

#### CLINICAL VINDICATION OF NUTRITION & HORMONES IN TODAY'S BIASED TOXIC WORLD

Dr. Devaki Lindsey Berkson

2023

#### NUTRITION & HORMONES BIGGEST RABBIT HOLES IN MEDICINE THAT HOLD BIGGEST PREVENTION & TREATMENTS





## VINDICATION/REVOLUTION

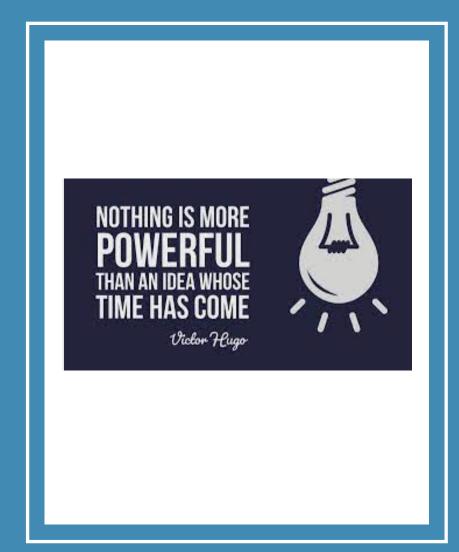
#### Hormone Vindication/Revolution

Those in-the-know can have "niche" practices

Helping many

#### Underappreciated facts:

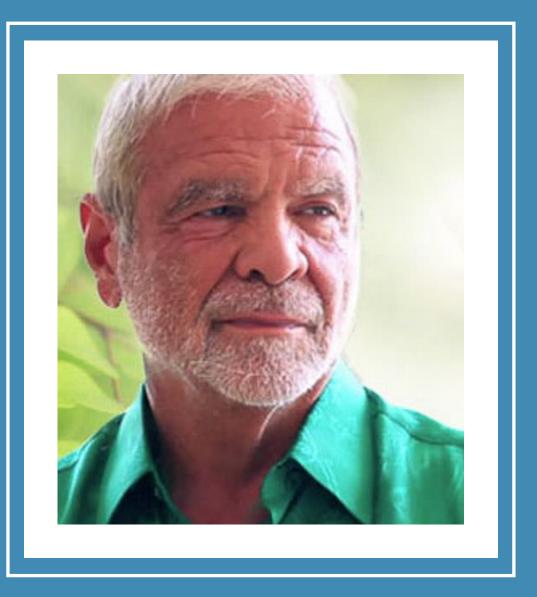
- Hormones are the most powerful signaling molecules in the body, more than exercise or food
- Hormone signals entirely depend on nutrients
- Which depends on food/digestion & more
- Hormones + Nutrition = Revolution whose time has come

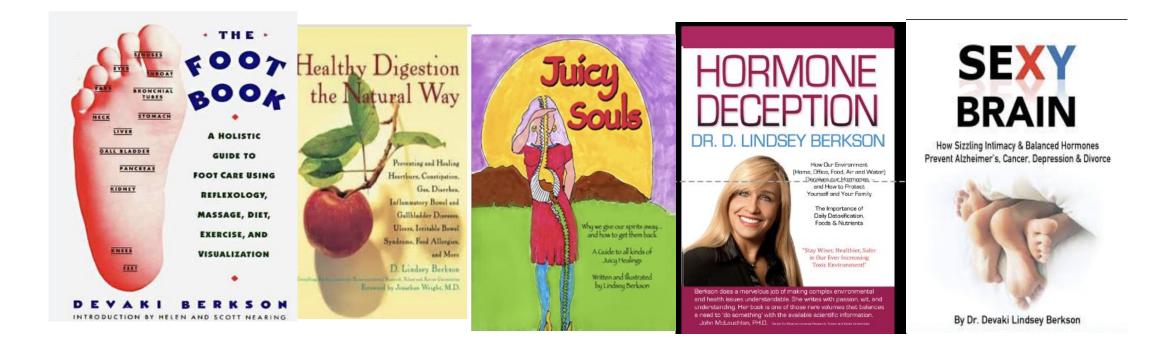


All our careers have their own "Fickle fingers of fate".

Jonathan V. Wright MD

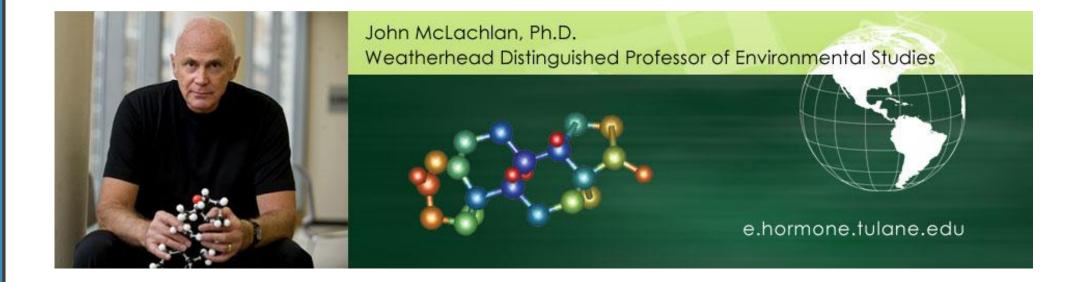
"Father of Bioidentical Hormones"





BOOKS

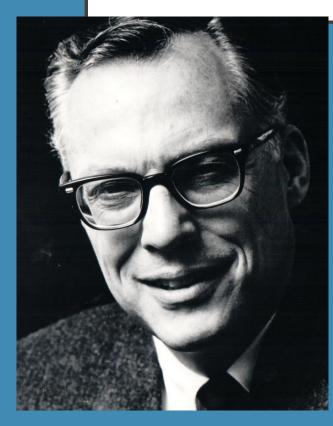
#### HORMONE SCHOLAR AT CENTER FOR BIOENVIRONMENTAL RESEARCH -ENVIRONMENTAL ESTROGEN THINK TANK.





# **MENTOR/MENTEE**

## GOT TO HANG WITH RECEPTOR SCIENTISTS



Elwood Jensen ER alpha Berkson Health copyrighted



Dr. Jan-ake Gustafson – ER beta

Receptors = malleable as built to "receive"

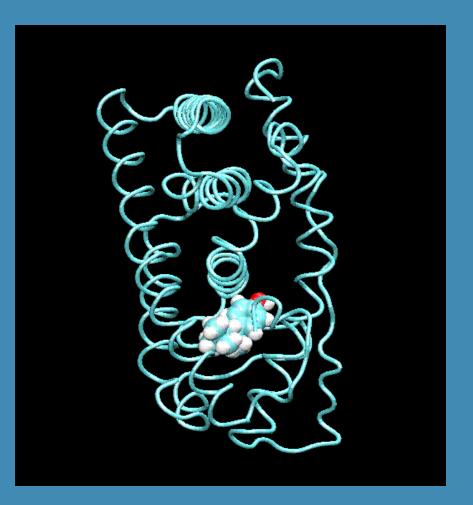
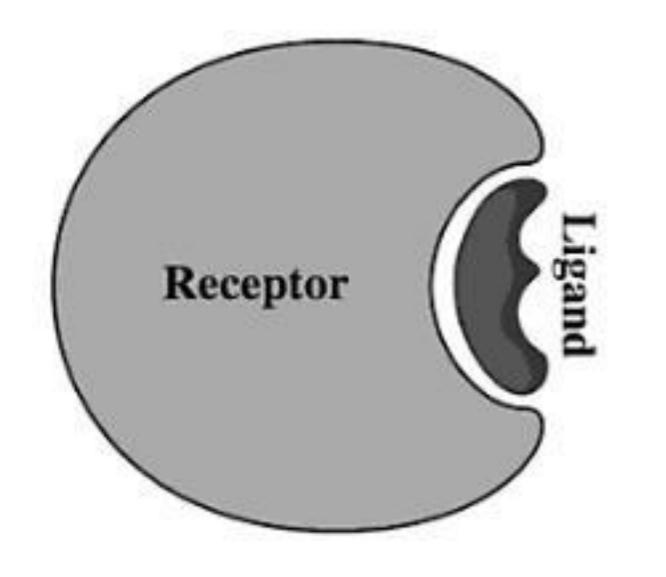
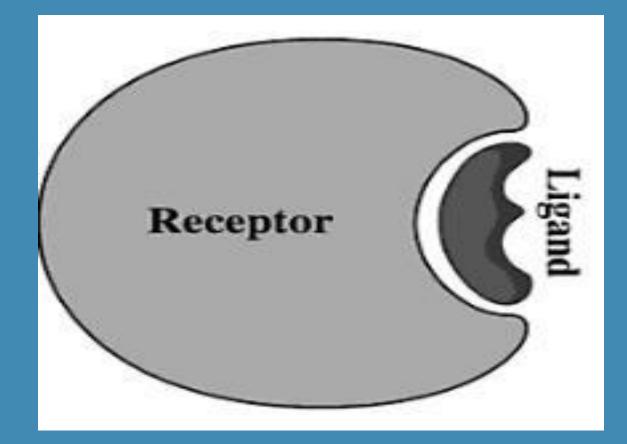


Image courtesy of T. Bishop, CBR



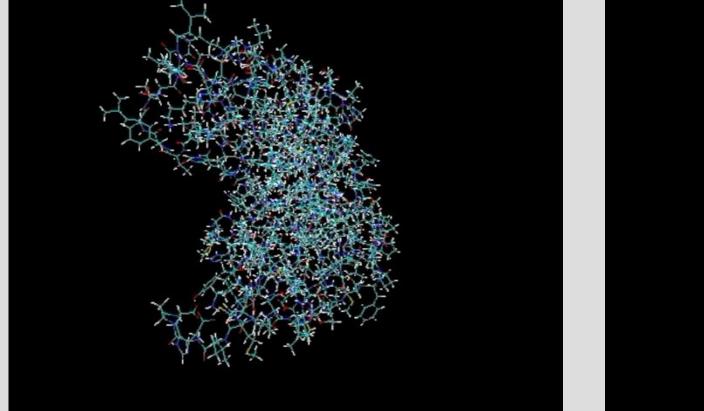
#### TARGET TISSUES HAVE RECEPTORS

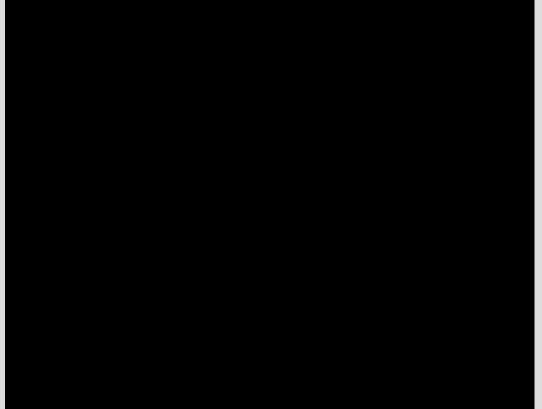
#### RECEPTOR FUNCTIONALITY DEPENDS ON NUTRIENTS



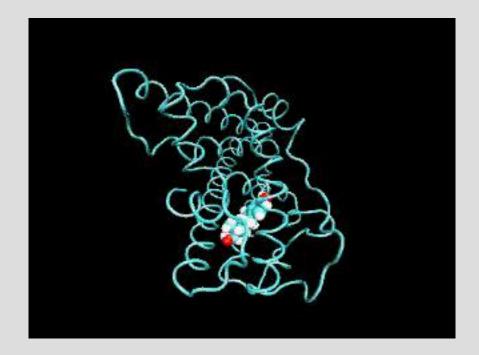
Nutrient Bowl Zinc (fingers) Vitamin B6 Magnesium Iodine Vitamin A Boron

#### TARGET TISSUE MOVIES: HORMONES DOCKING





#### **B6 – TIMING IS EVERYTHING –** DIFFERENCE BETWEEN ESTROGEN DOMINANCE & BALANCE



## B6 –HORMONE SIGNAL SQUATTING TIME

- Optimal level of B6 healthy signaling time
- Deficiency of B6 excessive signaling time
- Think of estrogen sitting on a receptor like sitting on a seat
- And the time on the seat is ruled by B6 blood and local tissue levels
- World Rev Nutr Diet. 1987;51:140-88. Oestrogens and vitamin B6--actions and interactions.
- <u>Br J Nutr.</u> 1989 May;61(3):619-28. Effects of vitamin **B6** deficiency and repletion on the uptake of steroid hormones into uterus slices and isolated liver cells of rats.
- <u>J Biol Chem</u>. 1992 Feb 25;267(6):3819-24. Vitamin B6 modulates transcriptional activation by multiple members of the steroid hormone receptor superfamily.

#### **B6 INSUFFICIENCY SYMPTOMS**

- Chronic hormonal imbalances like elevated estrogen signaling
- Difficulty with dream recall
- Wake up with swollen fingers
- History of moderate/severe PMS
- Symptoms of ER alpha excess
- Stress
- Insomnia
- Shakiness when holding a hand out
- Depression
- Carpal tunnel syndrome not due to impingement
- History of kidney stone
- Prone to arthritis and muscle spasms
- History of asthma
- History of Alcoholism

- History of moderate to severe tooth decay
- History of sensitivity to MSG
- History of severe nausea during pregnancy
- Fatigue
- Weakness
- **Dizziness**
- Peptic ulcers
- Acne
- Flaky scalp
- Light sensitivity
- History of herpes during pregnancy
- History of pre-eclampsia during pregnancy
- Parkinson's disease
- Dry eyes

#### B6 ANTAGONISTS

- Sugar
- Inorganic food (herbicides, plant-growth regulators, ripeners like Roundup®)
- FD&C Yellow 5 dye
- PCBs
- Jet fuel
- Cigarette smoke
- Oral contraceptive
- Penicillamine to treat RA & lead poisoning
- Hydralazine used to treat high blood pressure
- Phenelzine anti-depressant (Nardil®, Nardelzine, monoamine oxidase inhibitor (MAOI))
- Eating too many processed foods
- Eating refined sugar
- Button mushrooms
- Alfalfa seed sprouts
- Hydrogenated oils

# ZINC DEFICIENCY

- A deficiency of vitamin B6 has been reported to enhance estrogen responsiveness of the uterus in rats whereas zinc deficiency provokes a syndrome suggestive of a diminution in estrogen sensitivity.
- Without zinc, hormone cannot dock into receptor.
- Need RBC to check or symptoms of insufficient zinc.
- <u>J Steroid Biochem</u>. 1987 Mar;26(3):303-8. Effect of zinc and/or pyridoxine deficiency upon oestrogen retention and oestrogen receptor distribution in the rat uterus.

# HORMONES DICTATE MUCH OF OUR CELLULAR FATE AND GENE EXPRESSION

- Wherever there are receptors (target tissue) hormones deliver signals.
- ALL dependent on nutrients/digestion.

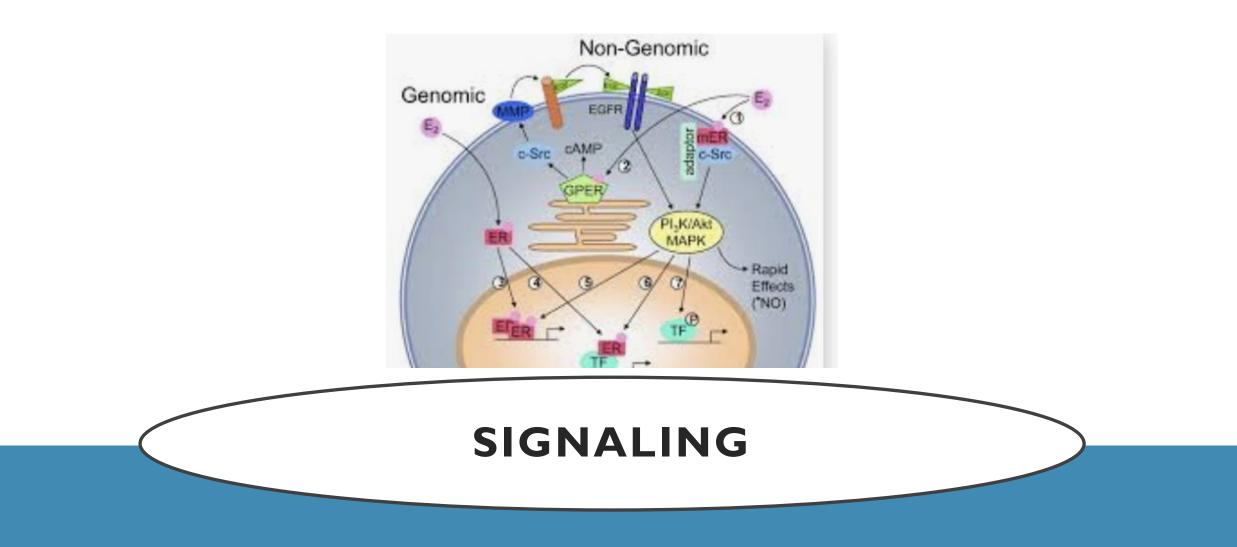
Mechanosensitive Steroid Hormone Signaling and Cell Fate. Endocrinology. 2022 Aug 1;163(8):bqac085. doi: 10.1210/endocr/bqac085. PMID: 35678467; PMCID: PMC9237634.

## WHEREVER RECEPTORS LIVE, HORMONES SIGNAL

- Reproductive Tissue
- Brain
- Gut
- Eyes
- Heart
- Lining of blood vessel
- Immune cells like T-reg cells

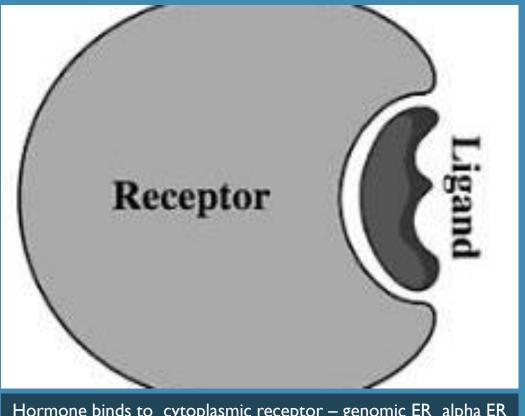
# HORMONE SIGNALING

- Genomic hormone signaling genes in nucleus needing nutrients to dock and shimmy in space.
  - Estrogen receptor Alpha Er I
  - Estrogen receptor Beta Er2
- GPER non-genomic instantaneous depending on membrane fluidity and health (EFAs, no heavy metals, etc.)



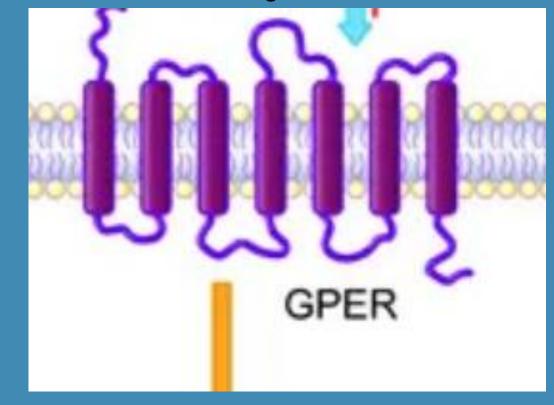
# HORMONE SIGNALING

Genomic



Hormone binds to cytoplasmic receptor – genomic ER alpha ER beta receptors

**Non-genomic** 



Hormone binds to membrane – non-genomic G-Protein Coupled Estrogen Receptor

## NUTRITION EFFECTS BOTH FORMS OF SIGNALING THOUGH NOT APPRECIATED

**Genomic Signaling** 

Needs receptor to be "available"

No endocrine disruptors

No excess cortisol

No excess chemicals

Non-genomic Signaling Needs fluid membranes EFA balance of 3:6 No hardening of fats

No trans-fatty acids

# **ESTROGEN RECEPTOR**

- Estrogen receptors (ERs) are expressed throughout the digestive tract.
- Their expression is lost during colorectal diseases such as carcinogenesis.
- With ER knock-out mice, deficiencies of these receptors cause a significant increase in intestinal abnormalities, inflamed bowel, leaky gut, tumor growth, number, and size.
- Estrogen receptors play a critical role in epithelium healing after injury.

Carcinogenesis vol.30 no.9 pp.1581–1590, 2009. Disruption of estrogen receptor signaling enhances intestinal neoplasia in ApcMin/1 mice Gastroenterology 2011 Jan. Role of Estrogen Receptor in the Regulation of intestinal Restitution After Mucosal Injury

# **ESTROGENS/PROGESTERONE**

- Gut wall: Up-regulate adhesive proteins and optimize gut wall permeability
- Prevent/treat leaky gut
- Lungs: Progesterone helps the lungs heal from injury
- Protect mitochondria
- Protects kidneys
- Protects bone
- Allows nitric oxide to protect the heart, all blood vessels, and many other tissues including the eyes.

## ESTROGEN RECEPTORS

- Hippocampus where memories live
- Endothelium which rules heart health
- Kidney cells
- Nitric Oxide

#### Free Radic Biol Med. 2013 May;58:46-51. doi: 10.1016/j.freeradbiomed.2013.01.020. Epub 2013 Jan 29.

Acute effects of hemodialysis on nitrite and nitrate: potential cardiovascular implications in dialysis patients Nathan S Bryan<sup>1</sup>, Ashley C Torregrossa, Asad I Mian, D Lindsey Berkson, Christian M Westby, Jack W Moncrief

#### Affiliation

<sup>1</sup>Texas Therapeutics Institute, Brown Foundation Institute of Molecular Medicine, The University of Texas Health Science Center at Houston, Houston, TX 77030, USA. Nathan.Bryan@uth.tmc.edu

#### COVID

- Evidence shows coronavirus disease 2019 (COVID-19)-induced symptom severity and mortality is more frequent in men than in women, premenopausal women, and postmenopausal women on HRT, suggesting sex steroids (which means their signals) play a protective role.
- Female reproductive steroids, estrogen and progesterone, and its metabolite allopregnanolone are anti-inflammatory, reshape competence of immune cells, stimulate antibody production, and promote proliferation and repair of respiratory epithelial cells, suggesting they may protect against COVID-19 symptoms.

Sex and COVID-19: A Protective Role for Reproductive Steroids. Trends Endocrinol Metab. 2021 Jan;32(1):3-6. doi: 10.1016/j.tem.2020.11.004. Epub 2020 Nov 9. PMID: 33229187; PMCID: PMC7649655

The Psychiatric Institute, Department of Psychiatry, College of Medicine, University of Illinois at Chicago, Chicago, IL 60612, USA. Electronic address: gpinna@uic.edu.

# COVID- 6-COUNTRY STUDY

- **Methods:** Healthcare workers (HCWs) from six countries (France, Germany, Italy, Spain, the UK, USA) with substantial exposure to COVID-19 patients completed a web-based survey from 17 July to 25 September 2020. Participants provided information on demographic characteristics, dietary information, and COVID-19 outcomes.
- **Results:** There were 568 COVID-19 cases and 2316 controls. Among the 568 cases, 138 individuals had moderate-to-severe COVID-19 severity, whereas 430 individuals had very mild to mild COVID-19 severity.
- After adjusting for important confounders, participants who reported following 'plant-based diets' and 'plant-based diets or pescatarian diets' had 73% lower odds of moderate-to-severe COVID-19 severity, respectively, compared with participants who did not follow these diets.
- Compared with participants who reported following 'plant-based diets', those who reported following 'low carbohydrate, high protein diets' had greater odds of moderate-to-severe COVID-19.
- **Conclusion:** In six countries, plant-based or pescatarian diets were associated with lower odds of moderate-to-severe COVID-19.
- These dietary patterns may be considered for protection against severe COVID-19.

# COVID

- Those who reported following plant-based diets or pescatarian diets had a higher intake of vegetables, legumes, and nuts, and a lower intake of poultry and red and processed meats.
- Our results suggest that a healthy diet rich in nutrient-dense foods may be considered for protection against severe COVID-19.

#### COVID

#### Affiliations

- <sup>1</sup>Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA.
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- <sup>4</sup>Envision Health Partners, Riverside, Connecticut, USA.
- <sup>5</sup>Department of Cardiology, Smidt Heart Institute, Cedars-Sinai Medical Center, Los Angeles, California, USA.
- <sup>6</sup>Department of Medicine, Stamford Hospital, Stamford, Connecticut, USA.
- <sup>7</sup>Department of Medicine, Columbia University Vagelos College of Physicians and Surgeons, New York, New York, USA.

- Plant-based diets, pescatarian diets, and COVID-19 severity: a population-based casecontrol study in six countries. BMJ Nutr Prev Health. 2021 Jun 7;4(1):257-266. doi: 10.1136/bmjnph-2021-000272. PMID: 34308134; PMCID: PMC8219480.
- CopyDownload .nbib

#### COVID – MASS. STUDY

- Diet may affect the risk and severity of COVID-19
- "Our models estimate that nearly a third of COVID-19 cases would have been prevented if diet improved." Merino one of the lead investigators.
- Diabetes Unit and Center for Genomic Medicine at MGH and an instructor in medicine at Harvard Medical School.
- For the study, Merino and his colleagues examined data on 592,571 participants of the smartphone-based COVID-19 Symptom Study. Participants lived in the U.K. and the U.S., and they were recruited from March 24, 2020, and followed until Dec. 2, 2020. At the start of the study, participants completed a questionnaire that asked about their dietary habits before the pandemic.
- Diet quality was assessed using a healthful Plant-Based Diet Score that emphasizes healthy plant foods such as fruits and vegetables.
- During follow-up, 31,831 participants developed COVID-19. Compared with individuals in the lowest quartile of the diet score, those in the highest quartile had a 9 percent lower risk of developing COVID-19 and a 41 percent lower risk of developing severe COVID-19.
- "These findings were consistent across a range of sensitivity analysis accounting for other healthy behaviors, social determinants of health, and community virus transmission rates," says Merino.
- Even one veggie meal a week makes a difference.
- Our findings also concur with a comparative risk assessment study suggesting that a 10% reduction in the prevalence of diet-related conditions such as obesity and type 2 diabetes would have prevented ~11% of the COVID-19 hospitalizations that have occurred among US adults since November 2020.

Diet quality and risk and severity of COVID-19: a prospective cohort study. Gut. 2021 Nov;70(11):2096-2104. doi: 10.1136/gutjnl-2021-325353. Epub 2021 Sep 6. PMID: 34489306; PMCID: PMC8500931.

#### **RECEPTOR FUNCTIONALITY**

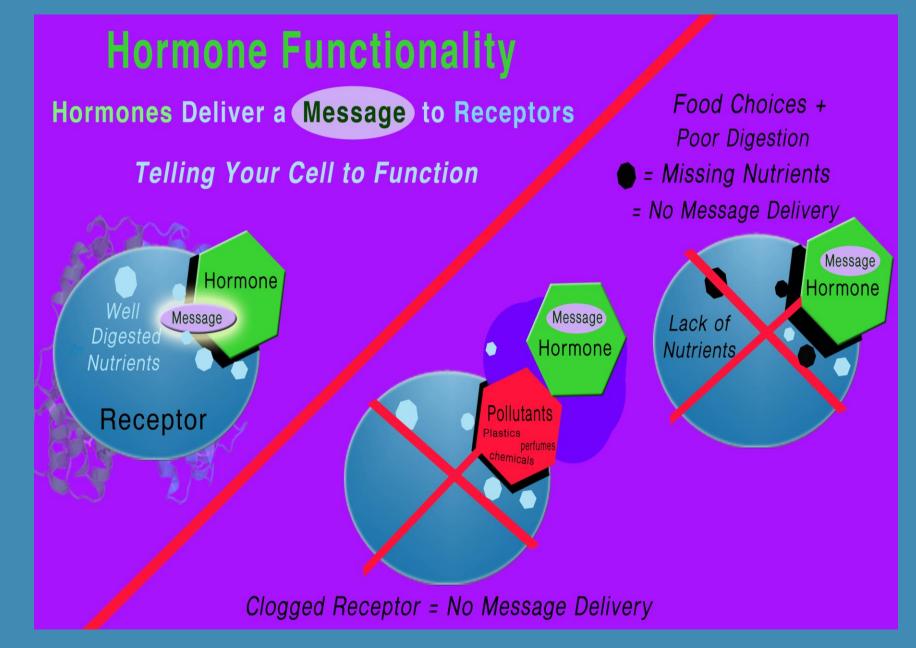
#### POOR DIET >>> POOR RECEPTOR FUNCTIONALITY

#### **Receptor Functionality**

Is where the hormone rubber meets the hormone road.







# HORMONES

Not just about levels

Tested and debated in blood, saliva, urine, etc.

There is a bigger picture

That relies on nutrients
At cellular level
Such as Zinc RBC
Magnesium RBC
Not just extracellular compartment in serum performed by most blood testing

## WHY IS NUTRITION SO MISUNDERSTOOD?

- On June 21-22, 2022, headlines were all over the news claiming that taking vitamins and other supplements is a waste of money.
- From WebMD: "Vitamins, Supplements a Waste of Money for Most, Task Force Says."
- From CNN Health: "Are you wasting your money on supplements?
- From New Scientist: "Vitamins and dietary supplements are a waste of money for most people."
- From the News Ticker on CBS Boston: "Experts say vitamin supplements are likely a waste of money."

#### TASK FORCE

- What the Task Force did state was, "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.
- Evidence is lacking and the balance of benefits and harms cannot be determined."

Mangione CM, et al. Vitamin, mineral, and multivitamin supplementation to prevent cardiovascular disease and cancer: US Preventive Services Task Force recommendation statement. JAMA. 2022;327:2326-2333.

O'Connor EA, 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;327:2334-2347.

#### TASK FORCE

- The Task Force also acknowledged that their report had a number of limitations.
- First, since the USPSTF focused on cardiovascular disease and cancer and secondarily on all-cause mortality, it did not exclude the possibility that there are other benefits of some supplements.
- Second, since the review was focused on healthy populations without known nutritional deficiencies, it did not cover the therapeutic use of supplements in persons with physical symptoms, medical conditions, or nutritional deficiencies.
- Third, there may be other dosages, formulations, or supplement combinations that could be beneficial.

#### TASK FORCE STUDY

- Among the 9 RCTs were 3 large trials that looked specifically at death, cardiovascular disease, and cancer.
- Those 3 RCTs comprised most of the evidence upon which the USPSTF report was based.

#### TASK

- In the first of those 3 trials, 13,017 French men and women (aged 35-60 years) were randomly assigned to receive, in a double-blind fashion, a daily nutritional supplement or placebo for a median of 7.5 years. The supplement provided daily 120 mg of vitamin C, 30 mg of vitamin E, 6 mg of beta-carotene, 100 µg of selenium, and 20 mg of zinc.
- In the group as a whole, the incidence of cancer was non-significantly lower by 8.9% and all-cause mortality was non-significantly lower by 20% in the supplement group compared with the placebo group.
- When the data for men and women were analyzed separately, marked differences were seen. Among men, the incidence of cancer was significantly lower by 31%, and all-cause mortality was significantly lower by 37% in the supplement group, compared with the placebo group.
- Among women, the incidence of these outcomes was non-significantly higher by 3-4% in the supplement group than in the placebo group.

Hercberg S, et al. The SU.VI.MAX Study: a randomized, placebo-controlled trial of the health effects of antioxidant vitamins and minerals. Arch Intern Med. 2004;164:2335-2342.

#### TASK

- It is noteworthy that the supplement used in this trial contained zinc but not copper.
- Zinc interferes with copper absorption, and long-term use of even modest doses of zinc can decrease body stores of copper. Animal studies have demonstrated that copper deficiency can cause cardiovascular disease. Therefore, the outcome for cardiovascular disease and possibly for all-cause mortality, as reported in this study, may have been better if the supplement had included copper.

Festa MD, et al. Effect of zinc intake on copper excretion and retention in men. *Am J Clin Nutr.* 1985;41:285-292. Gaby AR.Atherosclerosis and ischemic heart disease. In Gaby, AR. *Nutritional Medicine*, 2nd Edition. Concord, NH, 2017. doctorgaby.com; chapter 75.



- In the second trial, 14,641 U.S. male physicians were randomly assigned to receive, in double-blind fashion, a daily multivitamin (Centrum Silver) or placebo for a mean of 11.2 years. Compared with placebo, total mortality was non-significantly lower by 6%, and the incidence of major cardiovascular events was non-significantly higher by 1% in the supplement group compared with the placebo group.
- At the time this study was conducted, Centrum Silver contained (in addition to vitamins and minerals) FD&C Blue 2 Aluminum Lake, FD&C Red 40 Aluminum Lake, FD&C Yellow 6 Aluminum Lake, polyethylene glycol, polyvinyl alcohol, sodium aluminum silicate, sodium benzoate, talc, titanium dioxide, crospovidone, and butylated hydroxytoluene.
- It would be surprising if none of those chemicals were harmful with long-term use.
- Therefore, any potential benefit of the vitamins and minerals in Centrum Silver could conceivably have been negated by one or more of these other chemicals. In addition, until the year 2008, the zinc present in Centrum Silver was balanced with copper in the form of cupric oxide (personal communication, Pfizer Consumer Healthcare, December 7, 2012). According to animal research, cupric oxide cannot be absorbed. Thus, for about 70% of the time this study was conducted, the zinc in the product was not properly balanced with copper.

Sesso HD, et al. Multivitamins in the prevention of cardiovascular disease in men: the Physicians' Health Study II randomized controlled trial. JAMA. 2012;308:1751-1760. Baker DH. Cupric oxide should not be used as a copper supplement for either animals or humans. J Nutr. 1999;129:2278-2279.

#### TASK

- In the third trial, 21,442 US adults were randomly assigned to receive, in double-blind fashion, Centrum Silver or placebo for a mean of 3.6 years.
- All-cause mortality was non-significantly lower by 7%, the incidence of cardiovascular disease was non-significantly lower by 2%, and the incidence of cancer was non-significantly lower by 3% in the supplement group, compared with the placebo group.
- By the time this study was conducted, the cupric oxide in Centrum Silver had been replaced by an absorbable form of copper.
- However, the product still contained a wide range of potentially toxic chemicals.

Sesso HD, et al. Multivitamins in the prevention of cancer and cardiovascular disease: the COcoa Supplement and Multivitamin Outcomes Study (COSMOS) randomized clinical trial. *Am J Clin Nutr.* 2022;115:1501-1510.



- Thus, each of the 3 large trials cited by the Task Force showed a reduction in mortality ranging from 6% to 20%.
- One of these studies found a large and statistically significant decrease in both cancer and all-cause mortality in men but not in women.
- None of the products used in these studies could be considered optimal.
- All trials might have produced better results if the supplements had been better formulated and free of potentially toxic extraneous chemicals.
- The Task Force is correct in their assertion that there is no definitive proof that multivitamins prevent cardiovascular disease or cancer or decrease mortality among the general population.
- They failed to show some evidence of benefit in these studies.
- Nutritional supplements have demonstrated value for a wide range of health conditions, including fatigue, anxiety, depression, insomnia, cognition, hormone health, poor stress tolerance, arthritis, migraines, kidney stones, premenstrual syndrome, heart failure, osteoporosis, acne, respiratory infections, diabetes, age-related macular degeneration, and many others.
- Regardless of whether or not they can prevent two specific diseases or help you live longer, there is overwhelming evidence that nutritional supplements, when used properly, are **not** a waste of money.

#### FOLLOW WHOSE SCIENCE?

- Suicide the leading cause of death in the US 45,979 deaths in 2020.
- Oral vitamin D supplementation almost halved the rates of suicide and intentional self-harm in a newly published study of US veterans, with an even stronger effect among Black veterans. (darker-skinned persons have less ability to activate vitamin D from the sun, secondary to darker skin pigment).
- This retrospective cohort study showed:
  - Higher daily vitamin D supplement dosages appeared to offer greater protection against suicide and self-harm risk than lower doses,
  - ✓ The effect was greater among those with **baseline vitamin D deficiency or insufficiency**, and
  - ✓ Which Task Force did not evaluate though they eviscerated supplementation.
  - Both pharmaceutical vitamin D2 (ergocalciferol) and over-the-counter vitamin D3 (cholecalciferol) supplements were effective.
  - ✓ 1/3rd Of Military Members Are Vitamin D Deficient

#### **DEPRESSION IS INCREASING**

- Vitamin D has been shown to be helpful with depression.
- Anti-depressants are now shown to be linked to a higher risk of heart disease and mortality if taken long-term.

https://www.cdc.gov/suicide/suicide-data-statistics.html

The association between vitamin D serum levels, supplementation, suicide attempts, and intentional self-harm. PLoS One. 2023 Feb 1;18(2):e0279166. doi: 10.1371/journal.pone.0279166. PMID: 36724169; PMCID: PMC9891532.

Vitamin D Supplementation Linked to Fewer Suicide Attempts - Medscape - Feb 01, 2023.

Vitamin D deficiency and depression in adults: systematic review and meta-analysis. Br J Psychiatry. 2013 Feb;202:100-7. doi: 10.1192/bjp.bp.111.106666. PMID: 23377209.

#### COVID – VITAMIN D (BUT NOT IN MEDIA)

- Evidence Regarding Vitamin D and Risk of COVID-19 and Its Severity. Nutrients. 2020 Oct 31;12(11):3361. doi: 10.3390/nu12113361. PMID: 33142828; PMCID: PMC7692080.
- Role of vitamin D in preventing of COVID-19 infection, progression and severity. J Infect Public Health. 2020 Oct;13(10):1373-1380. doi: 10.1016/j.jiph.2020.06.021. Epub 2020 Jun 20. PMID: 32605780; PMCID: PMC7305922.
- Supplementation with vitamin D in the COVID-19 pandemic? Nutr Rev. 2021 Jan 9;79(2):200-208. doi: 10.1093/nutrit/nuaa081. PMID: 32679589; PMCID: PMC7454793.

#### VITAMIN D

- Vitamin (the body can't make)
- Hormone can signal gene (genomics) huge deal to be able to send directives to genes
- Very little mention in the COVID news
- But dissing supplementation

#### DIALOGUE BETWEEN OLE NUTRITIONAL DOC FRIENDS BEFORE THIS TALK

You know, nutrition is so misunderstood and ridiculed.

After working in it all these years, why do you think this is? The main reason. Is it money?

Does it always come down to money?

So wearisome.

Dr. Lindsey Berkson

#### **OPINIONS**

It's the money that drives the misinformation.

But I think it is the cognitive dissonance that drives the doctors. They get annoyed that they spent a decade training in how to give poisons, and then somebody comes along and says there is a simpler and safer way. They are just not capable of hearing it.

And, of course, there is money for the doctors, too. I once told a urologist that you can shrink prostates with EFAs and zinc, and he replied, "Why would I want to do that?"

And a GI guy (who I was friends with) referred me to an ulcerative colitis patient because the patient was sure he had hidden food allergies. My friend told me that if I cured this guy, he wouldn't send me any more patients.

#### OPINIONS

- I had an endoscopic exam with my last colonoscopy.
- The gut doc wanted me on PPIs.
- I said, "Hey, I have one kidney, and there are lawsuits against these companies for renal damage."
- He knew nothing of it.
- I simply stopped drinking so much bubbly water and eating later at night, and all my reflux went away.
- But he NEVER asked me about my diet or lifestyle.
- He did let me give a talk at Austin Regional Gastroenterology on how I saved (pre and postcolonoscopies) 6 of their young female patients were told they needed colectomies stat none with cancer.
- And within 6 months all had normal fu imaging.
- And at the end, several gut docs said, "We don't believe food, other than probiotics and fiber but hardly fiber, has anything to do with the gut."

#### OPINIONS

- Hard not to become crusty ole farts
- Thank God for BHRT
- Stay somewhat flexible ha!

#### NIH 7 MILLION ESTROGEN STUDY

• Effects of Hormone Therapy on survival, cancer, cardiovascular and dementia risks in 7 million menopausal women over age 65: a retrospective observational study

• May 2022

doi: https://doi.org/10.1101/2022.05.25.22275595

This article is a preprint and has not been peer-reviewed [what does this mean?]. It reports new medical research that has yet to be evaluated and so should not be used to guide clinical practice.

Yale BMJ Preprints

#### METHODS

- From 2007-2019, enrollment records of 100% Medicare beneficiaries, we identified 7 million female enrollees aged 65 or more.
- We identified estrogen type, route, and strength based on their prescription drug utilization records.
- Using vital status records and encounter records, we defined the first onset of thirteen patient outcomes; all-cause mortality;
- 5 cancers (breast, lung, endometrial, colorectal, ovarian cancers);
- CV conditions (ischemic heart diseases, heart failure, venous thromboembolism, stroke, atrial fibrillation, acute myocardial infarction);
- And dementia.
- Then, we implemented an extended Cox regression analysis to examine the effects of type, route, and strength of estrogens on each of 13 study outcomes.

#### LIVED LONGER -

- On average, ET use was associated with a significant 20% reduction in mortality risk relative to no ET use, which translated to 77,401 fewer expected deaths in our large population.
- All combinations of ET type, route, and dose were also associated with reduced mortality risk.
- Oral CEE medium dose, comparable to the drug in the WHI trial of ET, exhibited less risk reduction in mortality (9%) than overall ET.

#### VAGINAL DELIVERY BEST ANTI-AGING OUTCOMES

- Significantly reduced mortality rates in all 5 cancers
- Breast, ovarian, uterine, lung, colorectal.

#### ABSTRACT HIGH RISK CARDIAC PATIENTS HAD BEST LONGEVITY OUTCOMES NOT WORSE AS IS NOT STANDARD OF CARE.

- Menopausal hormone therapy (MHT) is indicated for menopausal symptom relief. However, MHT has also been shown to be beneficial for the prevention of long-term estrogen deficiency sequelae, including mortality.
- Based on a comprehensive literature review (**meta-analysis of 31 observational studies)** on MHT and mortality, the authors' recommendations are as follows:
  - in postmenopausal women, MHT appears to confer a **(significant) reduction in overall mortality;** the benefit especially applies to women who initiate **long-term** MHT early after menopause;
  - in women with prevalent cardiovascular risk factors (except for diabetes mellitus, where results are mixed), the benefit of MHT on overall mortality is even more pronounced; however, study results are difficult to compare due to heterogeneous study designs.

The impact of menopausal hormone therapy on overall mortality - a comprehensive review. Climacteric. 2020 Oct;23(5):447-459. doi: 10.1080/13697137.2020.1767568. Epub 2020 Jun 18. PMID: 32552066.

#### 7 MILLION STUDY

- Less neurodegenerative dx (like Alzheimer's)
- Only issue was increased stroke risk with oral supplementation
- The one BHRT FDA approved by ex-CEOs of Premarin/Prempro is 4 levels of oral
- So, the 7 million study has not been released out of "peer review."

BRAIN SCIENCE UNIV OF ARIZONA COGNITION STUDY

 Association between menopausal hormone therapy and risk of neurodegenerative diseases: Implications for precision hormone therapy. Alzheimer's Dement (N Y). 2021 May 13;7(1):e12174. doi: 10.1002/trc2.12174. PMID: 34027024; PMCID: PMC8118114.

#### ABSTRACT

- Introduction: The impact of menopausal hormone therapy (HT) on age-associated Alzheimer's and neurodegenerative diseases (NDDs) remains unresolved.
- To determine the effect of HT, formulation, type, and duration on the risk of NDDs, a retrospective analysis was performed using a 10-year Humana claims dataset.
- Methods: The study population included women aged 45 years or older with or without claim records of HT medications. Patients diagnosed with NDDs, including Alzheimer's disease (AD), Parkinson's disease (PD), dementia, multiple sclerosis (MS), and amyotrophic lateral sclerosis (ALS), were identified.
- Results: In 379,352 women with or without claim records of HT, the use of HT was associated with significantly reduced risk for combined NDDs (RR 0.42, 95% CI 0.40-0.43, P < 0.001). The average follow-up time was 5.1 [2.3] years.
- Greatest reduction in risk of NDD, AD, and dementia emerged in patients aged 65 years or older.
- Further, the protective effect of long-term therapy (>1 year) on combined NDDs, AD, PD, and dementia was greater compared to short-term therapy (≤1 year).
- **Discussion:** HT was associated with reduced risk of all NDDs, including AD and dementia, with greater duration of therapy and natural steroid formulations associated with greater efficacy. These findings advance precision HT to prevent NDDs, including AD.

#### ARIZONA STUDY

- Women on HRT are 58% less likely to develop neurodegenerative disease.
- Women who underwent menopausal hormone therapy for six years or greater were 79% less likely to develop Alzheimer's and 77% less likely to develop any neurodegenerative disease.
- "This is not the first study on the impact of hormone therapies on neurodegenerative disease reduction," said Roberta Diaz Brinton, Ph.D., director of the University of Arizona Center for Innovation in Brain Science and senior author of the paper.
- "But what is important about this study is that it advances the use of precision hormone therapies in the prevention of neurodegenerative disease, including Alzheimer's."

#### ARIZONA STUDY

---- They found that using the natural steroids estradiol or progesterone resulted in greater risk reduction than the use of synthetic hormones.

### JAN 2023

- Hormone replacement therapy is associated with improved cognition and larger brain volumes in at-risk APOE4 women: results from the European Prevention of Alzheimer's Disease (EPAD) cohort. Alzheimer's Research & Therapy, 2023; 15 (1) DOI: <u>10.1186/s13195-022-01121-5</u>
- Norwich Medical School
- Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, UK

#### HORMONES & NUTRIENTS PROTECT COGNITION

- The research team studied data from 1,178 women participating in the European Prevention of Alzheimer's Dementia initiative -- which was set up to study participants' brain health over time.
- The project spanned 10 countries and tracked participants' brains from 'healthy' to a diagnosis of dementia in some. Participants were included if they were over 50 and dementia-free.
- The research team studied their results to analyze the impact of HRT on women carrying the APOE4 genotype.
- Dr. Rasha Saleh, also from UEA's Norwich Medical School, said: "We found that HRT use is associated with better memory and larger brain volumes among at-risk APOE4 gene carriers.
- The associations were particularly evident when HRT was introduced early during the transition to menopause, known as perimenopause.
- "This is really important because there have been very limited drug options for Alzheimer's disease for 20 years, and there is an urgent need for new treatments.

#### HRT

- Protects against APOE4 Alzheimer's vulnerability gene
- Best started early
- Enlarges brain volume
- SIZE matters
- Hormones + Nutrition = Time has come



#### WHERE DID THIS HORMONE BIAS COME FROM?



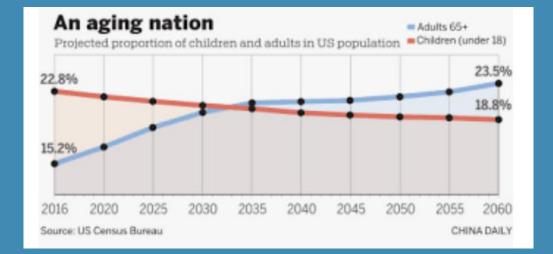






## WE ARE AN AGING NATION

As much as we worship youth, we are an aging demographic So how to keep us younger longer And the WHI wanted to protect Medicare from tanking.



# WHI

- Funded by the NIH
- From 1993 to 1998, more than 27,000 postmenopausal women aged 50 to 79 years with no prior breast cancer enrolled in one of two randomized, placebo-controlled WHI trials
- At 40 US centers
- Women with an intact uterus received CEE (0.625 mg/day) plus MPA (2.5 mg/day) or placebo (n = 8102)
- Women with prior hysterectomy received CEE alone (n = 5310) or placebo (n = 5429) for a median of 7.2 years.
- Prematurely stopped at median 5 years
- July 2002
- Tracked through Dec. 2019



### WHI FEAR SELLS

- Women no longer trusted HRT.
- Doctors were fearful of getting sued and feared estrogen, too.
- Wyeth was successfully sued after the initial WHI.
- FDA put warning labels on all estrogen products.
- **CONCLUSIONS:** Immediate post-WHI recommendations for MHT use were widely adopted.
- In US
- Not Europe
- Many socialized countries do track the effectiveness and safety and protection of country medical funds, that they offer for FREE.
- Used to be 40 million women on HRT, now 5-8 million women with half on synthetic and half on bioidentical.

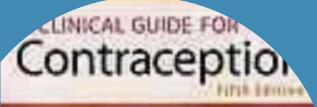
Menopause, 2017 Apr;24(4):355-357. doi: 10.1097/GME.000000000000845. The Women's Health Initiative: evolving insights over 15 years.

Menopause, 2018 Dec 21;26(6):588-597. doi: 10.1097/GME.00000000000001282. Menopausal hormone therapy trends before versus after 2002: impact of the Women's Health Initiative Study Results

## Speroff's Clinical Gynecologic Endocrinology and Infertility

Ninth Edition

HUGH S. TAYLOR LUBNA PAL



Leon Spende Thille D. Damey

#### CHAMPIONED PAST CLINICAL OUTCOMES

Wrote multiple studies urging physicians to not let a singular randomized trial stop what decades of clinical outcomes had shown.

- Physicians
- Patients
- Both

#### • But in US FEAR

Not Europe

• Where given for free in socialized countries like Finland to keep aging women safer and government health programs from toppling

on Health copyrighted

#### STOPPED PREMATURELY

- Increased risk of breast cancer
- Increased risk of clots
- Within months re-analysis shows "statistical fiasco"
- Methodology found to be fatally flawed
- Safe Hormones, Smart Women





#### Berkson Health copyrighted

#### DECEMBER 2019 – SAN ANTONIO YEARLY BREAST CANCER SYMPOSIUM

- All changed
- --San Antonio Breast Cancer Symposium 2019: <u>Abstract G55-00</u>. Presented December 13, 2019.
- --Medscape Medical Oncology, Dec.13, 2019

# **19-YEAR** RE-**ANALYSIS** WHI

#### **19-year Re-analysis**

- ESTROGEN ONLY: CEE (P... conjugated equine estrogens) alone resulted in a significant 23% reduction in breast cancer incidence (hazard ratio [HR], 0.77; P = .005),
- Estrogen for any length of time reduced the risk of dying from breast cancer by 44% if did get it.
- Protection 20 years+

#### WHI RE-ANALYSIS AUTHORS: WHO SAID THIS?

- The Los Angeles BioMedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA;
- Fred Hutchinson Cancer Research Center, Seattle, WA;
- Brigham and Women's Hospital, Boston, MA;
- Stanford Prevention Research Center, Stanford, CA;
- University of Washington, Seattle, WA;
- Pitt Public Health, Pittsburgh, PA;
- Karmanos Cancer Institute, Detroit, MI;
- Stony Brook University, Stony Brook, NY;
- University of Tennessee Health Science Center, Memphis, TN;
- Albert Einstein Cancer Center, Bronx, NY;
- The Ohio State University, Columbus, OH, and
- The UF Health Internal Medicine, Gainesville, FL.

2019 SABCS Abstracts Home GS5-00. Long-term influence of estrogen plus progestin and estrogen alone use on breast cancer incidence: The Women's Health Initiative randomized trials.

#### NONE OF THIS MADE HEADLINE NEWS

- Fear Sells
- Once fear settles into the cultural consciousness
- Velcroed in
- Hard to believe re-analysis

## SCARY HEADLINES SELL.

POSITIVE ONES DON'T.

- Did this positive re-analysis of the WHI make headlines? No
- Have most doctors heard about this? No.
- Had many compounding pharmacists heard about this? No.
- Have most patients heard about this? No.

## STANDARD OF CARE

- Is not reflecting the appropriate data
- For women without breast cancer
- For women with breast cancer
- Nor role of nutrients in keeping hormones signaling, safe and sound

Proc ASCO 2006l24L10012. Case-control study of hormone replacement therapy (HRT) and breast cancer in Japanese women.

Avrum Bluming MD, Carol Tavris PhD. Estrogen Matters: Why Taking Hormones in Menopause Can Improve Women's Well-Being and Lengthen Their Lives -- Without Raising the Risk of Breast Cancer 1st Edition. Hachett Book Group 2018.

## ANOTHER TODAY'S TOXIC WORLD

- Sex hormones, such as androgens, estrogens, and progestins, are naturally occurring compounds that tightly regulate endocrine systems in a variety of living organisms.
- Uncontrolled environmental exposure to synthetic mimetics has been widely documented.
- Furthermore, water contaminants penetrate the soil to affect flora, fauna, and ultimately humans.
- Because endocrine systems evolved to respond to very small changes in hormone levels, the low levels found in the environment cannot be ignored.
- The combined actions of sex hormones with glucocorticoids and other nuclear receptors disruptors create an additional level of complexity including the newly described "dynamic assisted loading" mechanism.

Endocrine disruptors of sex hormone activities. Mol Cell Endocrinol. 2022 Jan 1;539:111415. doi: 10.1016/j.mce.2021.111415.

Laboratory of Receptor Biology and Gene Expression, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA. Electronic address: varticol@mail.nih.gov.

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#### CALL FOR "GREEN PREGNANCIES"

- Exposure to endocrine-disrupting compounds (EDCs) especially during pregnancy linked to altered brain/hormone cross-talk
- And many proposed possible hormone issues at younger and younger ages
- Milestones of Reproduction changing
- I out of 10 women globally have PCOS
- Younger males today have less and less testosterone
- Our hormone imbalances are occurring younger and younger, not just peri, post, and andropause
- Much of this is starting in the womb
- Great niche for nutritional consulting
- Green Pregnancy slides -drlindseyberkson.com store

Hormone Deception Berkson DL McGraw-Hill 2000 Awakened Medicine Press

Effects of prenatal exposure to endocrine disruptors and toxic metals on the fetal epigenome. Epigenomics. 2017 Mar;9(3):333-350. doi: 10.2217/epi-2016-0112. Epub 2017 Feb 17. PMID: 28234024; PMCID: PMC5827796.

Prenatal and postnatal exposures to endocrine disrupting chemicals and timing of pubertal onset in girls and boys: a systematic review and meta-analysis. Hum Reprod Update. 2022 Aug 25;28(5):687-716. doi: 10.1093/humupd/dmac013. PMID: 35466359; PMCID: PMC9434240.

Clin Endocrinol Metab. 2007 Feb;92(2):549-55. Epub 2006 Dec 5. The relative contributions of aging, health, and lifestyle factors to serum testosterone decline in men.

#### HORMONES

- Hormones rule all physiologic real estate
- Hormones lean completely on nutrients
- Nutrients, methylation, and hormones are all under assault by endocrine-disrupting compounds
- Here, nutrition also makes a huge difference
- Heavy metals, for one example
- Detox must move mainstream

- Hormone Deception Berkson DL McGraw-Hill, Awakened Medicine Press
- Receptor Detox
- Hormone Balance and Protect

#### HORMONES & NUTRIENTS & DETOX

- \*Time has come.
- \*Will you be part of the answer/revolution?
- Drlindseyberkson.com/membership
  Drlindseyberkson.substack.com
  Podcast Dr. Berkson's Best Health Radio
  Consults @ drlindseyberkson.com at services
  QUESTIONS? Admin@drlindseyberkson.com



#### **Agile Thinking**

Where Health is AT! Dive into Science, Hormones, Nutrition and the "surrounding debates".

Subscrit

Agile Thinking drlindseyberkson.substack.com