LPI's Rx for Health—or
How to meet your micronutrient needs

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Micronutrients = 13 Vitamins & 14 Minerals

- Have to be obtained in small amounts from the diet (except vitamin D)
- Do not provide calories/energy (macronutrients)...
- ... but help convert food into energy, and have hundreds of other biological functions in the body:
  - Cofactors [coenzymes] of thousands of enzymes
  - Hormones
  - Structural elements of bone, teeth, proteins, DNA, and other biological macromolecules
  - Antioxidants
  - Etc.
13 Vitamins

<table>
<thead>
<tr>
<th>Water-Soluble (9)</th>
<th>Fat-Soluble (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>B-Vitamins:</strong></td>
<td>• Vitamin A (retinol)</td>
</tr>
<tr>
<td>• Thiamin (B1)</td>
<td>• Vitamin D (calciferol)</td>
</tr>
<tr>
<td>• Riboflavin (B2)</td>
<td>• Vitamin E (alpha-tocopherol)</td>
</tr>
<tr>
<td>• Niacin (B3)</td>
<td>• Vitamin K (phytoquinone)</td>
</tr>
<tr>
<td>• Pantothenic Acid (B5)</td>
<td></td>
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<tr>
<td>• Vitamin B6 (pyridoxal)</td>
<td></td>
</tr>
<tr>
<td>• Biotin (B7)</td>
<td></td>
</tr>
<tr>
<td>• Folic acid (B9, folate)</td>
<td></td>
</tr>
<tr>
<td>• Vitamin B12 (cyanocobalamin)</td>
<td></td>
</tr>
<tr>
<td>• Vitamin C (ascorbic acid)</td>
<td></td>
</tr>
</tbody>
</table>

14 Nutritionally-essential Minerals

**Macro-Minerals (5)**
- Calcium
- Magnesium
- Phosphorus
- Potassium
- Sodium (Chloride)

**Trace Minerals (9)**
- Chromium
- Copper
- Fluoride
- Iodine
- Iron
- Manganese
- Molybdenum
- Selenium
- Zinc
Essential Nutrients = Essential for Health
- cell and tissue function
- metabolism, growth, and development
- immune function
- cognitive function
- bone health
- etc.

By definition: Lack in diet results in overt symptoms of deficiency

Micronutrients = 13 Vitamins & 14 Minerals

- Scurvy killed a million seamen in 17th and 18th century (James Lind)
- Rickets and osteomalacia (soft bones); muscle pain, weakness
- Fatigue, lethargy; rapid heart rate, palpitations; rapid breathing on exertion; headaches; pallor

Deficiency vs. Inadequacy

- Micronutrient deficiencies
  - Low intake resulting in deficiency disease and overt symptoms
    - Rare—but not absent—in developed world
    - Common for iron, vitamin A, zinc, and iodine in developing world
Vitamin A Deficiency

- ~250 million preschool children world-wide (WHO)
- Causes death of ~650,000 children under 5y each year
- Blindness, severe infections

Deficiency vs. Inadequacy

- Micronutrient deficiencies
  - Low intake resulting in deficiency disease and overt symptoms
  - Rare—but not absent—in developed world
  - Common for iron, vitamin A, zinc, and iodine in developing world

- Micronutrient inadequacies
  - Intake sufficient to prevent deficiency disease but below the recommended dietary allowance (RDA)
  - Common in developed world
Risk of Inadequacy vs. Adverse Effects

- The **Recommended Dietary Allowance (RDA)** is the intake at which the risk of **inadequacy** is very small—0.02 to 0.03 (2 to 3%).
- At intakes between the RDA and the **Tolerable Upper Intake Level (UL)**, the **risks of inadequacy and of excess are both close to 0**.
- At intakes above the UL, the risk of adverse effects may increase.

Dietary Guidelines for Americans

- A fundamental premise of the **Dietary Guidelines for Americans** is that micronutrients (and other nutrients) should come primarily from the most nutrient-rich foods, because these foods also contain other dietary factors with positive health effects.

- However, people living in the US don’t eat according to DGA.

*Slide courtesy of Elizabeth M. Ward, M.S., R.D.*
How Do Typical American Diets Compare with Recommended Intake Levels or Limits?

<table>
<thead>
<tr>
<th>Eat more of these:</th>
<th>GOAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole grains</td>
<td>15%</td>
</tr>
<tr>
<td>Vegetables</td>
<td>69%</td>
</tr>
<tr>
<td>Fruits</td>
<td>62%</td>
</tr>
<tr>
<td>Dairy</td>
<td>52%</td>
</tr>
<tr>
<td>Seafood</td>
<td>52%</td>
</tr>
<tr>
<td>Oils</td>
<td>61%</td>
</tr>
<tr>
<td>Fiber</td>
<td>40%</td>
</tr>
<tr>
<td>Potassium</td>
<td>56%</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>28%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Eat less of these:</th>
<th>LIMIT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories from SoFAS*</td>
<td></td>
</tr>
<tr>
<td>Refined grains</td>
<td>110%</td>
</tr>
<tr>
<td>Sodium</td>
<td>149%</td>
</tr>
<tr>
<td>Saturated fat</td>
<td>300%</td>
</tr>
</tbody>
</table>

*SoFAS, solid fats and added sugars.


Percentage of major chronic diseases in the U.S. that is potentially preventable by diet and lifestyle modifications

Lung cancer: >80% preventable (non-smoking)

Willett, WC. Science 2002; 296, 695-698
Low Risk of Heart Disease:

1. Non-smoker
2. BMI < 25 kg/m²
3. Exercise ≥ ½ hr/day of brisk walking
4. Alcohol 5+g/day (≤ one drink in women; ≤ two drinks in men)
   One drink = 12 oz. beer (~5% alcohol), 5 oz. wine (~12% alcohol), 1.5 oz. liquor (~40% alcohol)
5. Good diet. Upper two quartiles (50%) of score based on:
   - low trans fat, high p/s ratio (polyunsaturated–to–saturated fat)
   - low glycemic load (whole vs. refined grains)
   - high fiber
   - high fish (omega-3s)
   - high fruit and vegetables

- Population Attributable Risk = 82% (95% CI = 58-93%)
- Proportion at low risk = 3.1%
How Do Typical American Diets Compare with Recommended Intake Levels or Limits?

**Usual Intake as a Percentage of Goal or Limit**

- Eat more of these:
  - Whole grains: 15%
  - Vegetables: 42%
  - Fruits: 52%
  - Dairy: 44%
  - Oils: 61%
  - Fiber: 40%
  - Potassium: 56%
  - Vitamin D: 28%
  - Calcium: 75%
- Eat less of these:
  - Calories from SfFAS*: 51%
  - Refined grains: 110%
  - Sodium: 149%
  - Saturated fat: 260%

*SoFAS, solid fats and added sugars.

**Standard American Diet (SAD): Energy-rich, nutrient-poor**

US Diet Not Improving

- The US population has made few dietary changes over time (2001–2004 to 2007–2010)
  - Fruit intake has remained low, but stable
  - Vegetable intake has declined, particularly among children of all ages, adolescents, and young adult males
    - Whole-grain intake has increased slightly, particularly among middle-aged and older adults
  - Dairy intake has been relatively constant over time, but has decreased for girls 4–8 years and young adult males, and has increased for adults 51–70 years


Slide courtesy of Elizabeth M. Ward, M.S., R.D.
Large Percentages of the U.S. Population have Micronutrient Inadequacies from their Diet

Results from the National Health and Nutrition Examination Survey (NHANES) 2003-2006: Usual Intakes from Food for U.S. Adults (≥19 Years)

Vitamin D “Insufficiency”: A World-wide Problem

Proportion of Population with 25(OH)D Status Below Recommended Levels (<20 ng/mL [<50 nmol/L]*)

*Institute of Medicine-defined level sufficient for bone health.

US Endocrine Society:
Deficient: ≤20 ng/mL (50 nmol/L)
Insufficient: 21-29 ng/mL (51-74 nmol/L)
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Shortfall Nutrients of Public Health Concern

Have been “linked in the scientific literature to adverse health outcomes”:

- **Calcium** Osteoporosis
- **Potassium** Hypertension and cardiovascular disease
- **Vitamin D** Skeletal health (growing body of evidence for role in preventing cancer, cardiovascular disease, and other chronic diseases; also: enhancing immune function)
- **Iron** Iron deficiency anemia (adolescent and pre-menopausal females)
- **Fiber** Colonic health, maintenance of proper laxation (role in preventing coronary heart disease, colorectal and other cancers, type 2 diabetes, and obesity)

Overconsumed Nutrients of Public Health Concern

- **Saturated fat**: Increased population risk of cardiovascular disease
- **Sodium**: Hypertension

“The SAD Brown Food Group”
Even the “Ideal Diet” Doesn’t Bridge All Nutrient Gaps

- Three food patterns were examined by DGA Committee:
  - The Healthy U.S.-style Pattern
  - The Healthy Mediterranean-style Pattern
  - The Healthy Vegetarian Pattern

- “For many nutrients, amounts of a nutrient in the patterns are well above the RDA”

- “In contrast, some nutrients are just above the RDA ... or marginally below [it]: calcium, iron, and magnesium.”

- “The nutrients for which adequacy goals are not met in almost all patterns are potassium, vitamin D, vitamin E, and choline.”

How to close Micronutrient Gaps?

1. DGA Committee: “Eat ideal diet and take a vitamin D supplement” (and vitamin E, potassium, choline; and possibly Ca, Mg, Fe)
2. Take a daily Multivitamin/Multimineral supplement with the RDA of most vitamins and minerals
Definition of a “Standard” Multivitamin/Multimineral (MVM)

- A dietary supplement that “is in compliance with all applicable government standards and provides at least two thirds [18] of the [27] essential vitamins and minerals at 100 percent of the daily value as determined by the Commissioner of Food and Drugs” (Older Americans Act; Congress, 2006)

### Supplement Facts

<table>
<thead>
<tr>
<th>Supplement</th>
<th>% Daily Value</th>
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<tbody>
<tr>
<td>Vitamin A 5,000 IU</td>
<td>100%</td>
</tr>
<tr>
<td>(as Beta Carotene)</td>
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<tr>
<td>Vitamin C 80 mg</td>
<td>100%</td>
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<tr>
<td>Vitamin D 400 IU</td>
<td>100%</td>
</tr>
<tr>
<td>Vitamin E 30 IU</td>
<td>100%</td>
</tr>
<tr>
<td>Vitamin K 25 mcg</td>
<td>33%</td>
</tr>
<tr>
<td>Thiamin (Vitamin B1) 1.2 mg</td>
<td>100%</td>
</tr>
<tr>
<td>Riboflavin (Vitamin B2) 1.7 mg</td>
<td>100%</td>
</tr>
<tr>
<td>Niacin 20 mg</td>
<td>100%</td>
</tr>
<tr>
<td>Vitamin B6 2 mg</td>
<td>100%</td>
</tr>
<tr>
<td>Folic Acid 400 mcg</td>
<td>100%</td>
</tr>
<tr>
<td>Vitamin B12 5 mcg</td>
<td>100%</td>
</tr>
<tr>
<td>Biotin 30 mcg</td>
<td>15%</td>
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<tr>
<td>Para-amino Acid 10 mg</td>
<td>100%</td>
</tr>
<tr>
<td>Calcium 150 mg</td>
<td>10%</td>
</tr>
<tr>
<td>Iron 18 mg</td>
<td>100%</td>
</tr>
<tr>
<td>Phosphorus 115 mg</td>
<td>11%</td>
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<tr>
<td>Iodine 150 mcg</td>
<td>100%</td>
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<tr>
<td>Magnesium 150 mg</td>
<td>25%</td>
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<tr>
<td>Zinc 15 mg</td>
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<tr>
<td>Selenium 20 mcg</td>
<td>29%</td>
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<tr>
<td>Copper 2 mg</td>
<td>100%</td>
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<tr>
<td>Manganese 5 mg</td>
<td>100%</td>
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<tr>
<td>Chromium 150 mcg</td>
<td>100%</td>
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<tr>
<td>Molybdenum 75 mcg</td>
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<tr>
<td>Chloride 27 mg</td>
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<tr>
<td>Potassium 80 mg</td>
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<tr>
<td>Boron 150 mcg</td>
<td>15%</td>
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<tr>
<td>Nickel 1 mcg</td>
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<tr>
<td>Silicon 2 mg</td>
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<tr>
<td>Tin 10 mcg</td>
<td>*</td>
</tr>
<tr>
<td>Vanadium 10 mcg</td>
<td>*</td>
</tr>
<tr>
<td>Iodine 250 mcg</td>
<td>*</td>
</tr>
</tbody>
</table>

* Daily Value (DV) not established

MVMs do not contain 100% of the DV (RDA) of Ca, Mg, and K; most provide less than the DV of vitamin K; they do not provide choline.
MVMM Effectively and Safely Close Most Dietary Micronutrient Gaps

N = 20 adults; 3-day food diaries; “Food Processor” (USDA National Nutrient Database)

**Group Analysis - No Supplements**

- Not meeting RDA: 15 of 27 Micronutrients
- Exceeding UL: Sodium

**Group Analysis - With Multi-Vitamin/mineral**

- Effective
- Safe
- Not meeting RDA: 3 of 27 Micronutrients (Vitamin K, Ca, K)
- Not exceeding UL of any Micronutrient (except Sodium)
Risk of Inadequacy vs. Adverse Effects

- The Recommended Dietary Allowance (RDA) is the intake at which the risk of inadequacy is very small—0.02 to 0.03 (2 to 3%).
- At intakes between the RDA and the Tolerable Upper Intake Level (UL), the risks of inadequacy and of excess are both close to 0.
- At intakes above the UL, the risk of adverse effects may increase.

Physicians’ Health Study II (PHS II)

- Large, randomized, double-blind, placebo-controlled, long-term trial (the “gold standard”)
- Evaluated the role of a standard MVM supplement in the primary prevention of:
  - Cancer
  - Cardiovascular disease (CVD)
  - Age-related eye diseases
  - Cognitive functioning

**Physicians’ Health Study II: MVM vs placebo**

**Total Cancer Incidence**

- Significant 8% reduction in total cancer incidence (HR: 0.92; 95% CI: 0.86–0.998; P=0.04)
- 12% reduction excluding prostate cancer
- 27% reduction for men with a baseline history of cancer (HR: 0.73; 95% CI: 0.56–0.96; P=0.02)
- Newly diagnosed cancer cases in US each year: 1.67M
  - 8% = 133,000 cases
  - 12% = 200,000 cases

**Physicians’ Health Study II: MVM vs placebo**

**Total Cataract Incidence**

- Primary endpoint
  - 1,817 confirmed cases of cataract
- 9% reduction in total cataract (HR: 0.91; 95% CI: 0.83–0.99; P=0.04)
- Prespecified secondary endpoint
  - 1,337 cataract extractions
  - 11% reduction in cataract surgery (HR: 0.89; 95% CI: 0.80–0.99; P=0.04)
  - Annual Medicare expenditure: $3.4B
  - 11% = $374M

**Notes:**

- CI=confidence interval; HR=hazard ratio. N=14,641 male US physicians initially 50 years or older, mean follow up 11.2 years
PHS II Findings: No Increase or Decrease in Incidence of Major Cardiovascular Events

**Primary Endpoint**

- Men taking MVM had no reduction in CV events (HR: 1.01; 95% CI, 0.91–1.10; \( P=.91 \))
- Rates of major CV events per 1,000 person-years were MVM, 11.0 and placebo, 10.8


PHS II Findings: No Significant Difference in Global Cognition Scores

- Age-related cognitive decline was assessed using a validated test of cognitive function in a substudy from PHS II (N=5,947)
- Included men ≥65 years (mean age at baseline, 72 y)
- No difference found in cognitive decline from initial to final assessment (average 8.5 years) for men taking MVM vs placebo

Three “tiers” of micronutrient health effects

1. Prevention and treatment of deficiency diseases (<RDA): developing world (Fe, I, Zn, vitamin A)
2. Prevention and treatment of nutritional gaps-micronutrient inadequacies (RDA): developed world (vitamins A, C, D, E, K; Ca, Mg, K)
3. Prevention of age-related chronic diseases (long-term maintenance of RDA) (multivitamin/mineral)

Summary and Conclusions (cont’d)

A daily “standard” (life-stage and gender-specific) MVM supplement is an effective and safe means of filling most micronutrient gaps in Western diets (energy-rich, nutrient-poor)

- Possible exceptions: Vitamin K; K, Ca, Mg
- Supports normal physiological and metabolic functions and, hence, good health
- PHS II showed that MVM supplementation lowers incidence of cancer and cataract
MVMs are supplements, not substitutes

Thank you for your attention!