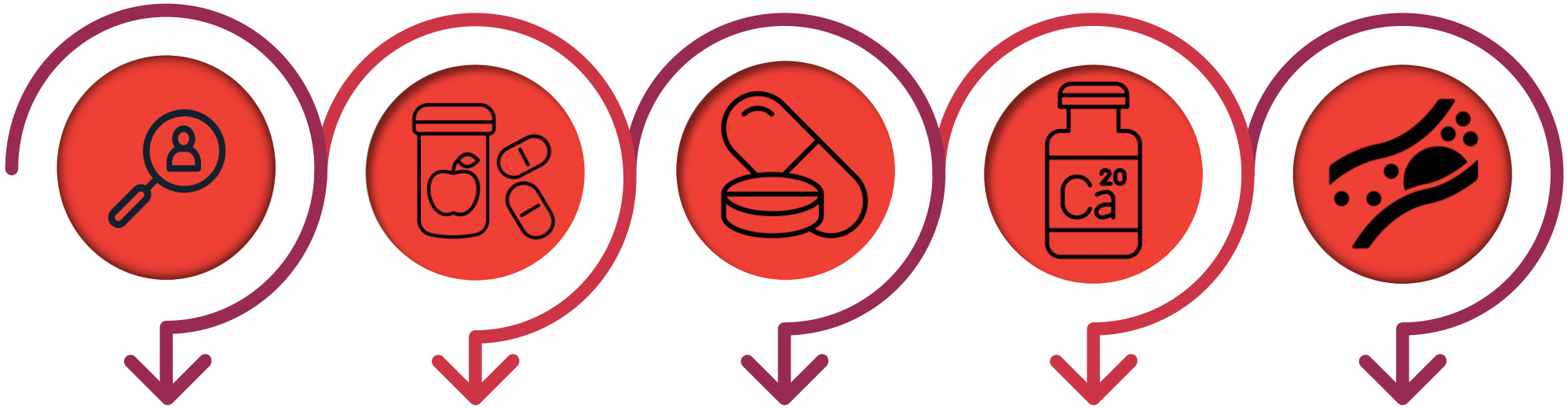
MITOS OU REALIDADES NA PREVENÇÃO CARDIOVASCULAR

SUPLEMENTOS NA SAÚDE E DOENÇA CARDIOVASCULAR

Bruno Miranda Castilho

Cardiologia – Hospital Distrital de Santarém

Supplements for the Primary Prevention of Cardiovascular Disease and Cancer



THE PROBLEM

MULTIVITAMINS

VITAMIN D

OTHER VITAMINS & Ca

SUPPLEMENTATION ON DYSLIPIDEMIAS

THE PROBLEM

- **Dietary supplementation is a very common practice in developed countries**
  - Half of U.S. adults (52%) take one or more dietary supplements.
  - Most commonly multivitamin supplements.

nutrients MDPI

Article

Dietary Supplement Use Differs by Socioeconomic and Health-Related Characteristics among U.S. Adults, NHANES 2011–2014

Alexandra E. Cowan [1], Shinyoung Jun [1], Jaime J. Gahche [2], Janet A. Tooze [3],

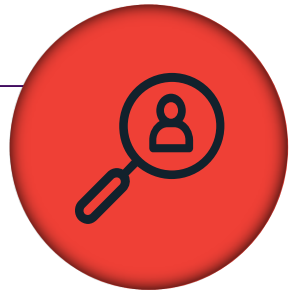
- **Common reasons appointed for using dietary supplements:**
  - Overall health and wellness.
  - **Disease prevention**, in particular **cardiovascular disease** and **cancer.**
  - Lose weight, have more energy.

JAMA Internal Medicine

Why US Adults Use Dietary Supplements

Regan L. Bailey, PhD, RD; Jaime J. Gahche, MPH; Paige E. Miller, PhD, RD; et al

THE PROBLEM



- Dietary supplements are **intensively advertised in the media.**
  - **Sales of nearly 50 billion** dollars annually in the United States
  - Frequently use expressions such as *"treat" and "prevent"* ,some advertisements use the authority of medical profession
  - **Many users feel so strongly** about the potential health benefits that they **reported that they would continue to take dietary supplements even if they were shown to be ineffective** in regulated scientific studies
  - Dietary supplements like multivitamins are **generally regulated as food products rather than pharmaceuticals**

Wierzejska R. [Whether the advertisement of dietary supplements is objective source of data about their impact on health? Analysis of broadcasting advertisements in the terms of the food law]. Wiadomosci Lekarskie (Warsaw, Poland : 1960). 2016 ;69(1):14-18. PMID: 27162289.

THE PROBLEM

Knowledge of dietary supplements is not a core competency for medical education and is often overlooked.

- Practicing physicians lack knowledge in these areas and rarely investigate supplements that they may not be familiar with
- Frequent sources of physician's information about dietary supplements were advertisements

Original Article

Medical Residents' Knowledge of Dietary Supplements

Authors: Bimal H. Ashar, MD, MBA, Tasha N. Rice, MHS, Stephen D. Sisson, MD

JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

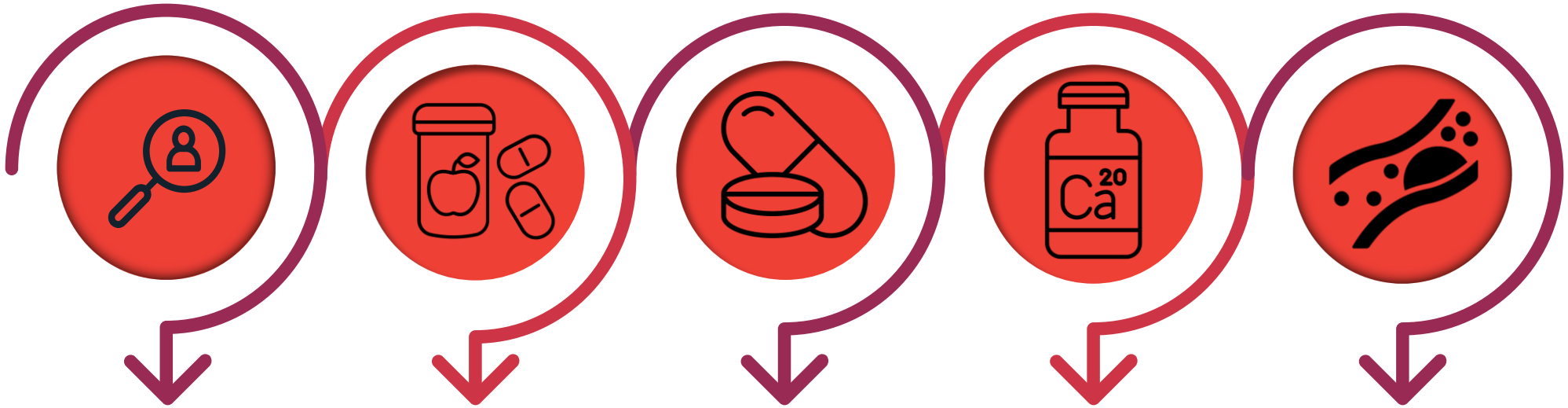
Vitamin, Mineral, and Multivitamin Supplementation to Prevent Cardiovascular Disease and Cancer

US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

Ashar, Bimal H.; Rice, Tasha N.; Sisson, Stephen D. (2008). Medical Residents' Knowledge of Dietary Supplements. Southern Medical Journal, 101(10), 996–1000. doi:10.1097/SMJ.0b013e31817cf79e

Supplements for the Primary Prevention of Cardiovascular Disease and Cancer



THE PROBLEM

MULTIVITAMINS

VITAMIN D

Ca & OTHER VITAMINS

SUPPLEMENTATION ON DYSLIPIDEMIAS

MULTIVITAMINS

MULTIVITAMINS

- **Most common dietary supplement** taken in the U.S., with more than one-third of adults reporting regular multivitamin use.

OBJECTIVE

- Prevent nutritional deficiency.

RATIONAL FOR MV use:

- The combination of essential vitamins and minerals contained in multivitamins may mirror healthier dietary patterns such as fruit and vegetable intake, which have been *modestly and inversely associated with cancer and CVD risk* in some studies

Gahche J, Bailey R, Burt V, Hughes J, Yetley E, Dwyer J, Picciano MF, McDowell M, Sempos C. Dietary supplement use among U.S. adults has increased since NHANES III (1988-1994). NCHS Data Brief 2011:1-8.

MULTIVITAMINS

Key question 1:

What is the efficacy of multivitamin supplementation for reducing cardiovascular disease, cancer, and mortality in the general adult population?

MULTIVITAMINS

MULTIVITAMINS

Is multivitamin supplementation effective?

Multivitamins in the Prevention of Cancer in Men
The Physicians' Health Study II Randomized Controlled Trial

J. Michael Gaziano, MD, MPH; Howard D. Sesso, ScD, MPH; William G. Christen, ScD; et al

Daily multivitamin supplementation modestly but significantly reduced the risk of total cancer (17.0 and 18.3 events, respectively, per 1000 person-years; hazard ratio [HR], 0.92; P = .04)

No effect on cancer mortality or site-specific cancers

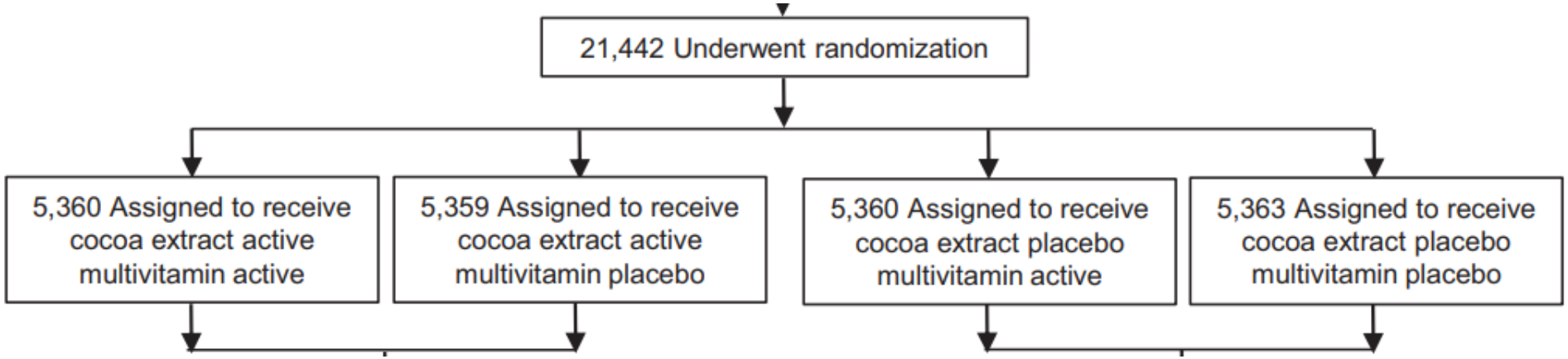
Gahche J, Bailey R, Burt V, Hughes J, Yetley E, Dwyer J, Picciano MF, McDowell M, Sempos C. Dietary supplement use among U.S. adults has increased since NHANES III (1988-1994). NCHS Data Brief 2011:1-8.

MULTIVITAMINS

MULTIVITAMINS

Largest randomized trial regarding **multivitamins and cocoa extract.**

COSMOS TRIAL



MULTIVITAMINS

MULTIVITAMINS

Largest randomized trial regarding multivitamins and cocoa extract

Mean Follow up 3,6 years

COSMOS TRIAL

No benefit on cancer mortality

No reduction of CV events

No reduction of all cause mortality

Daily MV supplementation was benefitial on cognition (P=0,007)

MULTIVITAMINS

MULTIVITAMINS

Pooled analisys of 4 RCTs
~37.000 participants

→

No association between **multivitamin** use and cardiovascular disease mortality.

O'Connor EA, Evans CV, Ivlev I, et al. 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. JAMA. 2022;327(23):2334–2347. doi:10.1001/jama.2021.15650

MULTIVITAMINS

Key question 2:

What are the harms of multivitamin supplementation in the general adult population?

Harms of multivitamin use were reported in 9 RCTs (n = 51614)

Very few adverse effects

Slight increase in RASH (OR 1.01-1.12)

Gahche J, Bailey R, Burt V, Hughes J, Yetley E, Dwyer J, Picciano MF, McDowell M, Sempos C. Dietary supplement use among U.S. adults has increased since NHANES III (1988-1994). NCHS Data Brief 2011:1-8.

MULTIVITAMINS

JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

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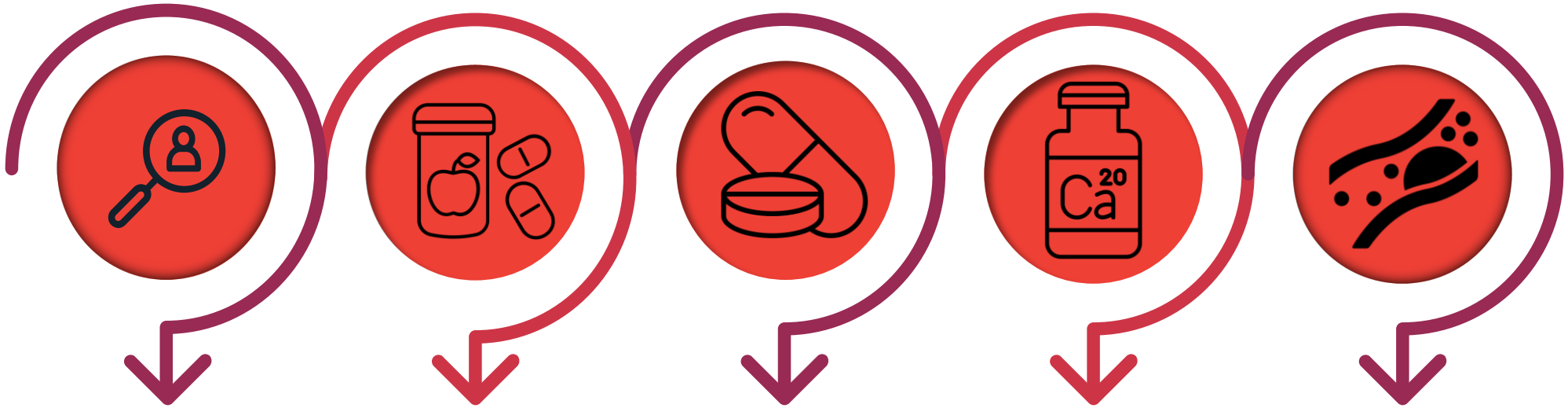
- The USPSTF concludes that the evidence is insufficient to determine the balance of benefits and harms of supplementation with multivitamins for the prevention of cardiovascular disease or cancer.

The largest randomized trial (COSMOS) as only a follow up of ~3.5 years

Small observational studies that suggest benefit

Supplements for the Primary Prevention of Cardiovascular Disease and Cancer



THE PROBLEM

MULTIVITAMINS

VITAMIN D

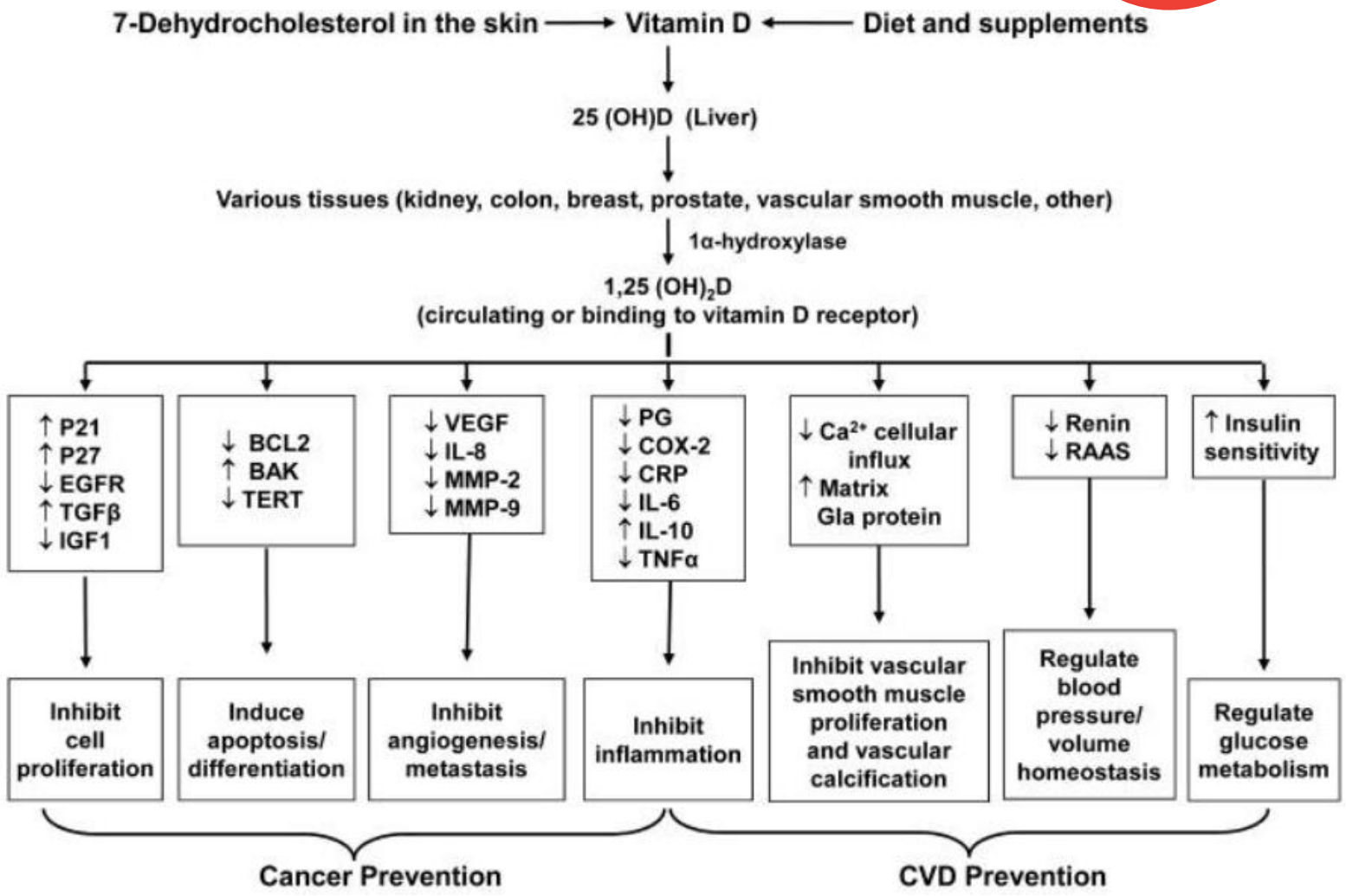
OTHER VITAMINS & Ca

SUPPLEMENTATION ON DYSLIPIDEMIAS

VITAMIN D

VITAMIN D

Approximately 20% of healthy adults in the UK take a supplement containing vitamin D.



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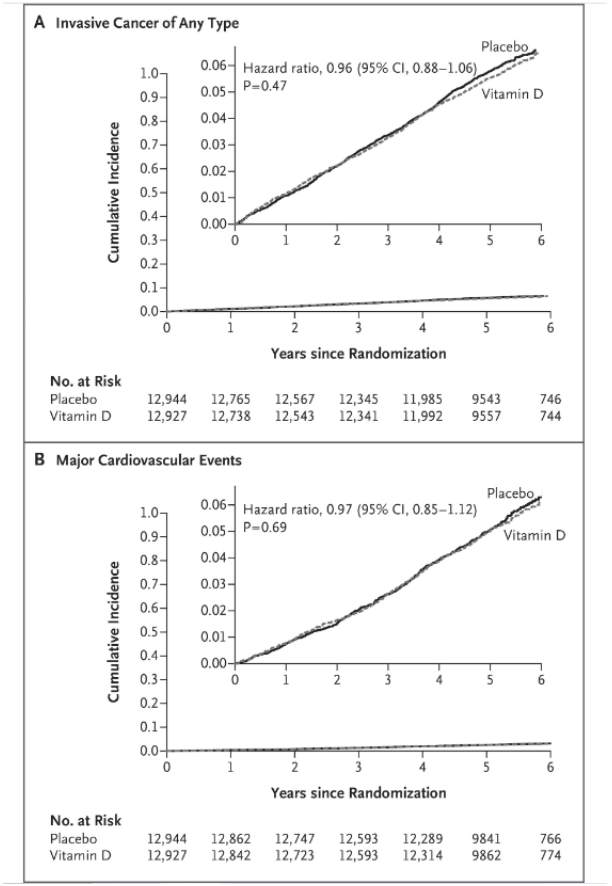
VITAMIN D

The NEW ENGLAND JOURNAL of MEDICINE

Vitamin D Supplements and Prevention of Cancer and Cardiovascular Disease

JoAnn E. Manson, M.D., Dr.P.H., Nancy R. Cook, Sc.D., I-Min Lee, M.B., B.S., Sc.D., William Christen, Sc.D., Shari S. Bassuk, Sc.D., Samia Mora, M.D., M.H.S., Heike Gibson, Ph.D., David Gordon, M.A.T., Trisha Copeland, M.S., R.D., Denise D'Agostino, B.S., Georgina Friedenberg, M.P.H., Claire Ridge, M.P.H., et al., for the VITAL Research Group*

- **~25.000 patients** > 50 years old
- Primary end points were **invasive cancer** of any type and **major cardiovascular events.**



Supplementation with vitamin D **did not** result in a **lower** incidence of **invasive cancer** or **cardiovascular events** than placebo.

No excess risks of hypercalcemia or other adverse events were identified.

VITAMIN D

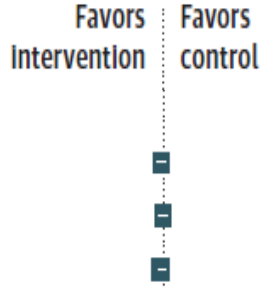
JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Vitamin, Mineral, and Multivitamin Supplementation to Prevent Cardiovascular Disease and Cancer

US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

Outcome	No. of studies	No. analyzed	% with event		Odds ratio (95% CI)
			Intervention	Control	
Vitamin D					
All-cause mortality	27	117 082	5	5.7	0.96 (0.91-1.02)
CVD events	7	74 925	8.1	8.2	1.00 (0.95-1.05)
Any cancer	19	86 899	6.7	6.8	0.98 (0.92-1.03)



No benefit in preventing cancer

No benefit in CV events

No benefit in all cause mortality

VITAMIN D

JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

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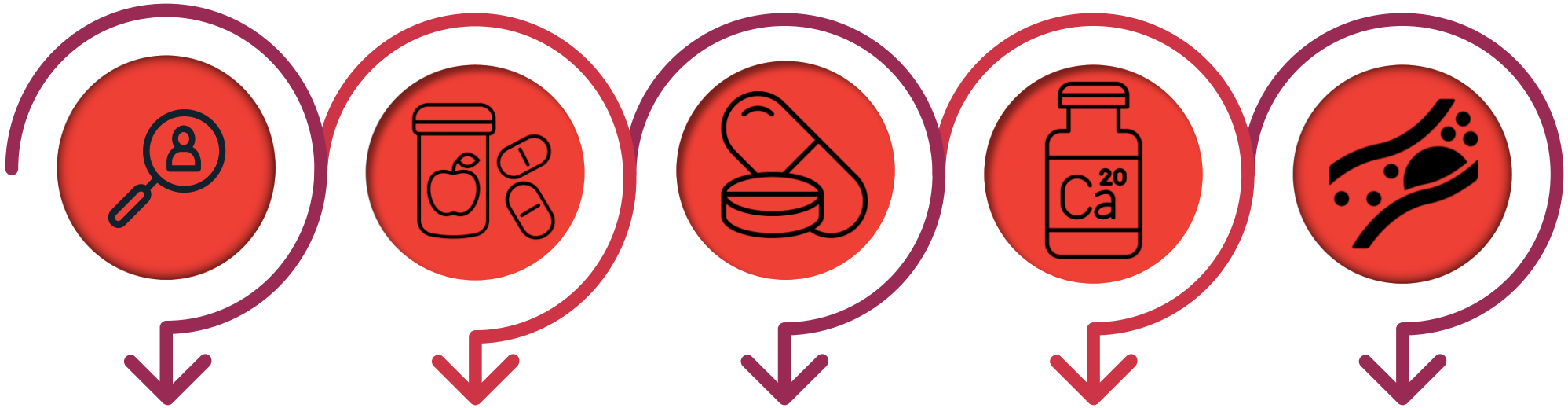
The USPSTF concludes that the evidence is insufficient to determine the balance of benefits and harms of supplementation with single or paired nutrients (other than beta carotene and vitamin E) for the prevention of cardiovascular disease or cancer.

- It is unclear whether the effect of vitamin D on health outcomes **might vary based on patient population characteristics** (eg, baseline vitamin D level or diet quality).
- **Follow-up** may be **too short** to detect an effect on cancer-specific mortality.

Supplements for the Primary Prevention of Cardiovascular Disease and Cancer



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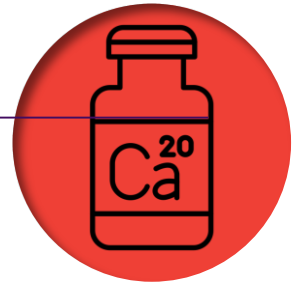
SUPPLEMENTATION ON DYSLIPIDEMIAS

CALCIUM



JCEM THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

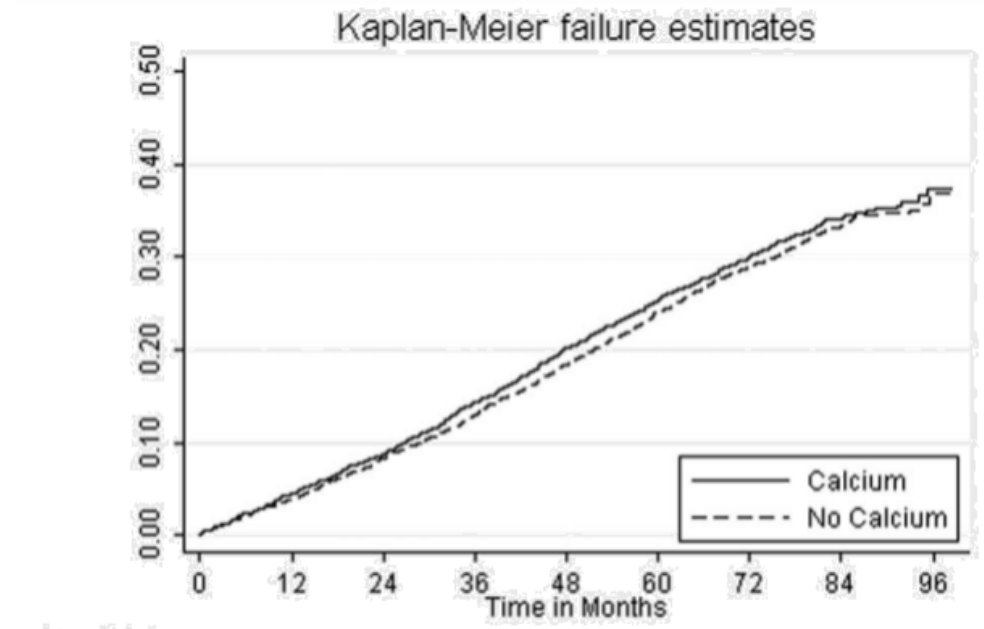
Long-Term Follow-Up for Mortality and Cancer in a Randomized Placebo-Controlled Trial of Vitamin D_3 and/or Calcium (RECORD Trial)

Alison Avenell, Graeme S. MacLennan, David J. Jenkinson, Gladys C. McPherson,

~5000 healthy individual

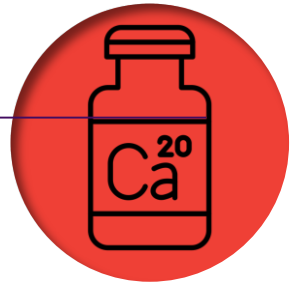
Randomized to calcium , vitamin D + calcium,

vitamin D or placebo



Gahche J, Bailey R, Burt V, Hughes J, Yetley E, Dwyer J, Picciano MF, McDowell M, Sempos C. Dietary supplement use among U.S. adults has increased since NHANES III (1988-1994). NCHS Data Brief 2011:1-8.

CALCIUM



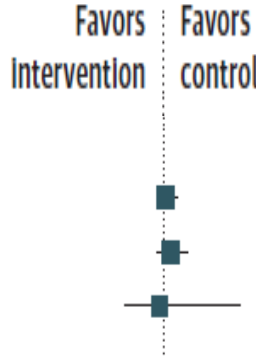
JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Vitamin, Mineral, and Multivitamin Supplementation to Prevent Cardiovascular Disease and Cancer

US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

Outcome	No. of studies	No. analyzed	% with event		Odds ratio (95% CI)
			Intervention	Control	
Calcium					
All-cause mortality	6	8394	13.1	12.7	1.05 (0.92-1.21)
CVD events	4	4076	10.7	9.7	1.11 (0.90-1.36)
Any cancer[a]	3	5051	8.7	8.9	0.94 (0.41-2.14)



No benefit in preventing cancer

No benefit in CV events

No benefit in all cause mortality

Gahche J, Bailey R, Burt V, Hughes J, Yetley E, Dwyer J, Picciano MF, McDowell M, Sempos C. Dietary supplement use among U.S. adults has increased since NHANES III (1988-1994). NCHS Data Brief 2011:1-8.

HARMS IN SUPPLEMENTATION

Are there serious harms in supplementation?

BMJ

RESEARCH

Effects of vitamin E on stroke subtypes: meta-analysis of randomised controlled trials

Rational: Vitamin E antioxidant properties might protect against cardiovascular disease.

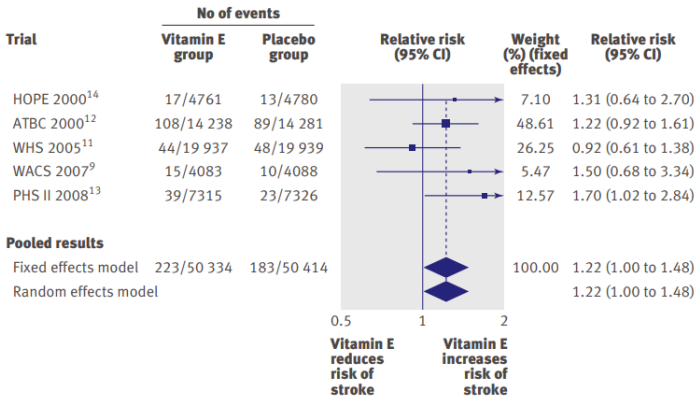


Fig 3 | Relative risks of the effect of vitamin E on haemorrhagic stroke for individual trials and for the pooled population

Increases Hemorragic stroke in 22%

Decreases risk of ischemic stroke in 10%

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HARMS IN SUPPLEMENTATION

Are there serious harms in supplementation?

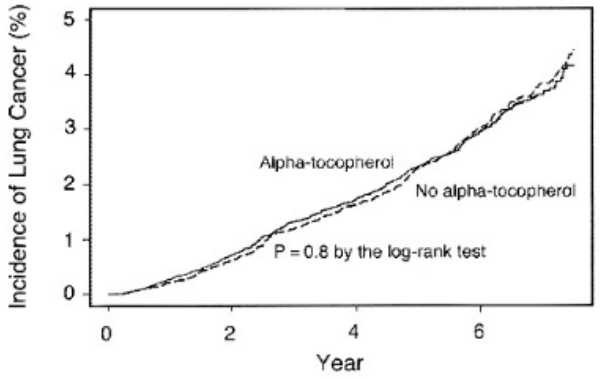
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

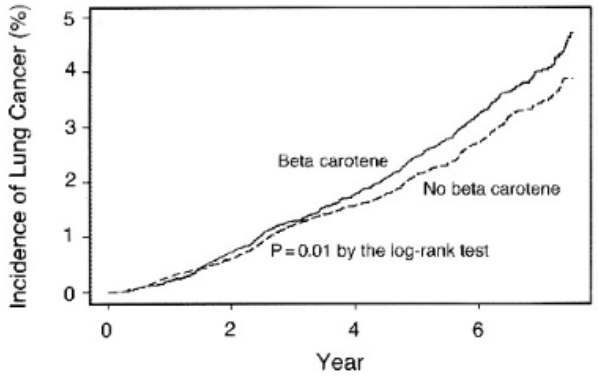
The Effect of Vitamin E and Beta Carotene on the Incidence of Lung Cancer and Other Cancers in Male Smokers

~30.000 male smokers healthy individual

Randomized to Vitamin E, Beta Carotene or placebo



Significant **increase of lung cancer** with **beta carotene** supplementation



No benefit with vitamin E

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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

OTHER VITAMINS

Outcome	No. of studies	No. analyzed	% with event		Odds ratio (95% CI)
			Intervention	Control	
Beta carotene					
All-cause mortality	6	112 820	5.4	5.1	1.06 (1.00-1.12)
CVD mortality	5	94 506	2.8	2.6	1.10 (1.02-1.19)
CVD events	2	61 947	3.5	3.5	1.01 (0.92-1.10)
Any cancer	2	61 947	5.3	5.4	0.99 (0.92-1.07)
Lung cancer[c]	4	94 830	1.2	1	1.20 (1.01-1.42)
Vitamin A					
All-cause mortality[d]	1	2297	5.4	4.6	1.16 (0.80-1.69)
Beta carotene or vitamin A					
All-cause mortality	7	115 117	5.4	5.1	1.06 (1.01-1.12)
Vitamin E					
All-cause mortality	9	107 772	6.9	6.8	1.02 (0.97-1.07)
CVD events	4	62 136	5.1	5.2	0.96 (0.90-1.04)
Any cancer	5	76 777	8.8	8.6	1.02 (0.98-1.08)
Vitamin D					
All-cause mortality	27	117 082	5	5.7	0.96 (0.91-1.02)
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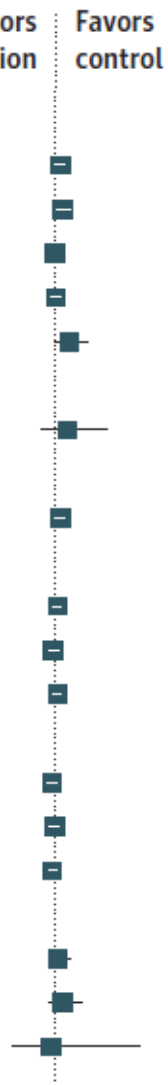

OTHER VITAMINS

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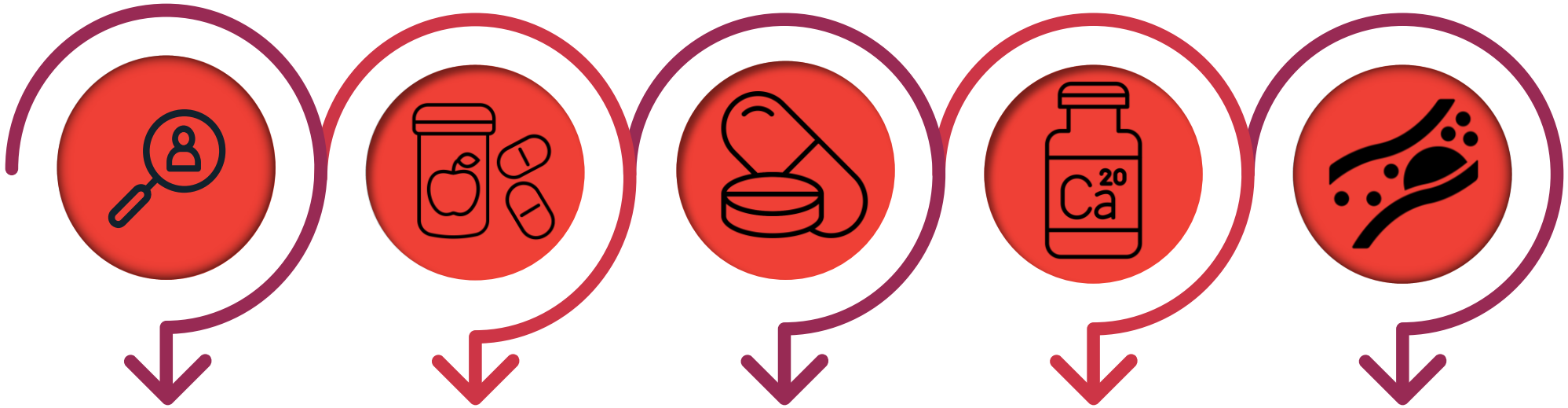
US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

USPSTF assessment	• The USPSTF concludes with moderate certainty that the harms of beta carotene supplementation for the prevention of cardiovascular disease or cancer outweigh the benefits. • The USPSTF concludes with moderate certainty that there is no net benefit of supplementation with vitamin E for the prevention of cardiovascular disease or cancer. • The USPSTF concludes that the evidence is insufficient to determine the balance of benefits and harms of supplementation with multivitamins for the prevention of cardiovascular disease or cancer. • The USPSTF concludes that the evidence is insufficient to determine the balance of benefits and harms of supplementation with single or paired nutrients (other than beta carotene and vitamin E) for the prevention of cardiovascular disease or cancer.

Supplements for the Primary Prevention of Cardiovascular Disease and Cancer



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SUPPLEMENTATION ON DYSLIPIDEMIAS

SUPPLEMENTATION ON DYSLIPIDEMIAS

For management of dyslipidemias, supplements are often used by patients in place of statins, in the absence of high-quality data.

Consumer research suggests most U.S. consumers believe cholesterol health supplements are safer than prescription medications.

Majority of the public also believe supplements are as effective, or more effective, than statins.

Gahche J, Bailey R, Burt V, Hughes J, Yetley E, Dwyer J, Picciano MF, McDowell M, Sempos C. Dietary supplement use among U.S. adults has increased since NHANES III (1988-1994). NCHS Data Brief 2011:1-8.

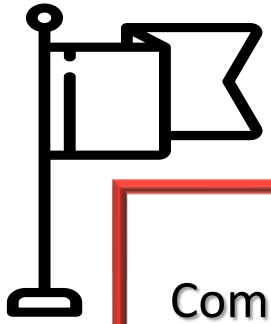
SUPPLEMENTATION ON DYSLIPIDEMIAS

SPORT trial

JACC Journals

Comparative Effects of Low-Dose Rosuvastatin, Placebo, and Dietary Supplements on Lipids and Inflammatory Biomarkers

Luke J. Laffin, MD,[a] Dennis Bruemmer, MD,[a] Michelle Garcia, RN,[b] Danielle M. Brennan, MS,[b] Ellen McErlean, MSN,[b] Douglas S. Jacoby, MD,[c] Erin D. Michos, MD,[d] Paul M Ridker, MD,[e] Tracy Y. Wang, MD,[f] Karol E. Watson, MD,[g] Howard G. Hutchinson, MD,[h] Steven E. Nissen, MD[a,b]



Compare the efficacy of a **low-dose statin** with placebo and **6 common supplements** in impacting lipid and inflammatory biomarkers

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SUPPLEMENTATION ON DYSLIPIDEMIAS

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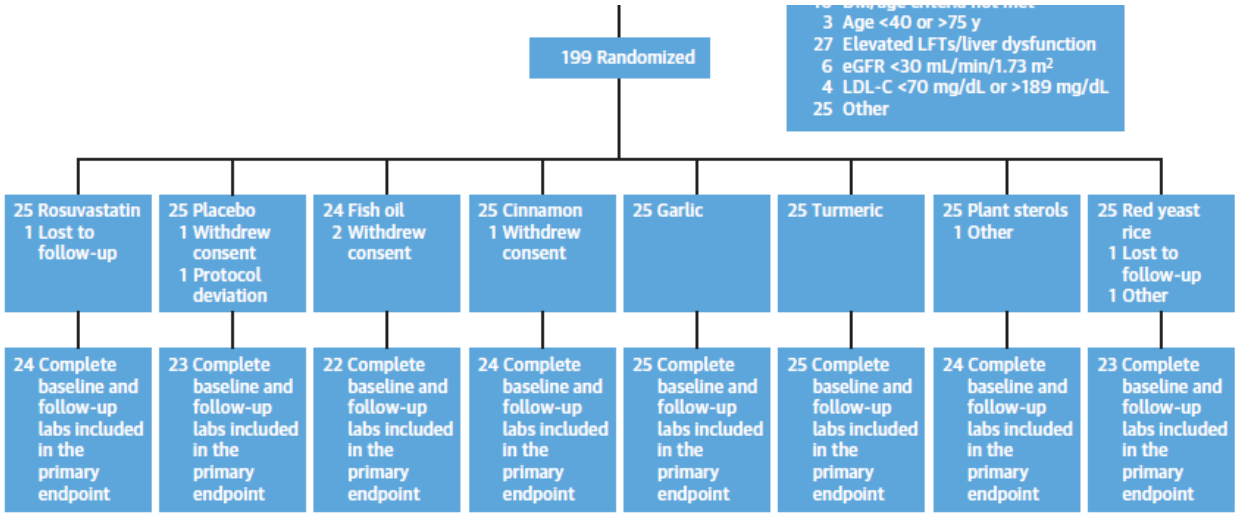

Inclusion Criteria

- **40 and 75 years**
- **LDL-C of 70 to 189 mg/dL**
- **no history of atherosclerotic cardiovascular disease**
- **not taking statins or other prescription lipid-lowering therapy**

Exclusion Criteria

- liver dysfunction
- fasting serum triglycerides >200 mg/dL.
- glomerular filtration rate of <30 mL/min/m2.

Gahche J, Bailey R, Burt V, Hughes J, Yetley E, Dwyer J, Picciano MF, McDowell M, Sempos C. Dietary supplement use among U.S. adults has increased since NHANES III (1988-1994). NCHS Data Brief 2011:1-8.

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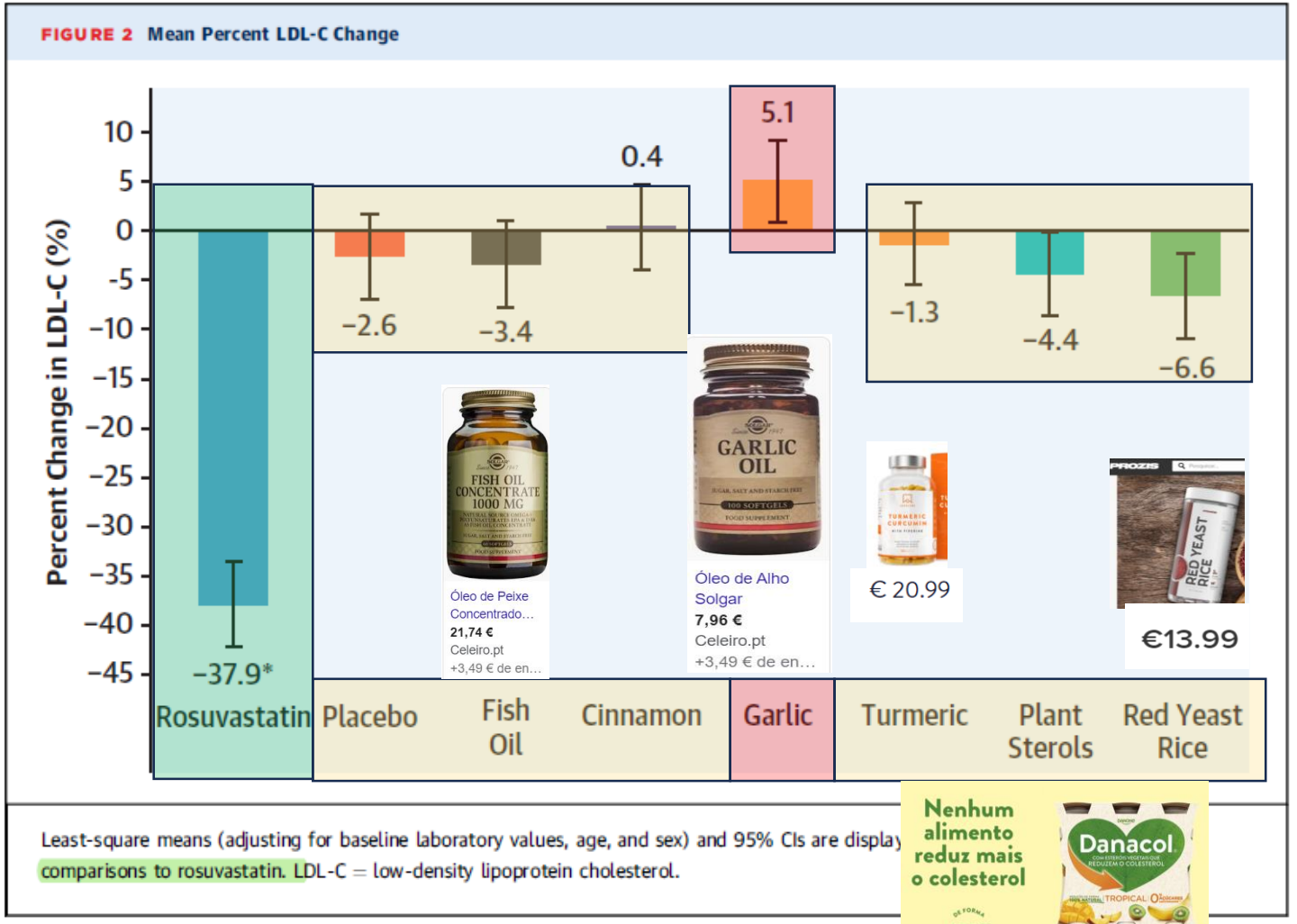
Primary endpoint: LDL reduction after 28 days



Gahche J, Bailey R, Burt V, Hughes J, Yetley E, Dwyer J, Picciano MF, McDowell M, Sempos C. Dietary supplement use among U.S. adults has increased since NHANES III (1988-1994). NCHS Data Brief 2011:1-8.

SUPPLEMENTATION ON DYSLIPIDEMIAS

JACC Journals

Comparative Effects of Low-Dose Rosuvastatin, Placebo, and Dietary Supplements on Lipids and Inflammatory Biomarkers

Luke J. Laffin, MD,[a] Dennis Bruemmer, MD,[a] Michelle Garcia, RN,[b] Danielle M. Brennan, MS,[b] Ellen McErlean, MSN,[b] Douglas S. Jacoby, MD,[c] Erin D. Michos, MD,[d] Paul M Ridker, MD,[e] Tracy Y. Wang, MD,[f] Karol E. Watson, MD,[g] Howard G. Hutchinson, MD,[h] Steven E. Nissen, MD[a,b]

Rosuvastatin Decreased LDL-C, Total Cholesterol, and Serum Triglycerides Significantly More Than Placebo and Each Supplement

LDL-C	Total Cholesterol	Triglycerides	HDL-C	hsCRP
↓	↓	↓	—	—

No difference in LDL-C reduction with any supplement compared to placebo

Supplements marketed or promoted for "cholesterol health" do not significantly lower LDL-C compared with placebo

No difference in adverse effects

Patients should be educated about the lack of benefit of these supplements on important cardiovascular risk factors.

Gahche J, Bailey R, Burt V, Hughes J, Yetley E, Dwyer J, Picciano MF, McDowell M, Sempos C. Dietary supplement use among U.S. adults has increased since NHANES III (1988-1994). NCHS Data Brief 2011:1-8.

TAKE HOME MESSAGES

- ✓ Dietary **supplementation is a very common** practice in developed countries.
- ✓ **Disease prevention (cardiovascular disease and cancer**) are common reasons appointed for supplement intake.
- ✓ **Multivitamins** do **not** seem to be **effective in CV disease.**
- ✓ **Supplementation may carry harms** in specific patients (Beta carotene, Vit E)
- ✓ **Supplements promoted for "cholesterol health" do not significantly lower LDL-C compared with placebo.**

MITOS OU REALIDADES NA PREVENÇÃO CARDIOVASCULAR

SUPLEMENTOS NA SAÚDE E DOENÇA CARDIOVASCULAR

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