Optimal Aging: Strategies for Life



Tieraona Low Dog, M.D.

Author of National Geographic's "Fortify Your Life" "Healthy At Home" and "Life Is Your Best Medicine"

www.DrLowDog.com

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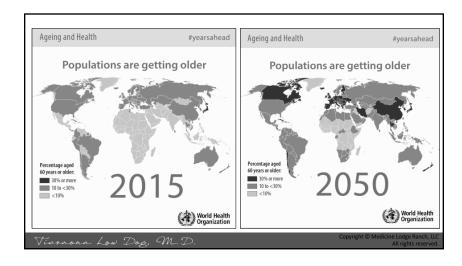
Reflection

- What if someone could predict with 90% accuracy how long you will live?
- Would you want to know?
- How would it affect the way you live?
- What if you planned to live to 50, 75, or 100?
- Would it change the way you...
 - work and play?
 - manage your money?
 - spend time with your family?



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When Does "Late Life" Begin?



- Studies have defined older populations in different ways: some as 65 and older, others at 60, and some at 50.
- Consensus seems to be growing:
 - Young-old: 65-70 years
 - Old-old: 80-99 years
 - Oldest-old: centenarians

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Life Span and Expectancy

- <u>Life Span</u>: the maximum number of years an individual can live; has remained between 120–125 years
- <u>Life Expectancy</u>: the number of years that the average person born in a particular year will probably live
 - Between 1975 and 2015, life expectancy at birth increased from 72.6 to 78.8 years for the total U.S. population.
 - Men 76.3 years
 - Women 81.2 years

www.cdc.gov/nchs/data/hus/hus16.pdf#015

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The Oldest of the Old



- In 1997, oldest person to have ever lived died at age 122 years and 164 days. Jeanne Louise Calment lived in France, took up fencing at age 85, and still rode a bicycle at 100.
- She was from a family of long-lived persons: her father died at age 93, her mother at 86, and her brother at age 97.
- She quit smoking when she was 117, reportedly because she was nearly blind and felt embarrassed asking for a light.
- Jeanne Calment as an example of "optimal aging."

 www.managedhealthcareconnect.com/article/7994

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What is "Optimal" Aging?



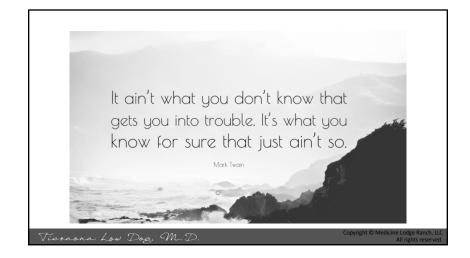
"The capacity to function across many domains—physical, functional, cognitive, emotional, social and spiritual—to one's satisfaction and in spite of one's medical conditions."

To live a life that is meaningful, fulfilling, and relatively independent.

Brummel-Smith K, Optimal Aging, Part I: Demographics and Definitions, *Annals of Long-Term Care*, 2007; 15: 26 – 28

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Changes....

- As we grow older we become less responsive to insulin, a hormone that regulates blood sugar. Approximately 50% of Americans ≥65 years have diabetes or insulin
- We also begin to store fat in strange places, such as within our muscle or liver cells rather than within fat cells where it is intended to be stored.
- Our mitochondria, the organelles that generate essential chemical energy, begin to fail
 at their jobs. All of these metabolic abnormalities are considered hallmarks of aging.
- However, this dogma is now being called into question: Are these metabolic derangements truly inevitable consequences of age, or do they simply reflect altered lifestyle with aging?

Lanza IR, et al. Aging metabolism: Evitable or inevitable? Science Translational Medicine 03 Feb 2016: 8 (324): 324ec19

Epigenetics



- The mapping of human genome was one of the greatest scientific undertakings of past century, detailing with incredible accuracy the blueprint of our species.
- It also paved the way for field of epigenetics, which has shown that when it comes to our genes, *nurture* is inextricably linked with *nature*.
- That it is the way we live our lives from the moment of conception to our last breath that influences the expression of our genes.



SCIENTIFIC AMERICAN.

PUBLIC HEALTH

The Hunger Gains: Extreme **Calorie-Restriction Diet Shows Anti-Aging Results**

A new study shows five days of hunger a month may reduce risk factors for aging and age-related diseases

Caloric Restriction?



Canto is 27 year old monkey on CR diet, Owen is 29 year old on unrestricted diet.

news.wisc.edu/monkey-caloric-restriction-study-shows-big-benefit-contradicts-earlier-study/

Ravussin E, et al.: A 2-Year Randomized Controlled Trial of Human Caloric Restriction: Feasibility and Effects on Predictors of Health Span and Longevity. J Gerontol A Biol Sci Med Sci. 2015;70(9):1097–104

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- 25 year study University of Wisconsin: 76 rhesus monkeys ages 7-14 years, fed a diet reduced in calories by 30%.
- Disease was 3 fold greater in control group. No evidence of diabetes in any caloric-restricted animal.
- NIA 2-year study randomized 218 nonobese people to current diet or 25% caloric restriction (11.7% on average).
 - Statistically significant reduction in inflammatory markers, weight loss, improved mood, sleep duration, etc.

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Fasting-Mimicking Diets



Wei M, et al. Fasting-mimicking diet and markers/risk factors for aging, diabetes, cancer, and cardiovascular disease. Sci Transl Med 2017; 9(377).

- USC study **100 healthy people** randomized into 2 study arms to test effects of FMD done 5 consecutive days each month for 3 months.
 - 1100 calorie first day, 700 calories for 4 days (plant based, multivitamin). Ate whatever they wanted rest of the month.
- Three cycles reduced body weight, total body fat; lowered blood pressure, cholesterol, triglycerides and IGF-1.
- Note: 25% drop-out rate
- Effects still noted 3 months AFTER study ended.

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Promising and.....



- Much of initial research on yeast and rodent models. Research in rhesus monkeys impressive.
- CALERIE study showed that even 11% reduction in calories can improve weight loss and certain biomarkers associated with aging. Most people could not sustain 25% reduction in cal.
- What is unclear: do these diets extend longevity in humans? The data suggest that they have a favorable impact on many metabolic parameters associated with better health.

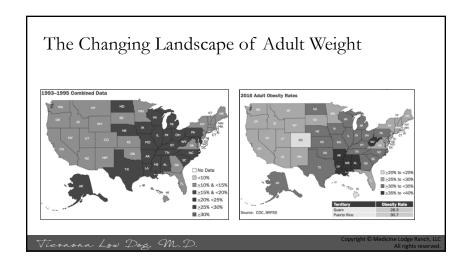
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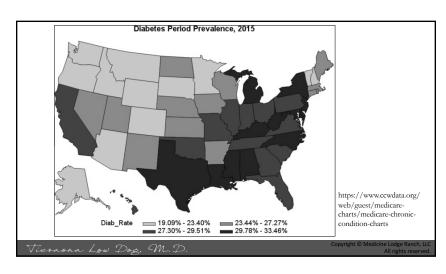
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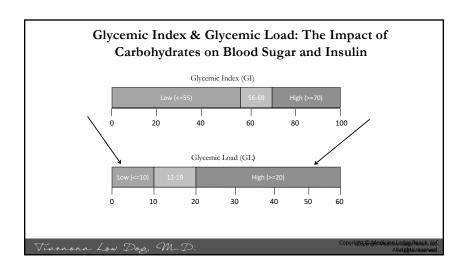
"THE FOOD YOU EAT
CAN BE EITHER
THE SAFEST
&
MOST POWERFUL
FORM OF MEDICINE
OF
THE SLOWEST
FORM OF POISON."

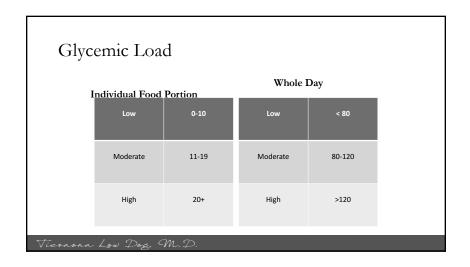
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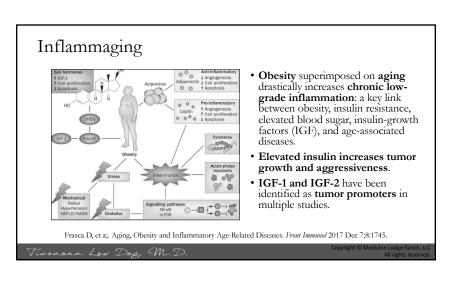
Glycemic Index/Load Low GI Diet Tracker App: \$3.99 • Glycemic load measurement of impact of carbohydrates on blood sugar/insulin. • International consensus conference concluded that given the consistency of the scientific evidence, diets low in glycemic index/load should be promoted in the prevention and management of 27 Cheese 1 slice diabetes and coronary heart disease, and are particularly important in individuals with 0 Egg insulin resistance. Avg GI: 35 Total GL: 3 Augustin LS, et al. Glycemic index, glycemic load and glycemic response: An International Scientific Consensus Summit from the International Carbohydrate Quality Consortium (ICQC). Nutr Metab Cardiovase Die 2015 Sep£25(9):795-815. coli, cooked, with cream sauci

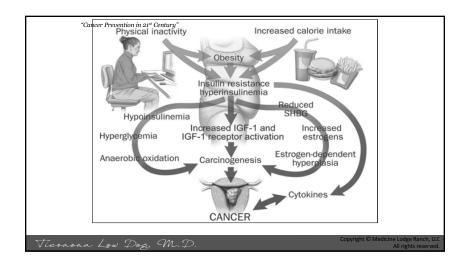


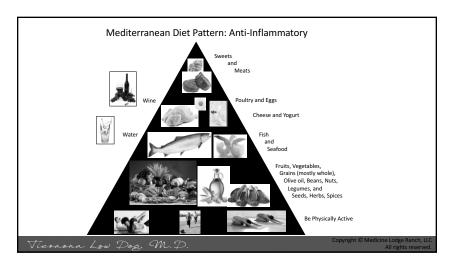


Food	Serving Size	Glycemic Load	Food	Serving Size	Glycemic L
Grapefruit	½ large	3	Asparagus	½ cup	2
Apple	1 medium	6	Broccoli	1 cup	4
Banana	1 large	14	Green beans	1 cup	3
Raisins	1 small box	20	Tomato	1 medium	2
Watermelon	1 cup	8	Subway sandwich	6 inch	17
Carrots	1 large	5	Turkey breast		
Orange	1 medium	6	Butter pecan ice cream	5.5 ounces (small)	22
Sweet potato	1 cup	17	Vanilla ice cream cone	4.5 ounces (small)	19
Baked potato	1 medium	28	Potato chips, fat free	1 bag (8 ounces)	49
French fries	1 medium serving	26	Tortilla chips, white corn	3.5 ounces	38
Snickers	1 bar	35	White bread	1 slice	10
Reese's cup	1 miniature	2	White rice	1 cup	33
White table wine	5 ounces	1	Brown rice	1 cup	23
Red table wine	5 ounces	1			38
Grape juice	6 ounces	12	Spaghetti	1 cup	36









Mediterranean Dietary Pattern

- 13 meta-analyses of observational studies and 16 meta-analyses of randomized controlled trials investigating the association between the adherence to the Mediterranean diet and 37 different health outcomes, for a total population of over than 12,800,000 subjects, were reviewed.
- Robust evidence (P-value<0.001) and large simple sizes showed that greater adherence to the Mediterranean diet was associated with *reduced risk* of overall mortality, cardiovascular diseases, myocardial infarction, overall cancer incidence, diabetes, and neuro-degenerative diseases.

Dinu M, et al. Mediterranean diet and multiple health outcomes: an umbrella review of meta-analyses of observational studies and randomized trials. Eur J Clin Nutr 2017; May 10. doi: 10.1038/ejcn.2017.58.

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Mediterranean Dietary Pattern and Memory

- The Mediterranean and DASH diets have both been associated with lower dementia risk. Researchers evaluated the inflammatory potential of these diets in relation to mild cognitive impairment or dementia risk using the DII during an average follow up of 9.7 years during Women's Health Initiative Memory Study.
- Higher DII scores were significantly associated with *greater* cognitive decline and earlier onset of cognitive impairment.

Hayden KM, et al. The association between an inflammatory diet and global cognitive function and incident dementia in older women: The Women's Health Initiative Memory Study. Alzheimars Dement 2017 May 19. pii: S1552-5260(17)30185-1.

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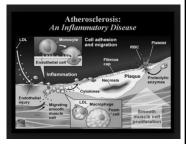
Dietary Inflammatory Index (DII)

- Inflammation often driven by dietary patterns. An anti-inflammatory diet may reduce sub-chronic inflammation and improve cardiovascular, metabolic, and neurologic parameters.
- The **Dietary Inflammatory Index** is based on measuring inflammation in the body in response to specific foods (many clinical trials).
- You can take the test by downloading the app for Dietary Inflammatory Index (Itunes: DII Screener)

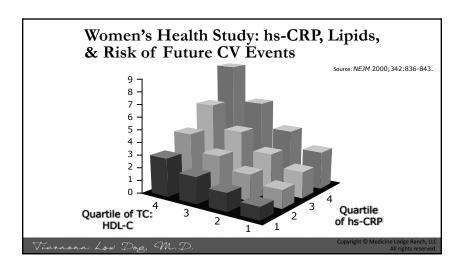
1 Per Week

Inflammatory Food AGAVE 1 TBSP 21 -74 NECTAR Ratings 100 ALMOND ¼ CUP 64 BUTTER CHEESE, 1 OUNCE 28.35 -20 CHEDDAR 200 or higher Strongly anti-inflammatory CHICKEN 3 OUNCES 85 -19 BREAST, RSTD 101 to 200 Moderately anti-inflammatory MILK, WHOLE 1 CUP 246 -46 0 to 100 Mildly anti-inflammatory OLIVE OIL 1 TBSP 14 74 240 ONIONS, ½ CUP 105 -1 to -100 Mildly inflammatory COOKED -101 to 200 Moderately inflammatory RICE, WHITE 1 CUP 158 -153 SPINACH 1 CUP 30 75 -201 or lower Strongly inflammatory SALMON. 3 OUNCES 85 450 SOHO BAKED TURMERIC 1.5 ½ TSP

- CAD once considered primarily a lipid accumulation mediated disease, now has been shown to involve ongoing inflammatory response.
- C-reactive protein (CRP) is a sign of inflammation in the body. There should be no detectable CRP in healthy individual, result of < 1 mg/L is normal.
- Levels of 2 mg/L or higher indicate higher risk for cardiovascular disease.

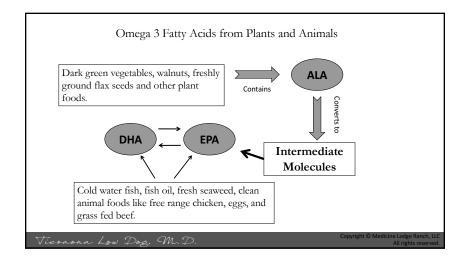


Christodoulidis G, et al. Cardiol Rev 2014 Jan 15



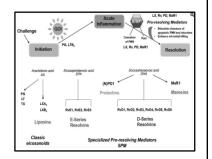
FOOD

SERVING SIZE | SERVING SIZE | IF RATING



Resolution Biology

- · Research shows that resolution of selflimited acute inflammation is an active, programmed response.
- *Omega 3 fatty acids* produce specialized *pro-resolving mediators* (SPM) – resolvins, protectins and maresins.
- These active resolvers of inflammation, show great promise as therapeutics for the treatment of periodontitis and other inflammatory diseases.



VanDyke TE. Pro-resolving mediators in the regulation of periodontal disease. Mol Aspects Med 2017 Dec;58:21-36

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."



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

No Fish Story



- Omega-3 Index test is the **gold standard for omega-3 biostatus** testing. It is used as a compliance marker for randomized controlled trials with fish oil supplements, and in epidemiological research.
- In 2008 Dr. Bernadine Healy, cardiologist and past President of the AHA and first woman Director of the NIH said, "Before long, your personal Omega-3 Index just could be the new cholesterol—the number you want to brag about."

Omega 3 Fatty Acids – Healthy Muscles

- Chronic low-grade inflammation also contributes to the loss of muscle mass, strength and functionality, referred to as sarcopenia, as it affects both muscle protein breakdown and synthesis through several signaling pathways.
- Omega-3 fatty acids stimulate muscle protein synthesis in older adults and may be useful for the prevention and treatment of sarcopenia.



Dalle S, et al. Front Physiol 2017; Dec 12;8:1045 Ticinesi A, et al. Nutrients 2016; Mar 29;8(4):186

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Omega 3 and Prostate Cancer?

- SELECT trial raised concerns about potential link between omega 3s and increased prostate cancer/aggressive cancer (link was weak)
- European Food Safety (EFSA) concluded, "there is no evidence for a role of EPA and/or DHA intake in the development of prostate cancer."
- Also, "supplemental intake of EPA and DHA combined at doses up to 5 g/d does not give rise to safety concerns for adults."

EFSA Journal 10(7): doi:10.2903/j.efsa.2012.2815

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Choose Your Seafood Wisely



https://www.seafoodwatch.org/seafood-recommendations/our-app

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Turmeric Rhizome

(Curcuma longa and others)

- Rhizomes provide bright yellow-orange culinary spice and dye.
- Yellow pigments = **curcuminoids**
- Long history of medicinal use for respiratory, skin, digestive and inflammatory conditions in India.
- More than 65 clinical trials have shed light on its potential role in CVD, diabetes, cancer, fatty liver, arthritis, neuro/psych disorders.



Kunnumakkara AB, et al. Br J Pharmacol 2016; Sep 17. doi: 10.1111/bph.13621.

Prasad S, et al. Biotechnol Adv 2014; 32(6):1053-1064

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Turmeric for Arthritis?

- Laboratory, translational and clinical trials, in general, support use of curcumin for osteoarthritis.
- 13 randomized clinical studies of varying methodological quality show turmeric/curcumin at sufficient dosing and in optimal preparations can reduce pain and improve the functionality of patients with knee osteoarthritis.



Chin K-Y. *Drug Des Devel Ther* 2016; 10: 3029–3042 Peddada KV, et al. Orth Surg 2015; 7(3):222-31

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Turmeric for Depression?

- Mini meta-analysis of 6 studies found curcumin reduced depression symptoms, particularly in middle-aged patients when given at higher doses for longer periods of time.
- Authors concluded, "there is supporting evidence that curcumin administration reduces depressive symptoms in patients with major depression."
- Is this an impact on microbiome? Is it due to systemic reduction in inflammation? Is it real?
 More research needed.



Al-Kawari D, et al. Phytother. Res 2016; 30(2):175-83

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"Cancer Prevention in 21st Century"

Absorption and Safety Issues



- Low aqueous solubility of curcumin and its rapid metabolism and elimination from the body have constituted *major obstacles* to clinical use.
- Nanoencapsulation, curcumin complexed with phosphatidylcholine, and black pepper alkaloid, piperine, enhance tissue distribution and bioavailability.
- Note: Piperine causes inhibition of CYP3A4 and doses of 20 mg can cause clinically relevant drug interactions especially for drugs with narrow therapeutic indices.
- Dose in clinical trials generally 1000-1500 mg per day of turmeric extract standardized to 95% curcumin, taken in divided doses.

Gurley BJ, et al. *Planta Med* 2012; 78(13):1490-514 Bedada SK, et al. *Drug Res* 2016; Oct 24

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Label Reading is Complicated Supplement Facts Serving Size: 10z. Supplement Facts Serving Size: 10z.

Servings Per Container: 16

Amt.
Per Serving Walue

Organic Turmeric
Root Extract
(Supercritical CO2 Extraction)

Organic Black Pepper Fruit Extract (Standardized to 95% Piperine)

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Supplement Facts
Serving Size: 1 Veggie Capsule
Servings Per Container: 60

Amount Per Serving % Daily Value

Turmeric (Curcuma Longa)(root) 600mg *

Turmeric 95% Curcuminoids 50mg *

* Daily Value not established

Other Ingredients: Vegetable Cellulose (Veggie Cap).

, ,

A Note on Protein



- Framingham Osteoporosis Study found higher protein intakes (60-83g/d versus 46g/d) in elder men and women (mean 75 years) were associated with a 37% decreased risk of hip fracture.
- Women's Health Initiative found 20% increase in protein intake (15-18% of energy intake) improved bone mineral density maintenance and marginally lowered forearm fracture risk.
- · European guidelines recommend 20-25 grams high quality protein with each meal for women over age 50 with regular physical activity/exercise 3-5 times/week.
- · Current recommendations are 0.8 grams protein per kg of body weight.

Misra D, et al. Does dietary protein reduce hip fracture risk in elders? The Framingham Osteoporosis Study. Osteoporosis Int 2011; 22(1):345-349. Beasley JM, et al. Biomarker-calibrated protein intake and bone health in the Women's Health Initiative clinical trials and observational study Am J Clin Nutr 2014; 99(4):934-940.

Rizzoli R, et. al. The role of dietary protein and vitamin D in maintaining musculoskeletal health in postmenopausalwomen: a consensus statement from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthniis (ESCEO). Maturitas 2014 Sep;79(1):122-32.

Nutrient Needs Change with Aging

- The need for certain micronutrients increases with age. These are current recommendations but they may not be sufficient.....
 - Vitamin D increases from 600 to 800 IU (20 mcg) per day
 - Calcium increases from 1000 to 1200 mg/day for women over the age of 50 and for men over the age of 70
 - Due to decreased ability to absorb food bound vitamin B12, the Institute of Medicine recommends adults over the age of 50 get their B12 from fortified foods or supplements.

Fragility Fractures

- Fragility fractures associated with decreased quality of life, increased disability, more frequent hospital admission and increased risk of mortality.
- While a multimodal approach is important, vitamin D supplementation alone, or in combination with calcium, has been shown to significantly reduce the risk of falling in elders.



http://www.who.int/nutrition/topics/ageing/en/in dex1.html Accessed January 3, 2018

- · Vitamin D deficiency can cause osteomalacia (lower bone mineralization), leading to musculoskeletal pain, usually in the pelvis, shoulders, low back, and proximal muscles.
- · Deficiency is common worldwide but often more severe in elders due to environmental and biological factors.
- Impaired mobility can limit time spent outdoors and decreased synthesis of vitamin D in skin makes it difficult to maintain adequate levels even with sun exposure.
- · As aging advances, intestinal resistance to 1,25(OH)2D impairs the uptake of calcium and a decline in renal function reduces activation of vitamin D.

Vitamin D



Wintermeyer E, et al. Crucial Role of Vitamin D in the Musculoskeletal System. Nutrients 2016; Jun 1;8(6). pii: E319.

Vitamin D: Bones and Balance

- Low vitamin D increases risk of falls and gait instability. Exercise, calcium and vitamin D supplementation all been shown to decrease falling in elders.
- Meta-analysis by National Osteoporosis Foundation: eight studies (n= 30,970 participants) showed calcium plus vitamin D supplementation produced a significant 15 % reduced risk total fractures and 30% reduced risk hip fracture.

Tricco AC, et al. Comparisons of Interventions for Preventing Falls in Older Adults: A Systematic Review and Meta-analysis. JAMA 2017; Nov 7;318(17):1687-1699.

Weaver CM. Calcium plus vitamin D supplementation and risk of fractures: an updated meta-analysis from the National Osteoporosis Foundation. Osteoporosis Int 2016 Jan;27(1):367-76

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Vitamin D and Respiratory Infection



Martineau AR, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. BMI 2017: 356: i6583.

- Acute respiratory infection kills ~2.65 million people/year.
- 25 eligible randomized controlled trials (n=10,933, aged 0-95 years).
- Vitamin D supplementation reduced risk of acute respiratory infection among all participants (NNT=33) and those who were vitamin D deficient experienced the most benefit (NNT=4), as did those who were receiving daily or weekly vitamin D and not receiving vitamin D boluses (NNT=20).

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Endocrine Society Guidelines

- Serum 25(OH)D level is used to determine vitamin D status
 - Sufficiency is 30 ng/mL (75 nmol/L) and above
 - Insufficiency defined as 21-29 ng/mL
 - **Deficiency** defined as <20 ng/mL
- 66.8 million Americans 1 year and older had levels between 12-20 ng/ml
- 23 million Americans 1 year and older had levels less than 12 ng/ml
 - Most at risk were women and non-Hispanic blacks.

CDC 2nd National Report on Biochemical Indicators of Diet and Nutrition in the U.S. Population Holick MF, et al. J Clin Endocrinol Metab 2011; 96(7):1911-30

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Endocrine Society Guidelines for Treating Deficiency

All adults who are vitamin D deficient should be treated with 50,000 IU of vitamin D2/D3 once per week for 8 weeks or 6000 IU of vitamin D2/D3 daily to achieve a blood level of 25(OH)D above 30 ng/ml, followed by maintenance therapy of 1500–2000 IU/d.

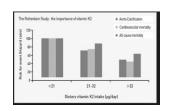


Holick MF, et al. J Clin Endocrinol Metab 2011; 96(7):1911-30

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Vitamin K and More

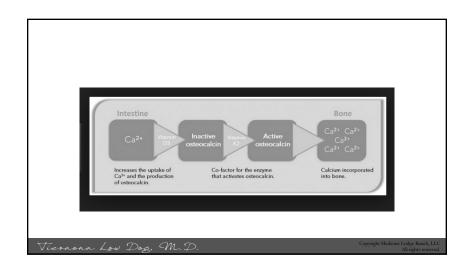
- Calcium, magnesium, vitamins D and K contribute independently and collectively to bone health.
- Beneficial role of vitamin K, particularly vitamin K2 as MK-7, in bone and cardiovascular health is reasonably well supported scientifically, with several preclinical, epidemiological, and clinical studies published over the last decade.

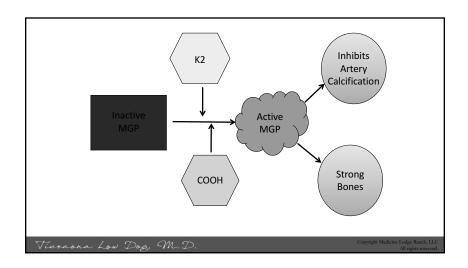


Karpinski M, et al. Roles of Vitamins D and K, Nutrition, and Lifestyle in Low-Energy Bone Fractures in Children and Young Adults. J Am Coll Nutr 2017 Jul;36(5):399-412.

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Prescription Meds and Nutrients: Just a Glimpse

- Widespread use of **prescription drugs** for management of chronic health conditions can make it difficult to **maintain adequate levels of specific nutrients.**
- **PPI drugs** are one of the most commonly prescribed medications and are also available over-the-counter in the United States. Long-term use can increase the risk of fracture, cause magnesium levels to plummet, and interfere with B12 absorption, as well as increasing the risk of *C. difficile* infection.
- With increasing prevalence of type-2 diabetes, we will continue to see increase in metformin use, a drug known to deplete vitamin B12.

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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.
- Deficiency associated with negative effects on calcium and vitamin D homeostasis. Magnesium required for the activation of vitamin D.
- FDA requires warning that proton pump inhibitors can cause dangerously low magnesium levels.

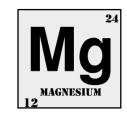


Rosanoff A, et al. Nutr Rev 2010;70(3):153-64

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Magnesium and Diabetes

- Insulin resistance repeatedly shown to decrease magnesium levels and diabetics with low magnesium show a more rapid disease progression and an increased risk for diabetes-related complications.
- A vicious forward feeding cycle is created. Magnesium supplementation has been shown to improve glucose metabolism and insulin sensitivity in those with type-2 diabetes.



Gommers LM, Hoenderop JG, Bindels RJ, de Baaij JH (2016) Hypomagnesemia in Type 2 *Diabetes*: A Vicious Circle? *Diabetes*, 65(1):3-1

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Magnesium and Heart Disease



- 2013 meta-analysis of 16 studies with more than 313,000 participants found:
 - Higher blood levels associated with a 30% lower risk of cardiovascular disease.
 - Dietary magnesium (per 200-mg/d increment) associated with a 22% lower risk of fatal ischemic heart disease.
- Magnesium important in maintaining blood pressure and supplementation (365 to 450 mg/d) shown to significantly lower blood pressure in those with insulin resistance, prediabetes, and other chronic diseases.

Del Gobbo LC, et al. Circulating and dietary magnesium and risk of cardiovascular disease: a systematic review and meta-analysis of prospective studies. Am J Clin Nutr 2013; 98(1):160-73.

Dibaba DT, et al. The effect of magnesium supplementation on blood pressure in individuals with insulin resistance, prediabetes, or noncommunicable chronic diseases: a meta-analysis of randomized controlled trials. Am J Clin Nutr 2017; 106(3):921-929.

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Magnesium Deficiency

- People with magnesium deficiency can present with insulin resistance, menstrual cramps, leg cramps, migraines, fatigue, anxiety and mild elevations in blood pressure.
- In more severe cases of deficiency, seizures, tingling and numbness in the arms and legs, bizarre muscle movements (especially of the eyes and face), personality changes, and coronary spasms can occur.
- Many medications can deplete magnesium (e.g., diuretics, PPIs, OCPs, gout medication, B2-agonists, steroids, etc.).

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Bird JK, et al. Risk of Deficiency in Multiple Concurrent Micronutrients in Children and Adults in the United States Nutrients **2017**; doi: 10.3390/nu9070655

Conzude R, et al. Prevalence and Predictors of Subclinical Micronutrient Deficiency in German Older Adults. Results from the Population-Based KOR-4-Age Study. Nutrients 2017; doi: 10.3390/nu9121276

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Vitamin B12 Deficiency

- Risk for deficiency increases with age:
 - 7% of those 51–70 years of age
 - 15% >70 years are B12 deficient
- Decline in gastric acid with advancing age makes it hard to absorb food-bound B12.
- Institute of Medicine recommends adults > 50 get B12 from **fortified foods/supplements**
- Risks: inadequate intake, malabsorption, medications, vegan, obesity, and aging.

Metformin and PPI Increase Risk for Low B12

- 2015 meta-analysis: 80% increased risk B12 deficiency after 10 months of regular proton pump inhibitor use.
- Meta analysis: 29 studies: 245% increased risk B12 deficiency with metformin use. Low B12 shown to increase progression of diabetic neuropathy.
- B12 deficiency can lead to difficulty walking, tingling/numbness in hands and feet, fatigue, shortness of breath, loss of appetite, joint pain, depression, loss of taste and smell, cognitive impairment, and dementia.
- B12 should be monitored every 1-2 years if taking these medications.

Jung SB, et al. Association between vitamin B12 deficiency and long-term use of acid-lowering agents: a systematic review and metaanalysis. Intern Med J 2015; 45(4):409-16.

Out M, et al. Long-term treatment with metformin in type 2 diabetes and methylmalonic acid: Post hoc analysis of a randomized controlled 4.3 year trial. J Diabetes Complications 2018; 32(2):171-178.

Niafar M, et al. Intern Emerg Med 2015; 10(1):93-1026

Vieraona Low Dog, M.I

Herbal Bitters: The Foundation

- Bitters may be one our most important remedies in modern times if we believe that an optimally functioning GI system is key to good health.
- Compounds in plants bind bitter receptors and increase salivation, stimulate the production of digestive juices from the stomach and pancreas, enhance bile flow from the gallbladder and increase the tone of the esophageal sphincter.
- Bitters enhance almost every aspect of digestion.
 "Low GI fire leads to gut inflammation, allergies and food intolerances."



Vieraona Low Dog, M.D.

Iberogast Ingredients

Botanical Name ^a	Plant Part	Extract Solvent (V/V)	Drug-Extract Ratio	% in 100 mL Iberogast
Iberis amara L.	Fresh whole plant	50% Ethanol	1:1.5-2.5	15
Mentha piperita L.	Dried herbs	30% Ethanol	1:2.5-3.5	5
Matricaria chamomilla L.	Dried flowers	30% Ethanol	1:2-4	20
Glycyrrhiza glabra L.	Dried roots	30% Ethanol	1:2.5-3.5	10
Angelica archangelica L.	Dried roots	30% Ethanol	1:2.5-3.5	10
Carum carvi L.	Dried fruits	30% Ethanol	1:2.5-3.5	10
Silybum marianum L. Gaertn.	Dried fruits	30% Ethanol	1:2.5-3.5	10
Melissa officinalis L.	Dried leaves	30% Ethanol	1:2.5-3.5	10
Chelidonium majus L.	Dried herbs	30% Ethanol	1:2.5-3.5	10

Vicraona Low Dog, M.D

Peppermint Essential Oil for IBS



Cash BD, et al. *Dig Dis Sai*. 2016;61(2):560–571. Chey WD, et al. *JAMA* 2015;313(9):949–958.

- Sustained-release formulation of enteric coated peppermint oil (0.2 ml) demonstrated efficacy in IBS.
- Antispasmodic (calcium channel blocking properties), peppermint oil and L-menthol normalize orocecal transit time, κ-opioid and 5-HT₃ antagonism.
- Abdominal pain/discomfort, bloating, pain at evacuation, and urgency are symptoms most improved.

Vieraona Low Dog, M.D.

Caraway Essential Oil

(Carum carvi)

- Caraway oil displays high degree of selectivity, inhibiting growth of potential bacterial intestinal pathogens at concentrations that had no effect on beneficial bacteria.
- Increases mucin secretion and PGE2 in stomach, protecting against NSAID damage.
- Carminative, antispasmodic
- Spirit of caraway 1 ounce EO in 10 ounces vodka. 5-10 drops PRN



Vieraona Low Dog, M. I

Ginger Rhizome

(Zingiber officinale)

- Ginger has beneficial effect on *lipids*, *blood* sugar, oxidative stress and *inflammation*.
- *Prokinetic*. Study 24 healthy volunteers found 1200 mg dried ginger accelerated gastric emptying and stimulated antral contractions greater than placebo.
- Ginger benefits those with gastroparesis with symptoms such as heartburn, early satiety, abdominal bloating, and nausea and/or vomiting several hours after eating a meal.
- Effective anti-emetic.



Wang J, et al. Beneficial effects of ginger Zingiber officinale Roscoe on obesity and metabolic syndrome: a review. Annals of the New York Academy of Sciences 2017; May 15. doi: 10.1111/nyas.

Wu KL, et al. Eur J Gastroenterol Hepatol. 2008 May;20(5):436-40. d

Vicraona Low Dog, M.I

Lemon Balm

(Melissa officinalis)

- The "gladdening herb" and "heart's delight."
- Has strong digestive affinity, can be *helpful* for functional GI disorders, IBS, etc.
- Carminative: Shown to *improve colic* in breastfed babies, especially when combined with chamomile and/or fennel.
- Exhibits numerous pharmacological effects, from which anxiolytic, antiviral and antispasmodic activities, as well as its effects on mood, cognition and memory have been shown in clinical trials.

Shakeri A, et al. J Ethnopharmacol 2016; 188:204-8

Vieranna Low Doc. M.D.



Iberogast

- STW 5 (Iberogast) is a combination-preparation "with proven clinical efficacy in the treatment of functional gastrointestinal diseases."
- According to German treatment recommendations, STW 5 may be recommended as evidence-based treatment for all IBS subtypes.
- Studies show that the combination increases mucin concentration, reduces gastric inflammation, decreases visceral hypersensitivity, has spasmolytic activity in gut, and had intestinal prosecretory effects (aids dysmotility/constipation).

Abdel-Aziz H, et al. Evaluating the Multitarget Effects of Combinations through Multistep Clustering of Pharmacological Data: the Example of the Commercial Preparation Iberogast. *Planta Med.* 2017 Oct;83(14-15):1130-1140.

Vicraona Low Doc, M.D

Bacopa Herb (Bacopa monnieri)

- Systematic review 5 studies found bacopa significantly improved memory span as well as verbal and visual memory in children and adolescents. Two studies found improvements in hyperactivity and attention in kids with ADHD.
- Systematic review: 8 of 9 placebo controlled trials demonstrated positive memory, attention or cognitive enhancing effect of bacopa, some found anxiolytic or improved mood effect.
- Very well tolerated.



Kean JD, Downey LA, Stough C. A systematic review of the Ayurvedic medicinal herb Baopa monnieri in child and adolescent populations. Complement Ther Med. 2016 Dec;29:56-62.
Pase MP, et al. The cognitive-enhancing effects of Baopa mounieri: A systematic review of randomized, controlled human clinical trials. J. Altern. Complement. Med. 2012;18:647-652.

Vieraona Low Dog, M. I

Holy Basil (Ocimum tenuiflorum; O. sanctum)

- Traditionally used in India for common cold and asthma but most widely revered as neural tonic and memory enhancer.
- Vedic scholars used to sharpen intellect and help memorize lengthy scriptures more than 1400 years ago.
- Anti-anxiety and anti-depressant activities reported. Calming effect said to lead to clarity of thought.
- Study (n=150) showed 1200 mg/d reduced general stress symptoms by 36% more than placebo.
- Study of 35 people with generalized anxiety disorder showed increased attention and improved mood with 500 mg BID.
- 100-300 mg/d extract or 1-2 grams crude herb equivalent per day.



Baliga MS, et al. Nutr Caner 2013; 658 1:26-35. Cohen MM. J Ayurveda Integr Med 2014; 5(4): 251-259. Saxena RC, et al. Erid Based Complement Alternat Med 2012; 894509 Bartacharyya D, et al. Nepal Med Coll J 2008; 10(5):176-9.

Vicraona Low Dog, M.D.

Lack of Sleep



- 1 in 3 Americans do not get sufficient sleep. Research shows chronic sleep problems can lead to weight gain, obesity, diabetes (33% increased risk type 2 DM), and heart disease.
- Biological clock most important regulator of the sleep wake cycle. Responsible for 24 hour fluctuations in hormone secretion, body temperature and other bodily functions.
- Lack of exposure to sunlight and use of bright lights at night increases the likelihood of disordered circadian clock. Consider dawn simulation device/app, use blue light blocking glasses at night with technology.
- · Controlled release melatonin now first line therapy for those older than 60 (2 mg)

Shan Z, et al. Diabetes Care 2015;38(3):529–37 Matheson E, et al. Insomnia: Pharmacologic Therapy. Am Fum Physician 2017; Jul 1;96(1):29-35.

Tieraona Low Dos, M.D

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Valerian (Valeriana officinalis)

- · Long history using roots for restlessness and sleep disorders dating back to Dioscorides.
- WHO monograph: "mild sedative, sleep promoting agent, milder alternative or substitute for stronger sedatives (e.g., benzodiazepines); and treatment of nervous excitation/sleep disturbances induced by anxiety."

apps.who.int/medicinedocs/en/d/Js2200e/29.html#Js2200e.29



European Medicines Agency: Valerian (2016)

- "For relief of sleep disorders, a single dose half to one hour before bedtime with an earlier dose during the evening if necessary."
- "Because of its gradual onset of efficacy valerian root is not suitable for acute interventional treatment of mild nervous tension or sleep disorders. To achieve an optimal treatment effect, continued use over 2-4 weeks is recommended."
- They do not recommend use in children under age 12 or during pregnancy.
- Single dose: 0.3-3 grams.
- For relief of mild symptoms of mental stress up to 3 times daily.

European Union herbal monograph on Valeriana officinalis L. www.ema.europa.eu/docs/en_GB/document_library/Herbal_-Herbal_monograph/2016/04/WC500205376.pdf

Lemon Balm (Melissa officinalis)

- Referred to as the "gladdening herb" and "heart's
- · Strong digestive affinity. Calms disordered energy.
- · Both valerian and lemon balm have GABAergic activity and anxiolytic activity in human trials.
- Studies of valerian root and lemon balm combination showed improvement in sleep in children and relieved test anxiety in healthy volunteers.

Streige K, et al. GABA-motivating psytometriene for artisety: A systematic review on presentate and united sciences of artisety of Systematic review on presentate and united sciences of a grant produced by the Martie G, et al. The Medical of Lemon Balm (Medisa affisinalis) and Valerian (Valerian affisial) as Natural Schrives Insight into their Intercolons with GABA Transmissions. Int. II Clin Pharmatel Promasaler Volume 1, 2016. 112



California Poppy (Eschscholzia californica)

- · Official state flower California. Native Americans used as food and medicine for millennia. Upper part of the plant used to relieve tooth pain, headache, and promote sleep.
- Basic science shows it acts on GABA-A receptors in the brain, similar to a benzodiazepine without habitforming tendency of the drug. Has anxiolytic, analgesic, sedative activity.

Fedurco M, et al. Modulatory Effects of Eschscholzia californica Alkaloids on Recombinan GABAA Receptors. Biochem Res Int 2015;2015;617620





California Poppy

- The European Union monograph recognizes the traditional use for relief of mild symptoms of mental stress and to aid
- It also discusses research that indicates that a "standardized extract of California poppy can be used in the management of chronic pain and as a hypnotic-mild-sedative for the management of pain-related insomnia."

European Union herbal monograph on Eschscholzia californica Cham., herba. January 28, 2015 www.ema.europa.eu/docs/en_GB/document_library/Herbal_Community_herbal_monograph/2015/05/WC500186552.pdf



D-mannose for Recurrent UTI



- After antibiotic treatment for acute cystitis, 308 women with history of recurrent UTI randomized to one of three groups:
 - 2 g/d mannose powder in 200 ml water
 - 50 mg/d nitrofurantoin
 - · No prophylaxis
- ~15% recurrent in D-mannose, 20% in nitrofurantoin and 61% no treatment group.

Kranjcec B, et al. World J Urol 2014; 32(1):79-84

Cranberry With D-Mannose (60 Veggie Caps) Supplement Facts SUPPLEMENT FACTS Serving Size: 2 VEGGIE CAPS Serving Per Container: 30 Vitamin C - (As Ascorbic Acid) 1,000 Mg N/A CRANRICH (CRANBERRY CONCENTRATE 400 Mg Now Foods D-Mannose (3 Ounces Powder) Supplement Facts Serving Size: 1 LEVEL TEASPOON (2 G) Serving Per Container: 40 2 Gri

Make Friends with Your Microbes!

- Rapidly expanding research on benefits of certain probiotic strains in women's health.
- · Gastrointestinal
 - · Reduce symptoms of irritable bowel syndrome
 - · Reduce incidence of antibiotic associated diarrhea
- · Genito-urinary
 - · Reduce the risk of recurrent bladder infections
 - Help reduce recurrent yeast infections
- Pregnancy
 - · Reduce allergies and eczema in high risk children, especially if born by Cesarean section, if taken last 2 months of pregnancy.

Grin PM, et al. Can J Urol 2013 Feb;20(1):6607-14; Ford AC, et al. Am J Gastroenterol 2014; 109(10):1547-1561

Loneliness, Social Isolation & Your Health

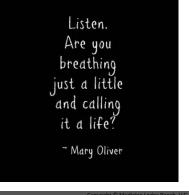
- Review found poor social relationships associated with 29% increase in risk of incident CHD and 32% increased risk of stroke.
- 148 studies on the effects of social isolation on health found it is:
 - As bad as smoking 15 cigarettes a day.
 - As dangerous as being an alcoholic.
 - As harmful as never exercising.
 - Twice as dangerous as obesity.



- · Valtorta NK, et al Loneliness and social isolation as risk factors for coronary heart disease and stroke: systematic review and metaanalysis of longitudinal observational studies. Heart. 2016 Jul 1;102(13):1009-16.
- Cacioppo JT, et al. Ann N Y Acad Sci 2011; 1231:17-22

Meaning and Purpose

- What truly gives a person a sense of meaning and purpose in life?
- · How does one feel the oneness, find the holy and sacred in the mundane?



Letting Go.....

"Healing may not so much be about getting better, but about letting go, of all the expectations, all of the beliefs, and becoming who you are."

— Rachel Naomi Remen, M.D.



