEDLINE (Ovid)**  

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<tr>
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</table>
Appendix II: Data extraction instrument

The de novo data extraction tool that will be used in this review is described in the text of the review. The following is a list of the data to be extracted from the included studies.

<table>
<thead>
<tr>
<th>Data extraction instrument</th>
<th>Overall study</th>
<th>Regular consumption group</th>
<th>Irregular consumption group</th>
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<td>Population</td>
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<td></td>
<td>Mean age and SD</td>
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<td></td>
<td>Male-to-female proportion</td>
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<td></td>
<td>Proportion with a prior history of cancer</td>
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<td>Proportion with a family history of cancer</td>
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<td></td>
<td>Mean BMI and SD</td>
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<td>Proportion of smokers</td>
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<tr>
<td>Exposure groups</td>
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<td>Classification method used for ascertainment of level of exposure (eg, quartiles, quintiles)</td>
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<td>Number of incident cancers</td>
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<td>Number of participants lost to follow-up, with reasons if provided</td>
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<td>Number included in the final analysis</td>
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<td>Unadjusted effect size data (RR, CI, p-value)</td>
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BMI, basal metabolic index; CI, confidence interval; RR, relative risk; SD, standard deviation.