

# Challenges in Addressing Extrapolation/Intrapolation in Unstudied Groups

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# Past Use of Extrapolation

- 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%

# Past Uses of Extrapolation

- Models varied within the DRIs (and globally in international standards)

## EXAMPLE – DRI for 6-12 mo age group

- **Extrapolation** up from 0-6 mo AI
  - niacin, choline, biotin, B-12, A, K
- **Extrapolation** down from adult EAR or AI
  - B-1, B-2, B-6, folate, pantothenic acid
- Extrapolation led to inconsistencies in recommendations between age groups

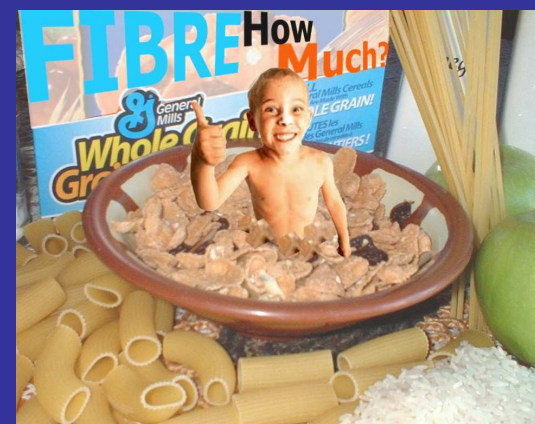
# Emerging Inconsistencies

Recommendations for 6-12 mo vs 1-3 y

Nutrient	6-12 mo	1-3 y
<b>Vit A (ug RAE)</b> Derivation	<b>AI=500</b> Extrap. 0-6 mo	<b>RDA=300</b> Extrap. adult
<b>Vit C (mg)</b> Derivation	<b>AI=50</b> HM + food	<b>RDA=15</b> Extrap. adults
<b>Molybdenum (ug)</b> Derivation	<b>AI=3</b> HM+food	<b>RDA=17</b> Extrap adults

**Why?** Extrapolation from adults adjusted for body weight is wrong model

# Emerging Inconsistencies: Fiber



- No AI for infants - not in milk; no data on food.
- AI extrapolated from adult AI of 14 g/1000 kcal based on reduction in CVD in adults.
- Low fiber intake is risk factor for constipation, but.....
- AI impossible to achieve?

Age (y)	AI (g/d)	Intake Range*
1-3	19	5-12 (1-2 y)
4-8	25	6-18
9-13	26-31	9-11 (10-12 y)
Adult	25-38	

\* Devaney et al 2004, Suitor & Gleason, 2002

# Emerging Inconsistencies: UL vs observed intakes in CSFII\*

## Observed intakes > the DRI UL

- **For 0-12 mo**
  - 90% exceed zinc UL
  - 39% exceed vitamin A UL
- **For 1-3 y**
  - 55% exceed zinc UL
  - 20% exceed vitamin A UL
  - 88% exceed Na UL
  - But < 1% exceed UL for Fe, Zn, B-6, C

\* Suitor & Gleason, 2002

# Extrapolation or Scaling?



**Adult**



**7-12mo 1-3 yr 4-8 yr**

# Terminology

- **Extrapolation**

- Calculation of the value of a function outside the range of known values
  - Used in DRIs to adjust for physiological differences between groups of varying body size or age

- **Scaling**

- Act of measuring or arranging or adjusting according to scale
  - Used since 1830s with regard to expressions of body weight or compartments scaled to height, e.g., BMI

# Models: Scaling/Extrapolation

- **Linear Models:**

- Body size (mass) – linear using reference BW for age & gender, e.g., AI for fiber for children
- Energy – median reference energy intake for age & gender, e.g. AI for water, K and Na for children

- **Issues:**

- no account of age variations in intermediary metabolic rates, energy intake or BMR

# Models: Scaling/Extrapolation

- **Exponent Model**

- Adjusts for metabolic differences related to body weight
- Example – UL from adults to children to  $BW^{0.75}$

- **Issues:**

- Assumes maintenance needs of nutrients as a function of metabolic weight are similar for adults and children; and similar across genders
- Assumes absorption, digestion, excretion similar across age groups
- Lack of consensus on adjustment factor that best reflects BMR, e.g. 0.6 – 0.8 used
- Values produced > from linear model

# Models: Scaling/Extrapolation

- **Relative body surface area**
  - Adjusts for metabolic differences between ages related to body surface area based on relation to BMR
- **Issues:**
  - Results in higher nutrient reference values than those based on body weight; almost 2-fold difference for infants  $< 1$  yr

# Relative Nutrient Intake (RNI) Reference Values by Extrapolation from Adults: Body Weight vs Surface Area *(Przyrembel 2005)*

<b>Age</b>	<b>RNI based on child/adult body weight</b>	<b>RNI based on child/adult body surface area</b>
Newborn	0.05	0.11
0.5 yr	0.1	0.19
1 yr	0.14	0.23
10 yr	0.46	0.59

# Models: Scaling

# Interpolation

- **Interpolation**

- Interpolate a value for an age group between known values of age groups older and younger
- Not used in DRIs
- Use in EU-SCF dietary standard (1993)

# Models: Accounting for growth

- **For extrapolation from adults to children**
  - DRI used approximate proportional increase in protein requirements for growth established in FAO/WHO/UNU (1985)

<u>Age Group</u>	<u>Growth Factor</u>
7 mo-3y	0.30
4-8 y	0.15
9-13 y	0.15
14-18 y (males)	0.15 (0 for females)

# Models: Reference body weights

- Reflect population-based standard for country(ies) i.e., USA/Canada
- Issues:
  - Used 3<sup>rd</sup> NHANES until Macronutrient report and then CDC/NCHS (2000) for median heights & weights computed from median BMI
  - Infants not based on breast-fed population
    - Now can use WHO reference growth standards for breast-fed infants (Acta Paediatr 2006;95:76) for 0-5 y
  - No Canadian reference data at time

# Challenges to address: Extrapolation

- Extrapolation is a proxy; thus yields a risk of error especially for values from adults to children
- Evaluation of physiology and scientific judgment needed for each nutrient
  - Need knowledge of substrate absorption, metabolism, deposition in tissues during growth phases, and renal or other excretion that may affect the EAR or UL as these may not be related to body size

# Challenges to address: Extrapolation

- For some nutrients, especially UL, extrapolation on basis of BW or BSA yields an UL for children incompatible with known nutrient requirements
  - Should not set such UL until direct experimental evidence is available

# Children are **NOT** just little adults

*.....they need their own evidence-based DRIs*

Inappropriately set DRIs can:

- Cause risks to health status
- Identify wrong nutrient intake problems (inadequacy & excess)
- Lead to inappropriate recommendations for child feeding programs, e.g. WIC



# Conclusions: Scaling/Extrapolation in Setting DRIs

- **Eliminate need for use of extrapolation/scaling models in DRIs**
- When it must be a second choice, apply the model that is most biologically plausible; scientific judgment is necessary
- If using energy intakes, body weights or activity levels as a basis for scaling, careful selection of relevant population-based data specific for age and gender is essential