



dutch®

Impacting Breast Cancer Risk with a Functional Medicine Approach

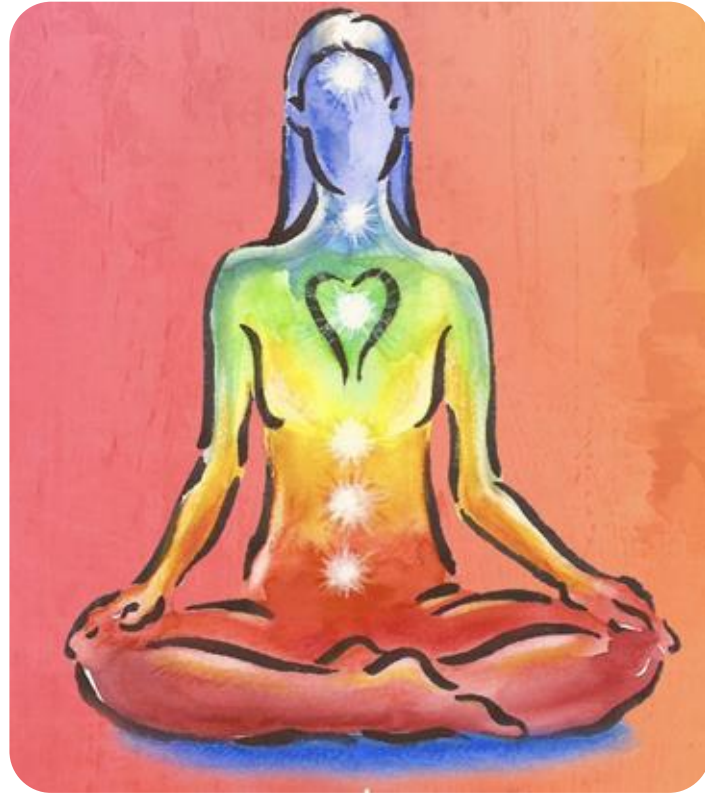
Elizabeth Boham, MD, RD, MS, FMCP-M

October 2026

Elizabeth Boham, MD, RD, MS, FMCP-M



- **Item 1:** Functional Medicine Approach / Creating Healthy Terrain
- **Item 2:** Inflammation and Insulin Resistance
- **Item 3:** Estrogen and Estrogen Metabolism
- **Item 4:** The Gut Microbiome and Cancer Risk
- **Item 5:** Toxins and Detoxification
- **Item 6:** Assessing Risk with Hormone Therapy
- **Item 7:** Patient with History of Breast Cancer

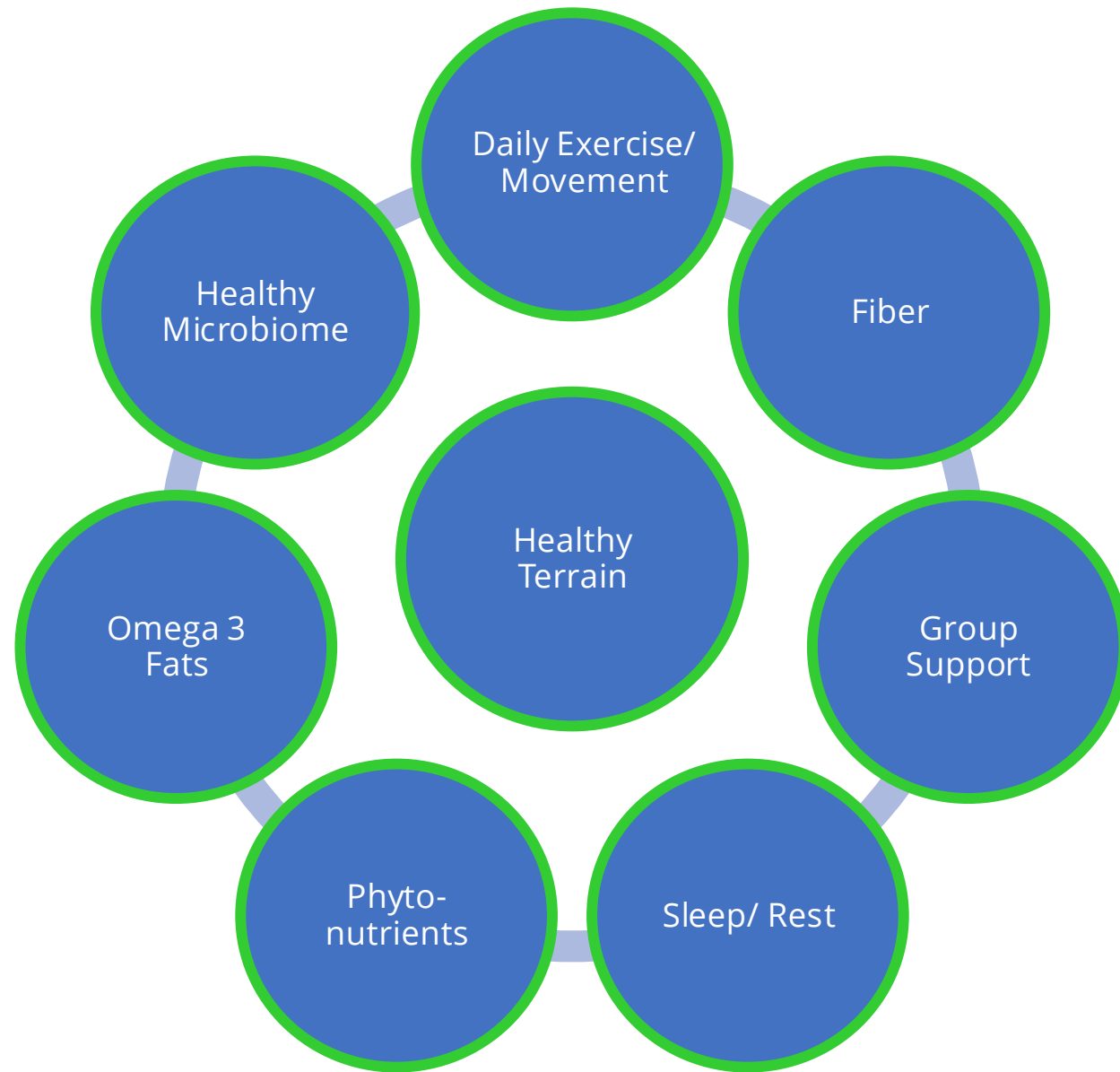


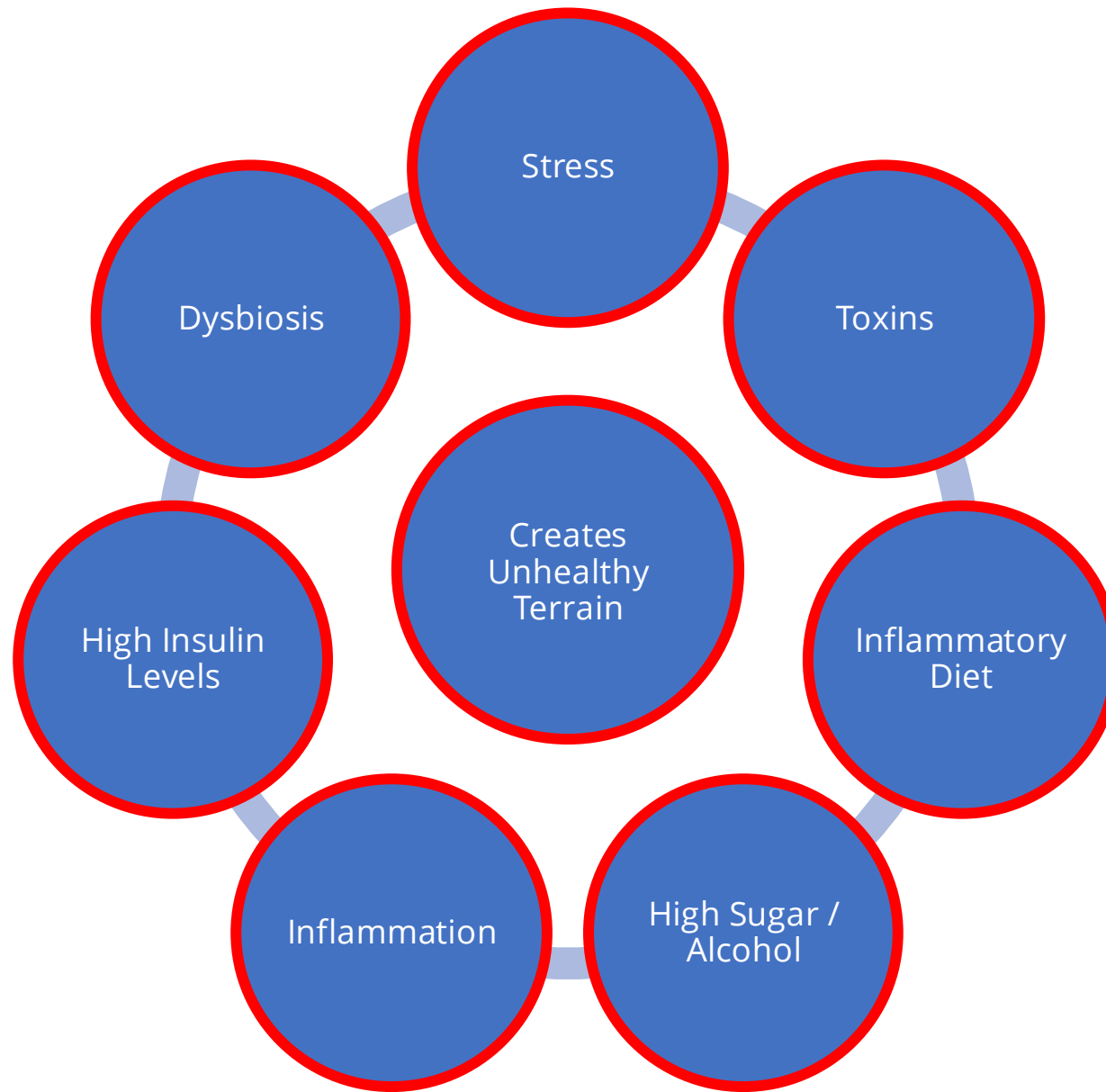
We can work
to create a
terrain in your
body that can
resist the growth
of cancer.

Create a Healthy Terrain



Remove what causes imbalance
Replace what is needed for balance





Inflammation and hsCRP

- Chronic inflammation can contribute to the development and progression of cancer
- Elevated levels of CRP at diagnosis is associated with increased aggressiveness of the tumor – increased angiogenesis, invasion and metastasis
- CRP is a well-established independent prognostic marker
- Breast cancer survivors with chronic inflammation are at increased risk of recurrence

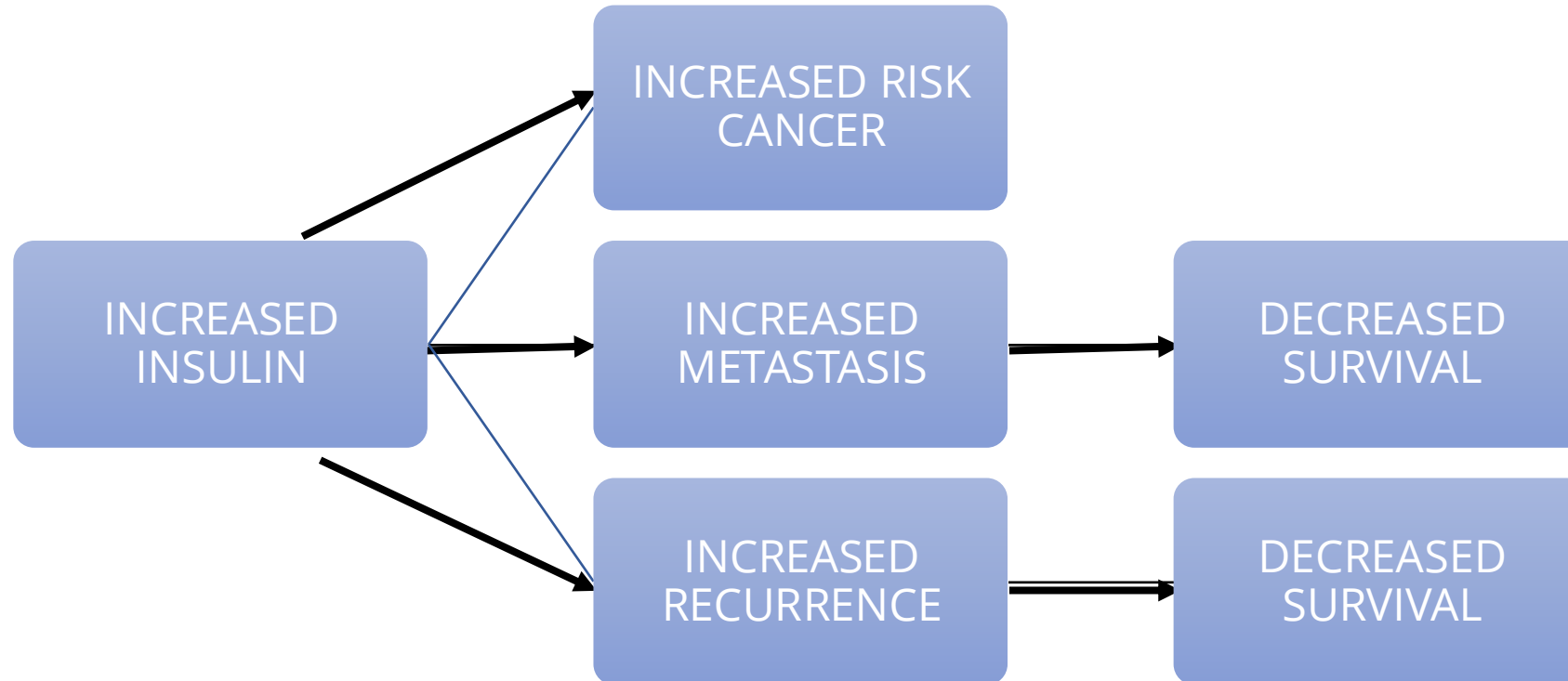
Zhu, M., et al., 2022
Aseganonkar, SB., et al., 2015

How to Decrease Inflammation

- Avoid refined and processed foods
- Decrease % Body Fat
- Increase Omega 3 fats
- Low glycemic impact diet
- Turmeric, resveratrol, ginger and green tea
- Decrease stress and increase sleep
- Look for underlying infections in the body (gums / gut)
- Trial of an elimination diet for some

Zivkovic AM, et al.,2011

Insulin Resistance



Srinivasan M, et al., 2022

Signs of Insulin Resistance

- Visceral Adiposity
 - Waist Circumference > 35 inches
 - Waist / hip ratio > 0.8 for women
 - Low lean muscle mass
- Elevated blood sugar >100mg/dL
- Elevated Insulin levels >10 uIU/mL
- Elevated blood pressure >140/90 or on medication
- High triglycerides >150mg/dL
- Low HDL (good cholesterol) <50mg/dL for women
- High LDL particles
- Elevated CRP >1.0mg/L

Freeman, AM., et al., 2023

Glycemic Load Linked to Breast Cancer Risk

High glycemic index and glycemic load diets are associated with cancer development and worse prognosis

Causing hyperinsulinemia, insulin resistance, oxidative stress and inflammation.

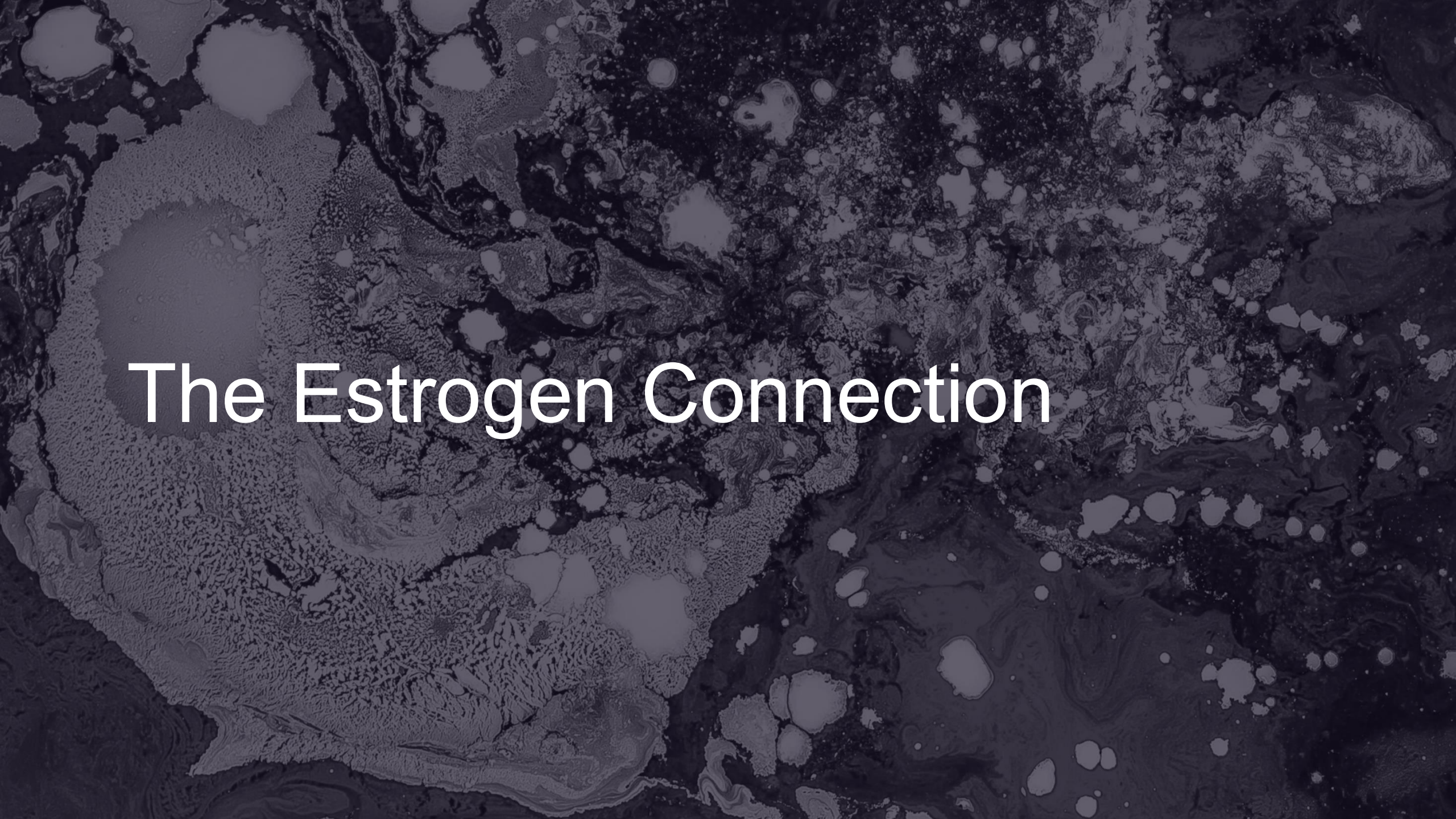


Peppas, M., et al., 2023

Conventional Biomarkers ... A Great Place To Start

- Fasting insulin
- Fasting glucose
- HgA1C
- Lipid panel with advanced lipid assessment
- Triglycerides, HDL, LDL-P, Pattern A vs B, IR score, Apo B
- hsCRP
- ESR
- Serum Zinc / Copper
- Vitamin D
- Homocysteine

Freeman, AM., et al., 2023

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The Estrogen Connection

The Estrogen Connection

Breast cancer progression is highly associated with level of circulating estrogens

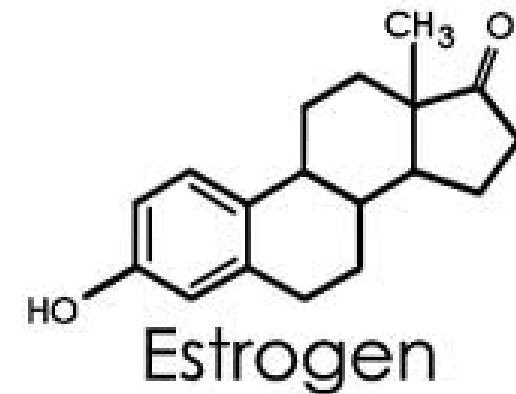
- Estrogens bind to ER- α receptor - enhance growth factor production - proliferation of breast cancer cells
- Genotoxic effect
- Phase 1 metabolism produces intermediate metabolites that can cause oxidative stress and genomic damage - increasing mutation rates and putting stress on the DNA repair system

Bernardo G, et al., 2023

The Estrogen Connection

Estrogen exposure and breast cancer risk

- Number of periods in your lifetime
- BCPs >5 years or current use - small
- HRT - ? Progestins / higher dose HRT
- High serum estrogen levels associated with increased breast cancer risk
- Endocrine Disrupting Chemicals
- Weight - % body fat



Starek-Świechowicz, B., et al., 2021

Estrogen Levels and Aromatase

Aromatase converts androstenedione into estrone (E1) and testosterone into estradiol (E2).

Aromatase is in body fat as well as other tissues in the body (breast, endometrial, fibroids).

Aromatase is increased with:

- Increased body fat
- Inflammation
- High insulin / insulin resistance
- Alcohol intake
- Genetic snps - CYP19A1

Bulun SE, et al., 2021

Decrease Aromatase Naturally

- Lower % body fat
 - Maintain healthy weight
 - Resistance exercise
- Decrease inflammation
 - Omega 3 fats
 - Decrease saturated fat
 - Turmeric
- Fiber
- Phytoestrogens
 - Lignans – Flax seed
 - Resveratrol
 - Soy
 - Green Tea



Lephart ED., 2015

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Estrogen Metabolism

Estrogen Metabolism – Phase 1

Phase 1 - Initial breakdown of estrogen in the Liver

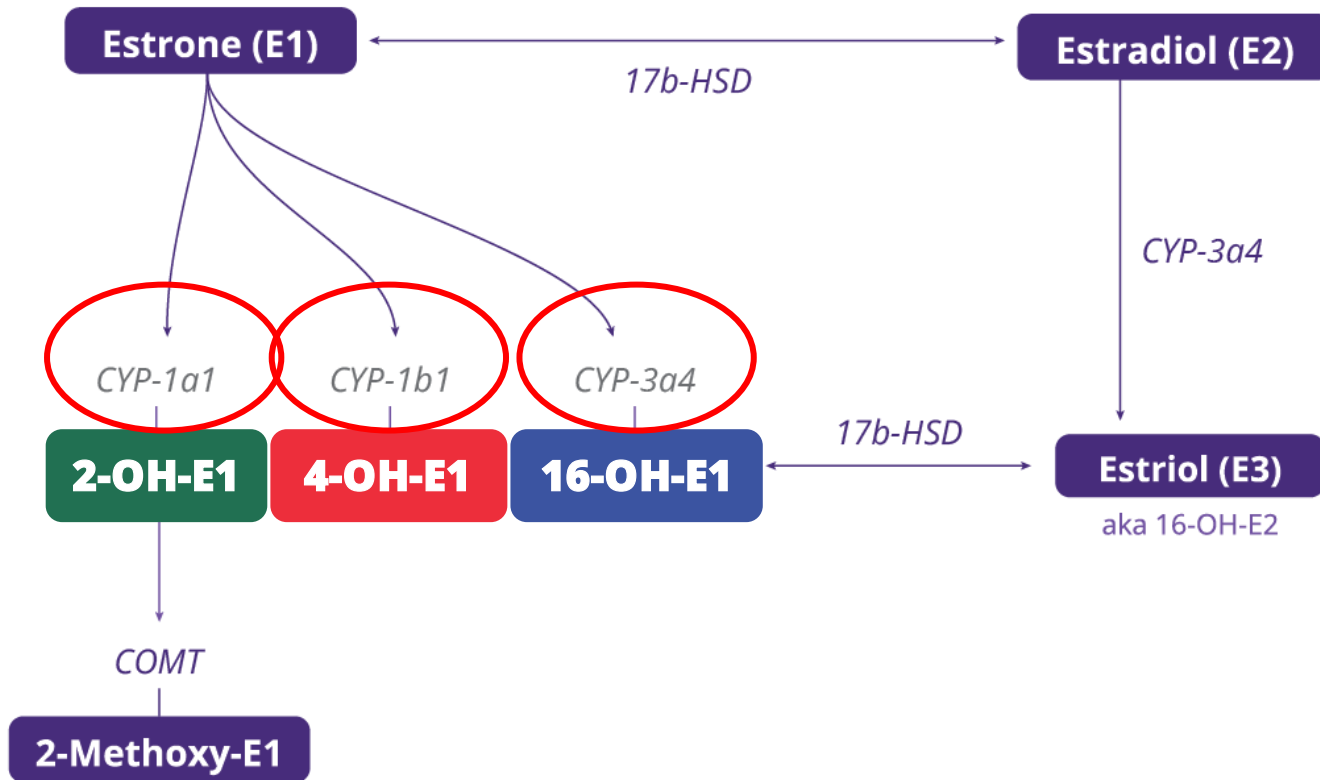
Hydroxylation -

- CYP1A1 - 2 OH E1/E2 - weaker estrogen - asst with lower cancer risk
- CYP3A4 - 16 OH E1/E2 - stronger estrogen / proliferative
- CYP1B1 - 4 OH E1/E2 - potentially carcinogenic

Active metabolites that need to be further broken down / neutralized into water soluble compounds for excretion in phase 2

Miao S, et al., 2019
Bukato K, et al., 2024

2-OH Preference (Phase 1)



In phase 1, parent estrogens (E1 and E2) are broken down via 3 main pathways.

- 2-OH is the **protective** pathway
- 4-OH is the **genotoxic** pathway
- 16-OH is the **estrogenic** pathway

Phase 1 CYP1B1 & Phase 2

CYP1B1 - Phase 1

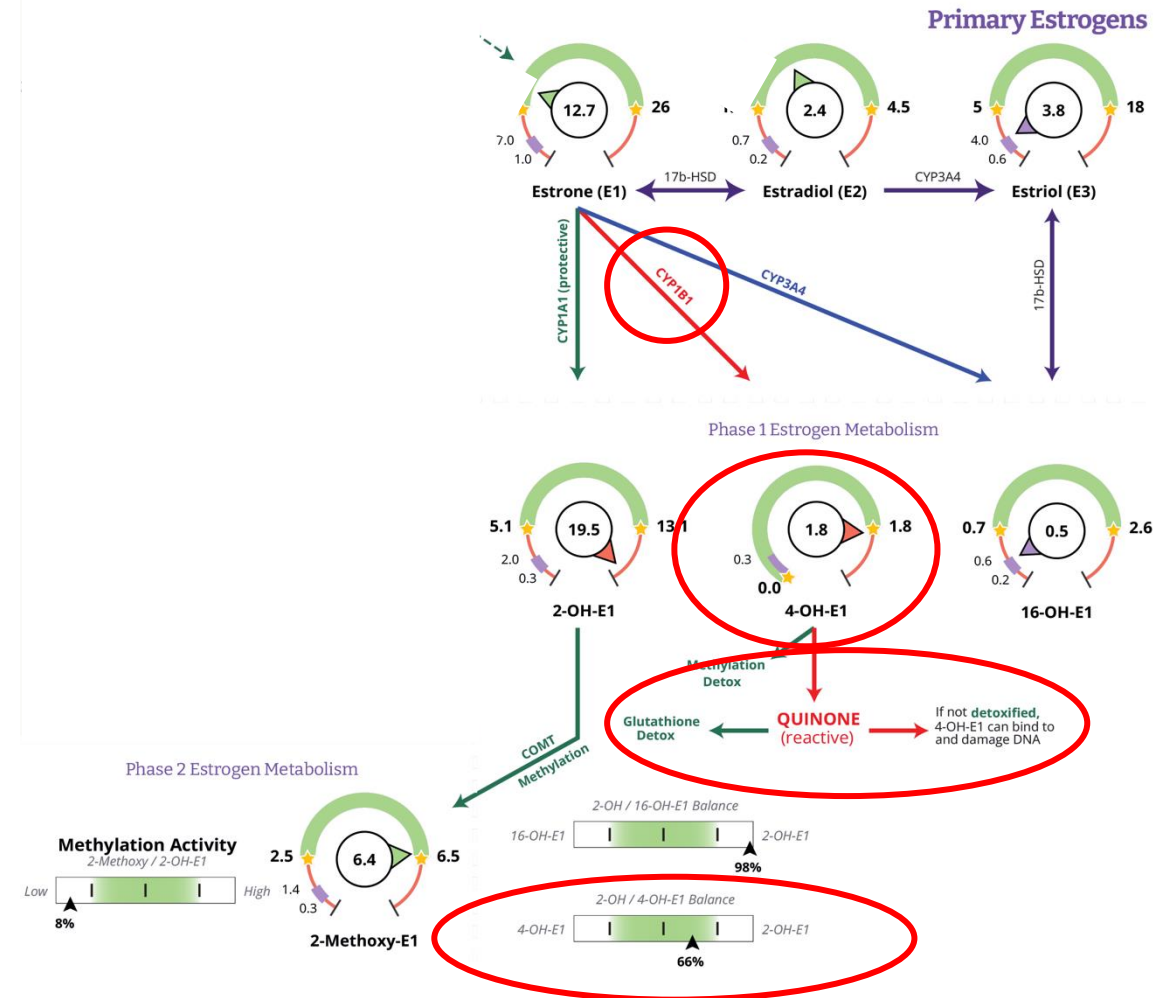
Catalyzes estrogens to 4OH metabolites

4 hydroxylation estradiol (E2) and estrone (E1)

4OH metabolites need to be neutralized with methylation or glutathione

Variations CYP1B1 drive increased 4OH metabolites that if not detoxified can drive increased reactive oxygen species and DNA adducts that have potentially carcinogenic properties

CYP1B1 is also involved in metabolism polycyclic aromatic hydrocarbons found in cigarette smoke and charbroiled meats



Kwon YJ, et al., 2024

Phase 1 CYP1A1 & Phase 2

CYP1A1 - Phase 1

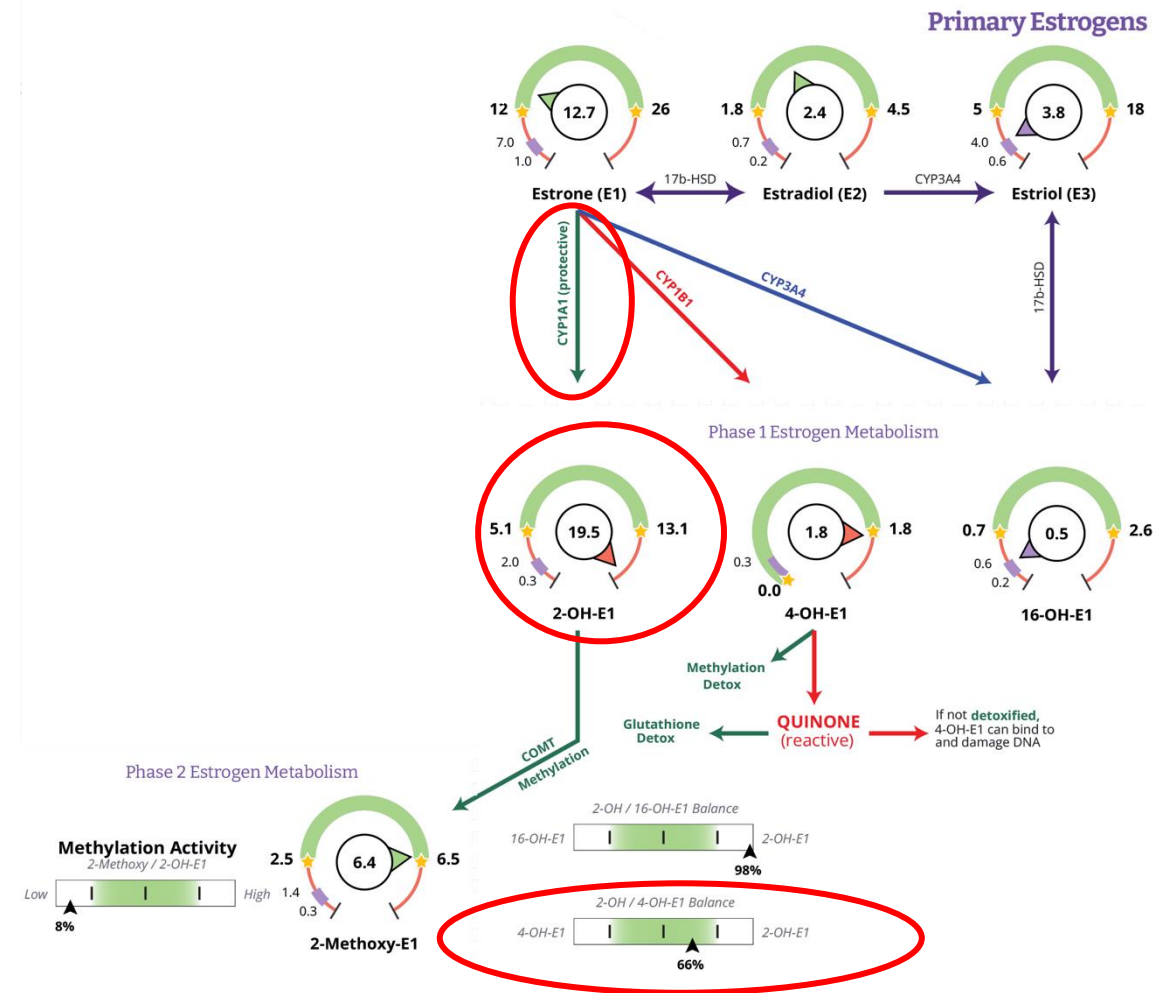
Increased activity increases phase 1 metabolites

Ensure support of phase 2 to prevent excess reactive oxygen species

Polyphenols can help decrease oxidative stress and activate phase 2

Also involved in metabolism polycyclic aromatic hydrocarbons found in cigarette smoke and charbroiled meats.

Increased risk of breast cancer seen in women with increased activity of the CYP1A1 enzyme who smoke.



Weber BL, et al., 2000

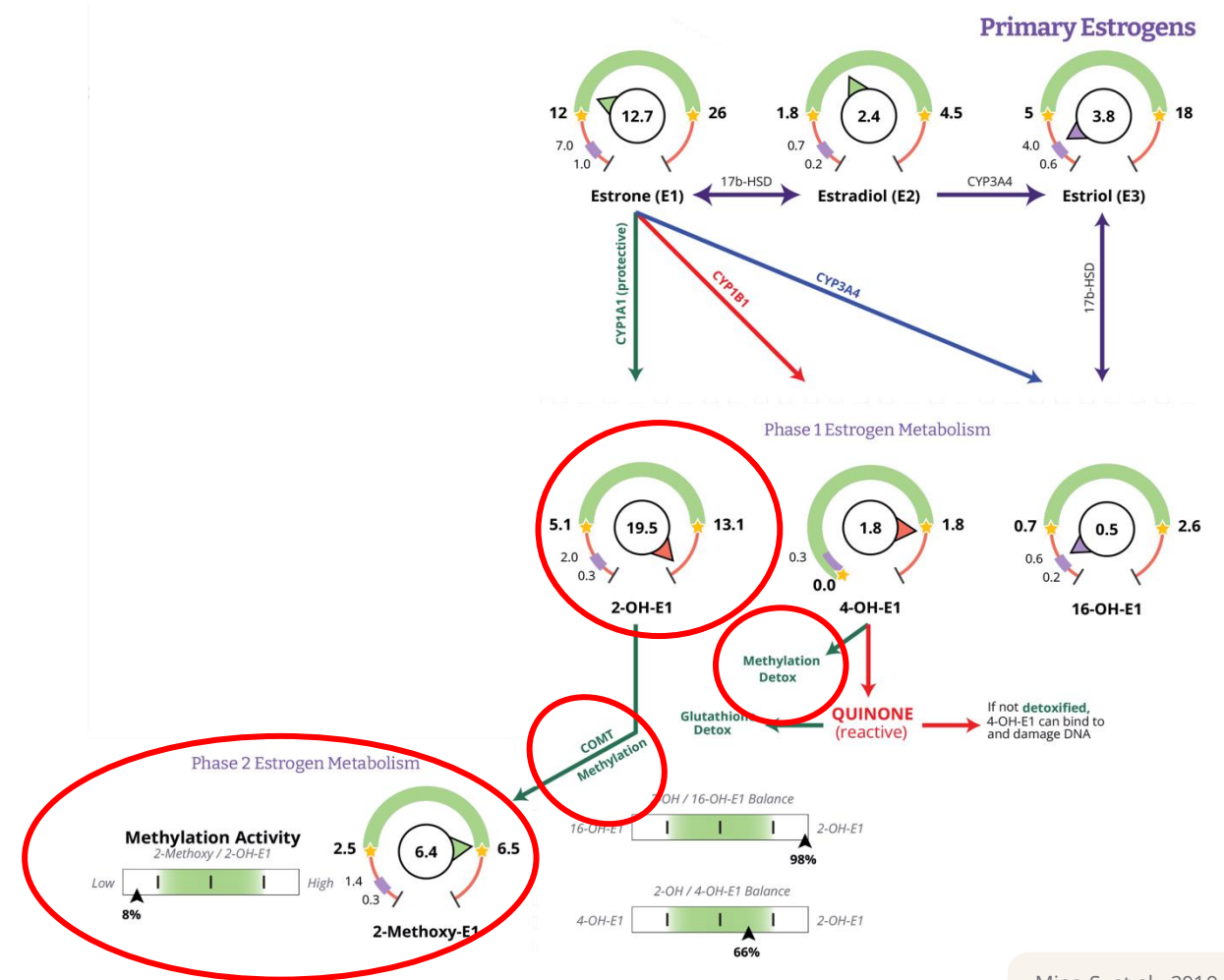
Estrogen Metabolism - Phase 2

Sulfation and Glucuronidation to allow biliary excretion of estrogen into the gastrointestinal tract.

Methylation

2 OH and 4 OH need to be methylated into 2 MeOH and 4MeOH to neutralize

COMT enzyme



Miao S, et al., 2019
Bukato K, et al., 2024

Estrogen Metabolism - Phase 2

Phase 2

2 OH E - methylated by COMT to 2 methoxy E - protective

16 OH E - reduced to estriol - neutralized

4 OH Estrogens - Increased levels associated with increased cancer risk

- CYP1B1 variations can increase 4OH estrogen levels
- methylated by COMT to 4 methoxy E - neutralized
- carcinogenic quinones - that need GST to be neutralized

Miao S, et al., 2019
Bukato K, et al., 2024

COMT

- Low Penetrance / High Prevalence
- 20-30% of the Caucasian population are homozygous variant of the COMT gene – Met / Met
- Resulting in a 25 % reduction in the Catechol O-Methyltransferase enzyme
- Decreased breakdown on catecholamines - dopamine, norepinephrine, epinephrine
- Decreased methylation of estrogens
- Increased risk of anxiety, worry, better focus, fibromyalgia, estrogen dominance – breast cancer
- Support methylated B complex, Magnesium, S-AdoMet
- Cruciferous vegetables, flax
- Stress reduction and self care
- Avoid caffeine / stimulants

Janacova L, et al., 2023
(Psychologytoday.com)

Glutathione S-Transferases

- Low Penetrance/ High Prevalence (23-60% populations have null variants)
- GSTT1, GSTM1, GSTP1
- Glutathione S-transferases are enzymes involved in utilization of glutathione, Phase 2 detoxification and elimination of carcinogenic metabolites
- Deletion on GST genes associated with increased risk of cancers (lung, bladder, gastric, cutaneous, colon, breast)
- EGCG upregulates GSTM1
- Sulforaphane – sulfur containing compound in cruciferous veggies – upregulates Nrf2, to help lower oxidative stress and increase glutathione production

Tanwar R, et al., 2015

Glucosinolates and Sulforaphane

1-2 Cups Cruciferous Vegetables per week

- Cruciferous vegetables (broccoli, broccoli sprouts, cauliflower, kale, Brussel sprouts) - Give bitter taste
- Pro apoptotic activity
- Decreases DNA damage and increases glutathione, decreases oxidative stress
- Microbes in our gut with myrosinase activate glucosinolate into isothiocyanate sulforaphane
- Feeds healthy gut bacteria
- Epigenetically increases tumor suppressor genes



Liu X, et al., 2013

Sulforaphane

- Downregulate CYP1B1
- Upregulate Phase 2
- Neutralize 4 OH estrogens decreasing their carcinogenic potential
- Activates Nrf2 a transcription factor that can decrease oxidative stress and lower inflammation in cells
- Increases glutathione production
- Lowers oxidative stress
- Activate the tumor suppressor gene
- Triggers apoptosis
- 1 Cup broccoli sprouts or 2.6 lbs (4 Cups cooked) broccoli will have 20mg of sulforaphane
- Many supplements contain 30 mg of glucosinolates with mustard seed powder for myrasinase

Baralić K., et al., 2024

Diindolylmethane (DIM) and Indole-3-Carbinol (I3C)

- I3C and DIM phytochemicals in cruciferous vegetables
- Increased intake of cruciferous vegetables is associated with lower risk of breast cancer
- Proapoptotic, anti-proliferative, anti-angiogenic, and anti-estrogenic
- Can bind to estrogen receptor and compete with estrogen
- Induces CYP1A1 and CYP1B1 - good and not so good
- Other genes impacted as well
- Newman et al. (with Precision Analytical) found that premenopausal women taking DIM had lower estrogen levels and that 2-OH-E1 metabolites increased more than 4-OH-E1 metabolites, leading to a higher (better) ratios vs women not taking DIM.

Newman, M, et al., 2024
Mulvey L, et al., 2007

Methylation Support

Methylation neutralizes dangerous phase 1 metabolites

Check methylation genes

- COMT
- MTHFR

Monitor homocysteine

- Other testing - Methylmalonic acid, serum B12, methylation panels

Folate rich vegetables

B complex with methylfolate

Miao S, et al., 2019
Bukato K, et al., 2024

Potential Testing

Estrogen metabolism

Genetic snp testing

Methylation activity

Homocysteine

Methylmalonic Acid

Assess Glutathione

GGT

Oxidative stress levels - 8OHdG

Pyroglutamate

Stool testing

butyrate

beta glucuronidase

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Gut Microbiota

Microbiome and Breast Cancer

Gut Microbiome

- Modulates the immune system
- Releases metabolites (i.e. SCFAs such as butyrate)
- Modulates estrogen levels
- Low diversity is associated with decreased survival in cancer patients
- Butyrate has anti-cancerous activity against breast cancer cells and has been shown to positively influence certain treatments

Bernardo G, et al., 2023

Glucuronidation

- Glucuronic Acid conjugates with estrogen in the liver
- E-GA - excreted in the stool
- Beta glucuronidase - cleave E-GA and increases free estrogen
- Beta glucuronidase is elevated:
 - High meat / Low fiber diets
 - Imbalanced gut flora
 - Pathogenic gut flora

Bernardo G, et al., 2023
Sui Y, et al., 2021

Estrobolome and Beta Glucuronidase

The enteric bacterial genes and their ability to metabolize estrogen and increase level of free estrogen

- Higher in Clostridia and Ruminococcaceae families
- Escherichia / Shigella genus

Beta glucuronidase production is higher in dysbiosis

- Poor diet
- High alcohol intake
- Increased antibiotic use

Bernardo G, et al., 2023

Heal the Gut

- Limit Antibiotic Use
- High Fiber Diet
- Phytonutrients
- Decrease Processed Red meat
 - Choose organic antibiotic free
 - <18 oz./wk (AICR)
- Probiotics
- Prebiotics
- Postbiotics
- Remove inflammatory foods
- Calcium D Glucarate



AICR website, March 2025

Calcium D Glucarate

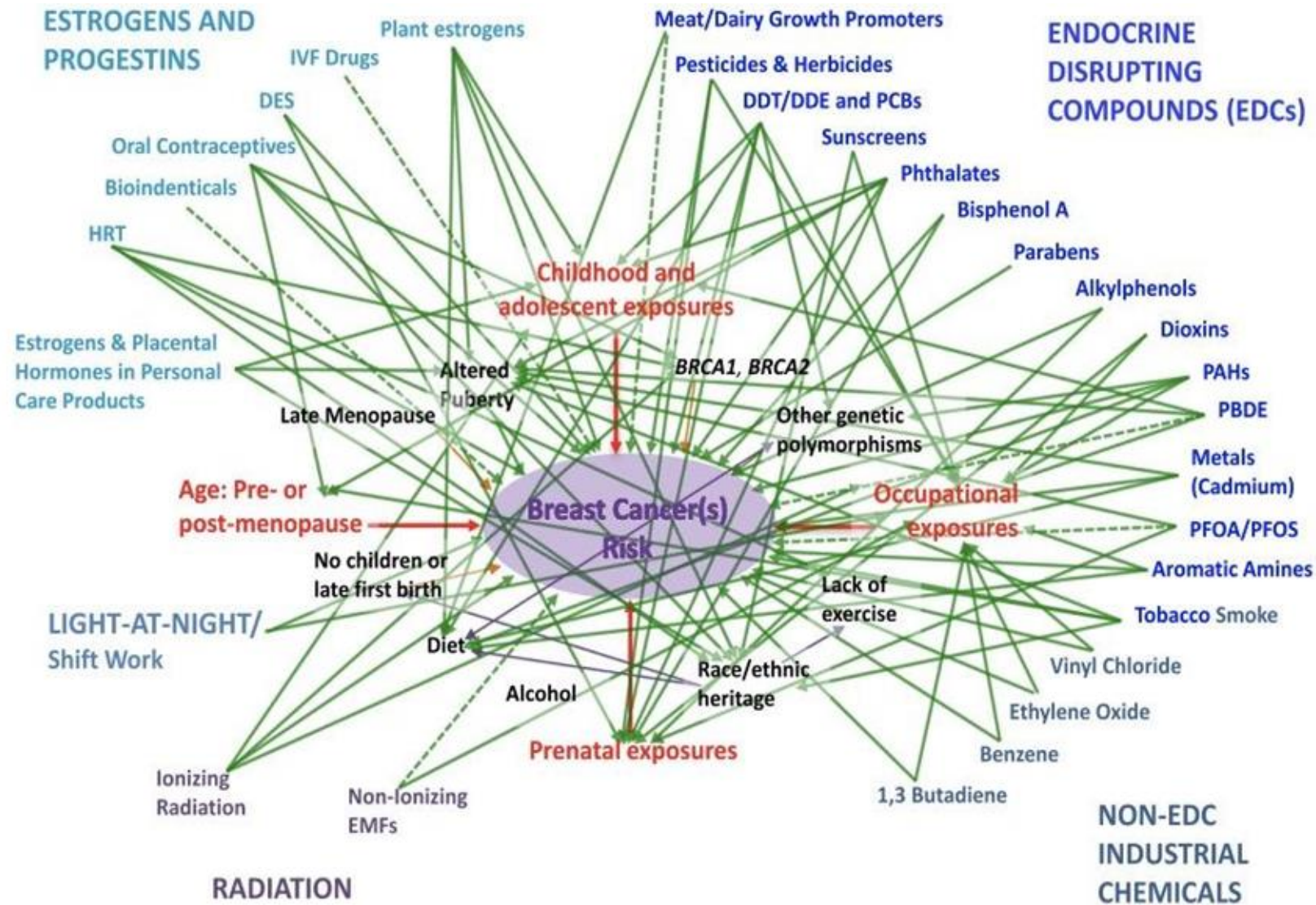
- Inhibits beta glucuronidase
- Binds to estrogens and toxins in the gut facilitating elimination
- Also found in foods - broccoli, cabbage, kale, apples, oranges, grapefruit, lettuce
- Supplement - 1000 mg twice daily

Calcium Glucarate. Memorial Sloan Kettering Cancer Center. Published March 22, 2022.

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Toxins and Detoxification

Complexity of Factors Impacting Risk of Breast Cancer



Gray, J.M., et al., 2017

Endocrine Disrupting Chemicals

An exogenous chemical or mixture of chemicals that interferes with any aspect of hormone action

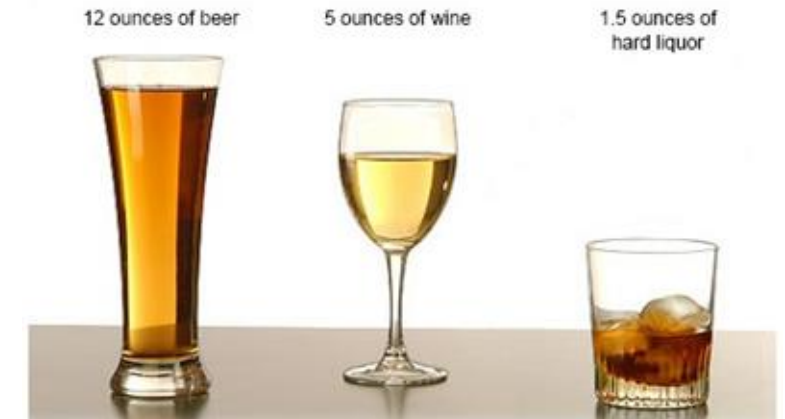
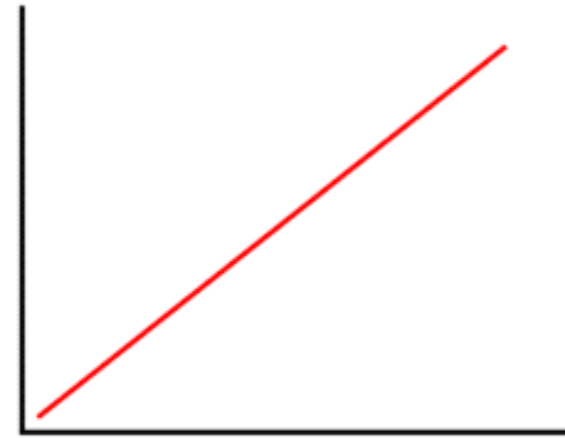
- BPA – bisphenol A – used in polycarbonate plastic, dental sealants, thermal receipts, food packaging and epoxy resins lining food cans
- Phthalates – fragrance ingredients in personal care and cleaning products, plastics, building materials, insecticides, food packaging, plastic wrap
- Parabens – (propyl-, isopropyl-, butyl-) antimicrobial preservatives in foods, personal care products, cosmetics, moisturizers, soaps, detergents and pharmaceuticals
- Alkylphenols – detergents, air fresheners, fertilizers, herbicides, and cleaning products
- Triclosan and triclocarban – antimicrobials in toothpaste, personal care and household products
- Pesticides - Carcinogens and endocrine disruptors



Gray, J.M., et al., 2017

Alcohol

- As alcohol intake increases, so does our risk of breast cancer
- Linear Relationship
- For every 1 drink increase per day, a women's risk of getting breast cancer increased by 12%
- >2 drinks per day = 3x increased risk



Rachdaoui N, et al., 2013
BCRF, 2024

Alcohol – Why?

- Liver and detox impact
 - Increased oxidative stress
 - Adds to the toxic load
- Increase free estrogen
 - by decreasing SHBG
 - Increased aromatase
- Associated with other unhealthy lifestyles
- Decrease B vitamins
 - Lower folate
 - Important for methylation

Rachdaoui N, et al., 2013
Starek-Swiechowicz B, et al., 2023
BCRF, 2024

Food for Detoxification

Focus on Whole Foods

- Greens
- Broccoli
- Beans / legumes
- Nuts – Brazil nuts
- Eggs
- Animal Protein
- Colorful Vegetables
- Spices
- Garlic / onions



Avoid Junk Food

- Devoid of nutrients necessary for all of the cells in your body to work properly
- Empty calories
- Not enough vitamins, minerals, phytonutrients
- SAD diet – nutrient deficient



Hodges RE, Minich DM., 2015

What Can You Do?

- Buy organic
 - Decreased pesticide exposure
 - Decreased growth hormone exposure
 - Decrease animal products in general - Balance
 - AICR <18 oz. red meat/ week
- Use glass whenever possible
- Store food in glass
- Do not heat or microwave plastic
- Switch to glass / stainless steel reusable water bottles
- Avoid pesticides on your lawn and garden
- Environmental Working Group – www.ewg.org



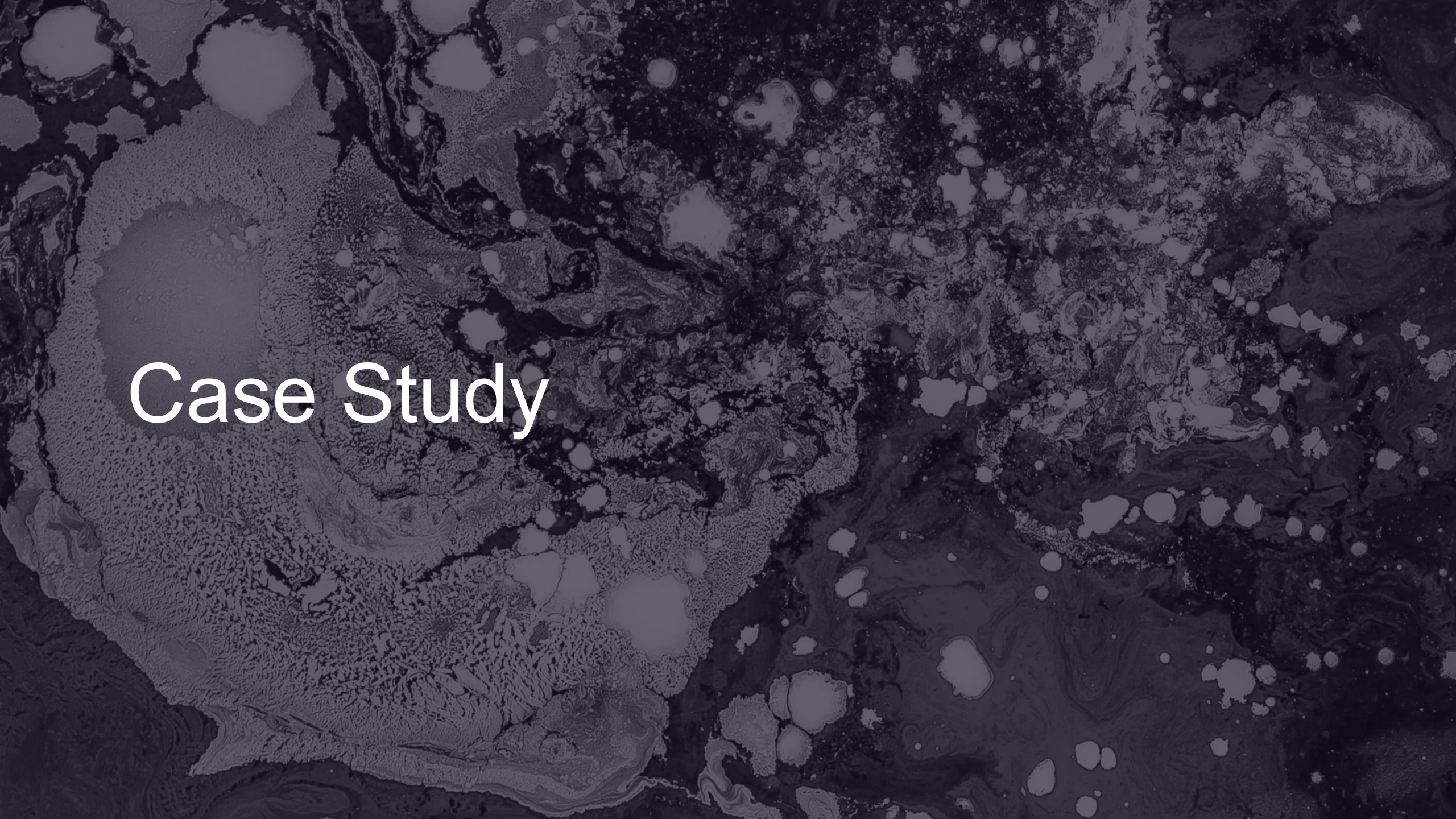
IARC Working Group, 2015

Improve Elimination of Toxins

- Have 1 to 2 bowel movements a day.
- Drink 6 to 8 glasses of water a day.
- Sweat regularly.
- Use exercise to help you sweat regularly.
- Use steam baths or saunas—infrared saunas may be even more beneficial.
- Regular exercise, yoga, and lymphatic massage can improve lymph flow and help flush toxins out of your tissues into your circulation so they can be detoxified.

Personalized Lifestyle Factors

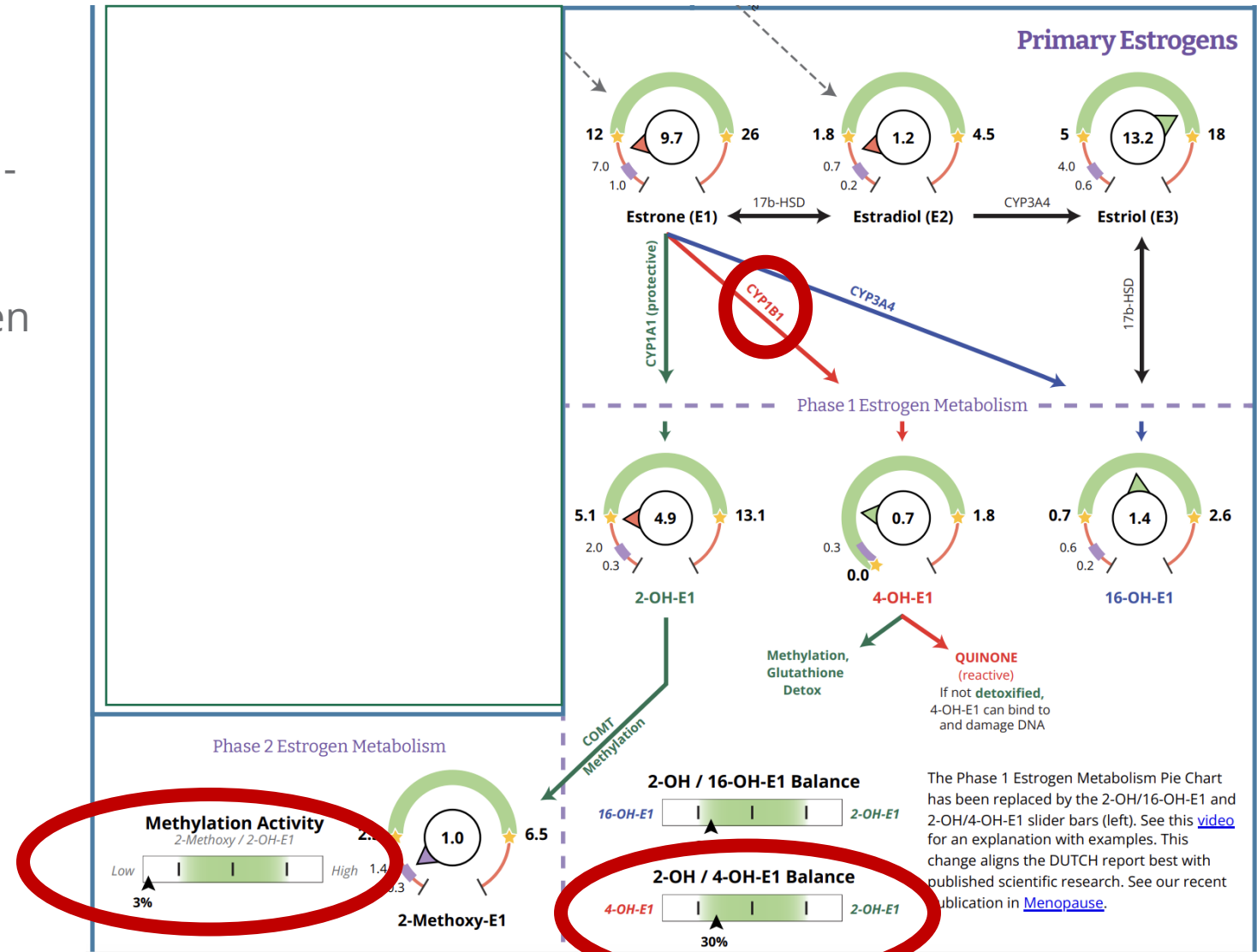
- Sleep and Rest
- Exercise and Movement
- Nutrition
- Stress Management
- Relationships and Community
- Mental, Emotional and Spiritual Wellbeing

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Case Study

Breast Cancer History / How to Decrease Risk

47 yo woman 1.2 cm breast cancer stage 1 -
ER+/PR+/Her2neg
oncotype score 25
4 cycles of T/C, radiation and then tamoxifen
CYP2D6 1/1 - good for tamoxifen
CYP1B1 ++
MTHFD1++
High beta glucuronidase on stool
4OH E1 high
Added sulforaphane
Methylated B complex with goal HC 8
Added calcium d glucurate



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Hormone Therapy and Risk for Breast Cancer

The Functional Medicine Approach

Gather a patient's history

Personalize care

Think about past hormone issues - PMS, fibroids, dense breast tissue, migraines, blood clots, breast cancer, uterine cancer, % body fat. (these are not necessarily contraindications, just considerations).

Consider why you are using the hormones

Start slow, assess effectiveness and work up as needed

Use bioidentical hormones, progesterone instead of progestins, transdermal estrogen

Monitor symptoms, levels, estrogen metabolism and consider genetics

Low doses can be helpful

Focus on the matrix to decrease overall risk -

Lower inflammation, lower insulin resistance, lower % body fat, support the microbiome, support detoxification and lower endocrine disrupting chemicals

Focus on lifestyle to lower overall risk of breast cancer and improve health.

Not needed for all women.

Things to Think About...

- Systemic vs local (vaginal)
- History of breast cancer (type and when) vs no history of breast cancer
- Has breast tissue or had mastectomy
- Uterus or hysterectomy
- Type of hormones used

Conventional Biomarkers ... A Great Place to Start

- Fasting insulin
- Fasting glucose
- HgA1C
- Lipid panel with advanced lipid assessment
 - Triglycerides, HDL, LDL-P, Pattern A vs B, IR score, Apo B
- hsCRP
- ESR
- Serum Zinc / Copper
- Vitamin D
- Homocysteine

Freeman, AM., et al., 2023

Additional Testing to Consider

Look deeper if high inflammation and / or high insulin - Ask yourself why?

Hormone levels and Estrogen metabolism

Stool testing

- Beta glucuronidase

- Butyrate

- Diversity index

Genetic snps

Toxin testing

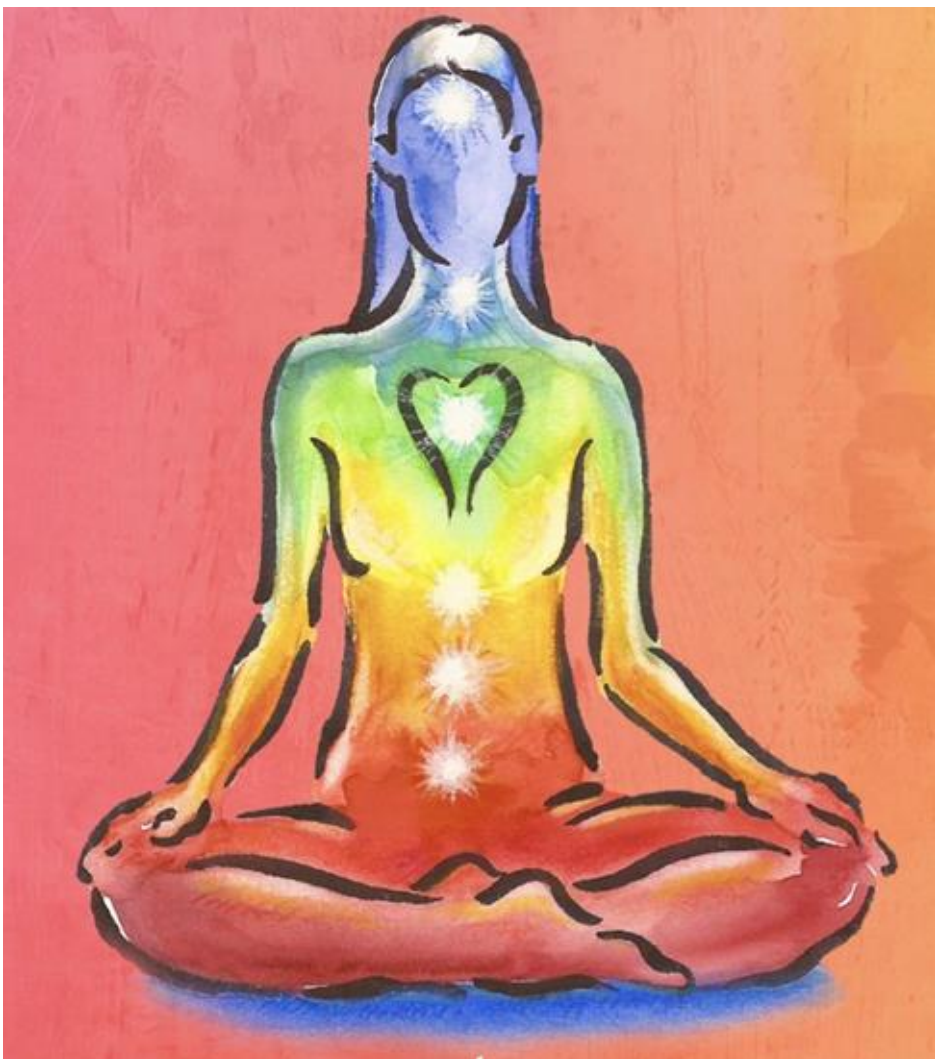
- GGT

- Heavy metal

- EDCs

- Oxidative stress markers / glutathione markers / pyroglutamate

Miao S, et al., 2019
Bukato K, et al., 2024



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