USDA Nutrition Evidence Library: Systematic Review Methodology

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USDA Center for Nutrition Policy & Promotion
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The National Academies of Sciences, Engineering, and Medicine, Health and Medicine
Division: Committee to Review the Process to Update the Dietary Guidelines for Americans
Background on the Nutrition Evidence Library (NEL)

Overview of NEL Systematic Review Methods
The NEL evaluates scientific evidence on food and nutrition to answer systematic review questions.

- Utilizes a rigorous, transparent process
- Meets Federal mandates
- Informs Federal nutrition policy and programs
The Nutrition Evidence Library implements a 6-step systematic review process.

1. Topic identification and question development
2. Literature search, screening, and selection
3. Data extraction and risk of bias assessment
4. Evidence description and synthesis
5. Conclusion statements and evidence grading
6. Identification of research recommendations
The Advisory Committee makes all substantive decisions; NEL staff ensure the process adheres to the established methods.

**Dietary Guidelines Advisory Committee**

**supported by NEL Analysts**

**NEL Librarians** support the literature search

**External Evidence Abstractors** assist with data extraction and risk of bias assessments
Step 1: Topic identification and question development
NEL systematic review questions are developed using the PICO framework.

- **Population:** Population of interest, and any relevant subpopulations
- **Intervention:** Intervention and/or exposure (independent variable) of interest
- **Comparator:** Main comparison of interest (e.g., main alternative to intervention or exposure)
- **Outcomes:** Public health outcomes (e.g., health or diet-related outcomes) of interest (dependent variables)

*Confounders and key definitions are also considered.*
The analytic framework lays the foundation for the systematic review.

What is the relationship between adherence to dietary guidelines/recommendations or specific dietary patterns, assessed using an index or score, and the risk of cardiovascular disease?

Target Population
Adults and children 2 years and older

Exposures
Dietary patterns indices and scores

Comparators
- Different levels of adherence to a dietary pattern
- Adherence to a different dietary pattern

Intermediate Outcomes
- Triglycerides
- LDL-cholesterol
- HDL-cholesterol

Clinic Outcomes
- Incidence of CVD
- CVD-related deaths

Dietary Patterns
Quantities, proportions, variety, or combination of different foods, drinks, and nutrients (when available) in diets, and the frequency with which they are habitually consumed.

Potential Confounders
- Total energy intake
- Physical activity
- Baseline weight status
- Smoking
- Age
- Gender

Hypertension
Blood pressure

Myocardial infarction
Stroke
Step 2: Literature search, screening, and selection
Inclusion/exclusion criteria ensure a relevant and appropriate body of evidence is identified.

<table>
<thead>
<tr>
<th>Category</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
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<tbody>
<tr>
<td><strong>Study Design</strong></td>
<td>• Randomized controlled trials</td>
<td>• Cross-sectional studies</td>
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<td>• Non-randomized controlled trials</td>
<td>• Uncontrolled studies</td>
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<td>• Prospective cohort studies</td>
<td>• Pre/post studies without a control</td>
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<td>• Retrospective cohort studies</td>
<td>• Narrative reviews</td>
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<td>• Case-control studies</td>
<td>• Systematic reviews</td>
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<td>• Pre/post studies with a control</td>
<td>• Meta-analyses</td>
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<tr>
<td><strong>Risk of Bias</strong></td>
<td>All studies regardless of NEL BAT</td>
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<tr>
<td><strong>Language</strong></td>
<td>Studies published in English</td>
<td>Studies published in languages other than English</td>
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<tr>
<td><strong>Publication Status</strong></td>
<td>Studies published in peer-reviewed journals</td>
<td>Grey literature, including unpublished data, manuscripts, reports, abstracts, conference proceedings</td>
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<td><strong>Health Status of Study Subjects</strong></td>
<td>• Studies done in generally healthy subjects</td>
<td>• Studies that exclusively enroll subjects with a disease</td>
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<td>• Studies done in samples with elevated chronic disease risk or that enroll some subjects with a disease or with the health outcome of interest</td>
<td>• Studies done in hospitalized or malnourished subjects</td>
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</table>
The Librarians develop and implement a literature search strategy.

Bibliographic databases (e.g., PubMed/MEDLINE, Cochrane, Embase)

Search terms and filters

DGAC, Peer-review librarian, Analyst
Title, abstract, and full text screening is completed by two independent screeners.
All steps of the process are documented to ensure transparency and reproducibility.
Step 3: Data extraction and risk of bias assessment
Key data relevant to the systematic review question are extracted into an Evidence Grid.

- Study design
- Study description
- List of independent variables
- Description of independent variables

**[DOMAIN FIELD NAME]: Duration**

**[INSTRUCTIONS]**: Record the total length of the intervention (for experimental studies), the total length of the observational period (for observational studies), the recall period (for retrospective studies), or the mean length and SD when total length is not provided. Specify components (e.g., run-in, intervention, and/or follow-up) in parentheses separated by commas, and do not include a space before the units (i.e., d, wk, mo, y).

**[EXAMPLES]**: 10y or 17d (SD=1.2d) or 20wk (2wk run-in, 8wk intervention, crossover)

- Race/ethnicity
- SES
- Baseline health status
- Funding source
- Supplemental publications
- Abstractor comments
The NEL Bias Assessment Tool (BAT) is an instrument that assesses studies’ internal validity.

**Selection Bias**
- Inclusion/exclusion criteria
- Recruitment
- Allocation
- Baseline distribution of confounders

**Performance Bias**
- Adherence (participants/ investigators)
- Unplanned concurrent exposures
- Blinding (participants/ investigators)

**Detection Bias**
- Blinding (outcome assessors)
- Outcome measures
- Statistical methods

**Attrition Bias**
- Follow-up length
- Attrition

**INTERNAL VALIDITY**

Reported effect vs True effect
Step 4: Evidence description and synthesis
Evidence synthesis is the process by which evidence from multiple studies is compared, contrasted, and combined.

- Overarching themes
- Similarities and differences
- Factors impacting the relationships
- Research gaps and limitations
Step 5: Conclusion statements and evidence grading
A conclusion statement is a brief summary statement that answers the systematic review question.

**Systematic Review Question:**
What is the relationship between the use of diet and weight self-monitoring strategies and of body weight outcomes in adults?

**Indicates strength of evidence**

**Conclusion Statement:**
Moderate evidence indicates that dietary patterns rich in vegetables, fruit and whole grains, and lower in animal products and refined carbohydrate, are associated with reduced risk of postmenopausal breast cancer. The data regarding this dietary pattern and premenopausal breast cancer risk point in the same direction, but the evidence is limited due to fewer studies.

**Grade:** Moderate: Postmenopausal breast cancer risk; Limited: Premenopausal breast cancer risk
Predefined criteria are used to evaluate and grade the strength of evidence supporting the conclusion statement.

<table>
<thead>
<tr>
<th>Elements</th>
<th>Grade I: Strong</th>
<th>Grade II: Moderate</th>
<th>Grade III: Limited</th>
<th>Grade IV: Grade Not Assignable</th>
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</thead>
<tbody>
<tr>
<td><strong>Internal Validity of the Evidence</strong></td>
<td>The body of evidence has a <strong>strong</strong> number of:</td>
<td>The body of evidence has a <strong>moderate</strong> number of:</td>
<td>The body of evidence has a <strong>limited</strong> number of:</td>
<td>A <strong>grade is not assignable</strong> for this element because it cannot be adequately assessed</td>
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<td>determined with the NEL Bias Assessment Tool</td>
<td>a) studies overall</td>
<td>a) studies overall</td>
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<td>b) studies by independent research groups</td>
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<td>c) studies with sample sizes that are sufficient to avoid type I and II errors</td>
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<td>d) participants overall</td>
<td>d) participants overall</td>
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<td><strong>Adequacy of Evidence</strong></td>
<td>Cross the body of evidence, the findings have a <strong>strong</strong> consistency in:</td>
<td>Cross the body of evidence, the findings have a <strong>moderate</strong> consistency in:</td>
<td>Cross the body of evidence, the findings have a <strong>limited</strong> consistency in:</td>
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<td>b) size of effect/degree of association</td>
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<td>c) statistical significance</td>
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<td>&amp;g, some explainable inconsistencies</td>
<td>&amp;g, some explainable inconsistencies</td>
<td>&amp;g, several explainable inconsistencies, some unexplainable inconsistencies</td>
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<tr>
<td><strong>Consistency of the Evidence</strong></td>
<td>The body of evidence demonstrates a <strong>strong</strong> impact, as evidenced by:</td>
<td>The body of evidence demonstrates a <strong>moderate</strong> impact, as evidenced by:</td>
<td>The body of evidence demonstrates a <strong>limited</strong> impact, as evidenced by:</td>
<td>A <strong>grade is not assignable</strong> for this element because it cannot be adequately assessed</td>
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<td>a) the directness with which the study designs examine the link between the</td>
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<td>c) the practical/clinical significance</td>
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<td>&amp;g, some studies were direct; some findings were statistically significant; there is some likelihood of practical/clinical significance</td>
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<tr>
<td><strong>Impact of the Evidence</strong></td>
<td>The body of evidence has <strong>strong</strong> generalizability to the U.S. population of</td>
<td>The body of evidence has <strong>moderate</strong> generalizability to the U.S. population of</td>
<td>The body of evidence has <strong>limited</strong> generalizability to the U.S. population of</td>
<td>A <strong>grade is not assignable</strong> for this element because it cannot be adequately assessed</td>
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<td>interest with regard to:</td>
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<td>a) the study samples</td>
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</table>
The grade communicates the strength of the evidence supporting the conclusion statement.

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<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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<tr>
<td><strong>Strong</strong></td>
<td>The conclusion statement is substantiated by a large, high quality, and/or consistent body of evidence that directly addresses the question. There is a high level of certainty that the conclusion is generalizable to the population of interest, and it is unlikely to change if new evidence emerges.</td>
</tr>
<tr>
<td><strong>Moderate</strong></td>
<td>The conclusion statement is substantiated by sufficient evidence, but the level of certainty is restricted by limitations in the evidence, such as the amount of evidence available, inconsistencies in findings, or methodological or generalizability concerns. If new evidence emerges, there could be modifications to the conclusion statement.</td>
</tr>
<tr>
<td><strong>Limited</strong></td>
<td>The conclusion statement is substantiated by insufficient evidence, and the level of certainty is seriously restricted by limitations in the evidence, such as the amount of evidence available, inconsistencies in findings, or methodological or generalizability concerns. If new evidence emerges, there could likely be modifications to the conclusion statement.</td>
</tr>
<tr>
<td><strong>Grade not assignable</strong></td>
<td>A conclusion statement cannot be drawn due to a lack of evidence or the availability of evidence that has serious methodological concerns.</td>
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USDA
United States Department of Agriculture
Center for Nutrition Policy and Promotion

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Step 6: Identification of research recommendations
Research recommendations describe the research needed with rationale.

- Identified and based on research gaps and limitations identified during the review process

Research Recommendations

In order to better assess the relationship between dietary patterns and risk of developing breast cancer, additional research is needed to:

- Improve and validate novel epidemiologic tools for the accurate assessment of dietary patterns over the life course, including the use of biomarkers
- Improve methodologic approaches for defining different dietary patterns such that patterns can be more consistently identified, scored and compared across studies
- Establish cohort studies that start earlier in life in order to capture dietary patterns contributing to risk of breast cancer risk later in life. It is particularly important to consider key phases of the life cycle relevant to breast cancer, including childhood and menarche, adolescence and periods of mammary gland development and growth, periods of reproduction and lactation and subsequent years prior to cancer development
- Assess associations of dietary patterns by subtypes of breast cancer defined by histopathologic outcomes, tumor hormone receptor status, molecular genotypes, gene expression patterns and other biological characteristics that influence the tumor behavior, for example, by tumor hormone receptor status and other relevant phenotypic characteristics (i.e., HER2 status)
- Examine how anthropometrics, physical activity and sedentary behaviors modify the relationship between dietary patterns and risk of breast cancer
- Examine the impact of SES, and ethnic/racial groups in regards to dietary patterns and breast cancer.
NEL Systematic Reviews are transparent and accessible.
For additional information visit
www.NEL.gov