

# CAN EVALUATION OF BIOACTIVES FIT THE CURRENT DRI (NRV) FRAMEWORK?

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CRN-I Annual Symposium

Nutrient Reference Value – Non-Communicable Disease  
(NRV-NCD) Endpoints

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Schlosshotel Kronberg, Kronberg im Taunus, Germany

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## Disclosures

- Member, Food and Nutrition Board, Institute of Medicine
- Member, National Academy of Medicine

# Working Definitions

- Bioactive. A substance, obtained from food, that promotes a beneficial physiological effect in humans and is not an essential nutrient.
- Essential Nutrient. A substance, obtained from food, that promotes a beneficial physiological effect in humans and must be obtained from the diet.

## Focus of the Talk

- Rationale for having a DRI/NRV process for bioactives?
- Is the current DRI process compatible with determining intake values for bioactives?
- What are the major obstacles to having a DRI-like process for bioactives?
- Where do we go next?

# Focus of the Talk

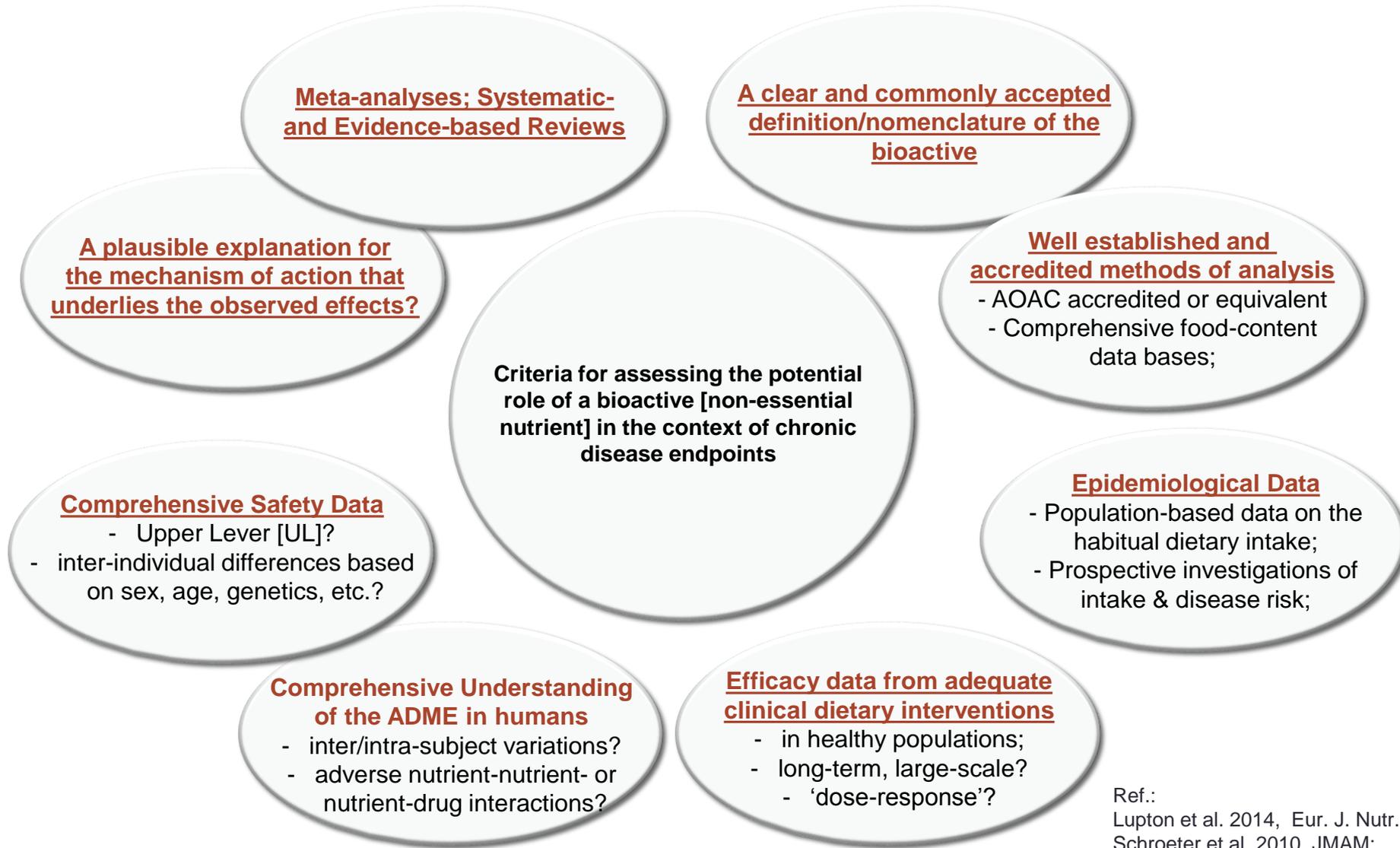
- Rationale for having a DRI/NRV process for bioactives?

# Why is it important to have a Framework for setting intake values for Bioactives?

- They are important to human health. There is a substantial scientific database on beneficial physiological effects of certain classes of bioactives.
  - Curcuminoids
  - Prenylated flavonoids
  - Carotenoids
  - Flavanols
  - Polyphenols
  - Omega 3 fatty acids (EPA and DHA)
- Research on bioactives is a significant part of Government, University and Food Manufacturer research portfolios.
- The quality of research would likely be enhanced if bioactives were subjected to the same standards as have the essential nutrients.

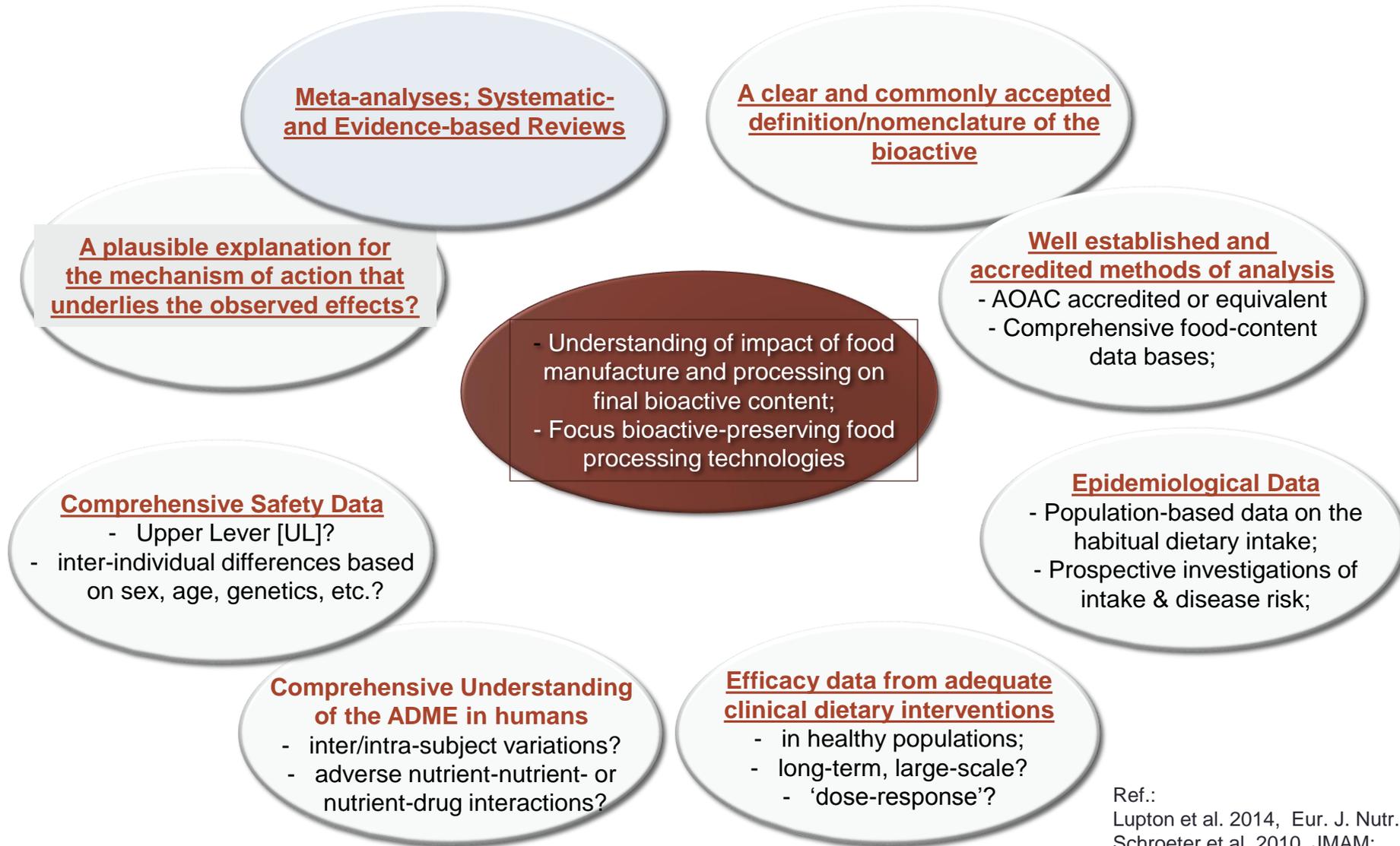
# Learning from the DRI

## Proposed Criteria for the Evaluation of bioactives by a DRI-like process



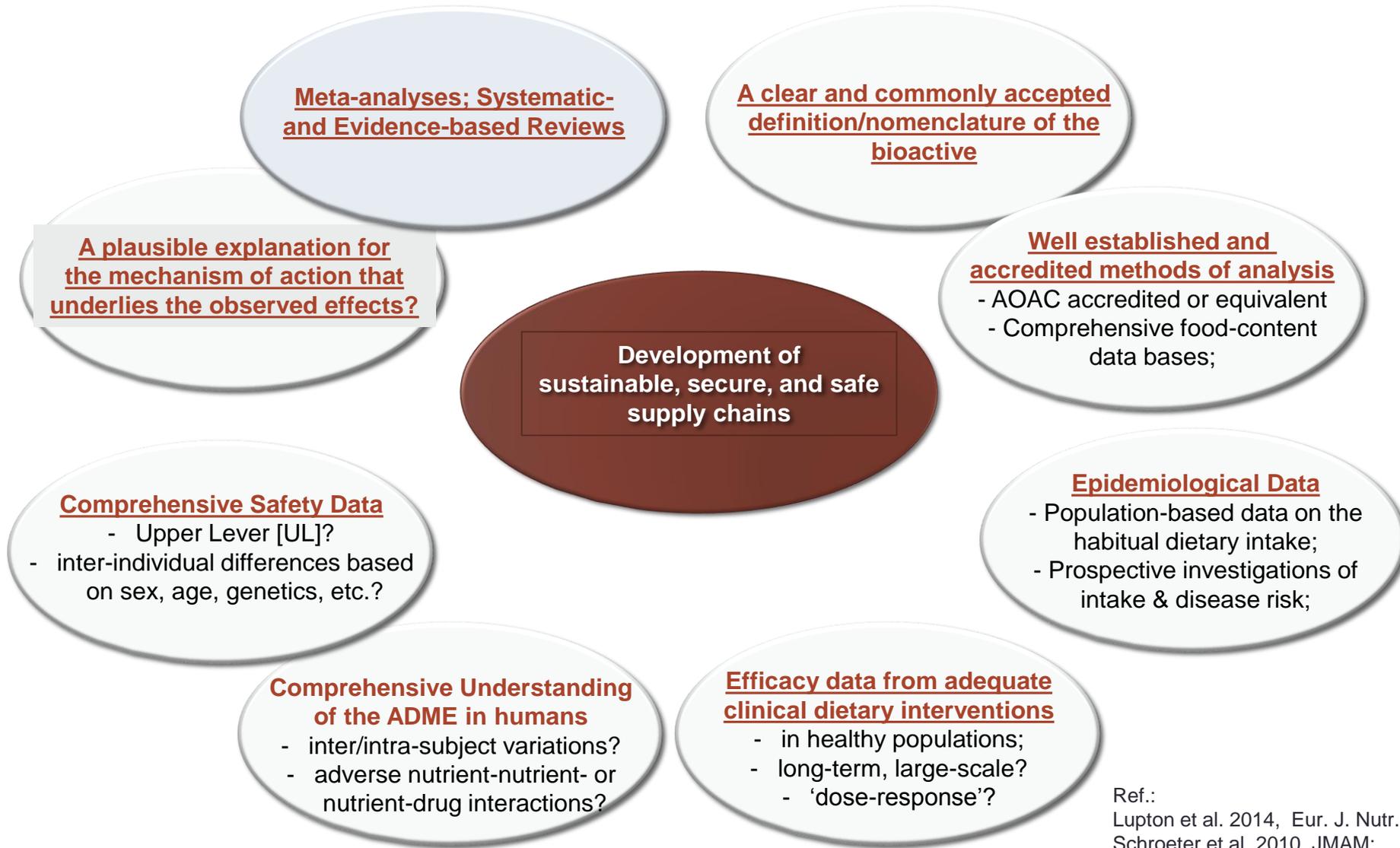
# Learning from the DRI

## Proposed Criteria for the Evaluation of bioactives by a DRI-like process



# Learning from the DRI

Proposed Criteria for the Evaluation of bioactives by a DRI-like process



# Why is it important to have a Framework for setting intake values for Bioactives?

- Consumers are interested in bioactives and are purchasing foods containing them.
- Food is now viewed as a source of substances to provide optimal health rather than just to protect against nutrient deficiency diseases
- It's important to provide consumers with information as to
  - How strong the science is behind purported benefits
  - How much they would need to eat to achieve these benefits
  - How much is too much

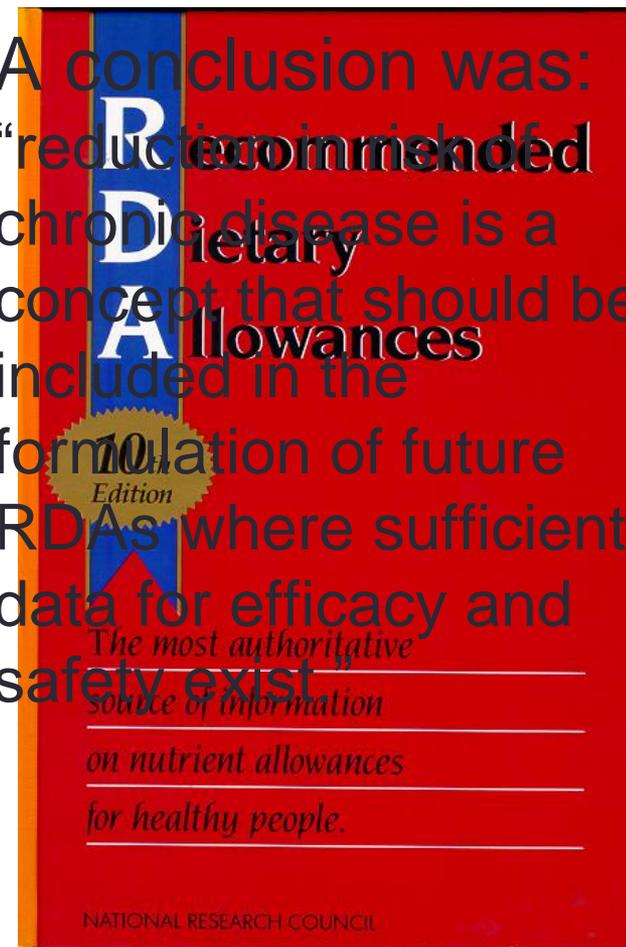
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# Three Key National Academies Press Publications

- **IOM.** 1994. *How should the Recommended Dietary Allowances be revised?*

- A conclusion was: “reduction of chronic disease is a concept that should be included in the formulation of future RDAs where sufficient data for efficacy and safety exist.”



# Applying the DRI framework to chronic disease endpoints

- **Affected how nutrients were grouped for review**
  - Calcium and related nutrients together because of their role in bone health and general health
  - Antioxidants and potential role in reduction of risk of cancer and CHD
- Electrolytes (blood pressure and hypertension)
- ...”A guiding principle conveyed to the DRI study committees was to review the evidence on chronic disease first in setting a DRI”

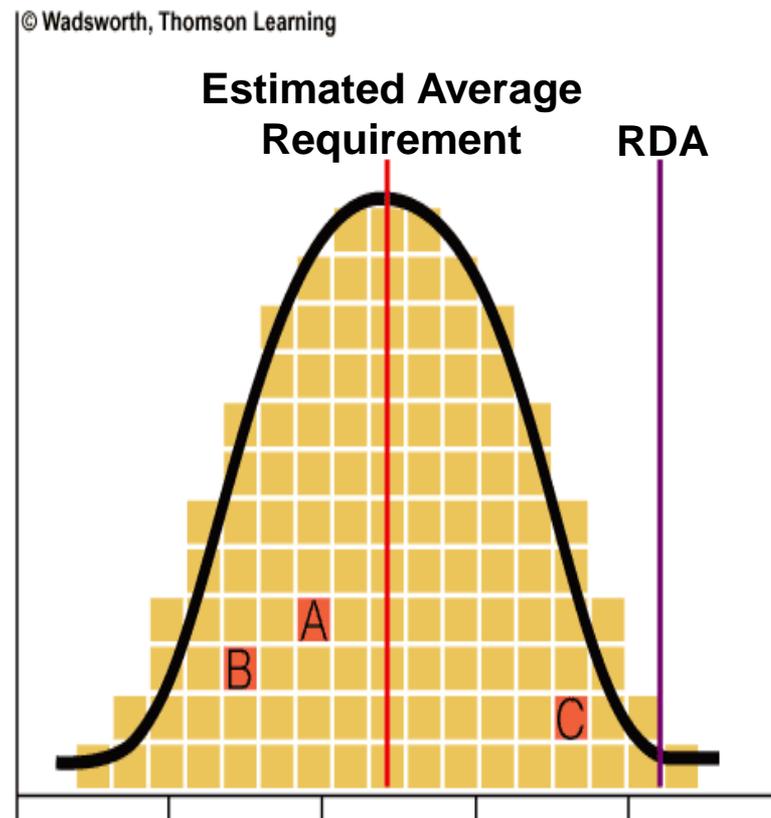
# There are two DRI intake values

- RDA
  - Derived from the EAR
- AI (Adequate Intake)

# Would setting an intake value for a bioactive fit the DRI paradigm?

## Recommended Dietary Allowance (RDA)

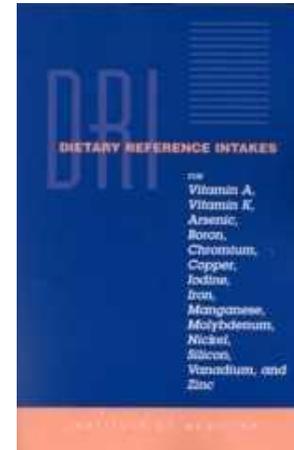
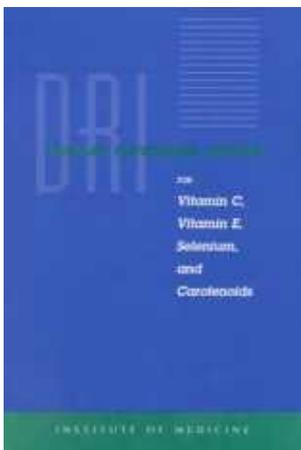
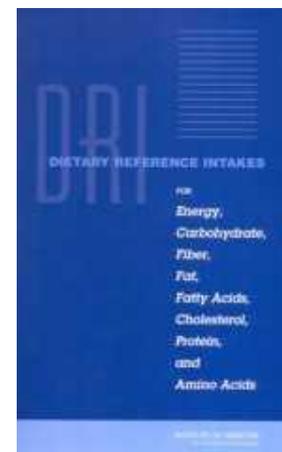
- The average daily dietary nutrient intake level sufficient to meet the nutrient requirement of nearly all (97-98%) healthy individuals in a particular life stage and gender group.



# Characteristics of an AI (Adequate intake)

- **Definition:** “The recommended average daily intake level based on observed or experimentally determined approximations or estimates of nutrient intake by a group (or groups) of apparently healthy people that are assumed to be adequate – used when an RDA cannot be determined”.
- “For adults, the AI may be based on data from a single experiment, on estimated dietary intakes in apparently healthy population groups, or on a review of data from different approaches that, when considered alone, do not permit a reasonably confident estimate of an EAR.”

# DRIs Established and Published as Nutrient Groups 1997-2005



Credit Dr. Linda Meyers

# Basing DRI values on chronic disease endpoints

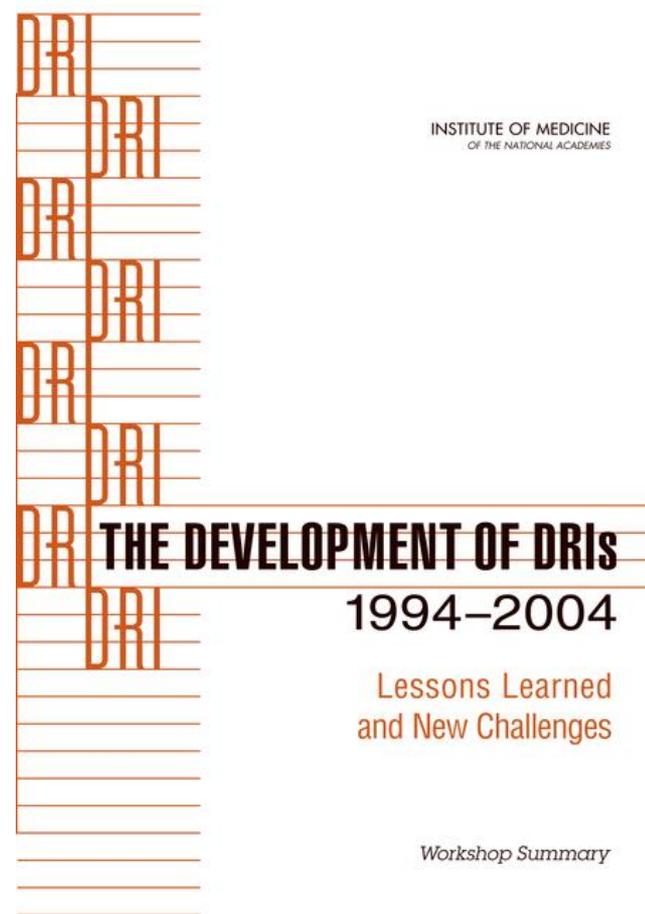
- Five, based on chronic disease, all were AIs.
  - Calcium and vitamin D (osteoporosis and fractures, also balance data)
  - Fluoride (dental caries)
- Fiber (CHD)
- Potassium (risk for hypertension, kidney stones, and blood pressure)

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# Applying the DRI framework to chronic disease endpoints

- The Development of DRIs 1994-2004: Lessons Learned and New Challenges: Workshop Summary, 2008
  - <http://.nap.edu/catalog/12086.html>
  - Dr. Paula Trumbo



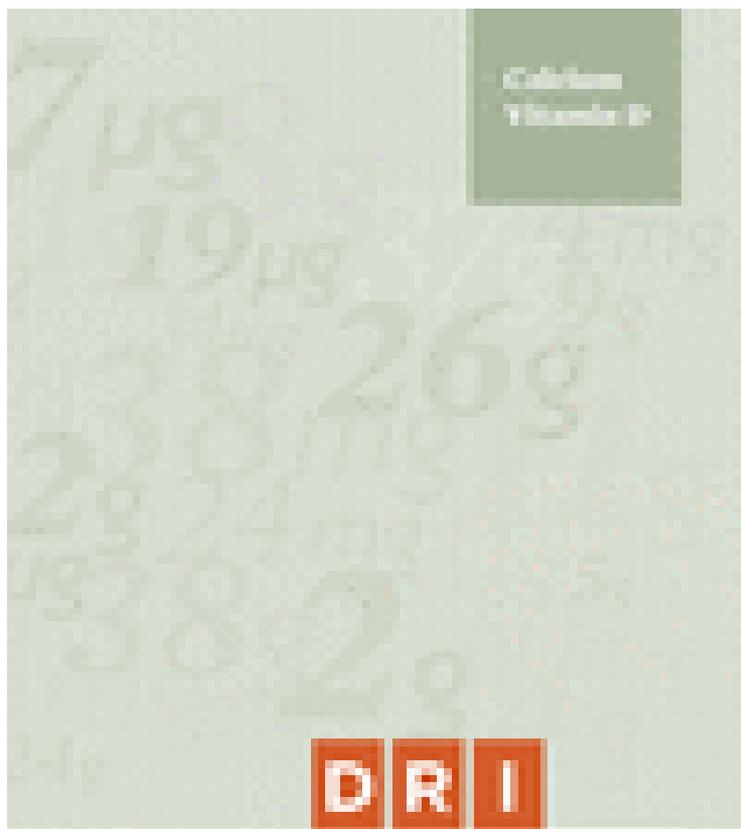
# The absence of a specific bioactive in the diet does not result in a deficiency disease

- The absence of an essential nutrient does result in a deficiency disease
  - Vitamin C
    - Scurvy
  - Thiamin
    - Beriberi
  - Iron
    - Microcytic Anemia
- The absence of a specific bioactive in the diet does not result in a deficiency disease
- Bioactives need a different type of “endpoint.”
  - Decreased risk of chronic disease
  - Optimal health\Ben Van Ommen
  - A beneficial physiological effect\Flow Mediated Dilation\Cesar Fraga

# Issues with applying the EAR to bioactives

- A nutrient specific indicator is not being applied.
  - Microcytic anemia vs CHD
- Endpoints of inadequacy assumed **ALL** individuals are at risk of inadequacy for essential nutrients.
  - Not true for bioactives and chronic disease
- Chronic diseases are not nutrient specific, but multifactorial
  - The absolute risk of most chronic diseases applies to only a portion of the population
  - Not likely that a bioactive would account for 50% of the risk reduction

# Calcium and Vitamin D revisited 2011



**DRI**  
DIETARY REFERENCE INTAKES

**Calcium  
Vitamin D**

Committee to Review Dietary Reference Intakes for Vitamin D and Calcium  
Food and Nutrition Board

A. Catharine Ross, Christine L. Taylor, Ann L. Yaktine, and  
Heather B. Del Valle, *Editors*

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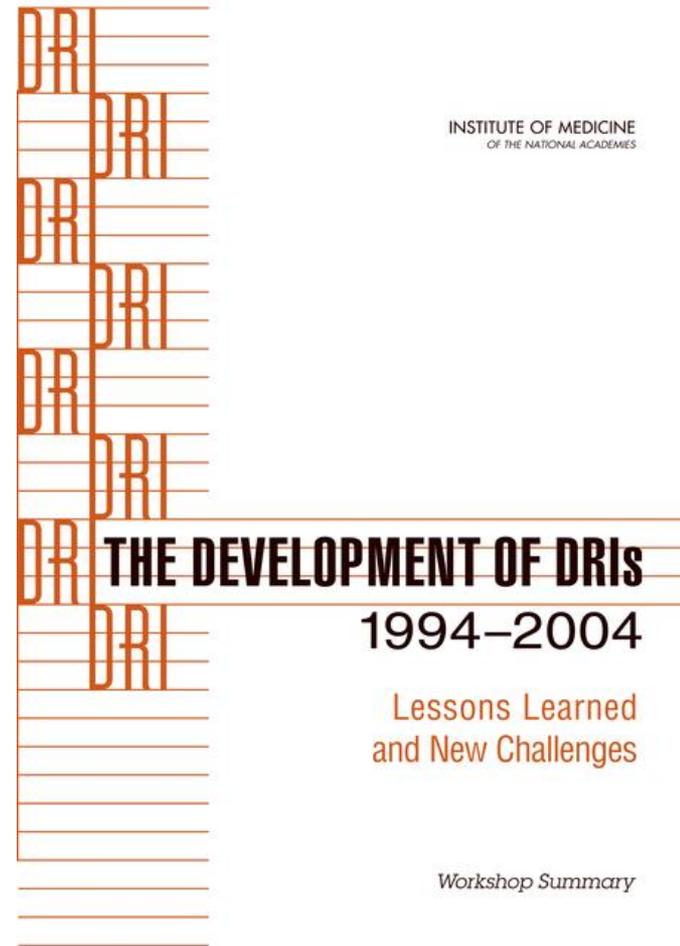
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# The Vitamin D/Calcium Report (two goals were described)

- 1) The framework should ensure and foster transparency of the decision making process.
- 2) the framework should anticipate the need to make decisions in the face of limited data and the interest in protecting public health and the reality that “**no decision is not an option**”—that is, a science-based judgment is more useful than no recommendation at all. In other words, the framework must operate under conditions of uncertainties.

# The Vitamin D/Calcium Report

- Is the only report that has come out after “Lessons Learned” Report.
- It characterizes setting DRIs as a “risk assessment process”
- It benefitted from a thorough evidence based review



# Summary

- There are multiple reasons why a framework for the evaluation of bioactives should be considered.
- The primary reason is to promote public health
  - What is an efficacious amount
  - How strong is the science
  - What are potential toxic effects
- Would setting an intake value for a bioactive fit the DRI paradigm?
  - A definite “maybe”
  - Probably not for an RDA value, but “yes” for an AI
- Where is the evaluative process for bioactives headed?

# Using chronic disease as an endpoint for intake values

- Committee from Canada and the USA
- Chair is Bert Garza, MD, PhD

# NIH VideoCasting and Podcasting

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- <http://videocast.nih.gov/summary.asp?Live=15713&bhcp=1>
- Joint Canadian-US DRI Working Group
- You need to know the dates, March 10,11, 2015

# Closing remarks from Dr. Bert Garza

Chair of the Committee on Options for Consideration  
of Chronic Disease Endpoints for DRIs

Chair of the Food and Nutrition Board, IOM

- ...”not having enough data will always be an issue, but we need to do the best we can at synthesizing what we have, for if we don’t – not doing so inevitably invites less rigorously derived guidance to fill perceived vacuums.”