Science for Women

Zoom in on Menopause

Naturally Informed

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March 27 2025

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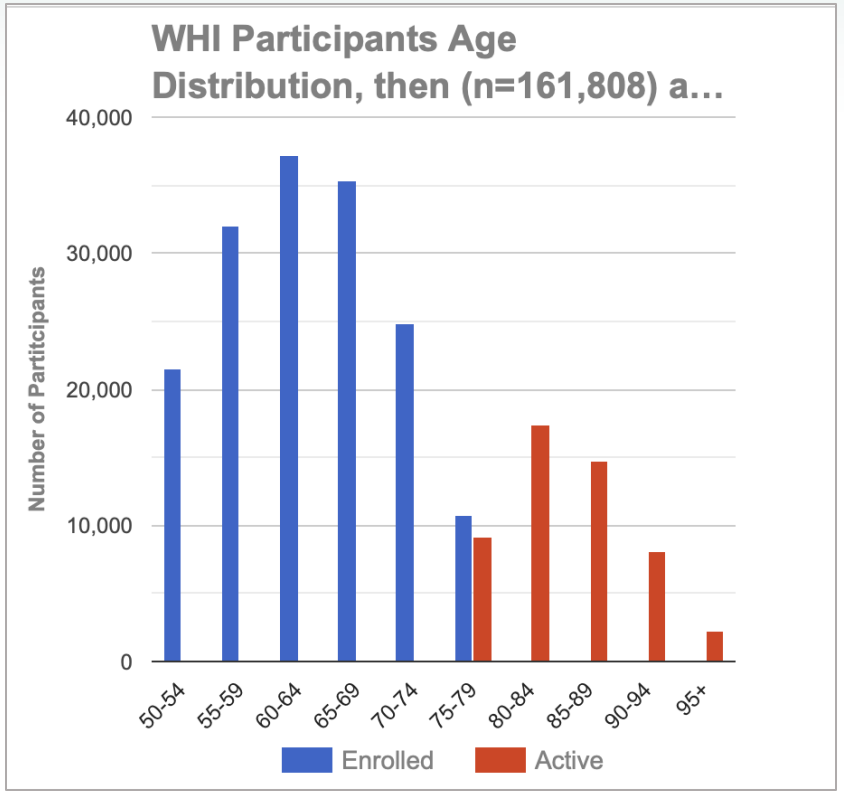
Women's Health Initiative (WHI)

A long-term national health study tracking cardiometabolic, cancer, osteoporosis

- The original WHI study began in the early 1990s and concluded in 2005.
- Since 2005, the WHI has continued as Extension Studies
- Study enrolled 93,500 women in 2010 and follow-up of these women continues annually.

Important insights:

- HRT is appropriate to treat bothersome vasomotor symptoms among women **in early menopause**, without contra-indications
- The WHI evidence does not support routine supplementation with calcium plus vitamin D for menopausal women to prevent fractures, However, supplementation is appropriate for women who do not meet national guidelines for recommended intakes of these nutrients



https://pubmed.ncbi.nlm.nih.gov/38691368/

What to expect today:

Deeper dive: wellness in the context of menopausal transition

Topics for today:

- Cognitive & mood
- Cardiometabolic health
- Active nutrition & weight management
- Latest on supplements in cardiovascular health

https://pubmed.ncbi.nlm.nih.gov/38691368/

Cognitive and Mood through the menopausal journey

Brain Fog, Stress & Mood

(in the context of Hormonal changes)

https://pubmed.ncbi.nlm.nih.gov/38691368/

Women and Chocolate…

Mood-boosting powers of chocolate:
This study finally puts it to the test!”

Study design

- 60 women, ages 45-65.
- 8-week intervention: 12 g chocolate (about 2 cubes) dark vs milk. (with the same nutritional composition)

Results

- Significant Improvement in depression scores
- No significant changes in sleep quality or in anthropometric indices (weight, BMI, waist / hip circumferences)

Key takeaway: Dark chocolate (78%) lowers depression score in menopausal women

Sci Rep. 2024 (Nature portfolio)

https://pubmed.ncbi.nlm.nih.gov/39397049/

Women and Chocolate…

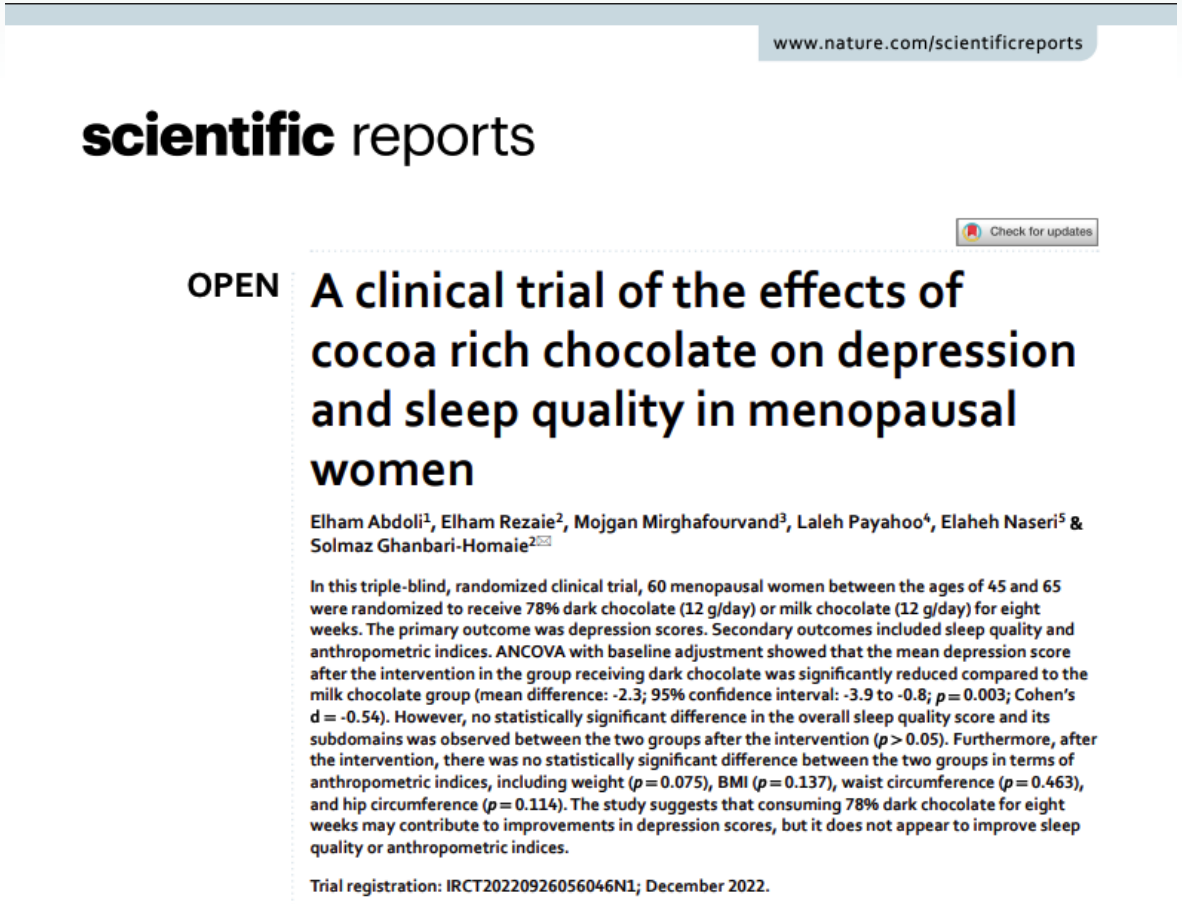
What I love about it:

Yes, chocolate is good for the soul ☺
(And science agrees!)

A daily dose of 78% dark chocolate (12g/day) significantly improved mood in menopausal women.

No stress about weight gain!
Even with milk chocolate –no significant changes in weight and BMI.
2 cubes of chocolate certainly won't hurt.

Eat with love and be kind to yourself



www.nature.com/scientificreports

scientific reports

Check for updates

OPEN

A clinical trial of the effects of cocoa rich chocolate on depression and sleep quality in menopausal women

Elham Abdoli[1], Elham Rezaie[2], Mojgan Mirghafourvand[3], Laleh Payahoo[4], Elaheh Naseri[5] & Solmaz Ghanbari-Homaie[2]✉

In this triple-blind, randomized clinical trial, 60 menopausal women between the ages of 45 and 65 were randomized to receive 78% dark chocolate (12 g/day) or milk chocolate (12 g/day) for eight weeks. The primary outcome was depression scores. Secondary outcomes included sleep quality and anthropometric indices. ANCOVA with baseline adjustment showed that the mean depression score after the intervention in the group receiving dark chocolate was significantly reduced compared to the milk chocolate group (mean difference: -2.3; 95% confidence interval: -3.9 to -0.8; $p = 0.003$; Cohen's $d = -0.54$). However, no statistically significant difference in the overall sleep quality score and its subdomains was observed between the two groups after the intervention ($p > 0.05$). Furthermore, after the intervention, there was no statistically significant difference between the two groups in terms of anthropometric indices, including weight ($p = 0.075$), BMI ($p = 0.137$), waist circumference ($p = 0.463$), and hip circumference ($p = 0.114$). The study suggests that consuming 78% dark chocolate for eight weeks may contribute to improvements in depression scores, but it does not appear to improve sleep quality or anthropometric indices.

Trial registration: IRCT20220926056046N1; December 2022.

https://pubmed.ncbi.nlm.nih.gov/39397049/

Brain fog? - Citicoline…

Improvement in accuracy and attentional performance:

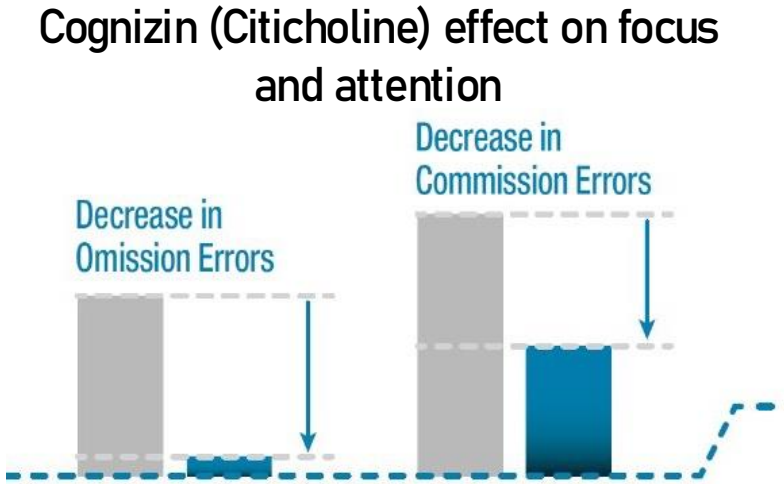
Study design

- 60 women, ages 40-60.
- 28 days intervention
- Citicholin (Cognizin, Kyowa) 250 mg or 500 mg

Results

- In Continuous Performance test (CPT-II) Significantly less **Omission and Commission** errors compared to placebo
- Mechanism includes increased energy utilization

Key takeaway: Supports “Brain energy”, mental clarity and focus in women (where are the keys?)



Mcglade E. et al. Food and Nutrition sciences 2021;3:769-773

Cardiometabolic and fitness journey in menopause

Active Nutrition, Healthy Weight Management, Cardiometabolic Outcomes

Menopause and Cardiometabolic Health

Decline in estrogen levels impacts almost any process in the body.

Risk factors in the context of cardiometabolic health:

- Increased LDL
- Decreased HDL
- Higher blood pressure
- Insulin sensitivity changes
- Fat and its distribution

Risk factors for:

- Atherosclerosis
- Hypertension
- Blood clots
- Insulin resistance/metabolic syndrome

Lifestyle modifications and proper nutrition are crucial to support cardiometabolic wellness

Role of Dietary Supplements in Supporting Cardiovascular Health in Menopausal Women

- Supplements can help manage cardiovascular health in menopausal women.
- Not a replacement for a balanced diet but can support overall well-being.
- Certainly not a replacement for drugs!

Healthy Weight management

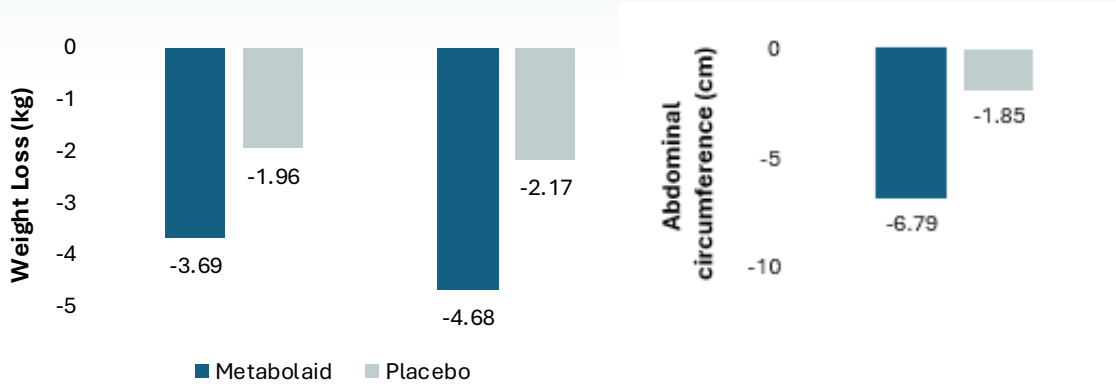
Weight loss, metabolic regulation, appetite & craving control

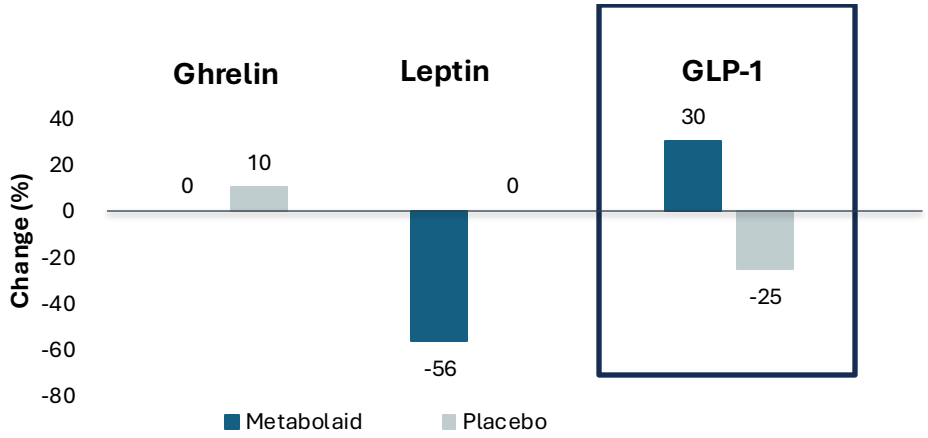
Study design

- 54-93 women, ages 36-69 (mean age 51).
- Overweight and Obese
- 60 days intervention alongside diet + 30 min walk
- 500 mg Lemon verbena + Hibiscus (Metabolaid, Monteloeder)

Results

- Higher weight loss: +88 % for over-weight (8.1 lb vs 4.3 lb) and +116% (10.3 lb vs 4.8 lb) for obese
- Majority from **visceral fat loss, (not muscle)**
- Significant Reduction in **Abdominal circumference**
- Improved **blood pressure and metabolic health**

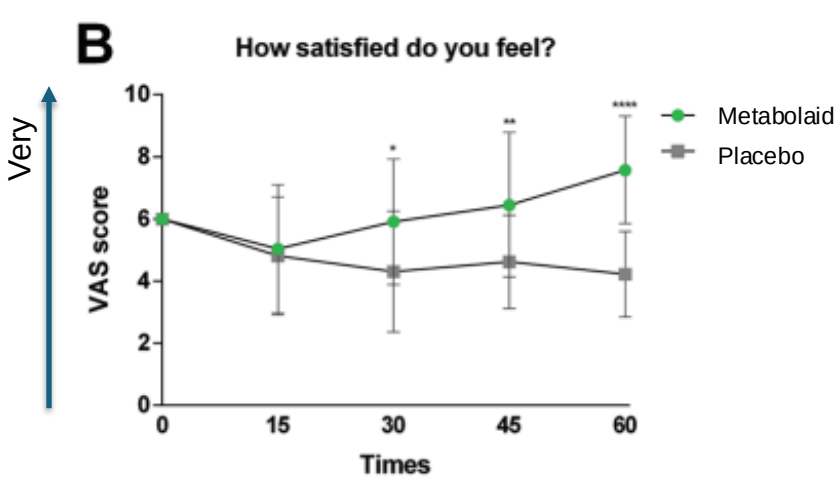




1. Herranz-López M, et al Sci Rep. 2019;9(1):2999. Published 2019 Feb 28. doi:10.1038/s41598-019-39159-5;
2. Boix-Castejón M, et al.. *Food Funct*. 2018;9(7):4037. doi:10.1039/c8fo90028k

Healthy Weight management

The human (or women) experience



Less hungry, more satisfied and less craving both sweet or savory

Important! Supplements are not a magic cure, and not meant to be
They reward good behavior

1. Herranz-López M, et al Sci Rep. 2019;9(1):2999. Published 2019 Feb 28. doi:10.1038/s41598-019-39159-5;
2. Boix-Castejón M, et al.. *Food Funct*. 2018;9(7):4037. doi:10.1039/c8fo90028k

Key Dietary Supplements to Support Cardiovascular Health in Menopausal Women

1.Magnesium

1.Regulates blood pressure

2.Supports heart function

2.Omega-3 Fatty Acids

•Reduces triglycerides

•Supports heart health

3.Coenzyme Q10 (CoQ10)

1.Helps in energy production

2.Acts as an antioxidant

4. Vitamin D and Calcium

- Essential for bone and heart health

5. Phytoestrogens (Soy Isoflavones, Flaxseed)

- May help balance hormones and reduce cholesterol levels

Magnesium to Support Cardiovascular Health in Menopausal Women

Relationship Between Dietary Magnesium Intake and Incident Heart Failure Among Older Women: The WHI

(Journal of the American Heart Association Volume 9, Number 7 https://doi.org/10.1161/JAHA.119.013570)

- Study design:
  - 97,725 postmenopausal women.
  - Magnesium intake: 122-item validated food-frequency questionnaire
  - Incident hospitalized HF (2153 events, median follow-up 8.1 years)
  - Analyses repeated on a sub-cohort (n=18 745; median-follow-up, 13.2 years)
  - HF cases were subclassified into preserved ejection fraction (526 events), reduced ejection fraction (291 events) or unknown (168 events).
- **Compared with the highest magnesium intake, women in the lowest quartile had an increased risk of incident HF**
- Results did not significantly vary by race.
- Sub-cohort analyses showed low residual magnesium intake was associated with HF with reduced ejection.

Low magnesium intake in a multiracial cohort of postmenopausal women was associated with a higher risk of incident HF

Magnesium to Support Cardiovascular Health in Menopausal Women

Relationship Between Dietary Magnesium Intake and Incident Heart Failure Among Older Women: The WHI: (Journal of the American Heart Association Volume 9, Number 7 https://doi.org/10.1161/JAHA.119.013570):

CLINICAL PERSPECTIVE

What Is New?

- The association between magnesium intake and heart failure in a multiracial cohort of women is unknown.
- This study showed that lower dietary intake of magnesium was associated with higher incidence rates of hospitalization for heart failure in postmenopausal women.
- In subgroup analyses, low dietary magnesium was associated with incident hospitalization for heart failure with reduced ejection fraction but not preserved ejection fraction.

What Are the Clinical Implications?

- These results suggest that ≈75% of postmenopausal women in this cohort have a median magnesium intake below US Recommended Daily Allowance levels, and a quarter of them are at increased risk of incident heart failure based on their dietary magnesium intake.

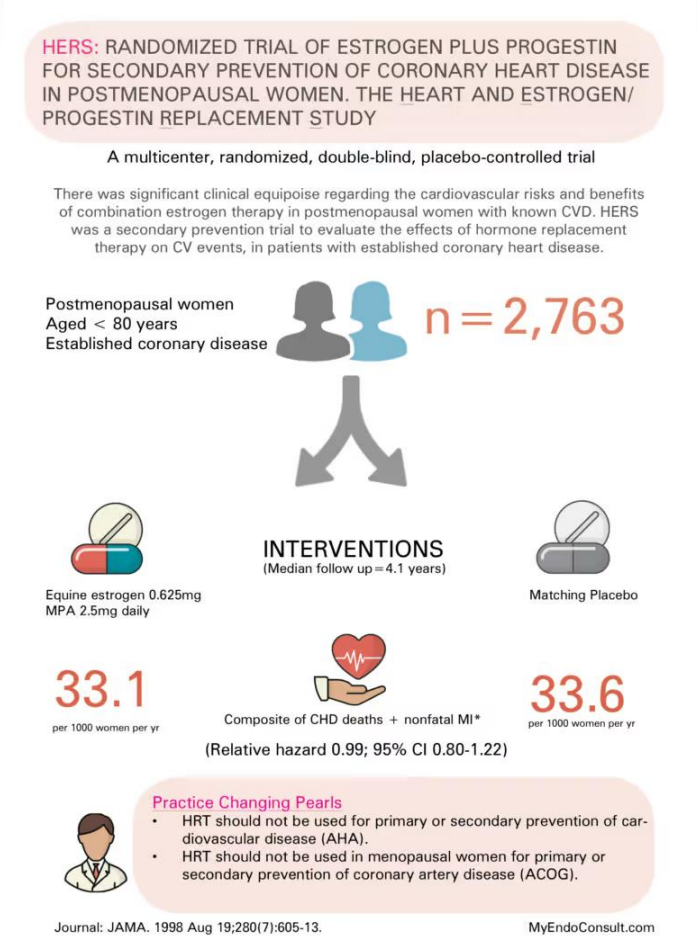
Estrogen and Cardiovascular Health in Menopausal Women: THE POSITIVES!

- **Coronary artery disease (CAD)**
- **Menopause increases CAD risk**
- **Surgical menopause**
- **Atherosclerosis**.
- **Observational studies:**
  - Women taking hormone therapy had about **50% lower cardiovascular risk**.
- **Clinical trials:**
  - Positive effects of estrogen on lipid profiles, endothelial function, vascular reactivity, and hemostatic factors in postmenopausal women.

Phytoestrogens and cardiovascular health. Lynette Wroblewski Lissin and John P CookeJACC. 2000 May, 35 (6) 1403–1410

Estrogen and Cardiovascular Health in Menopausal Women: THE NEGATIVES!

- **Heart and Estrogen/Progestin Interventions Trial:**
  - The trial found no cardiovascular benefits
- **Risks of estrogen therapy:**
  - Hypertriglyceridemia, endometrial hyperplasia, tumorigenesis, and hypercoagulable states, slight increase in breast cancer risk, increased thrombotic events



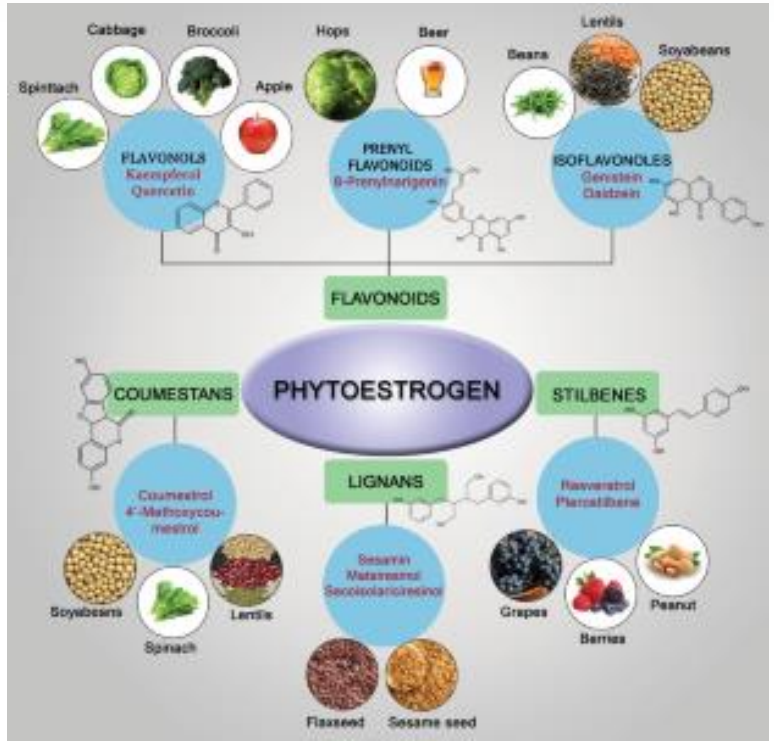
Hulley S, Grady D, Bush T, et al. Randomized Trial of Estrogen Plus Progestin for Secondary Prevention of Coronary Heart Disease in Postmenopausal Women. *JAMA.* 1998;280(7):605–613. doi:10.1001/jama.280.7.605

Phytoestrogens

What about Phytoestrogens?

- Plant-based estrogens
- Naturally occurring, plant based diphenolic compounds
- Similar in structure and function to estradiol
- Major categories: isoflavones, lignans, and coumestans.
- Common and significant sources: soybeans (isoflavones), cereals and oilseeds such as flaxseed (lignans) and alfalfa sprouts (coumestans).

Phytoestrogens and cardiovascular health. Lynette Wroblewski Lissin and John P CookeJACC. 2000 May, 35 (6) 1403–1410



Swathi Krishna, S., Kuriakose, B.B. & Lakshmi, P.K. Effects of phytoestrogens on reproductive organ health. *Arch. Pharm. Res.* **45**, 849–864 (2022). https://doi.org/10.1007/s12272-022-01417-y

Soy Protein: Meta analysis

- A meta-analysis:
  - 38 trials of soy protein consumption in humans
  - Average intake of soy was 47 g/day
  - Improvement in total cholesterol by 9% and LDL by 13%, and a decrease in triglyceride levels of 10%.
- Extent of reduction was dependent upon the baseline level of cholesterol
  - Subjects with moderate hypercholesterolemia (259–333 mg/dL), a decrease in total cholesterol of 7.4% was observed,
  - Subjects with severe hypercholesterolemia (>335 mg/dL) achieved a decline of 19.6%.

Three proposed mechanisms for the cholesterol-lowering effects of phytoestrogens

- Increased bile acid excretion enhancing LDL removal.
- Animal studies show induction of a hyperthyroid state
- Altered hepatic metabolism, leading to increased removal of LDL and VLDL by liver cells (hepatocytes).

Phytoestrogens and cardiovascular health. Lynette Wroblewski Lissin and John P CookeJACC. 2000 May, 35 (6) 1403–1410.

Meta-analysis of the effects of soy protein intake on serum lipids. Anderson J.W., Johnstone B.M. and Cook-Newell M.E. N Engl J Med 1995; **332**: 276.

Isoflavones to Support Cardiovascular Health in Menopausal Women

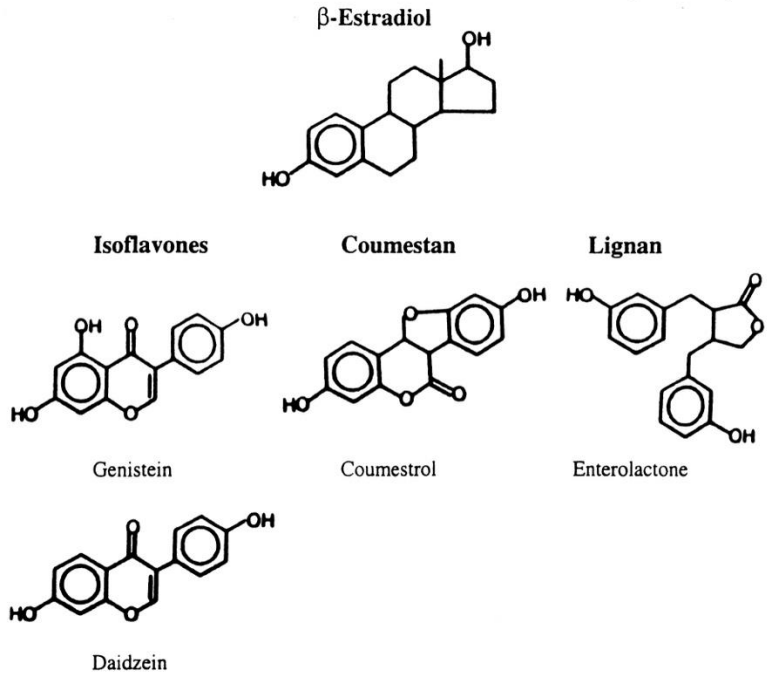
Potential advantages of phytoestrogens over conventional HRT:

May lower LDL cholesterol without increasing triglycerides.

May relieve menopausal symptoms **without raising the risk** of uterine or breast cancer.

May improve vascular function **without promoting harmful angiogenesis**.

No reported increase in thrombotic events.



Lack of large clinical trials prevents a definitive recommendation, but emerging evidence supports their potential as an alternative therapy for postmenopausal women at risk for CVD.

Phytoestrogens and cardiovascular health. Lynette Wroblewski Lissin and John P CookeJACC. 2000 May, 35 (6) 1403–1410

Studies on Isoflavones and Women's Health: WE NEED MORE STUDIES!!

- **Isoflavone Supplements for Menopausal Women: A Systematic Review.** Chen LR, Ko NY, Chen KH. Nutrients. 2019 Nov 4;11(11):2649. doi: 10.3390/nu11112649. PMID: 31689947; PMCID: PMC6893524.
- **Isoflavone Supplementation Does Not Potentiate the Effect of Combined Exercise Training on Resting and Ambulatory Blood Pressure in Non-Obese Postmenopausal Women: A Randomized Double-Blind Controlled Trial-A Pilot Study.** Dechichi JGC, Mariano IM, Giolo JS, Batista JP, Amaral AL, Ribeiro PAB, de Oliveira EP, Puga GM. Nutrients. 2020 Nov 13;12(11):3495. doi: 10.3390/nu12113495. PMID: 33203003; PMCID: PMC7697944.
- **Whole soy, but not purified daidzein, had a favorable effect on improvement of cardiovascular risks: a 6-month randomized, double-blind, and placebo-controlled trial in equol-producing postmenopausal women.** Liu ZM, Ho SC, Chen YM, Ho S, To K, Tomlinson B, Woo J. Mol Nutr Food Res. 2014 Apr;58(4):709-17. doi: 10.1002/mnfr.201300499. Epub 2013 Nov 24. PMID: 24273218.

Beetroot Juice and Active Nutrition

Domínguez R, Cuenca E, Maté-Muñoz JL, García-Fernández P, Serra-Paya N, Estevan MC, Herreros PV, Garnacho-Castaño MV. Effects of Beetroot Juice Supplementation on Cardiorespiratory Endurance in Athletes. A Systematic Review. Nutrients. 2017 Jan 6;9(1):43. doi: 10.3390/nu9010043.

Beetroot Juice to Support Cardiovascular Health in Menopausal Women

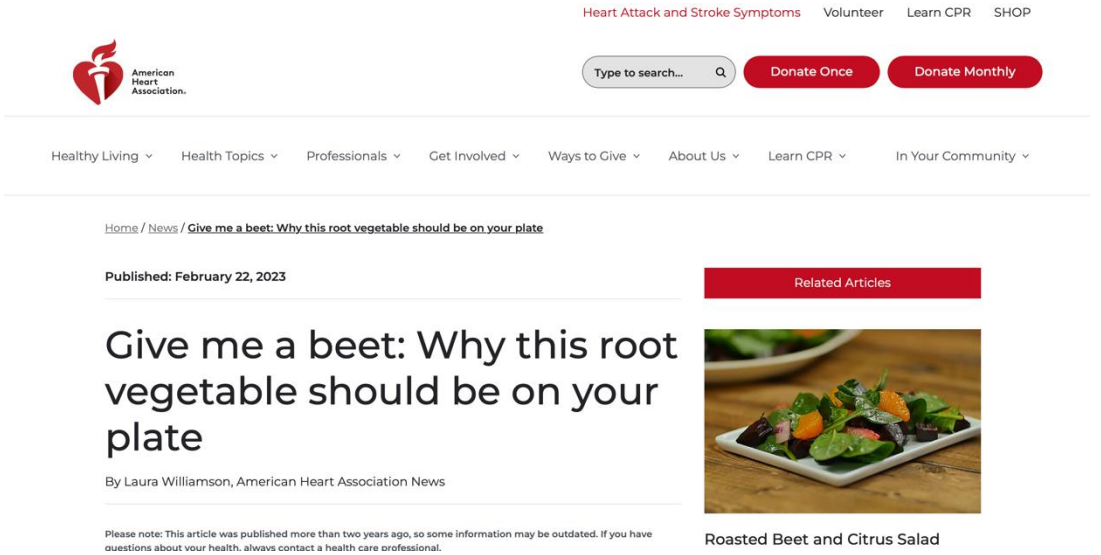
Does a beet a day keep heart disease away? ***Beetroot juice promotes healthy circulation in postmenopausal women, according to a new study (2024) led by Penn State researchers.*** Daily consumption of beetroot juice by postmenopausal women may improve blood vessel function enough to reduce future heart disease risk. ***(https://www.psu.edu/)***

WHAT DO WE KNOW ABOUT BEETROOT JUICE?

- Reduced Heart Attack Size & Improved Function
- Enhanced Nitric Oxide Production
- Blood Pressure Regulation
- Acute intake improves cardiovascular and autonomic responses in postmenopausal women with high blood pressure.
- Reduces Inflammation:
- Mixed Effects on Microvascular Function:

Mechanism of action:

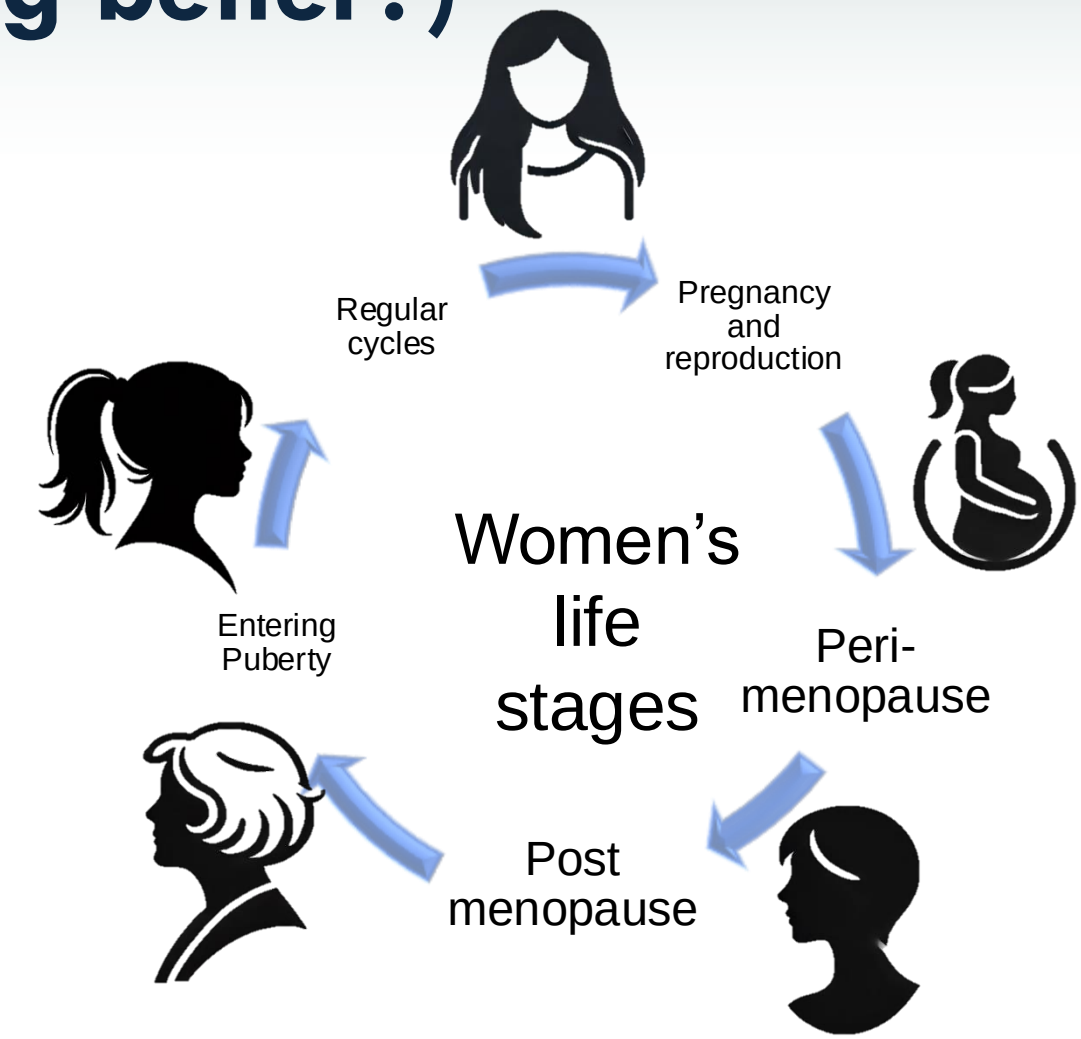
- Nitric Oxide Production:
- Anti-inflammatory Effects



What should we be doing? (Or doing better?)

Intentionally address:

- Specific life stages
- True understanding of the female "operating system"
- Better tailored to the context, lifestyle, needs and preferences of each stage
- Ethnicity and background
- By women for women!



Additional Slides

Studies on Mg and Women's Health

- Dietary Magnesium and Cardiovascular Disease: A Review with Emphasis in Epidemiological Studies. Rosique-Esteban N, Guasch-Ferré M, Hernández-Alonso P, Salas-Salvadó J. Nutrients. 2018 Feb 1;10(2):168. doi: 10.3390/nu10020168. PMID: 29389872; PMCID: PMC5852744.
- Effect of magnesium supplementation on women's health and well-being. Debora Porri , Hans K. Biesalski, Antonio Limitone, Laura Bertuzzo, Hellas Cena. NFS Journal, Volume 23, 2021, Pages 30-36, ISSN 2352-3646, doi.org/10.1016/j.nfs.2021.03.003.