Vitamins and aging: Vitamania?

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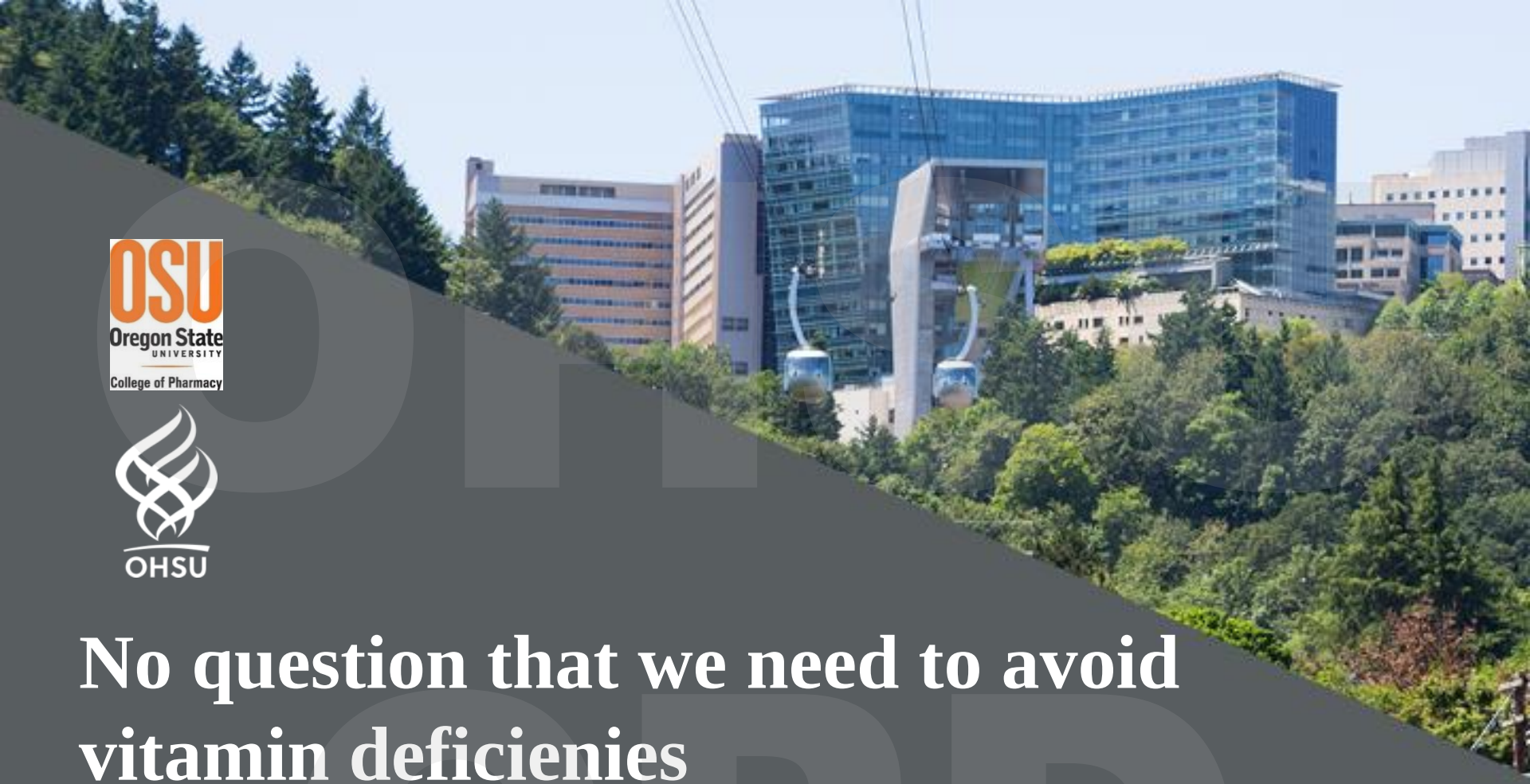
Declarations: No conflicts of interest with any content



No question that we need to avoid vitamin deficienies

Patient in mid-50's with alcohol use disorder admitted to OHSU March, 2022….

This is the early stages of scurvy

IRB 00024339

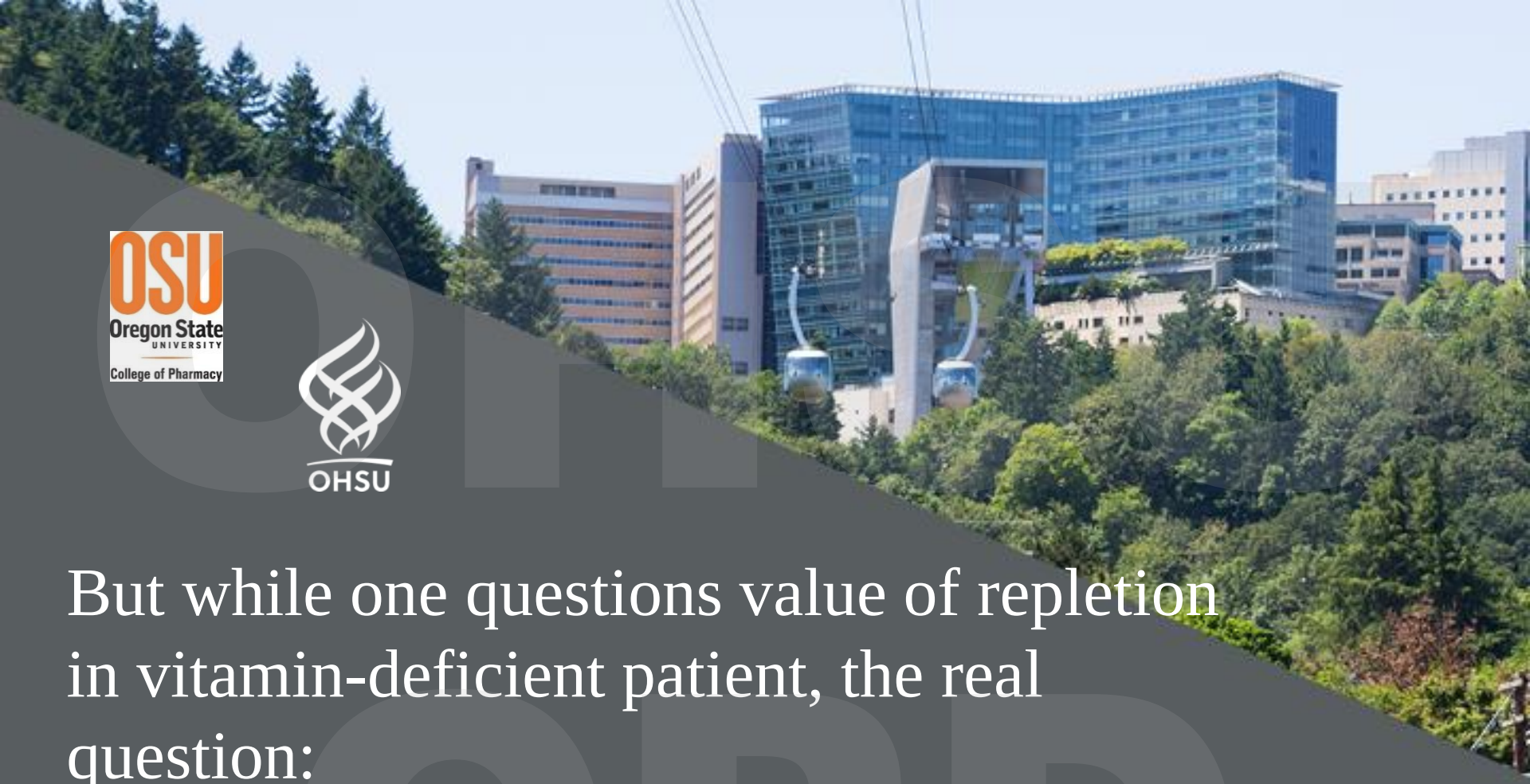
VITAMIN C, PLASMA

Status: **Final result** Visible to patient: **No (not released)**

0 Result Notes

Component	Ref Range & Units	8 d ago
VITAMIN C (LAB)	23 - 114 umol/L	<5 ⌄

Comment: `INTERPRETIVE DATA: Vitamin C (Ascorbic Acid), Plasma`



But while one questions value of repletion in vitamin-deficient patient, the real question:

What role does vitamin **supplementation** play in patients who are generally healthy

Objectives:

1. **What are vitamins?**
2. **A little background on regulatory environment**
3. **Why natural may not be the way to think about "natural products" including vitamins**
4. **The data – and do the elderly differentiate?**
5. **What now?**

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Background: What is a vitamin (vital amines):

There are 13 human vitamins (ADEK are fat soluble and C and the B vitamins [8 in all] are water soluble) and all are classified as essential micronutrients. Micronutrients to distinguish them from….

Macronutrients (fat, carbohydrate and protein) provide caloric nutrition whereas vitamins are essential enzymes which help to catalyze intracellular reactions…

And "essential" because we need them from our diet. Interestingly, mammalian cells have the DNA machinery to synthesize vitamins but it has been suppressed due to millennia of sufficient dietary consumption by our ancestors (we literally evolved to eat our vitamins in our food)

What do vitamins do, how much do we need for them to do their job?

Vitamins are … vital in the micro doses t… great example of the vital natu… own maritime history of scu…

Scurvy is a di… uction. Collagen is literally the… muscle, blood vessels, bones… procollagen and that react…

But it will be… truly at risk for scurvy (t… rs)…..or from Ricketts fro…

So how much… ence for ‘supplementi… ?

The RDA…..

Recommended Daily Allowance is poorly understood…It is the amount of a specific vitamin that is needed by the upper 97th percentile of the population (2 standard deviations from that mean) to avoid a deficiency.

The RDA is NOT the amount that the average person needs (97% could get by with less) and is also NOT a daily goal. Vitamins last a long time in our system and what is important is average consumption over time. Needed amounts for good health are tiny.

Example: Vitamin D. Popular vitamin past decade. RDA is 600 IU is 15 microgram (0.000015 gm) which is about 1/10 of a grain of table salt. The RDA for Vit. B12 is 1/7 that or 2.4 mcg!

So, vitamins work inside cells and last a long time and we don't need much of them at all for them to do their jobs

But this is America – if a little is good, more must be better

If micro doses of vitamins cure things like scurvy and Ricketts, imagine what larger doses could do?

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https://www.fda.gov/food/dietary-supplements/information-consumers-using-dietary-supplements

Labeling & Nutrition

Nutrition Facts Label, Label Claims, Menu & Vending Machine Labeling, Gluten-Free Labeling

Ingredients & Packaging

Food & Color Additives, GRAS, Food Allergens, Food Contact Substances, New Plant Varieties

Food Defense

Protecting the Food Supply, Intentional Adulteration, Food Defense Plan Builder

Dietary Supplements

Products & Ingredients, New Dietary Ingredients Notification Process, Structure/Function Claim Notifications

Science & Research

Laboratory Methods, Whole Genome Sequencing, Risk Analysis, Total Diet Study, Consumer Research

Compliance & Enforcement

Reportable Food Registry, Warning Letters, Inspections, Compliance Programs, Adverse Event Reporting

International & Interagency Coordination

International Outreach, Visitor's Program, Trade Agreements, Interagency Agreements

Chemical Contaminants & Pesticides

Acrylamide, Arsenic, Chemical Contaminants, Toxins & Pesticides in Food

Dietary Supplements

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https://www.fda.gov/food/dietary-supplements/information-consumers-using-dietary-supplements

Information for Consumers on Using Dietary Supplements

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Dietary Supplements can be beneficial to your health — but taking supplements can also involve health risks.

Because dietary supplements are under the "umbrella" of foods, FDA's Center for Food Safety and Applied Nutrition (CFSAN) is responsible for the agency's oversight of these products. The Dietary Supplement Health and Education Act (DSHEA) of 1994, which amended the Federal Food, Drug, and Cosmetic Act, created a new regulatory framework for the safety and labeling of dietary supplements. **FDA is not authorized to review dietary supplement products for safety and effectiveness before they are marketed.**

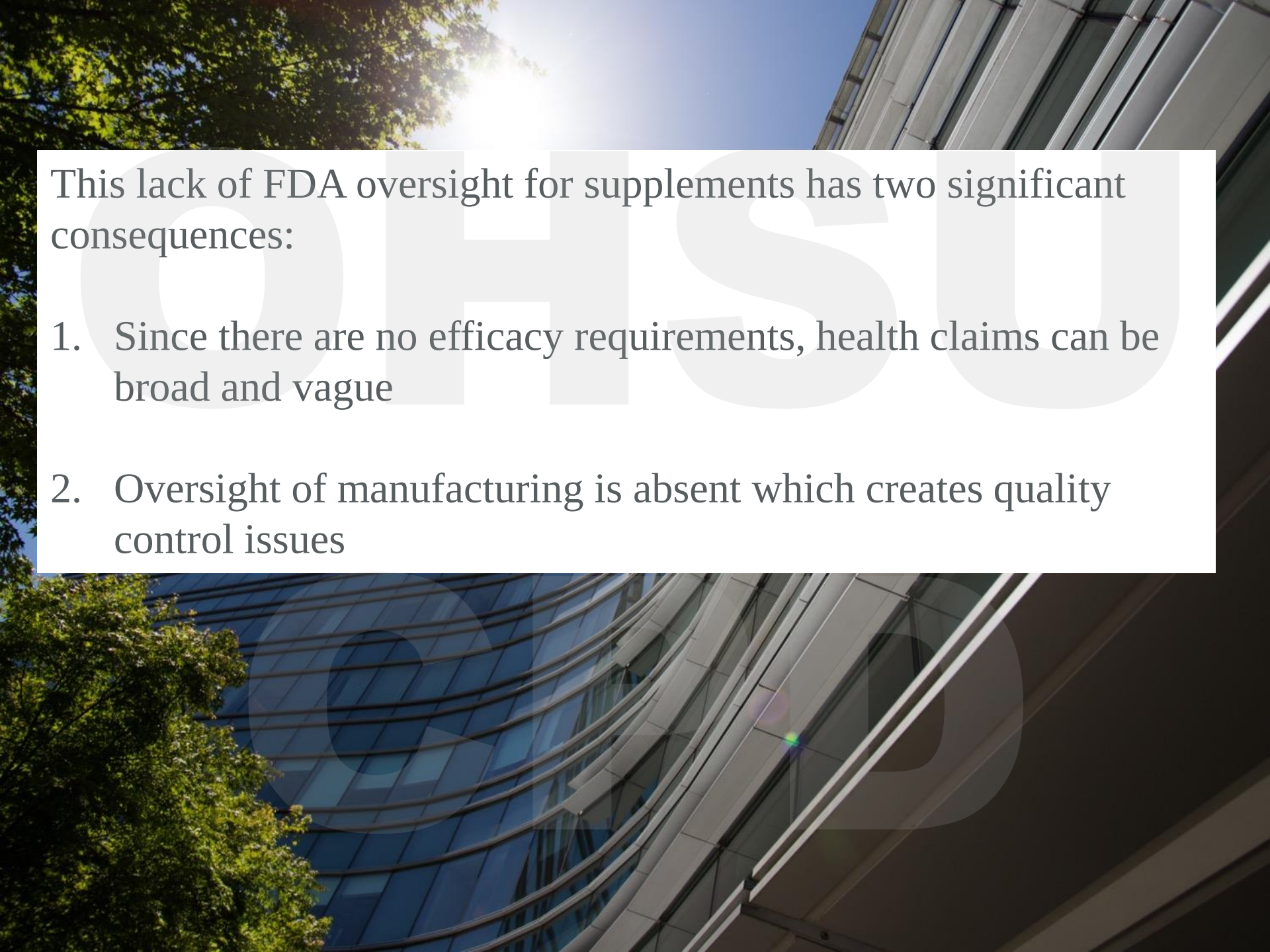
In 1990, congress passed NLEA (Nutrition Labeling and Education Act) in response to a number of incidents which culminated in a few dozen deaths from L-tryptophan (the turkey amino acid).

NLEA was aimed at both food and supplement labels with a goal of eliminating false advertising. Labeling changes were left to the FDA but….

Sen. Orin Hatch (from Utah - where about ½ of all supplements were manufactured at the time) along with the company and owner of NatureMade worked hard to pass DSHEA (Dietary Supplement Health and Education Act) which passed in 1994.

DSHEA exempted supplements (including vitamins) from NLEA and established the current legal standard that "supplements are to be considered safe unless the FDA can prove otherwise."

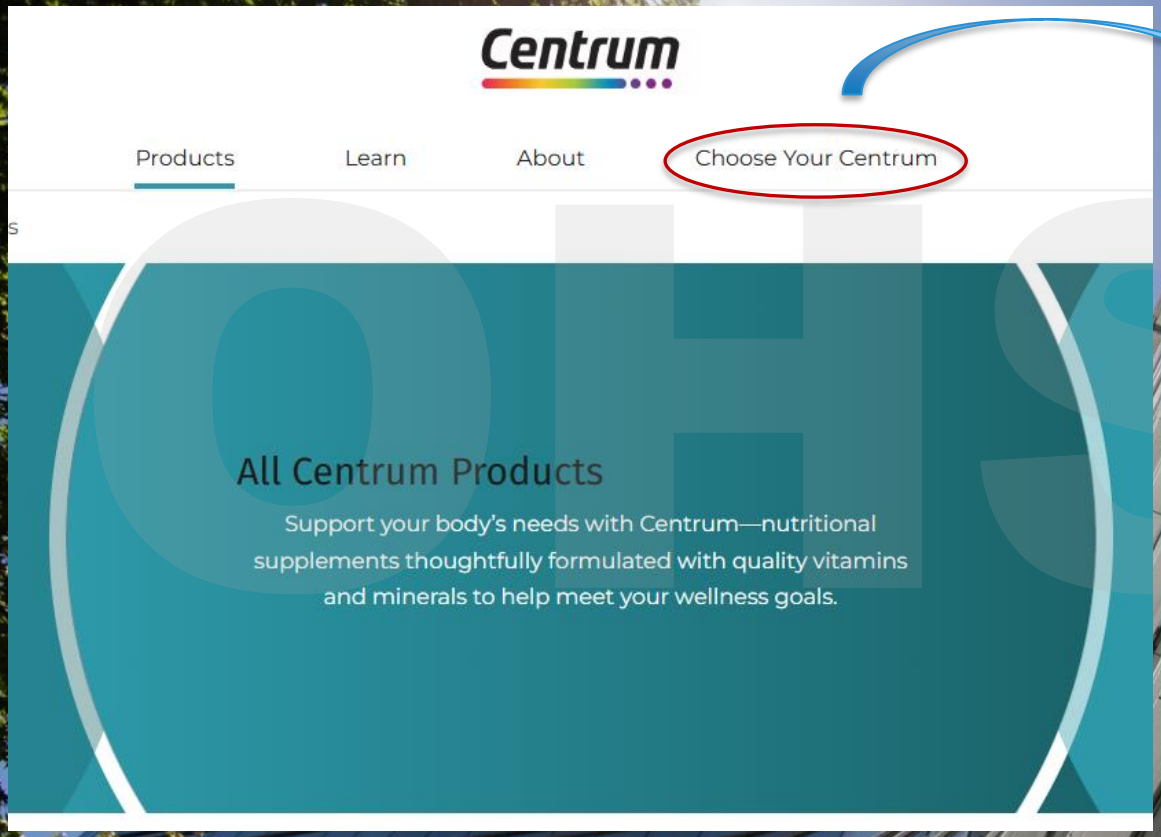
The opposite of how we treat prescription drugs and this remains in place in 2025



This lack of FDA oversight for supplements has two significant consequences:

1. Since there are no efficacy requirements, health claims can be broad and vague

2. Oversight of manufacturing is absent which creates quality control issues



Take this short quiz to find out which Centrum products could be right for you

Start

Centrum MultiGummies Adults 50+

4.5 (1204) Write a review

Product Benefits | Vitamins & Minerals | Usage | FAQs

Heart Health

B vitamins to help promote heart health.+*

Brain Function

Zinc and B vitamins – key nutrients to support your brain health.*

Bone Health

A combination of vitamin D and calcium helps maintain strong bones.*

General Wellness

Packed with key essential nutrients important in supporting your whole body and to help meet your nutritional needs.*

Product Benefits | **Vitamins & Minerals** | Usage | FAQs

B12 Vitamin B12

Vitamin B12 is a water-soluble B vitamin with a key role in the normal functioning of metabolism and formation of blood.*

E Vitamin E

Vitamin E mainly functions in the body as an antioxidant, supporting heart and eye health, and plays a role in immune function.*

B7 Biotin

Biotin is essential for enzymes involved in metabolism and it supports hair, skin, and nail cells.*

D Vitamin D

Vitamin D is central to healthy bones and influences cell growth and immune function, keeping inflammation in check.*

B6 Vitamin B6

Vitamin B6 plays a role in supporting the nervous system and the production of immune system cells.*

B5 Pantothenic Acid

Pantothenic acid is a B vitamin that assists in a wide variety of functions including generating energy from carbohydrates, fats, and proteins.*

**This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.*

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Especially since NLEA/DSHEA, Supplement use is big business:

The National Health and Nutrition Examination Survey (NHANES) added vitamins/supplements to their survey in the 1990s:
As of 2018, approximately ½ of adult Americans reported supplement use and ~1/3 reported their kids also took supplements

Current annual expenditure in the U.S. ~ $40,000,000,000 ($40 billion). For comparison, prescription drugs cost ~ $500 billion.
So, vitamins and supplements are big business

This lack of FDA oversight for supplements has two significant consequences:

1. Since there are not efficacy requirements, health claims can be broad and vague

2. Oversight of manufacturing is absent

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Synthetic vitamin manufacturing is about as far from natural foods as you can get:

From *Pandora's Lunchbox* by Melanie Warner:

Commercial vitamin C (ascorbic acid) typically begins as sorbitol which is fermented in bacterial broths to sorbose which is fermented further in a broth of genetically modified bacteria to 2-ketogluconic acid. That is treated with hydrochloric acid to form crude ascorbic acid which is filtered and purified to Vitamin C.

This lack of FDA oversight for supplements has two significant consequences:

1. Since there are not efficacy requirements, health claims can be broad and vague

2. Oversight of manufacturing is absent

    1. Unintended chemicals that shouldn't be in your OTC Vitamin C are in there and

    2. Intended chemicals that also shouldn't be there might be present

SPECIAL ARTICLE

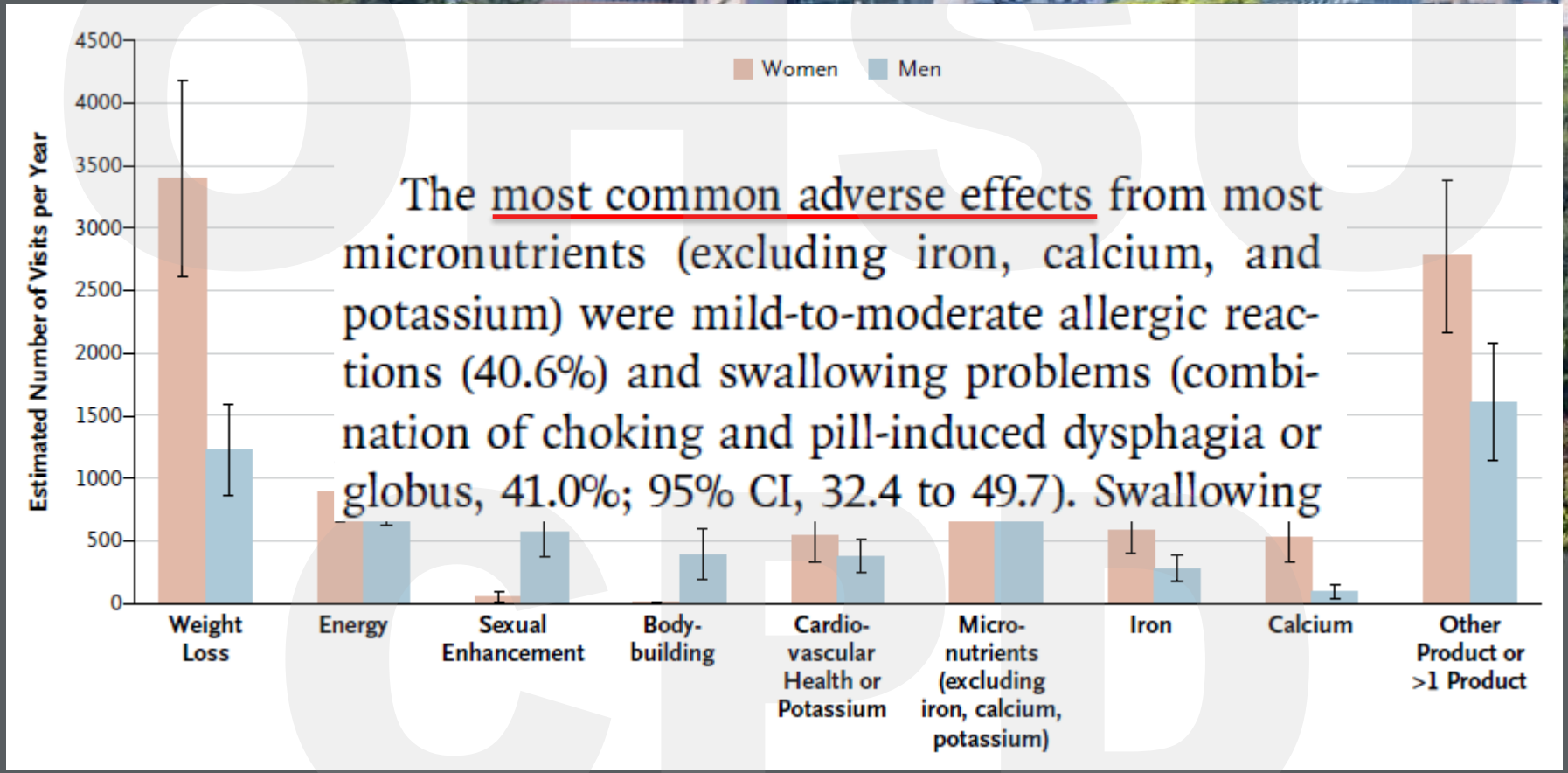
Emergency Department Visits for Adverse Events Related to Dietary Supplements

Andrew I. Geller, M.D., Nadine Shehab, Pharm.D., M.P.H., Nina J. Weidle, Pharm.D., Maribeth C. Lovegrove, M.P.H., Beverly J. Wolpert, Ph.D., Babgaleh B. Timbo, M.D., Dr.P.H., Robert P. Mozersky, D.O., and Daniel S. Budnitz, M.D., M.P.H.

NEJM, 2015;373:1531-40

63 ED departments surveilled for 10 years with data then extrapolated nationally. Estimate ~ 23,000 ED visits annually

Micronutrients which included vitamins accounted for about 1/3 of total….



The most common adverse effects from most micronutrients (excluding iron, calcium, and potassium) were mild-to-moderate allergic reactions (40.6%) and swallowing problems (combination of choking and pill-induced dysphagia or globus, 41.0%; 95% CI, 32.4 to 49.7). Swallowing

OSU Oregon State University College of Pharmacy

› Arch Environ Contam Toxicol. 1993 Jul;25(1):134-42. doi: 10.1007/BF00230724.

Contaminants in L-tryptophan associated with eosinophilia myalgia syndrome

R H Hill Jr [1], S P Caudill, R M Philen, S L Bailey, W D Flanders, W J Driskell, M L Kamb, L L Needham, E J Sampson

Affiliations + expand

PMID: 8346973 DOI: 10.1007/BF00230724

JAMA Network Open

August, 2022

Original Investigation | Public Health

Analysis of Select Dietary Supplement Products Marketed to Support or Boost the Immune System

Cindy Crawford, BA; Bharathi Avula, PhD; Andrea T. Lindsey, MS; Abraham Walter, MS; Kumar Katragunta, PhD; Ikhlas A. Khan, PhD; Patricia A. Deuster, PhD, MPH

CONCLUSIONS AND RELEVANCE In this case series study, most of the products tested had inaccurate labels and claims that were inconsistent with requirements the US Food and Drug Administration has put forward for dietary supplements. Quality control measures seem to be insufficient for most of these select products, and claims made on labels may be misleading consumers who purchase products.

JAMA Network Open. 2022;5(8):e2226040. doi:10.1001/jamanetworkopen.2022.26040

43% of products had ingredients listed on the label that were NOT contained in the bottle

30% had substances detected which were NOT listed on the label

This lack of FDA oversight for supplements has two significant consequences:

1. Since there are not efficacy requirements, health claims can be broad and vague

2. Oversight of manufacturing is absent

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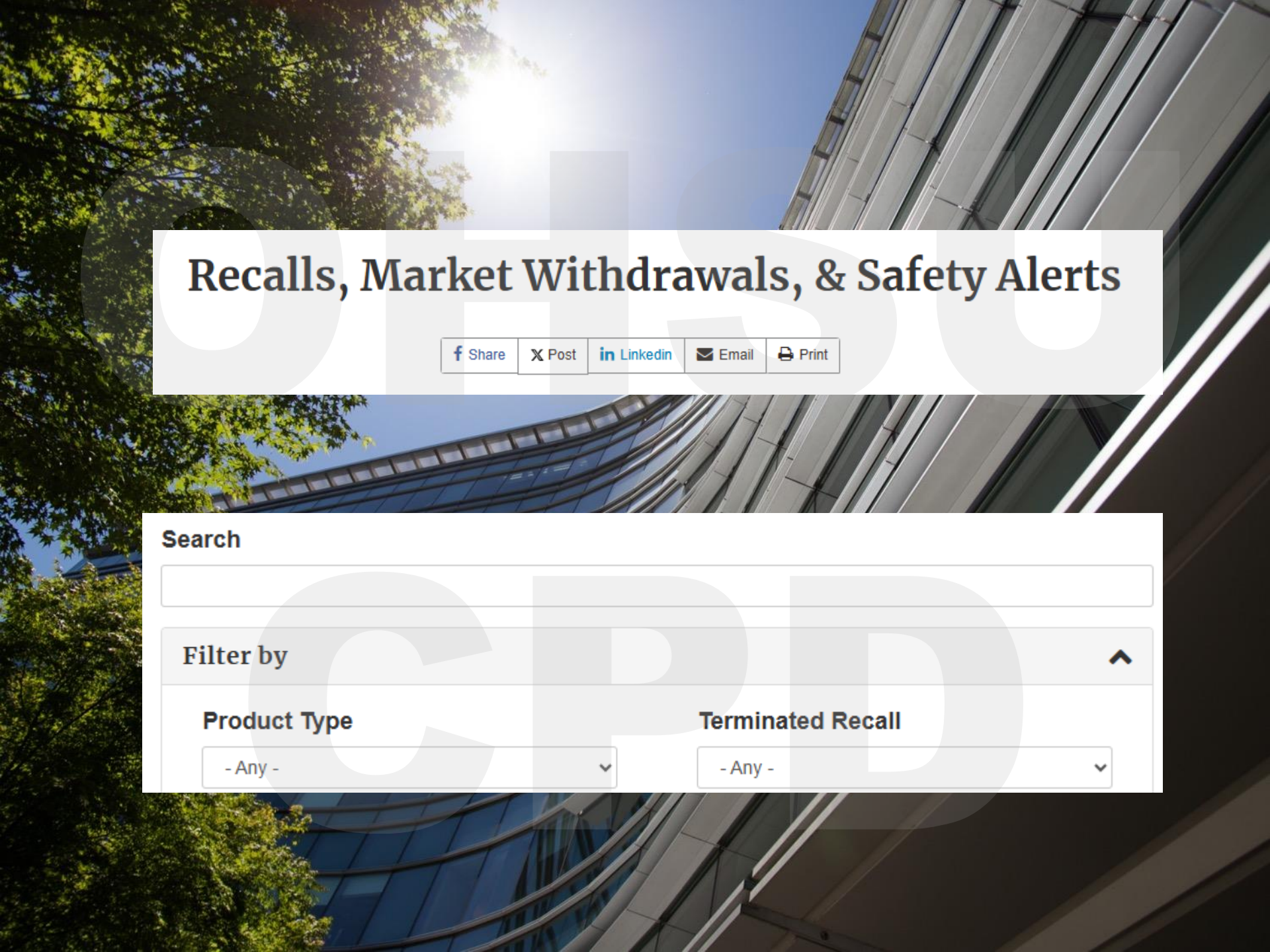
    2. Intended chemicals that also shouldn't be there might be present



Recalls, Market Withdrawals, & Safety Alerts

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Search

Filter by

Product Type

- Any -

Terminated Recall

- Any -

Showing 1 to 10 of 898 entries

Export Excel | Show 10 entries

Date	Brand Name(s)	Product Description	Product Type	Recall Reason Description	Company Name	Terminated Recall
12/16/2024	Force Forever	Dietary Supplement	Dietary Supplements	Product contains undeclared diclofenac and dexamethasone	GNMART Inc	
10/16/2024	AK Forte	AK Forte Dietary Supplement	Drugs	Device & Drug Safety – Unapproved Drug	C&A Naturistics	
07/15/2024	Umary	Umary Acido Hialuronica, Suplemento Alimenticio – 30 Capletas de 850mg	Drugs	Tainted with the drug ingredients, diclofenac and omeprazole	SoloVital.com	
07/12/2024	Supercore Products Group	Dietary Supplements for Male Sexual Enhancement.	Dietary Supplements	Tainted with Sildenafil and Acetaminophen.	Supercore Products Group	

If your email program has trouble displaying this email, view as a webpage.

MedWatch - The FDA Safety Information and Adverse Event Reporting Program

SHARE

TOPIC: Force Forever by GNMART INC: Recall - Due to Undeclared Drug Ingredients Diclofenac and Dexamethasone

AUDIENCE: Consumer, Health Care Professional, Pharmacy, Rheumatology, Cardiology

ISSUE: GNMART Inc. is recalling all lots of Force Forever for joint pain because FDA analysis has found product to contain undeclared diclofenac and dexamethasone. The affected product includes all lots and expiration date: 03/27/2030.

Risk Statement:

- Diclofenac is a non-steroidal anti-inflammatory drug (commonly referred to as NSAIDs). NSAIDs may cause increased risk of cardiovascular events, such as heart attack and stroke, as well as serious gastrointestinal damage, including bleeding, ulceration, and fatal perforation of the stomach and intestines.

- Dexamethasone is a corticosteroid commonly used to treat inflammatory conditions. Corticosteroid use can impair a person's ability to fight infections and can cause high blood sugar levels, muscle injuries and psychiatric problems.

Objectives:

1. **What are vitamins?**
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The wholesale movement of vitamin and supplement manufacturing oversees has removed the products from the purview of the FDA

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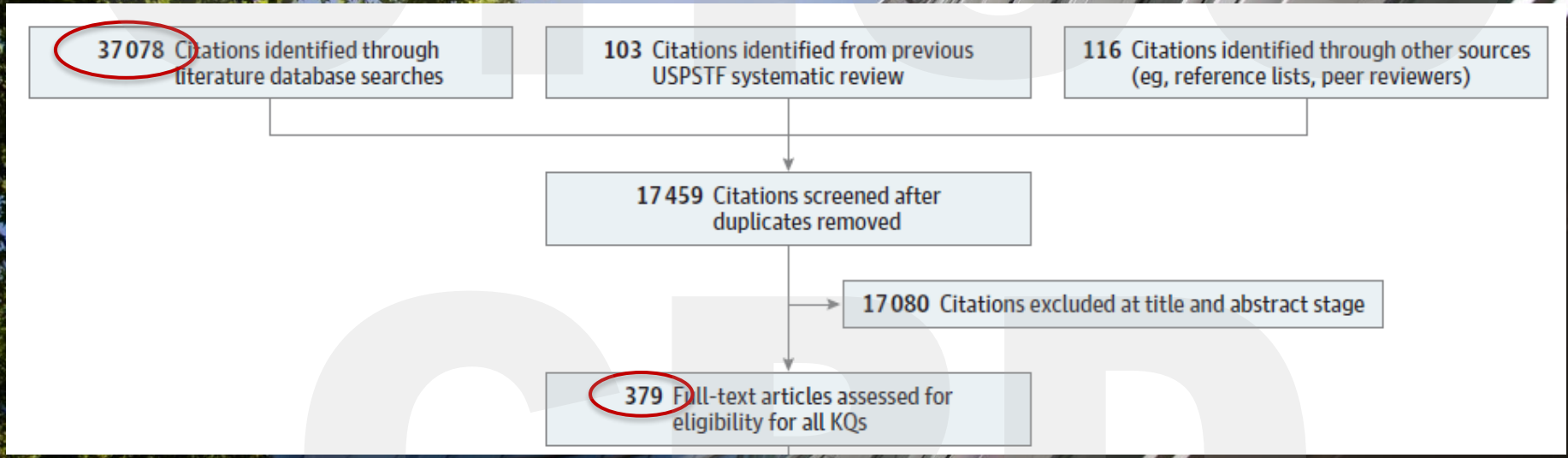
JAMA | US Preventive Services Task Force | EVIDENCE REPORT

Vitamin and Mineral Supplements for the Primary Prevention of Cardiovascular Disease and Cancer

Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

2022



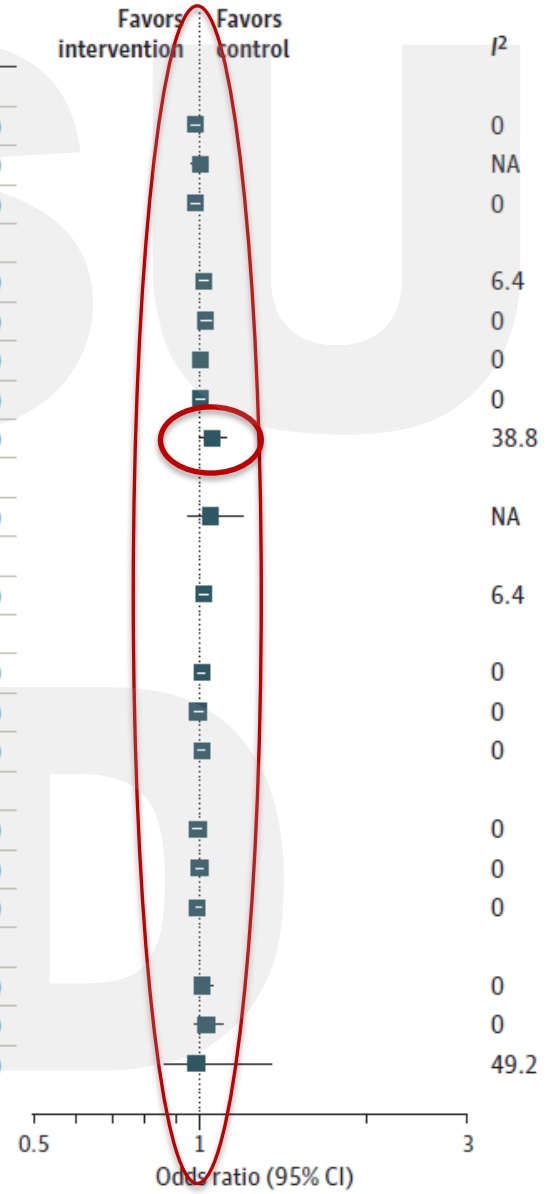
Goal: To answer four "Key Questions" using randomized, blinded trials with clear primary endpoints

Key questions

1. What is the efficacy of multivitamin supplementation for reducing cardiovascular disease, cancer, and mortality in the general adult population?
2. What are the harms of multivitamin supplementation in the general adult population?
3. What is the efficacy of supplementation with single nutrients or functionally related nutrient pairs for reducing cardiovascular disease, cancer, and mortality in the general adult population?
4. What are the harms of supplementation with single nutrients in the general adult population?

Figure 3. Summary of Meta-analysis Results or Best Evidence for Primary Key Question 1 and Key Question 3 Outcomes

Outcome	No. of studies	No. analyzed	% with event		Odds ratio (95% CI)	I^2
			Intervention	Control		
Multivitamin						
All-cause mortality[a]	9	51 550	7.3	7.7	0.94 (0.87-1.01)	0
CVD event[b]	1	21 442	4	4.1	0.98 (0.86-1.12)	NA
Any cancer[a]	4	48 859	8.5	9	0.93 (0.87-0.99)	0
Beta carotene						
All-cause mortality	6	112 820	5.4	5.1	1.06 (1.00-1.12)	6.4
CVD mortality	5	94 506	2.8	2.6	1.10 (1.02-1.19)	0
CVD events	2	61 947	3.5	3.5	1.01 (0.92-1.10)	0
Any cancer	2	61 947	5.3	5.4	0.99 (0.92-1.07)	0
Lung cancer[c]	4	94 830	1.2	1	1.20 (1.01-1.42)	38.8
Vitamin A						
All-cause mortality[d]	1	2297	5.4	4.6	1.16 (0.80-1.69)	NA
Beta carotene or vitamin A						
All-cause mortality	7	115 117	5.4	5.1	1.06 (1.01-1.12)	6.4
Vitamin E						
All-cause mortality	9	107 772	6.9	6.8	1.02 (0.97-1.07)	0
CVD events	4	62 136	5.1	5.2	0.96 (0.90-1.04)	0
Any cancer	5	76 777	8.8	8.6	1.02 (0.98-1.08)	0
Vitamin D						
All-cause mortality	27	117 082	5	5.7	0.96 (0.91-1.02)	0
CVD events	7	74 925	8.1	8.2	1.00 (0.95-1.05)	0
Any cancer	19	86 899	6.7	6.8	0.98 (0.92-1.03)	0
Calcium						
All-cause mortality	6	8394	13.1	12.7	1.05 (0.92-1.21)	0
CVD events	4	4076	10.7	9.7	1.11 (0.90-1.36)	0
Any cancer[a]	3	5051	8.7	8.9	0.94 (0.41-2.14)	49.2



ATBC trial, NEJM

The New England Journal of Medicine

Volume 330 APRIL 14, 1994 Number 15

THE EFFECT OF VITAMIN E AND BETA CAROTENE ON THE INCIDENCE OF LUNG CANCER AND OTHER CANCERS IN MALE SMOKERS

THE ALPHA-TOCOPHEROL, BETA CAROTENE CANCER PREVENTION STUDY GROUP*

Randomized, double-blind trial of 29,133 patients followed for 5-8 years; Ave age 57 years

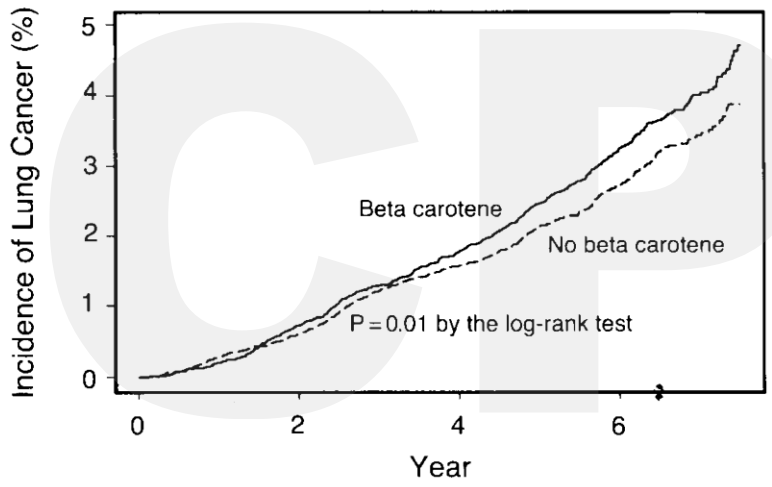


Figure 1. Kaplan–Meier Curves for the Cumulative Incidence of Lung Cancer among Participants Who Received Alpha-Tocoph-

Increased incidence of lung cancer in beta-carotene (Vit. A) group (p=0.01) and strong trend for increased lung cancer mortality (p=0.08)

The New England
Journal of Medicine

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Greater vitamin intake from the diet appeared protective…

Lung Cancer and Base-Line Alpha-Tocopherol and Beta Carotene Levels

When the placebo group was divided according to quartiles with regard to the base-line serum alpha-tocopherol or beta carotene concentration, the incidence of lung cancer was higher among the subjects in the lowest quartile group than among those in the highest (incidence per 10,000 person-years, lowest vs. highest quartile group: alpha-tocopherol, 56.8 vs. 41.8; beta carotene, 53.3 vs. 43.1). There was, moreover, an inverse association between dietary intake of alpha-tocopherol and beta carotene at base line and the risk of lung cancer during the trial (incidence per 10,000 person-years, lowest vs. highest: alpha-tocopherol, 61.4 vs. 40.6; beta carotene, 47.9 vs. 39.9).

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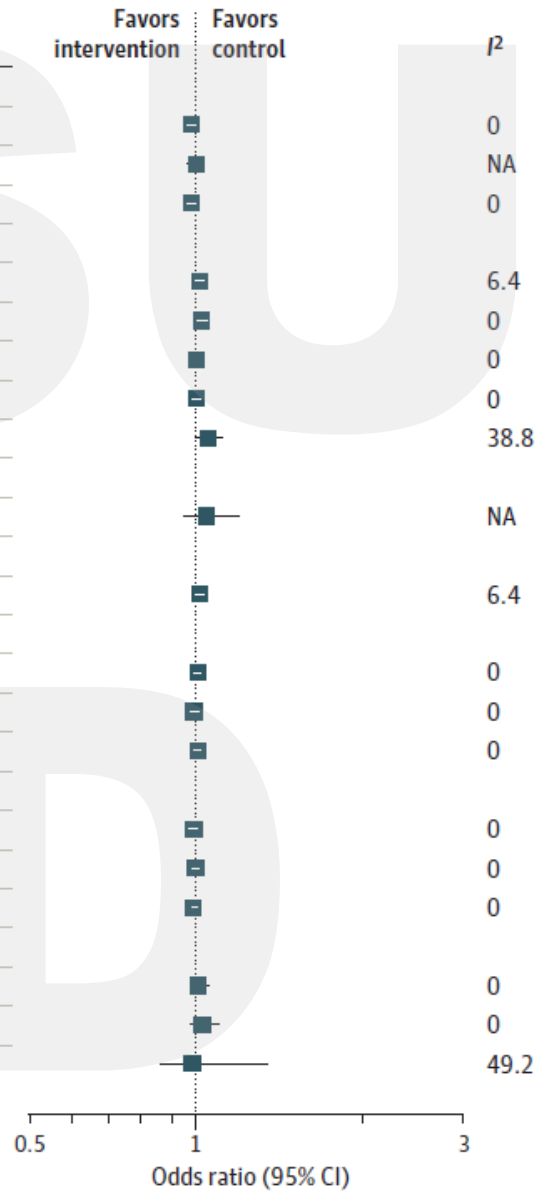


VITAL NEJM, Jan 3rd, 2019

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Vitamin D Supplements and Prevention of Cancer and Cardiovascular Disease

Randomized, double-blind trial of 25,871 participants followed for median of 5.3 years

CONCLUSIONS

Supplementation with vitamin D did not result in a lower incidence of invasive cancer or cardiovascular events than placebo. (Funded by the National Institutes of Health and others; VITAL ClinicalTrials.gov number, NCT01169259.)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

VITAL NEJM, Jan 3rd, 2019

Vitamin D Supplements and Prevention of Cancer and Cardiovascular Disease

Table 3. Hazard Ratios of the Primary Outcomes According to Subgroup, Comparing the Vitamin D Group with the Placebo Group.*

Subgroup	No. of Participants	Invasive Cancer of Any Type				Major Cardiovascular Events			
		Vitamin D	Placebo	Hazard Ratio (95% CI)	P Value for Interaction	Vitamin D	Placebo	Hazard Ratio (95% CI)	P Value for Interaction
		no. of participants with event				*no. of participants with event*			
Age	25,871				0.73				0.31
<Median of 66.7 yr	12,859	302	322	0.95 (0.81–1.11)		140	131	1.07 (0.85–1.36)	
≥Median of 66.7 yr	13,012	491	502	0.98 (0.86–1.11)		256	278	0.93 (0.78–1.10)	

No difference in lack of benefit for CVD or cancer outcomes in those older than median age of 67 years compared to younger

VITAL BONE; NEJM, July, 2022

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 28, 2022 VOL. 387 NO. 4

Supplemental Vitamin D and Incident Fractures in Midlife and Older Adults

Randomized, double-blind trial of 25,871 participants followed for median of 5.3 years

CONCLUSIONS

Vitamin D_3 supplementation did not result in a significantly lower risk of fractures than placebo among generally healthy midlife and older adults who were not selected for vitamin D deficiency, low bone mass, or osteoporosis. (Funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases; VITAL ClinicalTrials.gov number, NCT01704859.)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 28, 2022 VOL. 387 NO. 4

Supplemental Vitamin D and Incident Fractures in Midlife and Older Adults

No fracture benefit by age above or below median

Table 3. Hazard Ratios for Total Fractures with Vitamin D as Compared with Placebo, According to Subgroup.*

Subgroup	No. of Participants	Vitamin D Group (N=12,927)	Placebo Group (N=12,944)	Hazard Ratio (95% CI)
		no. of participants with event		
Age				
<Median of 66.7 yr	12,859	282	285	0.99 (0.84–1.18)
≥Median of 66.7 yr	13,012	487	497	0.97 (0.86–1.10)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 28, 2022 VOL. 387 NO. 4

Supplemental Vitamin D and Incident Fractures in Midlife and Older Adults

No fracture benefit by baseline Vit D level

Baseline 25-hydroxyvitamin D level, according to median				
<Median of 31 ng/ml	8,430	239	241	1.02 (0.85–1.22)
≥Median of 31 ng/ml	8,327	329	344	0.93 (0.80–1.08)
Baseline 25-hydroxyvitamin D level in quartiles				
Quartile 1: ≤24.0 ng/ml	4,270	115	112	1.04 (0.80–1.36)
Quartile 2: 24.1–30.0 ng/ml	4,104	122	128	0.98 (0.77–1.26)
Quartile 3: 30.1–36.9 ng/ml	4,097	151	154	0.98 (0.78–1.23)
Quartile 4: ≥37.0 ng/ml	4,286	180	191	0.89 (0.73–1.10)

A CLINICAL TRIAL OF BETA CAROTENE TO PREVENT BASAL-CELL AND SQUAMOUS-CELL CANCERS OF THE SKIN

E. Robert Greenberg, M.D., John A. Baron, M.D., Thérèse A. Stukel, Ph.D.,

1,805 patients with non-melanoma skin cancer;

51% over age 65 years

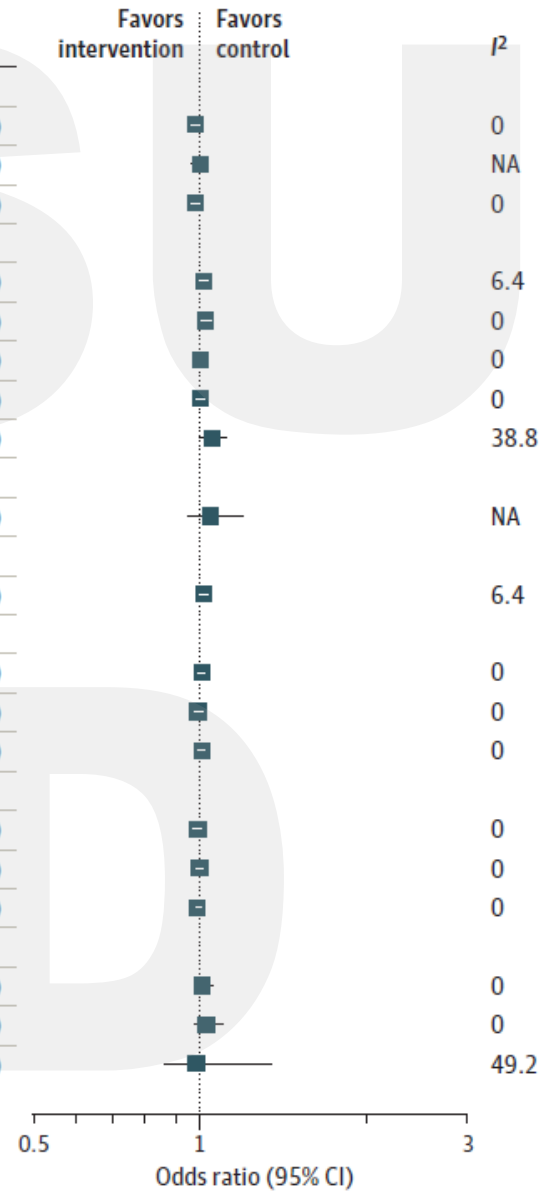
No benefit in older vs. younger patients by age at time of trial or age at onset of skin cancer

Table 5. Estimates of the Effect of Treatment with Beta Carotene in Subgroups of the Study Population.

Characteristic	Five-Year Risk of Skin Cancer*	Crude Relative Rate†	Adjusted Relative Rate‡
		rate (95% confidence limits)	
Sex			
Female	0.28	0.95 (0.69, 1.30)	0.94 (0.68, 1.31)
Male	0.48	1.09 (0.92, 1.29)	1.06 (0.90, 1.26)
Age (yr)			
<65	0.36	1.13 (0.90, 1.40)	1.14 (0.91, 1.42)
≥65	0.48	0.99 (0.81, 1.21)	0.96 (0.78, 1.18)
Center			
Hanover, N.H.	0.35	1.00 (0.73, 1.38)	1.01 (0.72, 1.41)
Los Angeles	0.59	1.09 (0.81, 1.46)	1.02 (0.76, 1.38)
San Francisco	0.50	0.93 (0.67, 1.29)	0.94 (0.67, 1.32)
Minneapolis	0.35	1.13 (0.87, 1.46)	1.13 (0.87, 1.47)
Previous skin cancers			
1	0.25	0.86 (0.65, 1.15)	0.86 (0.64, 1.15)
2	0.41	1.08 (0.78, 1.51)	1.05 (0.75, 1.47)
3	0.56	1.14 (0.75, 1.74)	1.13 (0.73, 1.74)
4 or 5	0.63	1.09 (0.77, 1.56)	1.05 (0.73, 1.53)
6–9	0.77	1.20 (0.77, 1.86)	1.21 (0.76, 1.92)
≥10	0.84	1.01 (0.65, 1.56)	1.02 (0.66, 1.59)
Age at first skin cancer (yr)			
<55	0.45	1.01 (0.81, 1.26)	1.02 (0.82, 1.29)
≥55	0.40	1.09 (0.89, 1.33)	1.05 (0.86, 1.29)

Figure 3. Summary of Meta-analysis Results or Best Evidence for Primary Key Question 1 and Key Question 3 Outcomes

Outcome	No. of studies	No. analyzed	% with event		Odds ratio (95% CI)	I^2
			Intervention	Control		
Multivitamin						
All-cause mortality[a]	9	51 550	7.3	7.7	0.94 (0.87-1.01)	0
CVD event[b]	1	21 442	4	4.1	0.98 (0.86-1.12)	NA
Any cancer[a]	4	48 859	8.5	9	0.93 (0.87-0.99)	0
Beta carotene						
All-cause mortality	6	112 820	5.4	5.1	1.06 (1.00-1.12)	6.4
CVD mortality	5	94 506	2.8	2.6	1.10 (1.02-1.19)	0
CVD events	2	61 947	3.5	3.5	1.01 (0.92-1.10)	0
Any cancer	2	61 947	5.3	5.4	0.99 (0.92-1.07)	0
Lung cancer[c]	4	94 830	1.2	1	1.20 (1.01-1.42)	38.8
Vitamin A						
All-cause mortality[d]	1	2297	5.4	4.6	1.16 (0.80-1.69)	NA
Beta carotene or vitamin A						
All-cause mortality	7	115 117	5.4	5.1	1.06 (1.01-1.12)	6.4
Vitamin E						
All-cause mortality	9	107 772	6.9	6.8	1.02 (0.97-1.07)	0
CVD events	4	62 136	5.1	5.2	0.96 (0.90-1.04)	0
Any cancer	5	76 777	8.8	8.6	1.02 (0.98-1.08)	0
Vitamin D						
All-cause mortality	27	117 082	5	5.7	0.96 (0.91-1.02)	0
CVD events	7	74 925	8.1	8.2	1.00 (0.95-1.05)	0
Any cancer	19	86 899	6.7	6.8	0.98 (0.92-1.03)	0
Calcium						
All-cause mortality	6	8394	13.1	12.7	1.05 (0.92-1.21)	0
CVD events	4	4076	10.7	9.7	1.11 (0.90-1.36)	0
Any cancer[a]	3	5051	8.7	8.9	0.94 (0.41-2.14)	49.2



Sanders, 2010 (Vital D)[116] Fair		2258 (90.0%)	1370 IU (500,000 IU annually)	5 (4)	AUS	Other: Falls and fractures	Women aged 70 years or older residing in southern Victoria, Australia (latitude 38 South) at higher risk of hip fracture	Mean age: 76 % Female: 100 % White: NR % Black: NR Mean BMI: NR % Curr. smoker: NR	NR	X	X	ACM: NR Ca: NR CVD: NR
Trivedi, 2003[88] Fair	X	2686 (100%)	1095.9 IU (100,000 IU every 4 months)	5 (5)	GBR	Other: Fractures and mortality	Age 65-85 years	Mean age: 75 % Female: 24 % White: NR % Black: NR Mean BMI: 24.4 % Curr. smoker: 4	NR	X	X	ACM: Full Ca: Self-report CVD: Self-report
Bischoff-Ferrari, 2020 (DO-HEALTH)[140] Good		2157 (88%)	2000 IU	3 (3)	AUT, FRA, DEU, PRT, CHE	Other : 6 primary outcomes (BP, Short Physical Performance Battery, Montreal Cognitive Assessment, nonvertebral fractures, infections)	Community dwelling adults 70 years or older	Mean age: 75 % Female: 62 Percent white: NR Mean BMI: NR % Curr. smoker: 6	Vit D: 55.91 nmol/L	X	X	ACM: Full Ca :NA CVD: NA
Sesso, 2022 (COSMOS)[152] Good		21442 (97.7%)	Broad	3.6	USA	CVD, Cancer	Age ≥65 (women) or ≥60 (men) years without history of MI, stroke, or recent cancer	Mean age: 72 % Female: 59 % White: 90 % Black: 5.3 Mean BMI: 26.8 % Curr. smoker: 44.6		X	X	ACM: Full Ca: Full CVD: Full

Mass General Brigham

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About Us > Newsroom > Daily Multivitamins Improve Memory and Slow Cognitive Aging

COSMOS trial

Third Major Study Finds Evidence that Daily Multivitamin Supplements Improve Memory and Slow Cognitive Aging in Older Adults

Jan 18, 2024

Healthy Aging | Brain & Nervous System Conditions | Research

Am J Clin Nut; 2024;119:692-701

The American Journal of Clinical Nutrition 119 (2024) 692–701

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Original Research Article

Effect of multivitamin-mineral supplementation versus placebo on cognitive function: results from the clinic subcohort of the COcoa Supplement and Multivitamin Outcomes Study (COSMOS) randomized clinical trial and meta-analysis of 3 cognitive studies within COSMOS

Check for updates

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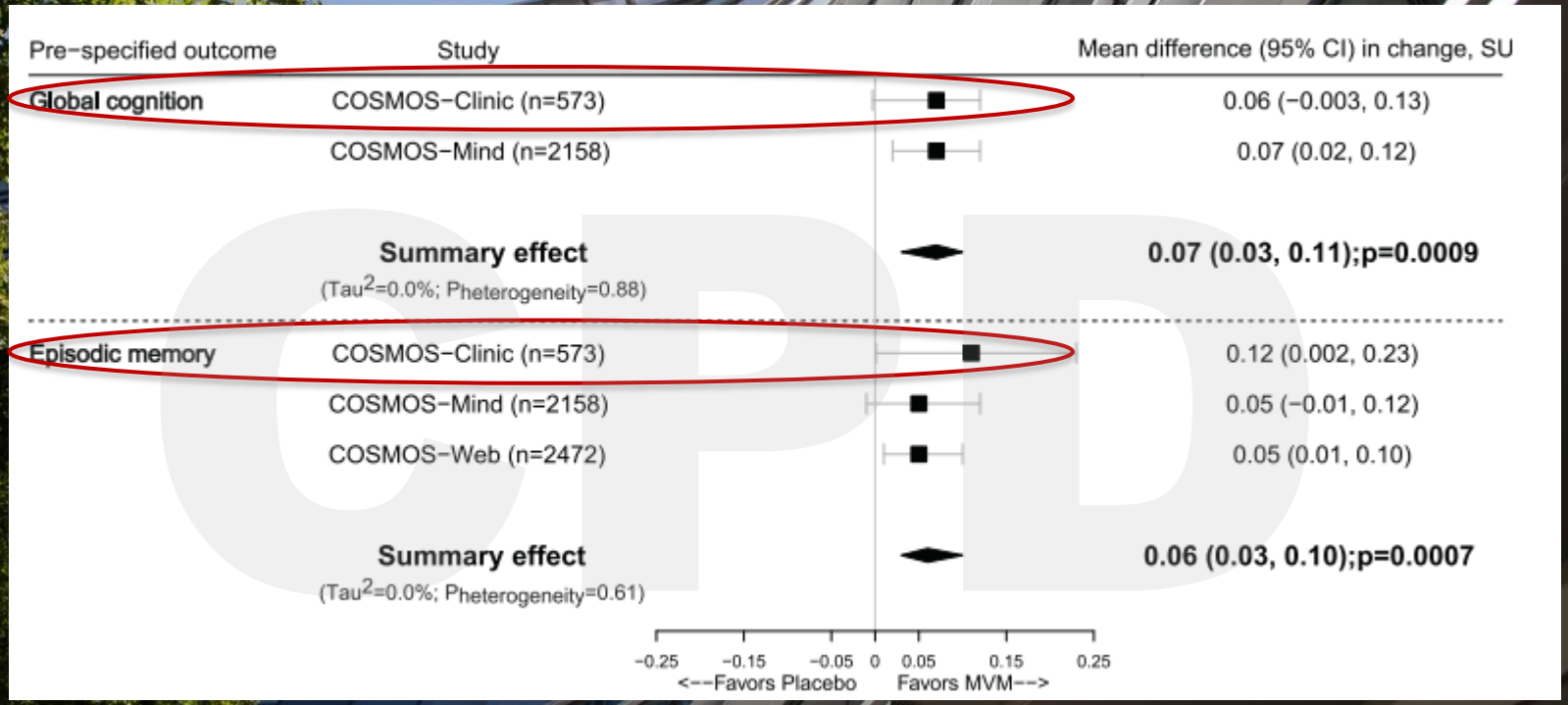

The American Journal of Clinical Nutrition 119 (2024) 692–701

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Original Research Article

Effect of multivitamin-mineral supplementation versus placebo on cognitive function: results from the clinic subcohort of the COcoa Supplement and Multivitamin Outcomes Study (COSMOS) randomized clinical trial and meta-analysis of 3 cognitive studies within COSMOS

Methods: COSMOS is a 2 × 2 factorial trial of cocoa extract (500 mg flavanols/d) and/or a daily MVM supplement for cardiovascular disease and cancer prevention among 21,442 United States adults aged ≥60 y. There were 573 participants in the clinic subcohort of COSMOS (that is, COSMOS-Clinic) who completed all cognitive tests administered at baseline. For the meta-analysis, we included nonoverlapping participants across 3 COSMOS cognitive substudies: COSMOS-Clinic (n = 573); COSMOS-Mind (n = 2158); COSMOS-Web (n = 2472).

Subgroup analysis of 573 patients from a study population of 21,442

Multivitamins in the prevention of cancer and cardiovascular disease: the COcoa Supplement and Multivitamin Outcomes Study (COSMOS) randomized clinical trial

Howard D Sesso,[1,2] Pamela M Rist,[1,2] Aaron K Aragaki,[3] Susanne Rautiainen,[1,4] Lisa G Johnson,[3] Georgina Friedenberg,[1] Trisha Copeland,[1] Allison Clar,[1] Samia Mora,[1,5] M Vinayaga Moorthy,[1] Ara Sarkissian,[1] Jean Wactawski-Wende,[6] Lesley F Tinker,[3] William R Carrick,[3] Garnet L Anderson,[3] and JoAnn E Manson,[1,2] for the COSMOS Research Group

Conclusions: A daily MVM supplement, compared with placebo, did not significantly reduce the incidence of total cancer among older men and women. Future studies are needed to determine the effects of MVMs on other aging-related outcomes among older adults. This trial is registered at www.clinicaltrials.gov as NCT02422745. *Am J Clin Nutr* 2022;115:1501–1510.

Trial designed to study older adults; average age 72 years, followed for nearly 4 years on average

The American Journal of CLINICAL NUTRITION

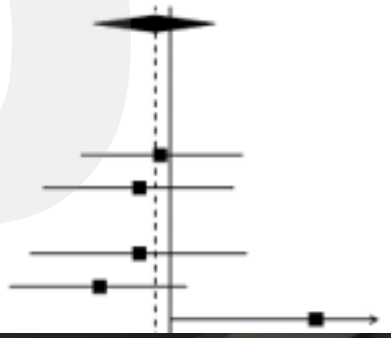
Online Supplementary Material

Multivitamins in the Prevention of Cancer and Cardiovascular Disease:

The COSMOS Randomized Clinical Trial

Supplementary Figure 2. Hazard ratios and 95% confidence interval[1] for the primary outcome[2] according to subgroup, comparing multivitamin group with placebo group.

Subgroup	No. of participants with event (Annualized rate,%) Multivitamin Group (N=10,720)	Placebo Group (N=10,722)	HR(95%CI)	P
Overall effect on invasive cancer events[2]	518(1.37)	535(1.42)	0.97 (0.86, 1.09)	0.57
Participant characteristics				
Sex				0.74
Female	301(1.33)	305(1.35)	0.98 (0.84, 1.15)	
Male	217(1.43)	230(1.51)	0.94 (0.78, 1.13)	
Age at randomization, y				0.11
60–69	169(1.10)	180(1.17)	0.94 (0.76, 1.16)	
70–79	236(1.35)	269(1.55)	0.87 (0.73, 1.03)	
>=80	113(2.23)	86(1.68)	1.33 (1.00, 1.76)	



Does vitamin supplementation have some small benefit in a subsets of older adults?

Maybe

But a ~ 600 patient subset of a negative trial of > 21,000 older adults is not compelling to me

USPSTF could not find convincing data for age or gender benefits

USPSTF recommendation:
For community-dwelling, non-pregnant adults, do not give beta-carotene or Vitamin E for CVD or cancer prevention (Grade D) and all other vitamins or vitamin combinations have insufficient evidence to recommend (Grade I)

Recommendation Summary

Population	Recommendation	Grade
Community-dwelling, nonpregnant adults	The USPSTF recommends against the use of beta carotene or vitamin E supplements for the prevention of cardiovascular disease or cancer.	D
Community-dwelling, nonpregnant adults	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the use of multivitamin supplements for the prevention of cardiovascular disease or cancer. See the "Practice Considerations" section for additional information regarding the I statement.	I

Objectives:

1. What are vitamins?
2. A little background on regulatory environment
3. Why natural may not be the way to think about "natural products" including vitamins
4. The data – and do the elderly differentiate?
5. What now?

How do we want to approach the data with our patients?

The USPSTF approach:

EDITORIAL | Annals of Internal Medicine

Enough Is Enough: Stop Wasting Money on Vitamin and Mineral Supplements

Ann Intern Med. 2013;159:850-851.

Three articles in this issue address the role of vitamin and mineral supplements for preventing the occurrence or progression of chronic diseases. First, Fortmann and

U.S. adults from 30% between 1988 to 1994 to 39% between 2003 to 2006, while overall use of dietary supplements increased from 42% to 53% (9). Longitudinal and

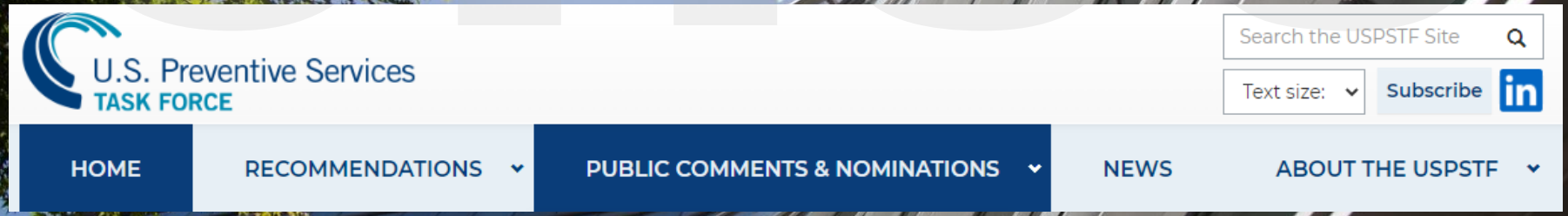
EDITORIAL

JAMA June 21, 2022 Volume 327, Number 23

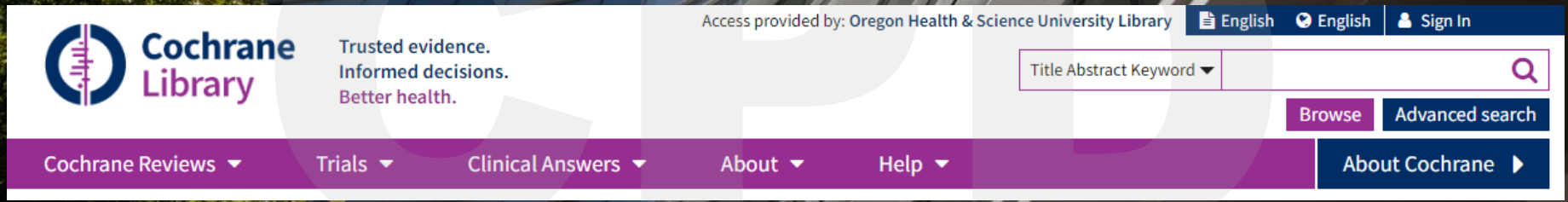
Multivitamins and Supplements—Benign Prevention or Potentially Harmful Distraction?

Jenny Jia, MD, MSc; Natalie A. Cameron, MD; Jeffrey A. Linder, MD, MPH

My approach: I am not here to take anyone's vitamins away if they feel they're helping (Benign Prevention).
However, I do think some patients may delay/avoid lifestyle interventions (Harmful Distraction) and I do offer advice when asked: Recommend save the $$ from supplements and buy the carrots farm-fresh strawberries instead

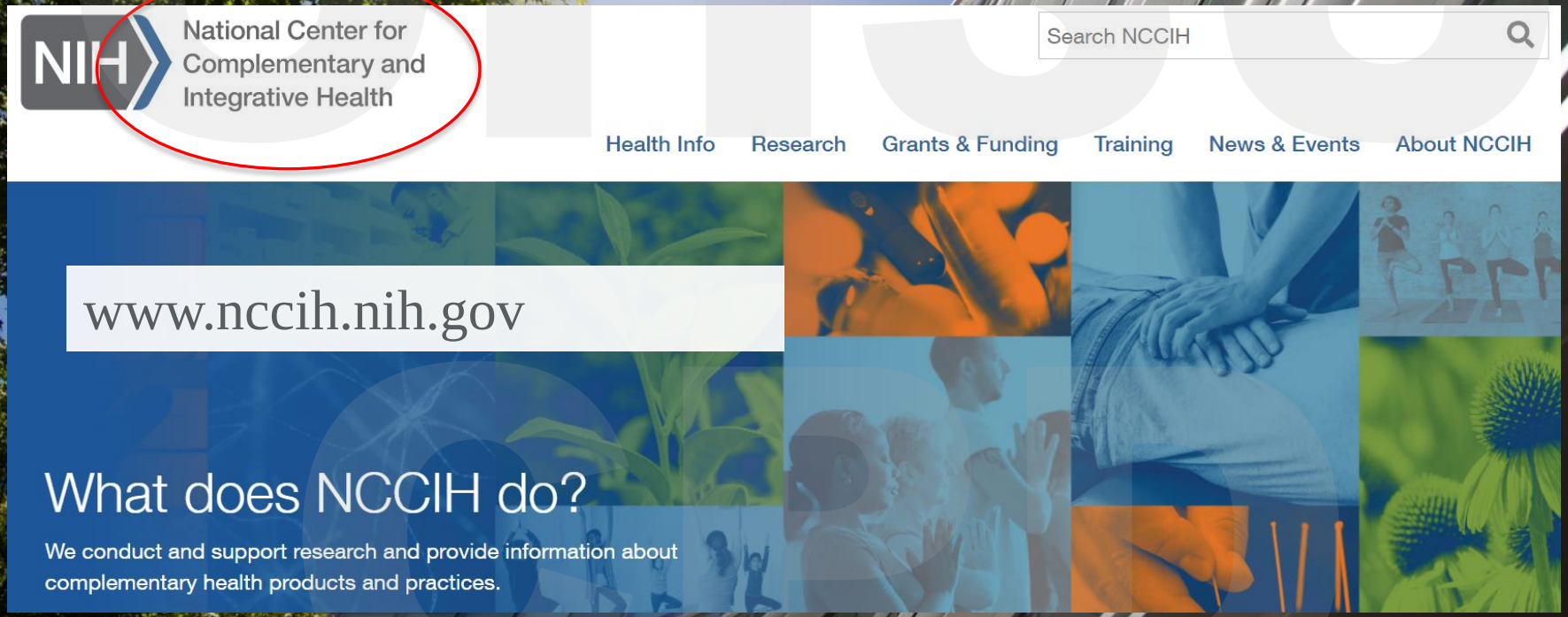


www.uspreventiveservicestaskforce.org



www.cochranelibrary.com

Given the interest in vitamins and other supplements and the often times disregard for data, another great source of information to be aware of is a branch of NIH….NCCIH (formerly NCCAM)



www.nih.gov and search "Dietary Supplements"….will lead you to NCCIH and a list of fact sheets for both patient and health care provider (hint – they're not very different)

Health Information

Share:

Home > Health Information > Dietary Supplement Fact Sheets

Dietary Supplement Fact Sheets

This collection of fact sheets and other resources from the NIH Office of Dietary Supplements and other federal government sources presents information about dietary supplements and their ingredients. These include vitamins, minerals, herbs and botanicals, probiotics, and more. Many of these resources are available in versions written for consumers (in both English and Spanish) and also for health professionals.

5 A B C D E F G H I K L M N O P Q R S T V W Y Z

General Supplement Information

- Dietary Supplements: Background Information
- Botanical Dietary Supplements: Background Information
- Vitamin and Mineral Fact Sheets

A

- Acai
- Activated charcoal
- African mango (see Weight Loss)
- Alfalfa
- Aloe vera
- Anabolic steroids
- Andrographis (see COVID-19)
- Antioxidants (see Exercise and Athletic Performance)
- Apple cider vinegar
- Arginine (see Exercise and Athletic Performance)
- Ashwagandha
- Astragalus
- Athletic and exercise performance (see Exercise and Athletic Performance)
- Vitamin A

www.nih.gov and search “Vitamins”….will lead you to NCCIH brand of NIH which is National Center for Complementary and Integrative Health

Vitamins and Minerals

Vitamins and Minerals

Vitamins and minerals are essential substances that our bodies need to develop and function normally. The known vitamins include A, C, D, E, and K, and the B vitamins: thiamin (B_1), riboflavin (B_2), niacin (B_3), pantothenic acid (B_5), pyridoxal (B_6), cobalamin (B_{12}), biotin, and folate/folic acid. A number of minerals are essential for health: calcium, phosphorus, potassium, sodium, chloride, magnesium, iron, zinc, iodine, sulfur, cobalt, copper, fluoride, manganese, and selenium. The Dietary Guidelines for Americans 2015–2020 recommends that people should aim to meet their nutrient requirements through a healthy eating pattern that includes nutrient-dense forms of foods.

5 A B C D E F G H I K L M N O P Q R S T V W Y Z

A

- Antioxidants (see Exercise and Athletic Performance)
- Vitamin A

D

- Vitamin D

Click on “Vitamin D” in NCCIH factsheets:

Vitamin D

- Vitamin D - Consumer
- Vitamin D - Vitamina D en español
- Vitamin D - Health Professional
- Vitamin D - ODS Activities and Resources for Researchers
- Vitamin D for weight loss (see Weight Loss)
- Vitamin D and COVID-19 (see COVID-19)
- Vitamin D and immune function (see Immune Function)
- NIH COVID-19 Treatment Guidelines on Vitamin D
  - *Source: National Institutes of Health (NIH)*

Overall, clinical trials show that vitamin D supplementation does not reduce CVD risk, even for people with low 25(OH)D status (below 20 nmol/L [12 ng/mL]) at baseline [91,122].

Taken together, studies to date do not indicate that vitamin D with or without calcium supplementation reduces the incidence of cancer,

Vitamin D “does not reduce CVD risk, even for people with low 25(OH)D status” …and “studies to date do not indicate that vitamin D with our without calcium reduced incidence of cancer.”

Using Dietary Supplements Wisely

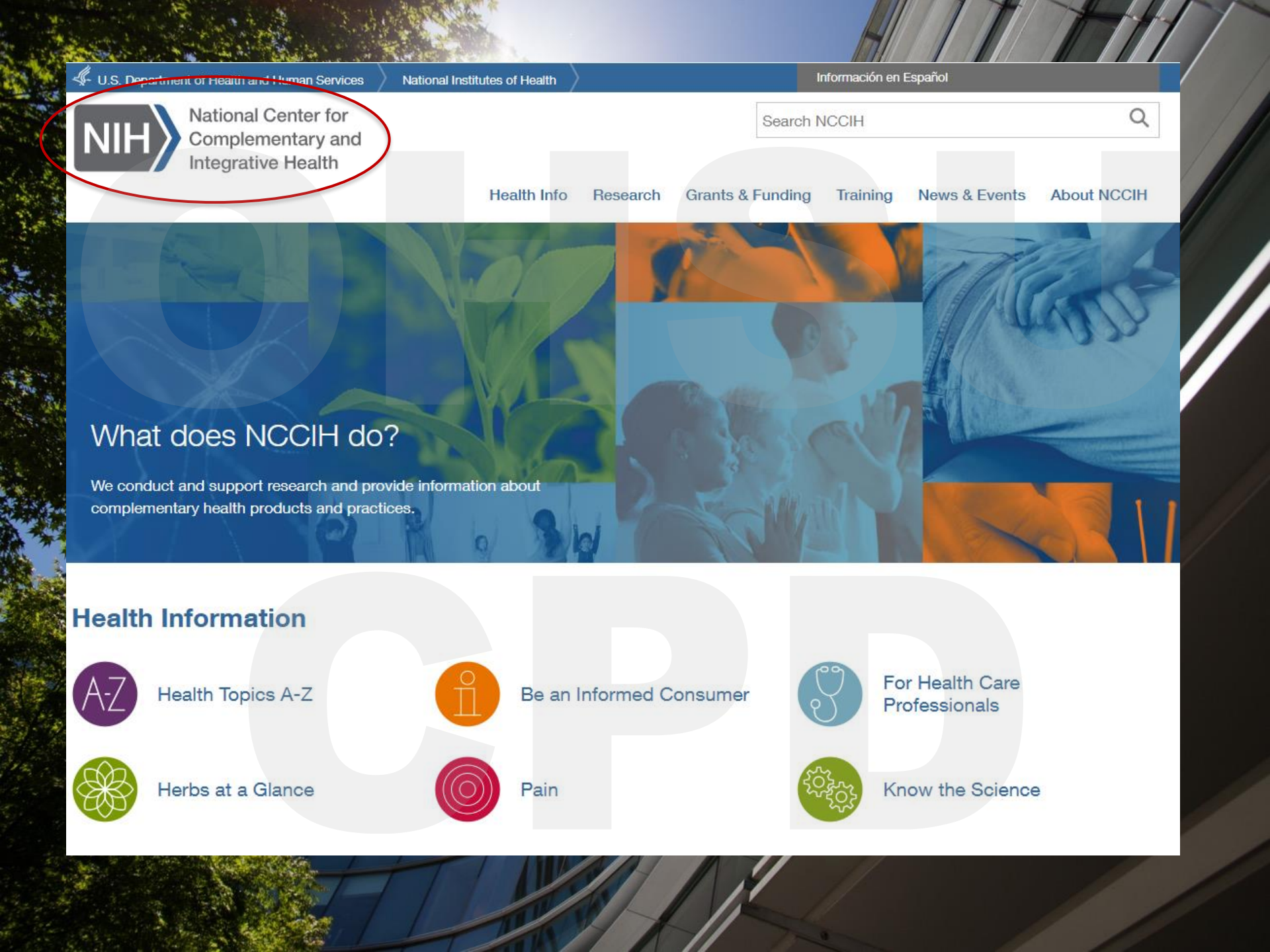
What's the Bottom Line?

How much do we know about dietary supplements?

The amount of scientific evidence we have on dietary supplements varies widely—we have a lot of information on some and very little on others.

What do we know about the effectiveness of dietary supplements?

- Studies have found that some dietary supplements may have some benefit, such as melatonin for jet lag, and others may have little or no benefit, such as ginkgo for dementia.
- Supplements you buy from stores or online may differ in important ways from products tested in studies.
- Most research shows that taking multivitamins doesn't result in living longer, slowing cognitive decline, or lowering the chance of getting cancer, heart disease, or diabetes.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For Health Care Professionals
Herbs at a Glance
Pain
Know the Science

Key take home points:

1. There are 13 human vitamins and all are vital but in very, very small doses, the benefits of which are averaged over time

2. The RDA is not a personal daily goal and 97% of people need less than the RDA to avoid deficiencies

3. While Vitamin C treats scurvy and Vitamin D treats Ricketts, prevention of any disease in patients without deficiencies has not been demonstrated across a variety of outcomes by age or gender

4. As providers, it's OK to be a skeptic but also Ok to support our patients choices if no harm is being done (Benign Prevention)

5. Be aware of safety issues: contaminants may be intended (sildenafil, dexamethasone, diclofenac) or unintended (chemical byproducts of industrial production techniques) and may result in real harms

Thank you

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