Nutrition and Policy: Evaluating Evidence

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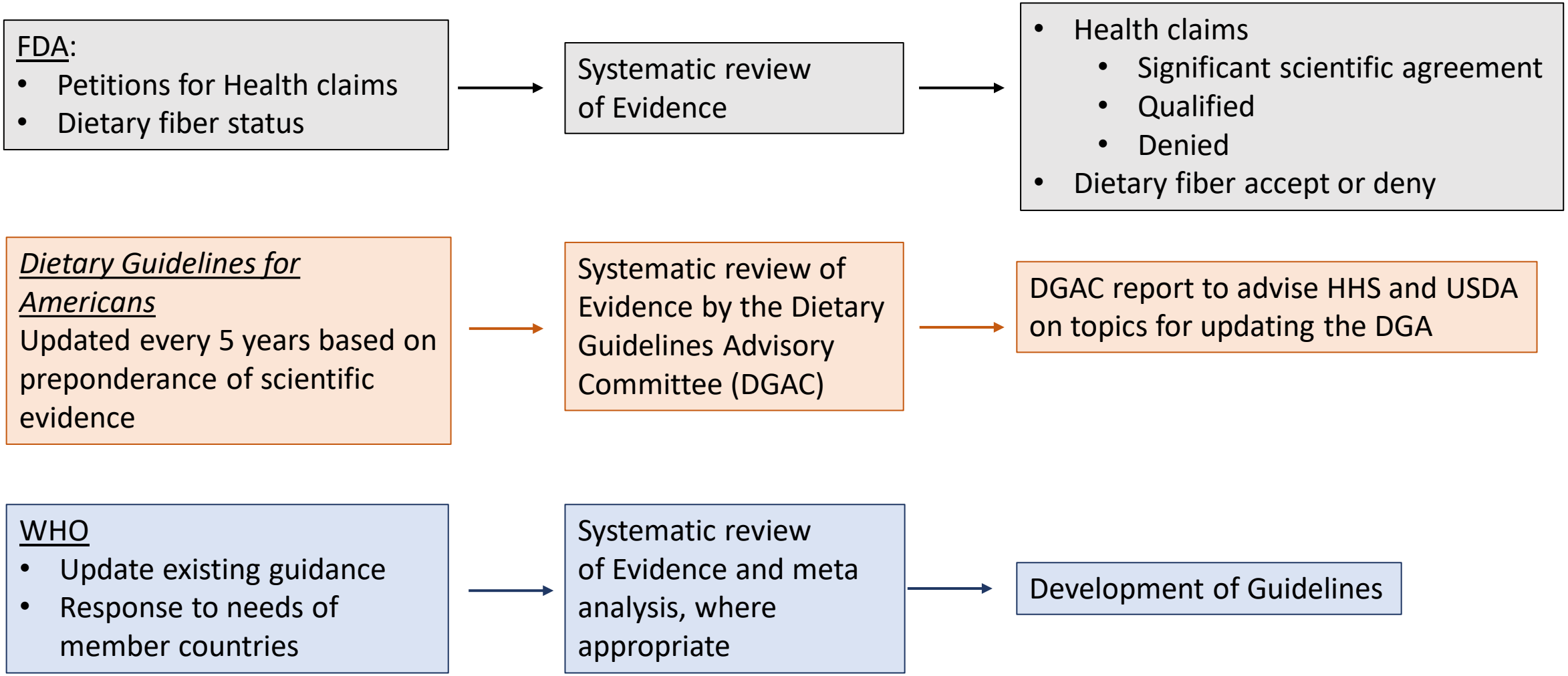
Disclosures

AFFILIATION/FINANCIAL INTERESTS (prior 12 months)	ENTITIES
Grants/Research Support	None
Scientific Advisory Board/Consultant/Board of Directors	McCormick Science Institute; International Food Information Council Trustee; International Advisory Board for Saudi Arabia National Nutrition Committee; Coalition for Grain fiber Science Advisory Committee
Speakers Bureau	None
Stock Shareholder	Mutual funds or managed accounts
Employee	N/A-Retired from UC Davis and Federal government
Other	2020 Dietary Guidelines Advisory committee, chair WHO NUGAG Diet and Health subcommittee WHO NUGAG Policy Actions subcommittee NASEM Food and Nutrition Board IUFoST Task Force on Food Classification

Main question for presentation

- What are examples of the application of meta-analysis in nutrition and policy?
  - Important to include use of systematic reviews
- Approach—based on my experience in 3 areas:
  - Food and Drug Administration: Food labeling, including health claims
  - Dietary Guidelines Advisory Committee: Scientific report for 2020-25 DGA
  - WHO: NUGAG Subcommittees on Diet and Health and on Policy Actions

Three examples (experiences) for discussion



From the WHO Handbook for Guideline Development, 2nd Edition

- "A "systematic review is "a review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to extract and analyse data from the studies that are included in the review" (1)"
  - WHO quote from Glossary of terms in The Cochrane Collaboration. Version 4.2.5. Oxford: The Cochrane Collaboration; 2005.
- A systematic review is different from a meta-analysis. The latter term refers to the quantitative synthesis (pooling) of an outcome across comparable studies to achieve a pooled estimate of effect...
- If the data extracted from the systematic review meet certain requirements (the most important one being a high level of homogeneity in study design and in population, intervention, comparator and outcomes across studies), then the data can be combined across comparable studies in a meta-analysis. A meta-analysis is a statistical method used to summarize the quantitative results of independent studies, providing a summary estimate of effect with a confidence interval."

In other words…

A systematic review differs from meta-analysis but is important for determining when a meta-analysis is useful.

Methodology Used for Evidence Evaluation

FDA:
- Petitions for Health claims
- Dietary fiber status

→ Guidance for industry: Evidence-Based Review System for the Scientific Evaluation of Health Claims. www.fda.gov
Use of authoritative reports

→
- Health claims
  - Significant scientific agreement
  - Qualified
  - Denied
- Dietary fiber accept or deny

Dietary Guidelines for Americans
Updated every 5 years based on preponderance of scientific evidence

→ Nutrition Evidence Systematic Review (NESR at USDA) methodology
https://nesr.usda.gov

→ DGAC report to advise HHS and USDA on topics for updating the DGA

WHO
- Update existing guidance
- Response to needs of member countries

→ WHO Handbook for Guideline Development, 2nd edition
https://www.who.int/publications/i/item/9789241548960

→ Development of Guidelines

Components of the process for using the systematic review

- A scoping review or evidence scan
- Structuring the systematic review and determining what can be used for a meta-analysis
- Criteria used for judging the quality of the evidence
- The process to move from evidence to decision or recommendation

Where is a Scoping Review or Evidence Scan useful?

Organization	Use of scoping review or evidence scan
FDA Health claim petitions; food labeling	-Re-evaluation of existing claims to determine if updates are needed. -A scoping review might identify major omissions in the literature submitted with the petition. -Monitoring tool
DGAC report	Enables monitoring of evidence to identify topics to be considered in updates to the *Dietary Guidelines for Americans*.
WHO Guideline Development	Scoping review is used to identify availability of relevant evidence and to facilitate development of protocols for the systematic review, including the drafting of relevant PI/ECO questions.

Components of the process for using the systematic review

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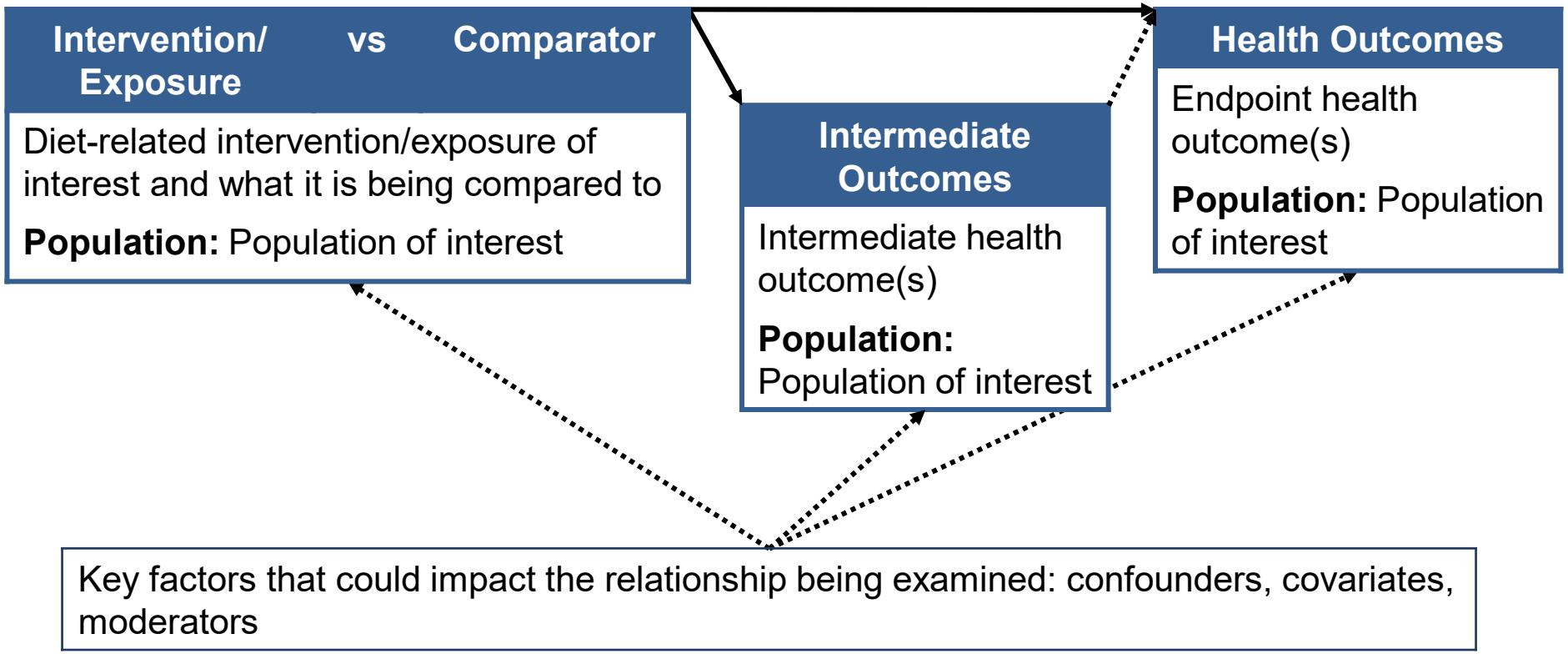
Some factors of the systematic review and meta-analysis that facilitate decision-making

- Clearly defined parameters for the PI/ECO elements and the inclusion and exclusion criteria, e.g.
  - Population: age ranges, sex, health status
  - Intervention/Exposure and Comparator: specificity; relevance to question
  - Outcomes: scope of outcomes examined; specify outcomes that are critical for decision-making; use of biomarkers that are validated
- Specifies the evidence that is included or excluded, e.g.
  - Type of studies included (e.g. RCT, Epidemiological) or excluded (e.g. case reports, animal); specified in guidelines for methodology
  - Minimal length of intervention/exposure studied
- Criteria to judge strength of the evidence
- Value of meta-analysis for understanding inconsistencies (heterogeneity) and for sub-group analysis

PICO Analytic Framework: Population, Intervention, Comparator, and Outcomes



Key definitions

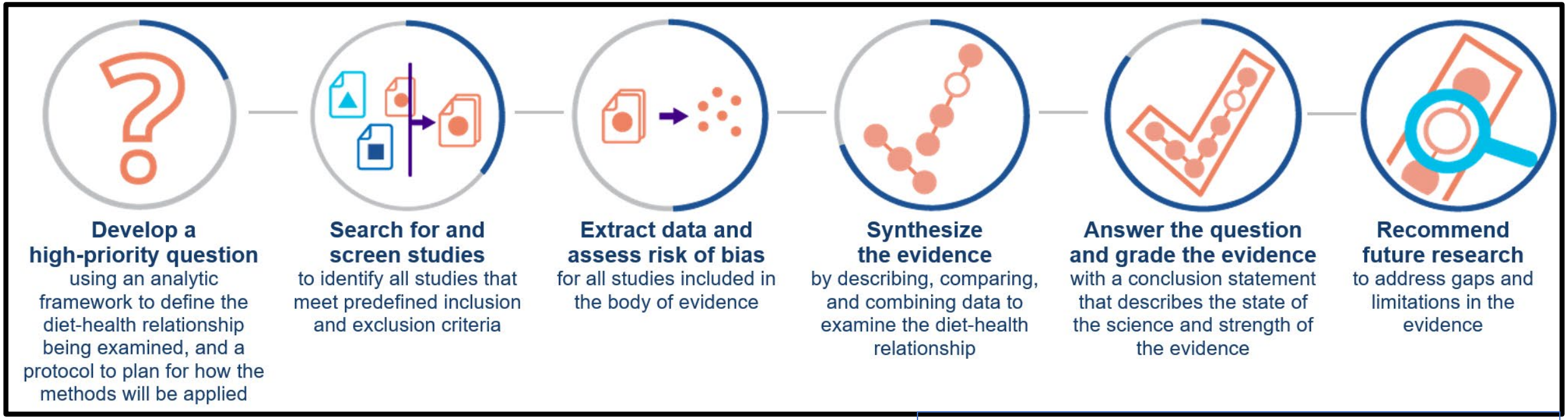
[Term] – [definition]
[Term] – [definition]
[Term] – [definition]

Legend

The relationship of interest in the systematic review
Factors that may impact the relationship of interest in the systematic review

Source: NESR

Structuring the Systematic review (NESR-USDA)



Key outputs:
-Synthesis of Evidence
-Conclusion based on the strength of the evidence
-Recommendation for future research

Structuring the systematic review

FDA Health claim petitions; food labeling	-Petition is used to identify the PICO elements -Inclusion and exclusion criteria are specified in FDA Guidance document
DGAC report	-NESR methodology specifies inclusion and exclusion criteria relevant to the DGA. -The DGAC develops the analytical framework and modifies criteria, as needed, to address the question. -The SR itself is conducted by methodology experts.
WHO Guideline Development	NUGAG subcommittee determines the PICO elements, identifies critical outcomes, and specifies inclusion and exclusion criteria, consistent with the WHO Handbook. -Systematic reviews and meta analysis are conducted by methodology experts

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Criteria for judging the strength of the evidence

Organization	Judging the strength of the evidence
FDA Health claim petitions and re-evaluation; Food labeling	-FDA guidance provides criteria used in the assessment of evidence for health claims -Final regulations or enforcement discretion letters illustrates FDA's assessment of evidence.
DGAC report	A grade of strong, moderate, limited, or not assignable is assessed by risk of bias, consistency, precision, directness, and generalizability to determine the level of certainty in the conclusion as determined by the DGAC.
WHO Guideline Development	The systematic review team uses GRADE* to assess quality of evidence for each outcome and considers study design as adjusted for limitations in study design and execution; indirectness; imprecision; inconsistency; and publication bias Ratings can be high, moderate, low, and very low.

*GRADE: Grading of Recommendations Assessment, Development and Evaluation

Moving from evidence to decision or recommendation

Organization	Evidence to decision or recommendation
FDA Health claim petitions and re-evaluation; food labeling	-Consider criteria and conditions that apply to the use of the claim or nutrition information on food labels (e.g acceptable wording of claim, amount of substance per serving, nutritional profile of food) -Process involves legal and economic input
DGAC report	Integrates systematic review conclusions with evidence from data analysis and food pattern modeling to develop advice for HHS and USDA to update the *Dietary Guidelines for Americans*
WHO Guideline Development	Integrates systematic review and meta-analysis with contextual factors* to determine the strength of the recommendation (strong or conditional) *(e.g. Confidence in the estimates of effect; Values and preferences related to the outcomes of an intervention or exposure; Balance of benefits and harms; Resource implications. Importance or priority of the problem being addressed; Equity and human rights; Acceptability; and Feasibility)

Approaches to Examine the Evidence

Data Analysis
A collection of analyses that uses national data sets to describe understand the current health and dietary intakes of Americans. These data help make the Dietary Guidelines practical, relevant, and achievable.

Food Pattern Modeling
Analysis that shows how changes to the amounts or types of foods and beverages in a pattern might impact meeting nutrient needs across the U.S. population.

NESR Systematic Review
Research project that answers a question on diet and health by searching for, evaluating, and synthesizing all relevant, peer-reviewed studies.

Using Meta-Analysis in Decision-Making—Observations from experience

- A well-designed systematic review is necessary for a meta-analysis.
  - Expertise in the appropriate methodology
  - Value of a Scoping review to set parameters
  - Fit for the specific purpose of the policy or guidance.
- Meta analysis allows for additional examination of the evidence to understand the strength of the evidence.
  - Value of Sub-group analysis
  - Additional tools are available for synthesis of findings across evidence when a meta-analysis is not possible (e.g. use of harvest plots for nutrition and policy guidelines)
- To move from evidence to decision or recommendation, the strength of evidence is considered along with other relevant or contextual factors related to the policy decision.

Using meta-analysis—Opportunities and Challenges

FDA Health claim petitions; Food labeling	-Can a graphic display such as a forest plot or harvest plot better illustrate the balance of evidence (i.e. studies that support or do not support the claim or labeling policy) and clarify inconsistencies in the evidence? -The meta-analysis should be derived from the relevant systematic review.
DGAC report	-Will a meta-analysis provide more transparency on rating the strength of evidence? -Will meta-analysis and subgroup analysis facilitate the development of recommendations? -Can the use of non-qualitative summary tools facilitate recommendations related to the food environment and policy?
WHO Guideline Development	Currently used for guideline development. Allows for experts in methodology to assess strength of the evidence and the expert guidance committees to use the analysis in the development of recommendations. - How can meta analysis be used to determine when evidence is insufficient for a recommendation?

References for WHO systematic reviews related to nutrition and policy decisions.

- Policy NUGAG references
  - Marketing restrictions: Boyland et al, Obesity Reviews
    - 2022;23:e13447. doi.org/10.1111/obr.13447
  - Fiscal policies: Andreyeva et al, JAMA Network Open (2 publications)
    - 2022;5(6):e2215276. doi:10.1001/jamanetworkopen.2022.15276
    - 2022;5(6):e2214371. doi:10.1001/jamanetworkopen.2022.14371
  - School food and nutrition policies: Durão et al
    - Nutrition Reviews nuad059, https://doi.org/10.1093/nutrit/nuad059doi.org/10.1093/nutrit/nuad059

References for WHO systematic reviews related to nutrition guidelines.

- Nutrient focused
  - Publication of systematic review available in IRIS at www.who.int include
    - Effect of reduced sodium intake on blood pressure, renal function, blood lipids and other potential adverse effects (2012).
    - Effect of increased potassium intake on cardiovascular disease, coronary heart disease and stroke (2012)
    - Effects of saturated fatty acids on serum lipids and lipoproteins: a systematic review and regression analysis (2016)
    - Effect of trans-fatty acid intake on blood lipids and lipoproteins: a systematic review and meta-regression analysis (2016)
  - Additional publications: Several of the systematic reviews are published in the peer-reviewed scientific literature and referenced in the relevant WHO Guideline.

Additional references

- FDA Letters of enforcement discretion for qualified health claims: https://www.fda.gov/food/food-labeling-nutrition/qualified-health-claims
- 2020 Dietary Guidelines Advisory committee report: https://www.dietaryguidelines.gov/resources/about-process-2020