Role of diet and environment in setting nutrient bioavailability factors for estimating dietary requirements

Rosalind S Gibson,
Emerita Professor,
Department of Human Nutrition,
University of Otago, New Zealand
Bioavailability and Bioefficacy

• To convert physiological requirements to *dietary requirements*, an adjustment is often needed to take into account factors that affect the proportion of the ingested nutrient that is absorbed and utilized through normal metabolic pathways (viz. bioavailability)*.

• Bioavailability may be influenced by factors related to:
  » Host (including health); Diet; Environment

• Bioefficacy is efficiency with which ingested nutrients are absorbed and converted to an active form
  » Currently applied to provitamin A carotenoids

If host conditions, diet or environment do NOT affect bioavailability, then physiological & dietary requirements *will be the same.*

* From Hurrell (2004)
Currently there is only sufficient data to quantitatively assess the impact of dietary factors on bioavailability/bioefficacy for the following nutrients:

- **Protein**
- **Trace elements**
  - Iron; Zinc
- **Vitamins**
  - Food Folate vs. synthetic folic acid
    - (*Dietary folate equivalents*)
  - Food vitamin B-12 vs. crystalline B-12
  - Preformed retinol vs. provitamin A carotenoids
    - (*Retinol activity equivalents*)
Dietary factors influencing bioavailability or bioefficacy

- **Chemical form:** Fe; Zn; folate; B-12; (B-6; Se; niacin)*
- **Nature of dietary matrix:** folate; carotenoids
- **Effects of other food components:**
  - Inhibiting interactions by organic food components
  - Enhancing interactions by organic food components
  - Interactions between >2 nutrients
    » for micronutrients: only occur with high doses of supplements *without* food; not a problem for levels in habitual diets
- **Pre-treatment of food:** preparation/processing/cooking

NB: * For many nutrients data are inadequate to quantify these effects
Examples: Food components & pre-treatment of food

- **Organic components that inhibit bioavailability:**
  - Phytate; Polyphenols; Oxalates: inhibit certain minerals
  - Dietary fibre: inhibits fat soluble vitamins, carotenoids, protein

- **Organic components that enhance bioavailability:**
  - Organic acids; enhance Fe, Zn; Vit C: enhances Fe
  - Animal protein: Fe, Zn, Cu, Mg; Fat: fat-soluble vits & carotenoids

- **Interactions between ≥2 nutrients:** with high supplement doses

- **Pre-treatment of food:**
  - **Milling:** ↓ phytate & minerals; **Soaking:** ↓ phytate, minerals, B vitamins
  - **Blending:** ↑ carotenoids; folates; **Germination/Fermentation:** ↓ phytate; ↑ Fe, Zn, Ca
Predictors of total absorbed Zn as a function of total dietary Zn at six levels of dietary phytate

EFSA dietary zinc requirements for adult females and males

<table>
<thead>
<tr>
<th>Phytate mg/d</th>
<th>≥18 y</th>
<th>Ave requirement mg/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>F, M</td>
<td>6.2, 7.5</td>
</tr>
<tr>
<td>250</td>
<td>F, M</td>
<td>7.6, 9.3</td>
</tr>
<tr>
<td>500</td>
<td>F, M</td>
<td>8.9, 11.0</td>
</tr>
<tr>
<td>1000</td>
<td>F, M</td>
<td>10.2, 12.7</td>
</tr>
<tr>
<td>2000</td>
<td>F, M</td>
<td></td>
</tr>
<tr>
<td>3000</td>
<td>F, M</td>
<td></td>
</tr>
</tbody>
</table>

From EFSA. Scientific opinion on Dietary Reference values for zinc. EFSA Journal 12(10):3844,1-76 (2014)
Methods to assess impact of dietary factors on nutrient bioavailability

- **Animal models**
- **In vitro methods**
  - Measurement of dialyzable or soluble Fe, Zn
  - Caco-2-cell systems: Fe, Zn, Ca
- **In vivo methods**
  - Balance & intake studies: Ca, Fe, Zn—yield *apparent* absorption
  - Isotopic methods: Fe, Zn, Ca; folate; vit A
    » isotope studies in *whole* diets & not single meals yield most accurate bioavailability data
- **Changes in biomarkers/functional outcomes**
- **Bioavailability algorithms**
  - Useful for *classifying* diets into high, medium, or low bioavailability
  - Based on mathematical models that take into account major absorption modifiers
Examples of diets with different iron bioavailability assessed by isotope techniques

<table>
<thead>
<tr>
<th>Type of diet</th>
<th>Bioavailability* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very high meat in two main meals daily &amp; high ascorbic acid</td>
<td>27.5</td>
</tr>
<tr>
<td>High meat, fish in two main meals per day</td>
<td>24.5</td>
</tr>
<tr>
<td>Moderate meat/fish in two main meals per day</td>
<td>19.5</td>
</tr>
<tr>
<td>Moderate meat/fish in two main meals daily; low phytate content</td>
<td>15.5</td>
</tr>
<tr>
<td>Meat, fish in 60% of two main meals daily; high phytate</td>
<td>11.5</td>
</tr>
<tr>
<td>Low meat intake; high phytate; often one main meal</td>
<td>9.2</td>
</tr>
<tr>
<td>Meat/fish negligible; high phytate; high tannin &amp; low ascorbic acid</td>
<td>5.5</td>
</tr>
</tbody>
</table>

*For 55 kg women with no iron stores & assuming an intake of 15 mg Fe/day From WHO/FAO (2004)
### WHO/FAO Algorithm: Iron

<table>
<thead>
<tr>
<th>High bioavailability 15%</th>
<th>Moderate bioavailability 10%</th>
<th>Low bioavailability 5%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diversified diet with generous amounts meat, poultry, fish &amp;/or w. high amounts ascorbic acid</td>
<td>Diets mainly of cereals, roots &amp;/or tubers Minimal amounts of meat, poultry, fish &amp; ascorbic acid</td>
<td>Simple, monotonous diet of cereals, roots, &amp;/or tubers Negligible amounts of meat, poultry &amp; fish or ascorbic acid-rich foods</td>
</tr>
</tbody>
</table>

### WHO/FAO Algorithm: Zinc

<table>
<thead>
<tr>
<th>High bioavailability 50%</th>
<th>Moderate bioavailability 30%</th>
<th>Low bioavailability 15%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low in cereal fiber; animal foods major protein source</td>
<td>Not based on unrefined cereal grains or high extraction rate (&gt;90%) flours</td>
<td>Cereal-based with &gt; 50% energy from unrefined cereals or legumes; negligible animal protein</td>
</tr>
</tbody>
</table>

| Phytate:Zn < 5 | Phytate:Zn 5 -15 | Phytate:Zn > 15 |

### IZiNCG: Algorithm: Zinc

<table>
<thead>
<tr>
<th>Mixed/Refined Vegetarian diet: Phytate:Zn 4-18</th>
<th>Unrefined cereal-based: Phytate:Zn &gt;18</th>
</tr>
</thead>
<tbody>
<tr>
<td>F: 34%; M: 26%;</td>
<td>F: 25%; M: 18%</td>
</tr>
</tbody>
</table>
Potential tools to estimate bioavailability across countries based on food supply* or food consumption data**

- **FAO Food Balance Sheets** (210 countries)
  - Per capita values for *supply* of 95 food commodities (g/d); energy, protein, fat per capita
  - Other nutrients can also be calculated (e.g. Zn & phytate)

- **WHO/FAO GEMS/Food cluster diets** (183 countries)
  - Data standardized into 13 cluster diets
  - Number & percent of children & adults consuming each commodity
  - Mean ± SD as g/kg BW/day of food/food grp for children & adults

- **FAO/WHO GIFT platform**
  - Mean daily *intakes* by life stage group of: standardized food groups (g/d); nutrients; antinutrients; food sources of nutrients (as %)
### Food Balance Sheet example: Mean daily per capita phytate: zinc molar ratios & fractional Zn absorption (FAZ) (as %) from available food supply

<table>
<thead>
<tr>
<th>Region</th>
<th>Phy:Zn Molar Ratios</th>
<th>FAZ* (as %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>South &amp; Tropical Latin America</td>
<td>9.6</td>
<td>26</td>
</tr>
<tr>
<td>China</td>
<td>10.6</td>
<td>23</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>21.3</td>
<td>27</td>
</tr>
<tr>
<td>South Asia</td>
<td>22.8</td>
<td>23</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Country</th>
<th>Phy:Zn Molar Ratios</th>
<th>FAZ* (as %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>8</td>
<td>25</td>
</tr>
<tr>
<td>Indonesia</td>
<td>19.4</td>
<td>28</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>20</td>
<td>28</td>
</tr>
<tr>
<td>Malawi</td>
<td>30.7</td>
<td>22</td>
</tr>
</tbody>
</table>

*Calculated from updated trivariate model of Miller et al. (2007): J Nutr 137:135-141

**Data from:**
doi:10.1371/journal/pone.0050565

PLoS ONE 7(II): e50568.
Doi: 10.1371/journal.pone.0050568
GIFT example: Indicators to estimate bioavailability/bioefficacy by country & life-stage grp*

<table>
<thead>
<tr>
<th>Food/food grp-based Indicators</th>
<th>Nutrient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selected food groups** (g/day; g/kg/BW/day)</td>
<td>Fe, Zn, vit A</td>
</tr>
<tr>
<td>Foods: red meat; liver; maize; rice; orange-yellow fruits &amp; veg; green leafy veg (g/d; g/kg/BW/day)</td>
<td>Fe, Zn, vit A</td>
</tr>
<tr>
<td><strong>Nutrient-based indicators</strong></td>
<td></td>
</tr>
<tr>
<td>Total protein, indispensable amino acids, dietary fiber</td>
<td>Protein</td>
</tr>
<tr>
<td>Major food/food group sources of nutrient intakes (e.g. proportion of iron or zinc from flesh foods)</td>
<td>Ca, vit A, Fe, Zn</td>
</tr>
<tr>
<td><strong>Potential indicators</strong></td>
<td></td>
</tr>
<tr>
<td>Heme Fe &amp; non-heme iron</td>
<td>Fe</td>
</tr>
<tr>
<td>Phy:Zn molar ratios; Fractional Zn absorption from trivariate model of Miller et al.*</td>
<td>Zn</td>
</tr>
</tbody>
</table>

Environmental factors with potential to influence nutrient requirements

• Exposure to ultraviolet light from sunshine:
  – influences extent of endogenous synthesis of vitamin D in skin
  – higher latitudes: decreased UV light & less vit D synthesised via skin so instead more needed from diet

Potential environmental factors not yet taken into account

• Extremes in ambient temperatures: affects nutrient losses via sweat
  – may impact Fe & Zn requirements estimated via factorial approach
• Exposure to high altitudes: increases BMR & may induce weight loss
  – may increase energy requirement
• Exposure to pollution: Antagonistic interactions e.g. Pb vs. Fe
  – may increase iron requirement
• Pesticide exposure: eg toxic levels of dioxin-type compounds
  – may lead to changes in carbohydrate metabolism & lipid peroxidation
Conclusions

• Physiological requirements must be adjusted to dietary requirements to account for bioavailability for certain nutrients.

• Current *quantitative* Fe algorithms may have limited use across populations whereas Miller trivariate model for estimating zinc bioavailability has potential with advent of new FAO/INFOODS/IZiNCG phytate database.

• Explore use of Food Balance Sheets, GEMS, & GIFT data in conjunction with WHO/FAO algorithms to classify Fe & Zn bioavailability in habitual diets across populations.

• Dietary requirement for vitamin D only nutrient adjusted for environmental exposure (e.g. UV light) at present time.
Approaches to harmonize methods for adjusting for bioavailability across countries

- Consensus on nutrients needing adjustment for bioavailability
- Consensus on isotope data selected for bioavailability estimates
- Explore use of GIFT indicators for classifying diets as low, intermediate, or high bioavailability for Fe or Zn across populations
- Calculate dietary phytate:Zn molar ratios across populations from GIFT data with new phytate database
  - Explore application of Miller trivariate model to estimate fractional zinc absorption
- Explore use of GIFT indicators on major food sources of provit A carotenoids to estimate bioefficacy across populations
- Calculate folate bioavailability from food folate + folic acid from fortificants & supplements (where relevant) across populations
Thank you!
Assessing nutrient bioavailability via algorithms

- Mathematical models to predict nutrient bioavailability based on general properties of major dietary enhancers & inhibitors

- Require information on:
  - Isotope data on bioavailability (as %) based on habitual whole diets
  - Habitual food consumption patterns including:
    » population nutrient intakes & potential dietary enhancers & inhibitors
    » major food sources of nutrients; food preparation & processing
  - Accurate food composition tables
  - For iron, data on host nutrient status where possible

- **WHO/FAO & IZiNCG**: semi-quantitative algorithms for Fe &/or Zn
  - Used to classify diets into high/medium/low bioavailability

- **BUT** algorithms have several limitations:
  - Eg: Cannot account for simultaneous effects of absorption modifiers in complex dietary matrix of whole diets