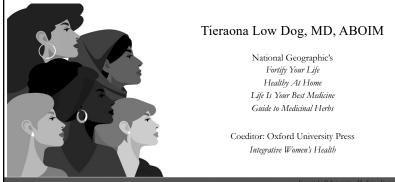
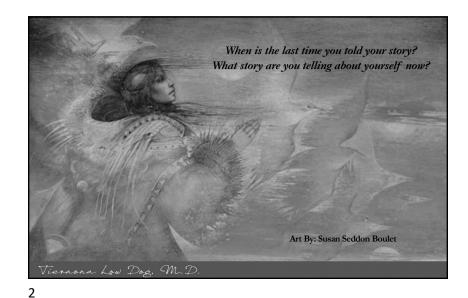
## Women's Health: A Woman's Guide to Wellness



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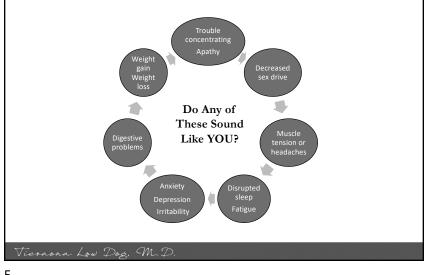


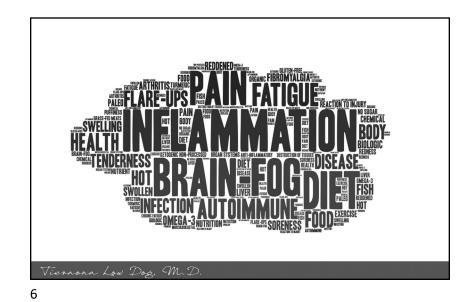


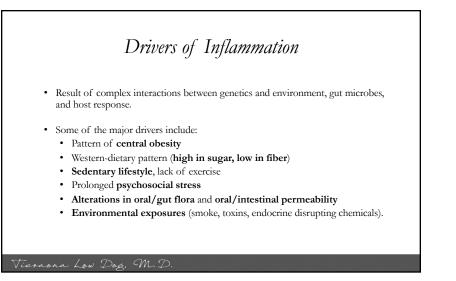
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The Gender Gap

- Alzheimer's Disease: 5.8 million people in US have AD, 2/3rds are women
- Bone Health: 10 million Americans have osteoporosis, 80% are women
- Mental Health: women 2x more likely than men to suffer from depression
- Migraines: women 3x more likely to have than men (post-puberty)
- Sleep: women are 2x more likely to have insomnia than men
- IBS: women 3x more likely than men to have IBS
- Autoimmune disease: 80 autoimmune diseases, women ~75% of patients
- Hypothyroidism: women 10x more likely to experience than men
- Fibromyalgia: women 2x more likely to experience than men
- Chronic fatigue syndrome: women 4x more likely to have than men
- Maternal Mortality: black women 69.9 deaths/100,000 births, 2.6 x higher than white women



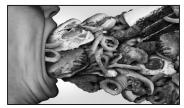




Diet & Lifestyle

Diseases linked to unhealthful diet and lifestyle choices, such as diabetes and cancer, are the leading causes of death in the United States, with high BMI and elevated blood glucose on the rise in all 50 states (tobacco use on the decline).

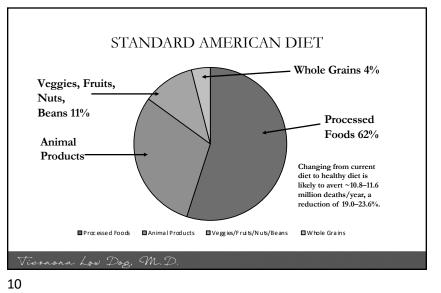
- · Dietary factors
- Tobacco consumption
- High blood pressure
- High BMI
- High plasma glucose
- Alcohol and drug use



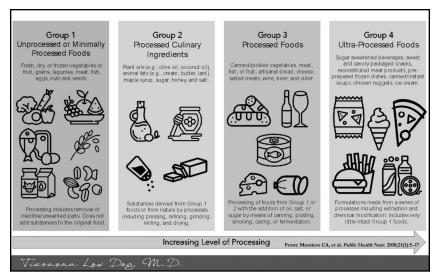
The US Burden of Disease Collaborators. The State of US Health, 1990-2016 Burden of Diseases, Injuries, and Risk Factors Among US States. JAMA. 2018;319(14):1444-1472.



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9



The Rise of Ultra-Processed Foods

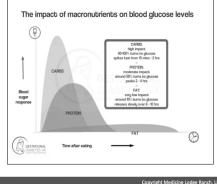
- UPF are "snacks, drinks, ready meals, and many other products created mostly or entirely from substances extracted from foods or derived from food constituents with little if any intact food."
- Quick, tasty, and often cheap. Increasingly found in "health" foods.
- UPF from *animals or plants* has been shown to harm the microbiome and drive inflammation.<sup>2</sup>
- In US, 57% of total calories for adults<sup>3</sup> and 67% for children<sup>4</sup> come from UPF.
- Observational studies show association between UPF and cancer, heart disease, obesity, and other chronic health problems.

Willett W, et al. Lancet 2019 February 2; 393, (10170): 447-492.
 Juul F, et al. Am J Clin Nutr 2022; 115(1):211-221.

Srour B, et al. Lancet Gastmenterol Hepatol 2022 Dec;7(12):1128-1140
 Wang I, et al. JAMA 2021; 326(6):519-530

## Refined Carbohydrates

- Overdo processed/refined carbs, blood sugar rises, insulin released, store extra glucose as fat, drives inflammation.
- Blood sugar goes up and then can plummet, **leaving one tired and disrupting sleep/wake cycle.**
- Eating lots of carbs makes one crave lots of carbs (dopamine rush).
- High-sugar diets cause **dysbiosis and degrade intestinal barrier, leading** to systemic inflammation.



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## Fiber, Processed Foods, and Depression

- Consumption of *sweetened beverages and* refined foods is associated with an increased risk of depression in longitudinal studies.
- Women's Health Initiative (n = 87,618): higher consumption of dairy products, fiber, fruit (not juice), and vegetables was significantly associated with LOWER odds of depression; refined grain consumption was associated with increased odds of depression in menopausal and post-menopausal women.



Gangwisch JE, et al. High Glycemic Index Diet as a Risk Factor for Depression: Analyses From the Women's Health Initiative. *Am J Clin Nutr* 2015 Aug;102(2):454-63.

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## Glycemic Load and Mood

- Glycemic load: measurement of how a serving of a particular food impacts blood sugar.
- 82 healthy weight or healthy overweight or obese adults enrolled in 28-day randomized, crossover-controlled feeding study.
- Compared to low GL diet, a high GL diet resulted in:
  - 38% higher score for *depressive* symptoms (P = 0.002)
  - 55% higher score for *total mood* disorder (P = 0.05)
  - 26% higher score for *fatigue/inertia* (P = 0.04)

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Breymeyer KL, et al. *Appetite* 2016; Dec 1;107:253-259.

# • Studies show high glycemic load meals

when compared to carbohydrates.

Glycemic Load & Cortisol

- significantly *increase cortisol* (stress hormone). • Protein and fat significantly *decreased cortisol*
- Low glycemic load diet beneficial for overall health and *particularly those with chronic stress*.

## Low GI Diet Tracker App



Marters MJI, et al. Effects of single macronutrients on serum cortisol concentrations in normal weight men. Physiology & Behavior 2010; 101(5): 563-67

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Grapefruit	½ large	3	Spaghetti	1 cup	38
Apple	1 medium	6	Brown rice	1 cup	23
Banana	1 large	14	White rice	1 cup	33
Raisins	1 small box	20	White bread	1 slice	10
Watermelon	1 cup	8	Whole grain bread	1 slice	5
Carrots	1 large	5	Bagel, cinnamon raisin	1 3.5 inch	24
Orange	1 medium	6	Pumpernickel bread	1 slice	6
Sweet potato	1 cup	17	Macaroni and cheese	1 cup prepared	31
Baked potato	1 medium	28	Chocolate doughnut	1 doughnut (80 g)	25
French fries	1 medium serving	26	Glazed doughnut	1 doughnut (80 g)	12
Snickers	1 bar	35			
Reese's cup	1 miniature	2	Kellogg's Frosted Flakes	% cup	20
White table wine	5 ounces	1	Kellogg's Special K	1 cup	14
Red table wine	5 ounces	1	Post Bran Flakes	% cup	12
Grape juice	6 ounces	12	Post Raisin Bran	1 cup	25

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uits	Serving size	Total fiber (grams)*	Vegetables	Serving size	Total fiber (grams)*
			Green peas, boiled	1 cup	9.0
laspberries	1 cup	8.0	Broccoli, boiled	1 cup chopped	5.0
Pear	1 medium	5.5	Turnip greens, boiled	1 cup	5.0
pple, with skin	1 medium	4.5	Brussels sprouts, boiled	1 cup	4.0
anana	1 medium	3.0	Potato, with skin, baked	1 medium	4.0
			Sweet corn, boiled	1 cup	3.5
ange	1 medium	3.0	Cauliflower, raw	1 cup	2.0
trawberries	1 cup	3.0		chopped	
			Carrot, raw	1 medium	1.5

https://www.mayoclinic.org/healthy-lifestyle/nutrition-and-healthy-eating/in-depth/high-fiber-foods/art-20050948

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## Eat More Fiber and Less Sugar



Bibbo S, et al. Eur Rev Mol Pharmacol Sci 2016; Nov;20(22):4742-4749.Weigh CAM, et al. Expert Rev Controventry Hypatol 2017 Nov;11(11):1031-1045.Young RP, et al. And N Expir Call Mol Biol 2016;54:161-160.Krauz X, et al. Adv Nare 2012; 3(1):47-53.

# Modulates immune system, 70% of immune system in GI tract. Diets low in fiber, high in sugar

*reduce Bifidobacterium* and degrade barrier function, key part of *innate immunity*.

• Gut bacteria ferment certain

fibers for fuel, increasing diversity of gut microbiota.

• Adequate Intake of dietary fiber: - 26 g/d women

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Grains	Serving size	Total fiber (grams)*	Legumes, nuts and seeds	Serving size	Total fiber (grams)*
Spaghetti, whole-wheat, cooked	1 cup	6.0	Split peas, boiled	1 cup	16.0
Barley, pearled, cooked	1 cup	6.0	Lentils, boiled	1 cup	15.5
Bran flakes	3/4 cup	5.5	Black beans, boiled	1 cup	15.0
Quinoa, cooked	1 cup	5.0	Baked beans, canned	1 cup	10.0
Oat bran muffin	1 medium	5.0	Chia seeds	1 ounce	10.0
Oatmeal, instant, cooked	1 cup	5.0	Almonds	1 ounce (23 nuts)	3.5
Popcorn, air-popped	3 cups	3.5	Pistachios	1 ounce (49	3.0
Brown rice, cooked	1 cup	3.5		nuts)	
Bread, whole-wheat	1 slice	2.0	Sunflower kernels	1 ounce	3.0

https://www.mayoelinic.org/healthy-lifestyle/nutrition-and-healthy-eating/in-depth/high-fiber-foods/art-20050948



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## Mediterranean Diet Inflammation & Memory



- Dietary Inflammatory Index measures inflammation in the body in response to specific foods (~1,900 studies).
- Mediterranean diet associated with lower dementia risk. Researchers evaluated inflammatory potential of diet in relation to mild cognitive impairment/dementia risk during ~9.7 years during WHI Memory Study.
- Higher inflammatory 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. Alzheimers Dement 2017 May 19. pii: S1552-5260(17)30185-1.

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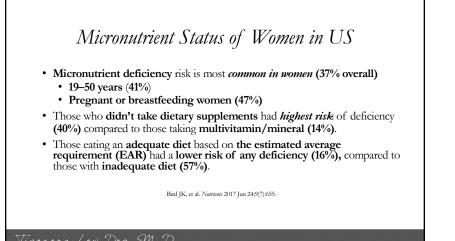
24

aflam	matom Food	FOOD	SERVING SIZE	SERVING SIZE (GRAMS)	IF RATING
Inflammatory Food Ratings		AGAVE NECTAR	1 TBSP	21	-74
		ALMOND BUTTER	¼ CUP	64	100
or higher	Strongly anti-inflammatory	CHEESE, CHEDDAR	1 OUNCE	28.35	-20
to 200	Moderately anti-inflammatory	CHICKEN BREAST, RSTD	3 OUNCES	85	-19
00	Mildly anti-inflammatory	MILK, WHOLE	1 CUP	246	-46
	Hitoty and Hittanin actory	OLIVE OIL	1 TBSP	14	74
-100	Mildly inflammatory	ONIONS, COOKED	½ CUP	105	240
io 200	Moderately inflammatory	RICE, WHITE	1 CUP	158	-153
orlower	Strongly inflammatory	SPINACH	1 CUP	30	75
		SALMON, SOHO BAKED	3 OUNCES	85	450
		TURMERIC	½ TSP	1.5	338



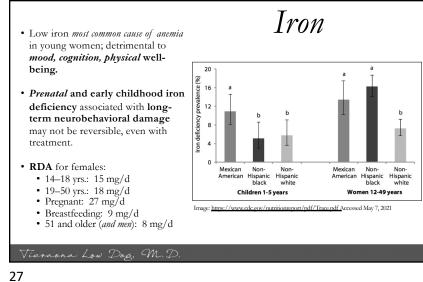


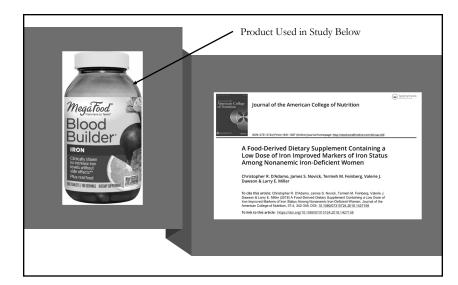
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## Calcium for PMS



- Majority of 14 studies showed serum calcium levels are lower in women with PMS, and calcium supplementation can significantly improve the incidence of PMS and its related symptoms.
- Dose: 600-1200 mg/d used in most studies. Absorption best with 500 mg or less. Calcium citrate better tolerated than carbonate.
- Most women only need to take 500 mg per day for PMS, along with vitamin D (helps calcium absorption).

Arab A, et al. Beneficial Role of Calcium in Premenstrual Syndrome: A Systematic Review of Current Literature Int J Prev Med 2020 Sep 22;11:156.



Verkaik S,. The treatment of premenstrual syndrome with menarations of Vitex acruss-castus: a systematic review and meta-analysis. Am J Obstet Gynecol. 2017;217(2):150-

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## Chaste Berry Fruit (Vitex agnus castus)

- Part used: dried ripe fruit
- · German health authorities approve for irregular menses, PMS, and cyclical breast tenderness.
- Meta-analysis PMS: 9/10 studies found Vitex superior to placebo (one negative study used ground fruit/not extract). Vitex similar to oral contraceptives in two studies, similar to fluoxetine in one study (PMDD), and not as effective on HAM-D as fluoxetine in another (PMDD).
- In summary: there is good evidence Vitex is beneficial for PMS/PMDD.

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• Dose: 400 mg dried fruit taken once per day.

33/4 cups

lontil

## Oral Contraceptives & Vitamin B6

- · Majority of women on OCPs have low serum B6 levels, even when meeting dietary RDA.<sup>1</sup>
- Oral contraceptive use in US 2017–2019:<sup>2</sup>
  - 19.5% of women aged 15-19
  - 21.6%
  - aged 20-29
  - 10.9% aged 30-39
  - 6.5% of women aged 40-49
- Low B6: microcytic anemia, depression, poor concentration, fatigue, etc.
- Women who discontinue OCs and become pregnant may be at increased risk for preterm birth and early pregnancy loss.<sup>3</sup>

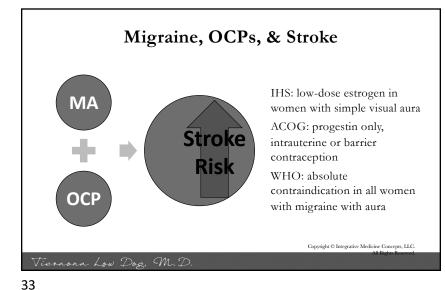


Morris MS, et al. Am J Clin Nutr 2008; 87(5):1446-54 www.cdc.gov/nchs/products/databriefs/db388.htm Wilson SMC. Nutr Rev 2011 Oct; 69(10):572-83



## Vitamin B6 in Women's Health

- ACOG recommends 10-25 mg vitamin B6 3-4 times daily for nausea/vomiting pregnancy.1
- Studies show B6 can improve PMS symptoms and reduce the risk for postpartum depression.<sup>2.3</sup>
- Low periconceptional B6 (PLP < 30 nmol/L) reduces probability of conception.4
- Do NOT exceed 100 mg per day.
- ACOG Practice Bulletin 189. Obstet Gyneod 2018 Jan;131(1):e15-e30. Retallik-Brown H, et al. J Altern Complanent Med 2020; 26(2):88-97 Khodadad M, et al. Journal Pharm Res International 2017; 19(1): 1-9 Ho CL, et al. Nutrients 2016; Sep 1;8(9).





## Magnesium for Migraines

MAGNESIUN

Parazzini F, et al. Magnes Res 2017 Feb 1;30(1):1-7. Garrison SR, et al. Cochrane Database Syst Rev 2020; 9(9):CD009402.

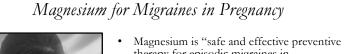
3. Pouteau E, et al. PLoS One 2018;13(12):e0208454.

- Migraine disproportionately affects women. Impacts 1 in 4 households. Studies show migraineurs have low brain magnesium during migraine attacks.
- American Academy of Neurology and American Headache Society concluded that magnesium therapy is "*probably effective*" for migraine prevention. Canadian Headache Society: strong recommendation for magnesium for prophylaxis of migraine (also for riboflavin).

Rajapakse T, et al. Nutraceuticals in Migraine: A Summary of Existing Guidelines for Use. Headache 2016; 56(4):808-16.

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- Magnesium is "safe and effective preventive therapy for episodic migraines in pregnancy."
- Decreases the frequency, severity, and duration of migraine headaches.
- When additional treatment was needed, 94% of migraines were controlled with the combination magnesium and riboflavin.
- May help reduce leg cramps in pregnancy

ssessing the efficacy of magnesium oxide and riboflavin as preventative treatment of migraines in preg ttps://doi.org/10.1016/j.ajog.2021.11.1136

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## Magnesium & Women's Health

- 2017 review: magnesium supplementation effective in preventing menstrual cramps, PMS, menopausal symptoms.<sup>1</sup>
- *May* relieve **leg cramps** in pregnancy.<sup>1</sup>
- 400–600 mg/d effective for preventing menstrual migraine.<sup>2</sup>
- Can reduce symptoms of **depression/anxiety** alone and in combination with **vitamin B6.**<sup>3</sup>
- Relaxing and calming in general.

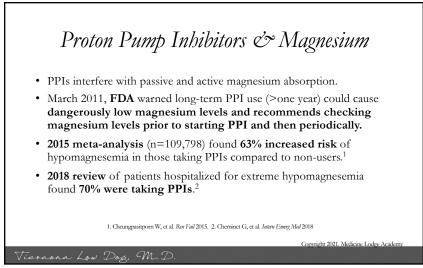
## Magnesium

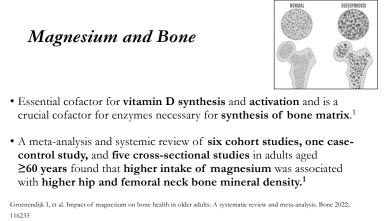
- Heart disease #1 cause of death for females.
- Rotterdam study 9,820 participants (mean 65.1yrs, 56.8% female): low serum magnesium associated with an increased risk of coronary heart disease mortality and sudden cardiac death.<sup>1</sup>
- 1 in 9 women have diabetes. Insulin resistance decreases magnesium levels, and diabetics with low magnesium show more rapid disease progression and increased risk for diabetes-related complications.<sup>2</sup>

1. Kieboom BCT, et al. J Am Heart Assoc 2016 Jan; 5(1): e002707. 2. Bertinato J, et al. Nutrients 2017 Mar; 9(3): 296

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SILU

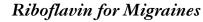
	Milligrams	
	(mg) per	Percent
Food	serving	DV*
Pumpkin seeds, roasted, 1 ounce	156	37
Chia seeds, 1 ounce	111	26
Almonds, dry roasted, 1 ounce	80	19
Spinach, boiled, ½ cup	78	19
Cashews, dry roasted, 1 ounce	74	18
Peanuts, oil roasted, ¼ cup	63	15
Cereal, shredded wheat, 2 large biscuits	61	15
Soymilk, plain or vanilla, 1 cup	61	15
Black beans, cooked, ½ cup	60	14
Edamame, shelled, cooked, ½ cup	50	12
Peanut butter, smooth, 2 tablespoons	49	12
Potato, baked with skin, 3.5 ounces	43	10
Rice, brown, cooked, ½ cup	42	10
Yogurt, plain, low fat, 8 ounces	42	10
Breakfast cereals, fortified with 10% of the DV for magnesium, 1 serving	42	10
Oatmeal, instant, 1 packet	36	9
Kidney beans, canned, ½ cup	35	8
Banana, 1 medium	32	8

## Magnesium

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	30 mg*	30 mg*		
7-12 months	75 mg*	75 mg*		
1-3 years	80 mg	80 mg		
4-8 years	130 mg	130 mg		
9-13 years	240 mg	240 mg		
14-18 years	410 mg	360 mg	400 mg	360 mg
19-30 years	400 mg	310 mg	350 mg	310 mg
31-50 years	420 mg	320 mg	360 mg	320 mg
51+ years	420 mg	320 mg		

High doses can lead to diarrhea and abdominal cramping. Forms most likely to cause diarrhea include magnesium carbonate, chloride, gluconate, and oxide.

ods.od.nih.gov/factsheets/Magnesium-HealthProfessional/



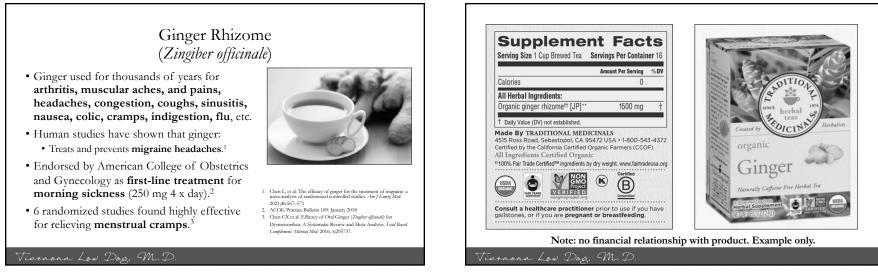


- CHS guidelines gave strong recommendation for benefit, and minimal side effects
- Teenage girls often low in riboflavin
- AAN/AHS give riboflavin Level B recommendation, probably effective and should be considered for migraine prevention (400 mg/d)
- Deficiency: increases light sensitivity

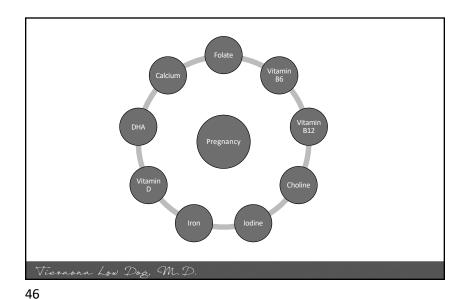
Rajapakse T, et al. Nutraceuticals in migraine: a summary of existing guidelines for use. Headache 2016; Apr;56(4):808-16.











## Folate/Folic Acid



- New RDA pregnancy: 360 mcg folic acid/d (600 mcg DFE).
- USPSTF recommends all women planning or capable of pregnancy take 400–800 µg per day of *folic acid*.<sup>1</sup> (*This recommendation currently under review*)
- Society of Obstetricians and Gynecologists Canada 2022: "Health care providers should advise all women aged 12–45 years considering or planning a pregnancy about the benefits of taking an **oral daily multivitamin** containing **folic acid (0.4–1.0 mg)** to optimize serum and red blood cell folate levels." (evidence: *strong, high*).<sup>2</sup>

1. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/folic-acid-for-the-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-of-neural-tube-defects-prevention-tube-defects-prevention-tube-defects-prevention-tube-defects-prevention-tube-defects-prevention-tube-defects-prevention-tube-defects-prevention-tube-defects-prevention-tube-defects-prevention-tube-defects-prevention-tube-defects-prevention-tube-def

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Choline in Pregnancy

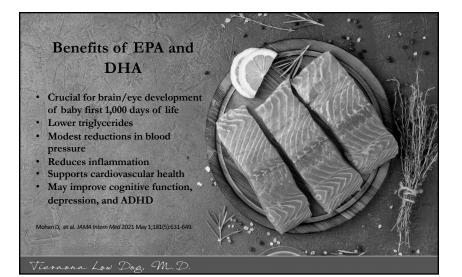


- ACOG, AMA, AAP, EFSA, WHO: all conclude that choline is *crucially important* during pregnancy.<sup>1</sup>
- Pregnant women: 450 mg/d, lactating women: 550 mg/d.
- ~90–95% pregnant women consume less than recommended amounts of choline.
- Review 38 animal & 16 human studies: supplementing mother/child's diet first 1,000 days of life:
  Supports normal brain development
  - Protects against neural/metabolic insults, particularly when fetus exposed to alcohol.<sup>2</sup>
  - Improves neural and cognitive functioning.<sup>3</sup>

1. Schwarzenberg SJ. Poliatrici. 2018:141. doi: 10.1542/peds.2017-3716. 2. Derbyshire E, et al. Natrinut/2020 Jun 10;12(6):1731. 3. Brunst KJ, et al. BMJ 2010 May 20;340:e2181.

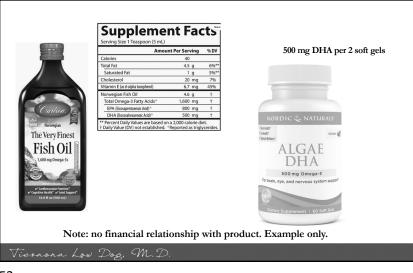
Choline Content Per Serving	(	rcent		Indian in Drogan anon d'~ I actation
Food	serving DV			Iodine in Pregnancy & Lactation
Beef liver, pan fried, 3 ounces	356	65		0 2
Egg, hard boiled, 1 large egg	147	27		
Beef top round, separable lean only, braised, 3 ounces	117	21	• Crucial	nutrient, especially during pregnancy.
Soybeans, roasted, ½ cup	107	19	infancy	nutrient, especially during pregnancy, and childhood when thyroid hormones
Chicken breast, roasted, 3 ounces	72	13	regulate	growth in developing brain.
Beef, ground, 93% lean meat, broiled, 3 ounces	72	13		
Fish, cod, Atlantic, cooked, dry heat, 3 ounces	71	13		enciency associated with autistic
Potatoes, red, baked, flesh and skin, 1 large potato	57	10		um disorder, ADHD, learning
Wheat germ, toasted, 1 ounce	51	9	disabili	ities, and dyslexia. <sup>1</sup>
Beans, kidney, canned, ½ cup	45	8	• Women	n in US (20–39 yrs) have median urine
Quinoa, cooked, 1 cup	43	8	iodine c	concentrations <i>borderline insufficient</i> . <sup>2</sup>
Milk, 1% fat, 1 cup	43	8	• Americ	can Thyroid Association: women
Yogurt, vanilla, nonfat, 1 cup	38	7		
Brussels sprouts, boiled, ½ cup	32	6	lactating	g on becoming pregnant, are pregnant or g, take supplement containing 150
Broccoli, chopped, boiled, drained, ½ cup	31	6	https://ods.od.nih.gov/factsheets/Choline_ mcg/d	potassium iodide. <sup>3</sup>
Mushrooms, shiitake, cooked, ½ cup pieces	27	5	HealthProfessional/#en16 Accessed July 17,	•
Cottage cheese, nonfat, 1 cup	26	5	2021	<ol> <li>Hay I, et al. Nativitat 2019 Aug 22;11(9):1974</li> <li>Pfeiffer CM, et al. J Natr 2013; 143(6): DOI:10.3945/jn.112.172858</li> <li>Stagnaro-Green A, et al. T/privid 2011;21(10):1081-1125</li> </ol>

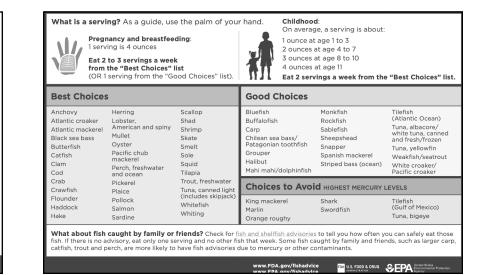
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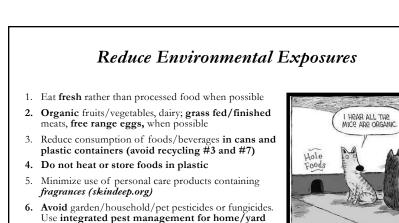


## Docosahexaenoic Acid (DHA)

- Cochrane analysis: high quality evidence preterm birth < 37 weeks and early preterm birth < 34 weeks reduced in women receiving omega-3 LCPUFA compared with no omega-3. Moderate evidence of reduced perinatal death.<sup>1</sup>
- Analysis of 2003–2012 NHANES data for 788 pregnant women in the US found daily consumption approximately **66 mg DHA and 34 mg EPA**.<sup>2</sup>
- Recommendation pregnant/breastfeeding women: consume 8-12 ounces lowmercury seafood per week. Many global scientific/expert committees recommend 200 mg/d DHA.<sup>3</sup> Algal-derived supplements are available for vegetarians/vegans.
- 1. Middleton P et al. Cochrane Database Syst Rev 2018 Nov 15;11(11):CD003402.
- 2. Nordgren TM, et al. Nutrients. 2017;9(3):197. doi: 10.3390/nu9030197
- GOED Global Recommendations for EPA and DHA Intake. https://www.jssfal.orp/assets/plobalrecommendationssummarv19nov2014landscape -3-.pdf.Accessed November 11, 2022

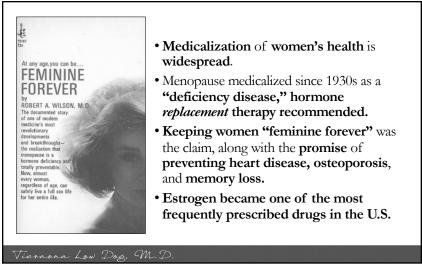






7. Use water filtration system (ewgs-water-filter-buyingguide), consider HEPA filters in home







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#### Three benchmark stages of natural menopause:

- 1. Perimenopause (or the menopause transition) is the span of time between the start of symptoms (such as erratic periods) and 1 year after the final menstrual period.
- 2. Menopause is confirmed 1 year (12 months) after the final menstrual period.
- 3. Post-menopause is *all the years* beyond menopause.

#### Symptoms can start up to 10 years prior

- Hot flashes
- · Sleep disturbances
- Vaginal dryness
- Mood changes
- · Difficulty concentrating
- Memory impairment
- Bladder irritability/urgency
- Changes in balance
- · Decreased interest in sex, decreased response to sexual stimulation

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# Hormone Therapy (HT)

- HT most effective treatment for **vasomotor symptoms** (VMS) and **genitourinary syndrome of menopause** (GSM).
- Risks of HT differ depending on type, dose, duration of use, route of administration, timing of initiation, and progestogen.
- Women <60 years or within 10 years of menopause onset without contraindications: benefit-risk ratio most favorable for treatment of VMS and those at higher risk for bone loss or fracture.
- Women >60 years or who initiate HT >10 years from menopause onset: benefit-risk ratio less favorable because of greater absolute risks of coronary heart disease, stroke, blood clots, and dementia.

Practice Guideline: Menopause 2017 Jul;24(7):728-753

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	Difference Associated With Combined Placebo in Postmenopausal Women	Table 2. Estimated Event Rate Difference Associated With Estroger Alone vs Placebo in Postmenopausal Women				
Outcome	Absolute Event Rate Difference per 10 000 Woman-Years (95% CI)	- Outcome	Absolute Event Rate Difference per 10 000 Woman-Years (95% CI)			
Harms		Harms				
Breast cancer (invasive)	9 (1 to 19)					
Coronary heart disease	8 (0 to 18)	Dementia (probable) <sup>a</sup>	12 (-4 to 41)			
Dementia (probable) <sup>a</sup>	22 (4 to 53)	Gallbladder disease	30 (16 to 48)			
Gallbladder disease	21 (10 to 34)	Stroke	11 (2 to 23)			
Stroke	9 (2 to 19)	Venous thromboembolism <sup>b</sup>	11 (3 to 22)			
Venous thromboembolism <sup>b</sup>	21 (12 to 33)	Urinary incontinence	1261 (880 to 1689)			
Urinary incontinence	876 (606 to 1168)	Benefits				
Benefits		Breast cancer (invasive)	-7 (-14 to 0.4)			
Diabetes	-14 (-24 to -3)	All fractures	-53 (-69 to -39)			
All fractures	-44 (-71 to -13)					
Colorectal cancer	-6 (-9 to -1)	Diabetes	-19 (-34 to -3)			
Women aged 65 years and olde	r.	<sup>a</sup> Women aged 65 years and olde	r.			
Includes deep vein thrombosis	and pulmonary embolism.	<sup>b</sup> Includes deep vein thrombosis	and pulmonary embolism.			

 $\label{eq:constraint} \begin{array}{l} \mbox{Hormone Therapy for the Primary Prevention of Chronic Conditions in Postmenopausal Women US Preventive Services Task Force Recommendation Statement. JAMA. 2017;318(22):2224-2233. \end{array}$ 

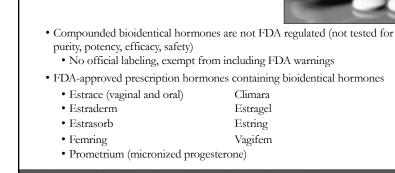
## Hormone Route and Type

- Transdermal estrogen LEAST likely to cause blood clots.1
- HT associated with increased risk of breast cancer; risk predominantly mediated by synthetic progestins. Micronized progesterone safer to use.<sup>2</sup>
- If symptoms primarily urinary and/or vaginal, vaginal estrogen should be used (has minimal systemic absorption).<sup>3</sup>
- ACOG: there is no biologically meaningful relationship between **salivary** sex hormone concentrations **and free serum hormone** levels. Salivary hormone levels **vary with diet, time of day, and other variables.**

Sobel TH, Shen W. Menopause 2022 Jan 14;29(4):483-490.
 Abenhaim HA, et al. Obstet Gynecol 2022 Jun 1;139(6):1103-1110.
 Practice Guideline: Menopause 2017 Jul;24(7):728-753

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**Bio-identical** 

Hormones

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## Vaginal Moisturizers and Lubricants

- Moisturizers (used regularly)
  - Replens-2 studies in breast cancer survivors, highly effective
  - Moist Again
  - K-Y Liqui-beads and K-Y Silk-E
- Lubricants (used during intercourse)
  - Pre-Seed—best tolerated
  - Slippery Stuff Gel (formerly Femglide)-hypo-osmotic (water-based)
  - K-Y Yours + Mine
  - YES (derived from flax extract, guar, locust bean, xanthan gum)
  - Astroglide-hyperosmotic, may cause irritation

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## Soy and Breast Cancer

- European Food Safety Authority concluded after a multi-year investigation that in postmenopausal women, soy isoflavones *do not* adversely affect the breast, thyroid, or uterus.
- North American Menopause Society concluded that soy isoflavones *do not* increase risk of breast or endometrial cancer.
- American Cancer Society and American Institute for Cancer Research confirm soy foods can be safely consumed by women with breast cancer.

Panel on Food Additives and Nutrient Sources added to Food Scientific opinion on the risk assessment for peri- and post-menopausal women taking food supplements containing isolated isoflavones. *EISA J.* 2015;13:4246. Messina M. Nutrients 2016; 8(12):754

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## Research & Traditional Use

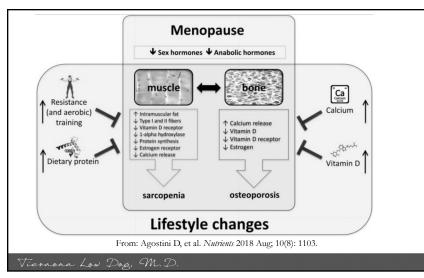


- Soy isoflavones may reduce severity and frequency of hot flashes
- Black cohosh not traditionally used for menopause; studies mixed
- St John's wort for hot flashes, moodiness, etc.\*
- $\bullet$  Maca for low libido and mood.
- Saffron for low libido and mood.
- Consider adaptogens (e.g., ashwagandha, bacopa, rhodiola)

\*Note: watch for drug interactions

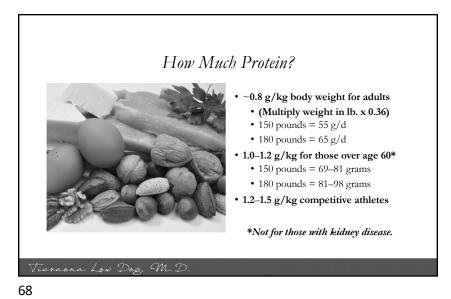
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Micronutrient	Ages 51-70 Years, % < EAR	Ages ≥71 Years, % < EAR	Women > 50 years
Folate 🗲	10.6 🗲	▶ 17.0	
Niacin	1.3	4.0	should take a good
Riboflavin	2.6	3.4	multivitamin, with
Thiamin	6.0	8.9	emphasis on
Vitamin A	39.2 🗲	▶ 37.2	*
Vitamin B <sub>6</sub>	15.6	22.4	vitamins B6, B12,
Vitamin B <sub>12</sub>	5.2	4.9	D, E, K; as well as
Vitamin C 🔸	42.1	▶ 44.2	calcium and
Vitamin D 🖌	94.6	95.5	
Vitamin E 🗕	85.0 4	91.7	magnesium.
Vitamin K*	48.7	62.9	
Calcium	51.4	72.9	
Copper	4.1	9.6	
Iron	<1	<1	
Magnesium 4	<b>-</b> 51.3 <b>-</b>	▶ 68.6	
Phosphorus	<1	2.1	Table from:
Selenium	<1	2.4	https://lpi.oregonstate.edu c/micronutrient-
Zinc 🔸	- 17.9 <b>-</b>	26.1	inadequacies/subpopulatio

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## Fast Facts on Calcium

- Most abundant mineral in body. Comprises most of bone and tooth structure; supports blood vessel contraction/dilation, muscle contraction, blood clotting, nerve transmission, etc.
- Absorption of dietary calcium: ~60% in infants/children, decreases to ~25% in adults, and continues to decline with age.
- **Deficiency** can lead to osteoporosis (low vitamin D levels, more Ca needed to maintain bone health); symptoms: **dry skin, muscle cramps, fatigue, etc.**
- Calcium content in **kale family** (broccoli, bok choy, cabbage, mustard, turnip greens) is as **bioavailable as in milk.**
- Don't take within 3 hours: antibiotics, thyroid meds, bisphosphonates.

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Table 2: Calcium Content of Selected Foods [12]							
Food*	Milligrams (mg) per serving	Percent DV*	C	alciu	m		
Yogurt, plain, low fat, 8 ounces	415	32					
Orange juice, calcium fortified, 1 cup	349	27					
Yogurt, fruit, low fat, 8 ounces	344	27					
Mozzarella, part skim, 1.5 ounces	333	26					
Sardines, canned in oil, with bones, 3 ounces	325	25	Age	Male	Female	Pregnant	Lactating
Milk, nonfat, 1 cup**	299	23	0-6 months*	200 mg	200 mg		
Soymilk, calcium fortified, 1 cup	299	23	7-12 months	* 260 mg	260 mg		
Milk, whole (3.25% milk fat), 1 cup**	276	21	1-3 years	700 mg	700 mg		
Tofu, firm, made with calcium sulfate, ½ cup***	253	19	4-8 years	1 000 mg	1.000 ma		
Salmon, pink, canned, solids with bones, 3 ounces	181	14	9-13 years		1,300 mg		
Cottage cheese, 1% milk fat, 1 cup	138	11					
Tofu, soft, made with calcium sulfate, ½ cup***	138	11	14-18 years			1,300 mg	
Soybeans, cooked, ½ cup	131	10	19-50 years	1,000 mg	1,000 mg	1,000 mg	1,000 m
Breakfast cereals, fortified with 10% of the DV for calcium, 1 serving	130	10	51-70 years	1,000 mg	1,200 mg		
Spinach, boiled, drained, ½ cup	123	9	>70+ years	1,200 mg	1,200 mg		
Frozen yogurt, vanilla, soft serve, ½ cup	103	8					
Turnip greens, fresh, boiled, ½ cup	99	8	*Adequate Int	ake (AI)			
Kale, fresh, cooked, 1 cup	94	7					
Chia seeds, 1 tablespoon	76	6				1.5 (24 (22)	
Chinese cabbage (bok choi), raw, shredded, 1 cup	74	6		both image		,	
Beans, pinto, canned, drained, ½ cup	54	4	ods.od.nih.j HealthProf	gov/factshee essional/#h4	ts/Calcium-		
Tortilla, corn, one, 6" diameter	46	4					

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## Vitamin D & Musculoskeletal Health

- Deficiency can cause rickets in children; osteomalacia in adults leading to musculoskeletal pain in the pelvis, shoulders, low back, and proximal muscles.
- In addition to its crucial role in **bone health**, vitamin D has been shown to **positively affect muscle strength**, **muscle size**, and neuromuscular **performance**.



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

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## Vitamin D & Respiratory Infection



Martineau AR, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. *BMJ* 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).

## Don't Forget the Vitamin K

- Calcium, vitamins D and K , and magnesium contribute independently and collectively to bones.
- Beneficial role of vitamin K, particularly vitamin K2, in bone and cardiovascular health is *reasonably* well supported scientifically, with preclinical, epidemiological, and clinical studies published over the last decade.
- Vitamin K2 (MK-7) 100-200 mcg per day.

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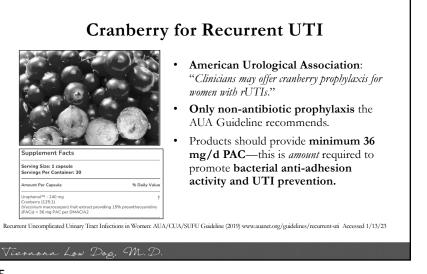
Karpinski M, et al. Roles of Vitamins D and K, Nutrition, and Lifestyle in Low-Energy Bone Fractures in Children and Young Adults. J Am Coll Nutr 2017 Jul;36(5):399-412.

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6-12 months         400 <sup>d</sup> 1,500           1-3 years         600         2,500	Intake 400-1,000 400-1,000 600-1,000	Upper Limit <sup>c</sup> 2,000
6-12 months         400 <sup>d</sup> 1,500           1-3 years         600         2,500	400-1,000	
1-3 years 600 2,500		0.000
	600-1 000	2,000
4-8 years 600 3,000		4,000
	600-1,000	4,000
9-18 years 600 4,000	600-1,000	4,000
19-30 years 600 4,000	1,500-2,000	10,000
31-50 years 600 4,000	1,500-2,000	10,000
51-70 years 600 4,000	1,500-2,000	10,000
71+ years 800 4,000	1,500-2,000	10,000
Pregnant or lactating women 600 4,000 (14-18 years)	600-1,000	4,000
Pregnant or lactating women 600 4,000 (19-50 years)	1,500-2,000	10,000

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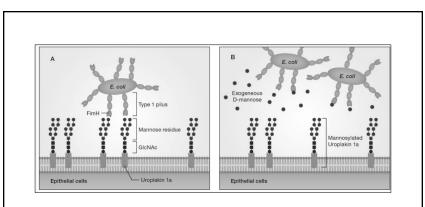


Image from: Antibiotics 2022, 11(3), 314; https://doi.org/10.3390/antibiotics11030314

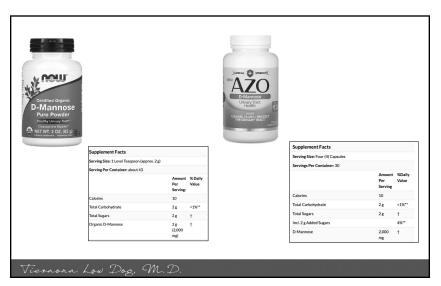
## **D**-mannose for Recurrent UTI



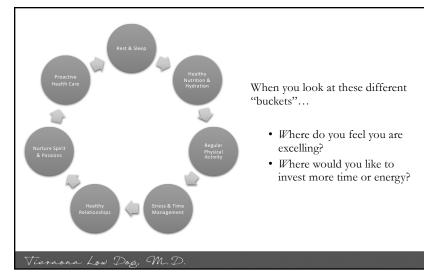
- After antibiotic treatment for acute cystitis, 308 women with history of recurrent UTI randomized to one of three groups:
  - 2 g/d mannose powder in 200 ml water
  - 50 mg/d nitrofurantoin
  - No prophylaxis
- ~15% recurrence in D-mannose, 20% in nitrofurantoin and 61% no treatment group.<sup>1</sup>
- 2020 Systematic Review: D-mannose protective for recurrent UTI (vs placebo) with
  possibly similar effectiveness as antibiotics. Overall, D-mannose appears well
  tolerated with minimal side effects—only a small percentage experiencing diarrhea.<sup>2</sup>

Kranjece B, et al. D-mannose powder for prophylaxis of recurrent urinary tract infections in women: a randomized clinical *livalIJ Uril* 2014; 32(1):79-84
 Lenger SM, et al. D-mannose yo other agents for recurrent urinary tract infection prevention in adult women: a systematic review and meta-analysis. Am J Ostatokis Granowog 200; 29:223: August 2010; Appe 235:62-435:621

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- Women's health is a state of well-being in which a woman feels creative, strong and wise.
- Her innate healing power is vital and intact.

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- She feels valued and heard.
- She is free to choose and decide; she honors her own rhythms and journey.

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