From Disease to Wellness and the Rise of Personalized Medicine and Health



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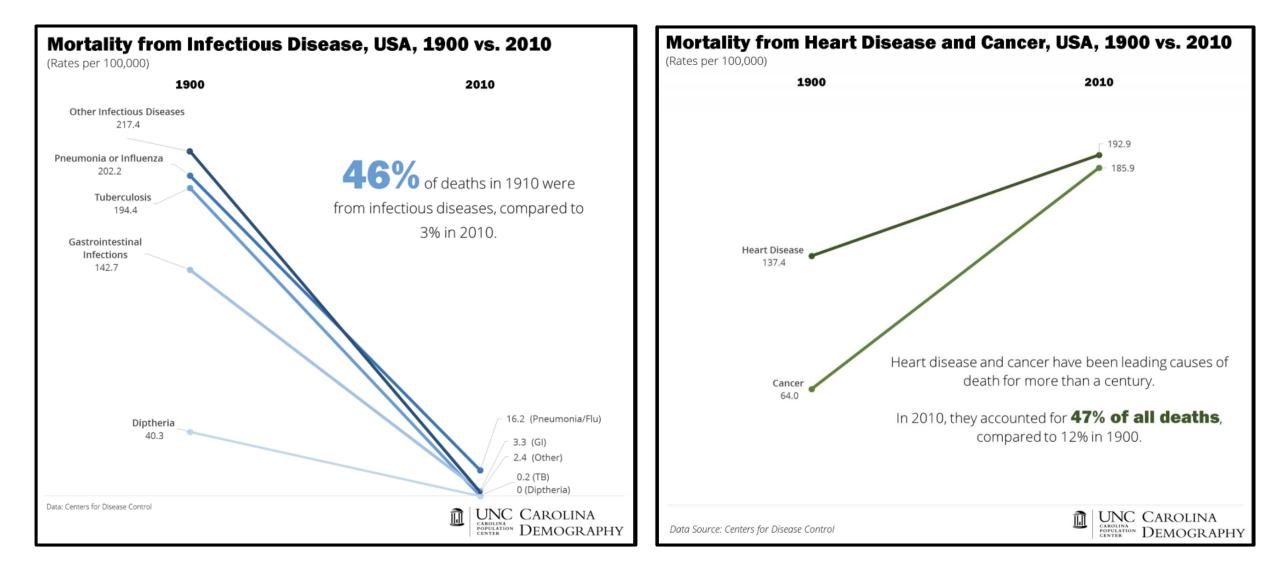
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Disease	Baseline 20 th Century Annual Morbidity	Year Vaccine Developed	1998 Provisional Morbidity	% Decrease
Smallpox	48,164	1798	0	100%
Diphtheria	175,885	1923	1	100%
Pertussis	147,271	1926	6279	95.7%
Tetanus	1,314	1927	34	97.4%
Poliomyelitis	16,316	1955	0	100%
Measles	503,282	1963	89	100%
Mumps	152,209	1967	606	99.6%
Rubella	47,745	1969	345	99.4%
Haemophilus influenza B	20,000	1985	54	99.7%

https://www.cdc.gov/mmwr/preview/mmwrhtml/00056803.htm#00003753.htm



The Times They Are A-Changing



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Modern Biomedicine

- Acute care is what drove medicine in the 20th century.
- Infectious disease and injuries dominated the landscape.
- Inevitably, this reinforced the view that being healthy meant not being sick.
- If you don't feel good, we look for a physical cause for your symptoms.
- We also assume that most everyone will present the same way and can be treated the same way. While this works well for appendicitis, collapsed lung, acute myocardial infarction in a man, it is woefully inadequate for the prevention and management of chronic disease.
- And it doesn't even begin to address the concept of *health promotion, a* process of enabling people to increase control over, and to improve, their health

Food is Foundational

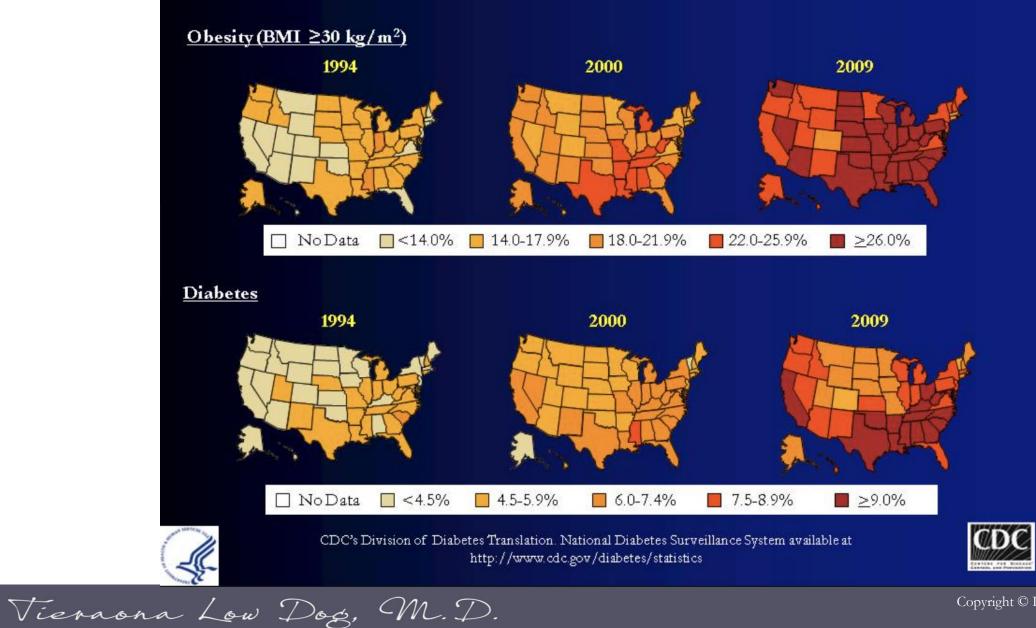


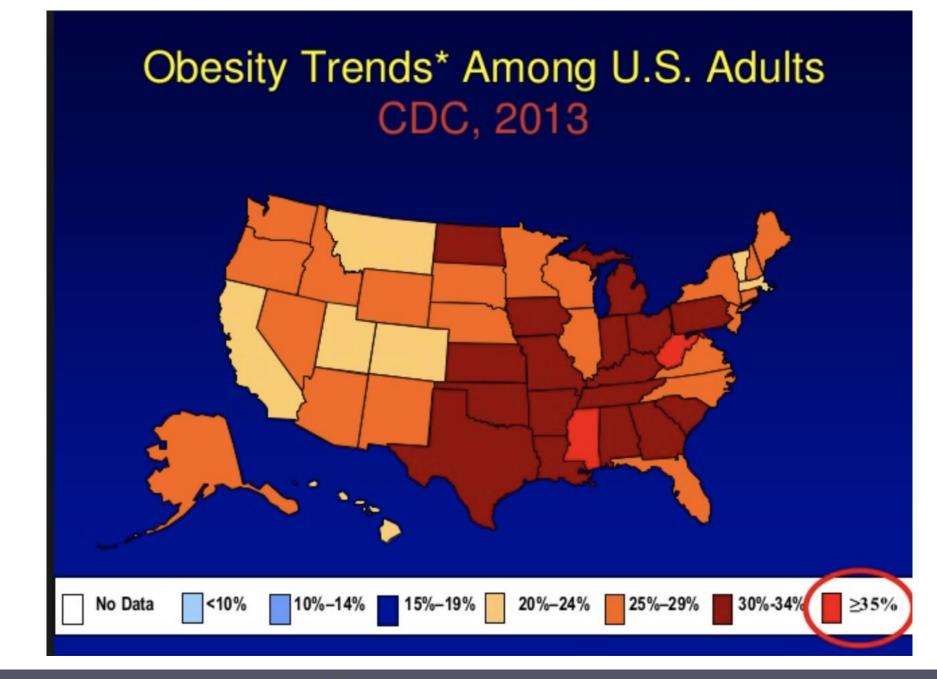
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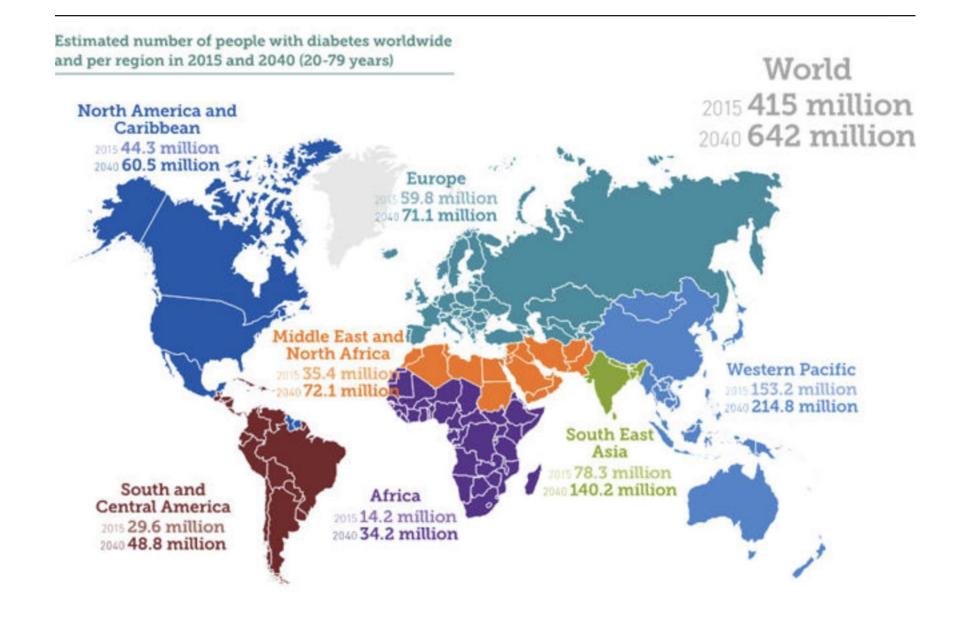
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Age-adjusted Percentage of U.S. Adults Who Were Obese or Who Had Diagnosed Diabetes

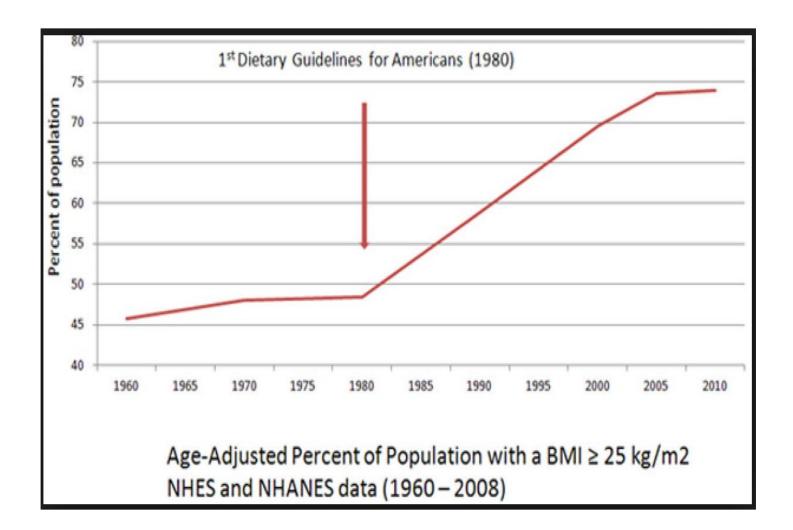




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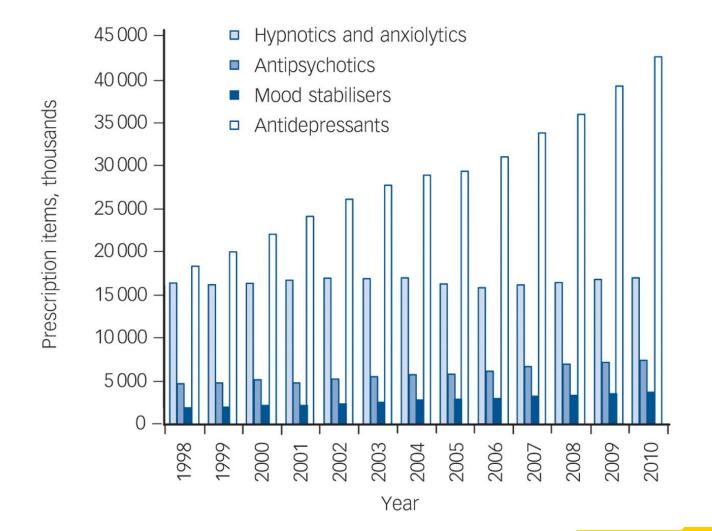








Trends in prescriptions of major classes of psychiatric drugs 1998–2010.



Stephen Ilyas, and Joanna Moncrieff BJP 2012;200:393-398



©2012 by The Royal College of Psychiatrists

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- According to CDC, 11% of Americans 12 and older take anti-depressant medications:
 - 400% increase from the 1980s, ~270 million prescriptions per year.
- 1 in 4 women 40-60 years take anti-depressants.
- Prevalence anxiety disorders ages 9 17 is 13%.
- 1 in 8 adolescents suffer from depression.





Effectiveness Questioned



- The magnitude of benefit for antidepressant medication compared with placebo may be *minimal or nonexistent*, on average, in patients with mild or moderate symptoms.
- For patients with very *severe depression*, the *benefit of medications over placebo is substantial*.

Fournier, et al. JAMA. 2010;303(1):47-53.

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Endocrine Society Second Scientific Statement

- EDCs contribute to outcomes related to impaired reproduction, neurodevelopment, thyroid function, metabolism, and increased propensity for hormone-sensitive cancers.
- Unfortunately, it is difficult to directly relate chronic disease burden to exposures in humans. The increased prevalence of such diseases underscores the need to invoke precaution in introducing new (and usually untested) chemicals into the environment.

Gore AC, et al. Endocr Rev 2015; 36(6):E1-E150.



Insecticides and Cancer

- Meta-analysis of 16 studies found childhood exposure to indoor residential insecticides associated with a significant increased risk of childhood leukemia and lymphomas.
- Positive but not statistically significant association also found for childhood brain tumors.



Chen M, et al. Pediatrics 2015; 136(4):719-29.



"The lesson from both our agricultural and medical experience is remarkable for its consistency: Ignoring the evolutionary attributes of biological systems can only be done at the peril of ecological catastrophe."

Marc Lappe, When Antibiotics Fail



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Personalized Diets

• Personalized diets based on an individual's genome to optimize the success of dietary intervention and reduce genetic cardiovascular disease (CVD) risk, (or to prevent/treat cancer is one of the challenges most frequently discussed in the scientific community.

Corella D, et al. Utilizing nutritional genomics to tailor diets for the prevention of cardiovascular disease: a guide for upcoming studies and implementations. Expert Rev Mol Diagn 2017 May;17(5):495-513.



Obesity and Insulin Growth Factors

- Obesity is associated with multiple factors that may cause an increased risk for cancer and cancer-related mortality including insulin resistance, high blood sugar and insulin-growth factors (IGF).
- Elevated insulin increases tumor growth and aggressiveness.
- IGF-1 and IGF-2 have been identified as tumor promoters in multiple studies.

Belardi V, et al. J Mammary Gland Biol Neoplasia 2013; 18(3-4



Cancer Cells Love Glucose

- Tumor cells have a remarkable up regulation of glucose transporter molecules on their surface. In addition, there is a frequent over expression of several key enzymes of glycolysis and attached pathway.
- This has sparked a great deal of interest in low carb, high fat diets, such as the ketogenic diet. While promising, there is still a dearth of clinical trials upon which to base recommendations and the studies that do exist yield conflicting results.
- It may be that some tumor types would be responsive to a ketogenic diet, while with others is might not be as beneficial.

Oliviera CL, et al. J Acad Nutr Diet. 2017 Mar 30.



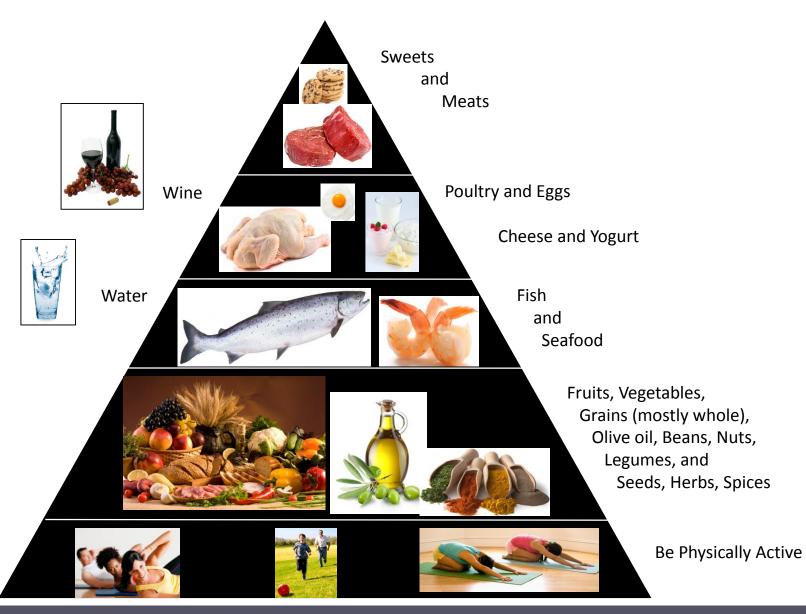
Breast Cancer and Low Carb Diet

- The Women's Healthy Eating and Living (WHEL) trial found that carbohydrate restriction was associated with a striking five-fold reduction in breast cancer recurrence in 50% of subjects, specifically those whose tumors expressed the IGF-1 receptor.
- Women who did not have this same tumor type did not see benefit.
- Unfortunately, IGF-1 testing of tumors is not yet a routine clinical practice.

Edmond JA, et al. Cancer Epidemiol, Biomarkers Prev 2014; DOI: 10.1158/1055-9965



FOR NOW



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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

Marra and Boyar. J Am Diet Assoc 2009



Position on Nutrient Supplementation by the Academy of Nutrition and Dietetics

- 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



State of Our Nutrition

- 90 million Americans are vitamin D deficient
- 30 million are deficient in vitamin B6
- 18 million people have B12 deficiency
- ~16 million have low serum vitamin C
- 13% of Latinas and 16% of African American black women (ages 12-49) are iron deficient
- Women 25-39 borderline iodine insufficiency
- 50% Americans don't meet RDI for magnesium



CDC: 2nd National Report on the Biochemical Indicators of Diet and Nutrition in the U.S. population

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Magnesium

- 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.
- 50% of U.S. population consumes less than the required amount of daily magnesium.
- FDA requires warning that proton pump inhibitors can cause dangerously low magnesium levels.

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Rosanoff A, et al. Nutr Rev 2010;70(3):153-64

Magnesium and Diabetes



- Study found that highest intake reduced development of metabolic impairment by 37% and T2DM by 32%, compared with the lowest.
- Patients with hypomagnesemia show more rapid disease progression and increased risk for diabetes complications.
- Clinical studies demonstrate that T2DM patients with hypomagnesemia have reduced pancreatic β-cell activity and are more insulin resistant.
- Magnesium supplementation for patients with T2DM improves glucose metabolism and insulin sensitivity.

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

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



Magnesium and Heart Disease



- 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) were associated with a 30% lower risk of CVD.
 - Dietary magnesium (per 200-mg/d increment) associated with a 22% lower risk of fatal ischemic heart disease.
- Few clinicians check RBC magnesium, deficiency is likely far greater than we know.

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



Thiamin and Diabetes

- Altered glucose metabolism associated with lower thiamin levels in diabetics, which in turn exacerbates hyperglycemia. Studies show that diabetics often are thiamin deficient.
- Simple sugars lack thiamin and metabolism of high sugar foods requires high amounts of thiamin and may accelerate its depletion.
- Magnesium deficiency increases risk of thiamin deficiency (need to make active form of thiamin (thiamin pyrophosphate)
- Studies suggest thiamin supplementation may improve/slow/prevent microvascular complications of diabetes.

Nix WA, et al. Diabetes Res Clin Pract 2015; 107(1):157-65.

Alaei-Shahmiri F, et al. Diabetes Metab Syndr 2015; 9(4):213-7.

Al Attas O, et al. Clin Med Insights Endocrinol Diabetes 2014; 7:1-6.



Thiamin: Marginal Deficiency

- Studies suggest a myriad of vague signs and symptoms, including mental fatigue and emotional lability, generalized weakness, myalgias, back pain, abdominal discomfort, poor memory, precordial pain, and a decreased ability to perform physical activity or work can occur with marginal thiamin levels.
- Virtually NO clinician checks thiamin levels, though deficiency is well-documented in those who are obese and in diabetes.

Kerns JC, et al. Adv Nutr 2015; 6(2): 147–153



Vitamin C

- Potent antioxidant, activates folate, needed to convert tryptophan to serotonin, cofactor in synthesis of carnitine, thyroxin, norepinephrine, dopamine and immune cells
- Vitamin C levels decline rapidly during periods of emotional and physical strain, and illness.
- As levels fall, collagen synthesis impaired: bruise more easily, skin becomes thick and dry, wounds take longer to heal, joints hurt, fatigue.
- Clinicians do NOT check vitamin C levels.

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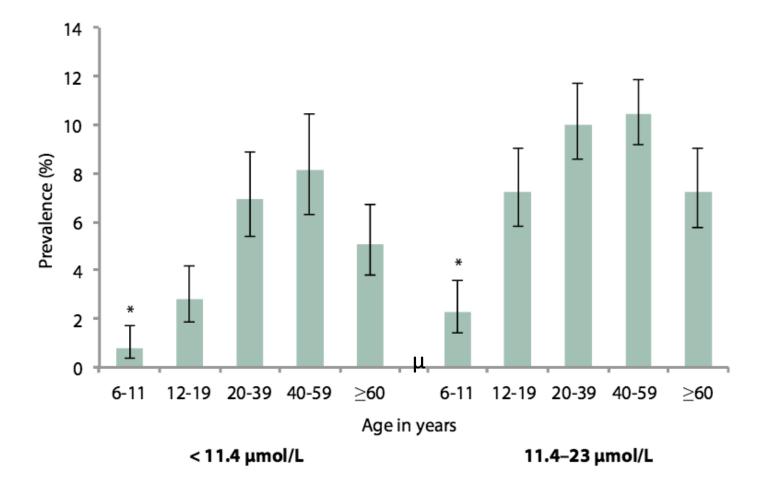


Figure H.1.f. Prevalence estimates of vitamin C deficiency (serum concentrations less than 11.4 μ mol/L) and low vitamin C concentrations (11.4-23 μ mol/L) in the U.S. population aged 6 years and older by age group, National Health & Nutrition Examination Survey, 2003-2006.

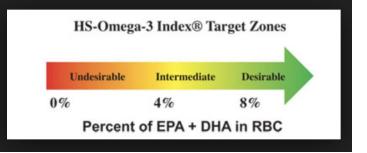
Error bars represent 95% of confidence intervals. *Prevalence in children is significantly lower than prevalence in persons 20 years and older (p <0.05).



American Heart Association

- "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."
- There was insufficient evidence to evaluate the role of fish oil supplements in primary prevention of CVD.
- Do YOU know your "O?"

Siscovick DS, et al. Circulation 2017; Mar 13.





Canadians and Omega 3

- The Omega-3 Index indicates the percentage of EPA+DHA in red blood cell fatty acids.
- Canadian government found that the mean Omega-3 Index level of Canadians aged 20-79 was 4.5%.
 - Levels higher for women, older adults, Asians and other non-white Canadians, omega-3 supplement users, and fish consumers; levels lower for smokers and people who were obese.
- Fewer than 3% of adults had levels associated with low CHD risk; 43% had levels associated with high risk.

Langlois K, et al. Health Rep 2015; Nov 18;26(11):3-11



Omega 3 and Asthma

- Reduced intake of omega-3 fatty acids may be a contributing factor to the increasing prevalence of wheezing disorders.
- Reviewers found that supplementation with omega-3 fatty acids in the third trimester of pregnancy *reduced the absolute risk of persistent wheeze or asthma and infections of the lower respiratory tract in offspring by approximately 33%.*

Bisgaard H, et al. N Engl J Med 2016; Dec 29;375(26):2530-9



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



Precision Medicine

Precision medicine that incorporates epigenetic analysis is a potentially powerful approach for evaluating the influence of environmental and lifestyle modifications on the heritability of hypertension and for personalizing patient care.

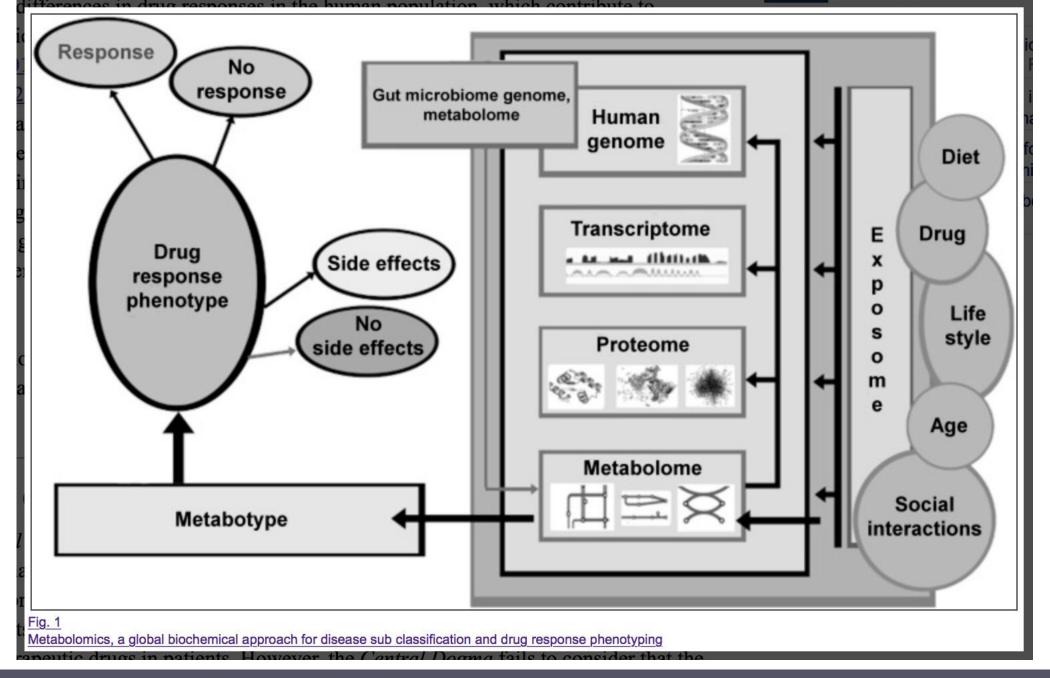
Clinical translation will require convergence, coordination, and integration among multidisciplinary teams with expertise in laboratory, clinical, and population-based research, as well as computational and modeling methods."

Kotchen TA, et al. Ushering hypertension into a new era of precision medicine. JAMA 2016; 315(4):343-44



Precision Medicine Initiative

- In 2016, the White House announced the precision medicine initiative (PMI) in the USA to help enable a new era of individualized care through cooperative efforts by researchers, providers, and patients
- A series of ground breaking studies supported by National Institute of Health (NIH) through the Pharmacometabolomics Research Network and its partnership with the Pharmacogenomics Research Network illustrate how a patient's metabotype at baseline, prior to treatment, during treatment, and post-treatment, can inform about treatment outcomes and variations in responsiveness to drugs (e.g., statins, antidepressants, antihypertensives and antiplatelet therapies).



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Patient: Doctor, I don't feel well and I'm not sure why.



Doctor: I want you to meditate for 20 minutes, twice a day, exercise for at least 30 minutes a day, avoid processed foods, eat plenty of organic fruit and veg, spend more time in nature and less indoors, stop worrying about things you can't control and ditch your T.V. Come back in 3 weeks.

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