The IOM DRI Framework and Definitions – Adaptation for Bioactives

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Outline

- History of Dietary Recommendations
- The Existing DRI Framework
- What are Essential Nutrients ?
- Levels of Evidence Needed
- What is Needed for Accreditation of Bioactives?
- Next Steps and Conclusions

History of Dietary Recommendations

- Initially established for armed forces
- British Merchant Seaman's Act (1835)
  - provision of lime or lemon juice

- Least cost prevention of starvation (UK,1862)
  - about 3,000 Kcal/d and 80 g protein

History of Dietary Recommendations

- Between 1860 – 1900 the UK, The Netherlands, Germany, France and USA began to develop dietary standards for:
  - Energy and protein
  - “Protective foods”
  - Healthy persons

History of Dietary Recommendations

In 1920's and early 1930's for the League of Nations began to investigate diets and foods in various countries (became the Food and Agriculture Organization of the United Nations)

FAO and other groups began to add recommendations for some essential nutrients like calcium, iron, vitamin A and some B vitamins

History of Dietary Recommendations

British Medical Association – 1933

USDA (Hazel Steebling) - 1933

–Broke down recommendations by age and sex for some nutrients

Revised USDA and Canadian standards in 1939

History of Dietary Recommendations

- Committee on Nutrition, appointed in 1940 by the US National Research Council on request from the Department of Defense for nutrition planning for entry into WW II

- This committee became the Food and Nutrition Board in 1941

The Existing Approach

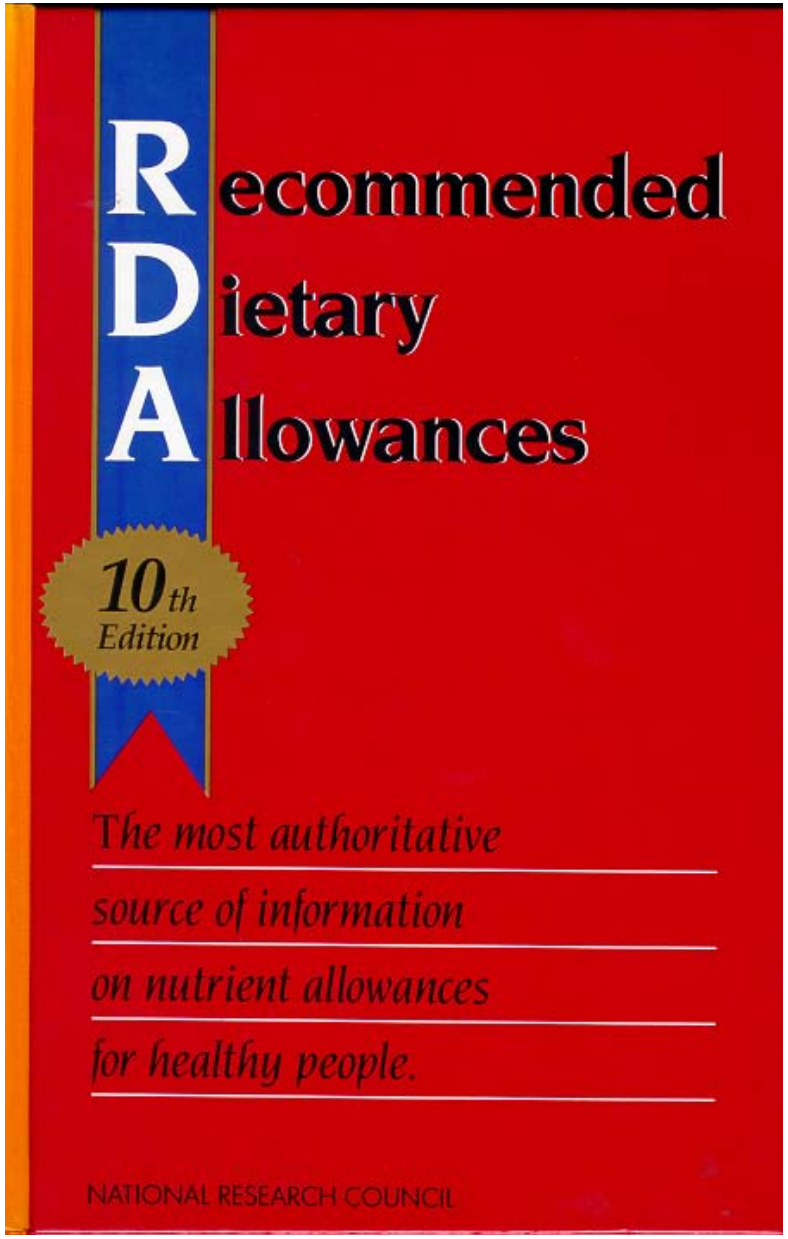
For more than 70 years we have relied upon the Recommended Dietary Allowances (RDAs) and the Dietary Reference Intakes (DRIs) for recommendations on essential nutrients for individuals and populations in the United States

Recommended Dietary Allowances First Edition 1941

- Energy
- Protein
- 2 minerals (Ca, Fe)
- 6 vitamins (A, C, D, thiamin, riboflavin, niacin)

Recommended Dietary Allowances
Tenth Edition 1989

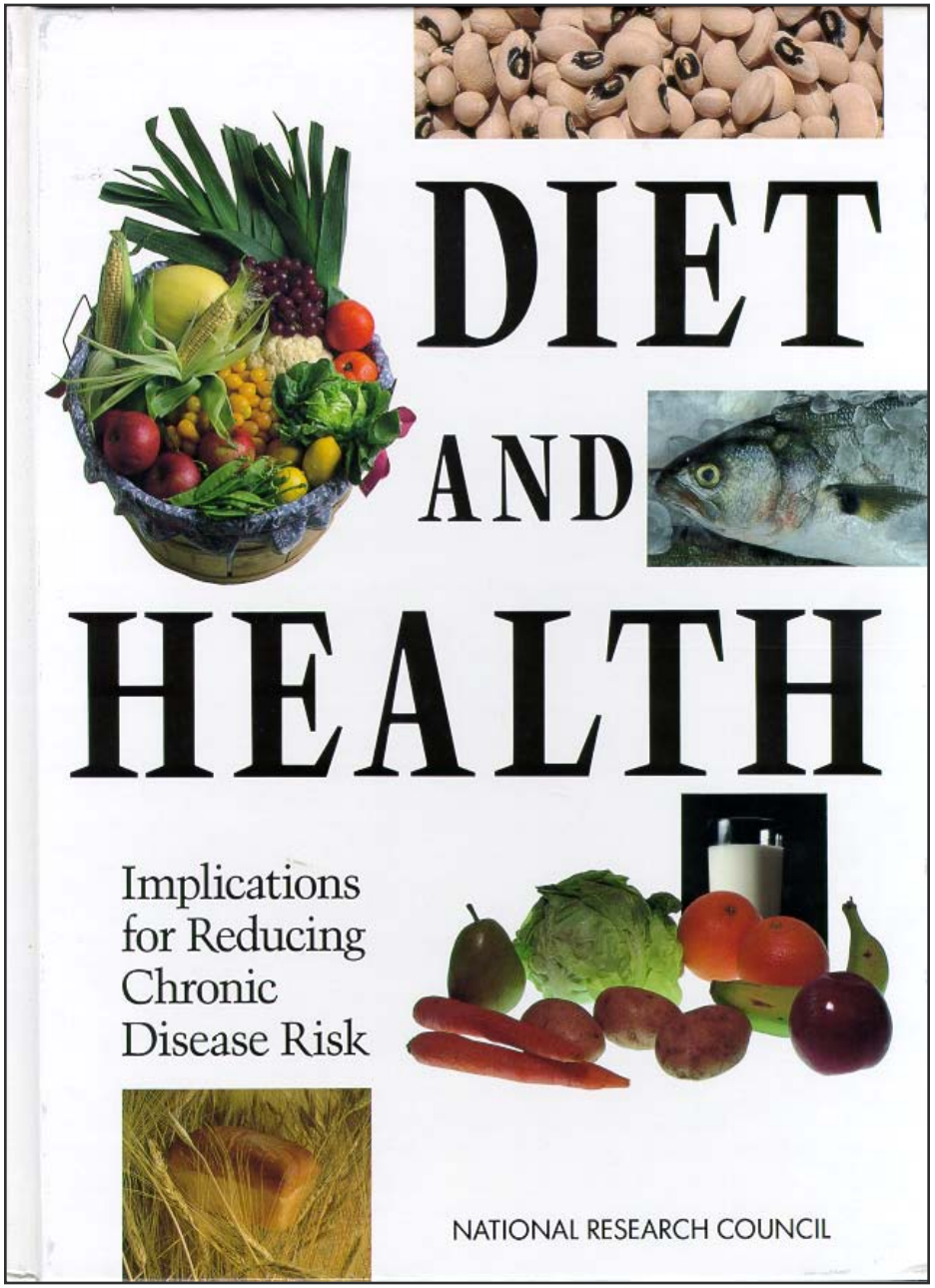
- Energy
- Protein
- 7 minerals (Ca, Fe, P, Mg, Zn, I, Se)
- 11 vitamins (A, C, D, thiamin, riboflavin, niacin, E, K, B_6, B_{12}, folate)
- Safe and adequate daily dietary intakes (biotin, pantothenate, Cu, Mn, F, Cr, Mo)


Recommended
Dietary
Allowances
10th Edition
The most authoritative source of information on nutrient allowances for healthy people.
NATIONAL RESEARCH COUNCIL

1989

Shift-Change

1989 marked a dramatic change in thinking among **some** nutritional scientists away from prevention of deficiency disease to optimizing health


DIET
AND
HEALTH
Implications
for Reducing
Chronic
Disease Risk
NATIONAL RESEARCH COUNCIL

1989

Why DRIs?
Conceptual Approach

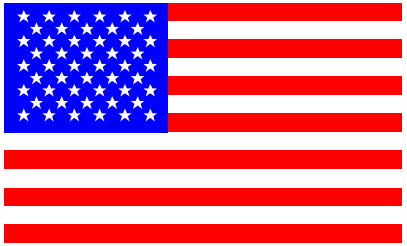
- In the early 1990's the Food and Nutrition Board discussed approaches to establish RDAs using the traditional approach of reduction of deficiency diseases with the emerging concerns of reduction of chronic disease risk
- They asked whether the concepts of RDA's and Diet and Health could be combined?

FNB 1994 Concept Paper for development of DRI's

Focused on Need to Include:

- Recommendations to meet variety of uses (food labeling, dietary assessment, etc)
- Concepts of reduction of risk to chronic disease
- Review of other food components
- Rationale for functional end points used
- Estimates of upper limits of intakes

DRIs



Dietary Reference Intakes

Food and Nutrition Board

1997 - 2005

Dietary Reference Intakes

- Estimated Average Requirement (EAR)
- Recommended Dietary Allowance (RDA)
- Adequate Intake (AI)
- Tolerable Upper Intake Level (UL)
- Acceptable Macronutrient Distribution Ranges (AMDR)

Definition of RDAs

". . . levels of intake of essential nutrients considered, in the judgment of the Food and Nutrition Board on the basis of available scientific knowledge, to be adequate to meet the known nutritional needs of practically all healthy persons."

NRC, 1974, 1980, 1989

Relationship of EAR and RDA

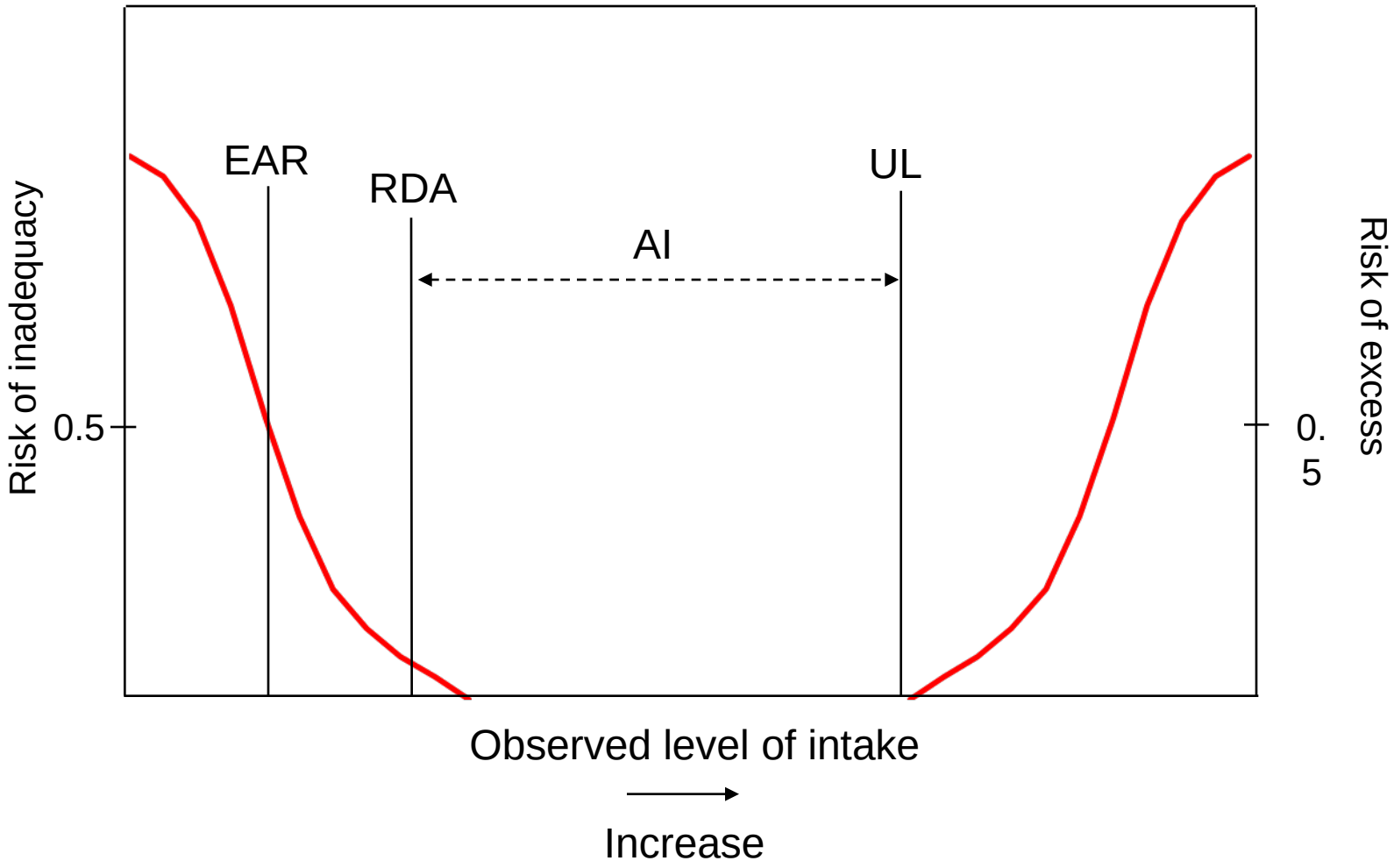
- Estimated Average Requirement (EAR) = requirement for 50% of the population

- Recommended Dietary Allowance (RDA) = requirement for 97.5% of the population, so plan diets for individuals using this DRI

RDA = EAR + 2 SD

(if symmetrically distributed)

Dietary Reference Intakes



Adequate Intake (AI)

The recommended average daily intake level based on observed or experimentally determined approximations or estimates of nutrient intake by a group (or groups of healthy people) that are assumed to be adequate — used when an RDA can't be determined.

Tolerable Upper Intake Level (UL)

The highest level of daily nutrient intake that is likely to pose no risks of adverse health effects to almost all individuals in the general population

- Not a recommended level of intake
- Not a level that is desirable to attain

Acceptable Macronutrient Density Ranges (AMDR)

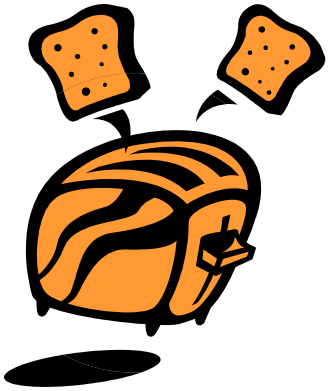
- Range of intakes for an energy source (e.g., fat) associated with reduced risk of chronic disease while providing adequate intakes of essential nutrients

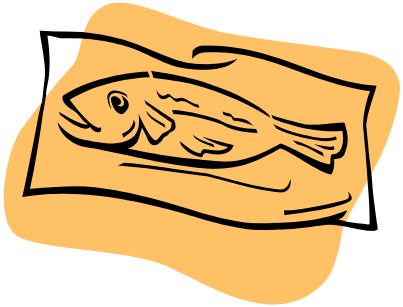
- Expressed as % total energy intake

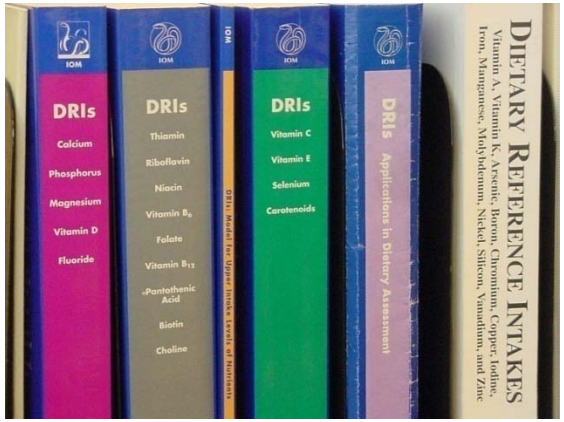
For example,

AMDR for adults

Nutrient	AMDR
Fat	20% – 35%
Carbohydrate	45% – 65%
Protein	10% – 65%







Dietary Reference Intakes

1997-2005

www.iom.edu/fnb

Dietary Reference Intakes

- Estimated Average Requirement (EAR)
- Recommended Dietary Allowance (RDA)
- Acceptable Macronutrient Distribution Ranges (AMDR)

Adequate Intake (AI) ⁎

Tolerable Upper Intake Level (UL) ⁎

⁎Applicably to bioactive food components?

Essential Nutrient Definition 1940 RDA Committee

Chemical substances found in foods that are essential for human life and tissue growth and repair.

Essential nutrients were identified when dietary deficiency led to the development of a well-defined disease or a failure to grow.

Source: NRC 1941

Classical Tests for “Essentiality”

- Feed a complete diet that is devoid of the substance
- Upon depletion, an adverse physiological or metabolic outcome occurs
- Addition of the substance back to the diet reverses the adverse event

Criteria for Establishing RDAs for Essential Nutrients

Scientific Database

- Observed intakes in healthy populations
- Epidemiological observations
- Balance studies
- Depletion/repletion studies
- Animal experiments
- Biochemical measurements

Should DRIs only include Essential Nutrients?

- Food and Nutrition Board subcommittee in 1992 decided not to define the term
- Why?
  - Decided not to "limit" the boundaries of the upcoming DRI process
  - The DRI committees were asked to consider both alleviation of deficiency diseases and reduction of chronic diseases risk as potential end points

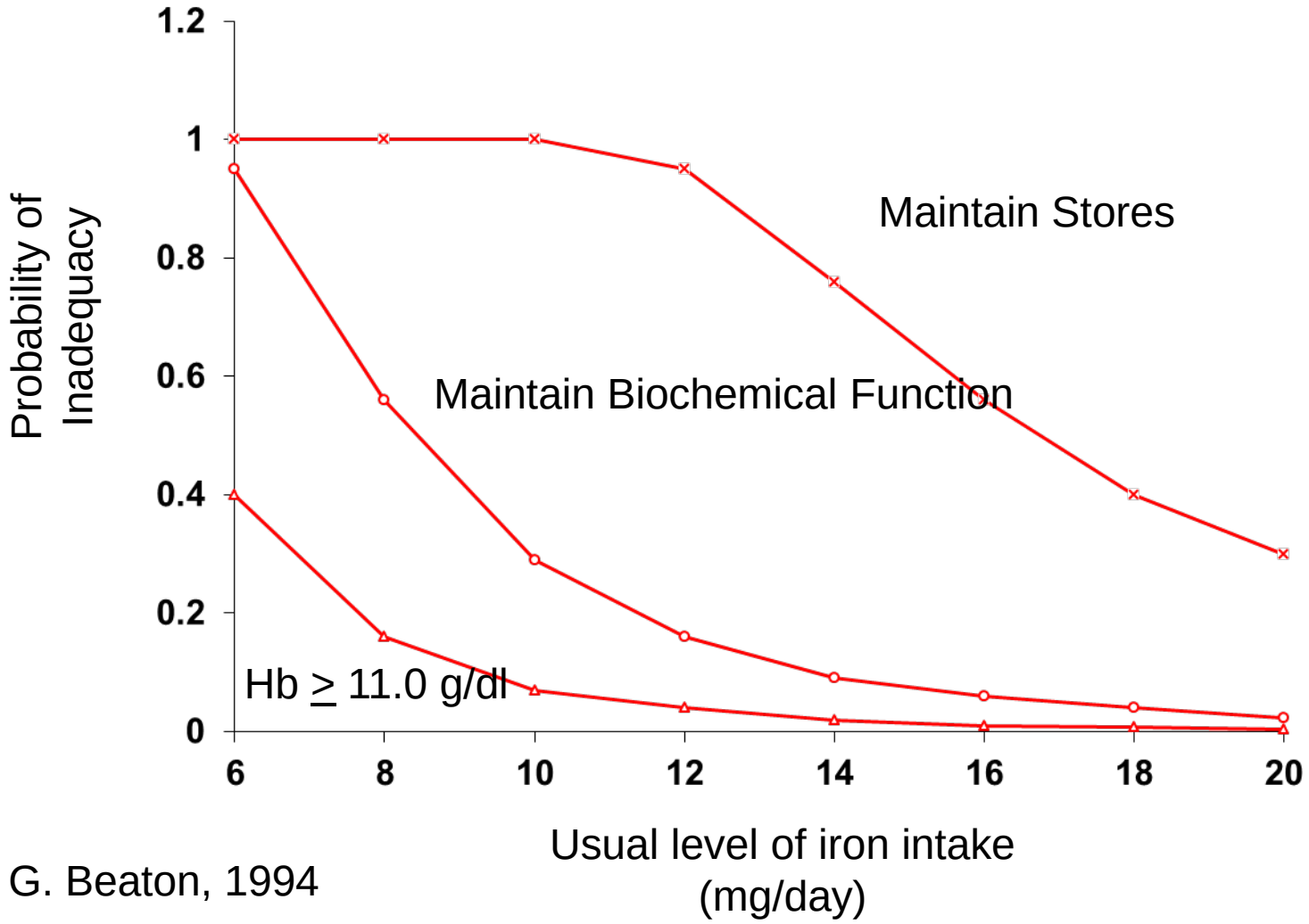
What is an Essential Nutrient?

- All will agree that vitamin C is essential to prevent scurvy in humans. Would other clinical endpoints related to vitamin C be considered essential?
- Are all DRI nutrients essential?
- Are fiber and fluoride essential?
- Are other food components that enhance health essential?
  - Probably not, but may enhance health never-the-less

Essential for What?

Multiple endpoint criteria are possible

Probability That Specified Usual Iron Intake would be Inadequate to Meet the Needs of a Randomly Selected Menstruating Woman[1]



G. Beaton, 1994

What types of evidence are needed?

"Because of limitations inherent in RCTs, particularly of nutrients, it is suggested that nutrient policy decisions will have to be made using the totality of available evidence. This may mean action at a level of certainty that is different from what would be needed in the evaluation of drug efficacy."

Blumberg, Heaney, Huncharek, Scholl, Stampfer, Vieth, Weaver and Zeisel. 2010 Evidence-based criteria in the nutritional context. Nutr. Reviews 68:478-84.

What types of evidence are needed?

"Similarly, it is judged that the level of confidence needed in defining nutrient requirements or dietary recommendations to prevent disease can be different from that needed to make recommendations to treat disease."

Blumberg, Heaney, Huncharek, Scholl, Stampfer, Vieth, Weaver and Zeisel. 2010 Evidence-based criteria in the nutritional context. Nutr. Reviews 68:478-84.

What amount of evidence is needed?

- Standards of Evidence should not change whether one is considering drugs, essential nutrients or other food components
- At issue is the Amount of Evidence that may be necessary
- The amount of evidence necessary depends upon Risk – Benefit of consuming the substance

What amount of evidence is needed?

- The amount of evidence necessary depends upon Risk : Benefit of consuming the substance

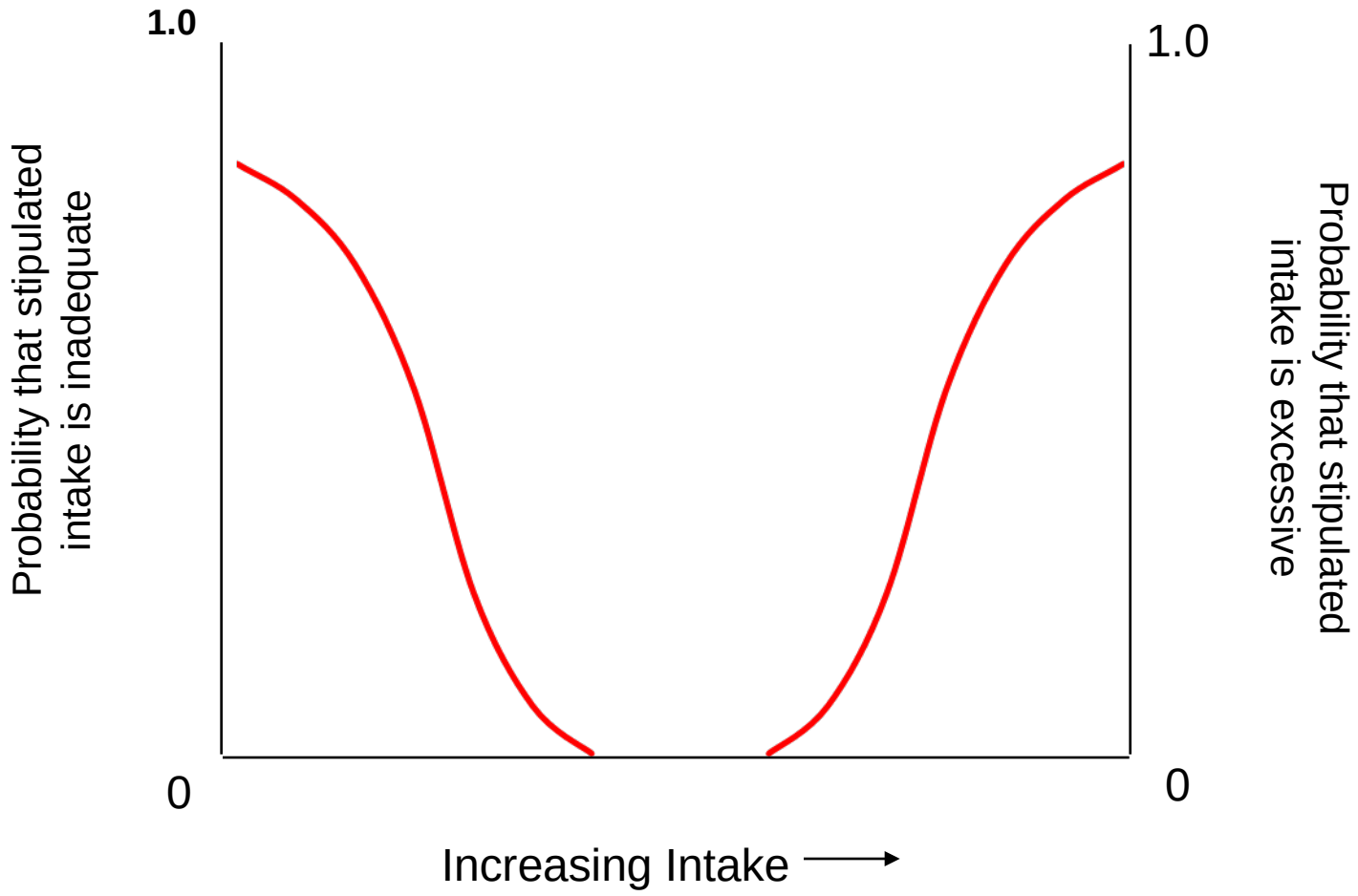
  – If high risk, lower benefit – more evidence

    A food component with higher potential for adverse side effects with marginal benefits (Selenium supplements for cancer prevention)

  – If low risk, higher benefit - less evidence

    A food component with few side effects but high benefit (Lutein and AMD)

Benefit/Risk Curve



What amount of evidence is needed for non-essential bioactive food components?

- Randomized Placebo Controlled Trials ?
- Evidence-Based Reviews ?
- “Totality of the Evidence” ?
- At issue is the Amount of Evidence that may be necessary

Challenges for "Accreditation" of Food Bioactives

- Lack of RCTs – perhaps impossible to use this approach
- Insufficient data for systematic evidence-based reviews
  - Costs of human intervention trials would be enormous considering the "small effects", long time needed to demonstrate efficacy, and huge population needed to complete such a trial with a bioactive food component

What types of information are needed?

- Baseline information absolutely required
  - Validated analytical technique
  - Food composition data base
  - Population intake patterns
  - Pharmacokinetics of substance
  - NOAEL and safety issues
- Other information needed
  - Epidemiological support
  - Biological plausibility
  - Specificity
  - “Hill’s Criteria”

Challenges for "Accreditation" of Food Bioactives

- Specificity of food component
- Non-validated biomarkers – broader issue than just with bioactives
- Who is going to pay for the research?
- Fear of fringe supplement/food companies by policy-making bodies which result in barriers for "accreditation"

Why Should We Care About "Accreditation" of Bioactive Food Components?

- Most food bioactives are components of plant-based foods
- Despite decades of promotion of 5-A-Day programs, consumers have not increased their consumption of fruits and vegetables
- This can be part of a new message to promote healthful eating

What are the Next Steps?

- The Food and Nutrition Board (IOM) should be funded to:
  - Evaluate paradigms that would facilitate assessment of the value of non-essential food components for improved health outcomes
  - Evaluate the public health value
  - Determine gaps in research knowledge

What are the Next Steps?

"A paradigm for assessing the effects of "bioactives is needed. Whether these are studied as nutrients or drugs must be established to properly inform future regulatory and policy decisions"

Shao and Mackay. 2010. Natural Medicine Journal 2:10 – 18.

What are the Next Steps?

Potential food components to consider could include:

- Carotenoids
- Classes of polyphenols
- Classes of dietary fiber
- Bioactive peptides
- Isothiocyanates, allyl sulfides, etc
- Omega 3 fatty acids

What are the Next Steps?

- Polyphenols classes:

  Daily intake recommendations (or AI) might be based upon amounts delivered by 5-A-day patterns that are associated with healthy endpoints.

  Williamson and Holst (2008) British J. Nutr. 99: Suppl. 3, S55-S58

Is there a consequences of inaction?

- Suppression of critical research to close gaps in knowledge
- “Open range” for supplement claims
- Further confusion among consumers
- Status quo for current food consumption patterns (i.e. poor consumption of fruits, vegetables and whole grains)

What are the Next Steps?

- "Development of Dietary Guidance for Non-Essential Nutrients" (June 8, 2010) Co-hosted by the Food Forum (FNB/IOM) and ILSI NA Project Committee on Flavonoids was a first step that began the dialog.

- "Are Dietary Bioactives Ready for Recommended Intakes?" EB symposium April, 21, 2013 (Boston)

Concluding Thoughts

- The DRIs provide a framework for assessment of “essential” nutrients
- The AI, UL and/or “Totality of Evidence” approaches could be applicable
- A modified evidenced-based systematic review approach (from what is used for drugs and essential nutrients) may be necessary

Overall Conclusions:

The current DRI framework may limit scholarly evaluation and potential "accreditation" of the contributions of bioactive substances.

The goal of public health recommendations should be to provide consumers with guidance about healthy food choices that provide both essential and "accredited" bioactive food components that enhance the quality of life.

Dietary Guidelines Versus RDAs

- Dietary Guidelines

  Qualitative advice to the public about diet (foods) and chronic disease prevention and maintaining health

- RDAs (or AIs)

  Quantitative advice to professionals about amounts of nutrients or food components found to be of benefit

FNB 1998 report on dietary antioxidants and related compounds

Criteria for selection (of dietary antioxidant)

- Substance is found in typical human diets
- Content of substance has been measured in foods commonly consumed
- In humans, the substance is associated with improved health outcome or decreased adverse effect

IOM. 1998. *DRIs. Proposed definition and plan for review of dietary antioxidants and related compounds.* National Academy Press.