Defining the process of Dietary Reference Intakes: framework for the United States and Canada¹–⁴

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ABSTRACT
The pioneering project of the harmonization of Dietary Reference Intakes (DRIs) for the United States and Canada resulted in the production of 13 reports from 1997 to 2006 that included 6 reports on specific nutrient groups, 3 reports in preparation for setting recommendations for fiber and antioxidants, 2 reports on applications of DRIs, a report of the synthesis of identified research gaps, and a summary report, Dietary Reference Intakes: The Essential Guide to Nutrient Requirements. This bicountry collaborative effort to harmonize values of reference nutrient intakes has continued through meetings to evaluate the strengths and weaknesses of the first harmonized DRI process in North America and to refine the framework for future revisions of DRIs. 

DEVELOPMENT OF DIETARY REFERENCE INTAKES FROM 1995 TO 2006
In 1995, the United States and Canada set out to establish a harmonized single set of nutrient-based Dietary Reference Intake (DRIs) through combined efforts of the Food and Nutrition Board of the Institute of Medicine, National Academies in the United States and the Office of Nutrition Policy and Promotion of Health Canada. Over the next decade, this effort resulted in the publication of 13 reports that included 6 reports on specific nutrient groups (1–6), one report on a risk-assessment model for the establishment of upper intakes for nutrients (7), on 2 reports on a definition for dietary fiber (8) and antioxidants (9), 2 reports on applications of DRIs for dietary planning (10) and dietary assessment (11), a report on identified research gaps that require additional investigation (12), and a summary report, Dietary Reference Intakes: The Essential Guide to Nutrient Requirements (13).

DRIs are quantitative reference values for recommended intakes and safe upper intakes of nutrients. Principles used included the review of nutrients for their roles in eliminating nutritional deficiencies and the reduction of risk of chronic diseases and the use of a risk-assessment model to evaluate the extent to which excess consumption may lead to health problems. Basic concepts underpinning the establishment of each nutrient reference intake were that intakes would meet the needs of healthy people (not individuals with disease), nutrients would be grouped by some element of functionality in each report, and age groupings would be revised to reflect the current knowledge of biological patterns. Sex-specific recommended intakes would only be established when there was reasonable scientific evidence, and chronic disease endpoints would be considered when scientific evidence was available.

Detailed information on the specific approach to define an estimated average requirement (EAR) intended for populations, the Recommended Dietary Allowance (RDA) for individuals, and an upper level (UL) for each nutrient and for all age groups is available in the introductory chapters of all reports (1–6). For energy, the approach to the derivation of the estimated energy requirement was based on the energy expenditure measured by using a stable-isotope tracer methodology that was adjusted for age, sex, physical activity level, weight, height, and a growth factor for children (5). Finally, values were established for the acceptable macronutrient distribution range that encompassed reference ranges for infants, children, and adults for the percentage of energy to be derived from protein, carbohydrate, fat and essential fatty acids (ie, linoleic and linoleic acids) thought to be associated with reduced risk of chronic disease and yet provide AI s of essential nutrients (5).

Despite an extensive assembly of published data and an a priori plan to establish an EAR, RDA, and UL for each nutrient for all age groups, many challenges arose primarily because of a lack of appropriate published scientific data, particularly for children. As a result, an AI was substituted for the RDA in cases where an EAR could not be established. The AI was generally based on observed intakes in healthy populations, such as for breastfed infants in the first 6 months of life or on experimentally derived intakes, such as for calcium. A major limitation in the application of an AI is that this value cannot be applied to population groups.

When insufficient data were available to derive an EAR in a specific age group, methods of extrapolation were applied. A full critique of the extrapolation methodology has been published (14). In the DRI process, extrapolation methods were used to derive “60% of DRI values for children aged 7 mo to 18 y. The most common method used was to extrapolate values for children

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dren down from those of adults by using a weight or metabolic factor and adjusting for growth. In some instances, values for young children were extrapolated up from infants; values for adults were extrapolated up from children, or values for older adults were extrapolated up from young adults. Extrapolation was used to estimate nutrient requirements or AIs and upper tolerable intakes.

Although the application of chronic disease endpoints was desirable, these were impossible to apply except in the case of EARs for fluoride, fiber, and potassium, ULs for sodium and chloride, and the acceptable macronutrient distribution range. The lack of specificity in the effect of a single nutrient, the variability in the effective dose, and the interaction with other nutrients were all factors that limited the use of chronic disease endpoints to derive DRI values.

Each nutrient panel was charged with defining gaps in scientifically valid knowledge that impeded the development of DRI values, and such recommendations were included in each nutrient chapter of the reports. A workshop that convened in 2006 engaged expert research scientists and nutrition practitioners from government, academia, and industry areas to review the identified knowledge gaps and research recommendations that were most critical to the future development of DRIs. A summary report of this research synthesis (12) and a searchable database (http://www.iom.edu/Activities/Nutrition/DRIResearchSynthesis.aspx) of the research recommendations is available.

FUTURE DRIs

Since the first published DRI reports, collaborative efforts between the United States and Canada have continued to evaluate strengths and weaknesses of the first harmonized DRI process in North America and to refine the framework for future revisions of DRIs (15, 16). Key areas that should be considered in refining the DRI process were as follows: an a priori definition of selection criteria and consistency in the approach of selecting endpoints, methodologies for approximating dose-response relations, especially when appropriate data are limited, methods for the extrapolation or scaling of values from a particular age or sex group to an unstudied group, adjustment for data uncertainty in establishing ULs by using a risk-assessment model, the usefulness of systematic reviews in the derivation of DRIs, and a consideration for the effect of environmental, genomic, and physiologic factors in establishing DRI values (15).

Several workshops and other outreach activities have addressed issues arising from the retrospective analysis of the initial DRI process and laid the groundwork for a way forward for future revisions of DRIs. A revised DRI framework was proposed that included the identification of gaps in scientific knowledge, guidance, criteria, and methods (15, 16). The pros and cons of this framework have been elucidated by Russell (17).

A possible new approach to define a reference intake value was proposed in a generic framework to link the dietary intake (exposure) with the clinical outcome for recommended intakes and ULs (18). This framework model was tested through a project aimed at the evaluation of the usefulness of systematic reviews by using vitamin A as an example (19), with the conclusion that an objective, unbiased systematic review of a defined question may assist in setting nutrient reference values while also increasing the transparency of the decision-making process. After an analysis of the triggers for undertaking a revision of nutrients from the initial DRI reports (20), a revision of DRIs for calcium and vitamin D was undertaken, and a prepublication report is available online (21). The panel deliberations were preceded by a systematic review (22) that explored the relations of vitamin D, calcium, or their combination on different health outcomes, but no consistent relations were elucidated. Although, to my knowledge, this was the first attempt to apply systematic reviews to support the development of nutrient reference intake values, it met with some challenges in both the process of the review and applications to the DRI paradigm (23). As outlined in the introduction to the report, the DRI review panel used the information from systematic evidence-based reviews prepared through the Agency for Healthcare Research and Quality in combination with other literature identified by the committee to establish potential indicators of health outcomes for the nutrient adequacy for calcium and vitamin D. In the end, the development of revised DRIs was only based on bone health outcomes. Data that related vitamin D or calcium intakes to other health outcomes such as cancer, cardiovascular disease, hypertension, or autoimmune disorders was not deemed adequate in terms of cause and effect or sufficiently informative regarding dose-response relations to be used to derive DRI recommendations.

The issue of how to use chronic disease indicators in the framework of the DRI was explored in a planning meeting organized in Washington, DC, by the Food and Nutrition Board of the Institute of Medicine and the Public Health Agency of Canada in 2009. The objective of the meeting was to consider what is known and what needs to be addressed to facilitate the development of nutrient reference values in cases where the most appropriate indicator is a measure of chronic disease. Perhaps the current model of the EAR is not applicable for use with chronic disease indicators. For example, chronic disease data are not readily compatible with the establishment of a threshold effect of benefit that is applicable to almost all healthy persons, as is used for setting the EAR. New approaches will have to be established that include the assessment of benefit and risk (beneficial to health and not harmful) and may provide opportunities to use multiple indicators as opposed to the selection of just one indicator, as is typical in the EAR-threshold model.

SUMMARY

This first collaboration of the United States and Canada to harmonize nutrient recommendations proved to be a practical and feasible approach. Except for differences in racial profiles between countries, differences in basic physiologic needs for nutrients between populations do not exist. The translation of DRI values into federal policies or recommended health practices may require the adjustment of DRI values. For example, DRI values for vitamin D assume minimal sun exposure with all vitamin D derived from the diet. On the basis of the geographical locale, populations or individuals may receive considerable sun exposure that, in turn, may reduce their need for dietary vitamin D. Ensuring adequate nutrients in the food supply to meet recommended DRI intakes for all age groups will require consideration by national regulatory agencies with respect to diversity in food-product availability or regulations for nutrient fortification.
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REFERENCES