



August 2017

Guiding Principles for Developing Dietary Reference Intakes Based on Chronic Disease

For decades, nutrient intake recommendations have been issued to the public through the Dietary Reference Intakes (DRI), the standards established by consensus committees of the Institute of Medicine,¹ and now the National Academies of Sciences, Engineering and Medicine (the National Academies) and used for planning and assessing the diets of apparently healthy individuals and groups.

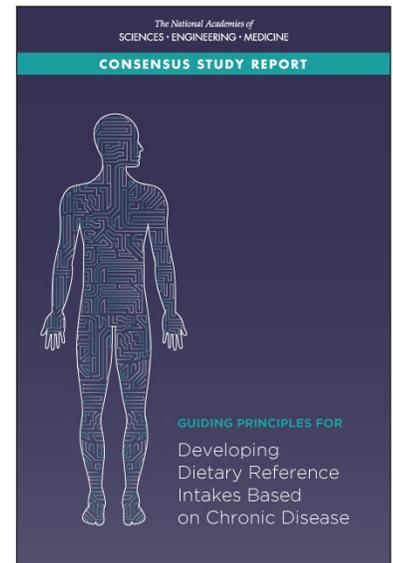
For each nutrient (e.g., vitamins, minerals, water, electrolytes, carbohydrate, or protein) deemed essential, the DRI committee reviews the scientific literature to help inform standards of adequacy and toxicity for groups of people of different genders and at different life stages. These traditional DRIs are required to guide efforts to ensure that populations meet essential nutritional needs to maintain health and prevent deficiency diseases.

Beyond meeting essential nutritional needs, there is an emerging body of evidence suggesting potential additional roles of nutrients or other food substances (NOFSs) in ameliorating chronic diseases, suggesting the need for additional DRIs—chronic disease DRIs—developed for this purpose. Although stakeholders have reflected on how to develop chronic disease DRIs, no agreement yet exists on methodological approaches that can be consistently applied.

The National Academies convened an ad hoc committee to determine guiding principles to support future DRI committees as they make decisions about recommending chronic disease DRIs. The resulting report, *Guiding Principles for Developing Dietary Reference Intakes Based on Chronic Disease*, addresses conceptual and methodological challenges and makes recommendations to develop chronic disease DRIs.

The pages that follow present the committee's recommendations in response to the methodological challenges identified in the report *Options for Consideration of Chronic Disease Endpoints for Dietary Reference Intakes (DRIs): Summary Report from a Joint US/Canadian-sponsored Expert Panel*, the primary reference resource for this consensus study.

¹ As of July 1, 2015, the National Academies continue the consensus studies and convening activities previously carried out by the Institute of Medicine.



MEASURING DIETARY INTAKE AND SELECTING CHRONIC DISEASE OUTCOMES

How should dietary intake measures be evaluated?

Recommendation 1

Until better intake assessment methodologies are developed and applied widely, DRI committees should strive to ensure that random and systematic errors and biases of NOFS exposure assessment methodologies are considered in their evidence review. In the long term, research agendas should include accelerated efforts to improve NOFS exposure assessments for application in studies of chronic disease risk.

How should chronic disease outcomes be selected?

Recommendation 2

The ideal outcome used to establish chronic disease DRIs should be the chronic disease of interest, as defined by accepted diagnostic criteria, including composite endpoints, when applicable. Surrogate markers could be considered with the goal of using the findings as supporting information of results based on the chronic disease of interest. To be considered, surrogate markers should meet the qualification criteria for their purpose. Qualification of surrogate markers must be specific to each NOFS, although some surrogates will be applicable to more than one causal pathway.

EVALUATING ACCEPTABLE LEVELS OF CONFIDENCE THAT THE RELATION OF A NOFS TO A CHRONIC DISEASE IS CAUSAL

What are acceptable levels of confidence that the relation is causal?

Recommendation 3

The committee recommends that DRI committees use Grading of Recommendations Assessment, Development and Evaluation (GRADE) in assessing the certainty of the evidence related to the causal association between NOFSs and chronic diseases. Using GRADE, the committee recommends that a decision to proceed with development of chronic disease DRIs be based on at least moderate certainty that a causal relationship exists and on the existence of an intake–response relationship.

APPROACHES TO IDENTIFY AND CHARACTERIZE THE QUANTITATIVE RELATIONSHIP AND ESTABLISH DIETARY REFERENCE INTAKES

What is the approach to selecting indicators and specifying intake–response relations?

Recommendation 4

The committee recommends the use of a single outcome indicator on the causal pathway. However, when a single food substance reduces the risk of more than one chronic disease, reference values could be developed for each chronic disease. The committee, however, does not recommend the use of “multiple indicators of a chronic disease” or “multiple indicators for multiple diseases,” unless there is sufficient experience with the use of algorithms or other strong evidence suggesting that multiple indicators point to risk of a chronic disease, due to potential lack of reliability or consistency in the results.

When should intake–response data be extrapolated?

Recommendation 5

The committee recommends extrapolation of intake–response data for chronic disease DRIs only to populations that are similar to studied populations in the underlying factors related to the chronic disease of interest.

What should be the different types of DRIs associated with benefit?

Recommendation 6

The committee recommends that DRIs for chronic disease risk take the form of a range, rather than a single number. Intake–response relationships should be defined as different ranges of the intake–response relationship where risk is at minimum, is decreasing, and/or is increasing (i.e., slope = 0, negative, or positive). When a NOFS reduces the risk of more than one chronic disease, DRIs could be developed for each chronic disease, even if the confidence levels for each chronic disease are different.

What should be the different types of DRIs associated with reduction in chronic disease risk?

Recommendation 7

The committee recommends retaining Tolerable Upper Intake Levels (ULs) based on traditional toxicity endpoints. In addition, if increased intake of a substance has been shown to increase the risk of a chronic disease, such a relationship should be characterized as the range where a decreased intake is beneficial. If the increase in risk only occurs at intakes greater than the traditional UL, no chronic disease DRI would be required, because avoiding intakes greater than the UL will avoid the chronic disease risk.

What are acceptable levels of confidence in the intake–response data?

Recommendation 8

The committee recommends that to develop a chronic disease DRI, the level of certainty in the intake–response relationship should generally be the same as the level of certainty for a determination of causality, that is, at least “moderate,” using GRADE. However, in some cases, for example when a food substance increases chronic disease risk, the level of certainty considered acceptable might be lower. In all cases, a thorough description of the scientific uncertainties is essential in describing quantitative intake–response relationships.

What approaches can be taken to make decisions when benefits and harms overlap?

Recommendation 9

The committee recommends that, if possible, health risk/benefit analyses be conducted and the method to characterize and decide on the balance be made explicit and transparent. Such a decision needs to consider the certainty of evidence for harms and benefits of changing intake and be based on clearly articulated public health goals. If DRI committees do not perform such risk/benefit analyses, it is still necessary to describe the disease outcomes and their severities, the magnitudes of risk increases and decreases over various ranges of intakes, and other factors that would allow users to make informed decisions.

INTEGRATING CHRONIC DISEASE DRIs IN THE CURRENT PROCESS

What should be the organizational process to set all DRIs?

Recommendation 10

Because of the need for close coordination and exchange of ideas when setting DRIs based on indicators of adequacy, toxicity, and chronic disease, one single National Academies parent committee should develop DRIs for the prevention of nutrient deficiencies and toxicities and for reducing the risk of chronic disease. Due to the need for different expertise and different methodological considerations, two subcommittees could be established at the discretion of the parent committee, for reviewing evidence on (1) adequacy and toxicity and (2) chronic disease, respectively.

What should be the starting point of chronic disease DRIs?

Recommendation 11

When sufficient evidence exists to develop chronic disease DRIs for one or more NOFSs that are interrelated in their causal relationships with one or more chronic diseases, a committee should be convened to review the evidence of their association with all selected diseases.

GUIDING PRINCIPLES FOR A RIGOROUS CHRONIC DISEASE DRI DEVELOPMENT PROCESS

As part of its response to the statement of task, the committee developed a set of guiding principles as a foundation for a scientifically credible chronic disease DRI process. To read the committee’s guiding principles with respect to systematic reviews and with respect to DRI committee reviews of the totality of the evidence, please see the “Guiding Principles for Establishing Chronic Disease DRIs” insert.

Committee on the Development of Guiding Principles for the Inclusion of Chronic Disease Endpoints in Future Dietary Reference Intakes

Shiriki Kumanyika (Chair)
Drexel University

Cheryl Anderson
University of California-San Diego

Susan I. Barr
University of British Columbia

Kathryn G. Dewey
University of California-Davis

Gordon Guyatt
McMaster University

Janet C. King
Children's Hospital Oakland
Research Institute

Marian L. Neuhouser
Fred Hutchinson Cancer
Research Center

Ross L. Prentice
Fred Hutchinson Cancer Research
Center

Joseph Rodricks
Ramboll Environ Inc.

Patrick J. Stover
Cornell University

Katherine Tucker
University of Massachusetts

Robert B. Wallace
The University of Iowa

Study Sponsors

Agricultural Research Service of the U.S. Department
of Agriculture

Centers for Disease Control and Prevention

U.S. Food and Drug Administration

U.S. Department of Health and Human Services—
Office of Disease Prevention and Health Promotion

Health Canada

National Cancer Institute

National Institute of Diabetes and Digestive
and Kidney Diseases

Office of Dietary Supplements at the National Institutes of Health

Study Staff

Maria P. Oria
Study Director

Alice Vorosmarti
Research Associate

Reneé Gethers
Senior Program Assistant

Faye Hillman
Financial Officer

Ann L. Yaktine
Director, Food and Nutrition
Board

Consultant

Weihsueh A. Chiu
Texas A&M University

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

The nation turns to the National Academies
of Sciences, Engineering, and Medicine for
independent, objective advice on issues that
affect people's lives worldwide.

www.national-academies.org