Harmonizing Micronutrient Recommendations World-Wide

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Why Harmonize?

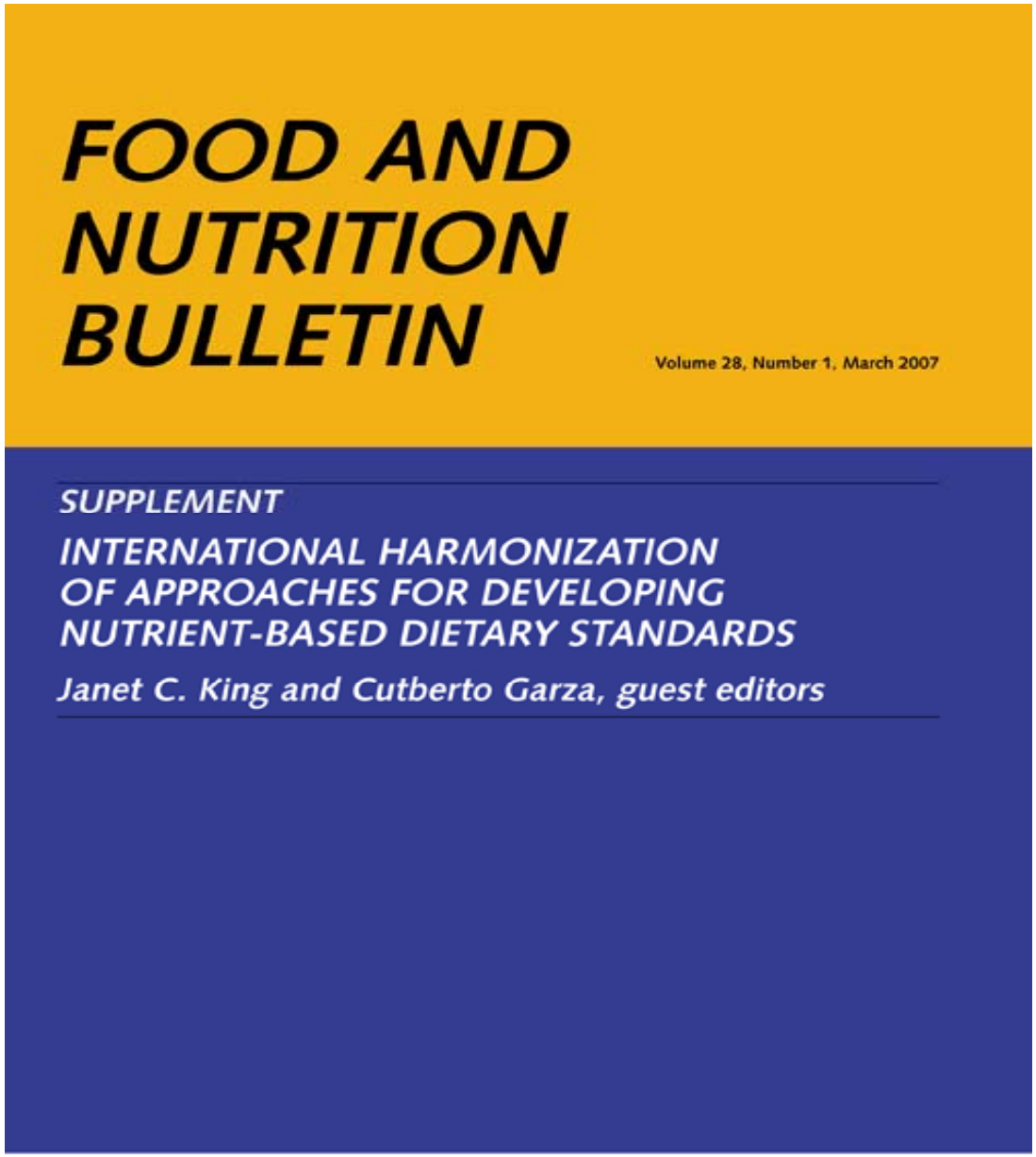
- Improves objectivity and transparency of recommendations
- Provides a common basis for recommendations by various groups
- Permits groups with limited resources to modify existing recommendations for their population
- Provides a common basis for establishing food and nutrition policies

We Live in an Evidence-based World!

Which means:

We must seek ways to <u>integrate</u>
the best available empirical
evidence with professional
wisdom for making decisions.

Courtesy: John Milner. ISLI-NA Workshop. December, 2008



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

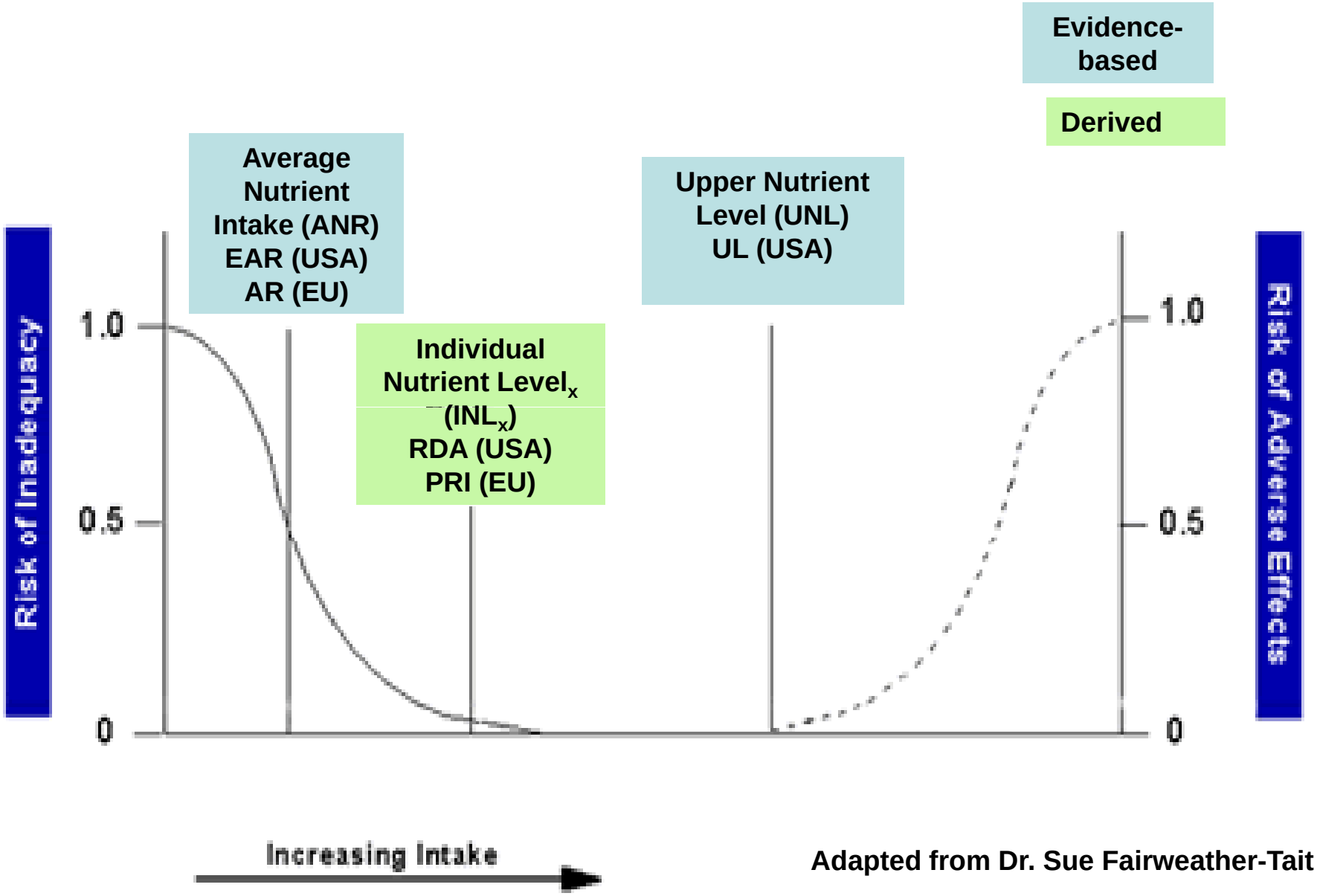
Applications

Regulatory issues & trade
Labeling
Public health planning
Fortification
Dietary guidance

Scientific Evidence-Based Values

- **Average Nutrient Value: mean nutrient intake to achieve a specific outcome in a specific population**
  - **Mean requirement**
  - **Variance**
- **Upper Nutrient Level: highest level of habitual nutrient intake that is unlikely to pose an adverse health effect in almost all individuals**
  - **NOAEL or LOAEL**
  - **Uncertainty factor (often based on judgment)**

Terminology is Inconsistent



Adapted from Dr. Sue Fairweather-Tait

Adequate for What?

Model criteria for adequacy:

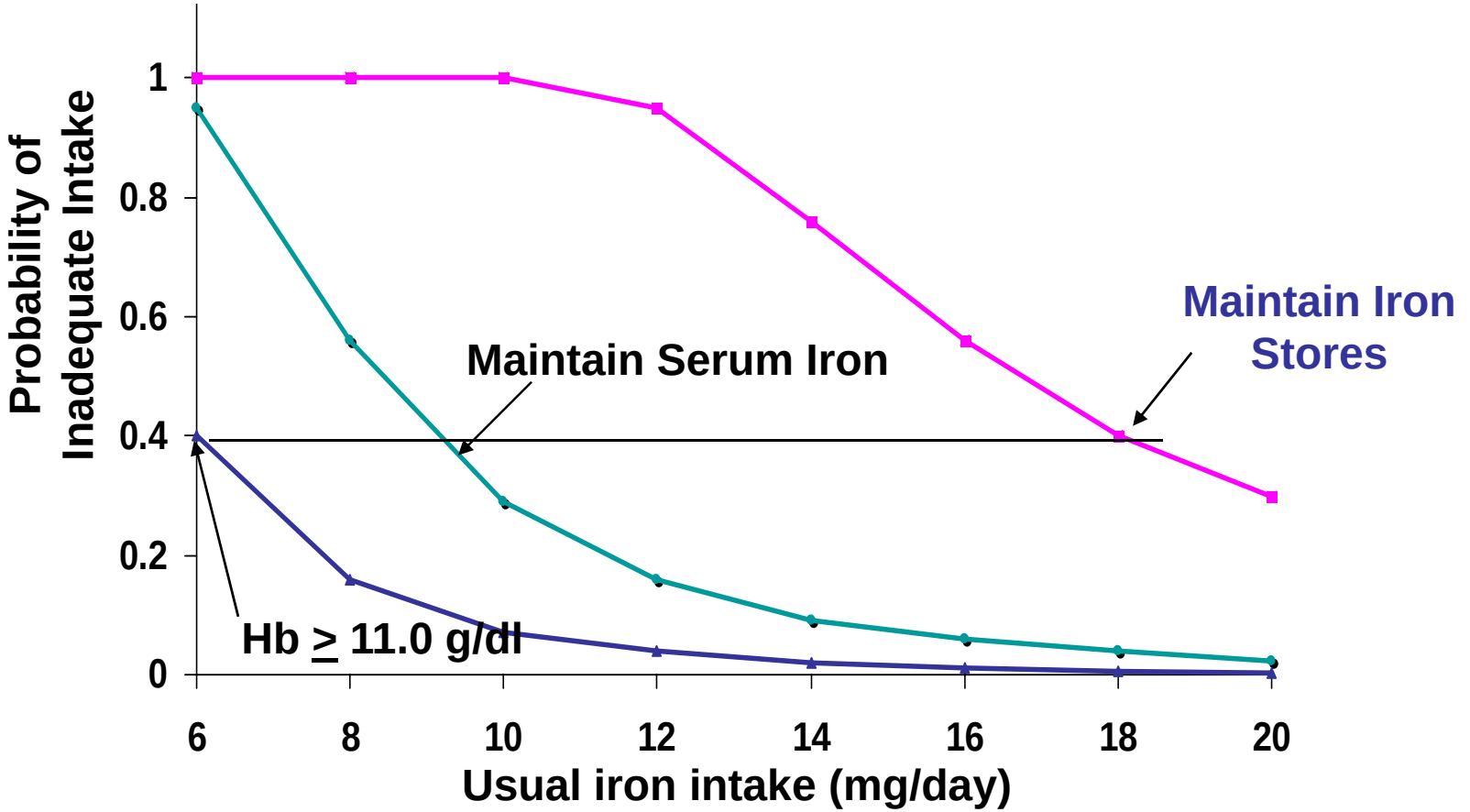
- **Measured without compromising health**
- **Does not fluctuate rapidly or markedly with intake**
- **A nutrient function that is not easily altered by other nutrients or environmental conditions**

Criteria for Micronutrient Requirements

Type of Study	Measurement	Examples
Dose-response studies (RCTs)	Functional outcome	BMD w/ ⇑ Calcium Glutathione peroxidase w/⇑ Se
	Biochemical measures	RBC folate 4-pyridoxic acid for B_6
Depletion/repletion	Biochemical measures	WBC ascorbic acid
Balance studies	Intake-excretion	Protein
	Factorial estimates	Zinc, Iron
Epidemiological observations	Functional outcome	Night-blindness—Vit A
Observed intakes	Dietary intake	Vitamin K

Average Nutrient Values Vary with Criterion

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



G. Beaton, 1994

Estimating Variance

Why? **Basis for planning diets for individuals (INL_x)**

Types of variability:

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

} ***control***

True biological variance often unknown

- **Assume a coefficient of variation of 10%**
- **Never validated**

A New Criterion for Nutrient Requirements

To Reduce the Risk of Chronic Disease

Nutrient Standards Based on Disease Endpoints, Institute of Medicine. USA. 2006

Calcium	Fracture Risk
Vitamin D	Fracture Risk
Fluoride	Dental Caries
Potassium	Hypertension, Renal Stones
Fiber	Coronary Heart Disease

Unable to establish EARs
Adequate Intakes (AIs) derived

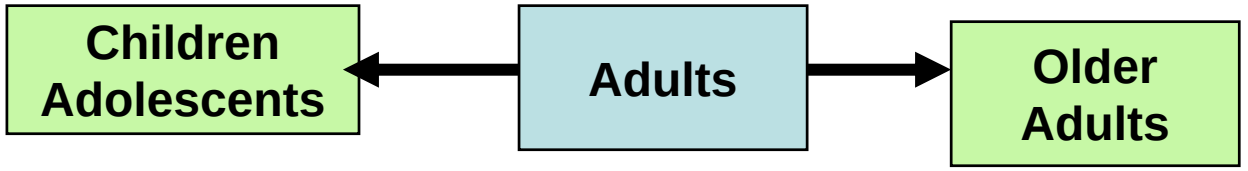
From Rob Russell, ILSI Workshop, 12/2008

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

Extrapolate When Necessary

- First choice—scientific evidence
- Second choice—extrapolation



- No one “correct” method
- Different approaches for different nutrients
- Examples:
  - Body size
  - Energy intakes
  - Factorial estimates based on growth or milk composition

Current Data Do Not Support Adjustments for Genetic Differences

- **The genome varies by 0.2 to 0.4% in humans**
- **Variations in a DNA sequence, or a polymorphism, accounts for different human phenotypes**
- **Challenging nutrient environments could induce genetic variations through natural selection**
  - ***Ex: Lactose Intolerance***
- **To date, no gene variant has affected nutrient requirements sufficiently to warrant geno-type specific recommendations**
  - ***Ex: MTHFR variant and folate requirements***

Unlikely gene-gene interactions will be a determinant of NIVs since highly penetrant genes have a low prevalence.

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.**

Diet-Related	Host-Related
Chemical form of nutrient Nature of diet matrix Interactions among nutrients or with other diet components Food pre-treatment: processing or preparation methods	Intestinal factors: atrophic gastritis, bacterial overgrowth, infection, altered mucosal structure, reduced transit time. Systemic factors: infection, nutritional status of host, maybe ethnicity

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 NIV to Use for What

	Individuals	Populations
Assessing Adequacy	**Average Nutrient Requirement**	**Average Nutrient Requirement**
Planning Diets	**Individual Nutrient Level$_x$**	**Distribute intakes between ANR and UNL**

Nutrient Intake Values: Summary

Criteria

- **Evidence-based; strong data sets**
- **Long-term disease is related more to diet pattern than specific nutrients**

Extrapolate if necessary

- **First choice—scientific data**
- **Transparency—essential**

Genetic Factors

- **An unlikely determinant of NIVs**
- ***Population-specific* recommendation for ethnicities/groups with nutrient sensitivities (e.g., salt sensitivity)**

Adjust for Bioequivalence

- **Based on country/region specific factors**
- **No scientific consensus—use judgment**