DRUG-SUPPLEMENT INTERACTIONS AND NUTRIENT DEPLETIONS IN OLDER ADULTS

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Disclosure

- Dr. Mathis has no conflict of interests to disclose.

Goals

Review the mechanisms of Drug Nutrient Interactions and Drug Nutrient Depletions

Discuss various drug nutrient interactions

Explore possible drug nutrient depletions

Increase the frequency of physician-patient dietary supplement discussions during office visits.

Question

- What percentage of older US adults with chronic disease use dietary supplements?

A. 0-20%

B. 20-40%

C. 40-60%

D. 60-80%

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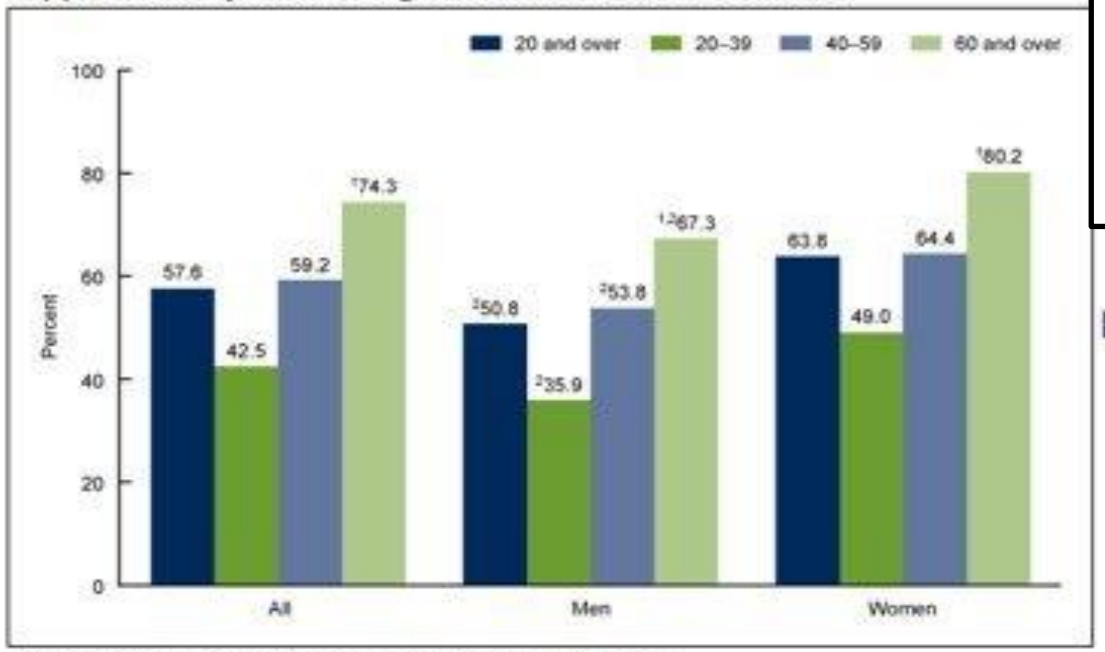
Figure 1. Percentage of adults aged 20 and over who used any dietary supplement, by sex and age: United States, 2017–2018



[1]Significant linear increasing trend with age.

[2]Significantly different from women of the same age group.

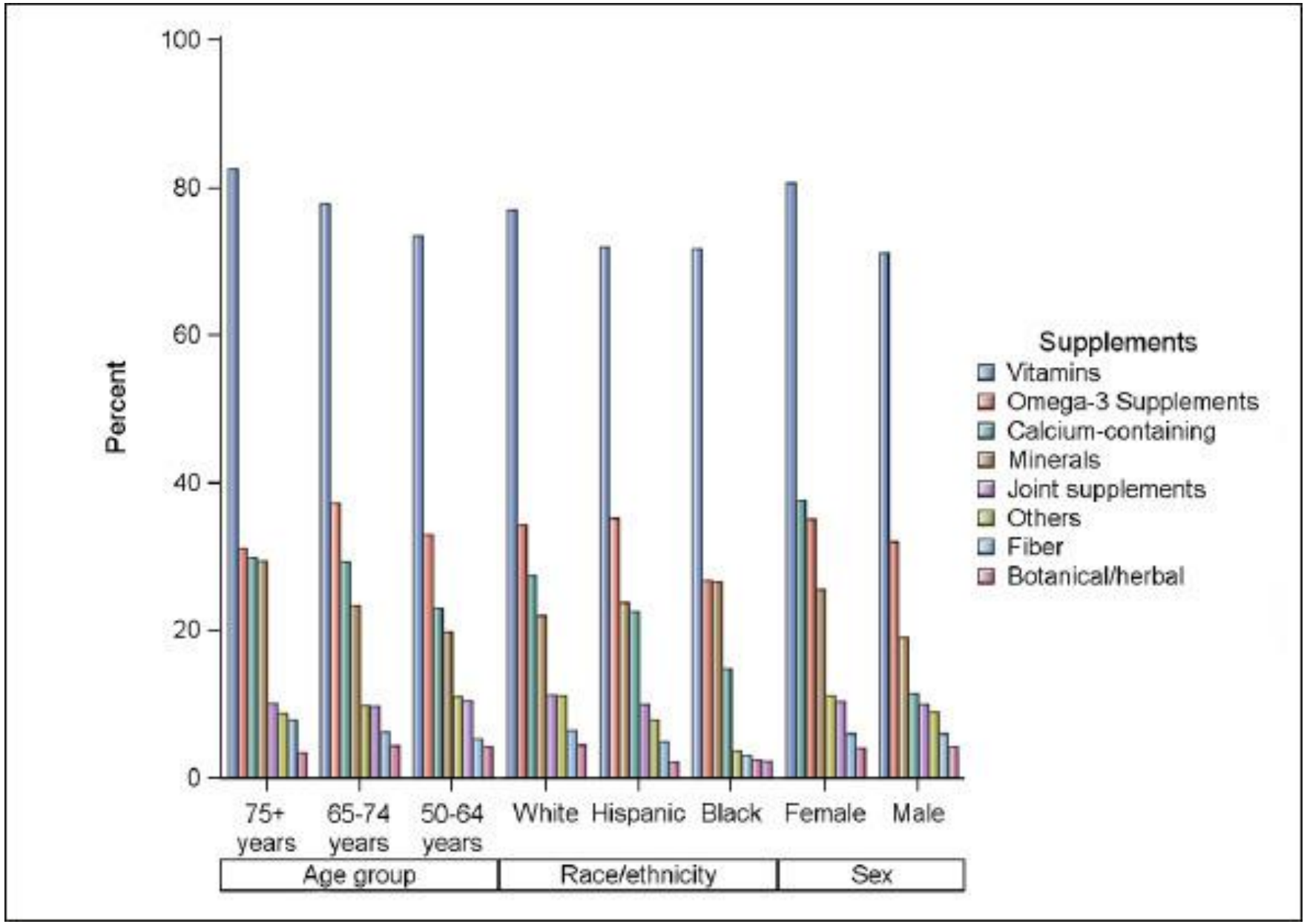
NOTES: Access data table for Figure 1 .

SOURCE: National Center for Health Statistics, National Health and Nutrition Examination Survey, 2017–2018.

Poll finds 86% of Americans Take Vitamins or Supplements Yet Only 21% Have a Confirmed Nutritional Deficiency

Osteopathic Physicians Say Vitamins Are Unnecessary for Most People

AOA
AMERICAN OSTEOPATHIC ASSOCIATION
TREATING OUR FAMILY AND YOURS



Tan ECK, Eshetie TC, Gray SL, Marcum ZA. Dietary Supplement Use in Middle-aged and Older Adults. J Nutr Health Aging. 2022;26(2):133-138. doi: 10.1007/s12603-022-1732-9. PMID: 35166304.

Why is this important?

- ~80% of older adult patients use dietary supplements
- 25% of patient's do not inform their physician of their supplement use.[1]
- Missing the main ingredient[2]
  - *No FDA testing requirements[3]*
  - *Mixed with medications/supplements*
  - *Label does not have to be true*
- Lack of solid research
  - *Mostly case reports on adverse reactions*
  - *No RCTs*

Understanding Drug-Supplement Interactions

- Pharmacodynamics:
  - *Synergistic vs Antagonistic interactions*
  - *Either increases or diminished the effect*
- Pharmacokinetic[6]
  - *Absorption*
  - *Distribution*
  - *Metabolism*
  - *Excretion*

Question

Mrs. Smith is a 67 y/o female with PMH of HTN, HLD, DM 2 that is controlled with rosuvastatin, lisinopril, and metformin. She reports that she does take some supplements and has recently started a new grapefruit juice protocol she heard about from a TV doctor. Since starting juicing she has noted increased muscle cramps and wants to stop her statin because her friend said that they cause muscle cramps. You inform her that the juice is likely causing this reaction through what pathway?

A. CYP450 3A4 enzyme blockage in the liver decreasing metabolism of the statin
B. CYP450 3A4 enzyme blockage in the intestines causing increased absorption of statin
C. Mercaptan competitively preferentially cleared by renal tubules, decreasing excretion of statin
D. The grapefruit juice tasted so good she forgot she took her medicine and has been taking an extra dose.

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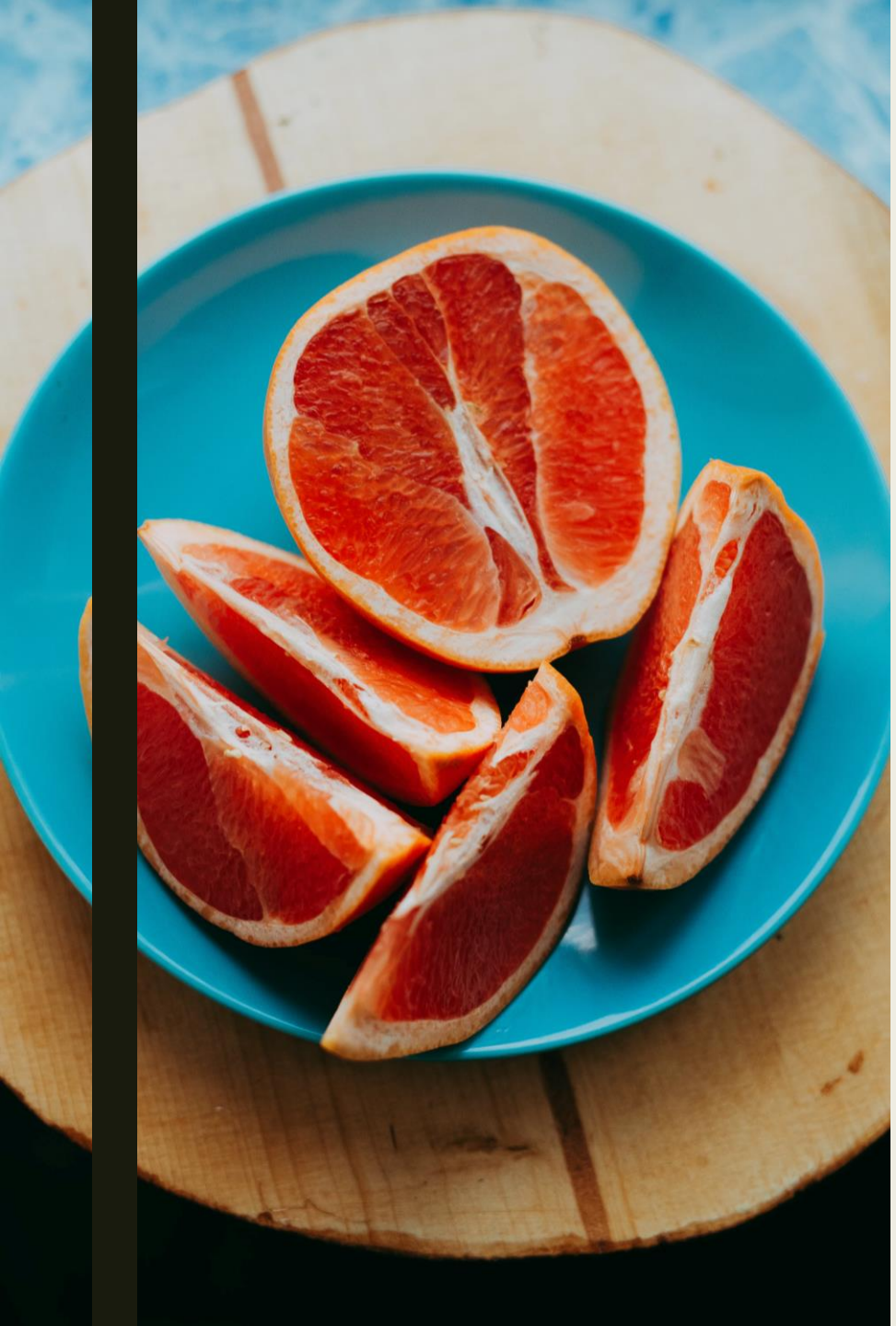

Grapefruit

- Most studied dietary supplement
- Interacts on CYP450 3A4 in the intestines.
- Interactions:[4]
  - *Calcium Chanel Blockers*
  - *Angiotension II Receptor Blockers*
  - *Beta Blockers*
  - *Antiarrythmics*
  - *Anti-cancer agents*
  - *Statins*
- Use it to our benefit?
  - *Increases simvastatin/lovastatin levels by 260%*[5]

Foods:

- Food as Medicine
- Numerous Food/Drug interaction possibilities[7]
  - *Milk: Ca^{2+} & Casein bind with tetracyclines and fluoroquinolones to reduce amount absorbed.*[8]
  - *Dark Leafy Greens:*
    - Potassium – Increased concentrations if taken with ACE Inhibitors
    - Vitamin K - Decreased INR with Warfarin
  - *Tyramine containing foods (matured cheese, red wine, yogurt, salami)*
    - Hypertensive crises if taken with MAOIs.

Coca-Cola

- Increased max concentration of ibuprofen if taken with Coca-Cola.[10]
- Recommend decrease amount or frequency of ibuprofen
- Study in rabbits – No human studies

Coumadin

Increase INR[9]

Acetaminophen
Amiodarone
Antifungal agents
Aspirin
Celecoxib
Clopidogrel
Anticoagulants
Ropinirole
Sulfamethoxazole-TMP
Tamoxifen
Acarbose
Allopurinol
Antibiotics
Levothyroxine
Vitamin E
Statins
SSRI Antidepressants
Antipsychotics
Diabetes medications
Influenza vaccine
EtOH

Decrease INR

Barbiturates
Phenobarbital
Phenytoin
Rifampin
St. John's Wort
Azathioprine
Carbamazepine
Coenzyme Q10
Colestipol
Estrogens
Green Tea
Ginseng
Vitamin K
Vitamin C
Soy
Methimazole
Mesalamine
Propylthiouracil
Primidone
Spironolactone
Sucralfate
Sulfasalazine

Question?

- Mrs. Smith returns to you a few months later complaining of depressive symptoms. She reports this is having significant impact on her competitive ballroom dancing. You recommend starting an antidepressant, which she is open to, but she suddenly remembers some integrative therapies she has read about that may also help. Which of the following IS NOT an appropriate adjunctive to her SSRI?

A. Regular exercise and a healthy diet

B. Adding 3,000mg of Fish oil daily

C. Adding 300mg St. John's Wort daily

D. Visiting her local acupuncturist for relaxation therapy

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St. John's Wort (*Hypericum perforatum*)

- Natural antidepressant
- Induces CYP3A4 and P-glycoprotein[11]
- Few case studies showing serotonin syndrome if taken with SSRIs[12]
- May cause decreased absorption of digoxin
- Breakthrough bleeding with oral contraceptives
- High doses to cause interaction[13]
- Avoid concurrent use with prescription and OTC medications
- May worsen photosensitivity with antibiotics

Ginseng (American/Asian)

- American Ginseng (panax quinquefolius)
  - *May cause small decrease in INR.*
- Asian Ginseng (panax ginseng)[11, 12]
  - *Root used for concentration, mood, memory, general well-being.*
  - *Decrease effect of Calcium Channel Blockers (blood pressure), chemotherapy, HIV, statins, and antidepressant medications*
  - *Warfarin: Decreased INR (Decreased bleeding)[13]*
  - *Phenelzine (MAOI): mania,[14] headache, tremors*
  - *Alcohol: Increased clearance in mice.[12]*

Goldenseal

- Used for URIs, UTIs, allergies, bleeding, infections, fatigue, etc.
- No great human trials for interactions
- Known to inhibit enzymes CYP2D6 & CYP3A4[11]
  - *Responsible for over half of all metabolized drugs.*
- Recommend against use as no good trials for or against it.

Ginkgo biloba

- Used for: improved cognition, blood flow
- No obvious interactions with metabolism
- Interactions
  - *ASA, coumadin, anticoagulants: Increased bleeding (case studies)*[11]
  - *Thiazides: One case of elevated BP*[12]
- Caution if taking other supplements or medications with antiplatelet or anticoagulant effects – could increase bleeding risk.
- Food Fraud?

https://www.youtube.com/watch?v=t6R-8ICyv7M

Food Fraud?

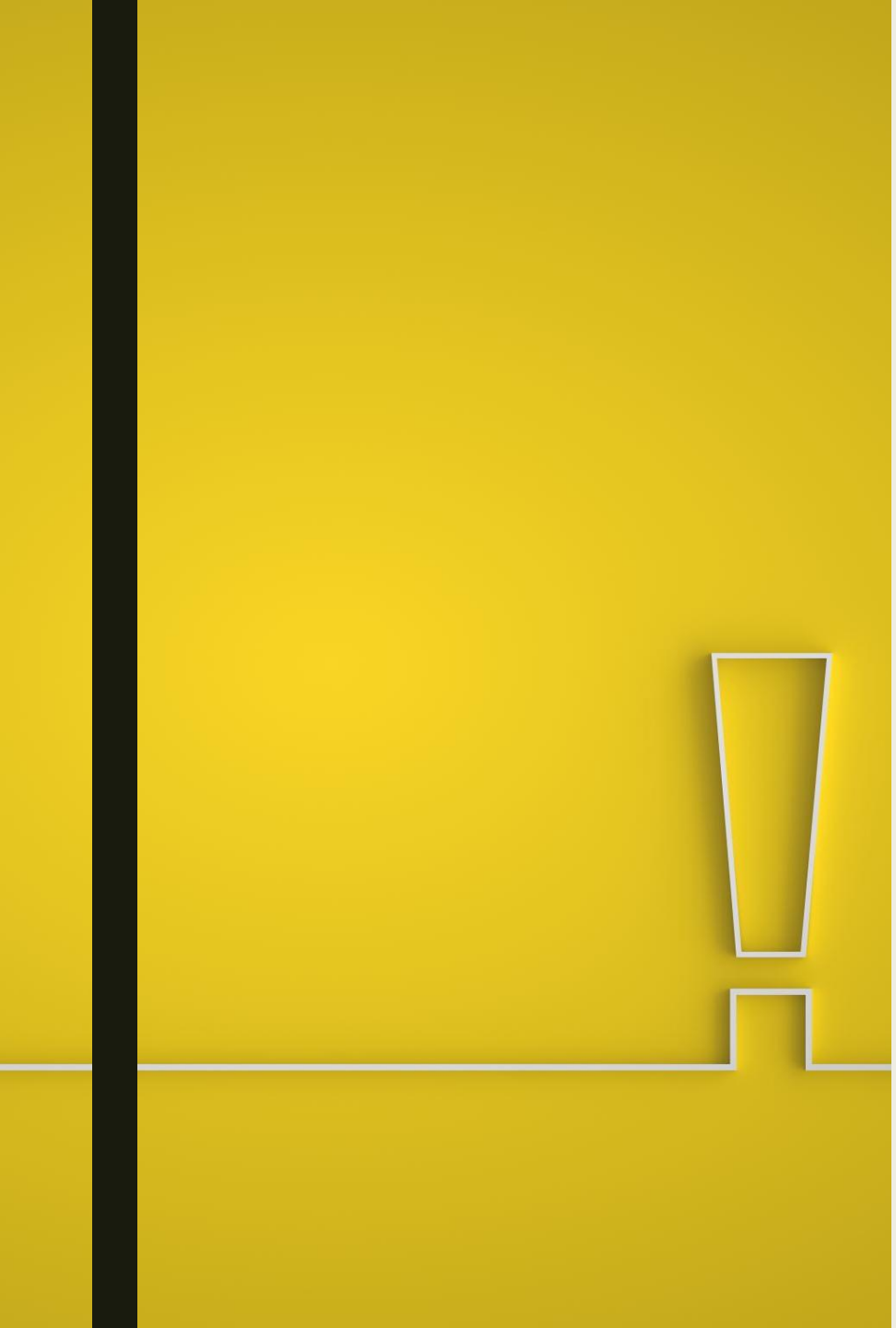
- 67% of all supplements contained undeclared adulterants [27]
- 2015 NY attorney general investigation:[28]
  - *80% of all supplements on Walmart, Walgreens, GNC, and Target walls were fake*

3rd party verification

- United States Pharmacopeial Convention
- NSF International
- Consumer Lab

Green Tea Extract

- “Jesus and Green Tea”
- Conflicting results In vitro vs human clinical trials
- May inhibit drug transporters[11]
  - *OATP1A1/OATP1A2*
  - *Involved in transport of statins, fluoroquinolones, beta blockers, antiretrovirals*
- Green Tea vs Extract



Milk Thistle (*Silybum marianum*)

- Used to help boost liver function
- CYP2C9
  - *Involved with losartan, warfarin, phenytoin, diazepam.*
  - *Depends on individuals genotype*[15]

Low Risk Supplements

- Cranberry
- Black Cohosh
- Curcumin
- Saw Palmetto
- Valerian[11]

DRUG NUTRIENT DEPLETIONS

Question

- Mrs. Smith comes to see you with a new complaint of fatigue. She reports that 2 months ago, her GI started her on a medication for her reflux. On physical exam, she appears slightly pale which prompts a CBC which shows she has anemia. You suspect the anemia is caused by what nutritional deficiency?

A. Vitamin B12 deficiency caused by proton pump inhibitor use

B. Iron deficiency caused by H2 Blocker use

C. CoQ10 deficiency caused by Bismuth subsalicylate

D. Copper deficiency caused by a zinc deficiency from proton pump inhibitor use

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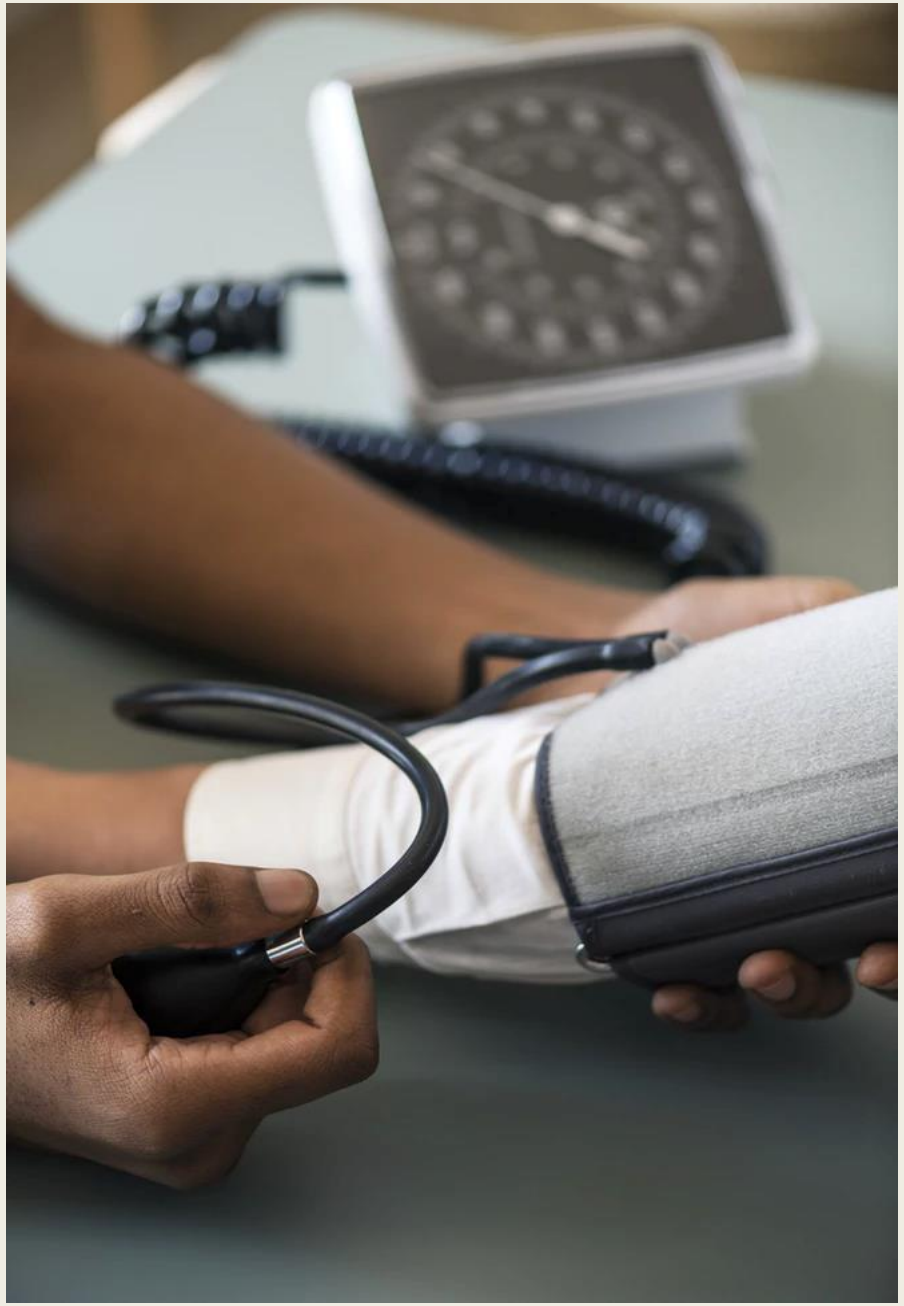
Acid Suppressing Medications

- H2 Antagonists[21]
  - *Deplete calcium, iron, zinc, folic acid, vitamin D, vitamin B12*
  - *Recommended supplementation:*
    - Calcium citrate: 500mg/day
    - Folic Acid: 400mcg/day
- Proton Pump Inhibitors[18]
  - *Deplete vitamin B12, magnesium*
  - *Recommended supplementation*
    - Vitamin B12: 25-400mcg/day
    - Magnesium: 250-400mg/day

Antihypertensives

- Angiotensin Converting Enzyme Inhibitors
  - *Depletes Zinc*[19]
  - *Recommended supplementation*
    - Zinc: <30mg/day
- Calcium Channel Blockers/ Thiazides
  - *Deplete Potassium*
  - *Recommended supplementation*
    - Potassium: <100mg/day
- Beta Blockers
  - *Deplete CoQ10*
  - *Recommended supplementation*
    - CoQ10: 100-200mg/day



Diuretics

- Loop Diuretics (lasix)[21]
  - *Depletes magnesium, potassium, zinc*
  - *Recommended supplementation*
    - Magnesium: 250mg/day
    - Potassium: <100mg/day
    - Zinc: <30mg/day
- Potassium-sparing diuretics (spironolactone)
  - *Depletes folic acid*
  - *Recommended supplementation*
    - Folic Acid: 400mcg/day

Hormonal agents

- Contraceptives & Hormone replacement therapy (Estrogens)[20]
  - *Depletes vitamin B6, folic acid, magnesium*
  - *Recommended supplementation*
    - Vitamin B6: 5mg/day
    - Folic Acid: 400mcg/day
    - Magnesium: 250-400mg/day

Psychotropics

- SSRIs[25]
  - *Deplete Folic Acid*
  - *Recommended supplementation*
    - Folic Acid: 400mcg/day
- Benzos[26]
  - *Depletes Calcium and melatonin*
  - *Recommended supplementation*
    - Calcium: 500-1000mg/day divided dosing
- Antipsychotics[24]
  - *Depletes Vitamin B2 (riboflavin)*
  - *Recommended supplementation*
    - Multivitamin: 1/day
    - B-complex: 1/day

Question

What supplement should be considered for all patients taking competitive inhibitors of the HMG-CoA reductase?

A. Turmeric
B. Fish Oil
C. Zinc
D. Coenzyme Q 10

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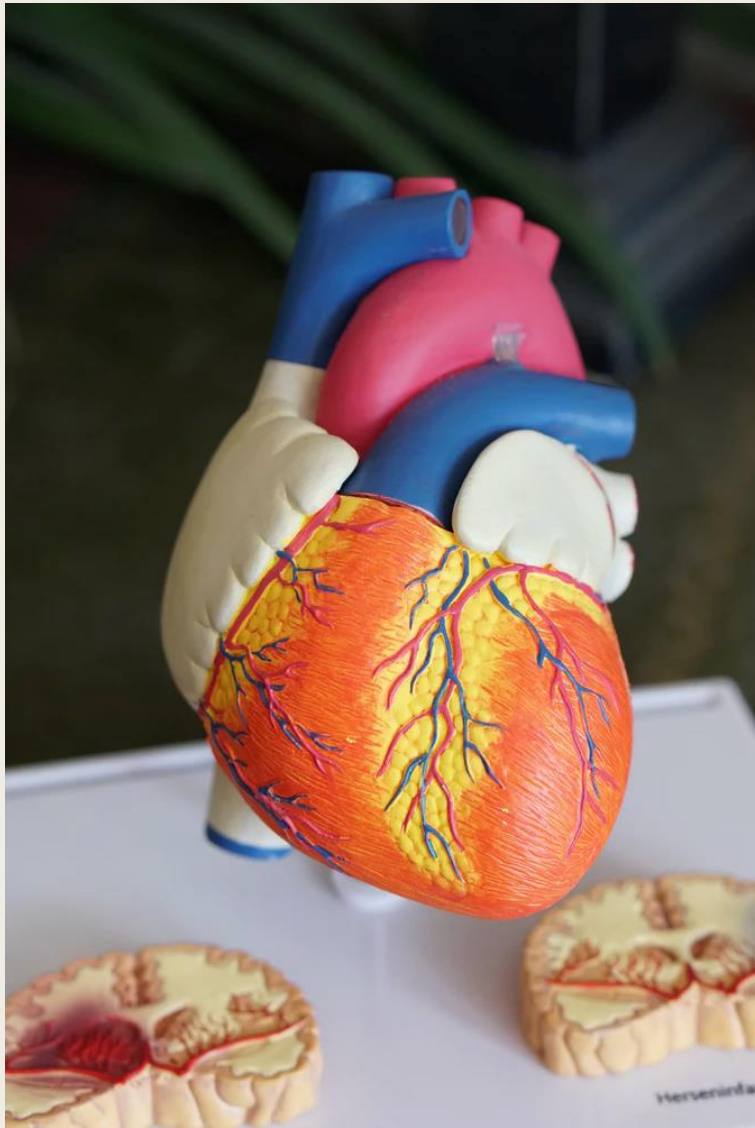
Cardiac

- Statins[17]
  - *Deplete Coenzyme Q 10*
  - *Recommended supplementation*
    - CoQ10: 100-200mg/day
- Digoxin
  - *Depletes calcium, magnesium, phosphorus, vitamin B1 (thiamin), potassium*
  - *Recommended supplementation*
    - Calcium: 500-1000mg/day
      - *High Calcium → toxic reaction to digoxin*
      - *Low Calcium → interference with digoxin's function*
    - Magnesium: 250-400mg/day
    - B-complex
    - Potassium: <100mg/day



Antibiotics

- Antibiotics[25]
  - *Deplete folic acid, vitamin B1, vitamin B2, vitamin B6, vitamin B12, calcium, magnesium, potassium, vitamin K*
  - *Recommended supplementation*
    - B-Complex
    - Calcium: 500-1000mg/day
    - Magnesium: 250-400mg/day
- Caution
  - *Many supplements can interfere with absorption of antibiotics.*
  - *Hold or take them separately*

Rules for Supplements

- Best way to get nutrition is through healthy diet[22]
- “Eat food, not too much, mostly plants.” – Michael Pollan
- Less is best
  - *3-5 supplements, no more than 10*
- Consumerlab.com
  - *~$50/year*
- Natural Medicines Database
- Be open

How to talk to patients[16]

- “Are you taking any herbal products, supplements, or other natural remedies?”
- “Have you used any herbal products or supplements recently?”
- “Do you use any natural or nutritional supplements?”

- No judgement!

Questions?


Thank You

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