Beyond Diabetes, Obesity, and Cardiovascular Disease: An Evidence Map of Anti-Inflammatory Diet and Related Dietary Interventions for the Prevention and Management of Chronic Health Conditions

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AUTHORS

Author roles, affiliations, and contributions (using the CRediT taxonomy) are listed below.

Author	Role and Affiliation	Report Contribution
Sydne Newberry, PhD	Research Communications Analyst, RAND Corporation Santa Monica, CA	Conceptualization, Data curation, Methodology, Investigation, Formal analysis, Visualization, Validation, Writing – original draft, Writing – review & editing
Dazhe Chen, PhD	Postdoctoral IRTA Fellow, National Institute of Environmental Health Sciences Durham, NC	Formal analysis, Data curation, Validation, Investigation, Writing – original draft, Writing – review & editing
Paul Shekelle, MD, PhD, MPH	Director, VA Greater Los Angeles Evidence Synthesis Program (ESP) Center Los Angeles, CA	Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing
Selene Mak, PhD, MPH	Program Manager, VA Greater Los Angeles ESP Center Los Angeles, CA	Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing
Meron Begashaw, MPH	Project Coordinator, VA Greater Los Angeles ESP Center Los Angeles, CA	Data curation, Project administration, Software, Validation, Writing – original draft
Gerardo De Vries, MPH	Project Coordinator, VA Greater Los Angeles ESP Center Los Angeles, CA	Data curation, Project administration, Software, Validation, Visualization, Writing – original draft, Writing – review & editing
Isomi Miake-Lye, PhD, MPH	Co-Director, VA Greater Los Angeles ESP Center Los Angeles, CA	Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to conduct timely, rigorous, and independent systematic reviews to support VA clinicians, program leadership, and policymakers improve the health of Veterans. ESP reviews have been used to develop evidence-informed clinical policies, practice guidelines, and performance measures; to guide implementation of programs and services that improve Veterans' health and wellbeing; and to set the direction of research to close important evidence gaps. Four ESP Centers are located across the US. Centers are led by recognized experts in evidence synthesis, often with roles as practicing VA clinicians. The Coordinating Center, located in Portland, Oregon, manages program operations, ensures methodological consistency and quality of products, engages with stakeholders, and addresses urgent evidence synthesis needs.

Nominations of review topics are solicited several times each year and submitted via the ESP website. Topics are selected based on the availability of relevant evidence and the likelihood that a review on the topic would be feasible and have broad utility across the VA system. If selected, topics are refined with input from Operational Partners (below), ESP staff, and additional subject matter experts. Draft ESP reviews undergo external peer review to ensure they are methodologically sound, unbiased, and include all important evidence on the topic. Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. In seeking broad expertise and perspectives during review development, conflicting viewpoints are common and often result in productive scientific discourse that improves the relevance and rigor of the review. The ESP works to balance divergent views and to manage or mitigate potential conflicts of interest.

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Operational Partners

Operational partners are system-level stakeholders who help ensure relevance of the review topic to the VA, contribute to the development of and approve final project scope and timeframe for completion, provide feedback on the draft report, and provide consultation on strategies for dissemination of the report to the field and relevant groups.

Tessa Johnson, MS, RDN, IFNCP, RYT
Clinical Dietitian; National Education Champion
Nutrition and Food Service Clinical Nutrition Committee, Integrative and Functional Nutrition Workgroup
Office of Patient Centered Care and Cultural Transformation, Eating for Whole Health

Katherine Dignan, MS, RD, LD, CDCES
Clinical Dietitian
Nutrition and Food Service Clinical Nutrition Committee, Integrative and Functional Nutrition Workgroup

Kwynn Mason, MPH, RDN, LDN, CLS, IFNCP
Clinical Dietitian
Nutrition and Food Service Clinical Nutrition Committee, Integrative and Functional Nutrition Workgroup

Glory Rodriguez-Gomez, MS, RDN, CDCES, LD, IFNCP
Employee Whole Health Coordinator
Nutrition and Food Service Clinical Nutrition Committee, Integrative and Functional Nutrition Workgroup

Technical Expert Panel

To ensure robust, scientifically relevant work, the technical expert panel (TEP) guides topic refinement; provides input on key questions and eligibility criteria, advising on substantive issues or possibly overlooked areas of research; assures VA relevance; and provides feedback on work in progress. TEP members included:

Shari Pollack, MPH, RDN, LDN
Employee Whole Health Coordinator
Jesse Brown VA Medical Center

Julie Obbagy, PhD, RD
Nutritionist
Center for Nutrition and Promotion, Food and Nutrition Service, U.S. Department of Agriculture

Wendy Kohatsu, MD, ABOIM
Techworks Consultant
VA Office of Patient Centered Care and Cultural Transformation

Disclosures

This report was prepared by the Evidence Synthesis Program Center located at the **VA Greater Los Angeles Healthcare System,** directed by Paul Shekelle, MD, PhD and Isomi Miake-Lye, PhD and funded by the Department of Veterans Affairs, Veterans Health Administration, Health Systems Research.

The findings and conclusions in this document are those of the author(s) who are responsible for its contents and do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. The final research questions, methodology, and/or conclusions may not necessarily represent the views of contributing operational and content experts. No investigators have affiliations or financial involvement (*eg*, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.

Executive Summary

KEY FINDINGS

- Proposed impacts of anti-inflammatory dietary patterns on—or associations of these dietary patterns with—risks for some chronic diseases and mortality lack a strong evidence base. This is partly due to the small numbers of original studies, most of which are observational in design.
- Although multiple anti-inflammatory dietary patterns, including the DASH diet, Mediterranean diet, and to a lesser extent, vegetarian/plant-based diets, appear to be associated with lower risks for some chronic conditions, including hypertension, some types of cancer, and liver diseases, these observations could be due to foods excluded from these dietary patterns, foods they include, or both.
- This evidence map was not intended to support recommendations regarding adoption of particular diets. Despite lack of a full understanding of how anti-inflammatory diets might be beneficial for preventing and managing some chronic conditions, the demonstrated benefits for other conditions and apparent lack of harms suggest that there may be no downside to adopting one of these diets. However, the larger finding is the gap in the evidence base underlying the possible effect of the diets on the conditions covered in this report.

BACKGROUND

Six out of 10 adults in the United States have at least one chronic health condition, and chronic diseases are the nation's leading cause of death and disability (causing 7 in 10 deaths each year). Chronic health conditions include heart disease, cancer, diabetes, chronic pain, asthma, inflammatory gastrointestinal disorders, degenerative diseases, obesity, and Alzheimer's disease/dementia. Some evidence supports a common role for inflammation as a contributory factor across these conditions. Other lines of evidence have supported a role for particular diets in reducing markers of inflammation. Thus, there is considerable interest in assessing the role of diets with anti-inflammatory properties in preventing or managing chronic disease conditions. Evidence is plentiful for some conditions, such as diabetes, obesity, and cardiovascular disease, but sparse for others. The aim of this synthesis is to develop evidence maps that provide a visual overview of the distribution of evidence for the role of anti-inflammatory dietary patterns on the prevention and management of chronic health conditions where anti-inflammatory diet and related interventions are not yet established as one standard of care. The evidence maps have accompanying narrative that helps stakeholders interpret the state of the evidence to inform policy and clinical decision-making. The aim of this report is to summarize the body of evidence to date linking dietary patterns believed to have anti-inflammatory properties with outcomes for a set of relatively understudied health conditions; this report is not intended to issue recommendations about pursuing any particular dietary pattern.

METHODS

DATA SOURCES AND SEARCHES

Search strategies were developed with an experienced medical librarian who is expert in literature reviews. Searches were conducted in bibliographic databases conducted searches from inception to July

2023 in bibliographic databases (Medline, Cumulated Index to Nursing and Allied Health Literature [CINAHL], Cochrane Database of Systematic Reviews [CDSR]), non-bibliographic databases (Canadian Agency for Drugs and Technologies in Health [CADTH]), National Center for Biotechnology Information [NCBI] Bookshelf, VA Dimensions), and in PROSPERO for reviews in development.

STUDY SELECTION

Titles of potentially eligible reviews were screened in duplicate for relevance by 5 authors independently; any article chosen by at least 1 reviewer based on the title went on for abstract screening. Abstracts were then reviewed in duplicate, with any discrepancies resolved by group discussion. All titles and abstracts were selected based on the eligibility criteria described in the section below.

Eligible publications were systematic reviews (SRs) of studies of 1) adults that examined the efficacy or effectiveness of 2) the Dietary Approaches to Stop Hypertension (DASH) diet, Mediterranean-type diets (MD), the Dietary Inflammatory Index (DII), vegetarian/plant-based diets, or other anti-inflammatory diets 3) for preventing or managing clinical outcomes related to blood pressure, cancer, autoimmune diseases, frailty, cognitive function, liver disease conditions, all-cause mortality, or mortality related to the conditions named; or assessed associations of adherence to these diets or diet indexes with those outcomes and 4) assessed the certainty of evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) or a comparable method.

DATA ABSTRACTION AND ASSESSMENT

Each included systematic review had data abstracted by 2 reviewers. Abstracted data included but were not limited to number of studies included in the review that had one of the diets of interest as the intervention or exposure, condition, type of diet, comparators, certainty of evidence rating, and certainty of evidence conclusion(s) relevant to the outcomes of interest.

SYNTHESIS

Our evidence mapping process resulted in visual depictions of the evidence for the role of anti-inflammatory dietary patterns on the prevention and management of chronic health conditions, excluding diabetes, obesity, and cardiovascular disease, as well as an accompanying narrative and table. Each visual depiction or evidence map uses a bubble plot format to display information on 4 dimensions: bubble size (numbers of relevant studies included in the review), bubble shape/color (study designs), bubble label (health condition), and y-axis (certainty of evidence underlying the conclusion). Each bubble represents a conclusion from an included systematic review. Thus, a systematic review may be represented multiple times, either in one map or multiple maps, but each conclusion appears only once.

RESULTS

We identified 2,309 potentially relevant citations. A total of 320 publications were retained and reviewed at full text. We excluded 292 publications for study design, outcomes that were not within scope, or failure to grade evidence, leaving 28 included publications. Based on these reviews, we created 6 evidence maps, one for each category of dietary patterns (*ie*, Mediterranean diet, DASH diet,

Dietary Inflammatory Index, vegetarian/plant-based diet, vegan diet, and other anti-inflammatory diets).

Of the 28 included studies, 4 reviewed more than 1 type of diet, while the other 24 focused on a single diet. While there are 28 included publications in total, some of those studies are counted multiple times across different diet categories because they examine more than 1 diet. From these reviews, 52 conclusions were made about 6 different types of diets. Two of the 6 diets were exclusively low or very low certainty of evidence. Of the 52 conclusions, 22 were drawn from 14 included reviews for the MD, 16 conclusions from 9 included reviews for the DASH diet, 5 conclusions from 5 included reviews for the DII, 5 conclusions from 4 included reviews for the vegetarian/plant-based diet, 3 conclusions from 3 included reviews for the anti-inflammatory diet, and 1 conclusion from 1 included review for the vegan diet (see Table 1).

Among the reviews that met our inclusion criteria of moderate or high certainty of evidence, 10 conclusions from 7 reviews considered the MD, 10 conclusions from 7 reviews considered the DASH diet, 3 conclusions from 3 reviews considered the DII, and 2 conclusions from 1 review considered the vegetarian/plant-based diet, for a total of 25 conclusions. Across the reviews of these 4 dietary patterns, 6 conclusions from the Mediterranean and DASH diets were supported by high certainty of evidence (see Table 8):

- The DASH diet was associated with significant reductions in systolic and diastolic blood pressure, compared with the consumption of other diets.
- A network meta-analysis suggested that the DASH diet might be the most effective dietary measure to reduce blood pressure among individuals with hypertension or pre-hypertension.
- A 5-point increase in adherence to the DASH diet reduced cancer-related mortality by 3%.
- A 5-point increase in adherence to the DASH diet reduced the risk for all-cause mortality by 5%.
- Better adherence to a Mediterranean diet was associated with decreased risk of frailty and pre-frailty (based on the findings of both randomized controlled trials and observational studies).

Moderate certainty of evidence supported 18 conclusions regarding the diets investigated and associated health outcomes, mainly the Mediterranean and DASH diets (See Table 9):

- SRs of observational studies found associations of the Mediterranean Diet, DASH diet, and lower DII scores with reductions in various cancer risk outcomes. For example, higher adherence to the Mediterranean diet and the DASH diet and lower DII scores are associated with lower risks for colorectal cancer and hepatocellular carcinoma and lower cancer-associated mortality.
- Adherence to both the Mediterranean diet and the DASH diet and lower DII scores are associated with lower risks for cirrhosis and nonalcoholic fatty liver disease (NAFLD).
- Adherence to the Mediterranean diet is associated with reduced risk for cognitive decline.

DISCUSSION

KEY FINDINGS AND CERTAINTY OF EVIDENCE

The proposed impacts of anti-inflammatory dietary patterns on—or associations of these dietary patterns with—risks for the chronic disease outcomes within scope of this study mostly lack a strong evidence base. This is partly due to small numbers of original studies and the challenges in examining these relationships via randomized controlled trials using clinical outcomes, rather than observational studies on biomarkers or other intermediate outcomes.

Multiple anti-inflammatory dietary patterns, including the DASH diet, Mediterranean diet, and to a lesser extent, vegetarian/plant-based diets, appear to be associated with lower risks for some chronic conditions, including high blood pressure, some types of cancer, and liver diseases (cirrhosis and NAFLD). However, these observations could be due to foods excluded from these dietary patterns as much as to foods or food combinations they include.

Despite lack of understanding of how anti-inflammatory diets might be beneficial for preventing and managing some chronic conditions, the demonstrated benefits for other conditions and apparent lack of harms suggest that there is no downside to promoting these diets.

This evidence map has a number of limitations, some inherent to the research and some inherent to the mapping process. As mentioned, most studies aimed at assessing the role of dietary patterns or individual foods or nutrients on chronic disease endpoints are relatively low-quality observational studies that rely on self-report or other potentially inaccurate methods of assessing exposures and adherence and on measures of intermediate outcomes of unclear value. In addition, because of the relatively large numbers of existing systematic reviews for some disease conditions of interest, we selected the most recent or most inclusive reviews for our map. Thus, we might have missed reviews that arrived at different conclusions. That being said, the proportion of reviews that assessed the certainty of the evidence supporting their conclusions was small for all outcomes and conditions of interest.

FUTURE RESEARCH

Definitively determining the impact of diets that might have anti-inflammatory properties on the risk of developing chronic diseases depends on first identifying several missing pieces in the biological plausibility chain. Most importantly, intermediate outcomes such as biomarkers that have consistent, significant associations—positive or negative—with disease risk must be identified and ideally, some chain of causality must be established. Inflammation is a natural process that serves vital physiological roles: Thus, the idea that a dietary pattern that non-selectively suppresses inflammation might have health benefits needs extensive clarification. Then it will be necessary to determine whether certain combinations of foods or nutrients or certain overall dietary patterns or the avoidance of certain foods or eating patterns are responsible for the observed health outcomes and whether these outcomes are also affected by other modifiable lifestyle characteristics.

CONCLUSIONS

Moderate or high certainty evidence linking diets with anti-inflammatory characteristics to chronic disease prevention or management outcomes is relatively sparse for conditions other than cardiovascular disease, diabetes, and obesity. Nevertheless, the evidence suggests that adherence to

diets such as DASH and Mediterranean-type eating patterns might have beneficial associations with reduction or management of chronic disease risks associated with blood pressure, liver diseases, cognitive function, and some types of cancer. Moreover, adverse events or harms associated with these diets are essentially non-existent.