

# *Life in the Margins: The Health Impact of Nutrient Insufficiency*



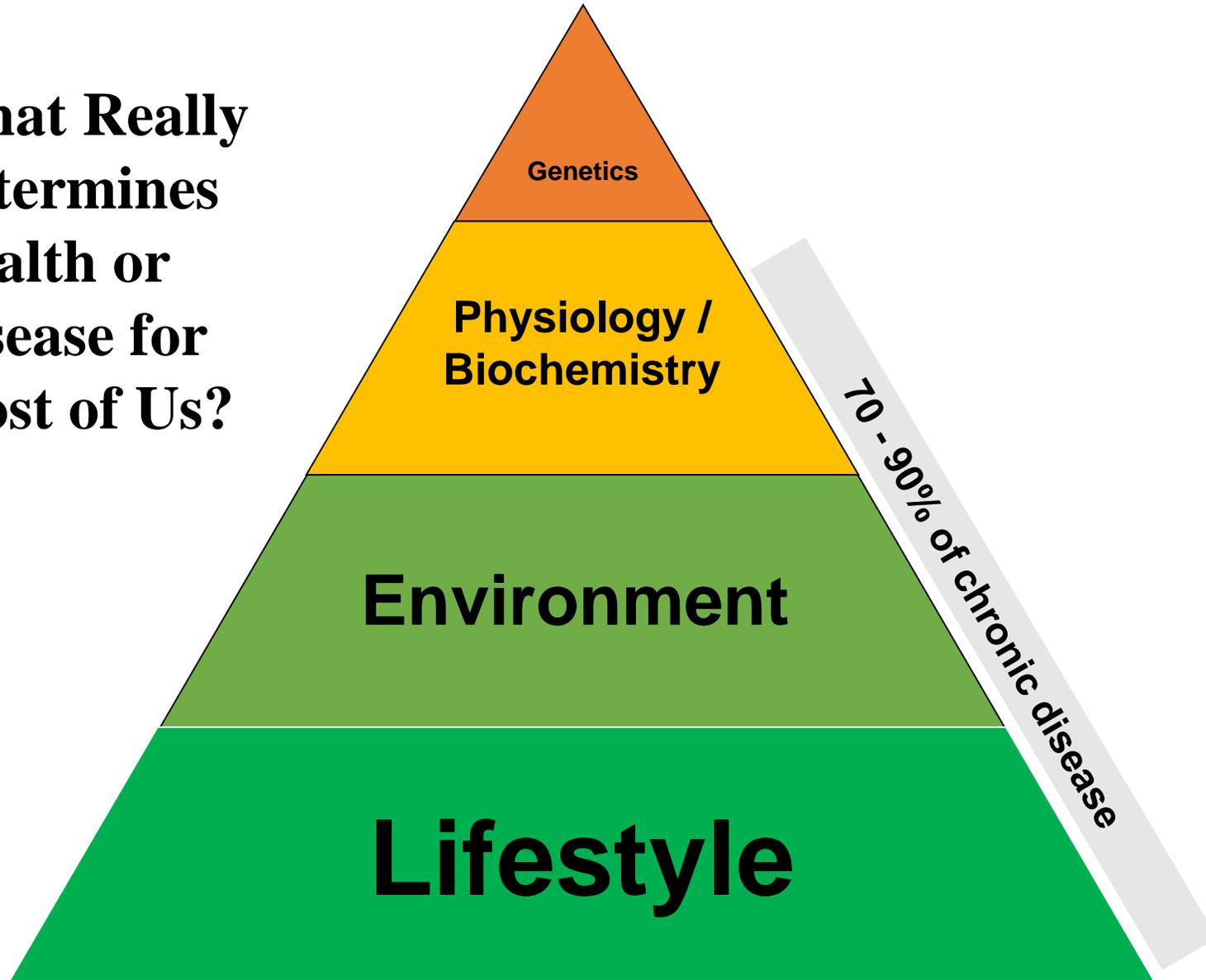
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Chair: US Pharmacopeia  
Dietary Supplements  
Admissions Joint Standard  
Setting Sub-Committee



*Vieraona Low Dog, M.D.*

**What Really  
Determines  
Health or  
Disease for  
Most of Us?**





"THE FOOD YOU EAT  
CAN BE EITHER  
THE SAFEST  
&  
MOST POWERFUL  
FORM OF MEDICINE  
*or*  
THE SLOWEST  
FORM OF POISON."

# Less Than *Optimal* Nutrient Levels

- Dietary deficiencies are well documented, and they have characteristic signs and symptoms.
- BUT recent findings have determined that *less than optimal* biochemical levels have been associated with risks of adverse health effects. Including **cardiovascular disease, stroke, impaired cognitive function, cancer, eye diseases, poor bone health, depression,** and other conditions.

*CDC: 2<sup>nd</sup> National Report on Biochemical Indicators of Diet and Nutrition in the U.S. Population*

# Who is at Risk?

- Obese individuals
- Ethnic/racial minorities
- Those with chronic disease
- Chronic medication use
- Families with food insecurity
- Those on restricted or poor diets
- Elders



# *Real State of American Nutrition*

- **90 million** Americans are **vitamin D deficient** (using Endocrine Society guidelines defining deficiency as  $<20\text{ng/ml}$  or  $50\text{ nmol/L}$ )
- **30 million** are deficient in **vitamin B6** (PLP  $< 20\text{nmol/L}$ )
  - **Women** twice as likely to be deficient as men and deficiency rates for **blacks** (15.7%) are higher than for whites (10.7%).
- **18 million** people have **B12 deficiency** (MMA  $>271\text{ nm/L}$ )
  - More common in those over 50 years of age
- **~16 million** are **deficient in vitamin C**
- **13% of Latinas and 16% of African American women** (ages 12-49) and **8% of white women** are **iron deficient**
- Women ages 25-39 overall have **borderline iodine insufficiency**



*CDC: 2<sup>nd</sup> National Report on the Biochemical Indicators of Diet and Nutrition in the U.S. population*

# Nutritional Needs Change As We Age

- Change in body composition
  - Energy requirements
  - Sarcopenia
  - Osteopenia
- Change in energy expenditure
- Disease related alterations
  - Immune disorders
  - Inflammation
  - Metabolic disorders
  - Malignant diseases
  - Cardiovascular Diseases

# Vitamin B12

- Found in animal and fortified foods.
- Risk for deficiency: **inadequate intake, impaired absorption, vegan, medications (e.g. metformin), obesity, elders, alcoholism**
- Deficiency: **numbness/tingling hands and/or feet, difficulty walking, memory loss, disorientation, depressed mood.**
  - Note: **25% of cases of B12 deficiency present with these symptoms and no megaloblastic anemia.**
- **Atrophic gastritis affects 10%-30% of people over 60 years of age causing malabsorption of food bound vitamin B12.**

Zdilla MJ. *Clin Diabetes* 2015; 33(2):90-5

# Metformin and B12

- 29 studies (8,089 patients); 19 studies rated intermediate or high quality.
  - **Metformin was significantly associated with an increased incidence of B12 deficiency** and reduced serum B12 levels.
- Combination of **metformin and proton pump inhibitors** create a polypharmacy recipe for B12 deficiency.
- **B12-deficient patients have 2.4 times higher chance of depression and 1.79 point lower cognitive performance score.**
- Routine screening is recommended in elders and/or if on long-term metformin.

Niafar M, et al. *Intern Emerg Med* 2015; 10(1):93-102.

Biemans E, et al. *Acta Diabetol* 2015; 52(2):383-93.

Zdilla MJ. *Clin Diabetes* 2015; 33(2):90-5



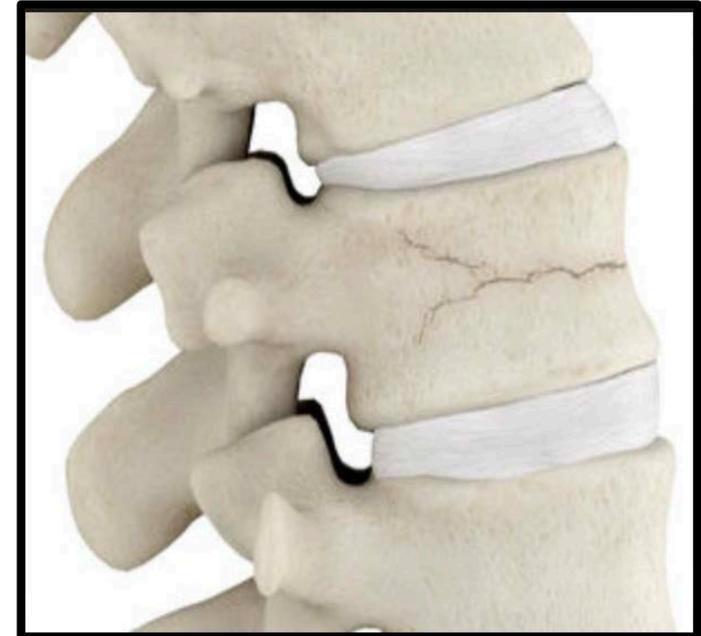
# Endocrine Society Clinical Practice Guidelines for Vitamin D

- Serum 25(OH)D level used to evaluate high-risk folks
  - **Insufficiency defined as 21-29 ng/mL**
  - **Deficiency defined as <20 ng/mL**
- Maximum tolerable limits for vitamin D (*without supervision*):
  - 1,000 IU/day for infants to age 6 months
  - 1,500 IU/day for ages 6 months to 1 year
  - 2,500 IU/day ages 1 to 3 years
  - 3,000 IU/day for ages 4 to 8 years
  - 4,000 IU/day anyone older than 8 years

Holick MF, et al. *J Clin Endocrinol Metab* 2011; 96(7):1911-30

# Drug Induced Osteoporosis

- **Glucocorticoids** (steroids) – 1:5 cases of osteoporosis
- **Aromatase inhibitors** (breast cancer)
- **Anti-androgen** therapy (prostate cancer)
- **Proton pump inhibitors** (heartburn) – principally in those taking > 1 year (OR 4.55 for fracture if taking 7 or more years)
- **Antiretroviral drugs** (HIV, hepatitis)
- **SSRIs** (antidepressants) and **antipsychotics**
- **Antiepileptic drugs** (epilepsy, migraines, chronic pain, neuropathy)
- **Loop diuretics** (e.g. lasix)
- **Heparin and oral anticoagulants**



Mazziotti G, et al. *Am J Med* 2010; 123:877-84

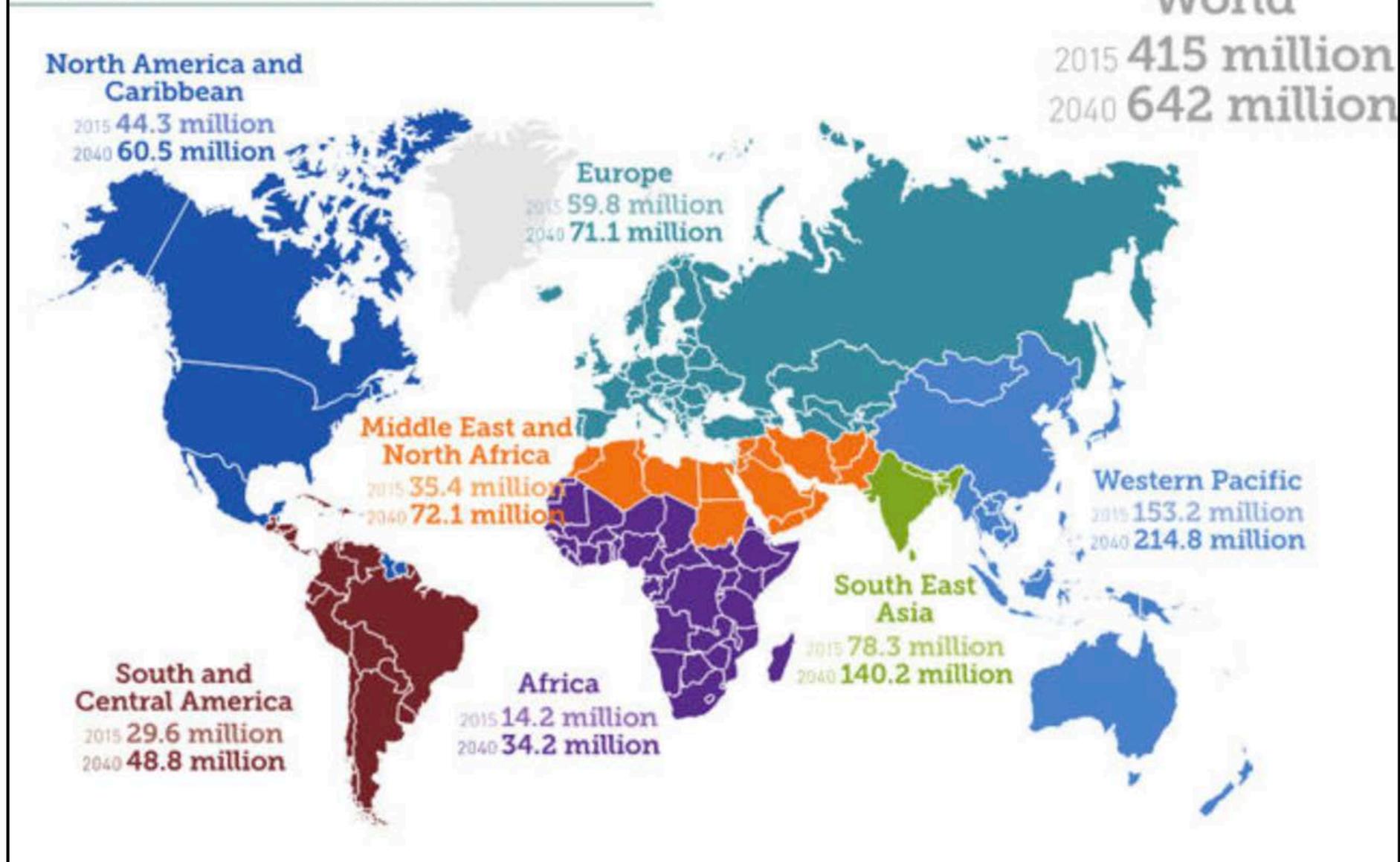
# Magnesium Status

- Low magnesium intakes and serum levels associated with type 2 diabetes, metabolic syndrome, inflammation, high blood pressure, atherosclerotic vascular disease, sudden cardiac death, osteoporosis, migraine headache, asthma, and colon cancer.
- Canadian Health Measures Survey (2012-2013), study of serum magnesium concentrations (ages 3-79) **9.5–16.6% of adults and 15.8–21.8% of adolescents aged 12–19 years had a serum Mg concentration below lower reference cut-off**, raising strong suspicions of significant Mg deficiency in Canadian population. **Diabetes was a strong predictor of lower magnesium levels.**
- FDA requires warning that **proton pump inhibitors can cause dangerously low magnesium levels**. Many **diuretics** used to treat hypertension cause magnesium loss (as well as potassium and often zinc).



Rosanoff A, et al. *Nutr Rev* 2010;70(3):153-64  
Bertinato J, et al. *Nutrients* 2017 Mar; 9(3): 296

Estimated number of people with diabetes worldwide and per region in 2015 and 2040 (20-79 years)



# Magnesium: Heart and Diabetes



- 2013 meta-analysis that included 16 studies and more than 313,000 participants found:
  - Higher blood levels of magnesium (per 0.2 mmol/L increment): **30% lower risk of CVD.**
  - Dietary magnesium (per 200-mg/d increment): **22% lower risk fatal ischemic heart disease.**
- For patients with type 2 DM, **low magnesium leads to more rapid disease progression and increased risk for diabetes complications.**
- **Magnesium supplementation for patients with T2DM improves glucose metabolism and insulin sensitivity.**

Del Gobbo LC, et al. *American Journal of Clinical Nutrition* 2013; 98(1):160-73.

Hruby A, et al. *Diabetes Care* 2014; 37(2):419-27

Gommers LM, et al. *Diabetes* 2016; 65(1):3-13

# Each of Below = ~400 mg Magnesium

- 115 almonds, whole
- 2.5 cups boiled spinach
- 6.5 cups soymilk
- 15 slices whole wheat bread
- 3.5 cups cooked black beans
- 4.7 cups cooked brown rice
- 9 cups raw, cubed avocado OR
- 3 cups pumpkin seeds



# Marine Omega 3 Fatty Acids



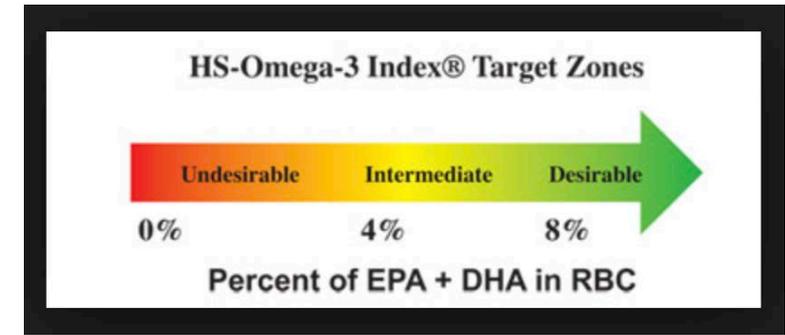
- DHA and EPA involved in modulation of neuroinflammation and cognitive decline.
- Epidemiological studies find frequent consumption of fatty fish protective against cognitive decline. In Okinawa, **higher serum EPA and DHA + EPA** levels independently associated with better scores on **global cognitive function** among the oldest old (mean age 84 years), free from dementia.”
- Prospective cohort study 6501 women (65-80 yrs) in **Women's Health Initiative Memory Study** (enrollment began 1996), after median of 14.9 years of follow-up, 1851 women (28.5%) had died. **RBC levels of EPA and DHA higher in survivors** ( $P < .002$  for each). No significant associations of alpha-linolenic acid, arachidonic acid or linoleic acid with total mortality.

Devassy JG, et al, *Adv Nutr* 2016 Sep 15;7(5):905-16

Nishihira J, et al. *J Alzheimers Dis* 2016; ;51(3):857-66.

Harris WS, et al. *J Clin Lipidol* 2017; Jan - Feb;11(1):250-259.e5.

# Marine Omega 3

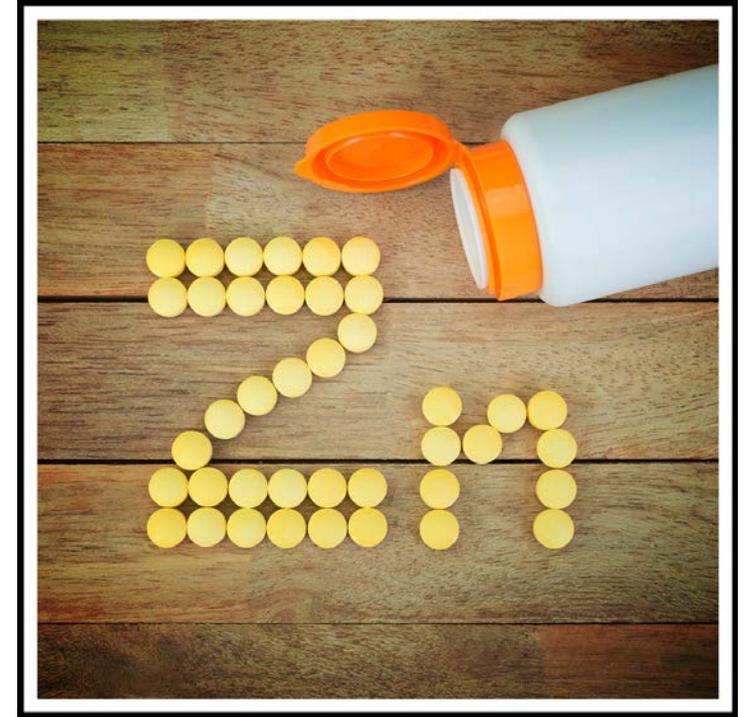


- Studies should use **blood analysis pre- and post-supplementation** to ensure adequate omega 3 levels and difference with control group.
- **Omega-3 fish oil supplements** prescribed by a healthcare provider may help **prevent death from heart disease** in patients who recently had a **heart attack** and may **prevent death and hospitalizations in patients with heart failure.**”

Siscovick DS, et al. Omega-3 Polyunsaturated Fatty Acid (Fish Oil) Supplementation and the Prevention of Clinical Cardiovascular Disease: A Science Advisory From the American Heart Association. *Circulation* 2017; Apr 11;135(15):e867-e884

# Zinc and Taste

- Zinc vitally important for **immune health, as well as vision and taste.**
- Many elders have altered smell and taste, which influences appetite.
- Many elders have marginal zinc status.
- A review of clinical trials found **“moderate quality evidence that zinc supplements improve overall taste improvement in patients with zinc deficiency or idiopathic taste disorders.”**



Nagraj SK, et al. *Cochrane Database Syst Rev* 2014; 2014 Nov 26;11:CD010470.

# Position on Nutrient Supplementation by the Academy of Nutrition and Dietetics

- Among the groups most vulnerable to inadequacy of one or more nutrients are:
  - **Older** adults
  - **Pregnant** women
  - People who are **food insecure**
  - **Alcohol** dependent individuals
  - **Strict vegetarians and vegans**
  - Those with increased needs due to a **health condition** or the **chronic use of a medication** that decrease nutrient absorption or increase metabolism or excretion
- Nutrient supplementation can be used to help meet a nutrient requirement for those:
  - **Restricting energy intake** for weight loss/control
  - Not consuming an adequate amount of food to meet energy requirements as a result of **poor appetite or illness**
  - **Eliminating one or more food groups** from their diet on a regular basis
  - Consuming a diet **low in nutrient rich foods** despite adequate or excessive energy intakes.

Marra and Boyar. *J Am Diet Assoc* 2009

# Vitamin and Mineral Deficiency: A Global Progress Report

“The control of vitamin and mineral deficiencies is one of the most extraordinary development-related scientific advances of recent years. Probably **no other technology available today offers as large an opportunity to improve lives and accelerate development at such a low cost and in such a short time.**”

*The World Bank*

[www.unicef.org/media/files/vmd.pdf](http://www.unicef.org/media/files/vmd.pdf)

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