Breast Cancer Prevention & Nutrition:
A Review of the Dose-Response Relationship between Various Foods/Nutrients & Risk for Breast Cancer

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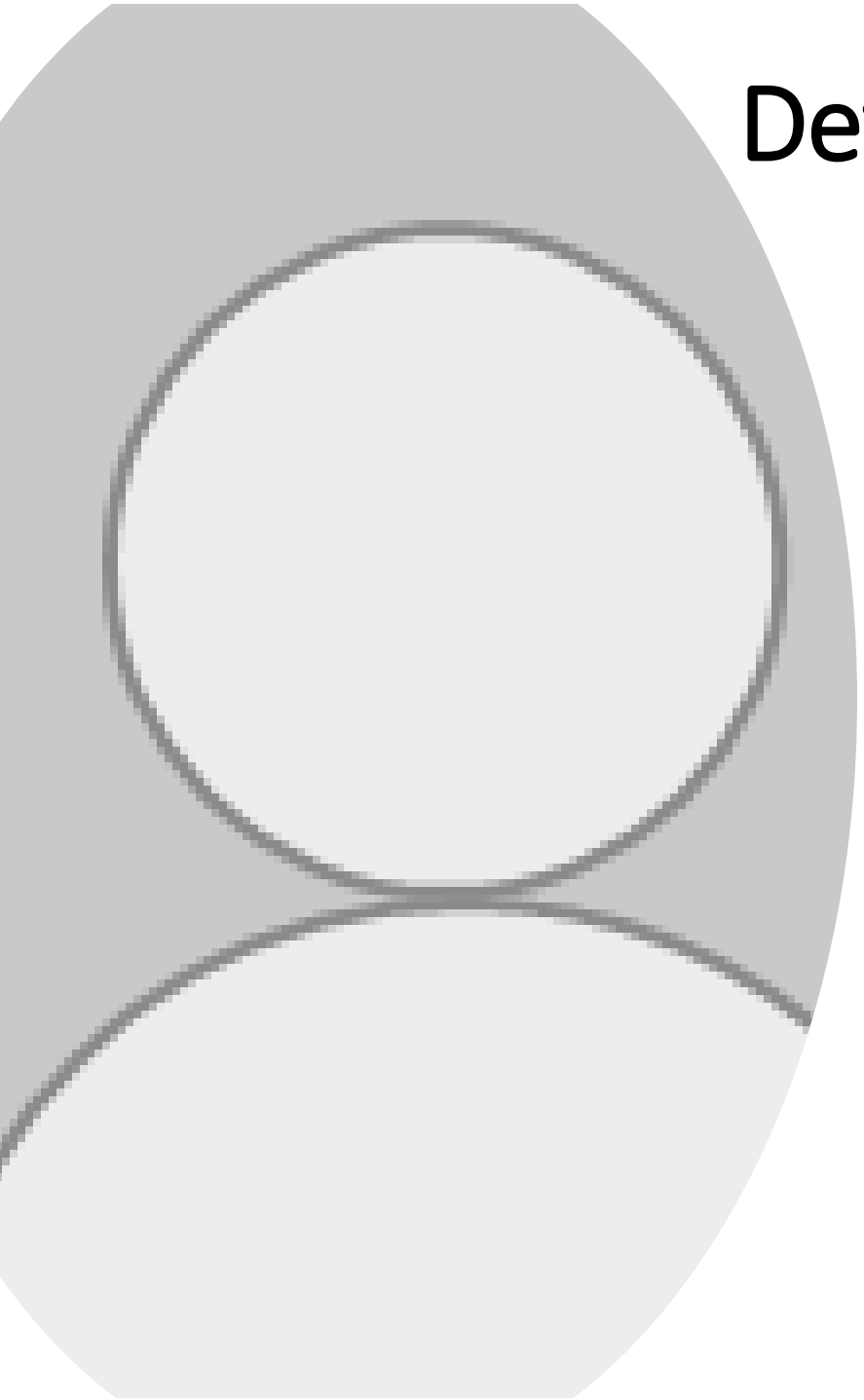
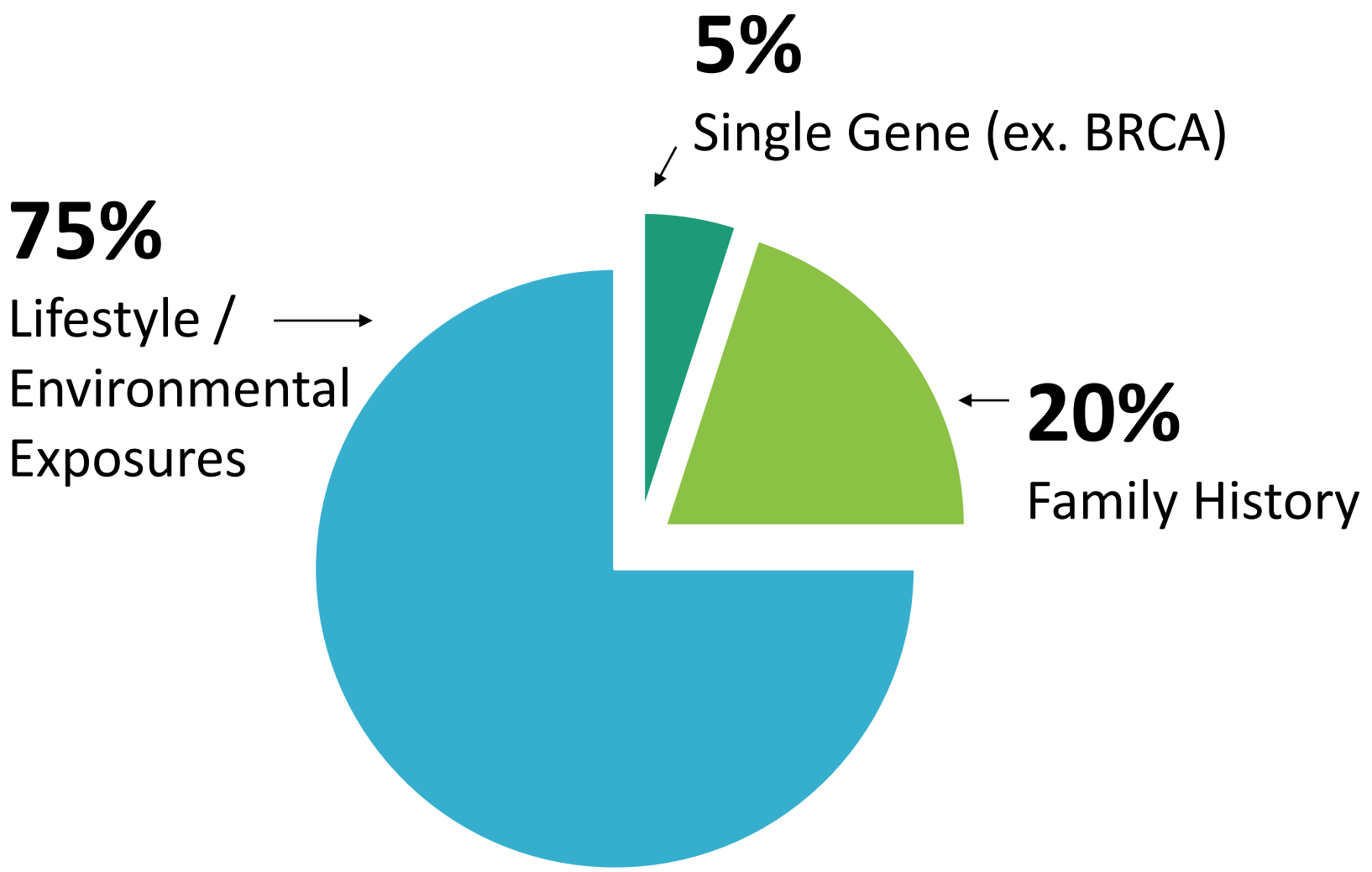
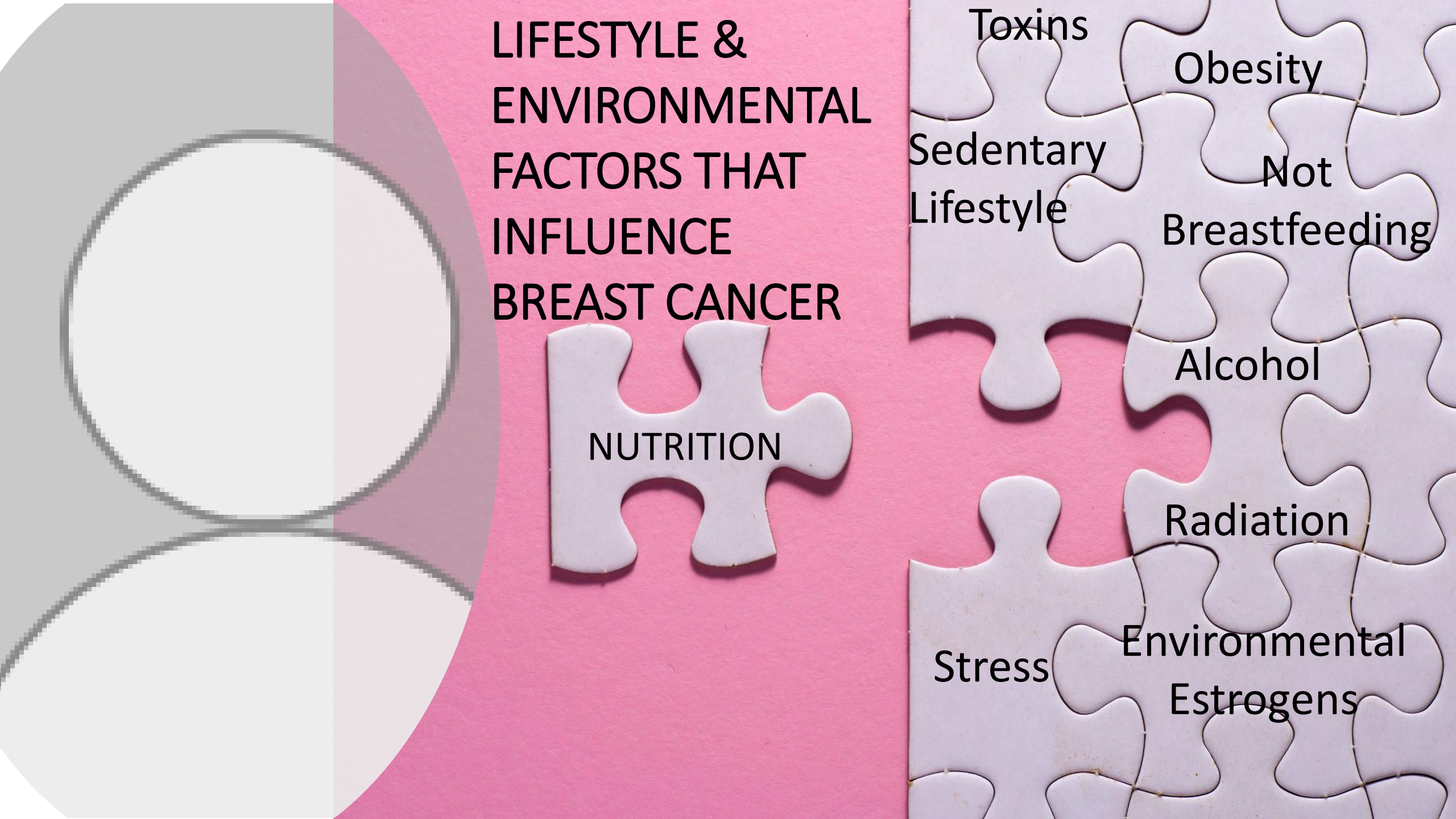
Determinants of Risk for Breast Cancer





www.breastcancer.org/facts-statistics

LIFESTYLE & ENVIRONMENTAL FACTORS THAT INFLUENCE BREAST CANCER



Mediterranean Diet prevents Breast Cancer

Randomized Controlled Trial, Toledo et al, JAMA IM, 2015

JAMA Internal Medicine | Original Investigation

Mediterranean Diet and Invasive Breast Cancer Risk Among Women at High Cardiovascular Risk in the PREDIMED Trial

A Randomized Clinical Trial

Estefanía Toledo, MD, MPH, PhD; Jordi Salas-Salvadó, MD, PhD; Carolina Donat-Vargas, PharmD; Pilar Buil-Cosiales, MD, PhD; Ramón Estruch, MD, PhD; Emilio Ros, MD, PhD; Dolores Corella, DPharm, PhD; Montserrat Fitó, PhD; Frank B. Hu, MD, PhD; Fernando Arós, MD, PhD; Enrique Gómez-Gracia, MD, PhD; Dora Romaguera, MSc, PhD; Manuel Ortega-Calvo, MD; Lluís Serra-Majem, MD, PhD; Xavier Pintó, MD, PhD; Helmut Schröder, PhD; Josep Basora, MD, PhD; José Vicente Sorlí, MD, PhD; Mònica Bulló, BSc, PhD; Merce Serra-Mir, RD; Miguel A. Martínez-González, MD

IMPORTANCE Breast cancer is the leading cause of female cancer burden, and its incidence has increased by more than 20% worldwide since 2008. Some observational studies have suggested that the Mediterranean diet may reduce the risk of breast cancer.

OBJECTIVE To evaluate the effect of 2 interventions with Mediterranean diet vs the advice to follow a low-fat diet (control) on breast cancer incidence.

DESIGN, SETTING, AND PARTICIPANTS The PREDIMED study is a 1:1:1 randomized, single-blind, controlled field trial conducted at primary health care centers in Spain. From 2003 to 2009, 4282 women aged 60 to 80 years and at high cardiovascular disease risk were recruited after invitation by their primary care physicians.

INTERVENTIONS Participants were randomly allocated to a Mediterranean diet supplemented with extra-virgin olive oil, a Mediterranean diet supplemented with mixed nuts, or a control diet (advice to reduce dietary fat).

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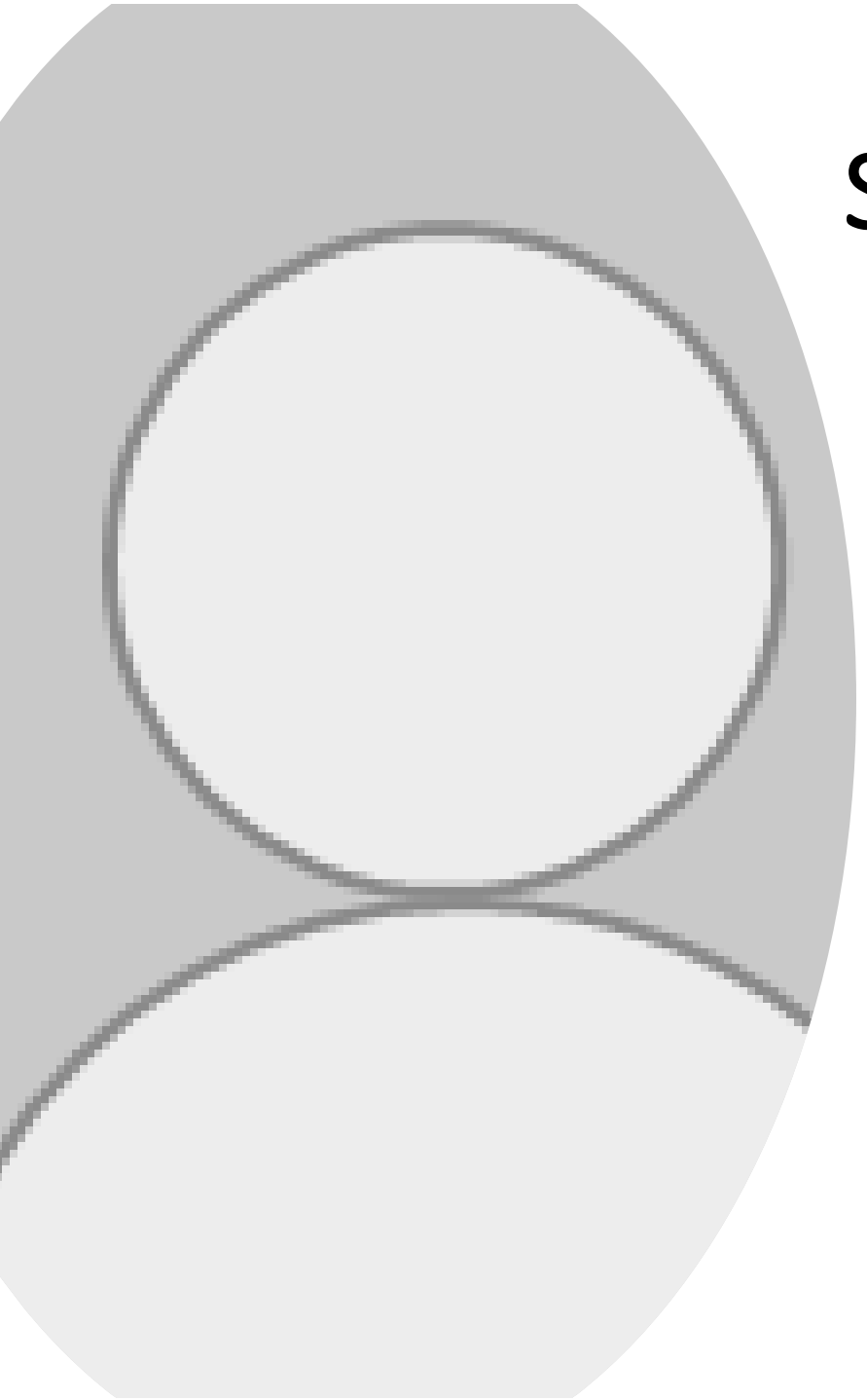
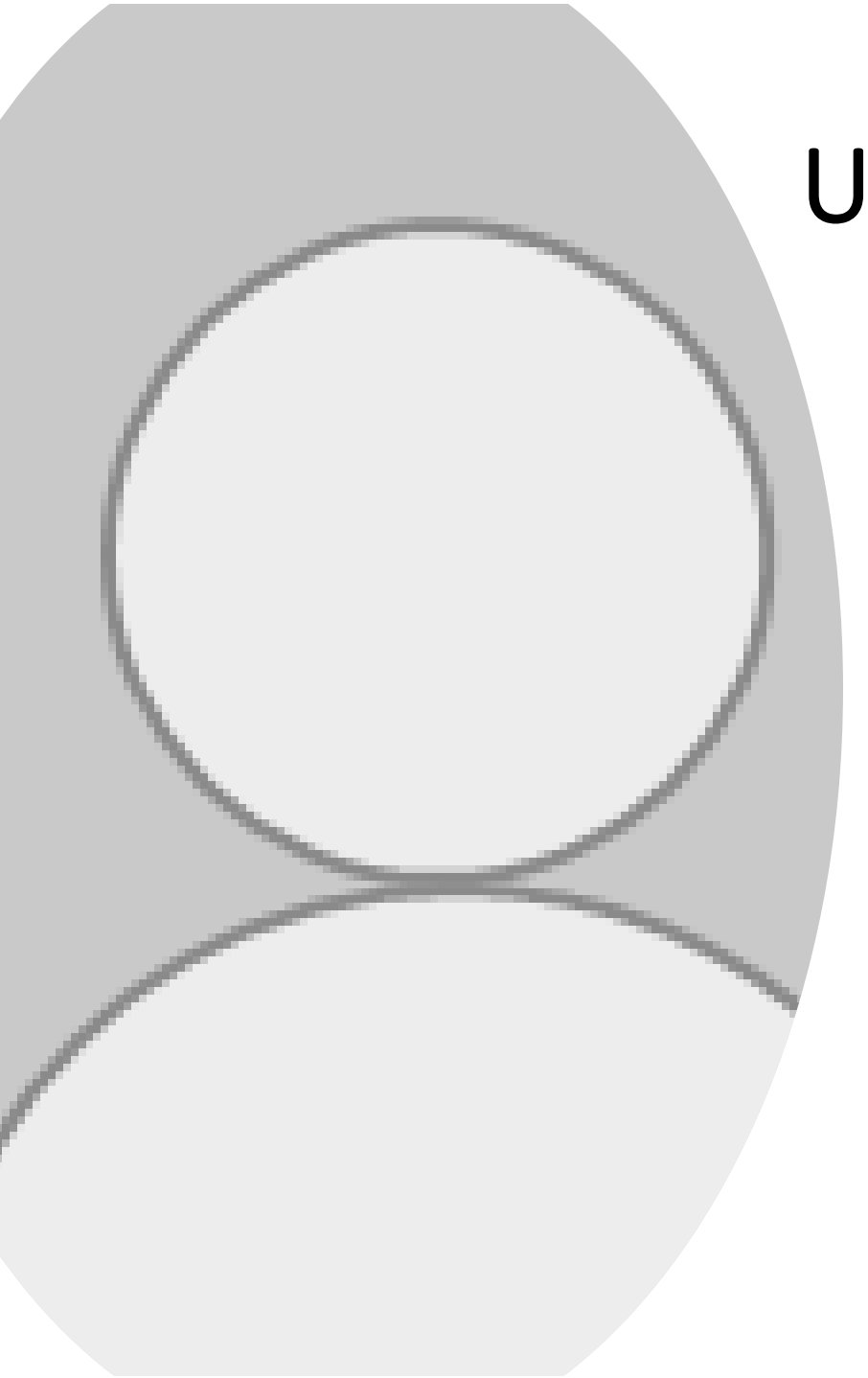
Supplemental content at jamainternalmedicine.com



So what do we tell our patients?

“Adopt a Mediterranean Diet” =

Not Ideal Messaging

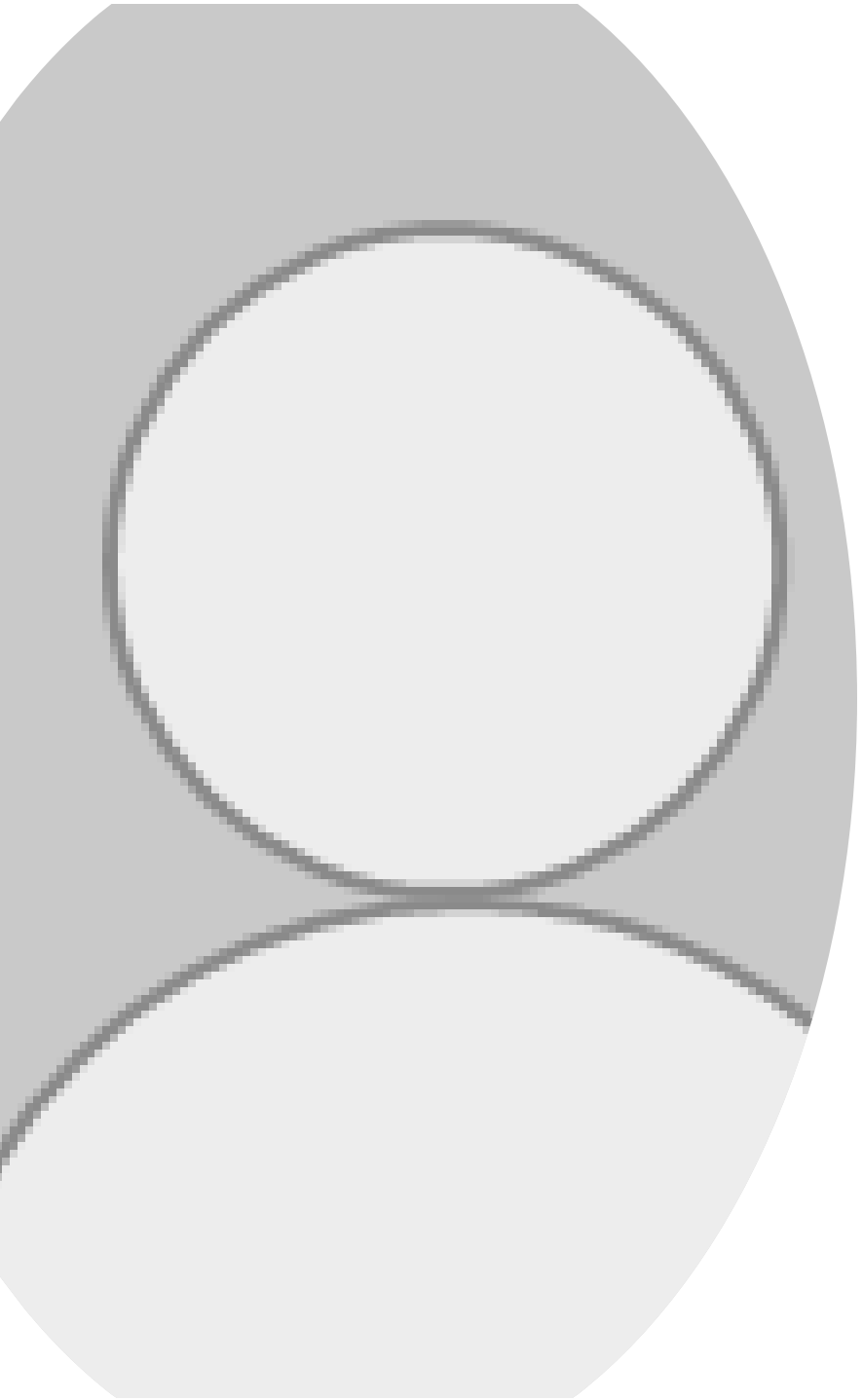


Umbrella Review – Buja et al, 2020

- Review of Meta-Analyses & Systematic Reviews
  - Cohort
  - Case Control
- Identified a **13 foods/nutrients** associated with increased/decreased risk for breast cancer

Foods that Increase Risk:
-Red/processed meat
-High Glycemic Index Foods
-Eggs

Foods that Decrease Risk:
-Vegetables
-Citrus Fruit
-Mushrooms
-Calcium
-Folate
-Vitamin D
-Lignans
-Carotenoids
-Soy
-Fiber



Research Gap

- Buja et al did not report quantities of consumption

- Patients wants to know
  - What to eat?
  - How much?
  - How often?

Objective

- To re-examine and **update** Buja et al's 2020 review in order to extract data regarding the **quantity** of the foods/nutrients that are associated with breast cancer
- To **compare** the evidence-based quantities **with established dietary recommendations** (ex. Dietary Reference Intake Levels)
- To **translate the findings** into dietary advice for patients

Buja et al, 2020 Review
13 foods/nutrients

Updated Search (Scopus & PubMed)
2017 - Oct. 2022

33 meta-analyses

74 abstracts

No dose response reported
3 foods

Dose-response reported
10 foods

Updated dose-response meta-analyses
5 foods

New contradictory data
2 foods

New meta-analysis
1 food

2 foods
~~Calcium~~

4 foods
~~Eggs~~

9 cohort & case-control studies

3 studies reported doses

Lignans
Citrus Fruit

Mushrooms
Fiber
Folate
Carotenoids

Vegetables
Vitamin D
Red/Processed Meat
High GI Foods
Soy Isoflavones

~~**Eggs**~~
~~**Calcium**~~

Fruit

Study Characteristics

9 meta-analyses, 2 prospective cohorts, 1 case-contorl

Author	Type of Study	Studies Included/sample size (if applicable)	Food/Nutrient
Aune et al, 2012	Meta-analysis	16 cohort studies	Fiber
Chen et al, 2014	Meta-analysis	16 cohort studies, 23 case-control studies	Folate
Guo et al, 2015	Meta-analysis	14 cohort/nest-case control studies	Red & Processed Meat
Hu et al, 2012	Meta-analysis	6 cohort studies, 6 case control studies	Carotenoids
Li et al, 2014	Meta-analysis	2 cohort, 8 case-control studies	Mushrooms
Malin et al, 2003	Case-Control	1459 cases	Citrus Fruit
Suzuki et al, 2008	Prospective cohort	51823 participants	Lignans
Touillaud et al, 2007	Prospective cohort	58049 participants	
Kazemi et al, 2021	Meta-analysis	14 cohort studies	Vegetables and Fruits
Schlesinger et al, 2017	Meta-analysis	19 cohort studies	Glycemic Index
Hossain et al, 2019	Meta-analysis	22 cohort studies	Vitamin D
Wei et al, 2020	Meta-analysis	9 cohort studies	Soy Isoflavones

Fruits & Vegetables

Kazemi et al, 2021

Meta-Analysis of
14 Cohort Studies

- 100 g/day

  ↓RR 3%

What does 100 g of fruits/veg look like?

½ Apple = 100 g

Banana = 120 g

¾ cup Blueberries = 113 g

1 ¼ cups broccoli = 100 g

1/2 cup cooked spinach = 90 g

1.5 carrots = 91 g

Mushrooms

Li et al, 2014

Meta-Analysis

2 Cohort + 8 Case-Control Studi

- 1 g/day ↓RR 3%

Mushrooms

Li et al, 2014

Meta-Analysis

2 Cohort + 8 Case-Control Studi

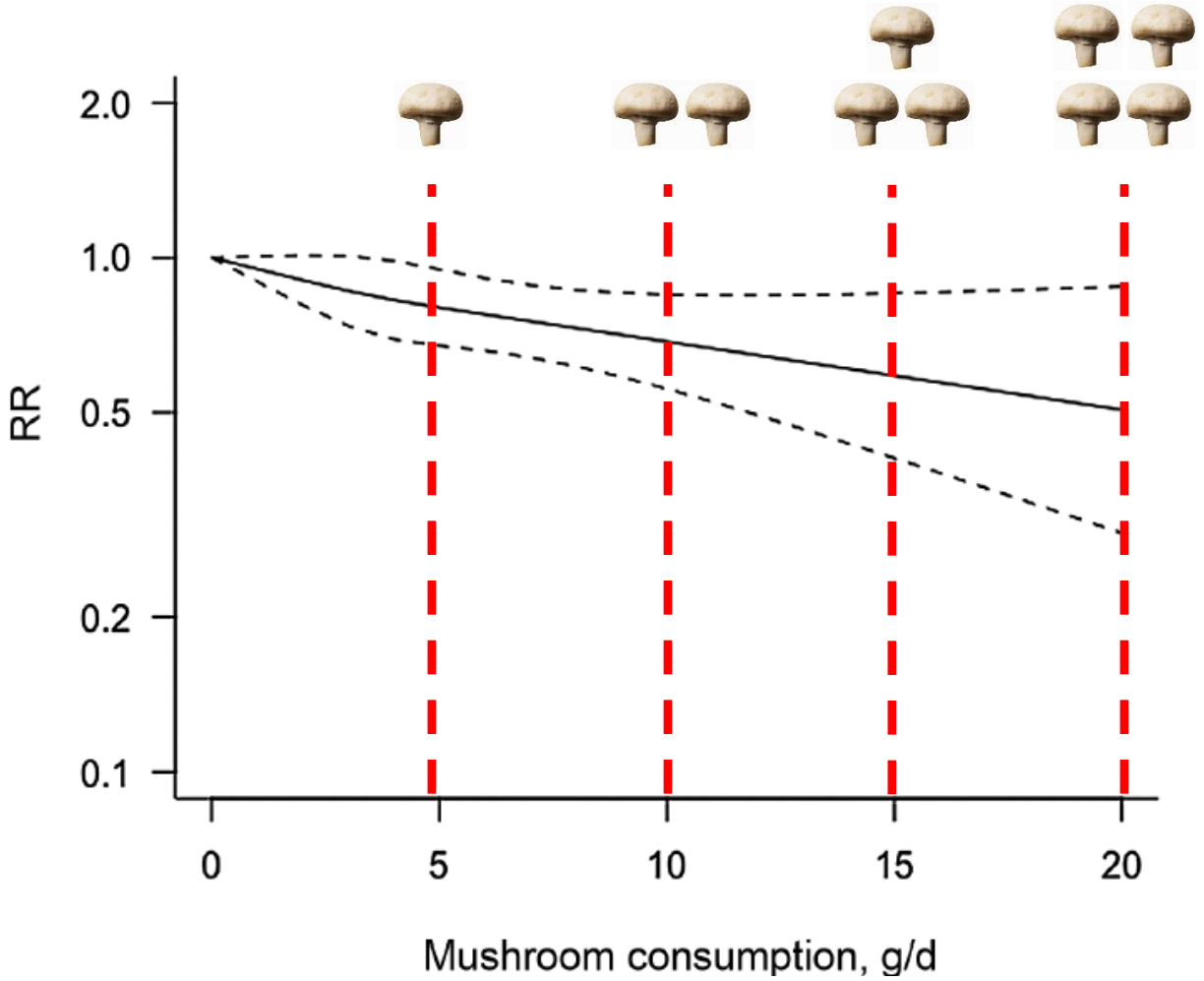
- 1 g/day ↓RR 3%

1 mushroom

=

5 g

Dose Response:
Mushrooms & Breast Cancer
Li et al, 2014



*logarithmic scale

Dietary Folate =Vitamin B9

Chen et al, 2014

Meta-Analysis
16 Cohort Studies +
23 Case-Control Studies

- 100 ug/day

↓RR 5%

Dietary Folate =Vitamin B9

Chen et al, 2014

Meta-Analysis
16 Cohort Studies +
23 Case-Control Studies

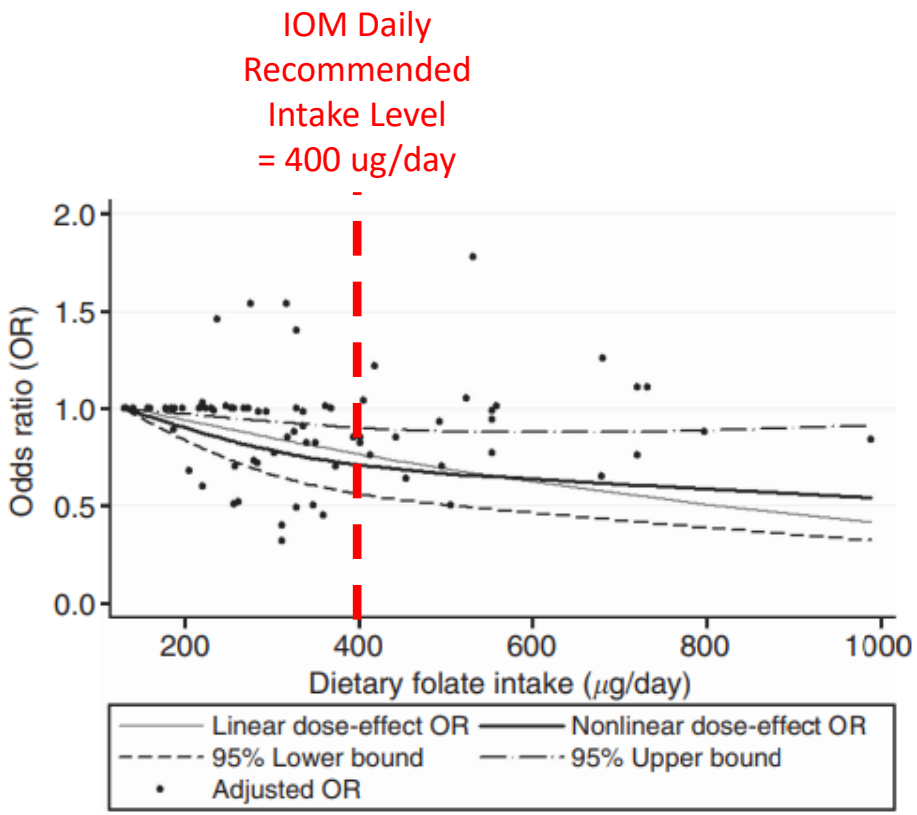
- 100 ug/day

↓RR 5%

½ cup beans
= >100 ug

2 cups of raw dark green leafy veg or ½ cup if cooked = >100 ug

Dose Response:
Dietary Folate & Breast Cancer
Chen et al, 2014



Fiber

Aune et al, 2012

Meta-Analysis
16 Cohort Studies

- 10 g/day

↓RR 5%

Fiber

Aune et al, 2012

Meta-Analysis

16 Cohort Studies

- 10 g/day

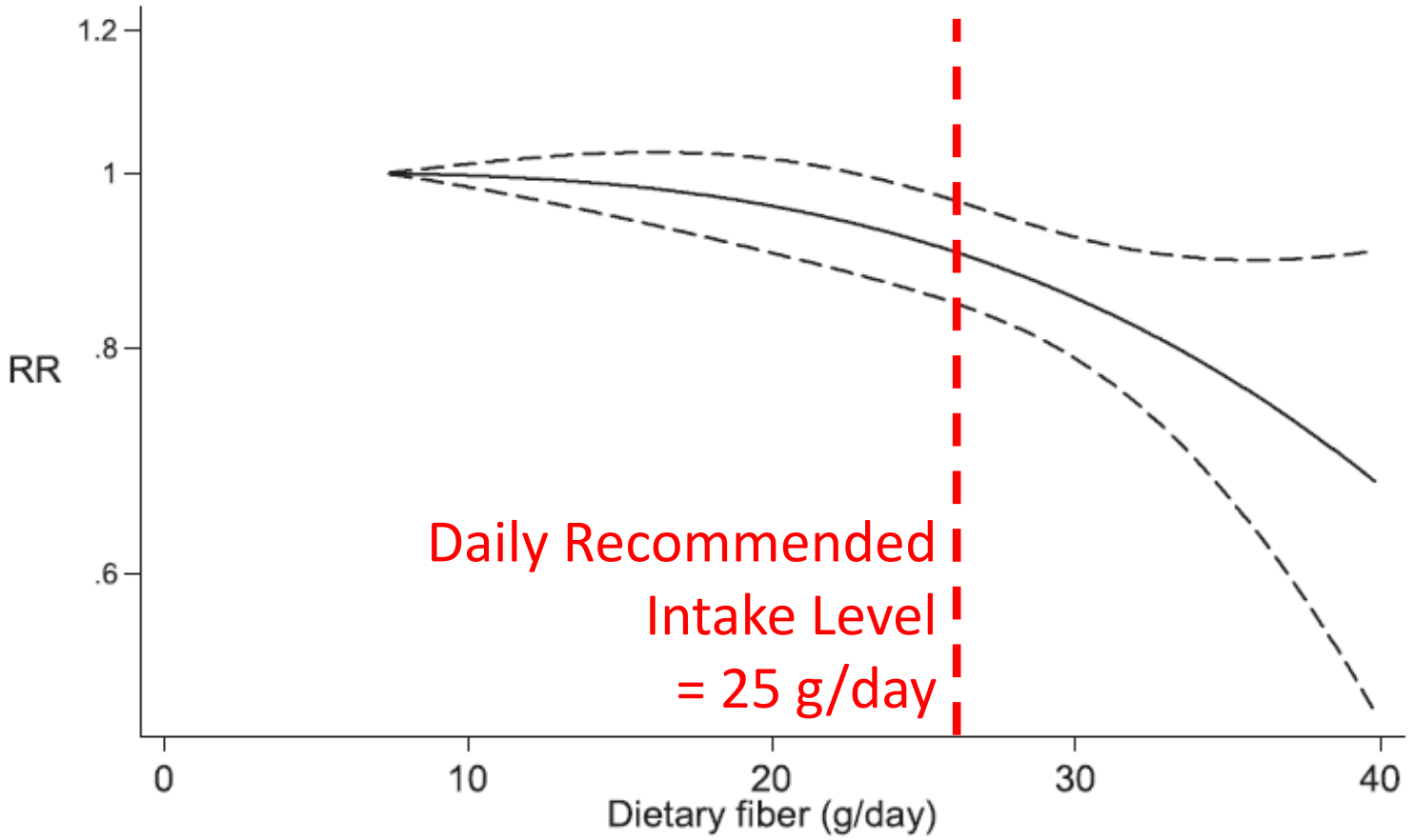
↓RR 5%

½ cup beans = 10 g

Apple + Pear = 10.5 g

¾ cup Pistachios = 9.75 g

Dose Response:
Fiber & Breast Cancer
Aune et al, 2012



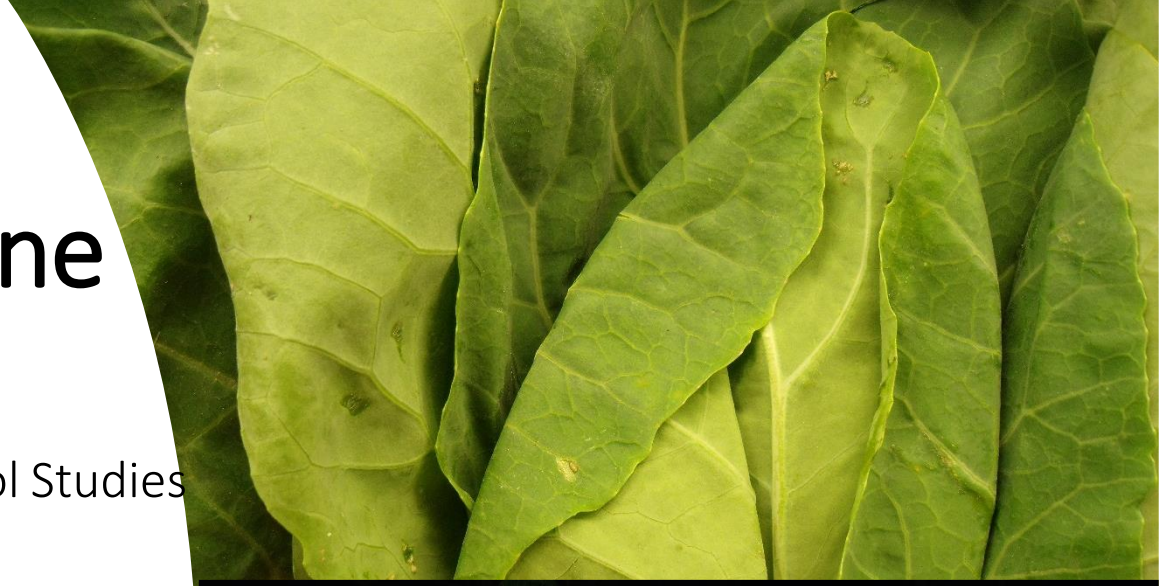
Beta-Carotene

Hu et al, 2012

Meta-Analysis

6 Cohort + 6 Case-Control Studies

- 5 mg/day ↓RR 7%



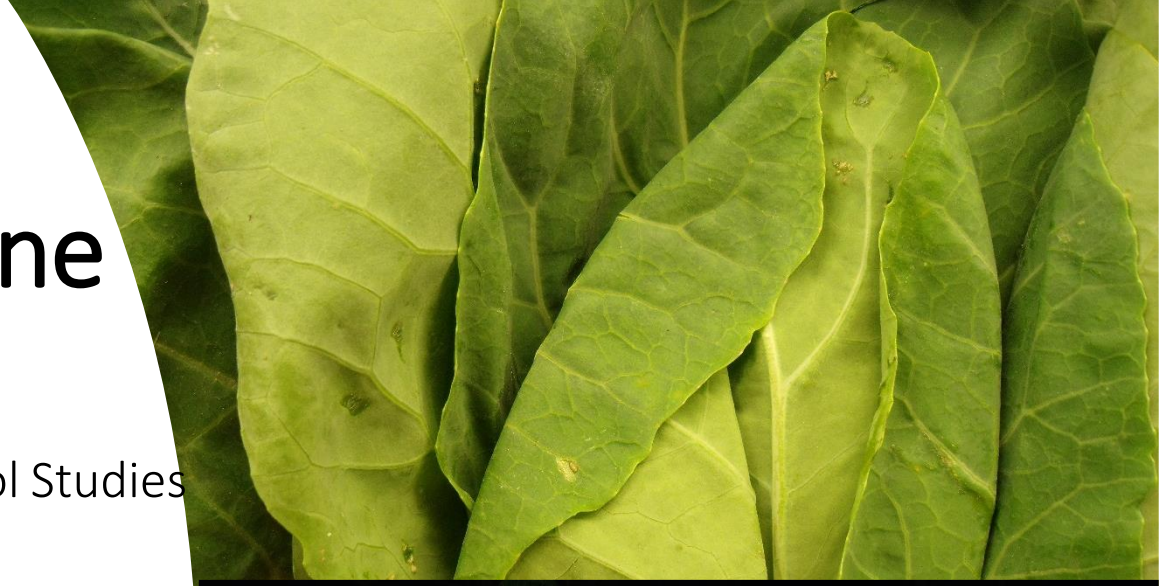
No dose response graph was reported

Beta-Carotene

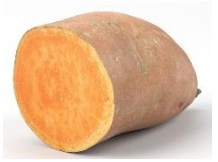
Hu et al, 2012

Meta-Analysis

6 Cohort + 6 Case-Control Studies



- 5 mg/day ↓RR 7%



<½ Sweet Potato= 7 mg

<½ cup raw leafy green vegetables = 5.5 mg

No dose response graph was reported

Lignans = a type of phytoestrogen

Suzuki et al 2008 & Touillard et al 2007

Cohort Studies

- 1.2 mg/day

OR 0.85

No dose response graph was reported

Lignans = a type of phytoestrogen

Suzuki et al 2008 & Touillard et al 2007

Cohort Studies

- 1.2 mg/day

OR 0.85

1 tbsp crushed flaxseeds = 30 mg lignans

No dose response graph was reported

Soy Isoflavones =

a type of phytoestrogen

Wei et al, 2020

Meta-Analysis

9 Cohort Studies

- 10 mg/day

↓RR 3%

Soy Isoflavones =

a type of phytoestrogen

Wei et al, 2020

Meta-Analysis

9 Cohort Studies

- 10 mg/day

↓RR 3%

1/8 cup soybeans
= 10 mg

½ cup edamame
= 16 mg

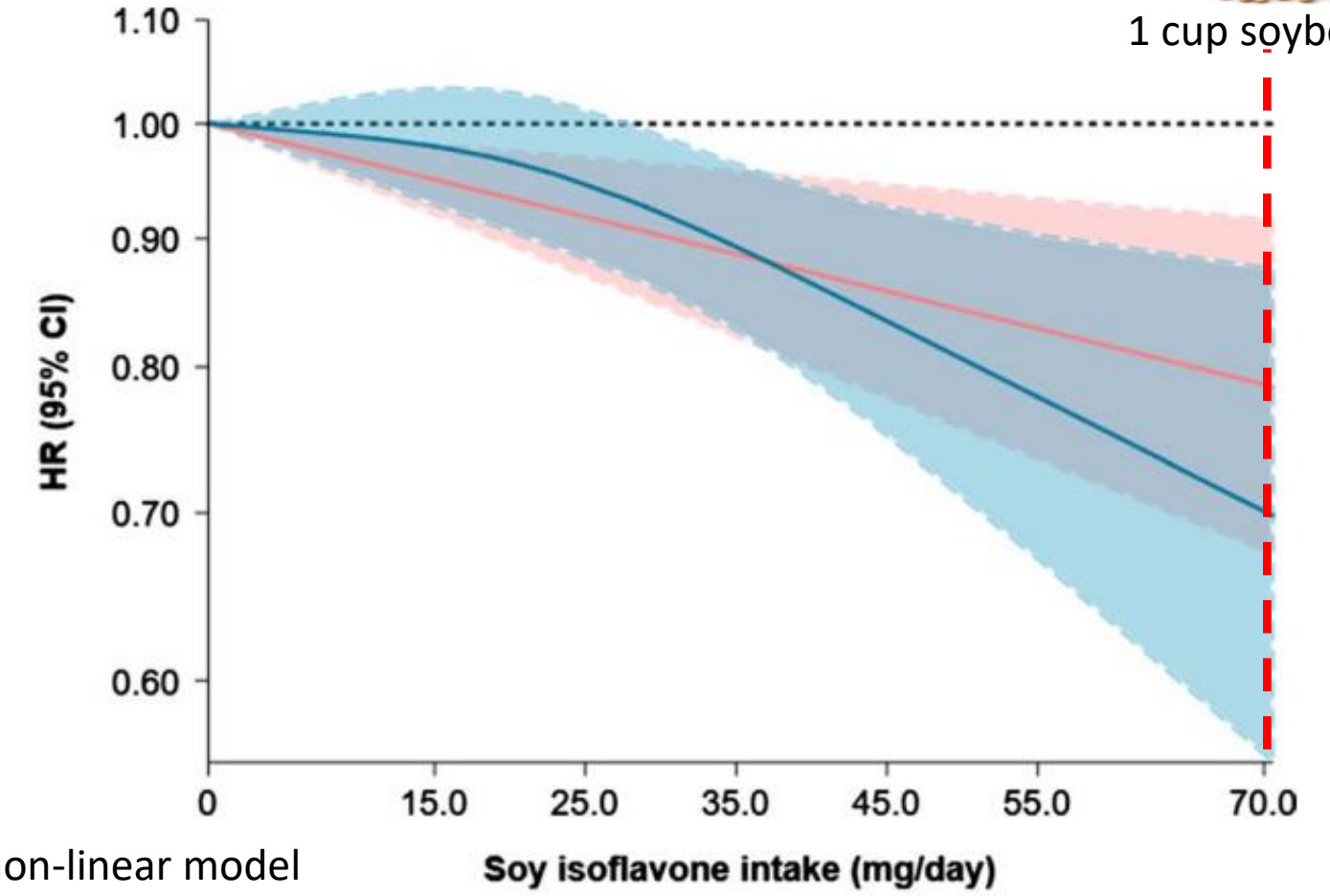
~1/4 cup tofu
= 10 mg

Dose Response:

Soy Isoflavones & Breast Cancer

Wei et al, 2020

1 cup soybeans



Blue = non-linear model

Red = linear model

Relative Risk Comparison

Beta-Carotene — 7% RR↓

Folate

Fiber

5% RR ↓

Fruits

Vegetables

Mushrooms

Soy Isoflavones

3% RR ↓

Vitamin D — 1% RR ↓

Lignans exempt due to odds ratio (vs RR) reported

Relative Risk Comparison

<½ cup sweet potato
< ½ cup leafy greens

Beta-Carotene — **7% RR↓**

½ cup beans

Folate

Fiber

5% RR ↓

½ apple

Fruits

½ cup spinach

Vegetables

1/5 of a mushroom

Mushrooms

3% RR ↓

<¼ cup soybeans

Soy Isoflavones

100 IU

Vitamin D — **1% RR ↓**

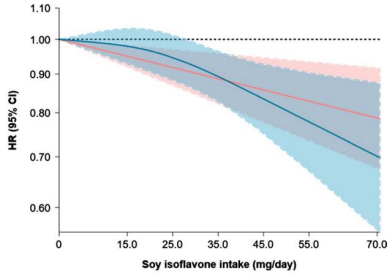
Lignans exempt due to odds ratio (vs RR) reported

Maximal risk reduction?

Beta-carotene, lignans, vitamin D did not provide dose-response graphs

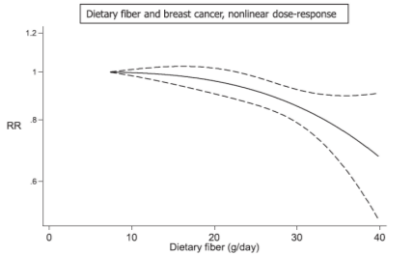
Mushrooms
4 mushrooms/day

45% RR↓

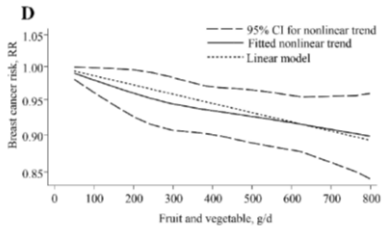


Soy Isoflavones
>1 cup/day soybeans

30% RR↓



Fiber
2 cups beans/day



F&V
8 servings/day

10% RR↓

Foods the Increase Risk for Breast Cancer

Red Meat

Processed Meat

9% RR ↑

High Gl Foods

4% RR ↑

Knowledge Translation Product

Nutrition & Breast Cancer

Nutrition is only one of many factors that can influence risk for breast cancer. Nevertheless, numerous studies have demonstrated that certain foods/nutrients are associated with increased or decreased risk.

Foods that DECREASE risk for Breast Cancer

Mushrooms[1]
As little as one mushroom per day makes a difference, and more is better

Crushed Flaxseed[2,3]
1-4 tablespoons per day

Vegetables & Fruits[4]
Aim for 7-10 servings per day

Nutrients that DECREASE risk for Breast Cancer

Beta-Carotene[5] - aim for 5 mg per day, examples include:
-<½ of a sweet potato
-½ cup cooked spinach
-½ cup cooked carrots
-½ cup raw green leafy vegetables
-1 cup squash/pumpkin

Soy Isoflavones[7] - aim for 10 mg per day, examples include:
-<⅛ cup mature (beige) soybeans
-<½ cup edamame
-¼ cup tofu/tempeh

Folate[8] - aim for 400 ug per day
-Lentils [180 ug/½ cup]
-Beans [150 ug/½ cup]
-Asparagus [134 ug/½ cup]
-Cooked spinach [131 ug/½ cup]

Fiber[6] - aim for at least 25 grams per day
-Beans [15g/cup]
-Oats [8g/cup]
-Nuts [6g/half cup]
-Avocado [9g]
-Pear [5.5g]
-Apple [4g]

Vitamin D[9]
-1000-2000 IU of supplemental Vit D per day

Foods That INCREASE Risk for Breast Cancer

Red Meat[10]
-Beef
-Pork
-Veal
-Lamb
-Goat

Processed Meat[10]
-Deli meats
-Hot dogs
-Canned meats

Sugar[11]
-Baked Goods
-Candy
-Desserts
-Processed cereals

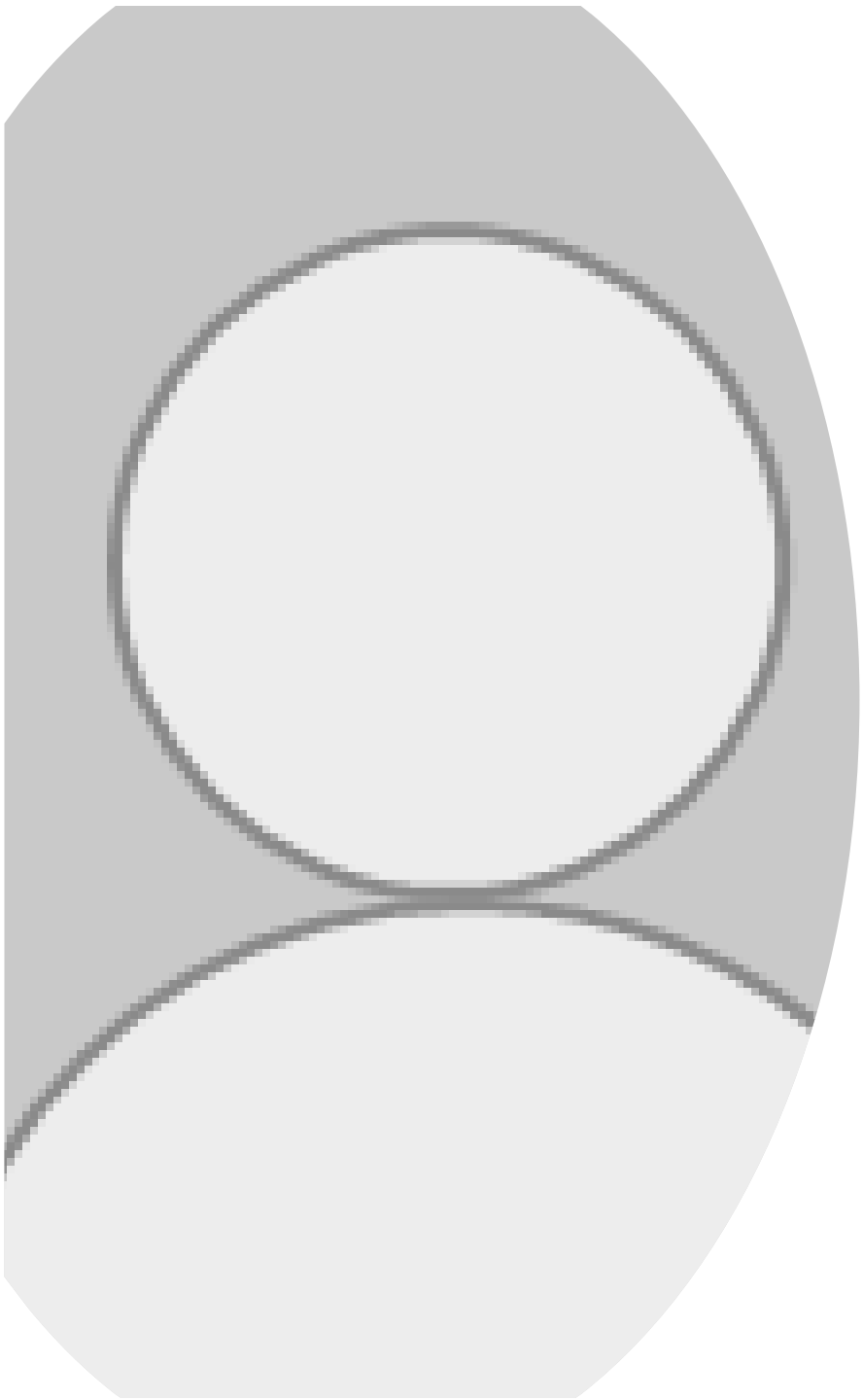
Refined Carbs[11]
-White bread
-White Rice
-Jasmine, Arborio & Sticky rice
-Crackers
-Bagels

Alcohol[12]
Very light drinking (less than half of a standard drink per day) can increase risk for breast cancer

www.**nutrition-prescriptions**.com
Resident Academic Project Created By: Dr. Mary Sco. & Dr. Melinda Wu ©2023

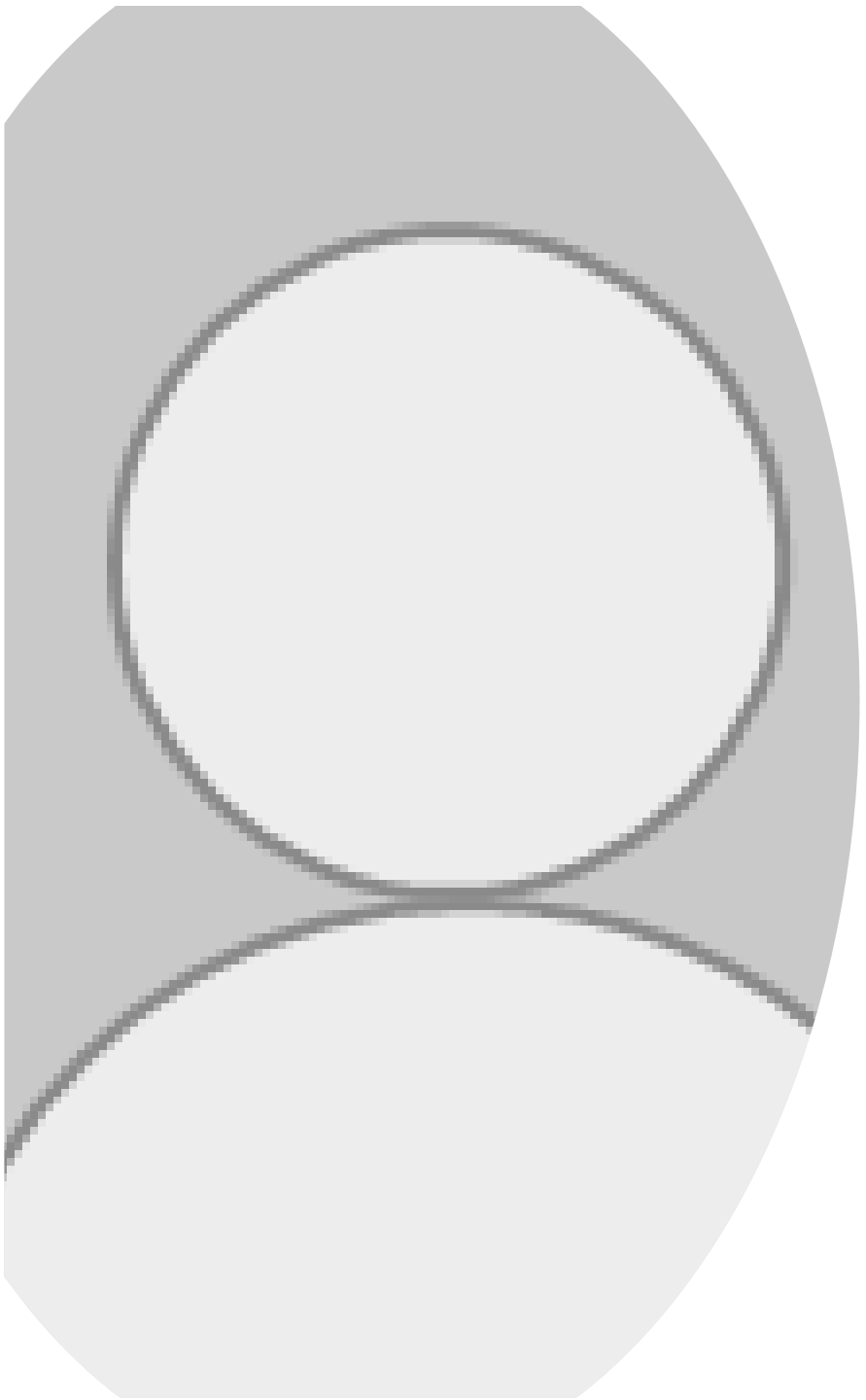
1-Li, PloS one, 2014; 2-Suzuki, Br J Cancer, 2008; 3-Thompson, Clin Cancer Res, 2005; 4-Kazemi, Adv Nutr, 2021; 5-Hu, Breast Cancer Res Treat, 2012; 6-Aune, Ann Oncol, 2012; 7-Wei, Eur J epidemiol, 2020; 8-Chen, Br J Cancer, 2014; 9-Hossain, Clin Nutr ESPEN, 2019; 10-Guo, Breast Cancer Res Treat, 2105; 11-Schlesinger, Nutr Rev, 2017; 12-Choi, Can Res Treat, 2018.

Available From: www.**nutrition-prescriptions**.com



Limitations

- **Observational data (cohort & case-control studies)**
  - Self-reported data/recall bias
  - Dietary assessment inaccuracies
- **Association ≠ causation**
  - Impossible to do a 30 year RCT (CIHR cannot afford this!)
- **Breast Cancer is not one entity**
  - Pre versus post menopausal
  - ER+/-, PR+/-, HER2+/-, inflammatory
- **Additive effects for maximal risk reduction??**
- **Primary Prevention vs Secondary Prevention**



Conclusion

- Meta-analyses demonstrate that a large number of foods & nutrients are associated with increased/decreased risk for breast cancer

- Quantities associated with decreased/increased risk were consistent with reasonable/standard portions that can easily recommended to patients