US-Canada Dietary Reference Intakes: Merits and Limitations

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World Health Organization, February 26, 2010
1994: How should the RDAs be revised?

1989—10th Edition:
“the levels of intake of essential nutrients that, on the basis of scientific knowledge, are judged by the Food and Nutrition Board to be adequate to meet the known nutrient needs of practically all healthy persons.”

1994 Report:
Reduction of chronic disease should be included in future RDAs.
Multiple reference points needed for expanded uses.
Framework for DRIs: EAR, RDA, AI & UL

(Figure from Development of DRIs (IOM) at http://books.nap.edu/topics.php?topic=380)
## Comparison of RDAs and DRIs

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>A single value/nutrient</td>
<td>4 values reflecting the requirement distribution</td>
</tr>
<tr>
<td>Essential nutrients</td>
<td>Essential nutrients + food components that may benefit health</td>
</tr>
<tr>
<td>For healthy persons</td>
<td>For <em>apparently</em> healthy populations</td>
</tr>
<tr>
<td>To reduce nutrient deficiencies</td>
<td>To optimize health, prevent disease, and avoid consuming too much of a nutrient</td>
</tr>
</tbody>
</table>
The DRIs:

Two new features:
- Based on an explicit functional criterion
- Distribution for each criterion assumed to be normal

Misinterpretations:
- Different applications need different criterion
- Distribution of intakes and requirements are known for populations

Framework implied a specificity and precision of knowledge that doesn’t exist.
Adequate for What?

Model criteria for adequacy:

- Measured without compromising health
- Does not fluctuate rapidly or markedly with intake
- A nutrient function that is not easily altered by other nutrients or environmental conditions
# Criteria for Micronutrient Requirements

<table>
<thead>
<tr>
<th>Type of Study</th>
<th>Measurement</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose-response studies (RCTs)</td>
<td>Functional outcome</td>
<td>BMD w/ ( \uparrow ) Calcium Glutathione peroxidase w/( \uparrow ) Se</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Biochemical measures RBC folate</td>
</tr>
<tr>
<td>Depletion/repletion</td>
<td>Biochemical measures</td>
<td>4-pyridoxic acid for B(_6) WBC ascorbic acid</td>
</tr>
<tr>
<td>Balance studies</td>
<td>Intake-excretion</td>
<td>Protein</td>
</tr>
<tr>
<td></td>
<td>Factorial estimates</td>
<td>Zinc, Iron</td>
</tr>
<tr>
<td>Epidemiological observations</td>
<td>Functional outcome</td>
<td>Night-blindness—Vit A</td>
</tr>
<tr>
<td>Observed intakes</td>
<td>Dietary intake</td>
<td>Vitamin K</td>
</tr>
</tbody>
</table>
Nutrient Requirements Vary with Criterion

Amount of Dietary Iron to Meet the Needs of 60% of Population

Maintain Serum Iron

Hb > 11.0 g/dl

Maintain Iron Stores

Usual iron intake (mg/day)

Probability of Inadequate Intake

G. Beaton, 1994
Assumed Distribution of Nutrient Requirements

Requirement distribution reflects variability between individuals
Variance of Requirements: Unknown

Types of variability:

- Biological differences in response between individuals
- Day-to-day variation within an individual
- Environmental variables not controlled
- Measurement error

True biological variance unknown
- Assume a coefficient of variation of 10%
- Never validated
Looking Back: Lessons Learned:

1. Nutrient requirements are only known for small groups of *individuals* at one point in time in one setting.

   Recommendations for populations are *estimates* based on the judgment of the Committees.
DRIs only as good as the science base: Limits of metabolic studies.

- Healthy people are studied; to change the parameter of interest requires a large increase or decrease in intake.

- Large changes in nutrient intakes are required to overcome homeostatic control of biochemical or functional endpoints.

- Studies are limited to small numbers; unable to estimate true variance in requirements.
Body Zn Remains Constant Over a Wide Range in Intakes
Models of Extrapolation

- Models varied within the DRIs
- Within an age group, extrapolation up from 0-6 mo AI (e.g., B12, A & K) or down from adult EAR or AI (e.g., B-6, folate)
- Extrapolation → inconsistencies in DRIs between age groups and compared to observed dietary intakes

Atkinson & Koletzko. Food Nutr Bull 2007;28:S61-77,
Lack of science → Scaling models

- Scaling/extrapolation models used to derive
  - AI, EAR/RDA and UL
  - % of DRIs derived by extrapolation

- 7-12 mo → 40%
  - 1-3 y → 64%
  - 4-8 y → 60%
  - 9-13 y → 58%
  - 14-18 y → 60%
  - 31-50 → 11%
  - 51-70 y → 27%
  - > 70 y → 33%

- Iron and zinc by factorial
- Vitamin A and folate by extrapolation from adult EAR
Adjust for Bioequivalence

- Efficiency of nutrient absorption from typical dietary sources and conversion to active forms.
- Diet- and host-related factors specific to a country or region need to be considered.

<table>
<thead>
<tr>
<th>Diet-Related</th>
<th>Host-Related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical form of nutrient</td>
<td>Intestinal factors: atrophic gastritis, bacterial overgrowth, infection, altered mucosal structure, reduced transit time.</td>
</tr>
<tr>
<td>Nature of diet matrix</td>
<td><strong>Systemic factors:</strong> infection, nutritional status of host, maybe ethnicity</td>
</tr>
<tr>
<td>Interactions among nutrients or with other diet components</td>
<td></td>
</tr>
<tr>
<td>Food pre-treatment: processing or preparation methods</td>
<td></td>
</tr>
</tbody>
</table>
How to Adjust for Bioequivalence

No Consensus

Algorithms available to estimate bioavailability of some nutrients

- Accuracy may vary by complex interactions within the whole diet
- Fixed bioavailability factors often used even though the efficiency of absorption varies with level in the diet

Prevalence of infection usually not considered
## What DRI to Use for What

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<tr>
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<th>Individuals</th>
<th>Populations</th>
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<tbody>
<tr>
<td>Assessing Adequacy</td>
<td>Estimated Average Requirement</td>
<td>Estimated Average Requirement</td>
</tr>
<tr>
<td>Planning Diets</td>
<td>Recommended Dietary Allowance</td>
<td>Distribute intakes between EAR and UL</td>
</tr>
</tbody>
</table>
Lessons Learned:

1. Nutrient requirements are only known for small groups of *individuals* at one point in time in one setting.

   Recommendations for populations are *estimates* based on the *judgment* of the Committees.

2. Goals and process for estimating nutrient requirements differs from that of estimating healthy food patterns to prevent chronic disease.

   *Can not mix the two.*
### Nutrient Standards Based on Disease Endpoints, US-Canadian DRIs.

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Disease Endpoint</th>
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<tr>
<td>Calcium</td>
<td>Fracture Risk</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Fracture Risk</td>
</tr>
<tr>
<td>Fluoride</td>
<td>Dental Caries</td>
</tr>
<tr>
<td>Potassium</td>
<td>Hypertension, Renal Stones</td>
</tr>
<tr>
<td>Fiber</td>
<td>Coronary Heart Disease</td>
</tr>
</tbody>
</table>

*Unable to establish EARs

Adequate Intakes (AIs) derived*
Associations between Diet and Chronic Disease Are Complex

- Long latency for disease onset
  - Chronic diseases have multiple etiologies
- Risk linked to more than one dietary component
  - Nutrients or diet components affecting risk (or prevention) may differ from treatment
  - Long-term disease related more to diet pattern than specific nutrients
Acceptable Macronutrient Distribution Ranges (AMDRs) for Adults

Goals:
- To reduce risk of chronic disease
- To provide adequate intakes of essential nutrients

Implication: Intake outside the range increases disease risk.

- Carbohydrates
  - 45-65% of kcal
- Lipids
  - 20-35% of kcal
- Protein
  - 10-35% of kcal
- N-6 polyunsaturated fatty acids
  - 5-10%
- α-linolenic (n-3) – protective against heart disease
  - 0.6-1.2%
AMDRs—Gaps or Flaws

- Types of carbohydrates and fat may be more important than total amounts.
- Qualitative standards (or guidelines) given for cholesterol, trans fatty acids, saturated fatty acids, and added sugars.
- No data to support upper protein intake; value derived from carbohydrate and fat AMDRs.
- Two protein recommendations (AMDR & EAR)
Setting DRIs vs Standards for Reducing Chronic Disease.

- Two clearly different goals
- Two different scientific committees
- Two different scientific documents providing evidence-based standards
US Nutrition Policy Components

- DRIs: the science back-bone
- DGAC Report: Translates DRIs and science linking food, physical activity and chronic disease into DGs

Food pattern for individuals

MyPyramid.gov
Overall DRI Process: Challenges

- Framework not well defined
  - Varied approach between nutrient panels
- Alternate to EAR/RDA not anticipated when science not available → AI
- Paucity of data for EAR in children
  - no alternate approach planned
- Criteria for selection of endpoints not well defined
  - Data availability often drove criteria selection
1. Systematic evidence-based reviews – must inform not replace expert judgment
2. Risk assessment as an organizing scheme
Systematic Reviews

- An objective, unbiased systematic review of a defined question may assist in setting nutrient reference values

- Provide increased transparency of the decision making process


When to Revise Nutrient Recommendations?

TRIGGERS

- Request/interest by sponsors
- Established criteria indicating that significant new, relevant scientific research is available.
  - Example: A review of the 1997 DRIs for vitamin D
  - Yetley, EA et al. Dietary reference intakes for vitamin D: justification for a review of the 1997 values  
    Am J Clin Nutr 2009;89 719-727
Provides a generic structure for integrating empirical evidence with professional wisdom.
**Nutrient Intake Values: Generic Framework**

**Concepts**
- Evaluate criteria
- Extrapolate as necessary
- Consider
  - Genetics
  - Long-term health
- Adjust for
  - Food sources
  - Host factors

**Average nutrient requirement (ANR)**
Estimated from a distribution of requirements for a specific criterion in healthy individuals

**Individual Nutrient Level\(x\) (INL\(x\))**
Derived from the distribution of the ANR; \(x=\)percentile chosen

**Upper Nutrient Level (UNL)**
Estimated from LOAEL/NOAEL using an appropriate uncertainly factor

**Methods of using NIVs**
- Assessment
  - Individuals
  - Populations
- Diet Planning
  - Individuals
  - Populations

**Applications**
- Regulatory issues & trade
- Labeling
- Public health planning
- Fortification
- Dietary guidance
**Terminology is Inconsistent**

- Average Nutrient Intake (ANR)
- EAR (USA)
- AR (EU)
- Upper Nutrient Level (UNL)
- UL (USA)
- Individual Nutrient Level\(_x\) (INL\(_x\))
- RDA (USA)
- PRI (EU)

Adapted from Dr. Sue Fairweather-Tait
Acknowledgments

Some slides courtesy of
Linda Myers, PhD
Christine Taylor, PhD
FNB/IOM
Stephanie Atkinson, PhD
Sue Fairweather-Tait, PhD