

Nutraceuticals in Heart Failure Prevention

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**15th Annual Orange County
Symposium for Cardiovascular
Disease Prevention**

A faint, stylized illustration in the background shows a person running, overlaid with a red heart rate monitor line. The runner is depicted in a light blue and white color scheme, moving from left to right. The heart rate line is a vibrant red, showing a typical pulse pattern. The overall aesthetic is clean and medical.

Disclosures

- none



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Complementary and Alternative Medicines

“A group of diverse medical and healthcare systems, practices, and products that are not presently considered to be part of conventional medicine”

– *National Institutes of Health (NIH)*

- Alternative whole medical systems (ex. homeopathic, Chinese medicine, Ayurveda)
- Mind-body interventions (ex. meditation, art, tai chi)
- Biologically based therapies (vitamins, herbals, dietary supplements)
- Manipulative body-based methods (ex. osteopathic, chiropractic, massage)
- Energy Therapeutics (ex. therapeutic touch, Reiki)

Complementary vs. Alternative Medicine

- **Complementary Medicine**
 - Used **together** with conventional medicine
- **Alternative Medicine**
 - Used **in place** of conventional medicine



Contributing factors

- Ads and television
- “Alternative medicine and therapies are natural and therefore safe”
- “OTCs are too weak to cause any harm”
- Self-prescribing and easy access
- Cost
- Cultural and ethnic influence



“You the guy who asked for the least expensive generic alternative?”

Background

- 1/3 of HF patients use CAM
- 1 in 5 adults use herbal therapy within a year
- Increasing trend
- Used across different populations
 - Age
 - Gender
 - Income level
 - Education



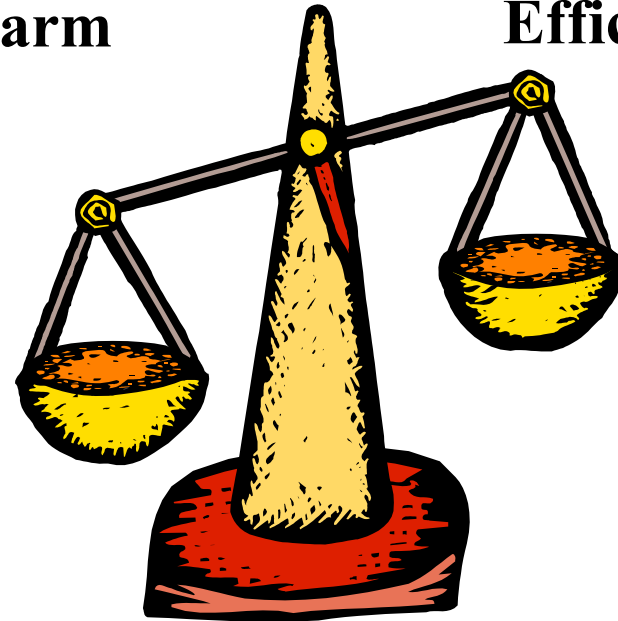
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The problem in HF

- Regulation
- Lack of efficacy
- Priority over conventional therapies
- Interactions
 - Drug-Drug
 - Drug-Nutrient
- Adverse effects
- Informing healthcare providers

**Risk of
Harm**

**Proven
Efficacy**



First Do No Harm

- Consider whether alternative therapy is
 - Effective and safe with evidence of efficacy and safety
 - Effective but evidence of potential danger or side effects
 - Inadequately studied but safe
 - Both ineffective and dangerous



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Oversight and Regulation of CAM

Dietary Supplements

- 1994 Dietary Supplement Health and Education Act (DSHEA)
 - Maintain health in some manner
 - Regulated like foods
 - Requires identity, quantity, nutrition, ingredients, name/place of manufacturer
 - Exempted premarket safety and efficacy testing

Which could be toxic?



Standards and Transparency

US Pharmacopeia

- Standards for drugs and supplements
- Ensures compliance with standards
 - Quality, quantity, purity, strength, packaging, labeling
- Many dietary supplements are not endorsed!
- www.usp.org/verification-services/dietary-supplements-verification-program
- Nature made and Kirkland

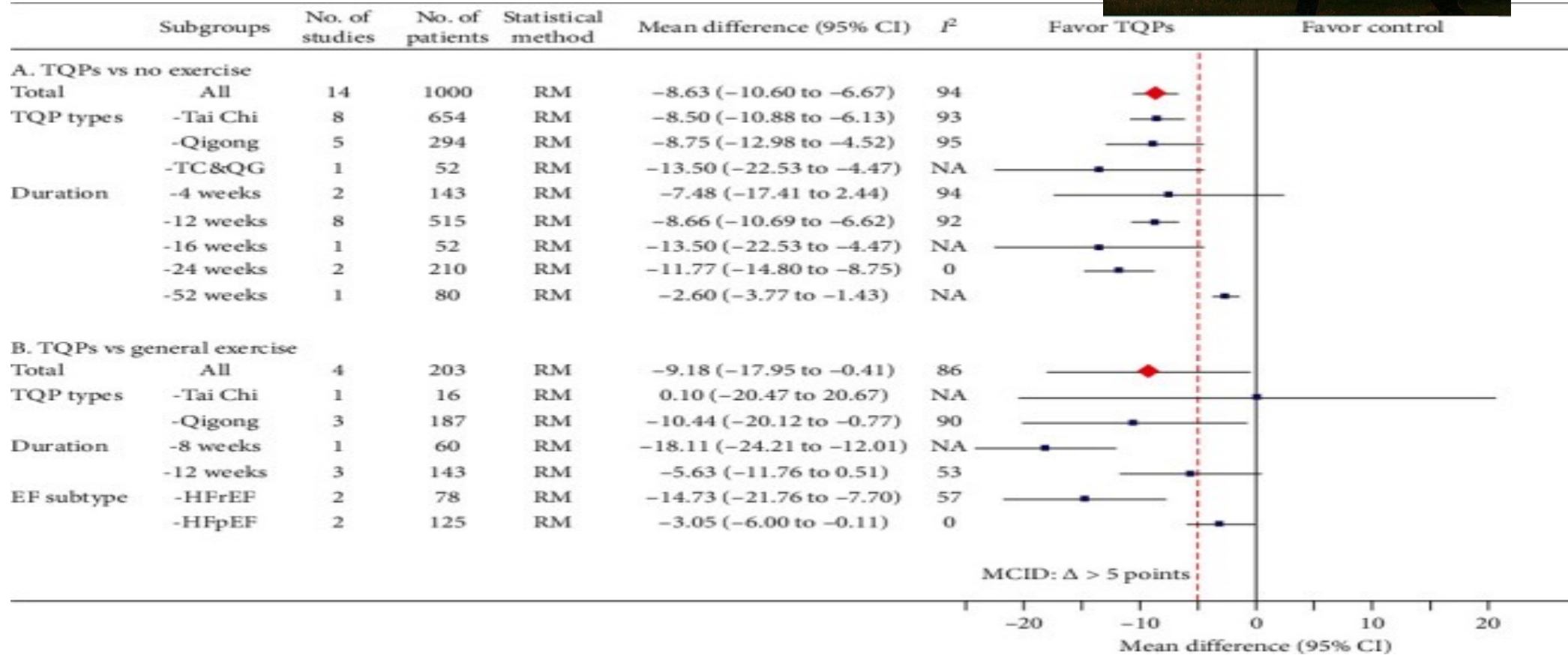
Nutrition Facts	
Serving Size 100 tons	
Serving Per Container About 50	
Amount Per Serving	
Calories	1 million
Total Fat	2 pounds
Vitamins	Zero
Cholesterol	50%
Sodium	20%
Sugar	20%
Total Carbohydrate	10%
Dietary Fibre	0%
Vitamin A 0% • Vitamin C 0%	
Vitamin D 0% • Vitamin F 0%	
Calcium 50% • Iron 50%	
INGREDIENTS: Dog hairs, sheep dip, deck varnish, pond scum, parts cleaner, squid ink, mouthwash, dandruff flakes, barnyard slops, bicyanalyticalthrombolysis, expired dairy products, wheel grease, military de-icing solution, crushed glass particles, nail polish remover, FDA approved colors and artificial flavorings.	



despite optimization of GDMT.

2. Many nutritional supplements and hormonal therapies have been proposed for the treatment of HF.^{3–9,30,31} Ultimately, most studies are limited by small sample sizes, surrogate endpoints, or nonrandomized design.^{32,33} In addition, adverse effects and drug-nutraceutical interactions remain unresolved. There is a lack of evidence of benefit from vitamin D,^{3–5} thiamine,^{34–36} carnitine,³⁷ and taurine^{38,39} and potential harm from vitamin E.^{6,7} The largest RCT of coenzyme Q10—Q-SYMBIO (Coenzyme Q10 as adjunctive treatment of chronic heart failure with focus on SYMptoms, Blomarker status [Brain-Natriuretic Peptide], and long-term Outcome [hospitalisations/mortality])—showed no changes in NYHA functional classification at 16 weeks, although the incidence of major adverse cardiovascular events at 2 years was significantly reduced (hazard ratio, 0.50; 95% CI, 0.32–0.80; $P=0.003$).⁸ Despite these findings, concerns about slow recruitment in this trial have tempered enthusiasm for coenzyme Q10 supplementation in clinical practice.^{9,31} Hormonal therapies have been proposed

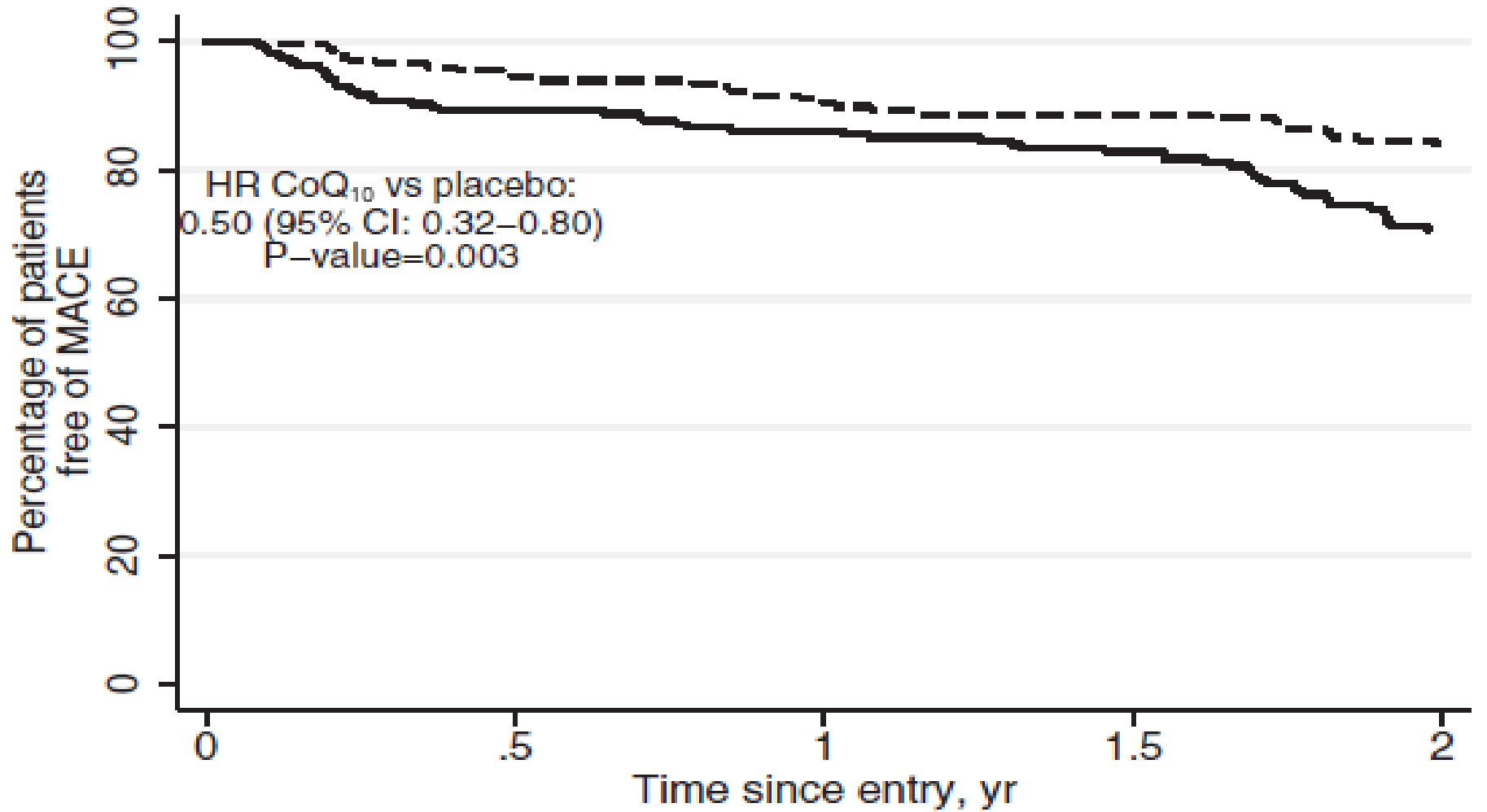
Tai Chi



Tai Chi is safe and well tolerated adjunctive therapies for HF.
Improves mood and QOL

CoQ10 Q-SYMBIO trial

- 420 pts, randomized, double blind, placebo controlled trial.
- CoQ10 – 100mg three times daily x 2 years
- Major endpoint – composite of worsening HF, CV death, mechanical assist implant, urgent transplant.
- 88% Class III, 90% ACE, 72% BB, 46% Dig, 34%AA.
- EF = 31%

A

Number at risk

CoQ ₁₀	202	179	154	147	138
Placebo	218	180	162	150	127

--- CoQ₁₀ — Placebo

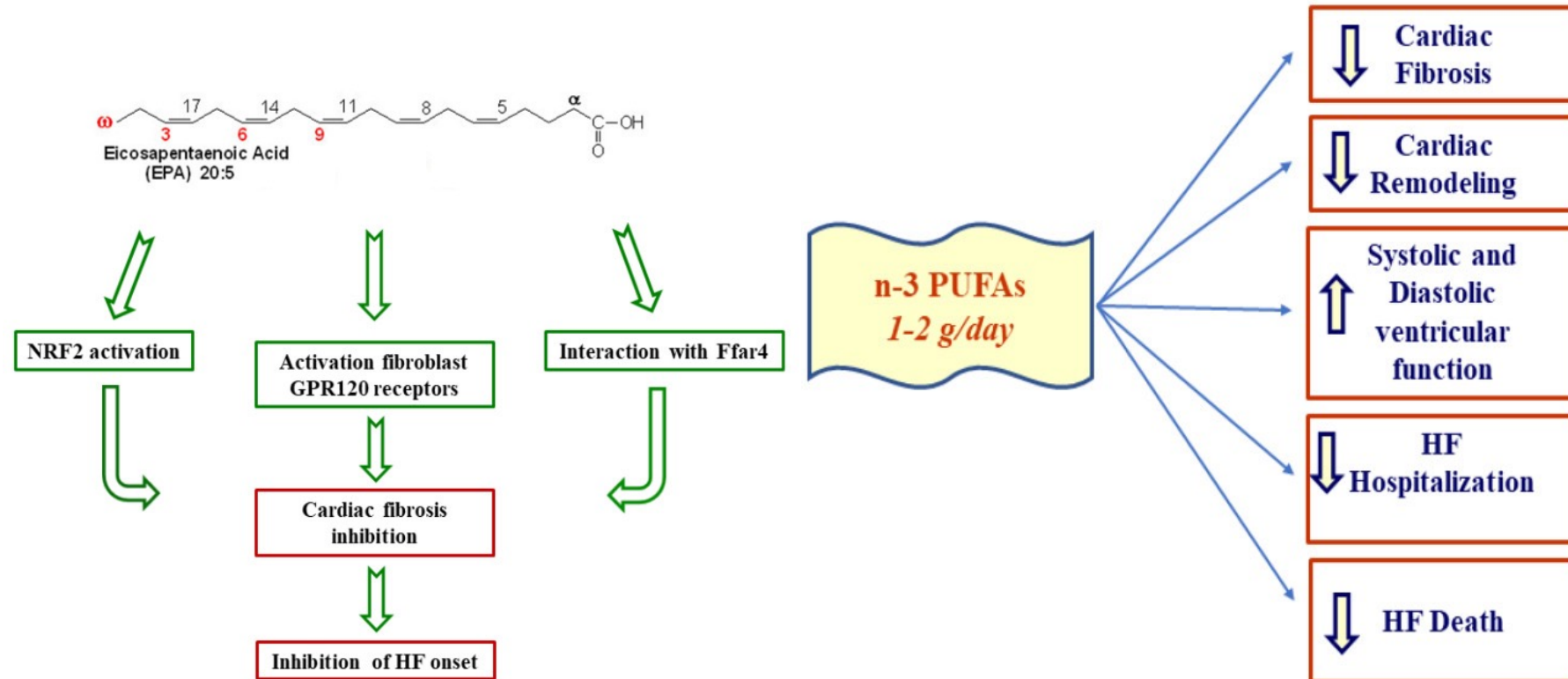
7.3.6. Other Drug Treatment

Recommendations for Other Drug Treatment

Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	Recommendations
2b	B-R	1. In patients with HF class II to IV symptoms, omega-3 polyunsaturated fatty acid (PUFA) supplementation may be reasonable to use as adjunctive therapy to reduce mortality and cardiovascular hospitalizations. ¹⁻⁴

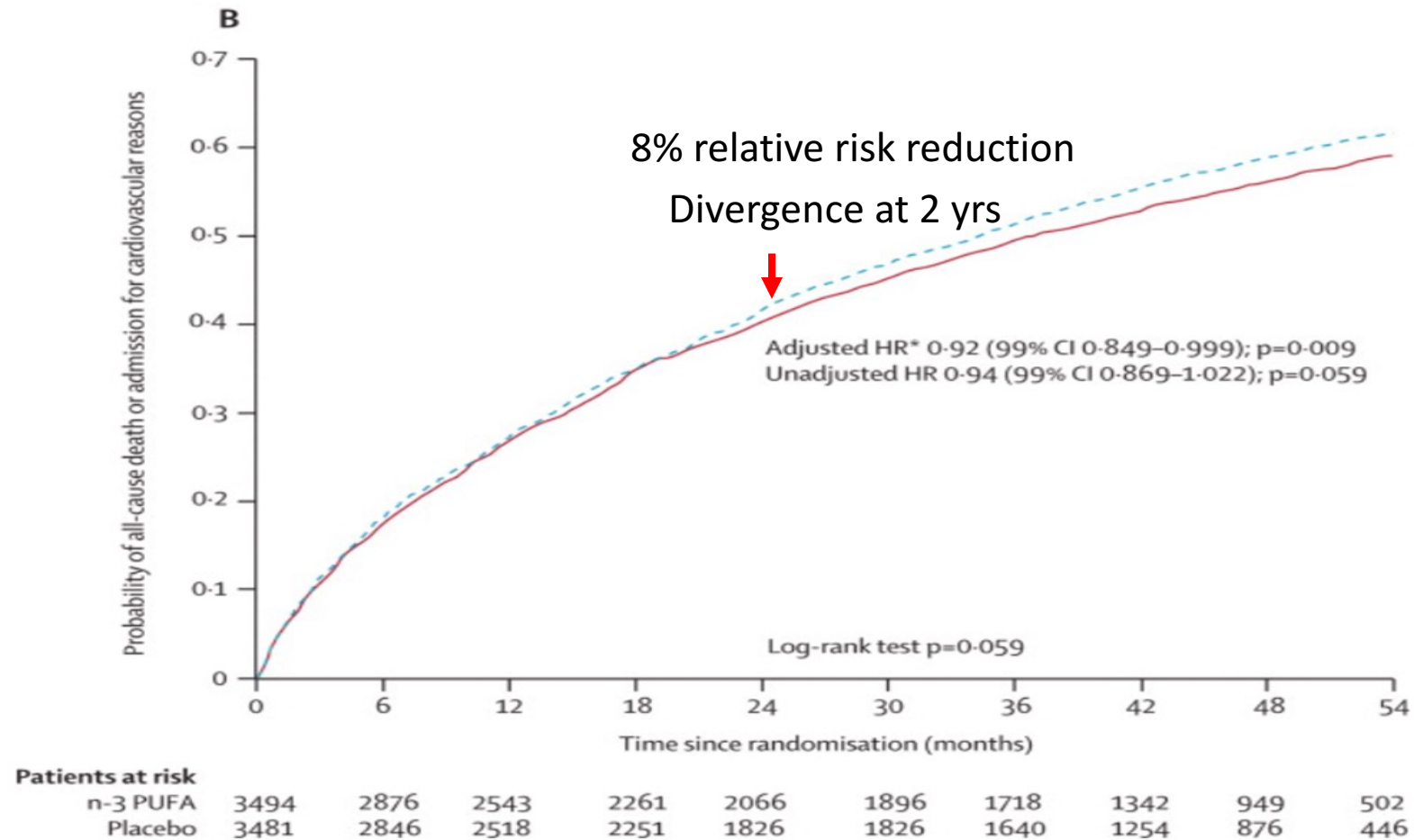
Fish oil on HF



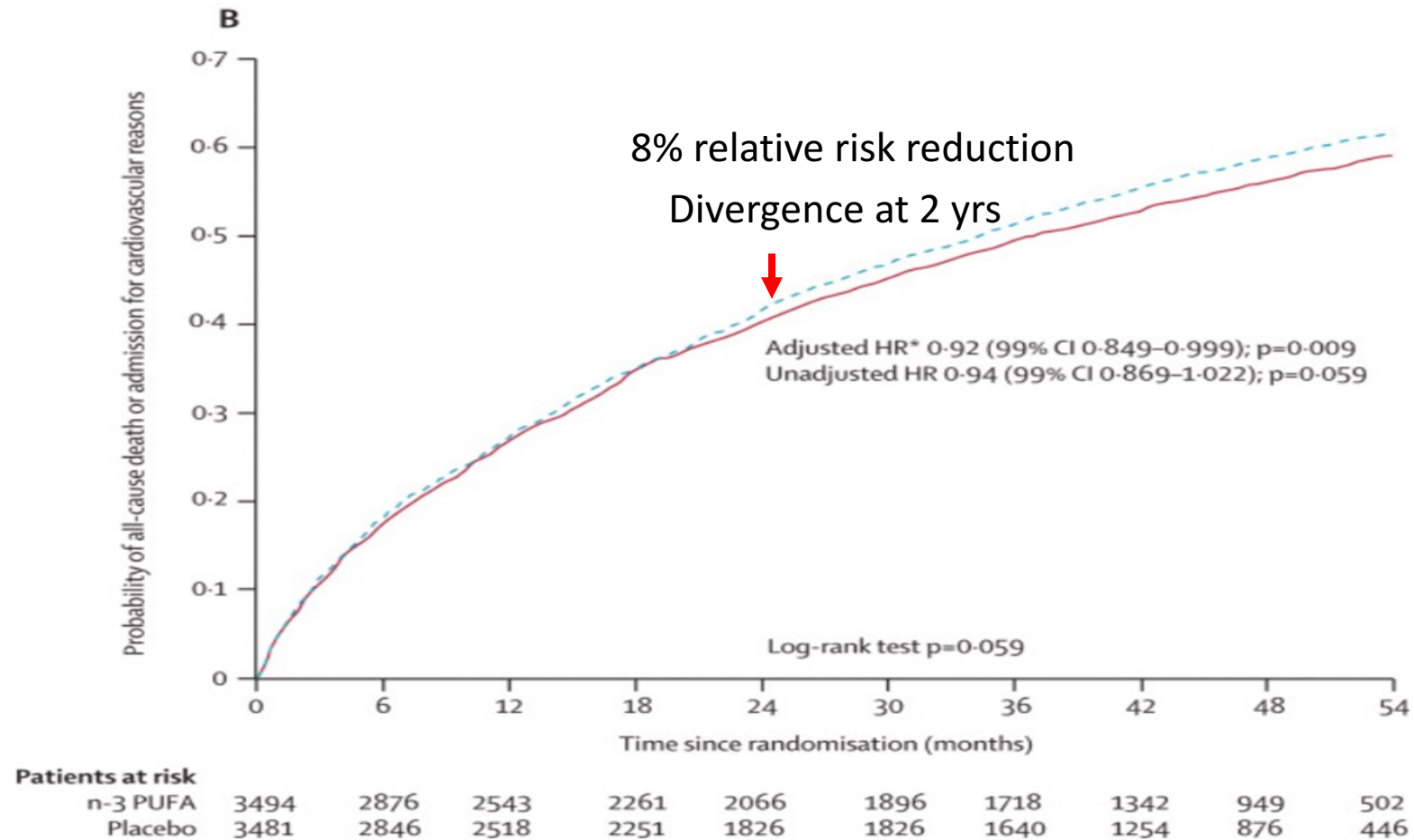
GISSI-HF Trial

- Randomized double-blind, placebo-controlled trial
- N=6,975 NYHA Class II-IV, HFrEF
- PUFA 3 fa <1 g daily vs. placebo
- Mean 3.9 yr f/u
- Primary endpoint: time to death, and time to death or CV hospitalization

GISSI-HF: Time to all-cause death or CV hospitalization



GISSI-HF: Time to all-cause death or CV hospitalization



Risk of Afib with Fish Oil

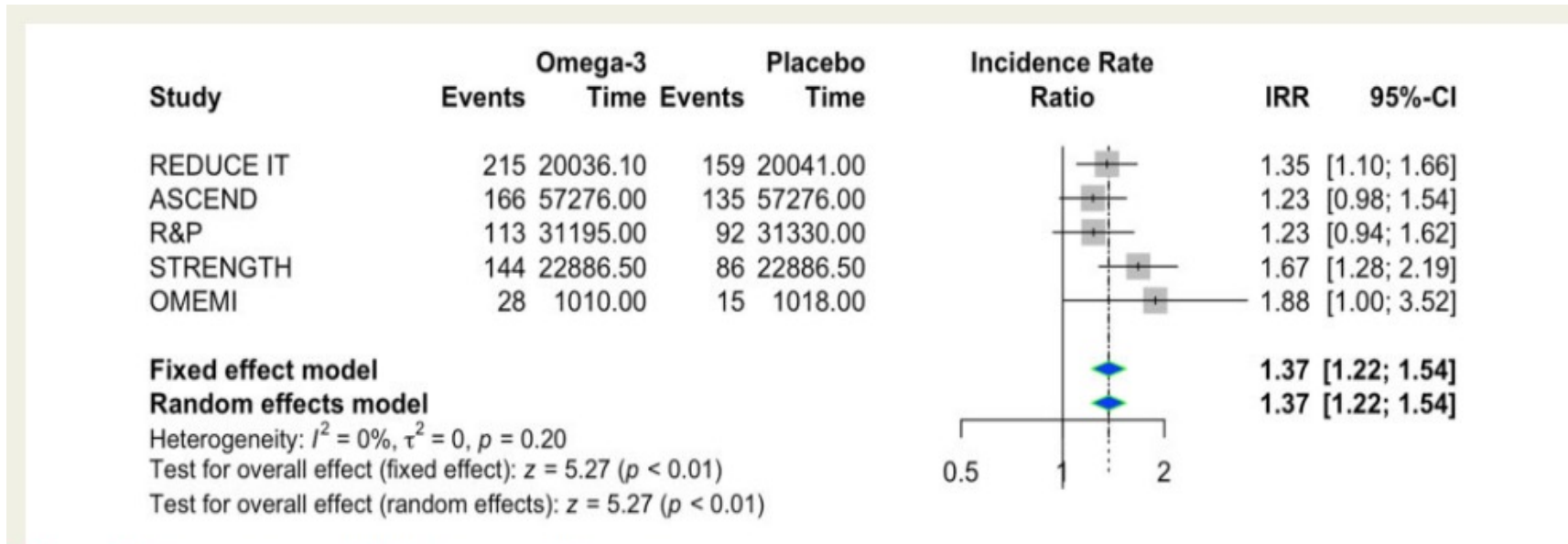


Figure 1 Forest plot for atrial fibrillation events. IRR, incidence rate ratio.

More than 2g/d of Fish oil may increase risk of Afib.

Circulation

AHA SCIENTIFIC STATEMENT

Complementary and Alternative Medicines in the Management of Heart Failure: A Scientific Statement From the American Heart Association

Sheryl L. Chow, PharmD, FAHA, Chair; Biykem Bozkurt, MD, PhD, FAHA, Vice Chair; William L. Baker, PharmD, FAHA; Barry E. Bleske, PharmD; Khadijah Breathett, MD, MS, FAHA; Gregg C. Fonarow, MD, FAHA; Barry Greenberg, MD, FAHA; Prateeti Khazanie, MD, MPH; Jacinthe Leclerc, RN, PhD, FAHA; Alanna A. Morris, MD, MSc; Nosheen Reza, MD; Clyde W. Yancy, MD, FAHA; on behalf of the American Heart Association Clinical Pharmacology Committee and Heart Failure and Transplantation Committee of the Council on Clinical Cardiology; Council on Epidemiology and Prevention; and Council on Cardiovascular and Stroke Nursing

Safety of CAM in HF

Agent

- Hawthorn



- Oleander



- Vitamin E
 ≥ 400 IU/day



- Caffeine 500 mg within 5 hrs
 3-5 cups coffee



ADRs/ Interactions




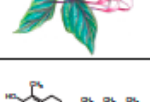
- \uparrow HF progression, digoxin?

- Cardiac glycoside

\uparrow risk of new onset HF

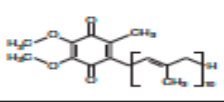
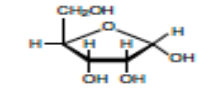
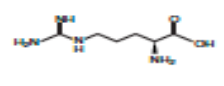
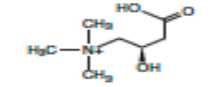
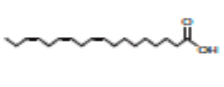
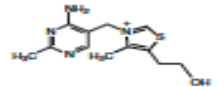




- Increases BP, \uparrow diuresis

Chow SL, et al. Circulation.
2023;147:e4-e30

	Potentially harmful	Interactions
	Bitter Orange	√
	Blue Cohash	
	Devil's claw	√
	Ginkgo	√
	Gossypol	
	Grapefruit Juice (dose dependent)	√
	Khella	
	Licorice	
	Lily of the Valley	√
	Oleander	√
	Strophanthus	√
	Vitamin E	



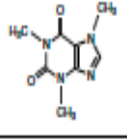


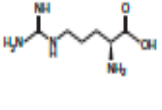
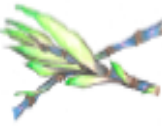


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Potentially beneficial	
	Co-Q10
	D-Ribose
	L-arginine
	L-carnitine
	Omega-3 fatty acids
	Thiamine (with deficiency)
	Vitamin C (with deficiency)
	Vitamin D (with deficiency)
	Yoga with GDMT
	Tai-Chi with GDMT

Chow SL, et al. Circulation. 2023;147:e4-e30

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	Bidirectional	Interactions
	Alcohol	
	Aloe Vera	
	Caffeine	
	Guar gum	
	Hawthorn	√ PD, theoretical
	L-arginine	
	Policosanols	

Chow SL, et al. Circulation.
2023;147:e4-e30

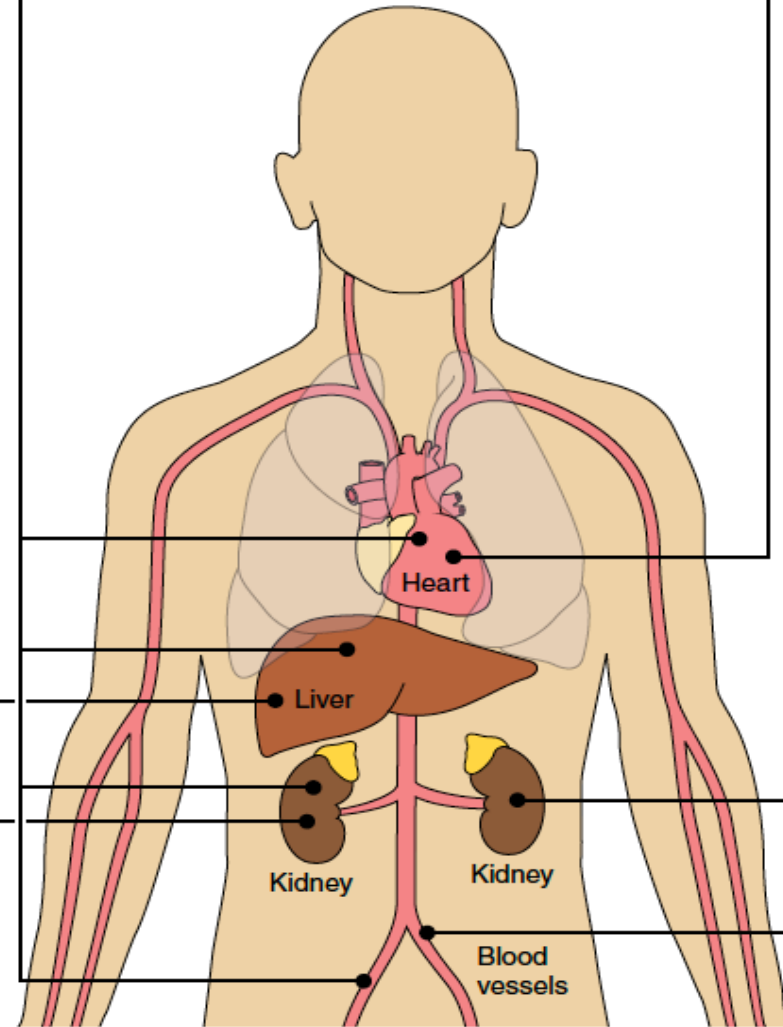


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Decreased heart rate
 Rx:
 • Beta blockers (carvedilol, metoprolol succinate, bisoprolol)
 • Ivabradine
 CAM:
 ↑ Bitter Orange
 ↑ Blue Cohash
 ↓ Khella

Metabolism of cardiac drugs
 ↑ St. Johns Wort
 ↓ Grapefruit juice
 ↓ Bitter Orange
 ↓ Devils Claw
 ↓ Ginko

Increased fluid loss
 Rx:
 • Diuretics (furosemide, torsemide, bumetanide)
 • Mineralocorticoid antagonists (spironolactone, eplerenone)
 • SGLT2 inhibitors (dapagliflozin, empagliflozin)
 CAM:
 ↑ Caffeine
 ↓ Licorice root
 ↑ Alcohol



Increased force of contraction
 Rx:
 • Digoxin
 • Milrinone
 • Dobutamine
 • Dopamine
 CAM:
 ↑ Hawthorn
 ↑ Lily of the Valley
 ↑ Oleander
 ↑ Strophanthus
 ↓ Khella

Decreased blood pressure
 Rx:
 • ARNI (sacubitril, valsartan)
 • ACE inhibitors (lisinopril, captopril, quinapril, etc.)
 • ARBs (losartan, candesartan, valsartan)
 CAM:
 ↑ Bitter Orange
 ↑ Licorice root
 ↓ Khella
 ↑ or ↓ Caffeine
 ↑ Blue Cohash
 ↑ Devils Claw

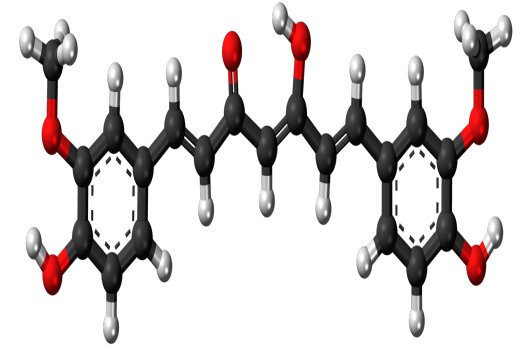
Electrolytes
 ↑ K⁺ Licorice
 Lilly of the Valley
 Aloe Vera
 Gossypol
 ↑ Na⁺ Licorice
 ↑ Ca²⁺ Vitamin D

Turmeric in CVD?

- Curcumin: polyphenol compound from turmeric
- Anti-inflammatory
- Anti-oxidant effects
- Normally poor absorption
- Reduced activation of LVH and BNP (hypertensive rats)



Curcumin for the prevention of hypertensive heart disease

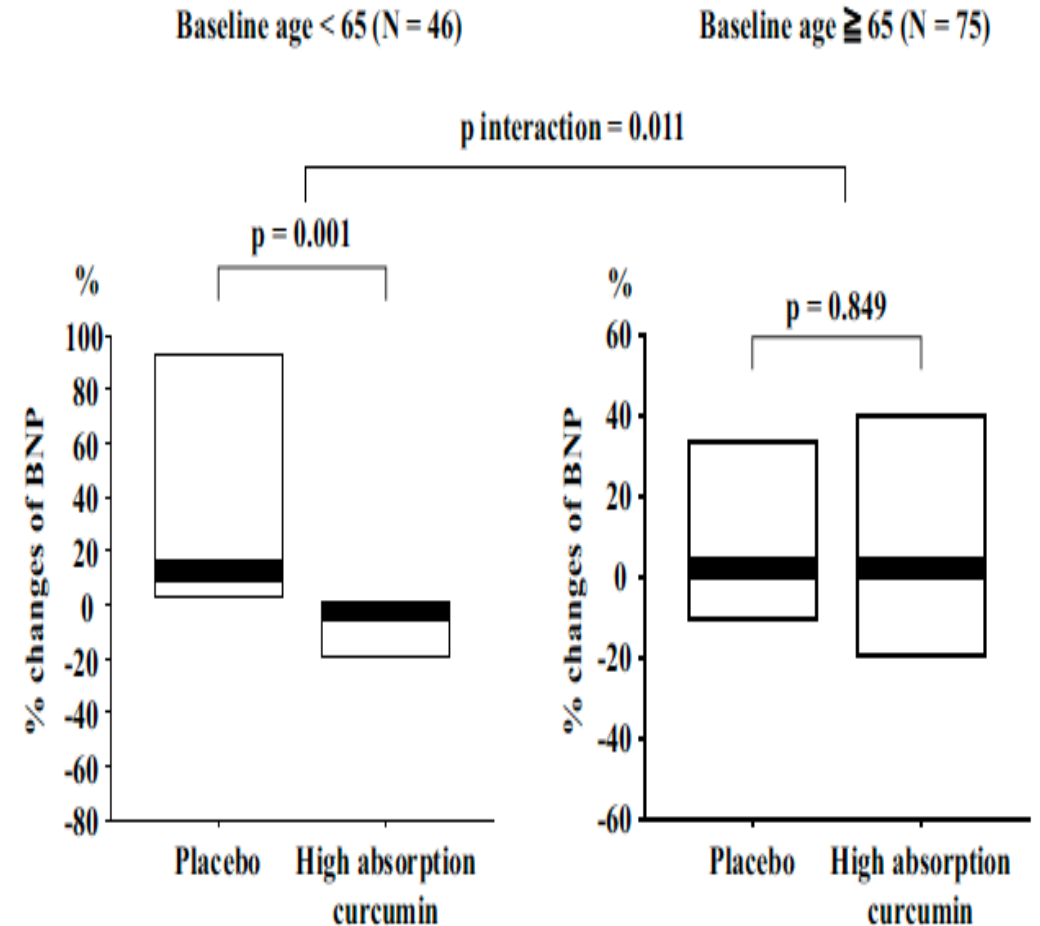


- Randomized double-blind, placebo-controlled trial
- N=142 LVEF $\geq 60\%$ <https://en.wikipedia.org/wiki/Curcumin>
- Curcumin 90 mg twice daily vs. placebo (n=73 vs. 69)
- 24 weeks
- Primary endpoint: E/E' from baseline to 6 months
- Secondary endpoint: % change in BNP

Curcumin: Change in BNP based on age

End points	Placebo, n=25	Curcumin, n=24	p
• Δ SBP (%)	3.8	-5.3	0.022
• Δ DBP (%)	1.2	-4.2	0.112
• Δ E/A (%)	-7.1	-5.9	0.826
• Δ E/E' (%)	1.4	-3.9	0.386

Percent change
Baseline age <65 years



Turmeric (Curcumin) conclusions

- High-absorption curcumin did not affect E/E' ratio
- Attenuated an increase in BNP with early hypertensive heart disease/LV diastolic dysfunction
- Unknown if prevents progression to HFpEF

Low Antihypertensive Med Adherence CoSMO Humana population

N=2180 Black and White adults ≥ 65 years of age on antihypertensive medications

	Prevalence %	P	Prevalence Ratio	P	Multivariable adjusted Ratio	P
Blacks						
No CAM	26%	<0.001	1.71	0.001	1.56	0.006
CAM	15%					
Whites						
No CAM	12.3%	0.956	0.97	0.872	0.95	0.728
CAM	12.2%					

Adherence based on Morisky Medication Adherence Scale (MMAS-8)

How Does CAM Influence Adherence?

- Higher educational status associated with CAM use
- Blacks were less likely than whites to discuss health food supplements
- Hispanics and Asians are also less likely to disclose CAM use to their physician or pharmacist
- White participants with more comorbidities were more likely to use CAM
- Lack of federal oversight can lead to misuse and misunderstanding

Closing gaps to improve counseling

- 72% of patients do not report use of alternative therapy to healthcare providers
- Healthcare professionals do not routinely ask, document, or monitor dietary supplements
 - Physicians lack resources to answer patient inquiries
 - Community retail pharmacists less likely to inquire about supplements than inpatient pharmacists.
 - Utilize multidisciplinary team care
 - Consult pharmacy to counsel patient and assess for nutrient-drug interactions.
 - Include CAM during Medication Reconciliation (nurses and pharmacists). Ask patients directly about diet, supplements and herbs.



Counseling patients

Do NOT

- Avoid asking patients about CAM use
- Criticize or judge patients
- Make demands , paternalistic approach



Do

- Reserve judgement
- Be ethnically sensitive
- Provide objective lack of evidence and potential safety concerns.



Summary

- Studies show that healthcare professionals need further knowledge, confidence, and training in CAM therapy.
- CAM agents are frequently used in conjunction with traditional therapies and careful consideration of efficacy and safety are important.
- Modest improvements on CV outcomes have been observed with select CAM agents but larger, more robust randomized trials are needed
- Discussions between clinician and patient should occur routinely to improve safety and adherence.



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