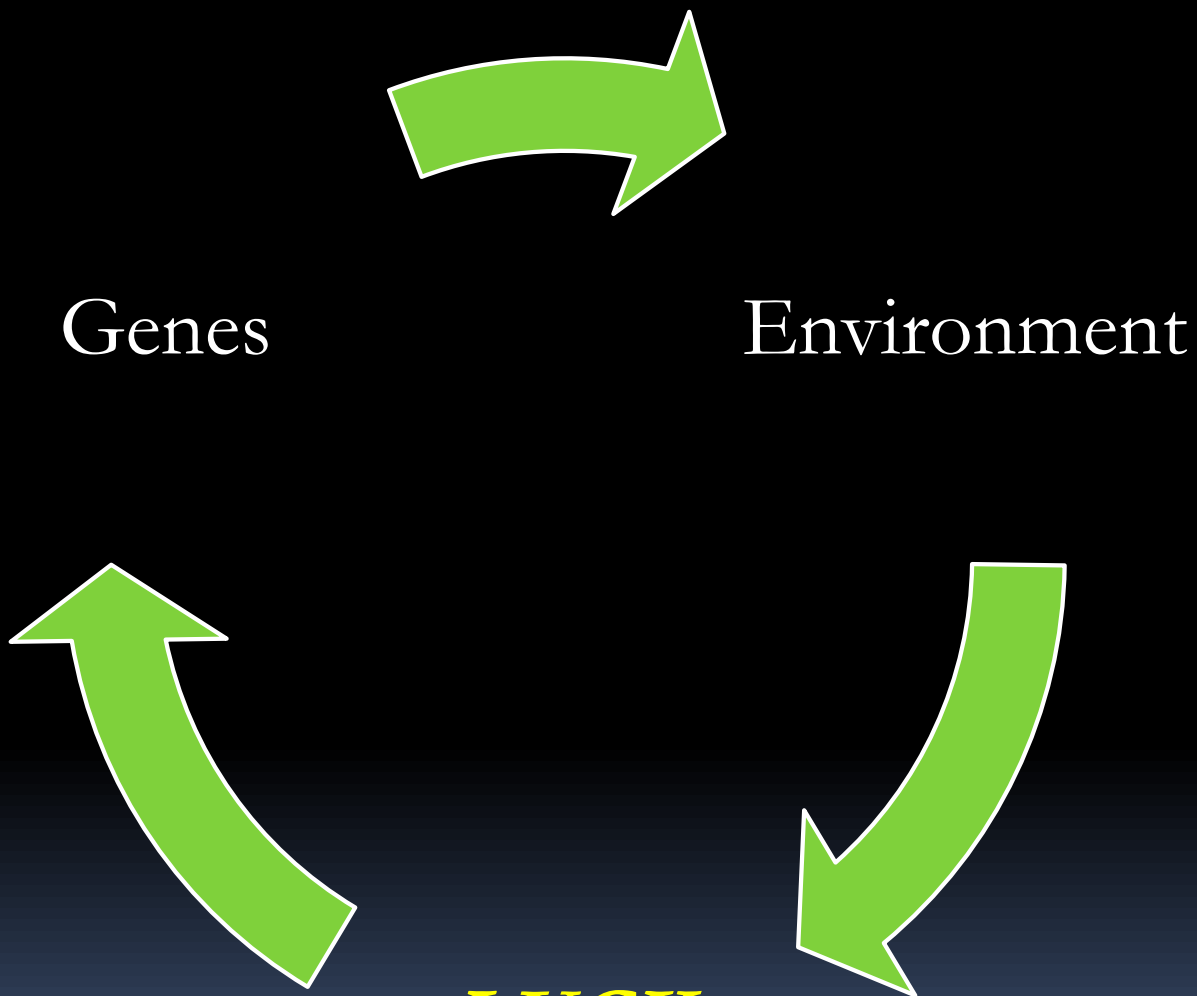
NUTRITION, LIFESTYLE & CANCER SURVIVAL

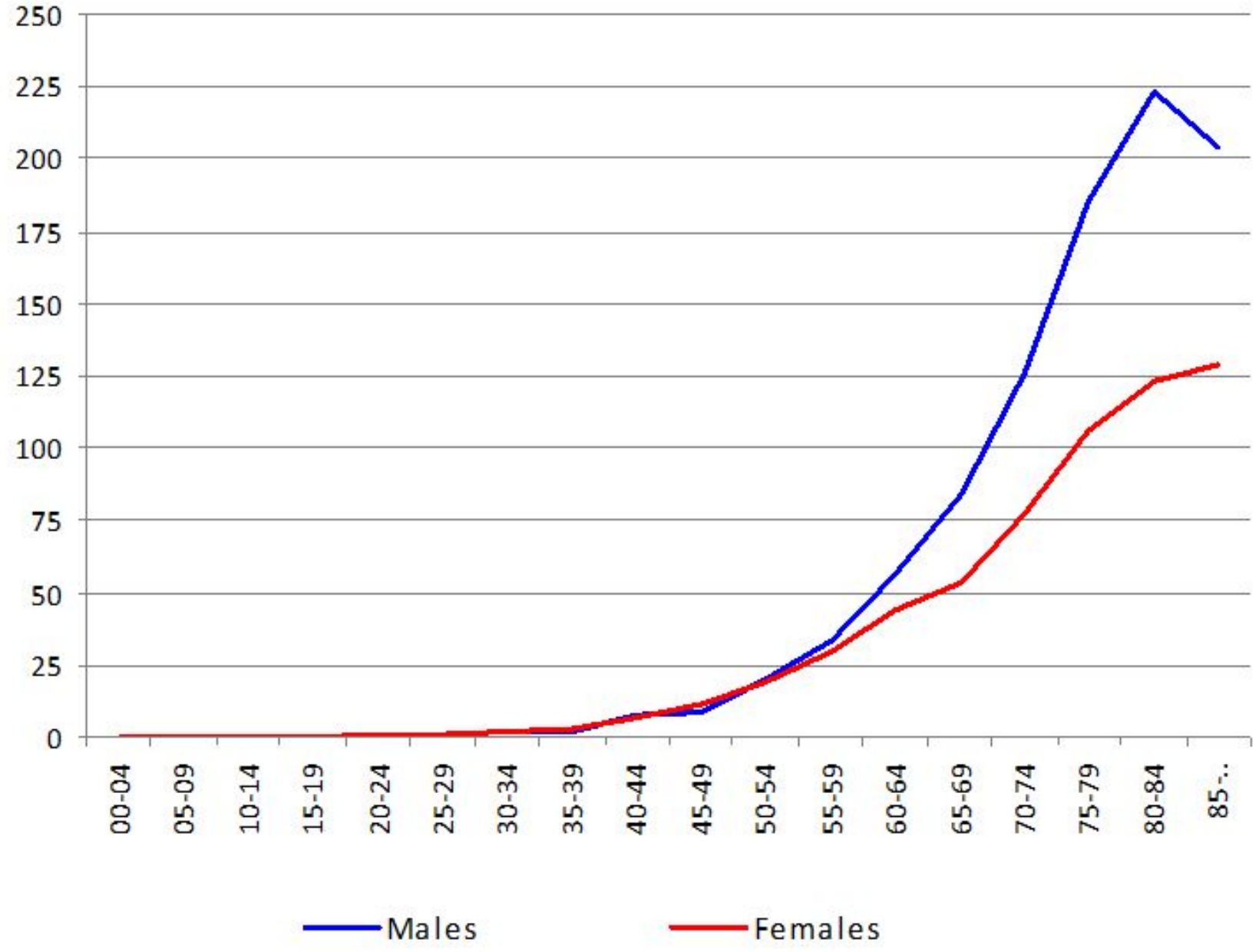
THE HEART OF INTEGRATIVE CANCER CARE

D. Barry Boyd, M.D., M.S.

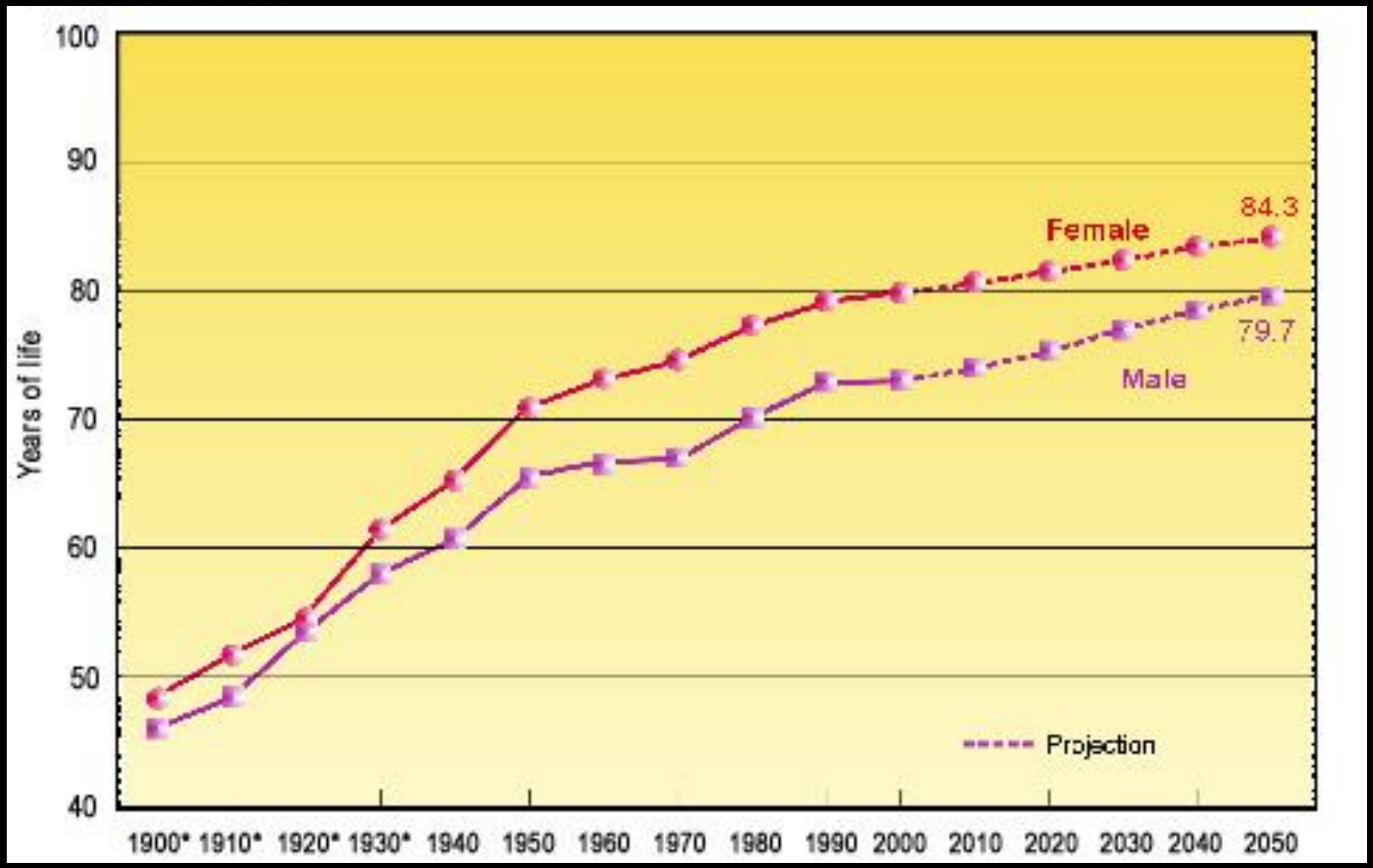
WHY DO WE GET CANCER?



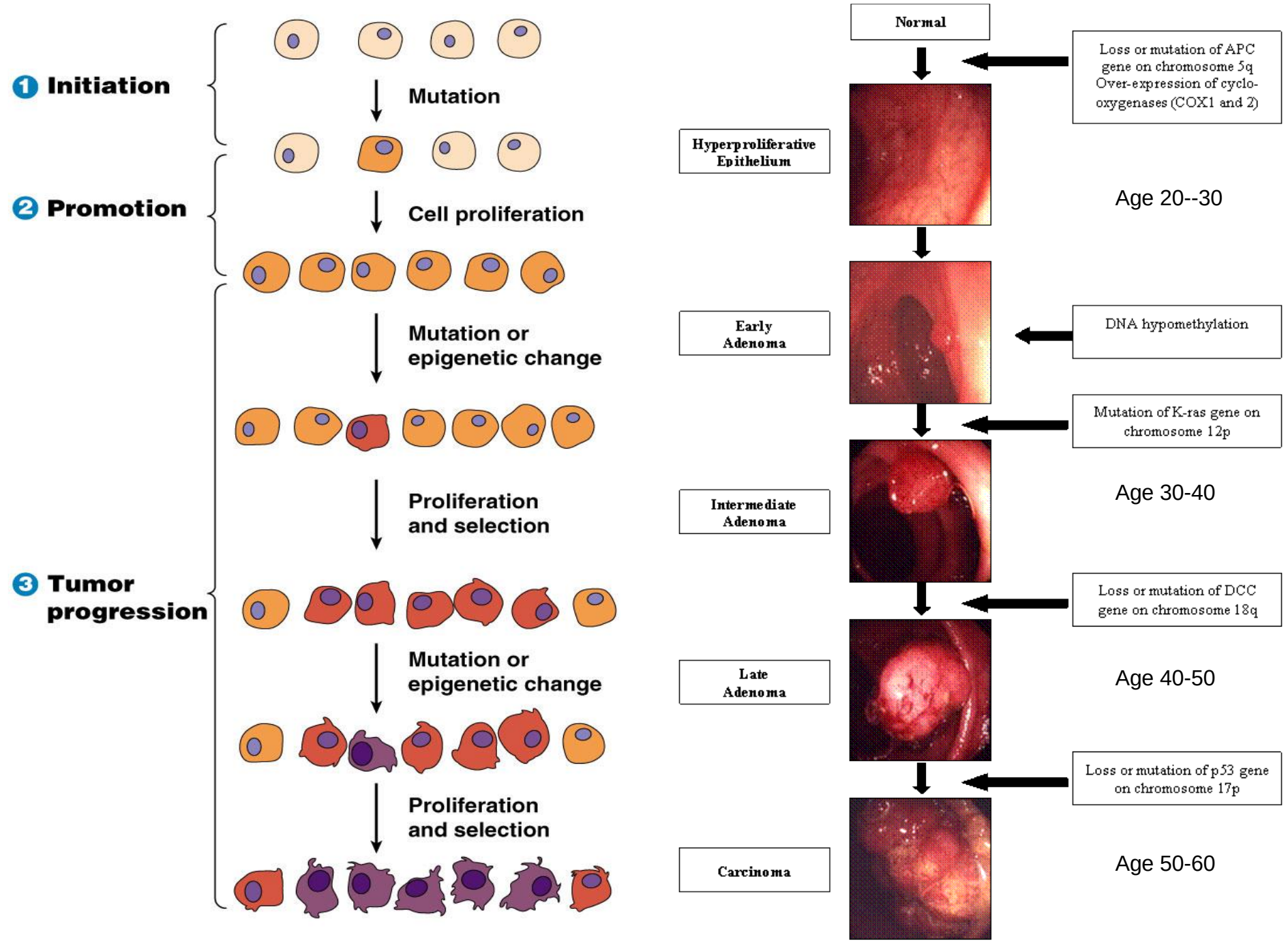
Cancer Incidence (per 100,000) by Age



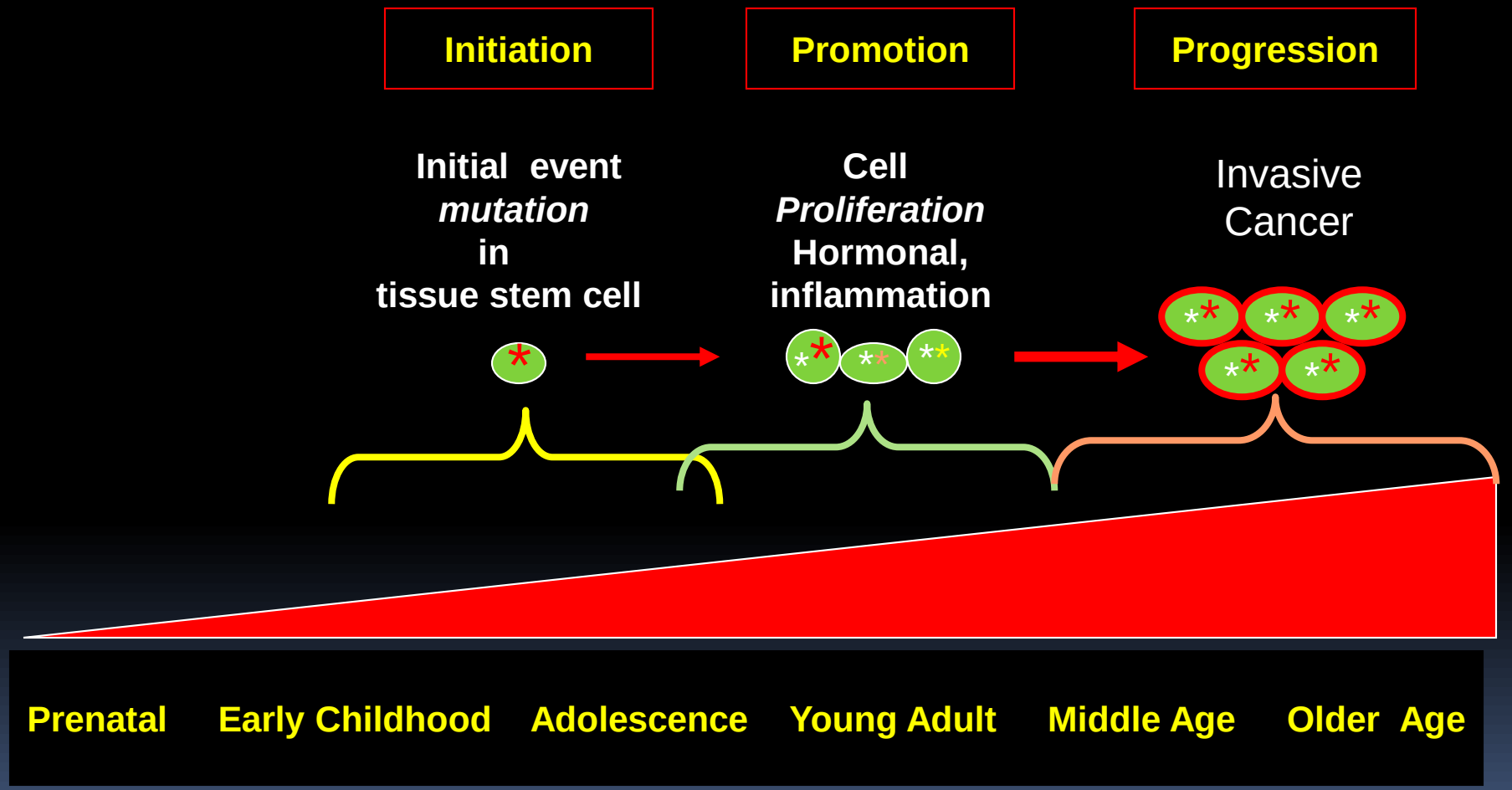
Life Expectancy, by Year of Birth



Multistage Carcinogenesis- Colorectal Cancer (B Vogelstein)



Evolution of Adult Cancer

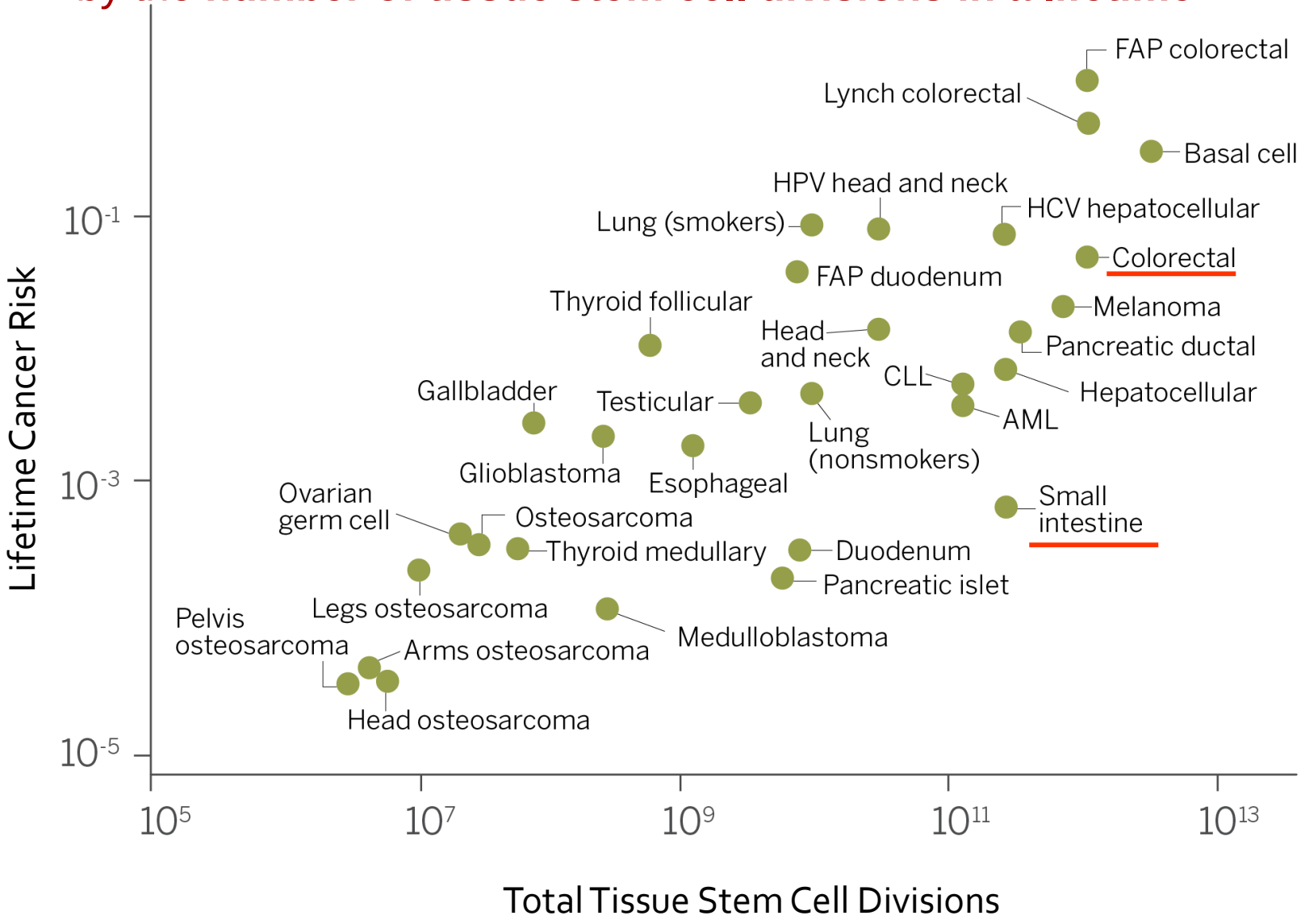


The New York Times

JAN. 19, 2015

Random Chance's Role in Cancer

Variation in **cancer risk** among tissues can be explained by the **number of tissue stem cell divisions in a lifetime**



C Tomasetti B Vogelstein. Variation in cancer risk among tissues can be explained by the number of stem cell divisions Science 347;(6217):78-81, 2015

Variation in **cancer risk** among tissues can be explained by the **number of tissue stem cell divisions in a lifetime**

FAP colorectal

*The majority (65%) is **due to "bad luck,"** that is, **random mutations** arising during DNA replication"*

C. Tomasetti , B. Vogelstein

*"Lifetime risk of cancer strongly correlated (0.81) with the **total number of divisions of the normal self-renewing cells** maintaining that tissue's homeostasis"*

*"Only **a third** of the variation in cancer risk among tissues is attributable to **environmental** factors or **inherited** predispositions.*

If true, diet plays limited role in cancer risk and ?survival

How do we reconcile cancer biology and epidemiology

Total Tissue Stem Cell Divisions

C Tomasetti B Vogelstein. Variation in cancer risk among tissues can be explained by the number of stem cell divisions Science 347;(6217):78-81, 2015

Epidemiology of Cancer and Nutrition

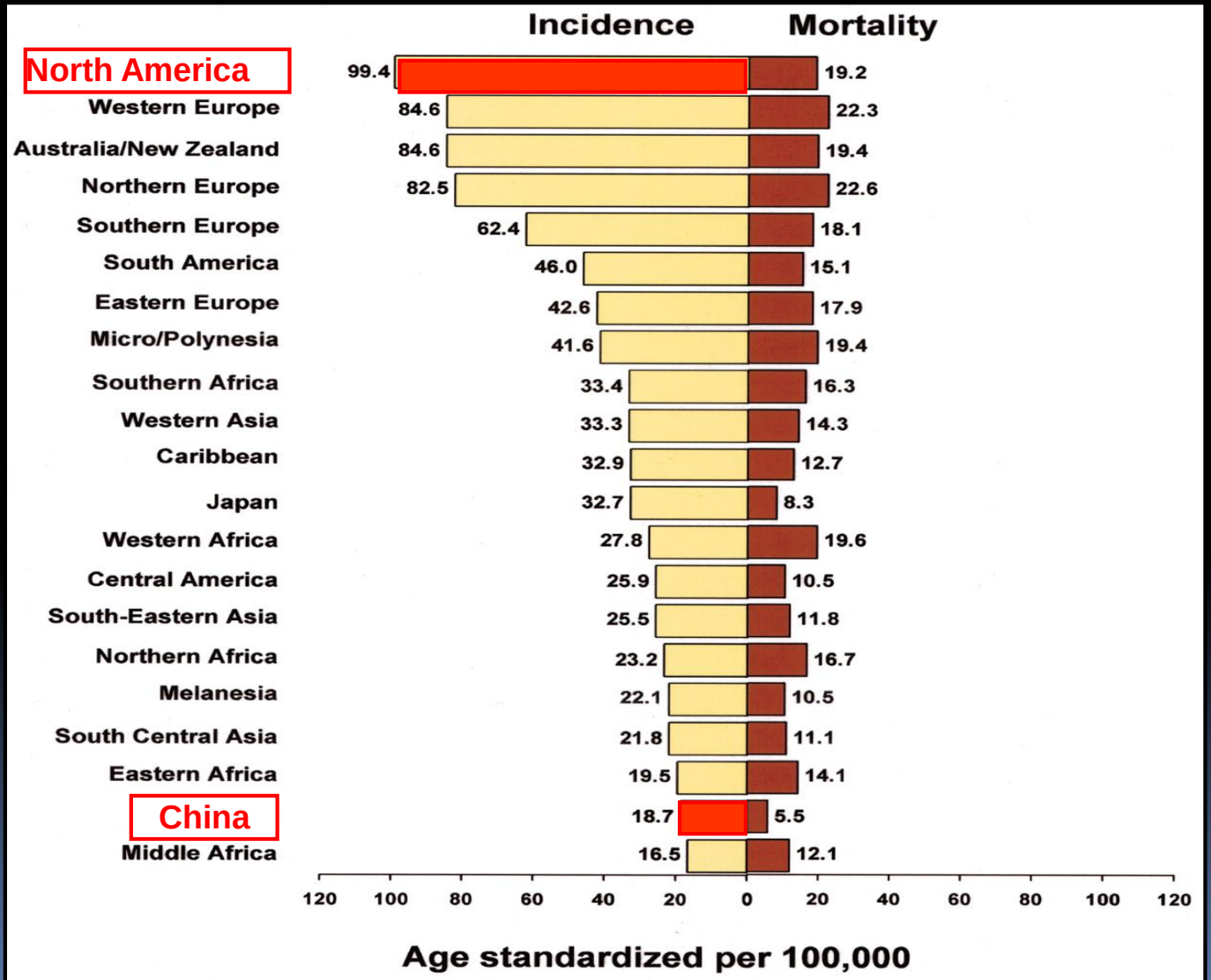
Causes of Cancer Deaths
(Doll & Peto)

INTRODUCTION

- EPIDEMIOLOGY
- **NUTRITION**
- SUPPLEMENTS
- SUMMARY

	1980	2000
Pollution	2%	2%
Geophysical	3%	3%
Smoking	30%	30%
Alcohol	3%	3%
Diet/ Lifestyle	35%	5%
Food Additives	1%	0
Reproductive/Sexual	7%	7%
Occupational	4%	4%

Age-Adjusted Rate - Breast Cancer



Age-Adjusted Rate - Prostate Cancer

- INTRODUCTION
- EPIDEMIOLOGY
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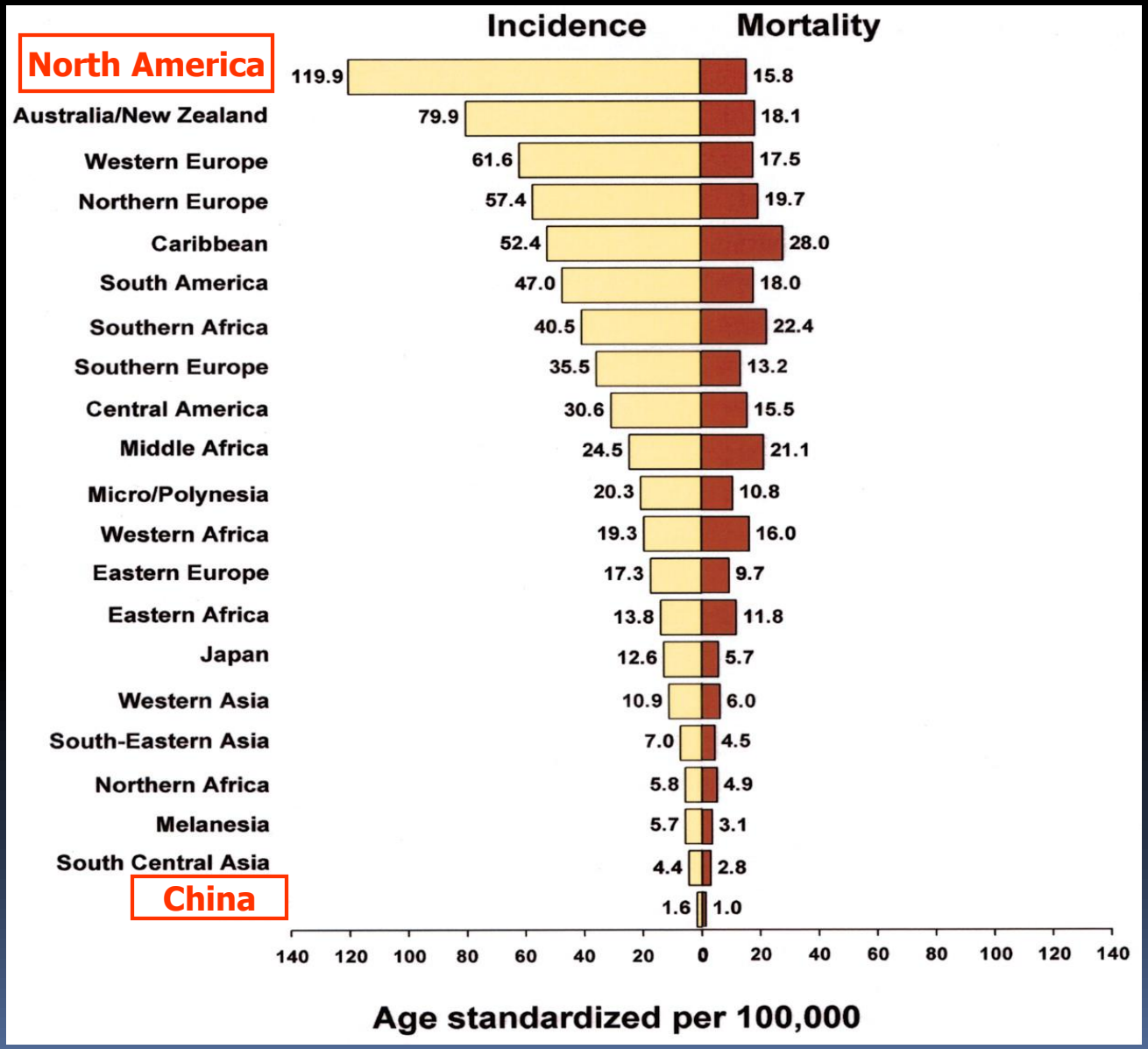
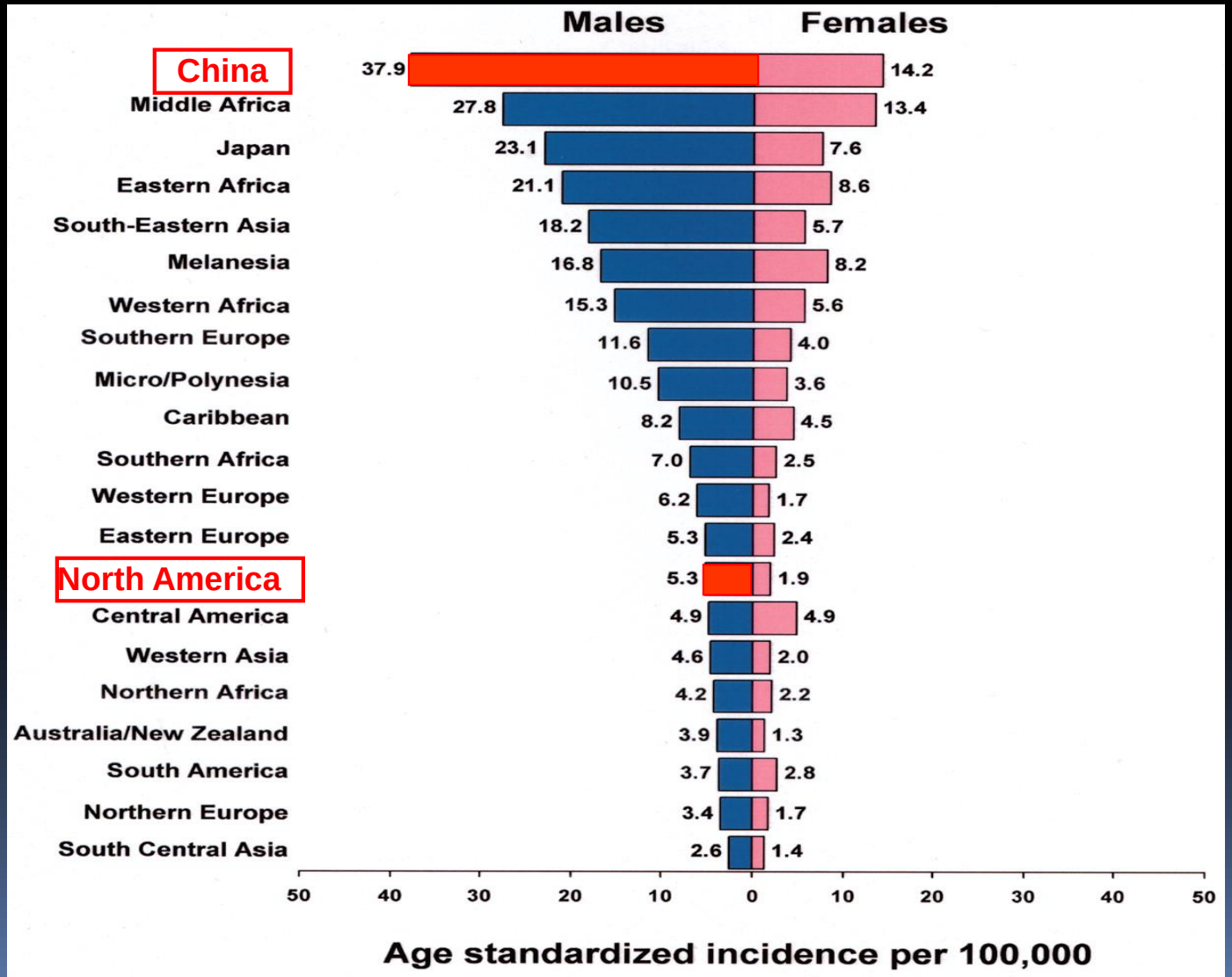


Age-Adjusted Rate - Hepatocellular Carcinoma



The Causes of Cancer: Quantitative Estimates of Avoidable Risks Of Cancer in the United States Today

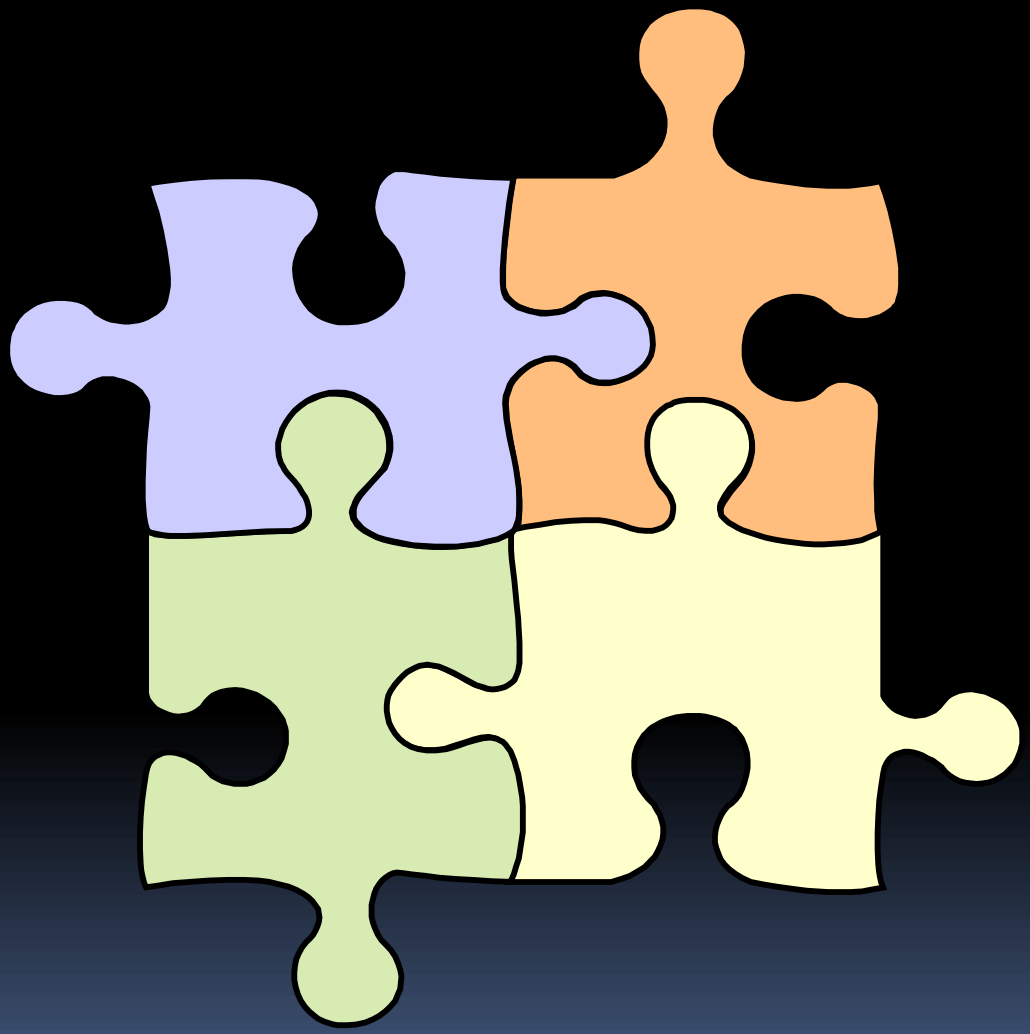
Richard Doll, Honorary Director, Imperial Cancer Research Fund Cancer Epidemiology and Clinical Trials Unit, and Warden of Green College, Oxford, United Kingdom

Richard Peto, Imperial Cancer Research Fund Reader In Cancer Studies, Nuffield Department of Clinical Medicine, University of Oxford, Radcliffe Infirmary, Oxford OX2 6HE, United Kingdom

J. Natl. Cancer Inst. 66:1191-1308, 1981.

"Diet probably plays a major role in controlling Between 1/3 and 2/3 of human cancers"

Nutrition, Lifestyle and Cancer



"Let food be thy medicine and medicine be thy food"

Hippocrates

"Let food be thy medicine and medicine be thy food"

"There are in fact two things, science and opinion; the former begets knowledge, the latter ignorance"

Hippocrates

Nutrition and Cancer

- Critical in cancer risk and *outcome*- *How?*
- Central concern of many cancer patients
- Conflicting messages
- MD's- limited knowledge, dismiss concerns Media- changing messages, no context
- Industry- Food / Supplement ($$$$)

  CAM / IM- Often non-science based
- Why the conflict ?
- Failure to "connect the dots"

  Biase- $$, Strongly held beliefs

  Like life, knowledge evolves

The Story of nutrition, lifestyle and cancer

Dietary & Nutrition Change

- 40-80 % of Cancer Patients seek Dietary Advice
- Highly Motivated for change
- Goal – Improve QOL & Disease Outcome
- Highly Vulnerable

  "I'll do whatever it takes"
- High % utilize Supplements/ Nutriceutical

Dietary Factors

- Overall diet vs. individual nutrients and constituents

  Meal size and frequency

  Nutrient synergy

  Role of Dietary Pattern

- Interaction with Dietary-related Factors:

  Obesity/ body mass index (BMI)

  Physical activity

  Genetic differences (nutrigenomics)

  individual/ population

- Non-food contaminants –*1st Paradigm*

  Dietary and Food borne Carcinogens (1970-80"s)

Nutrition and Cancer – Myths & Perceptions

- **Magic Foods**

  Confusing phytonutrient research vs cancer survival

- **Good Food vs. Bad Food**

  Green tea is good, Coffee is bad

- **Sugar "*Feeds Cancer*"**

  Mistaking diet and metabolism

  ie. Warburg Effect / PET Scan

  Fructose vs glucose (IR, wt gain, tumor proliferation)

- **An "*Alkaline Diet*" can inhibit cancer growth**
- **The "*Right Diet* " can inhibit my cancer and prevent future cancer**
- **Dietary supplements are natural, safe and an critical part of a "cancer survival plan"**

  "Nutritional Insurance"

Dietary Fat vs. Breast Cancer

INTRODUCTION

- **EPIDEMIOLOGY**
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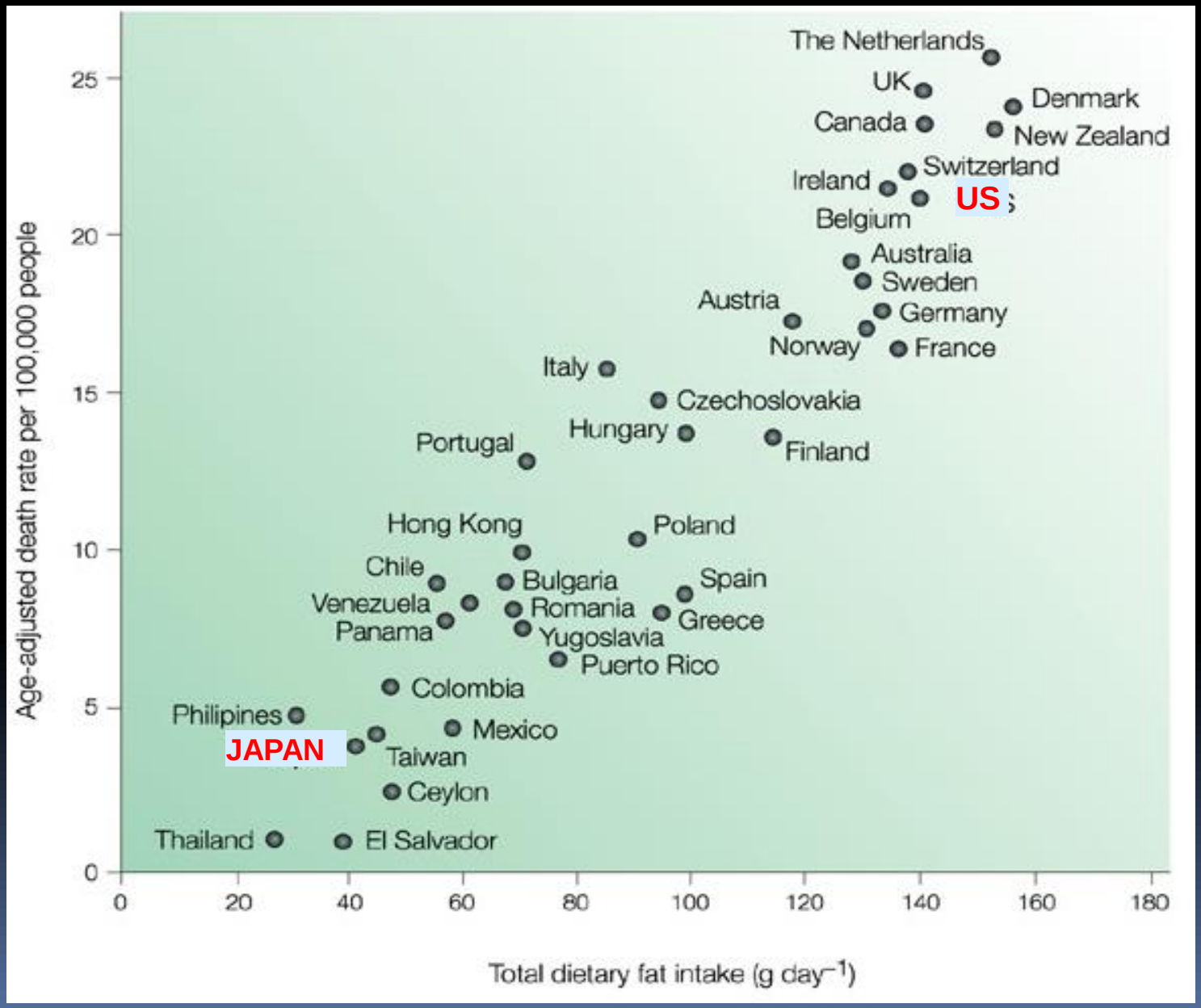

It must be the fat !

2nd Paradigm - 1980's to early 1990's

Dietary fat % is not associated with Breast Cancer Risk ?

INTRODUCTION

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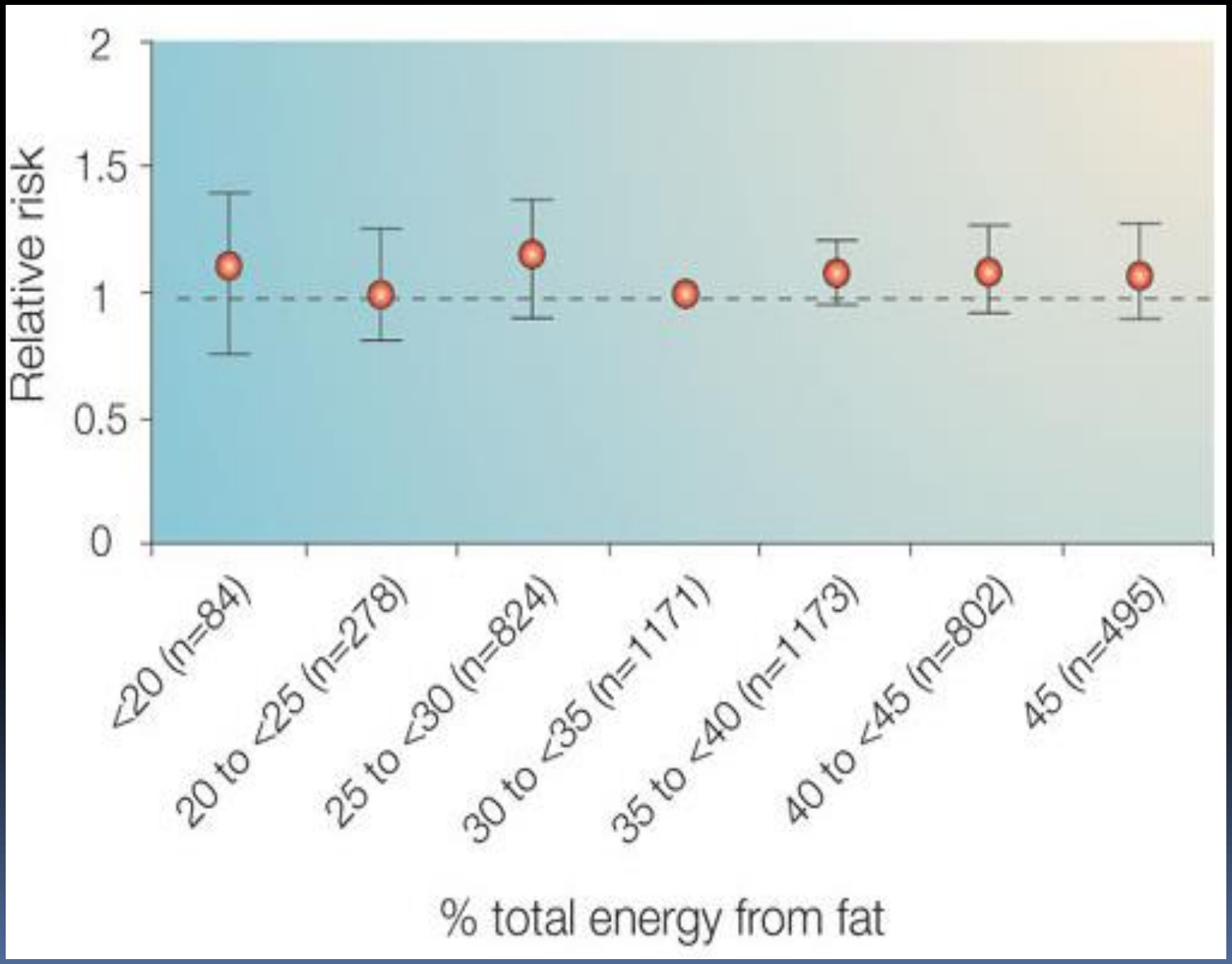
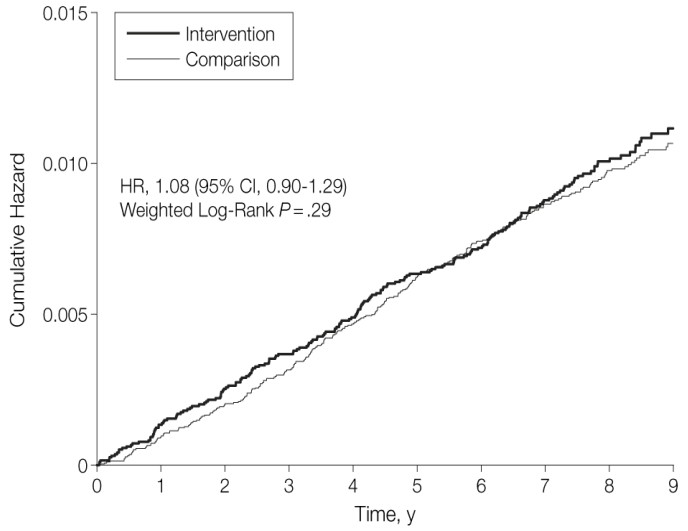


WHI – Low Dietary Fat Intervention Trials

Decreased Dietary Fat ***does not reduce*** Breast or CRC Risk

Colorectal Cancer Risk

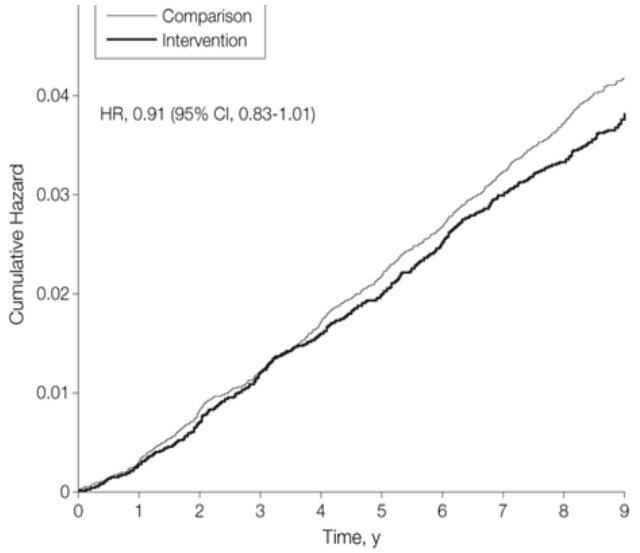


No. of Events									
Intervention	26	23	22	23	27	16	28	18	9
Comparison	27	32	32	43	44	33	33	22	11

No. at Risk										
Intervention	19541	19402	19218	19004	18784	18576	18290	15909	10507	5260
Comparison	29294	29070	28806	28554	28259	27916	27622	23991	15806	7913

Hazard Ratio Estimates for Colorectal Cancer Based on Cumulative Data Through Each Follow-up Year

Breast Cancer Risk

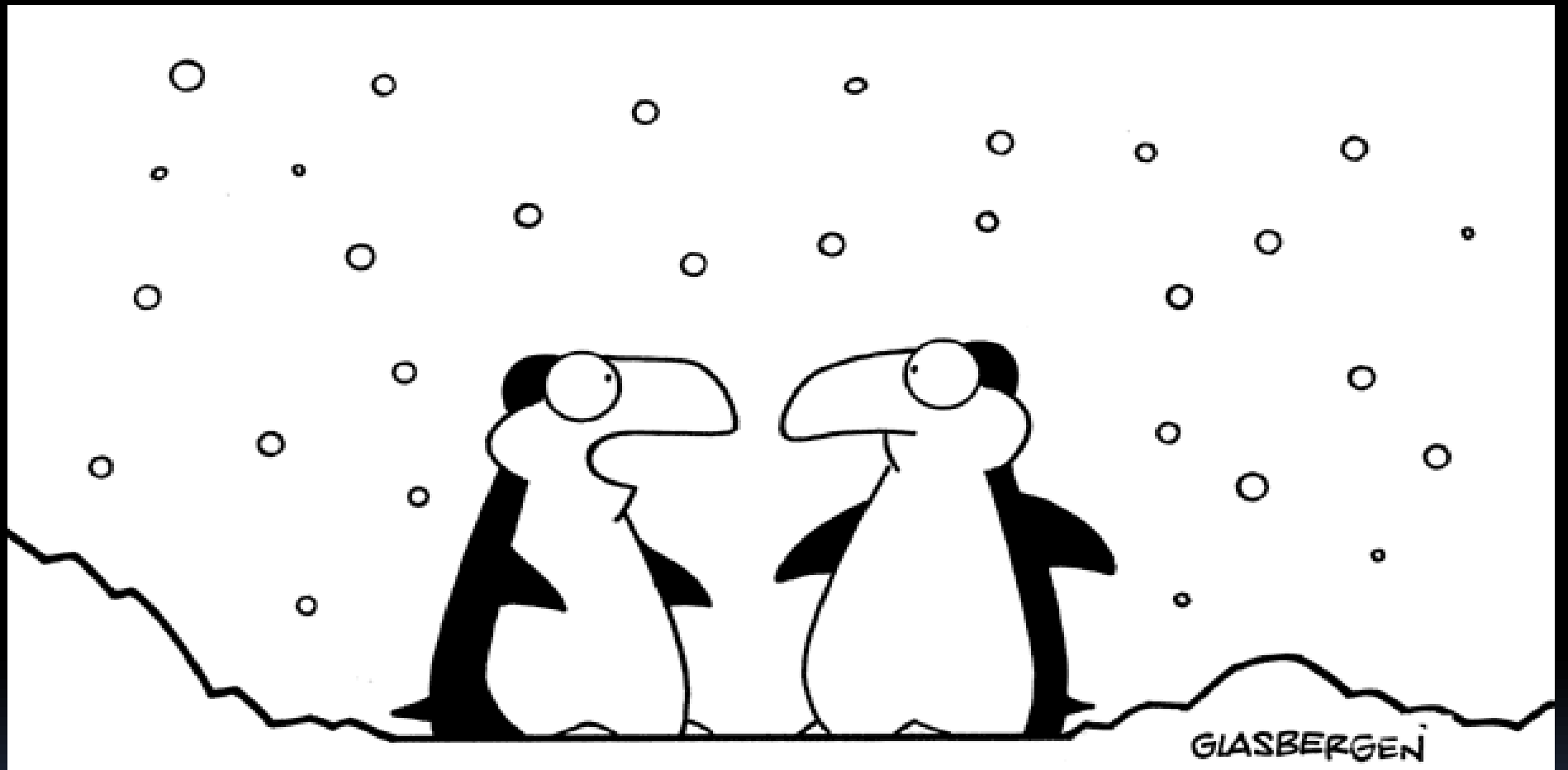


Events									
Intervention	47	79	92	80	72	94	89	46	33
Comparison	74	140	123	137	136	137	145	97	58

No. at Risk										
Intervention	19541	19328	19084	18798	18520	18263	17900	15507	10245	5075
Comparison	29294	28908	28536	28195	27806	27372	26977	23337	15373	7580

Hazard Ratio Estimates for Invasive Breast Cancer Based on Cumulative Data Through Each Follow-up Year

Much Confusion Exists



"Low fat diets don't work. I eat fish every day and my butt still drags on the ground!"

Fruit, vegetables, and cancer prevention: a review of the epidemiological evidence

Block G, Patterson, S et al.
Dept. of Social and Administrative Health Sciences, School of Public Health, University of California, Berkeley 94720.
Nutr Cancer. 1992;18(1):1-29.

Abstract

Approximately 200 studies that examined the relationship between fruit and vegetable intake and cancers of the lung, colon, breast, cervix, esophagus, oral cavity, stomach, bladder, pancreas, and ovary are reviewed. A statistically significant protective effect of fruit and vegetable consumption was found in *128 of 156 dietary studies* in which results were expressed in terms of relative risk. For most cancer sites, persons with *low fruit and vegetable intake* (at least the lower one-fourth of the population) experience *about twice the risk of cancer* compared with *those with high intake*, even after controlling for potentially confounding factors. For lung cancer, significant protection was found in 24 of 26 studies after control for smoking in most instances. Fruits, in particular, were significantly protective in cancers of the esophagus, oral cavity, and larynx, for which 28 of 29studies were significant. Strong evidence of a protective effect of fruit and vegetable consumption was seen in cancers of the pancreas and stomach (26 of 30 studies), as well as in colorectal and bladder cancers (23 of 38 studies). For cancers of the cervix, ovary, and endometrium, a significant protective effect was shown in 11 of 13 studies, and for breast cancer a protective effect was found to be strong and consistent in a meta-analysis.

"It would appear that major public health benefits could be accomplished antially increasing consumption of these foods"

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128 of 156 dietary studies

Persons with low fruit and vegetable intake experience about twice the risk of cancer

"It would appear that major public health benefits could be accomplished by substantially increasing consumption of these foods"

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It must be the fruits and vegetables !

3rd Paradigm - 1990's- 2000's

Dietary Fruits and Vegetables are not associated with Breast Cancer Risk ?

INTRODUCTION

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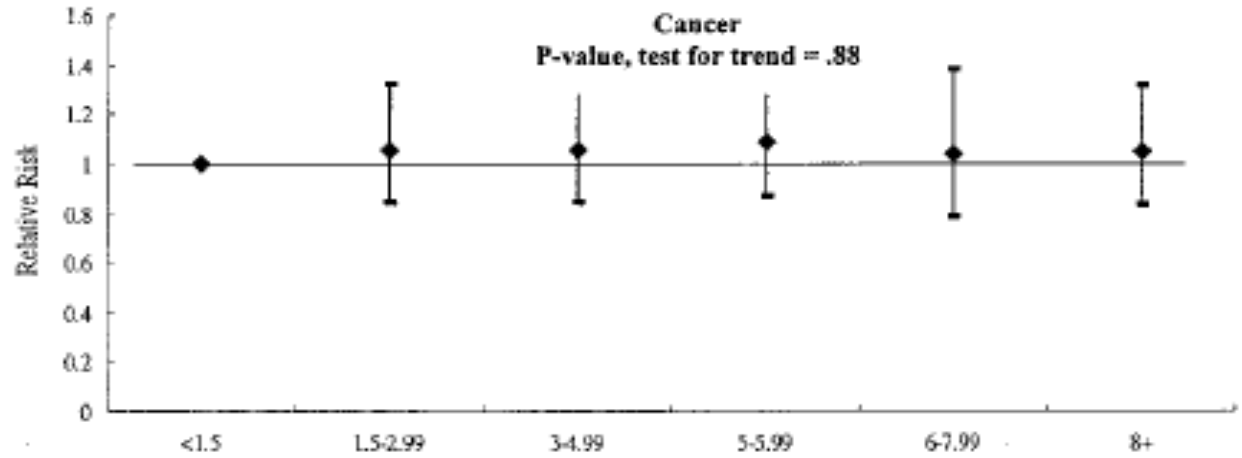
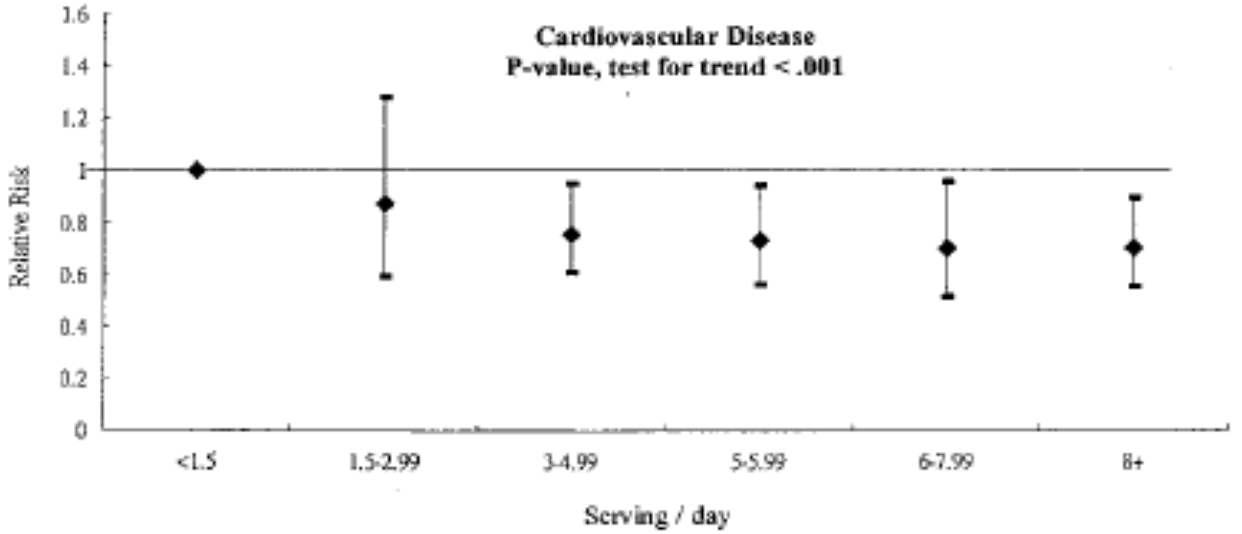
Study‡	Relative Risk (95% Confidence Interval) for 100 g/d Intake Increment†		
	Total Fruits	Total Vegetables	Total Fruits and Vegetables
Adventist Health Study	0.97 (0.87-1.08)	1.10 (0.88-1.38)	0.99 (0.91-1.09)
Canadian National Breast Screening Study	0.98 (0.92-1.05)	0.98 (0.89-1.07)	0.98 (0.94-1.03)
Iowa Women's Health Study	1.01 (0.98-1.04)	0.98 (0.93-1.03)	1.00 (0.98-1.02)
Netherlands Cohort Study	0.97 (0.91-1.04)	0.90 (0.81-1.00)	0.96 (0.91-1.01)
New York State Cohort	1.01 (0.94-1.08)	1.04 (0.93-1.15)	1.01 (0.96-1.06)
New York University Women's Health Study	1.00 (0.95-1.05)	0.97 (0.90-1.04)	0.99 (0.95-1.03)
Nurses' Health Study (a)	0.98 (0.95-1.02)	1.01 (0.95-1.07)	0.99 (0.96-1.02)
Nurses' Health Study (b)	0.98 (0.95-1.01)	1.01 (0.98-1.05)	0.99 (0.97-1.01)
Sweden Mammography Cohort	0.99 (0.94-1.03)	1.01 (0.93-1.11)	0.99 (0.96-1.03)
Pooled	**0.99 (0.98-1.00)**	**1.00 (0.97-1.02)**	**0.99 (0.98-1.00)**

Fruit and Vegetable Intake and Risk of Major Chronic Disease

Hung H-C, Joshipura KJ, et al. (NHS, HPSF)





Increased Fruits and Vegetables linked to lower CV Disease risk, *not Cancer Risk*

Fruit and Vegetable Intake and Overall Cancer Risk in the European Prospective Investigation Into Cancer and Nutrition (EPIC)

Boffetta P et al J Natl Cancer Inst 2010;102:529-537

Prospective, cohort analysis, 10 European countries

142,605 men, 335,873 women, 8.7 years follow-up

Assess total fruits, total vegetables, total fruits and vegetables vs .risk

200 g Fr&Vg- HR =0.98, 100 g Vg- HR=0.98, 100 g Fr HR= 0.99

High vegetable- *benefit in women only,* High Fr Vg – heavy drinkers, tobacco only

*How much decrease in risk – **1-2%***

A very small inverse association between intake of fruits and vegetables and cancer risk was observed in this study

"Given the small magnitude of the observed associations, caution should be applied to their interpretation"

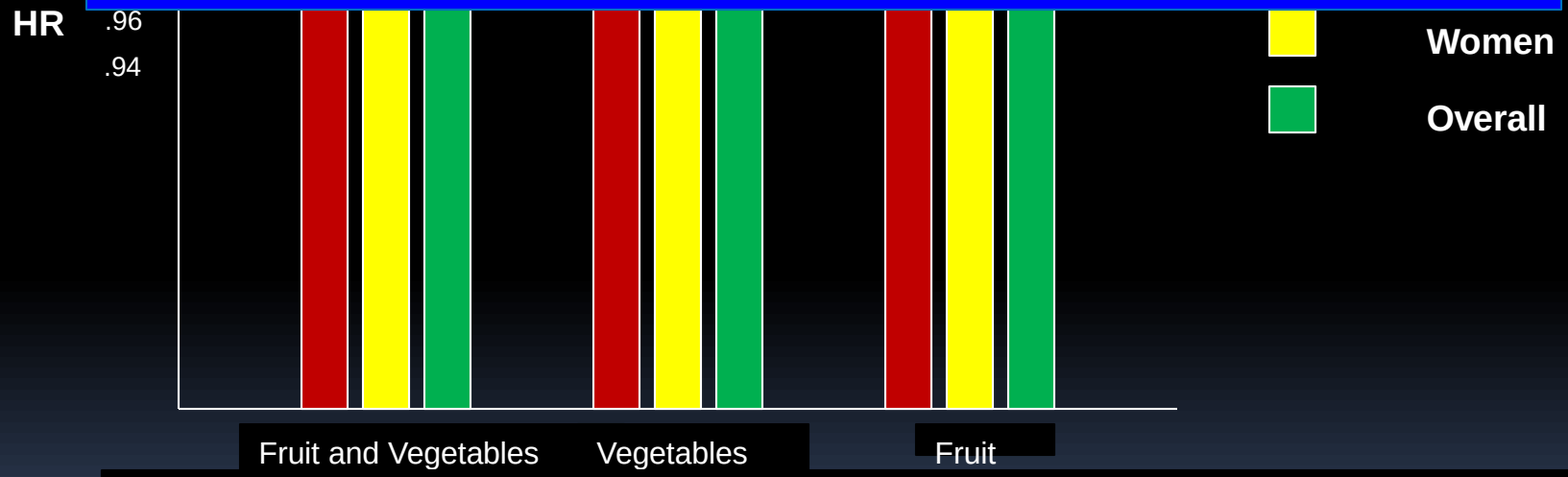
Fruit and Vegetable Intake and Overall Cancer Risk in the European Prospective Investigation Into Cancer and Nutrition (EPIC)

Boffetta P et al J Natl Cancer Inst 2010;102:529-537

"Turmoil in the Produce Section"

The findings from the EPIC cohort add further evidence that a broad effort to increase consumption of fruits and vegetables will not have a major effect on cancer incidence

W. Willett



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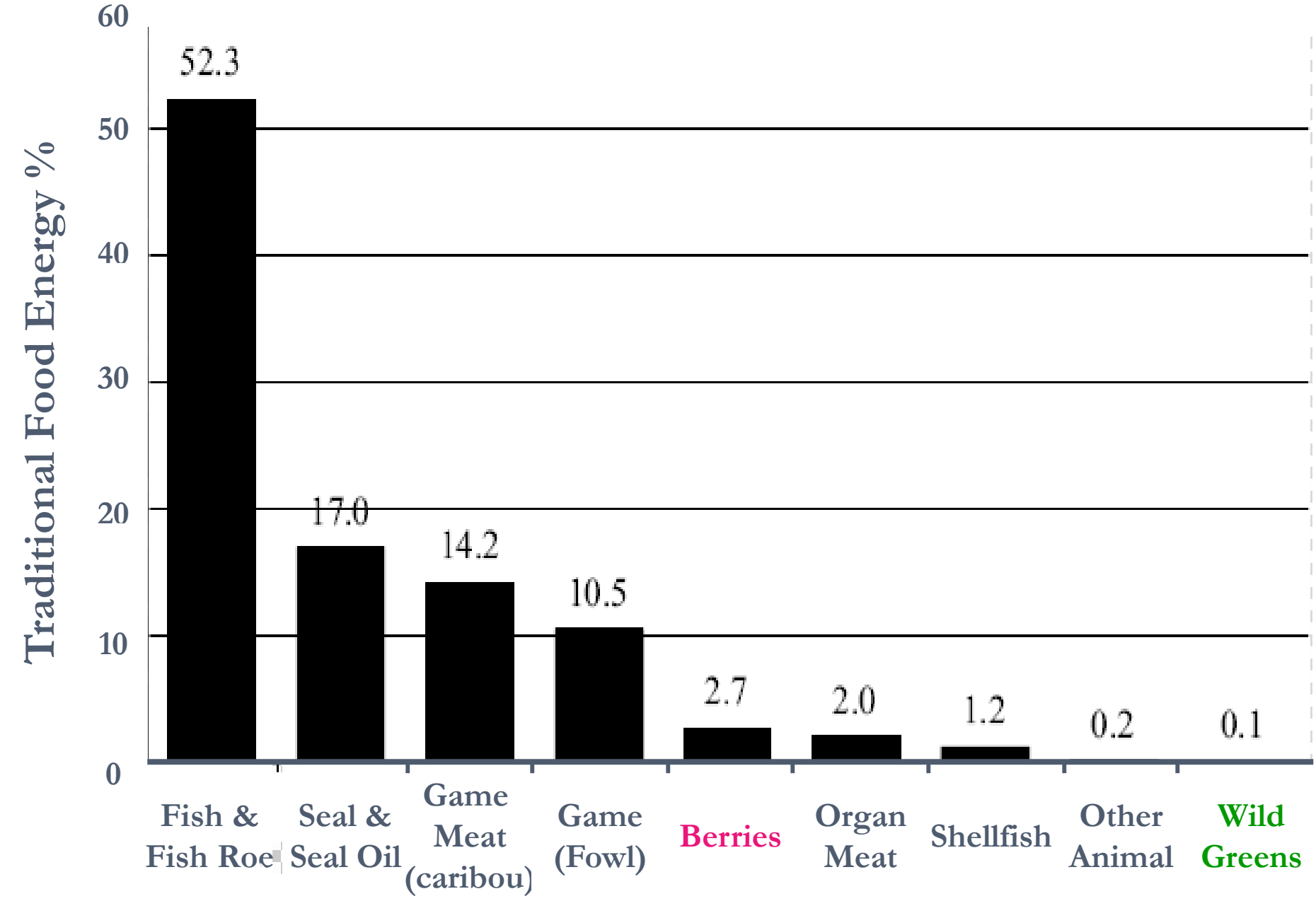
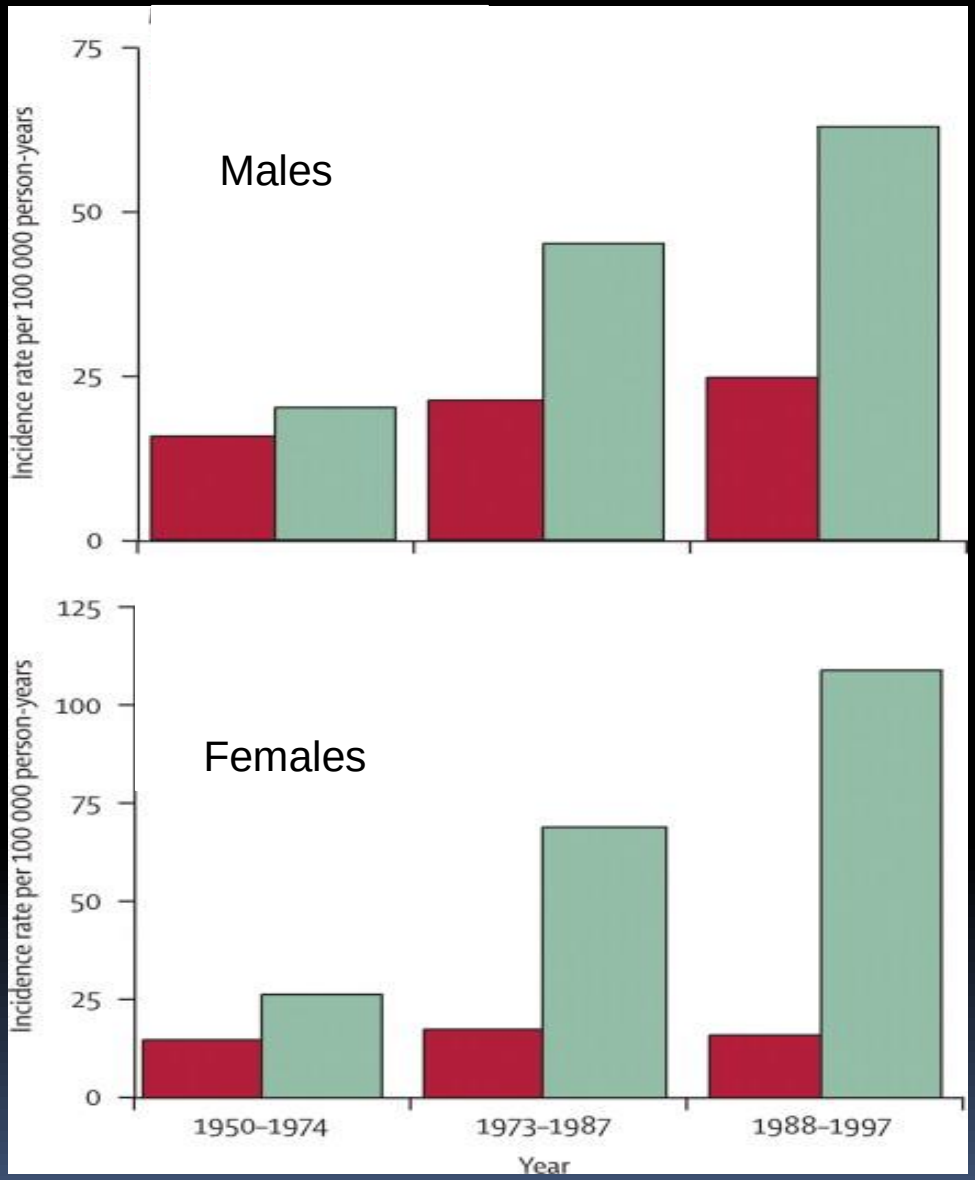
NIH 5 – a - Day Campaign

Eskimo / Inuit Diet and Disease



Contribution of nine food groups to traditional inuit food intake (% energy

Westernization of Inuits and Rising Incidence of 20th Century Cancers



Traditional
Nasopharyngeal
Salivary Gland
Sq Esophageal

Western
Lung
Colon
Rectal
Breast
Prostate

Incidence of traditional and lifestyle-associated cancers in Greenland in 1950–74, 1973–87 and 1988–97

Vegetables, Fruits and Carotenoids and the Risk of Cancer

Regina G Ziegler Am J Clin Nutr;53:251S-9S, 1991.

- ***Low intake*** of vegetable, fruits and carotenoids is consistently associated with increased risk of lung cancer in both prospective and retrospective studies
- ***Low levels*** *of* ***β-carotene in serum or plasma*** are consistently associated with subsequent development of lung cancer

" The simplest explanation- β-carotene is protective"

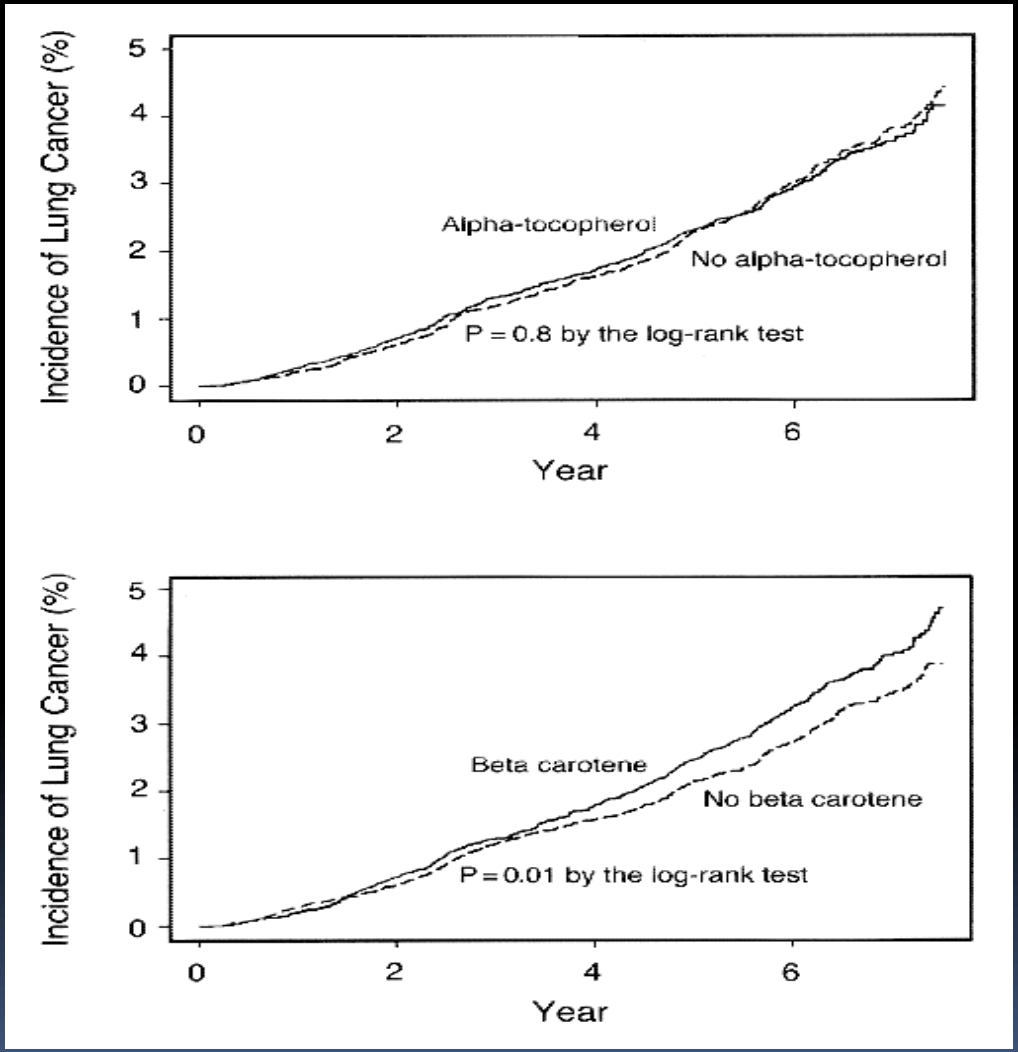
Can beta-Carotene materially reduce human cancer rates?

Peto R, Doll R, Buckley JD, Sporn MB.

Nature 1981; 290 (5803): 201-208

ATBC Lung Cancer Prevention Trial

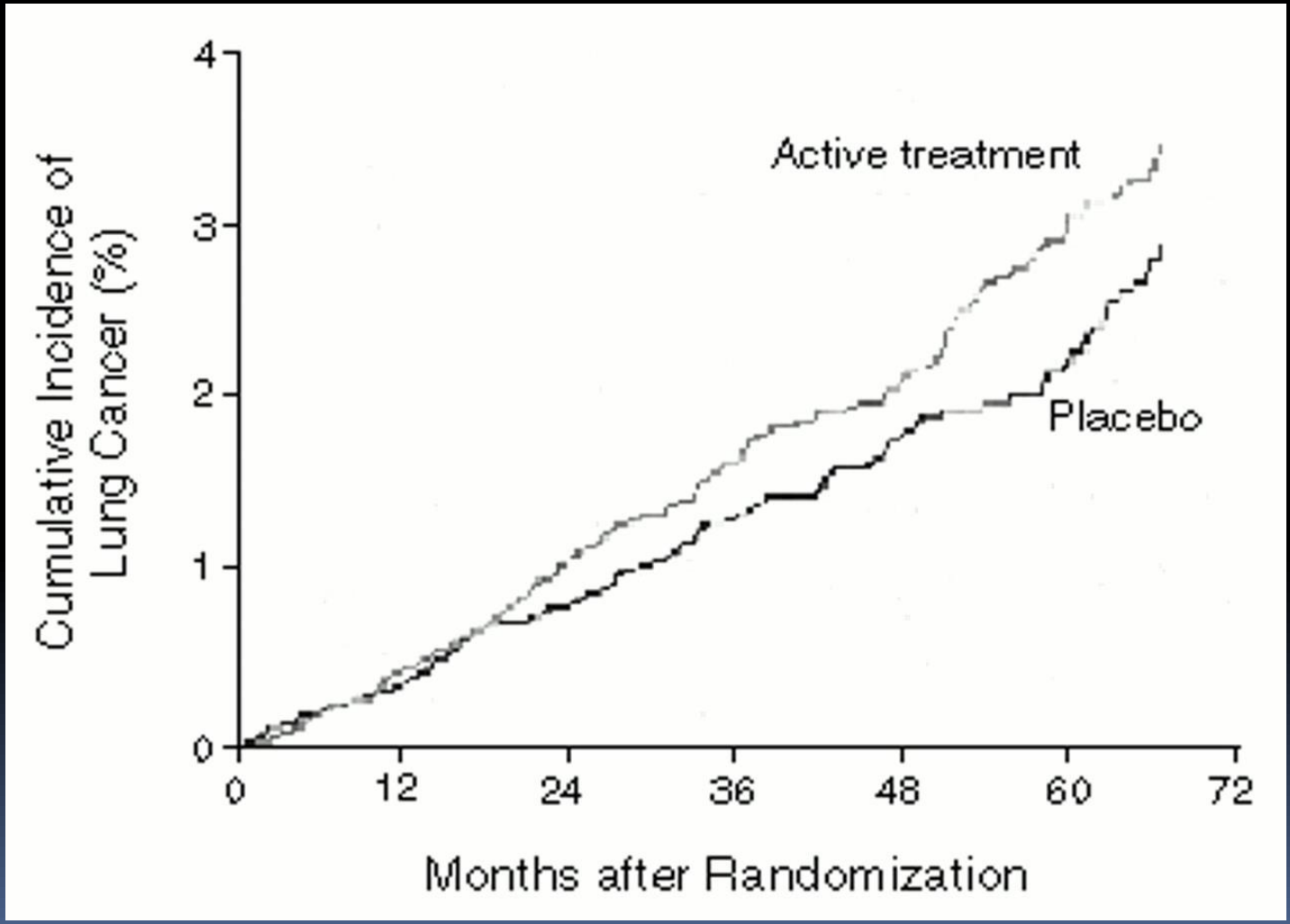
β-Carotene Raised Lung Cancer Risk in Smokers - 18%



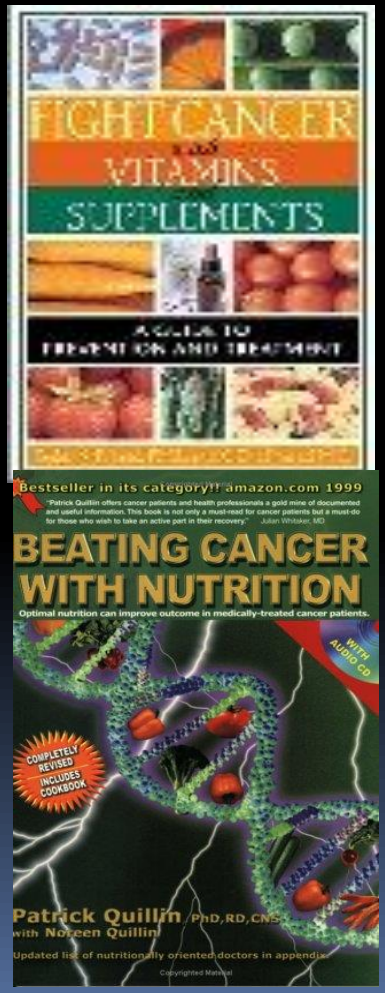
β-Carotene vs. Placebo – CARET Trial

US –Smokers + Asbestos Exposure

β-Carotene ***Raised*** *Risk* ***- 28%***

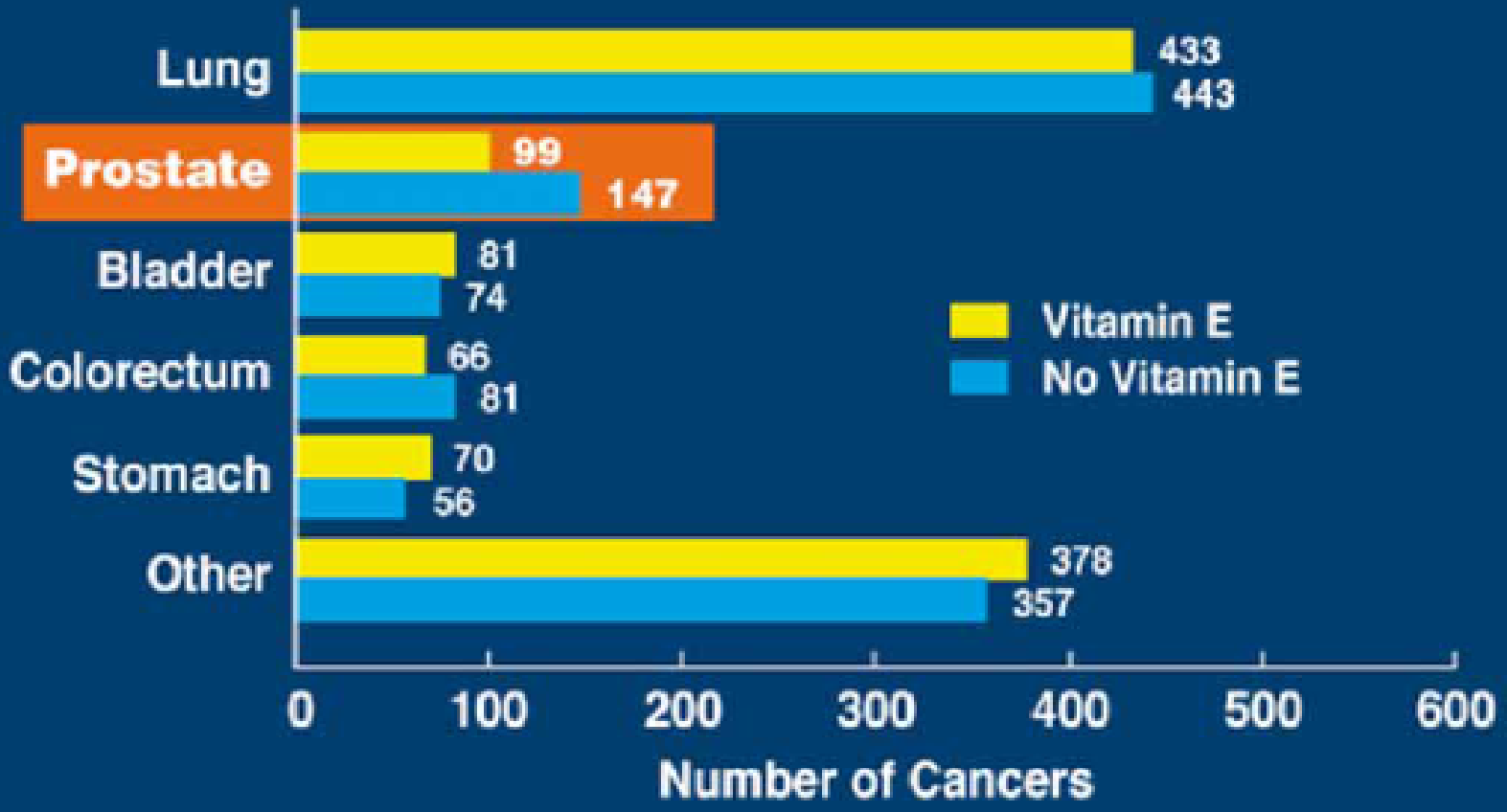


Cancer Treatment Centers of America

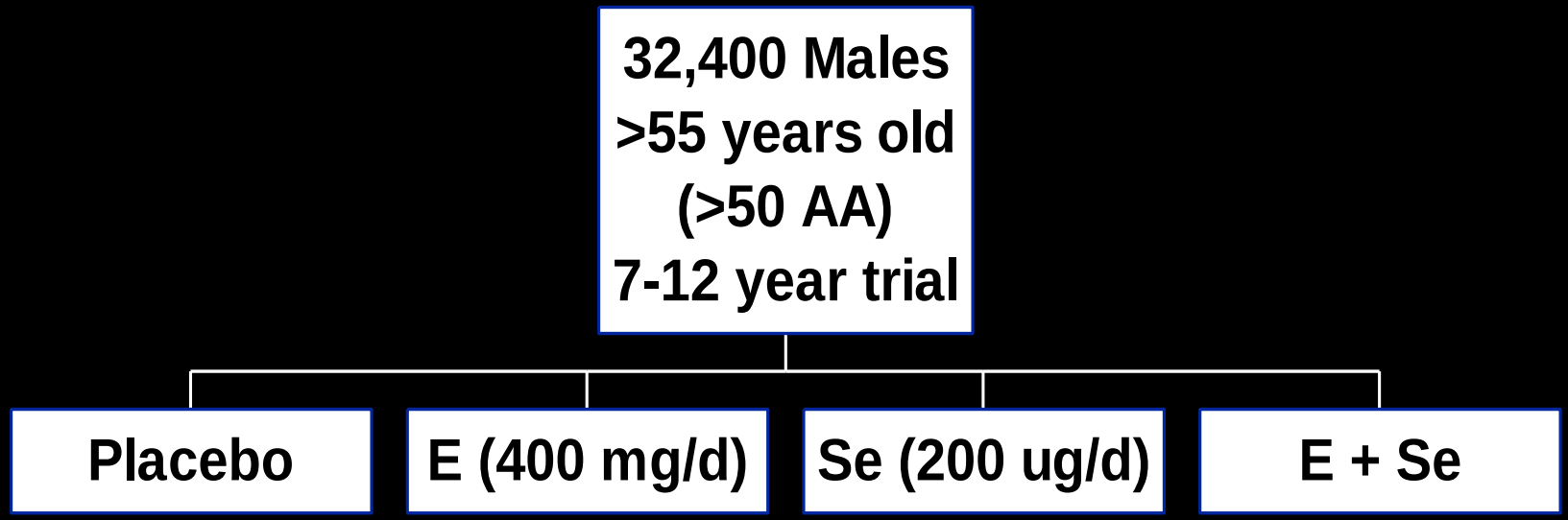


ATBC Study

Cancers According to Vitamin E Treatment Status



Selenium and Vitamin E Chemoprevention Trial (SELECT)

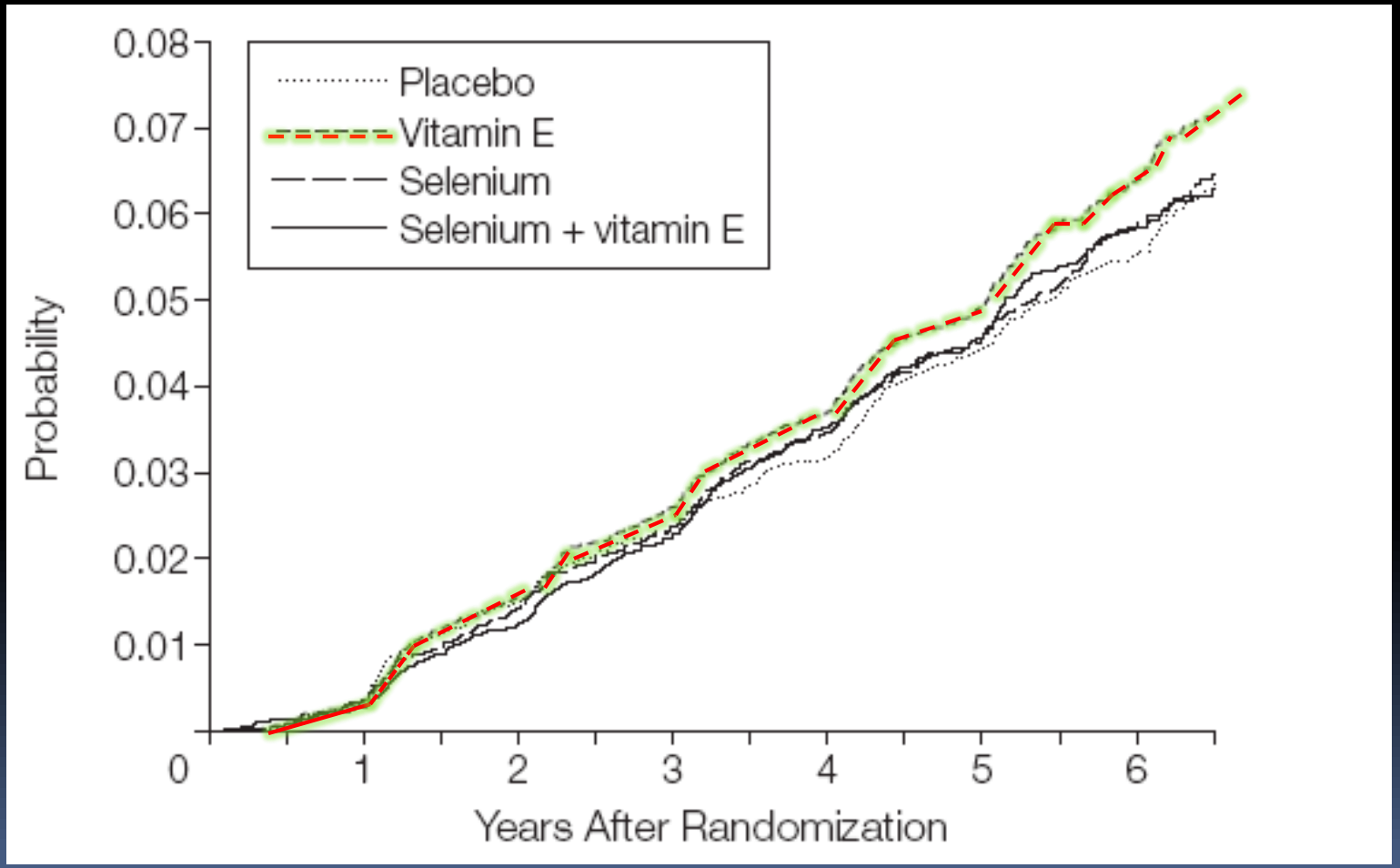


Outcome: Vitamin E - *Increased* Prostate Cancer
Selenium - *Increased* Diabetes Mellitus

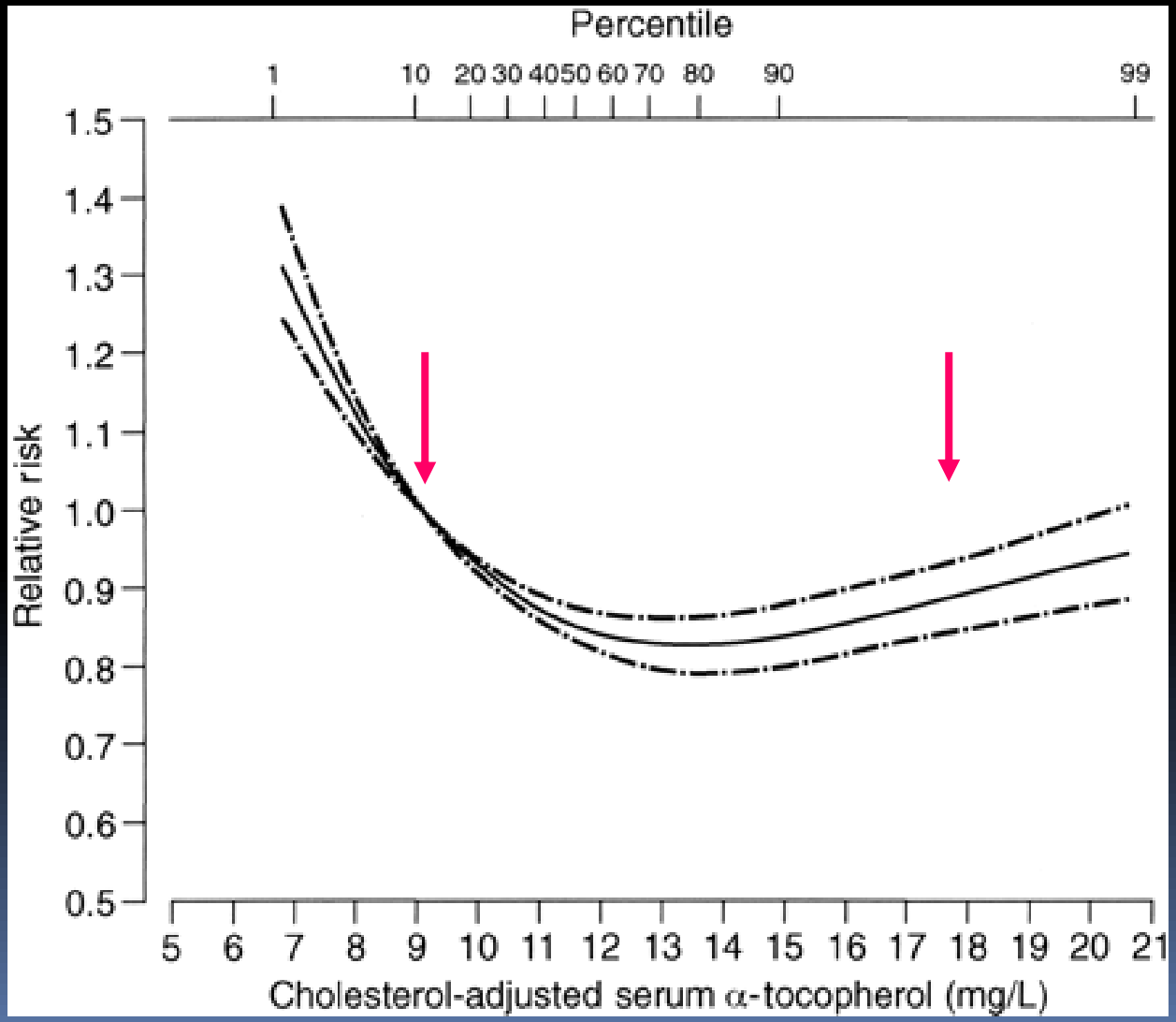
Effect of Selenium and Vitamin E on Risk of Prostate Cancer and Other Cancers: The Selenium and Vitamin E Cancer Prevention Trial (SELECT)

Scott M Lippman; Eric Klein; Phyllis J Goodman; et al

JAMA 2009; 301:39-51



Total Mortality- Adjusted for Serum a-Tocopherol Levels - ATBC Trial

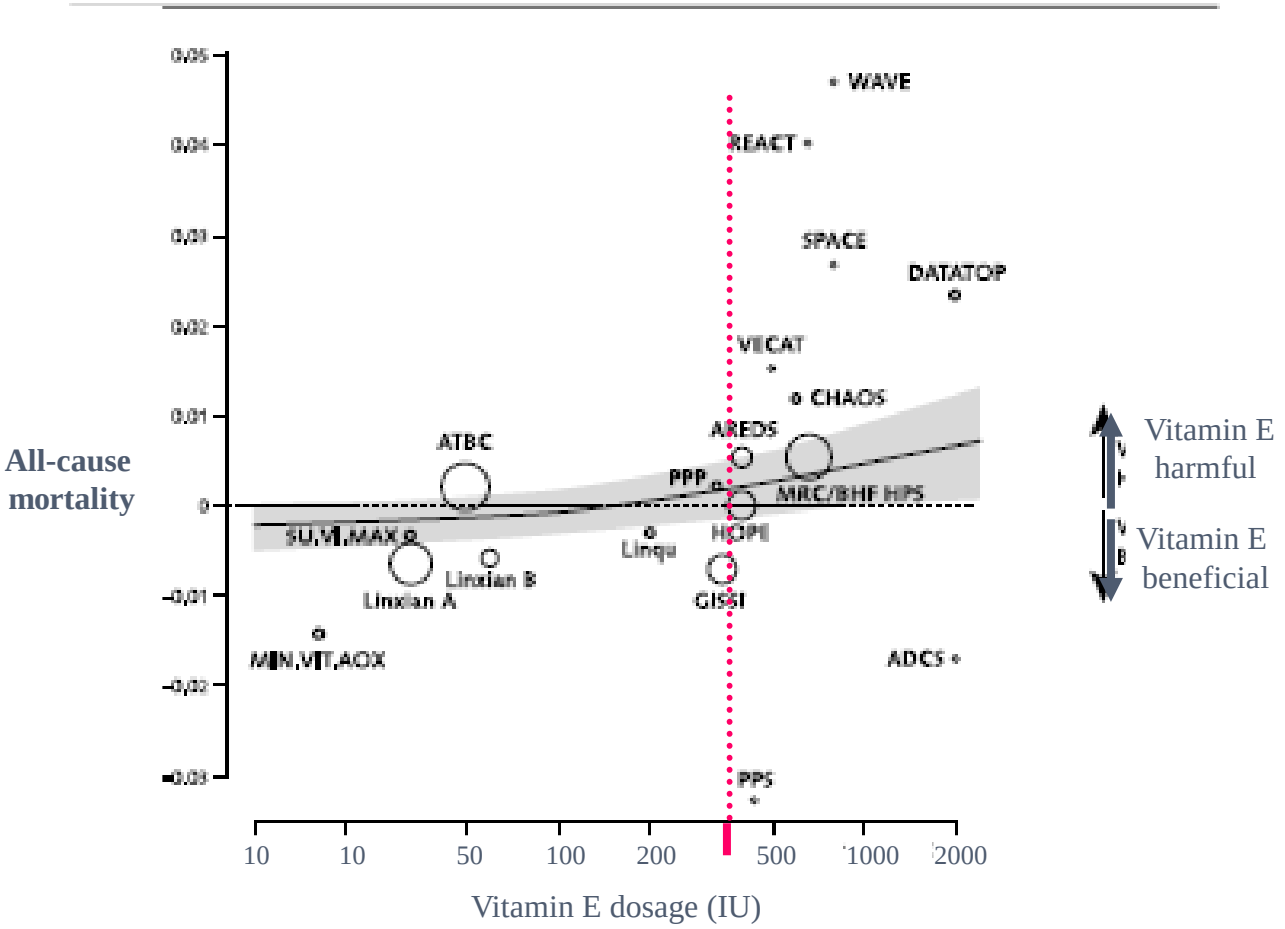


Increased Mortality

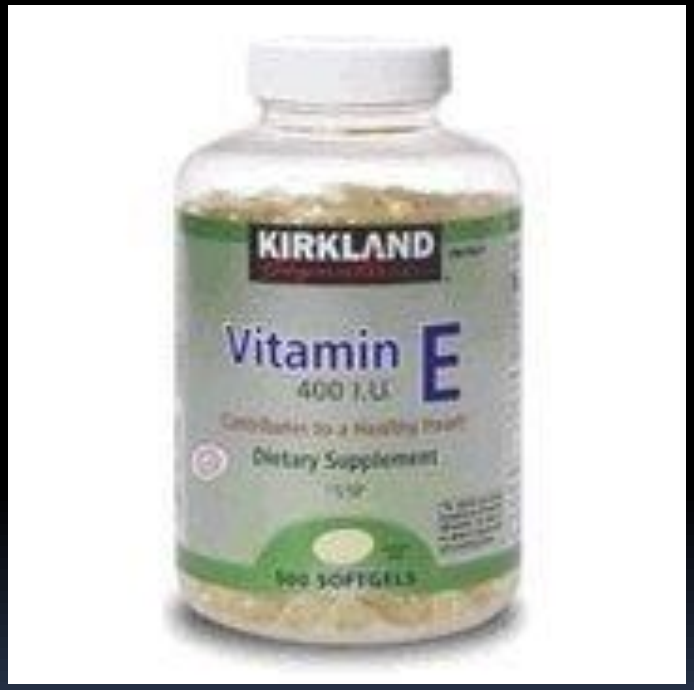
Below 40th Percentile

Upper 10th Percentile

Dose –response relationship between vitamin E supplementation and all-cause mortality in randomized controlled trials



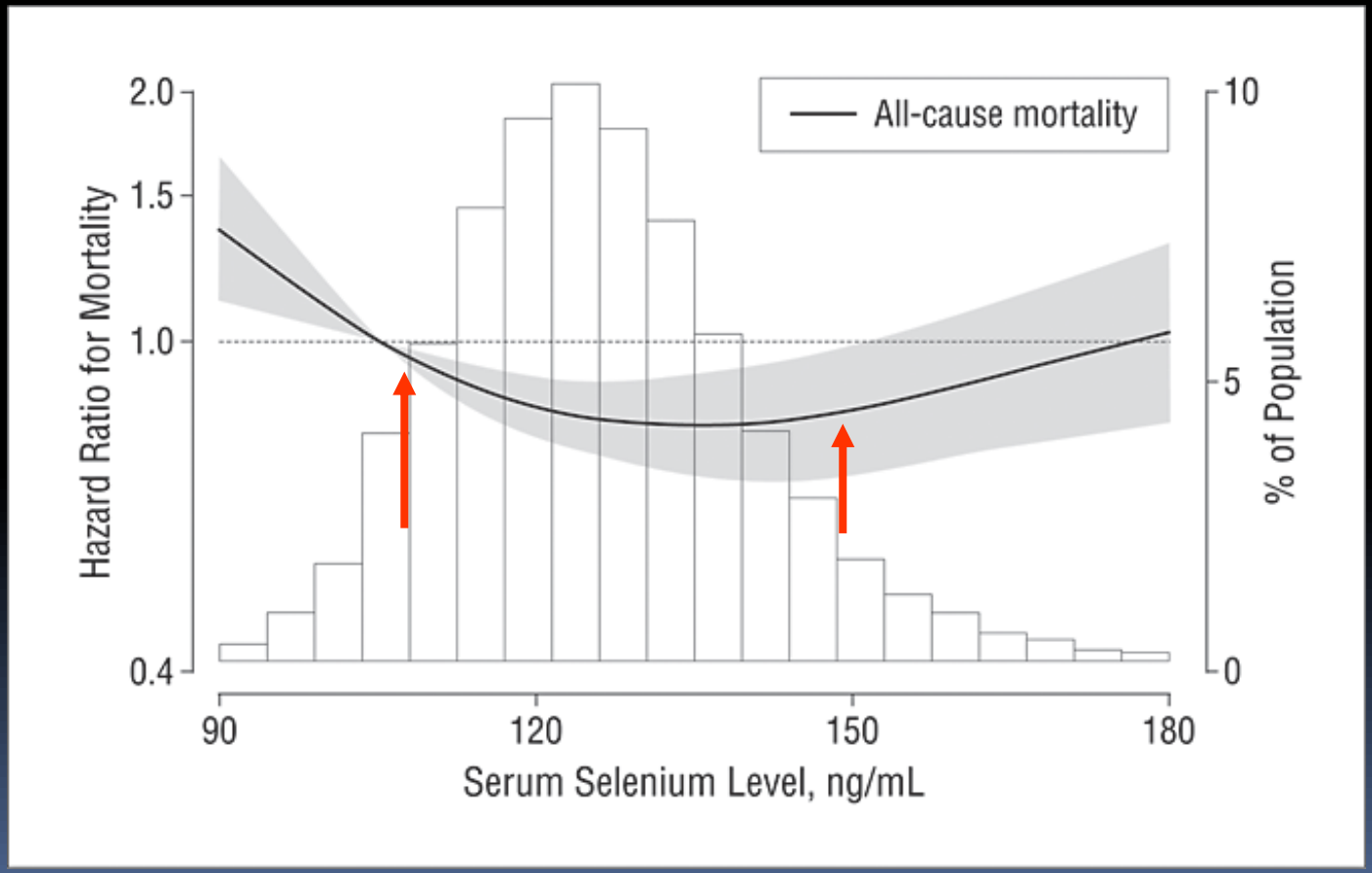
Usual Vitamin E Capsule = 400 IU



400 IU = 1333% of ADR

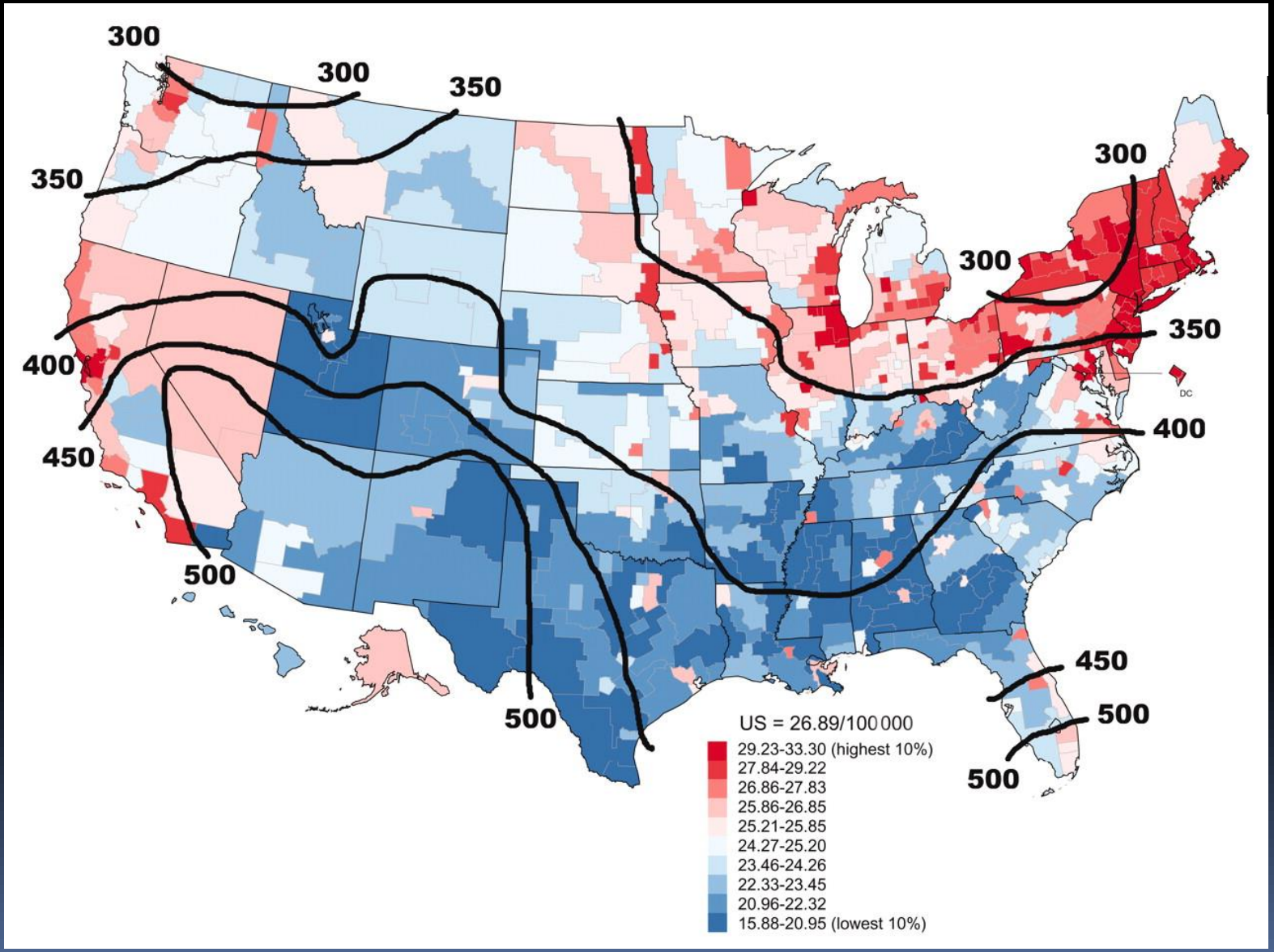
Risks for Cancer and all-cause Mortality by serum selenium levels (NHANES)

Increased risk below 100ng / ml and above 150 ng / ml



Bleys, J. et al. Arch Intern Med 2008;168:404-410.

Age-adjusted *breast cancer* mortality rates, by county area, and contours of annual mean daily solar irradiance in Langleys (calories/cm2), United States, 1970-1994

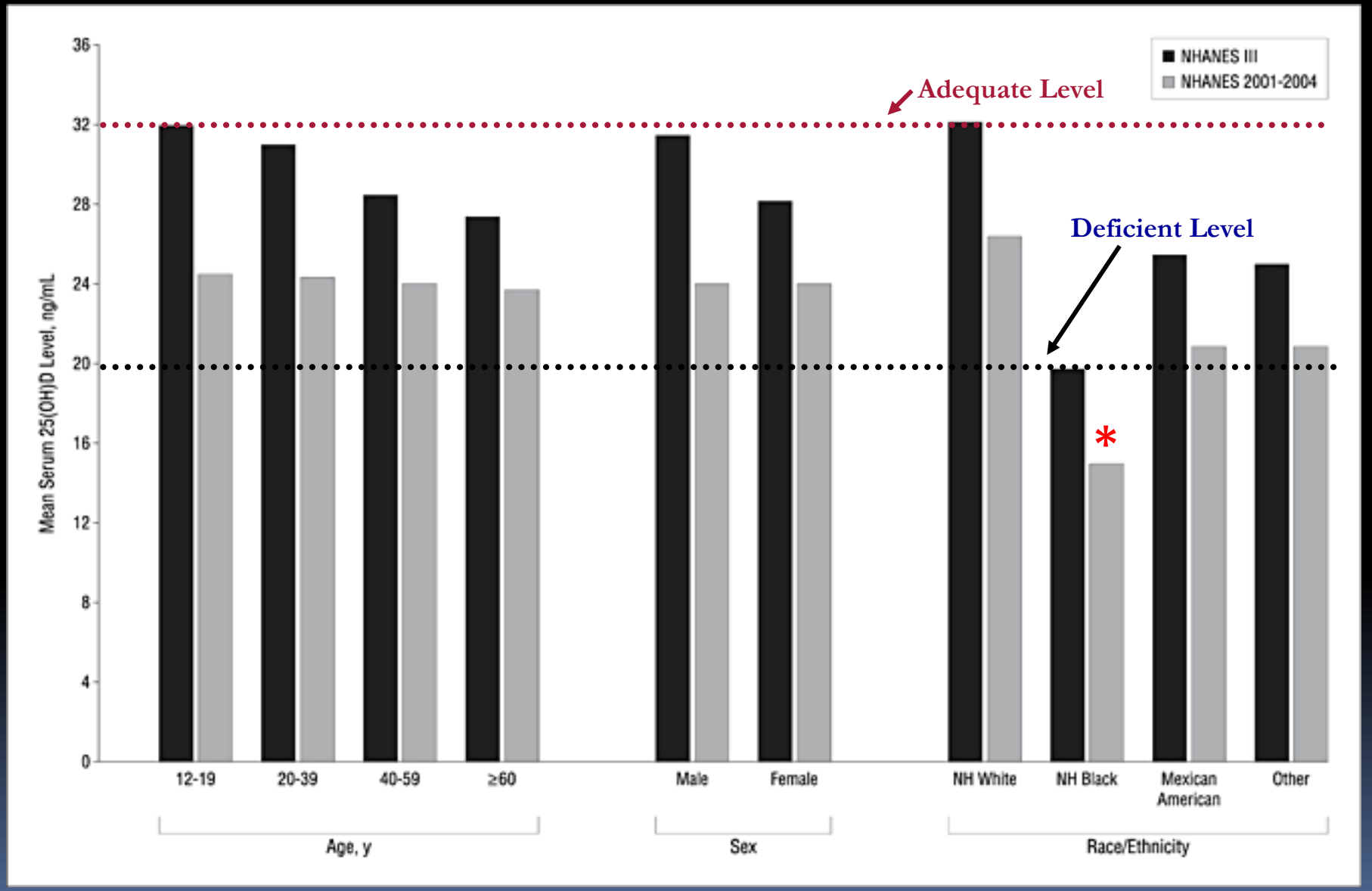


Garland, C. F. et al. Am J Public Health 2006;96:252-261

Vitamin D and Cancer Prevention

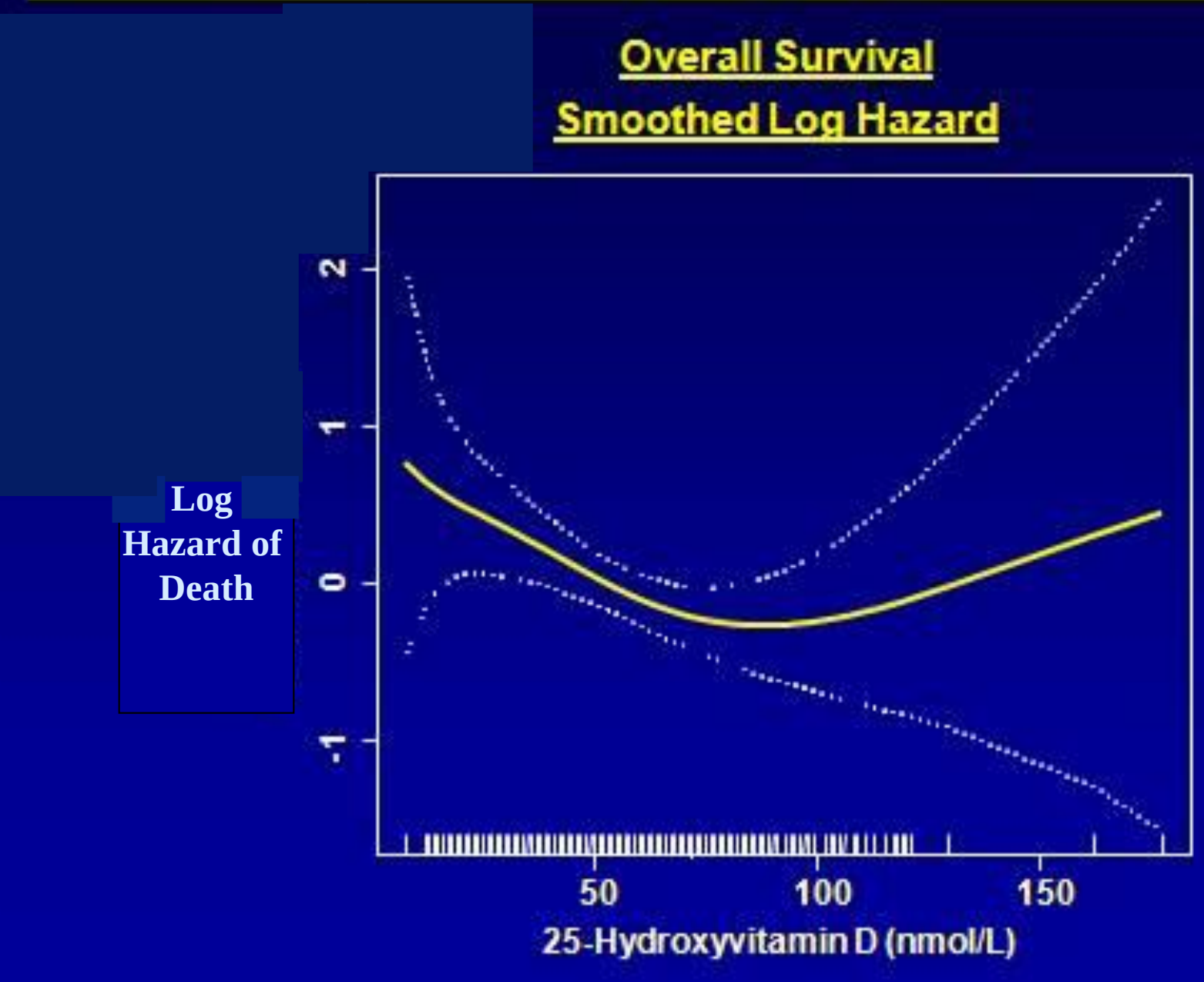
- Randomized clinical trials with cancer outcomes lacking; concerns about adverse effects (e.g., hypercalcemia) noted
- Observational epidemiologic data suggest that lower vitamin D status is associated with higher risk of various cancers (breast, prostate, colorectal, etc).

Mean serum 25-hydroxyvitamin D (25[OH]D) levels in the NHANES 1988-1994 vs 2001-2004

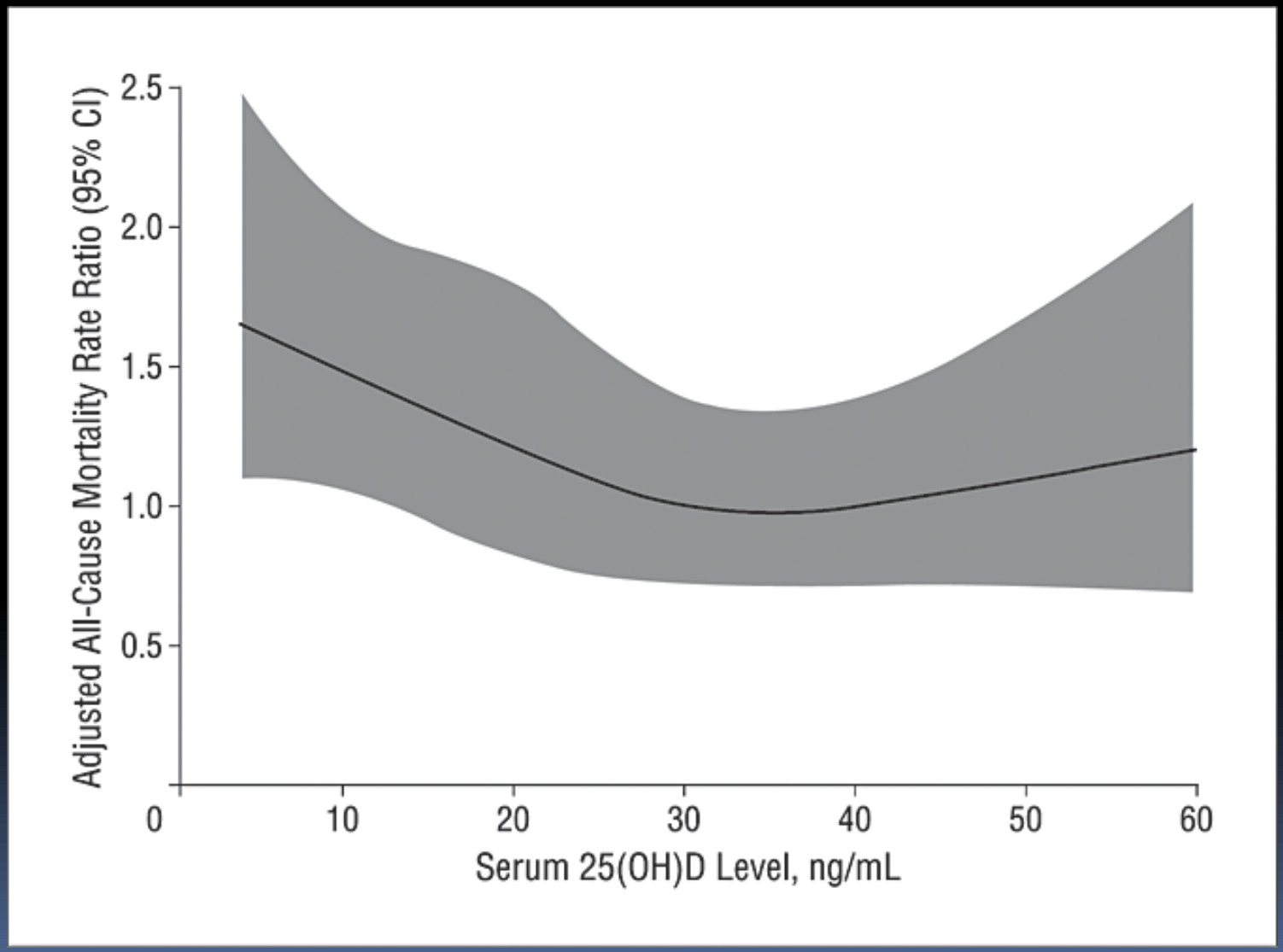


Ginde, A. A. et al. Arch Intern Med 2009;169:626-632.

Vitamin D Deficiency and Breast Cancer Survival



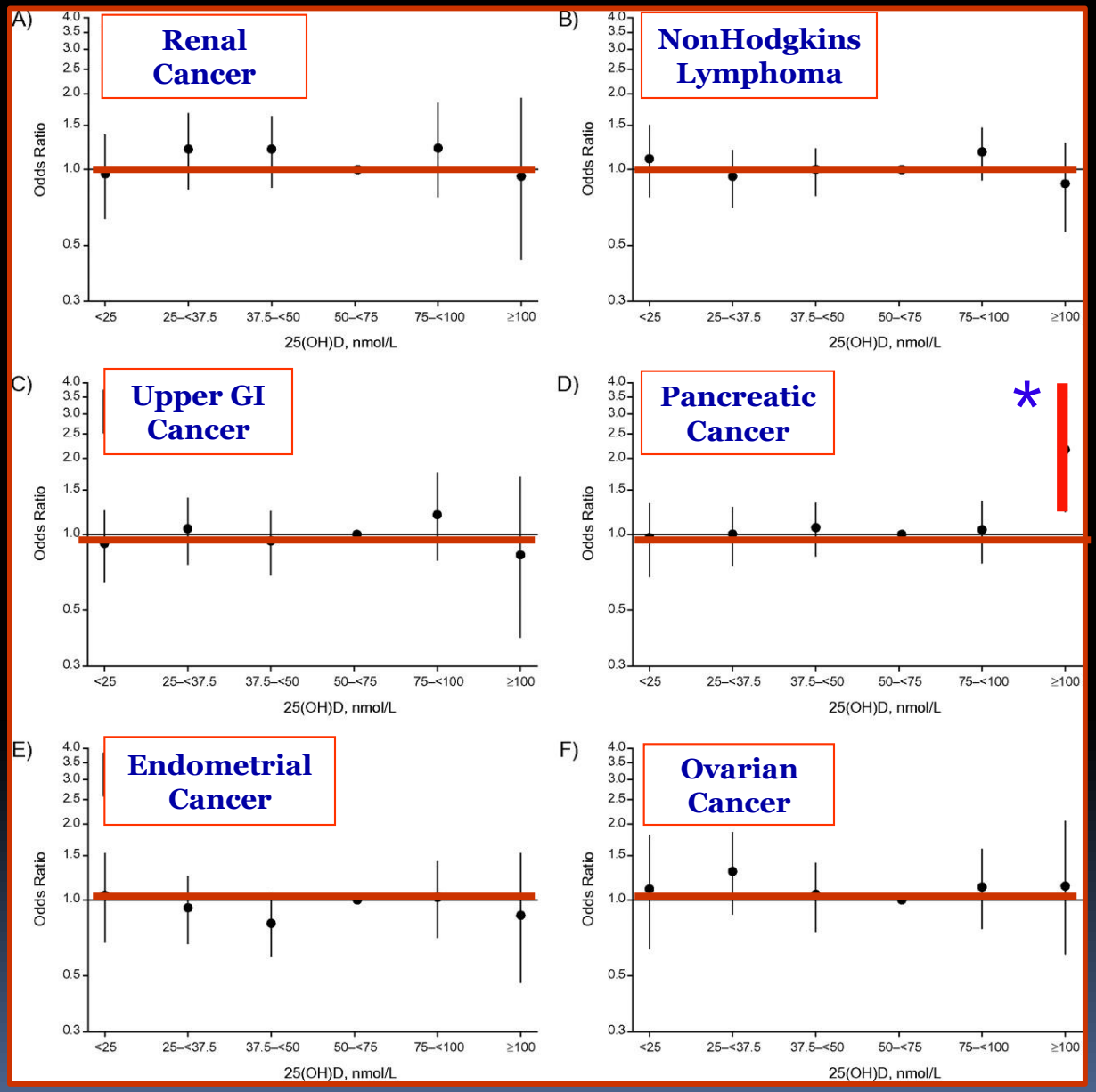
25-Hydroxyvitamin D Levels and the Risk of Mortality in the General Population - 3rd NHANE Survey



Arch. Intern Med. 168(15):1629-37, 2008

Consortium Vitamin D Pooling Project of Rarer Cancers

Cancer Risk, by site, vs. serum vitamin D level



No Relationship* between Vitamin D and Cancer Risk except *higher risk of Pancreatic Cancer at highest level

Helzlsouer, K. J. et al. Am. J. Epidemiol. 2010 172:4-9

B Vitamins and Cancer

- Presumed safe- water-soluble, minimal storage(x B12)
- Renal excretion – "you pee it out, no risk!!" **WRONG!!**
- Role: Single carbon metabolism- CH-3 transfers
  Transmethylation reactions
  Amino Acid metabolism (Homocysteine → Methionine)
  Nucleotide metabolism (Uridine → Thymidine)
  Fatty acid metabolism (Malonyl)
  Promoter methylation (altered gene expression)

Folate, B-12, B-6, Betaine

Concerns: Altered cancer risk: deficiency vs. excess (folic acid)

Polyp Prevention Trial -1000 mcg folic acid vs. placebo

↑ Advanced Polyps ↑ Prostate Cancer

Limited data – high dose folic acid, B12 in common use

Cofactors in Intermediary Metabolism

Glucose, Lipid, AA metabolism

Thiamine (B-1),Riboflavin (B-2),Niacinamide (B-3),Pyridoxine (B-6), Biotin, Pantothenic Acid (B-5)

Sidney Farber -1903-1973

Benefits of Vitamin- B100 Complex

Livestrong, 2014

- B-complex vitamins are nutrients that ***help your body convert calories into energy.***

  Important for vision, normal appetite, and healthy skin, hair and nails.

  Play role in the formation of red blood cells and the functioning of the nervous system.

- **Vitamin B-100 complex** supplements contain most of the B vitamins in doses of 100 milligrams, except for *a few B vitamins that you need in much smaller doses*.

  The 100-milligram dosage is ***much higher*** than the recommended daily value.

- Because B vitamins are ***not stored*** in the body's fat tissues the way other vitamins are, B-vitamin toxicity is not generally an issue

- B-complex vitamins **help "*convert the food you eat into usable energy*"**, they may also be effective in ***increasing energy levels***

- Study published in "*Psychopharmacology*" in 2010:

Male participants : 33 days of supplementation with B-complex vitamin, vitamin C and mineral supplement.

Significant improvement in mental well being

Increased vigor, overall improvements in mood, reduction in stress levels.


Nature Made
Balanced B-100
Complex
TIMED RELEASE
DIETARY SUPPLEMENT
60 TABLETS
Helps
Convert
Food Into
Energy†

Linking vitamin B1 with cancer cell metabolism

Jason A Zastre*, Rebecca L Sweet, Bradley S Hanberry *Cancer & Metabolism* 2013, **1**:16

Thiamine (B-1) is critical for the activity of four key enzymes in cellular metabolism:

Circulating plasma levels of thiamine in healthy individuals : 10 and 20 nM

Recommended daily intake (RDI) thiamine for adult men and women: **1–1.5 mg/day**

Thiamine- found naturally in many foods (breads, fish, meat, eggs, legumes, milk)

Used in fortification of many processed foods, in dietary supplements

Problem: Central role in cancer cell proliferation

Thiamine-degrading enzyme **thiaminase**: decreases thiamine and cell proliferation through reduced ATP levels in cancer cells, key role in support of cancer cell bioenergetics.

Hypothesis:

Western diet - Excess thiamine supplementation - ? Role in Increased cancer risk

- Commonly supplemented in processed foods, over-the-counter supplements in western countries with high cancer incidences.

Asian diet - Naturally high in ***thiaminase*** (natural thiamine-degrading enzyme)

- Limits dietary thiamine exposure
- Correlated with low cancer risks in populations

B 100 -Ingredients

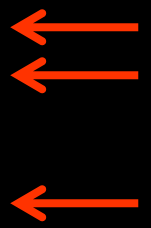
Supplement Facts

Serving size: 2 vegetable capsules

	Amount Per Serving	% Daily Value
Thiamine (vitamin B-1)	100 mg	6667%
Riboflavin (vitamin B-2)	100 mg	5882%
Vitamin B-3 (niacinamide)	100 mg	500%
Vitamin B-6 (pyridoxine HCl)	100 mg	5000%
Folic Acid	400 mcg	100%
Vitamin B-12 (cyanocobalamin)	100 mcg	1667%
Biotin	100 mcg	33%
Vitamin B-5 (pantothenic Acid)	100 mg	1000%
PABA (para-aminobenzoic acid)	100 mg	*
Choline bitartrate	100 mg	*
Inositol	100 mg	*

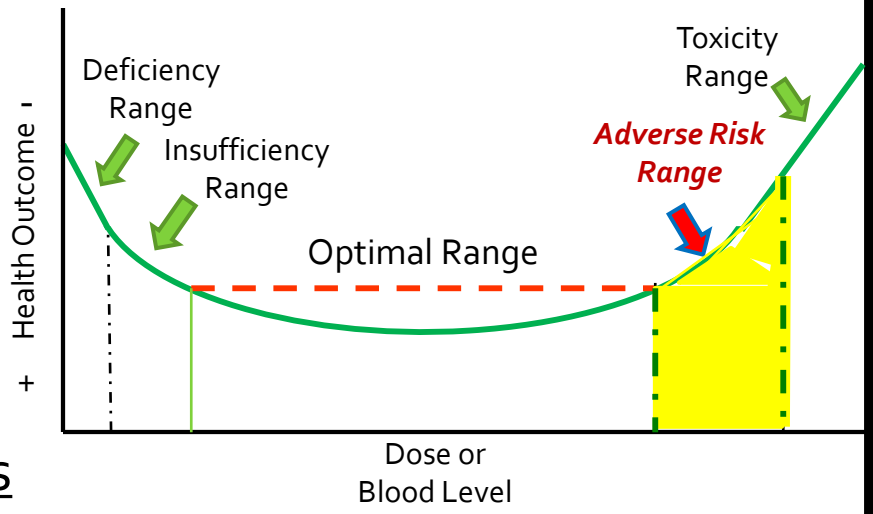
* Daily value not established

Other Ingredients: vegetable capsule. Contains no fillers, excipients or artificial substances.



Dietary Supplement Use
"Boyd's Rules"

- Respect the U-shaped curve
- Toxic Risk - High Risk
  - High Probability
- Adverse Risk - *Low Risk*
  - *Low Probability*
  - **Why?**



- Law of Unintended Consequences

  Adverse risks *not predicted* by knowledge of nutrient physiology

  Low probability events *hard to notice* without careful follow/up

- Respect Nature

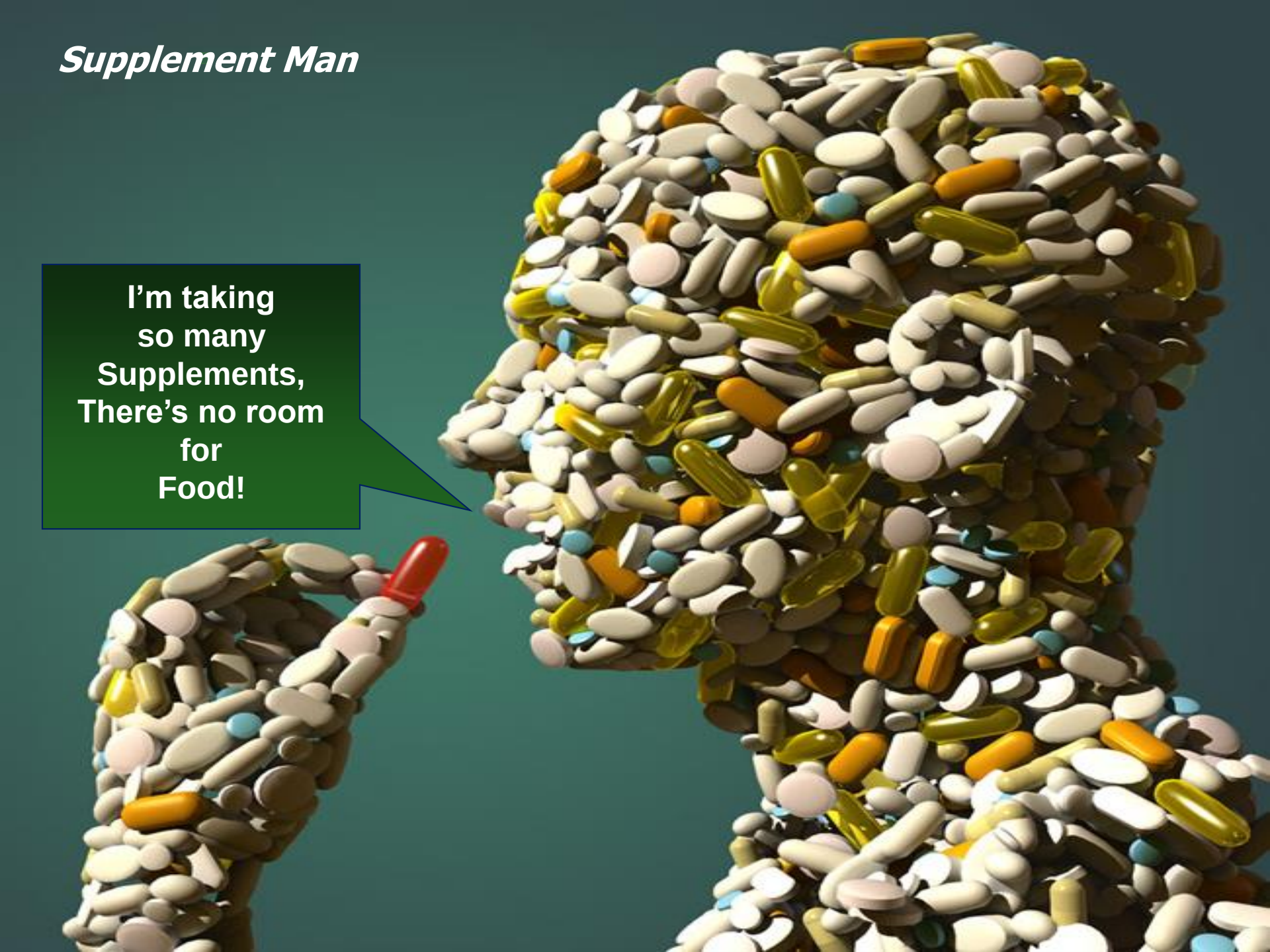
  Nutrient intakes in *non-physiologic ranges* unattainable in "nature" ie. diet!

- Economic Rules of Supplement Industry

  Target by income - Consequence

"The people who need it don't take it, the people who take it don't need it!"

Supplement Man



Where are the antioxidants in our food ?

Foods with the Highest Antioxidant Contents per Serving Size

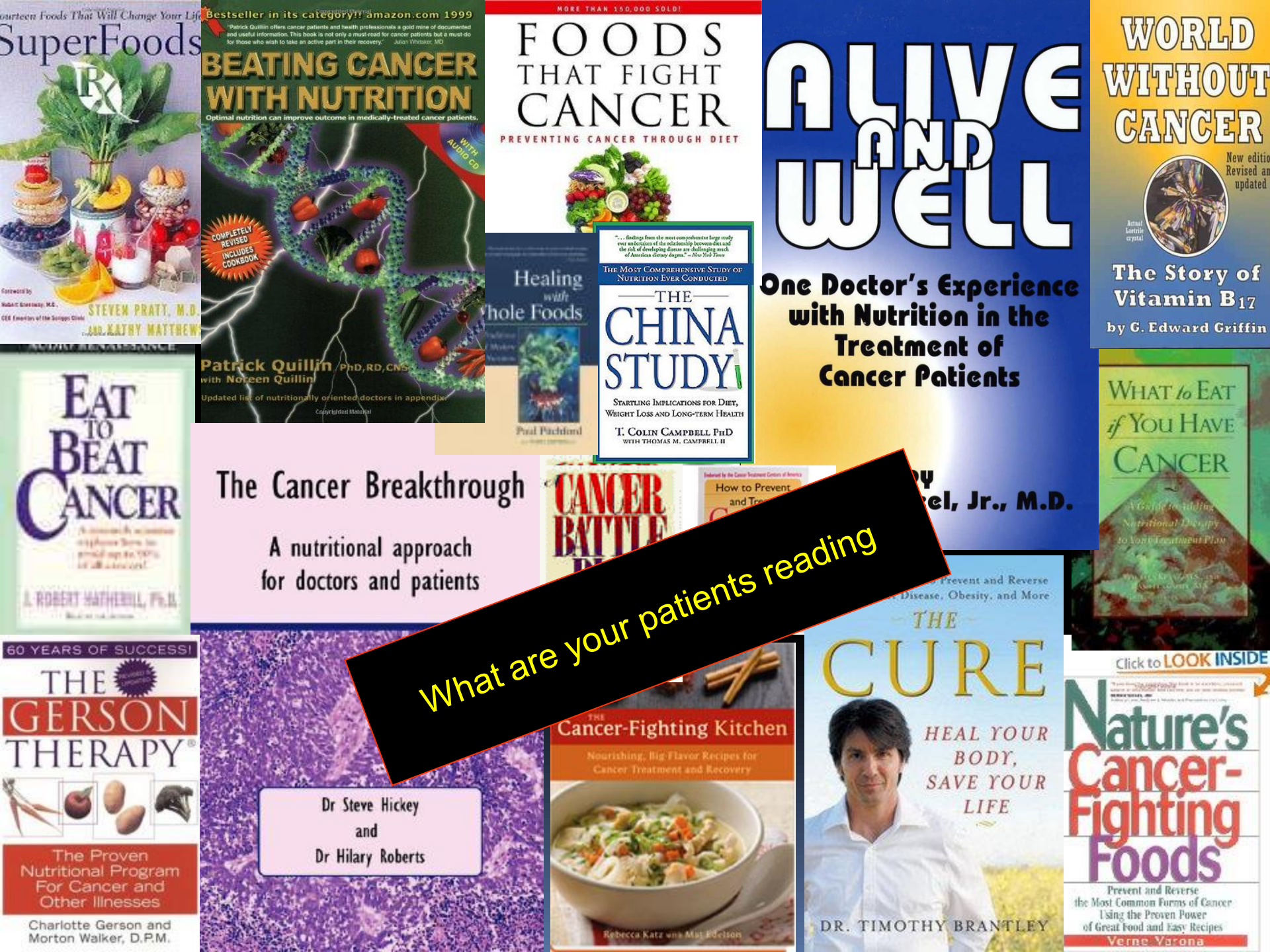
Product	Antioxidant content
	mmol/serving
Blackberries	5.746
Walnuts	3.721
Strawberries	3.584
Artichokes, prepared	3.559
Cranberries	3.125
Coffee	2.959
Raspberries	2.870
Pecans	2.741
Blueberries	2.680
Cloves, ground	2.637
Grape juice	2.557
Chocolate, baking, unsweetened	2.516
Cranberry juice	2.474
Cherries, sour	2.205
Wine, red	2.199

50 Foods with the Highest Anti-Oxidant Content

Product	Antioxidant content[1]
	mmol/100 g
Cloves, ground	125.549
Oregano leaf, dried	40.299
Ginger, ground	21.571
Cinnamon, ground	17.647
Turmeric powder	15.679
Walnuts	13.126
Basil leaf, dried	12.307
Mustard seed, yellow, ground	10.527
Curry powder	9.980
Pecans	9.668
Chocolate, baking, unsweetened	8.876
Paprika	8.601
Chili powder	8.372
Parsley, dried	7.430
Molasses, dark	4.900
Pepper, black	4.444
Artichokes, prepared	4.237
Chocolate, dark	4.188
Blackberries	3.990
Whole-grain cereal	3.412
Cranberries	3.289
Pudding mix, chocolate, cook-and-serve	3.026
Bran cereal	2.925
Power bar, chocolate flavor[2]	2.757
Chocolates, sugar-free	2.567
Raspberries	2.334
Strawberries	2.159
Blueberries	2.154
Cabbage, red, cooked	2.153
Wine, red	2.135
Barley malt syrup, organic	2.121
Prunes	2.018
Cherries, sour	1.814
Peppers, red, cooked	1.640
Chocolate cookies with vanilla creme filling	1.604
Cocoa Krispies cereal[3]	1.558
Chocolate chip cookies	1.524
Mustard, yellow, prepared	1.501
Milk-chocolate candy	1.483
Pistachios	1.426
Plums	1.330
Kiwi fruit	1.325
Corn flakes	1.255
Coffee	1.249
Spinach, frozen	1.226
Flaxseed, ground or milled	1.125
Rice and corn cereals	1.121
Toasty peanut crackers	1.101
Cupcakes, chocolate	1.059
Grape juice	1.011

Contribution of Different Food Groups to Antioxidant Intake in 7-Day Weighed-Record Study and NORKOST2 Study

	7-d weighed-record study	NORKOST2[1]
Total intake of antioxidants,[2] *mmol*	17.3 ± 9.4	17.6 ± 10.6
	% of total antioxidant intake	
Cereals	5	4
Fruits and berries	11	7
Fruit juices	2	2
Vegetables	2	2
Coffee	64	68
Tea	8	9
Wine	5	2
Other foods	5	8


What are your patients reading
SuperFoods
Steven Pratt, M.D.
Bestseller in its category!! amazon.com 1999
BEATING CANCER WITH NUTRITION
Optimal nutrition can improve outcome in medically-treated cancer patients.
Patrick Quillin PhD,RD,CNS
with Noreen Quillin
FOODS THAT FIGHT CANCER
PREVENTING CANCER THROUGH DIET
ALIVE AND WELL
One Doctor's Experience with Nutrition in the Treatment of Cancer Patients
WORLD WITHOUT CANCER
The Story of Vitamin B17
by G. Edward Griffin
Healing Whole Foods
THE CHINA STUDY
Startling Implications for Diet, Weight Loss and Long-term Health
T. Colin Campbell PhD
with Thomas M. Campbell II
EAT TO BEAT CANCER
The Cancer Breakthrough
A nutritional approach for doctors and patients
WHAT to EAT if You Have CANCER
60 YEARS OF SUCCESS!
THE GERSON THERAPY
The Proven Nutritional Program For Cancer and Other Illnesses
Charlotte Gerson and Morton Walker, D.P.M.
Dr Steve Hickey
and
Dr Hilary Roberts
Cancer-Fighting Kitchen
Nourishing, Big-Flavor Recipes for Cancer Treatment and Recovery
THE CURE
HEAL YOUR BODY, SAVE YOUR LIFE
DR. TIMOTHY BRANTLEY
Click to LOOK INSIDE
Nature's Cancer-Fighting Foods
Prevent and Reverse the Most Common Forms of Cancer Using the Proven Power of Great Food and Easy Recipes
Verne Varona


Zola
BRAZILIAN SUPERFRUITS
Energy SMOOTHIE
Immunity SMOOTHIE
Antioxidant SMOOTHIE
Superfood SMOOTHIE
Açaí with pineapple JUICE
Açaí original JUICE
Açaí with blueberry JUICE


Eating for life
anti-cancer foods


ORGANIC SINCE 1957
USDA ORGANIC
Biotta
BEET JUICE
FOR YOUR IMMUNE SYSTEM


Acai Berries and Cancer
www.AcaiAdvisors.com
www.AcaiAdvisors.com


GOJI POWER
Himalayan Superfruit


Acai Berry
Purple Grape
Pomegranate
White Grape
Bilberry
Lychee
Passion Fruit
Pear
Wolfberry
Banana
Blueberry
Acerola
Kiwi
Camu Camu
Cranberry
Aronia
Apricot
Nashi
Prune


THE MOST POWERFULL and potent acai berry available
MAXIMUM STRENGTH FORMULA
PURE ACAI BERRY
1500mg of high grade Acai Berry per serving
Certified organic with a high ORAC rating
60 capsules
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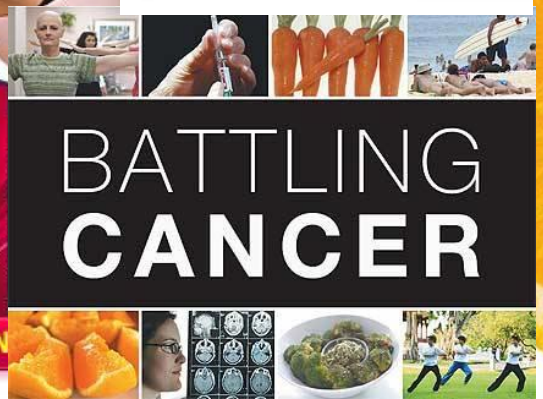
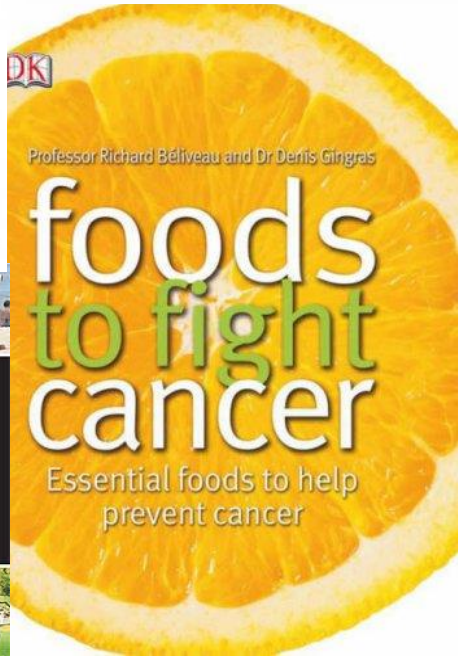
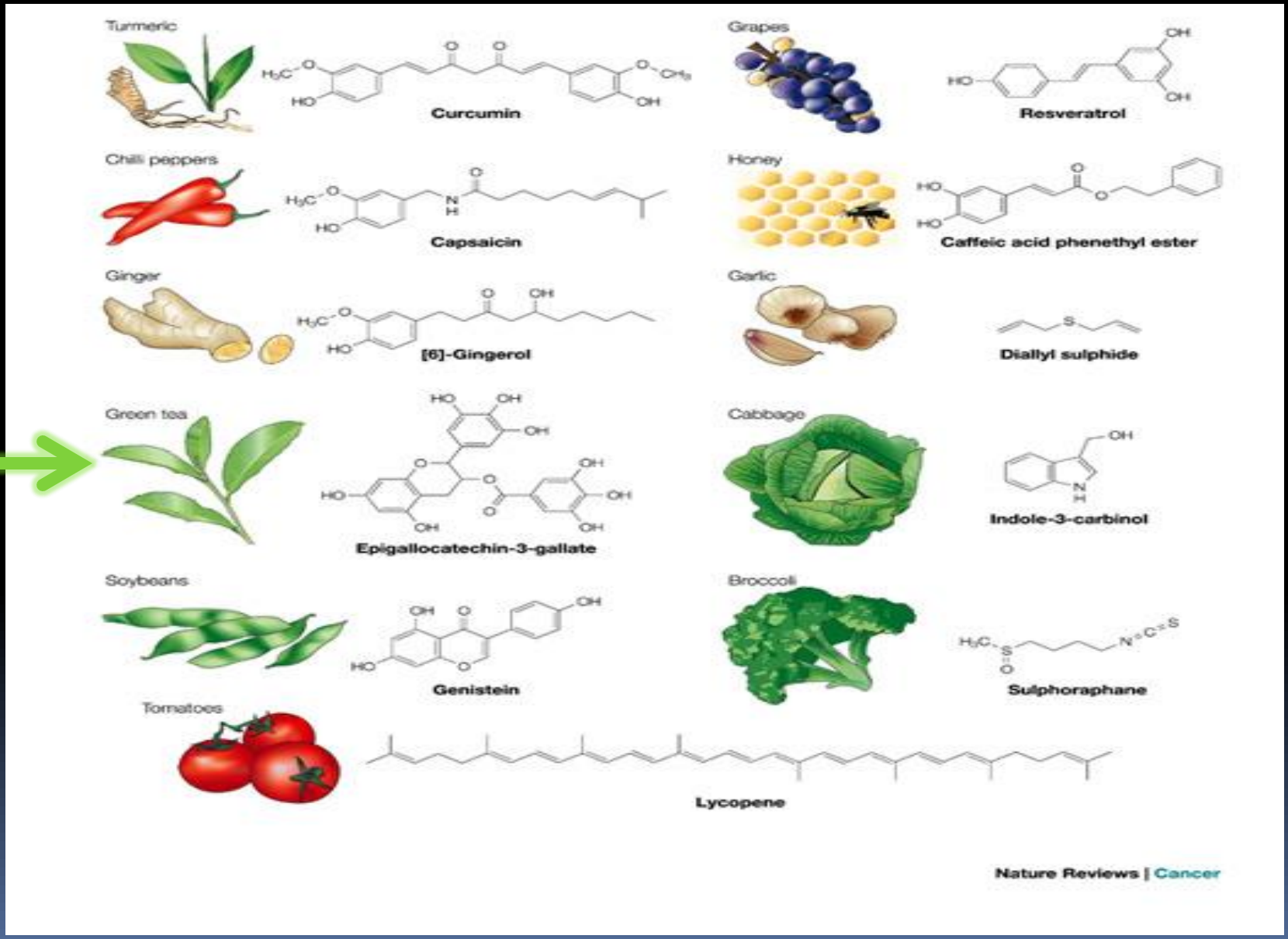
ULTIMATE MAQUI BERRY
Maximum Strength

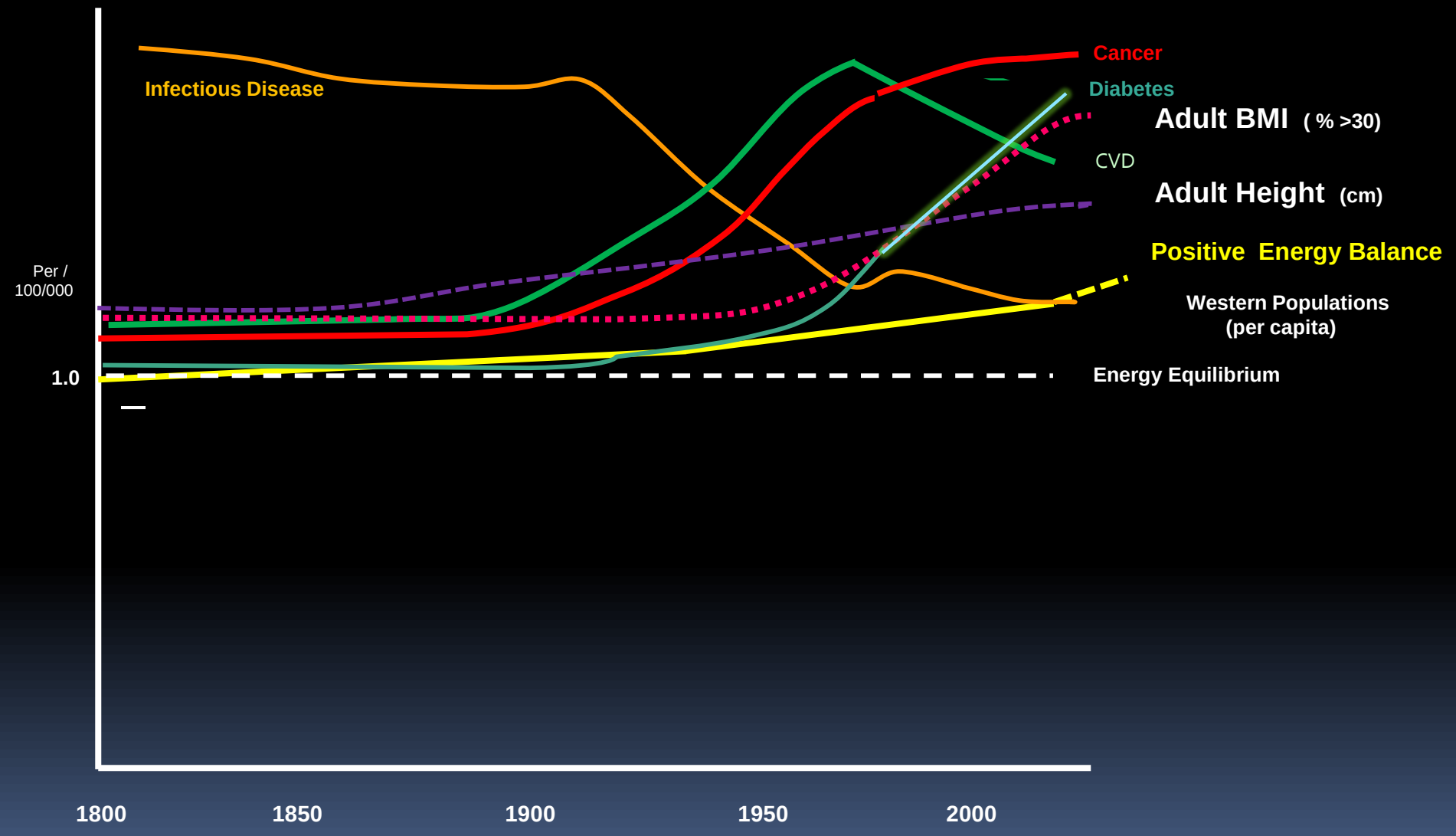

BATTLING CANCER


DK
Professor Richard Béliveau and Dr Denis Gingras
foods to fight cancer
Essential foods to help prevent cancer

Phytonutrients and Cancer



Origins of the Era of Chronic Metabolic Disease



Variation in **cancer risk** among tissues can be explained by the **number of tissue stem cell divisions in a lifetime**

FAP colorectal

*"The total number of stem cells in an organ and their proliferation may, of course, be influenced by genetic and environmental factors such as those that affect **height and weight**"*

Tomasetti , Vogelstein

Fundamental endocrine driver of height and weight- ***Insulin – IGF system***

Explains the **epidemiology** of cancer
Over time
Geographic Disparity
Nutrition transition

Total Tissue Stem Cell Divisions

C Tomasetti B Vogelstein. Variation in cancer risk among tissues can be explained by the number of stem cell divisions Science 347;(6217):78-81, 2015

Variation in **cancer risk** among tissues can be explained by the **number of tissue stem cell divisions in a lifetime**

FAP colorectal

20th Century Cancers:
Breast, Endometrial, Ovarian, Prostate,Pancreas,Colorectal

What features do they share?

All Hormonally Influenced
Endocrine hormones drive stem cell proliferation
*(Estrogen, Progesterone, Testosterone, and **INSULIN**)*

Enhanced stem proliferation by GF's increase both total stem cell divisions and may increase mutation rate per cell division

Total Tissue Stem Cell Divisions

C Tomasetti B Vogelstein. Variation in cancer risk among tissues can be explained by the number of stem cell divisions Science 347;(6217):78-81, 2015

What Do Traditional Early Human Societies Share ?

Australian Aborigine

Masaii

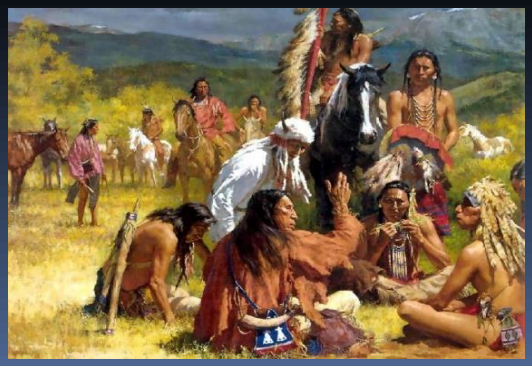
Kung bushman

Mongol Herdsman

Inuit

Asian

Yanamamo



Native American

Pastoralist- Crete

High Cancer Risk Populations

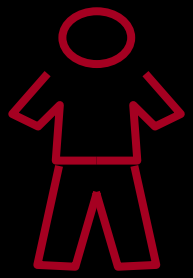
Modern Western Man

vs.

Early Man

Energy Balance and Cancer

The 4th Paradigm – 2000's to Present



Energy in | Energy out

- Amount
- Type
- Pattern

Energy Balance:

kcal in = kcal out

- Physical Activity
- Routine Metabolism
- Thermoregulation
- Growth
- Storage

Air, Food and Exercise

Rabagliatti (19th Century)

“ Overfeeding is the predisposing cause of cancer”

Caloric Restriction Increases Longevity in All Organisms

EARLY CHILDHOOD INFLUENCES

- **AGING, INSULIN, AND CANCER**

Caloric Restriction Limits Tumor Growth

Tannenbaum, 1940

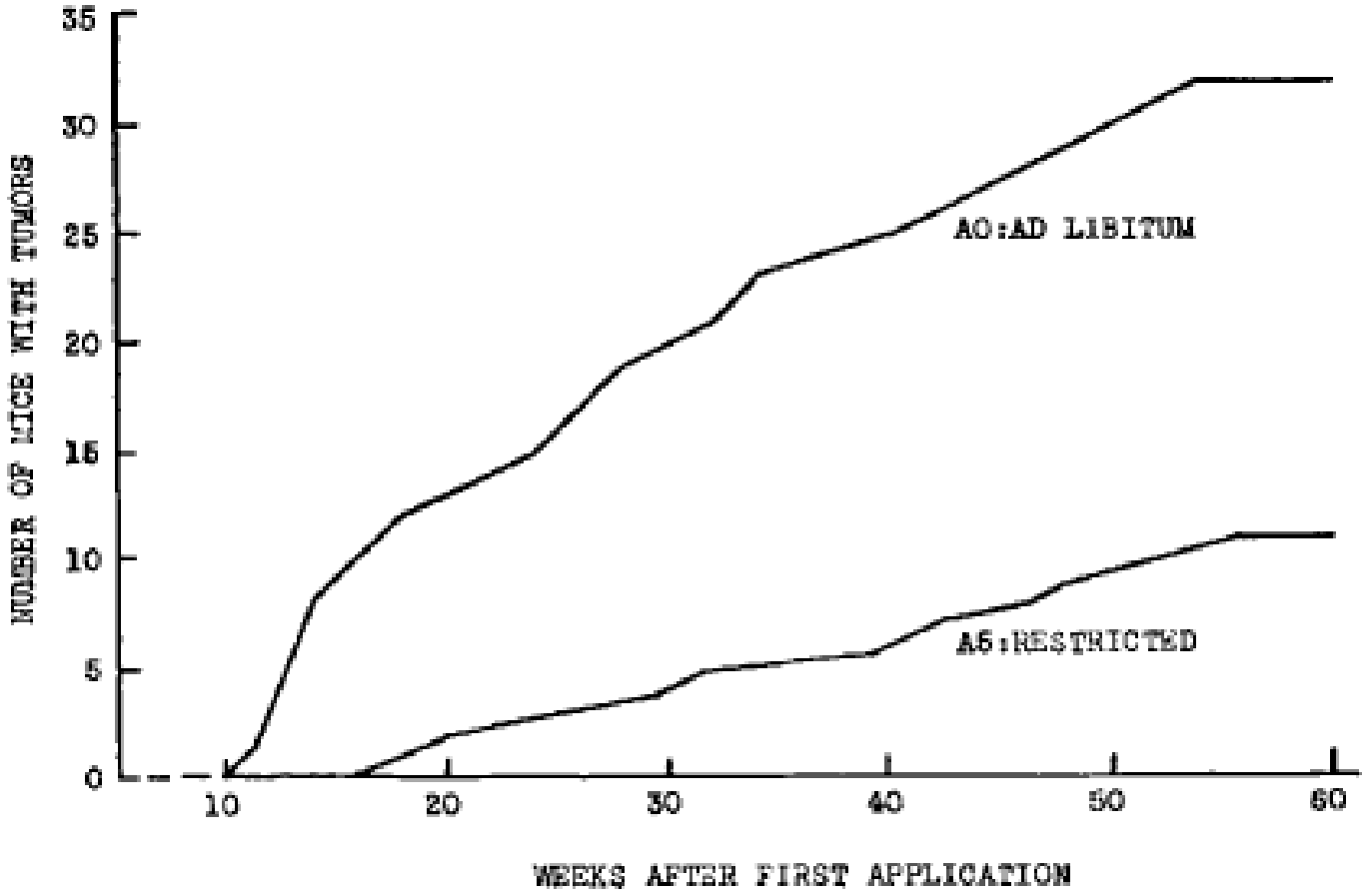
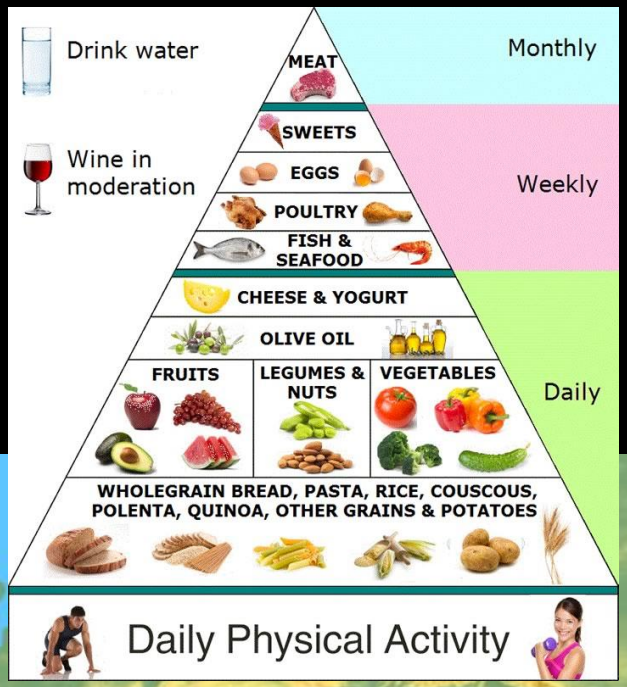


FIG. 1.—Inhibition of the formation of induced epithelial tumors by means of a caloric-restricted diet. Curve of cumulative number of tumors. Time in weeks after first application

Mediterranean Diet and Health: Are we missing something?



Greek Orthodox fasting rituals: a hidden characteristic of the Mediterranean diet of Crete

Sarri K A, Linardakis M K, Bervanaki F N, Tzanakis N E and Kafatos A G
University of Crete, School of Medicine, Iraklion 71003, Crete, Greece

- The Mediterranean diet of Crete -protective for CHD, DM and some cancers (Keys, 1980) – The "Original Mediterranean Diet Studies"
- Confirmed in the Seven Countries Study - Crete had the lowest CHD mortality rate and the longest life expectancy (Ancel Keys)
- Diet of Crete (early 1960s):

  Wheat-based products, legumes, abundant seasonal fruits and vegetables

  Moderate dairy-product consumption, Limited meat and fish consumption

  Olive oil and olives - main fat source
- The Orthodox Church specifies dietary restrictions, *fasted 180–200 days/yr*

The Mediterranean Diet Studies have not accounted for the role of ritual fasting in these populations (Christian, Muslim, Jewish)

Energy Balance across the Life Course

- Excess calorie intake and reduced calorie burning (activity)

Childhood Energy Imbalance

- In pregnancy (maternal diet) and early childhood

→ *Increase in childhood growth in height*

Adult Energy Imbalance

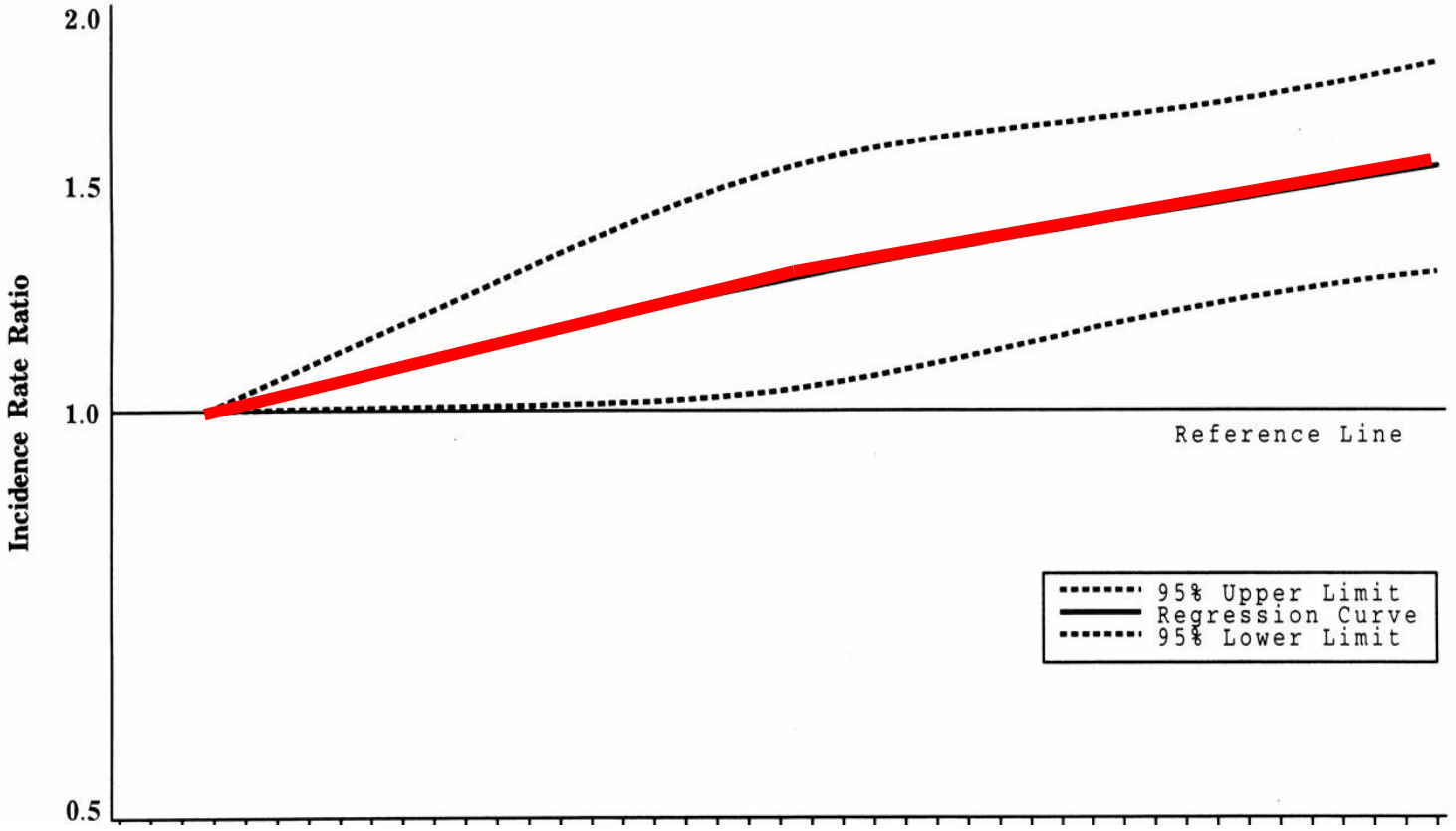
- In adolescence and adulthood

→ *Increase in body weight, obesity*

Increased Breast Cancer Risk Increasing Height

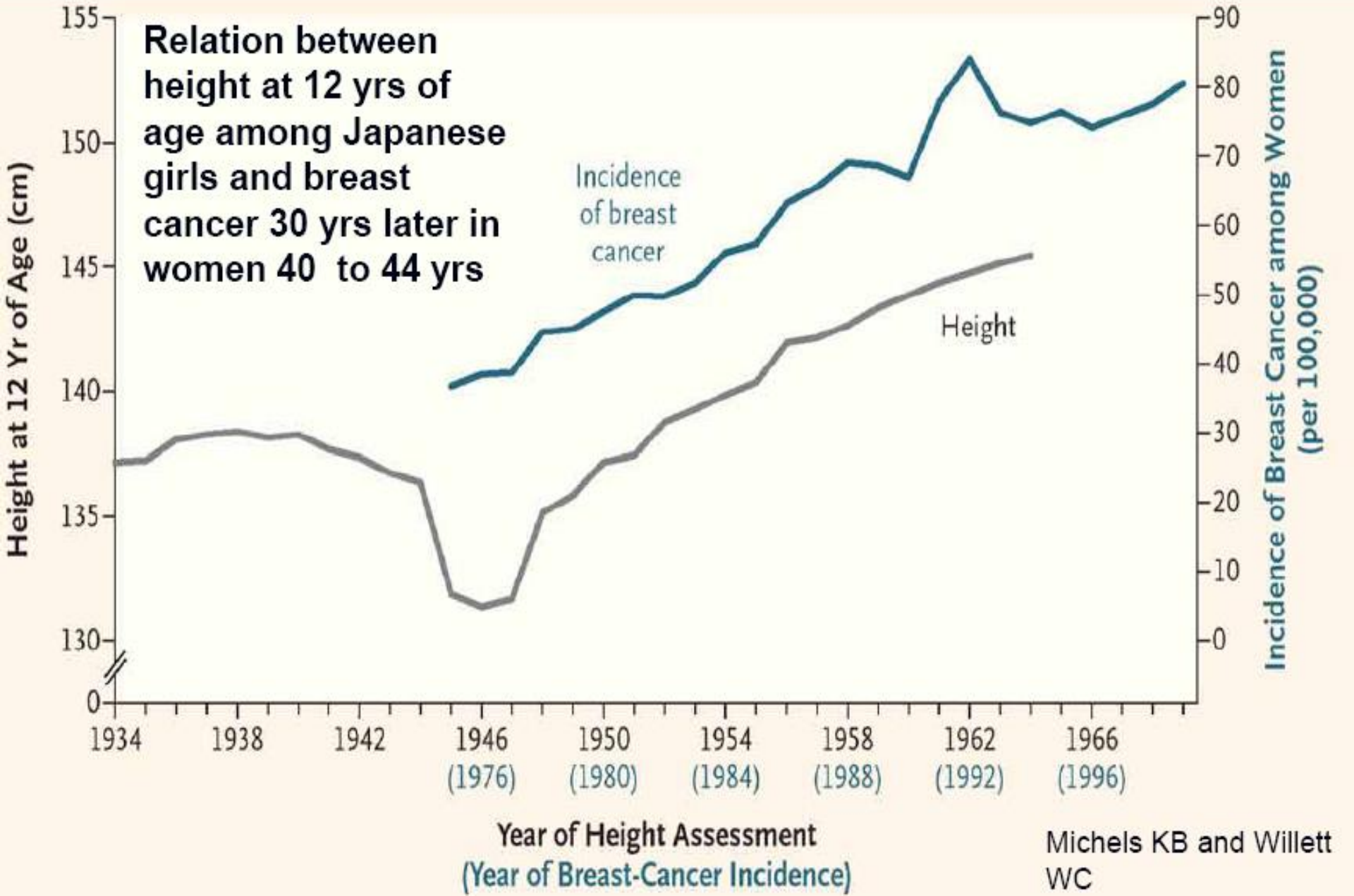
EARLY CHILDHOOD INFLUENCES

- AGING, INSULIN, AND CANCER
- **HEIGHT and CANCER RISK**

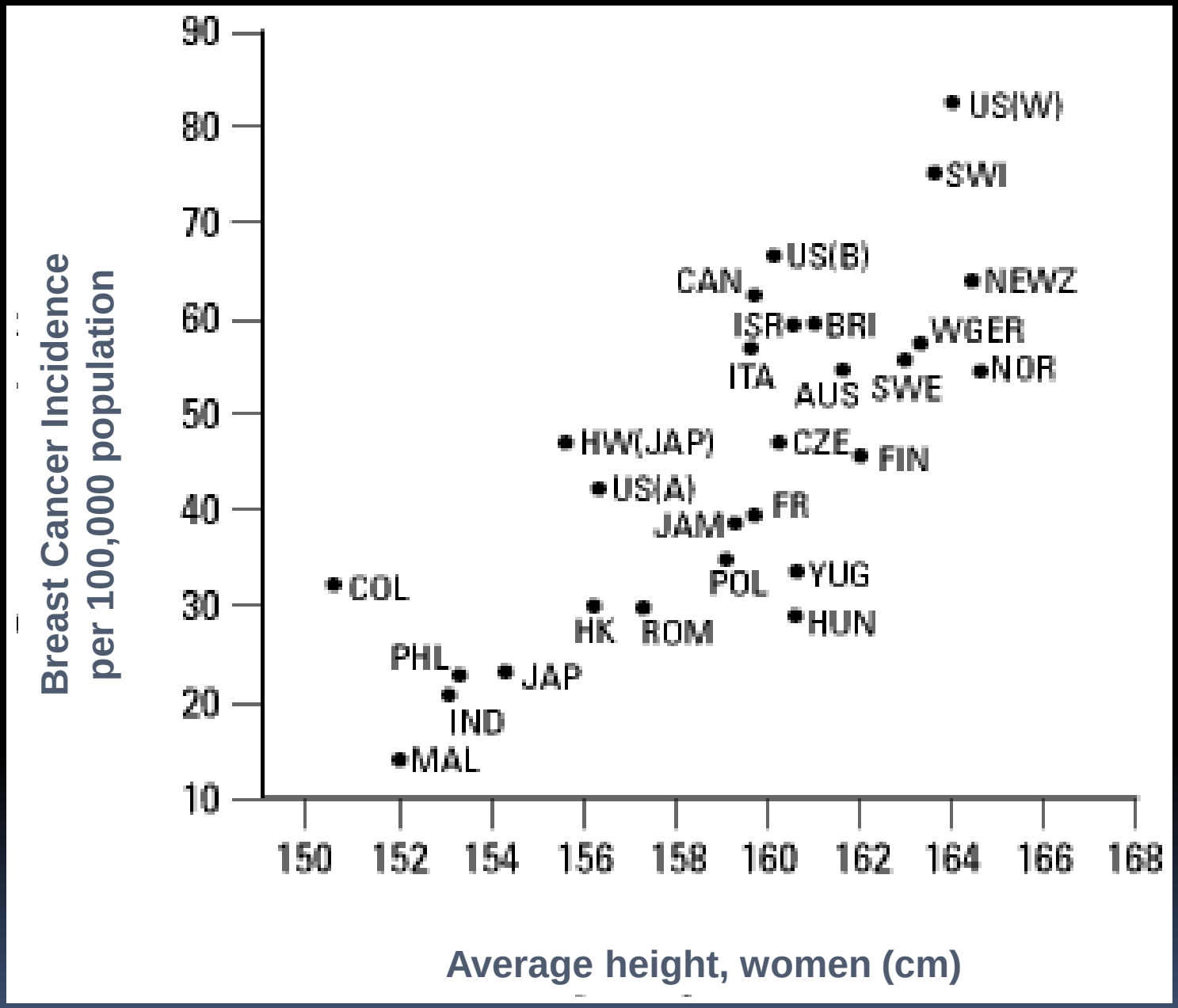


Pooled Analysis of Prospective Cohort Studies on Height, Weight, and Breast Cancer Risk

Breast Cancer – Early Life Matters



Michels KB and Willett WC

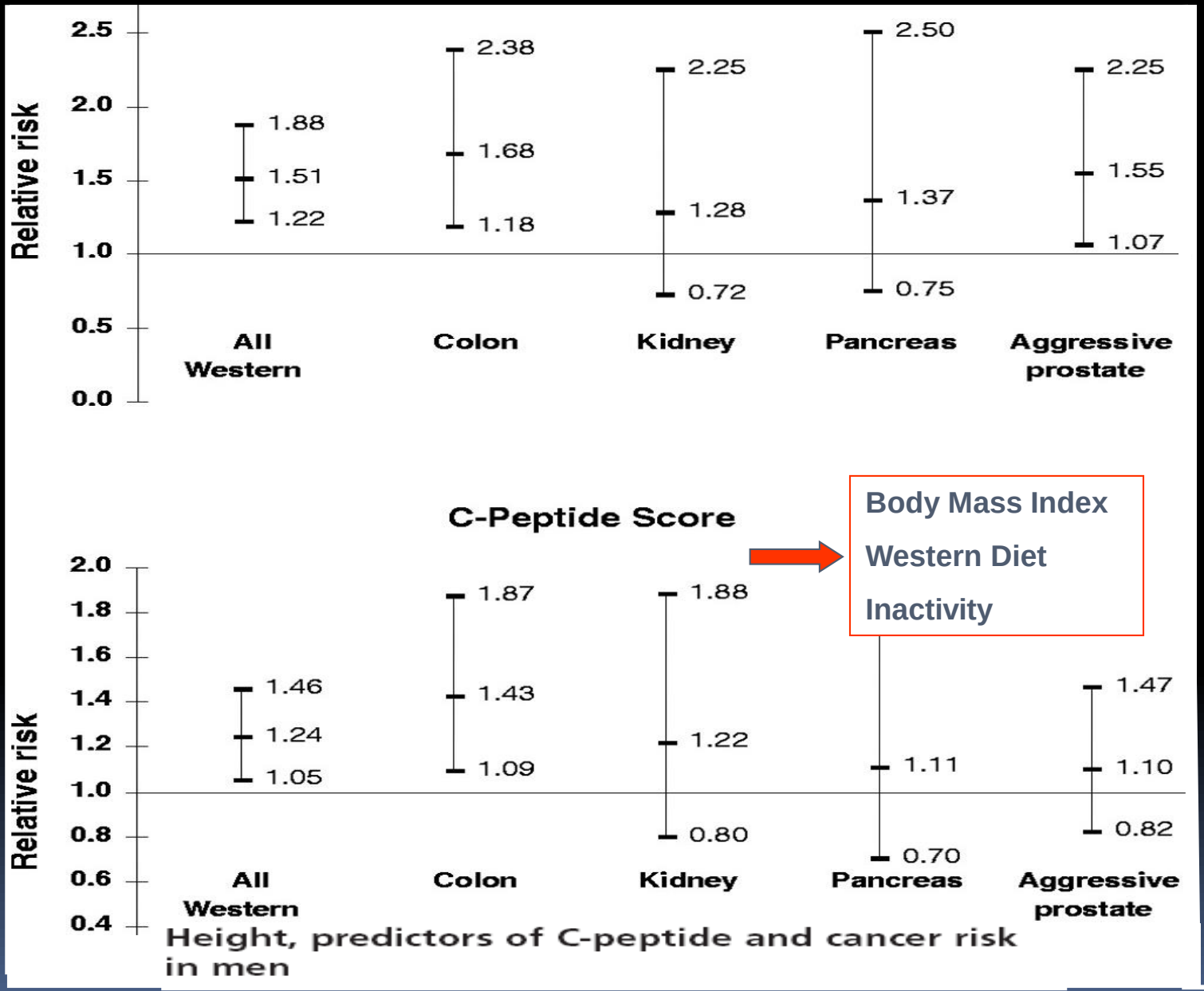


Per Capita Height correlates with Breast Cancer Risk

Height and C-Peptide Score vs. Cancer Risk in Men

EARLY CHILDHOOD INFLUENCES

- AGING, INSULIN, AND CANCER
- **HEIGHT and CANCER RISK**



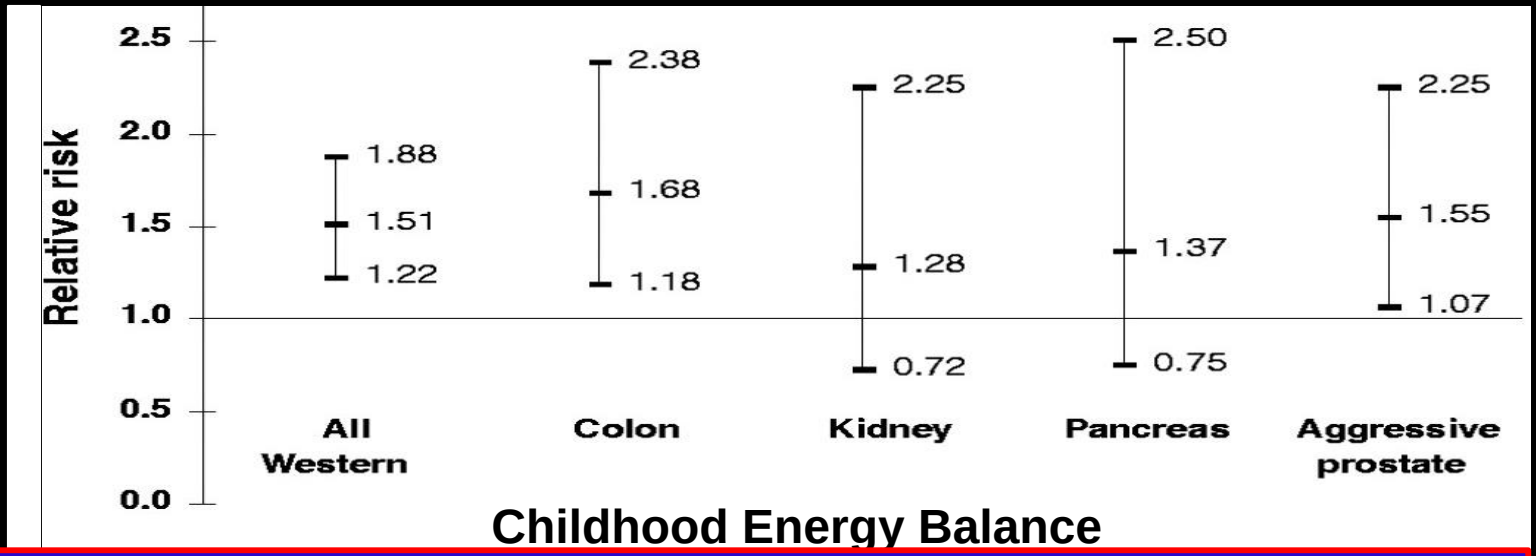
Height, predictors of C-peptide and cancer risk in men

Giovannucci E et al Int J Epidemiol 33(1): 217-225, 2004

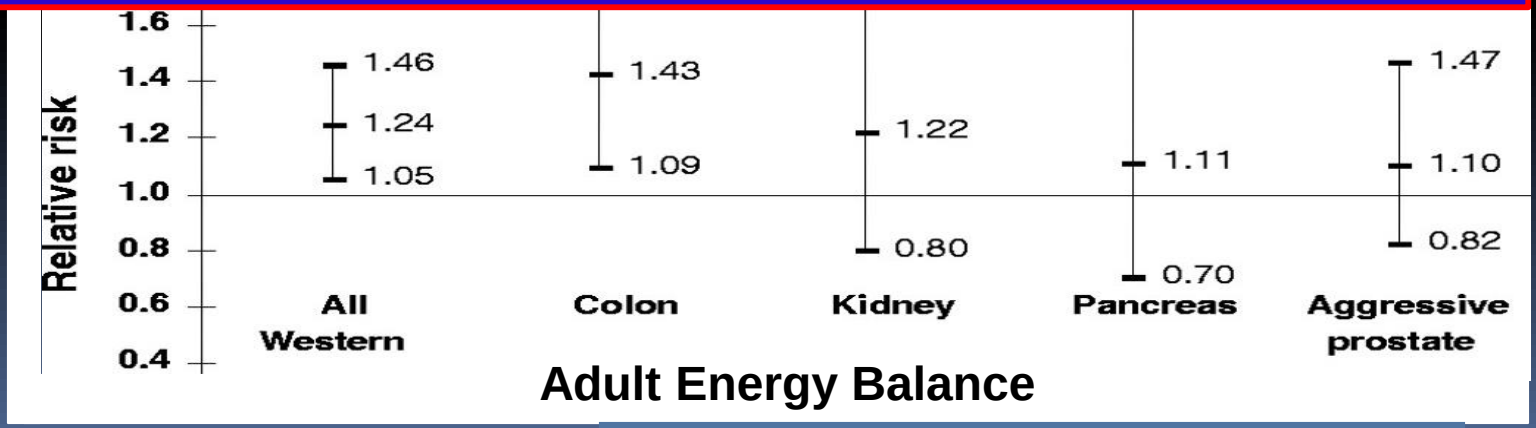
Height and C-Peptide Score vs. Cancer Risk in Men

EARLY CHILDHOOD INFLUENCES

- AGING, INSULIN, AND CANCER
- **HEIGHT and CANCER RISK**



Over 50% of cancer risk of "Western Cancers" explained by combination of positive early childhood energy balance (height) and positive adult energy balance (increased weight–related IR)



Giovannucci E et al Int J Epidemiol 33(1): 217-225, 2004

Childhood Growth and Risk

Height has increased *on average 3 inches* in Western populations in last 150 years

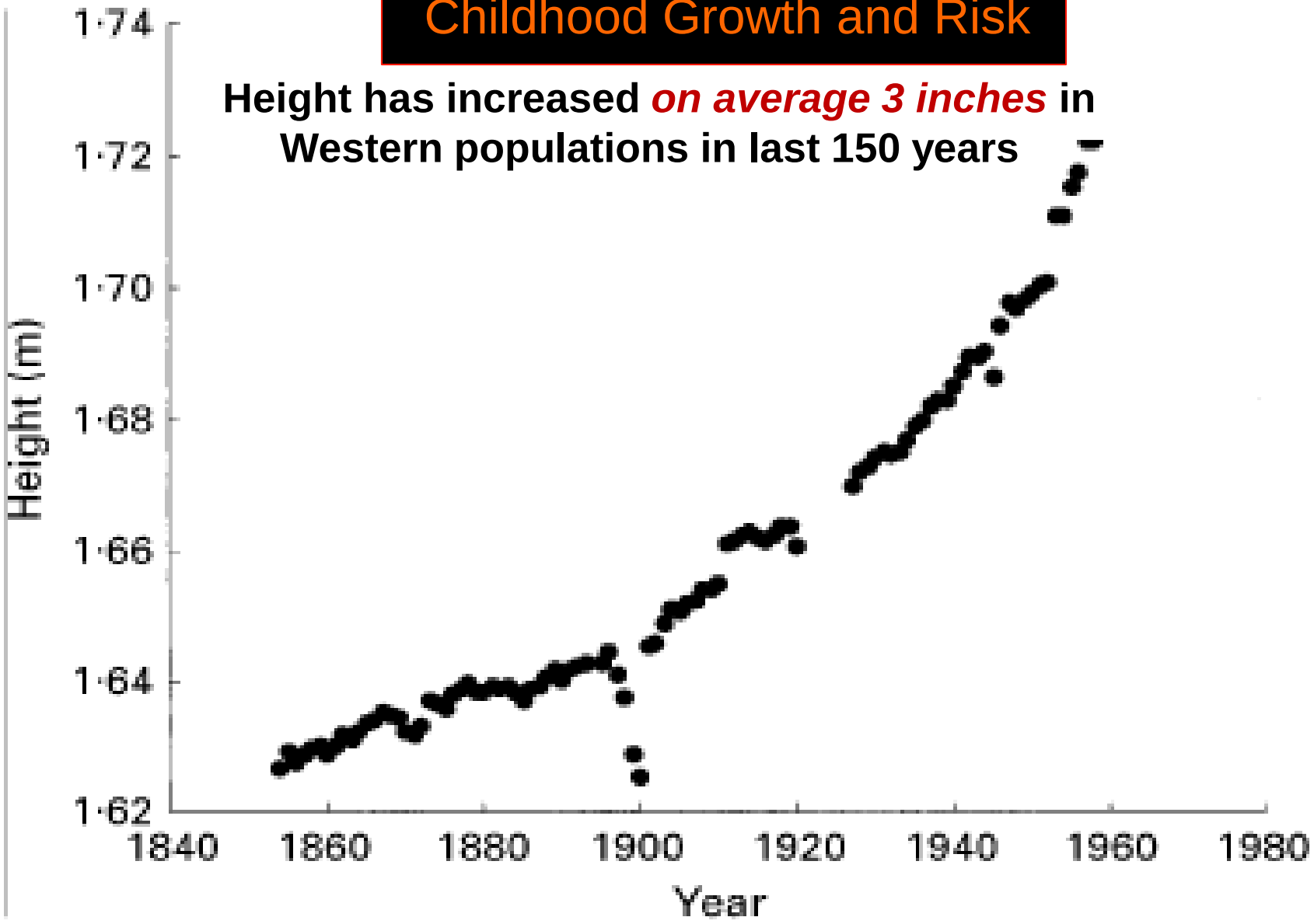


Fig. 1. Mean height in Italian conscripts from 1854 to 1963. (From Hermanussen *et al.* 1995)

Are Cell Number and Cell Proliferation Risk Factors for Cancer?[1]

Demetrius Albanes,[2] *Myron Winick*[3]

Relatively little is known about the mechanisms underlying carcinogenesis in humans. ***Caloric restriction strongly inhibits the development of neoplasia*** in rodents, and there is evidence of a ***positive relationship between cancer and body weight in humans***. **Caloric restriction** early in life is also known to ***permanently diminish organ cellularity***.

A ***recent link between adult stature and cancer incidence similarly implicates a lasting effect for growth and possibly for early nutrition in carcinogenesis***. It is postulated that ***cancer risk is proportional to the number of proliferating cells***, which in turn ***depends on both the number of cells and the rate of cell division within the tissue***. This hypothesis is consistent with several aspects of human carcinogenesis, including multistage models and the epithelial origin of most cancers.

J Natl Cancer Inst 1988; 772-775

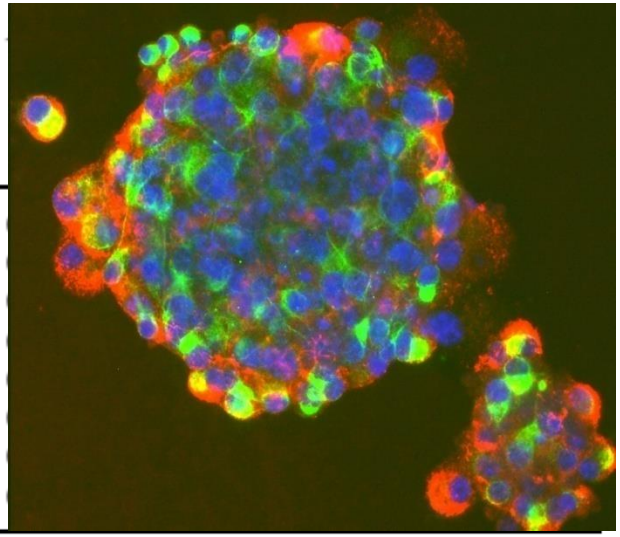
Association of Fetal Hormone Levels with Stem Cell Potential: Evidence for Early Life Roots of Human Cancer

Inkyung Baik,[1,4] William J. DeVito,[1] Karen Ballen,[5] Pamela S. Becker,[7] William Okulicz,[2] Qin Liu,[1] Ellen Delpapa,[3] Pagona Lagiou,[8] Susan Sturgeon,[4] Dimitrios Trichopoulos,[6] Peter J. Quesenberry,[9] and Chung-Cheng Hsieh[1]

[1]Cancer Research Center and Department of Cancer Biology and [2]Department of Physiology, ILAT Steroid RIA Laboratory, University of Massachusetts Medical School; [3]Department of Obstetrics and Gynecology, University of Massachusetts Memorial Medical Center, Worcester, Massachusetts; [4]Department of Biostatistics and Epidemiology, University of Massachusetts, Amherst, Massachusetts; [5]Division of Hematology and Oncology, Massachusetts General Hospital; [6]Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts; [7]Division of Hematology, University of Washington, Seattle, Washington; [8]Department of Hygiene and Epidemiology, School of Medicine, University of Athens, Athens, Greece; and [9]Department of Research, Roger Williams Medical Center, Providence, Rhode Island

Cord Blood Stem Cells highly correlated with IGF-1

Hormones	% Change (95% confidence interval)	*P*	% Change (95% confidence interval)
	$CD34^+$ cells/10^3 MNC		$CD34^+$ $CD38^-$ cells/10^3 MNC
Estradiol	9.5 (−11.8 to 35.9)	0.40	38.0 (−9.8 to 111.2)
Estriol	30.5 (8.8, 56.4)	0.006	34.4 (−10.4 to 101.4)
Testosterone	22.6 (1.6, 47.9)	0.04	30.5 (−12.4 to 94.4)
SHBG	−1.4 (−22.0 to 24.5)	0.90	53.1 (−1.8 to 138.7)
Progesterone	7.4 (−14.2 to 34.3)	0.52	51.1 (−1.6 to 132.1)
Prolactin	−4.0 (−25.2 to 23.3)	0.74	−21.1 (−52.1 to 29.9)
IGF-I	**40%** 10.0, 80.5)	0.008	**108%** (27.6, 241.7)
IGFBP-3	32.3 (5.0, 66.7)	0.02	97.3 (26.3, 208.1)

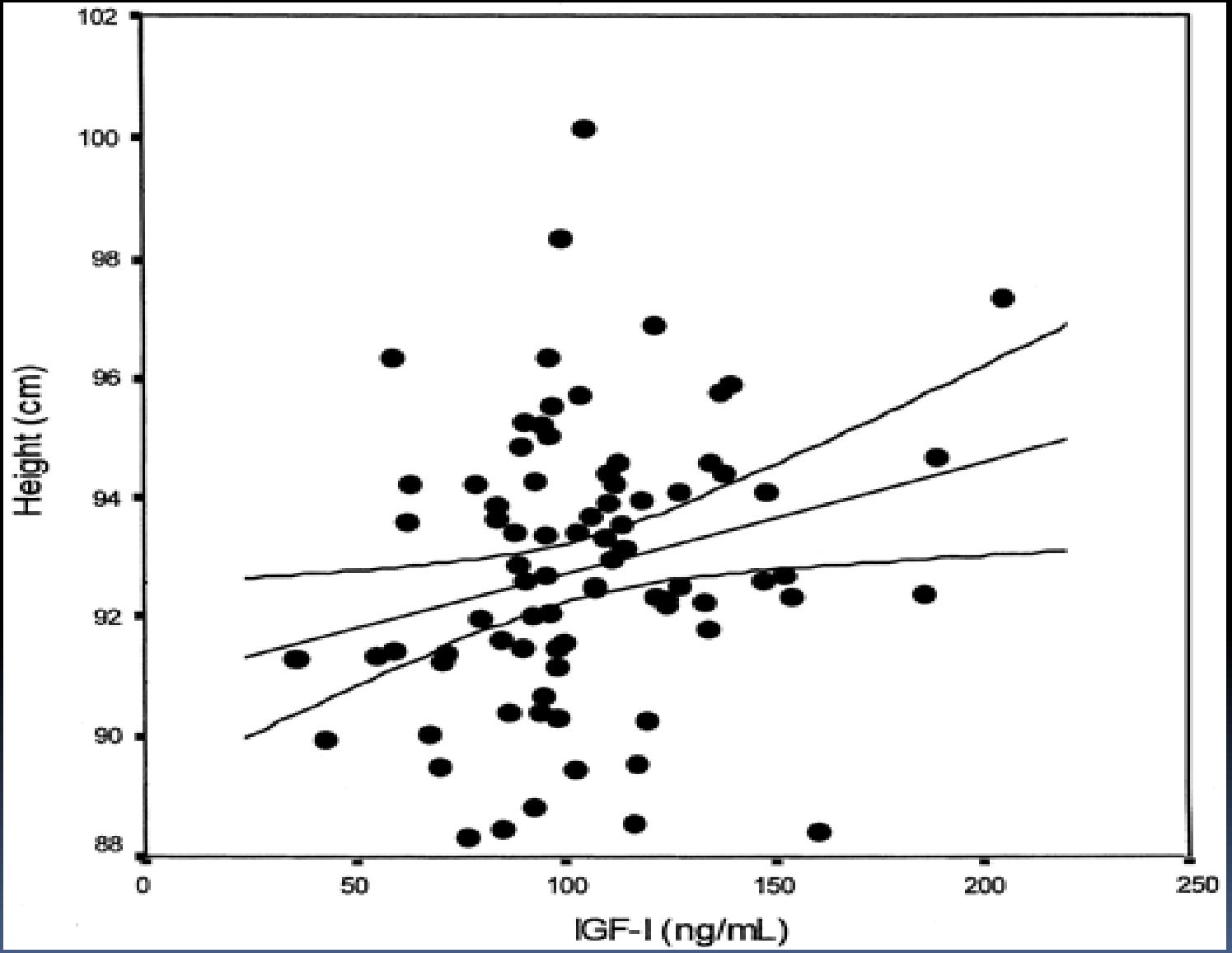


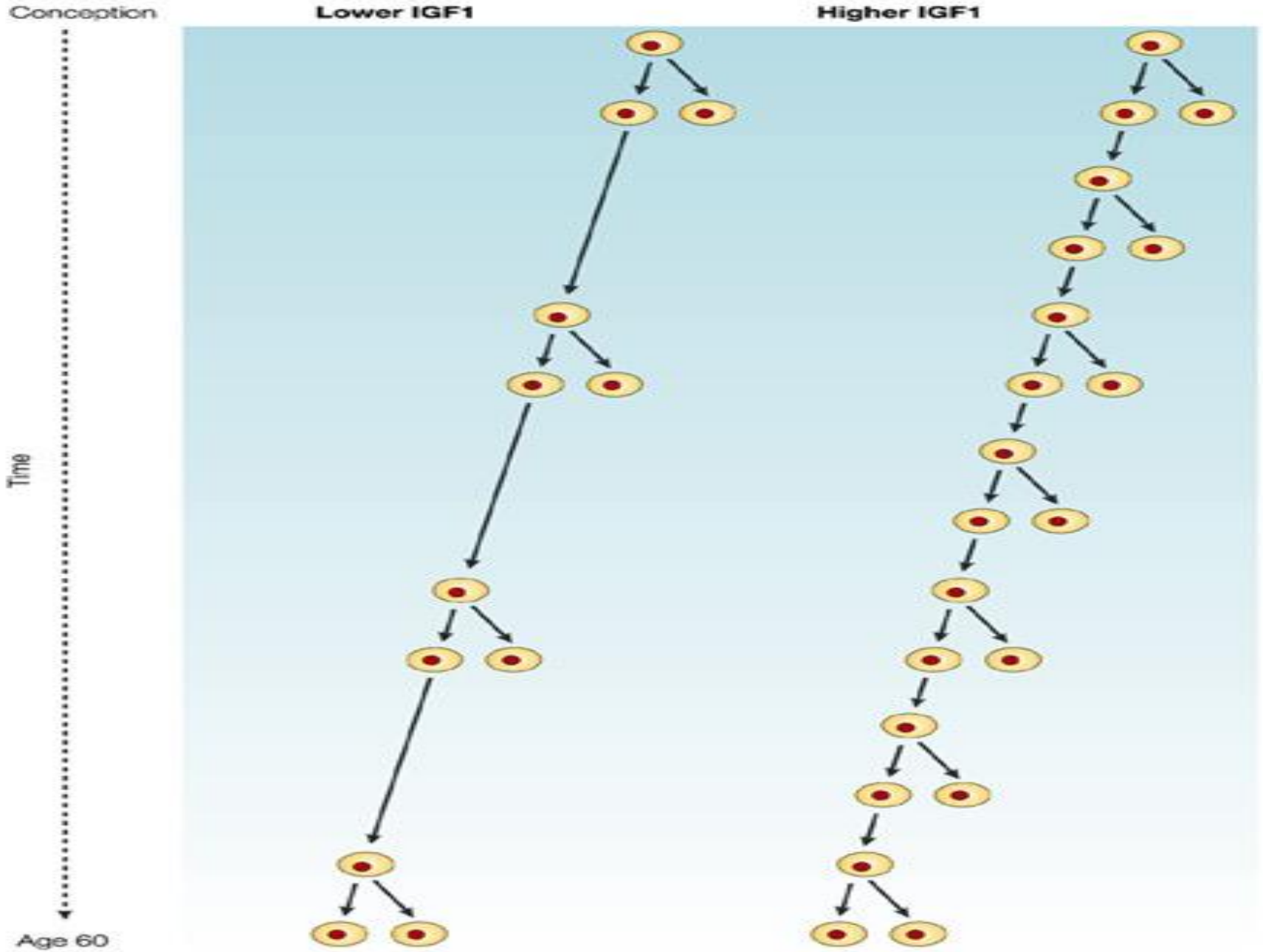
NOTE: From multiple regression model, adjusting for mother's age, race of parents, number of live births, gestation duration, gender of baby, delivery time, and birth weight of baby. % Change: expected proportional change in dependent variable associated with 1 SD increase per independent variable. *P*s for the estimated coefficients.

Adult Height Correlated with Increased IGF-1

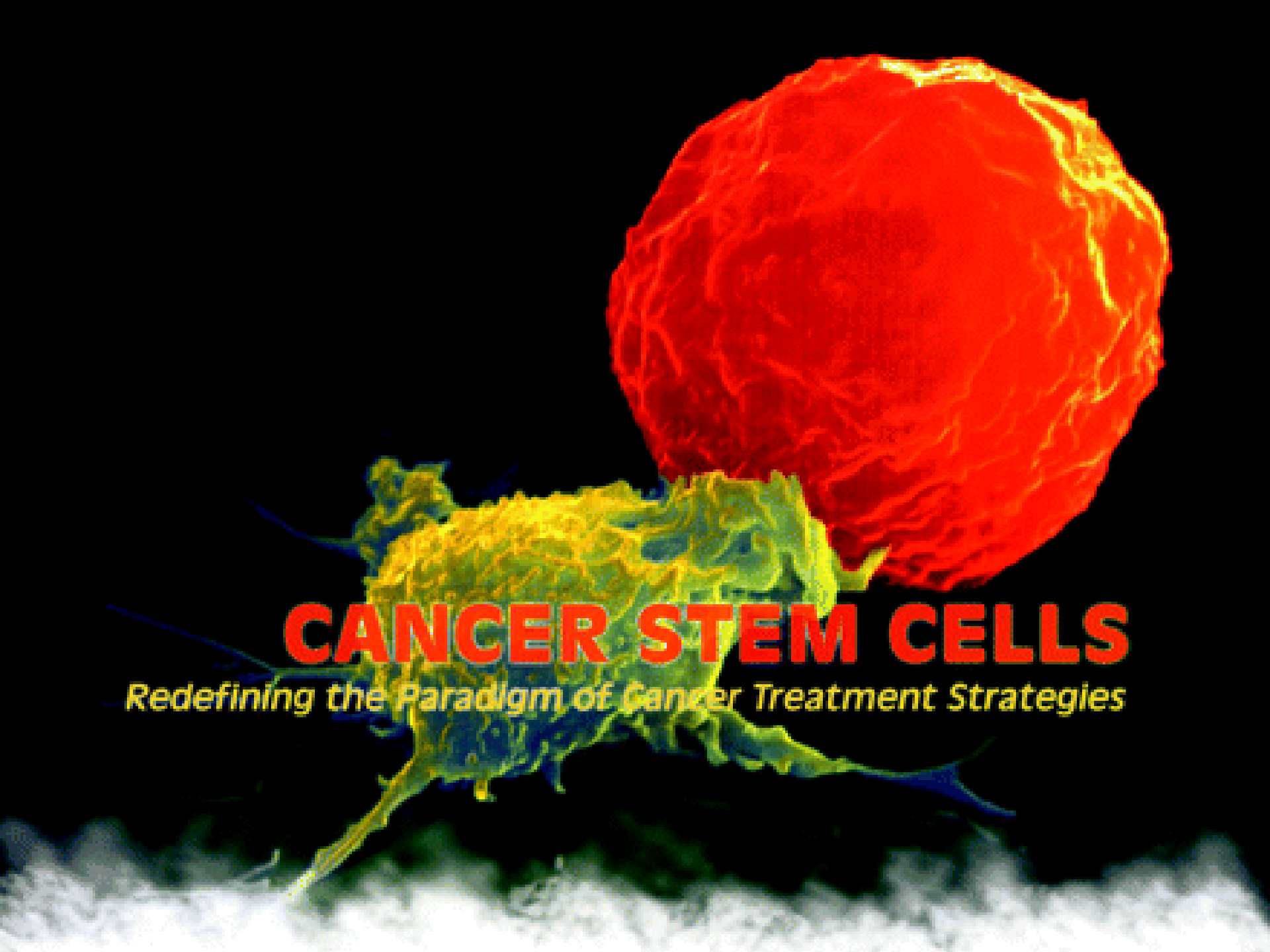
EARLY CHILDHOOD INFLUENCES

- AGING, INSULIN, AND CANCER
- **HEIGHT and CANCER RISK**

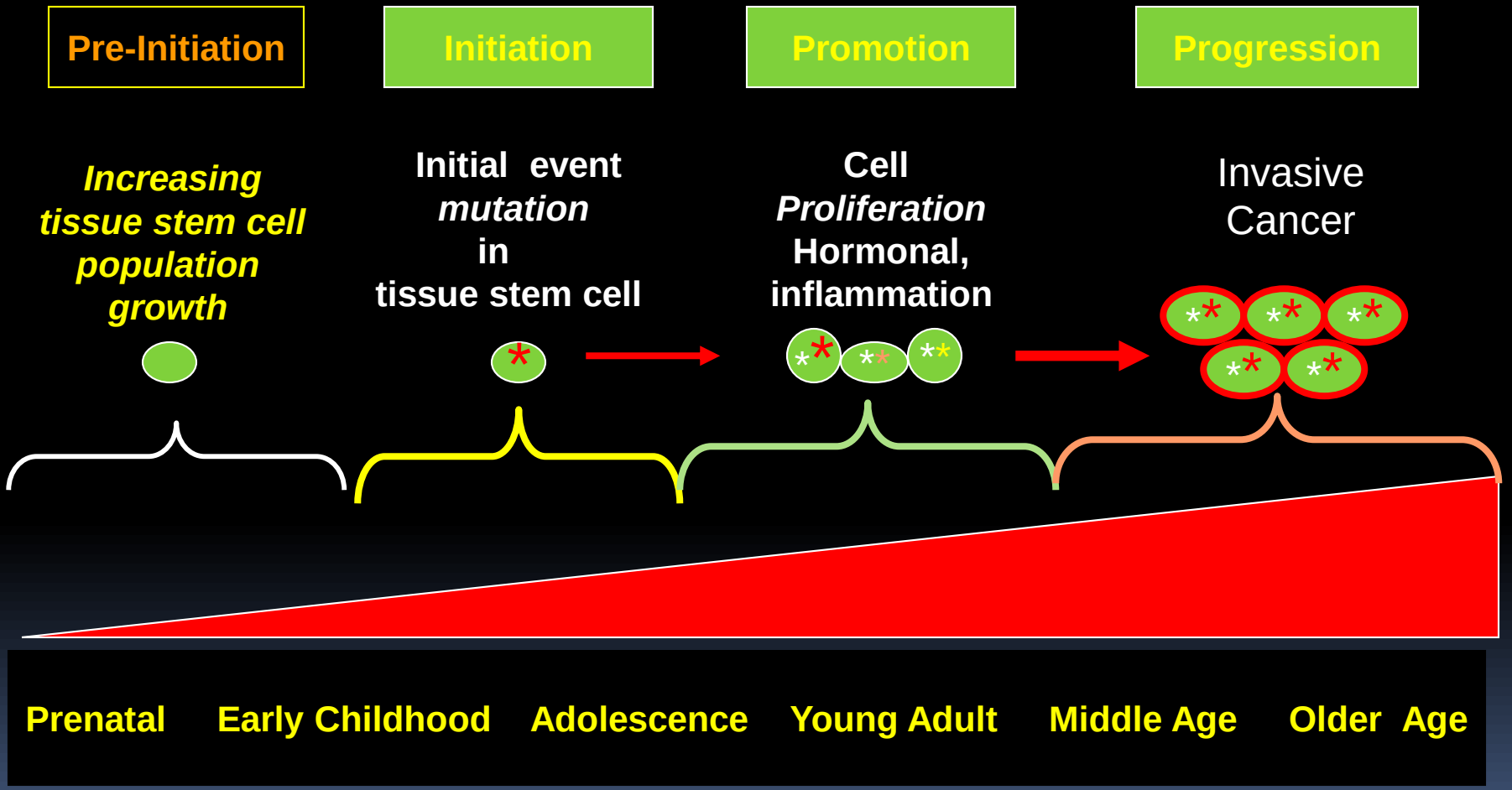


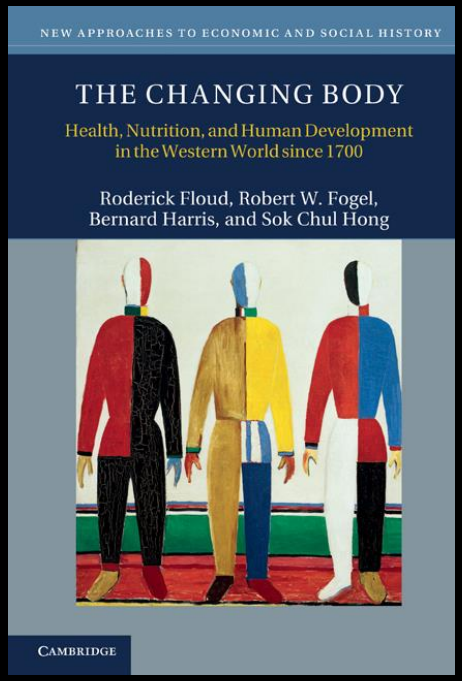


Nature Reviews | Cancer


CANCER STEM CELLS
Redefining the Paradigm of Cancer Treatment Strategies

Evolution of Adult Cancer





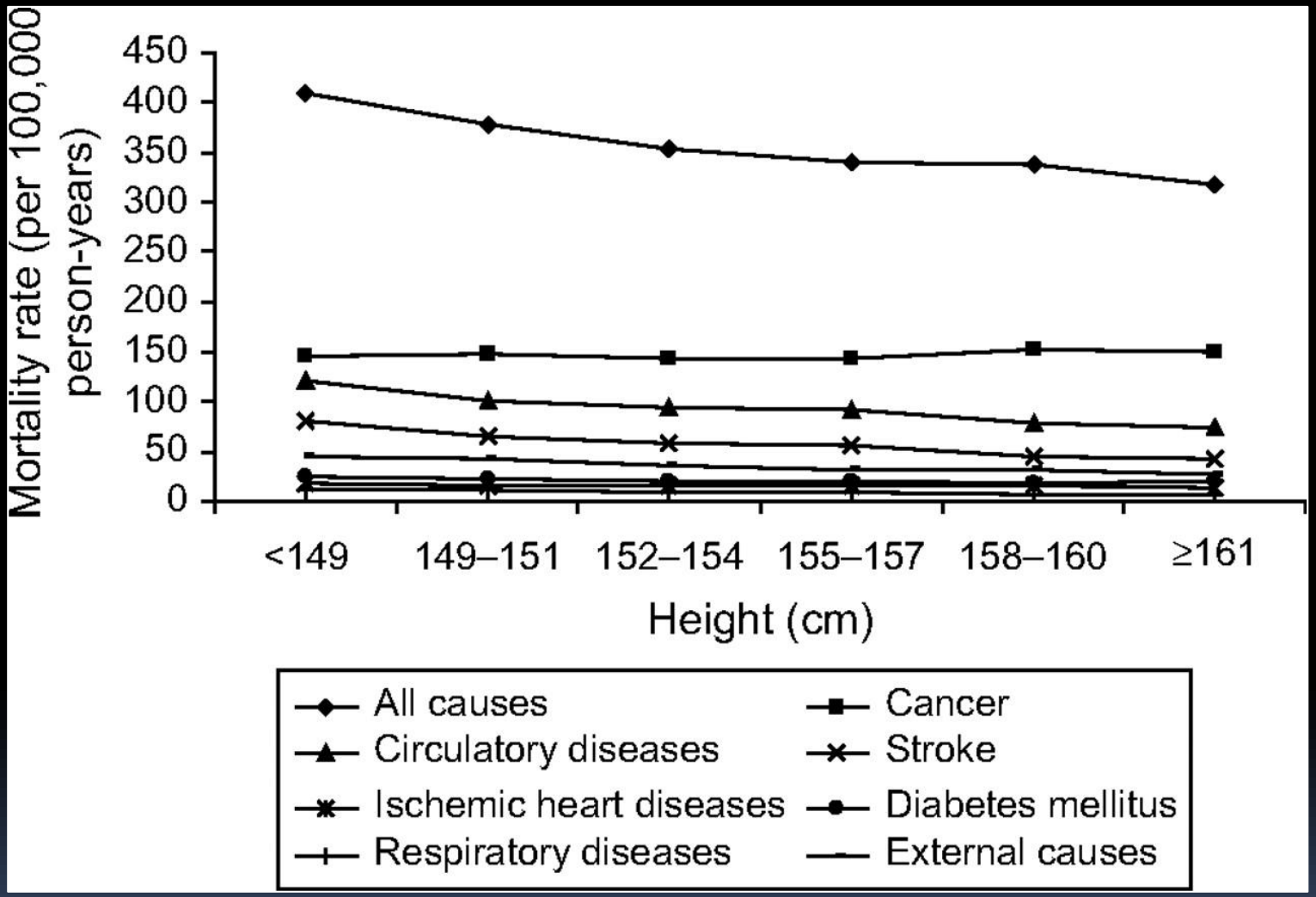
Robert W. Fogel

The Changing Body: Health, Nutrition, and Human Development in the Western World since 1700

Sir Roderick Floud, Robert W. Fogel, Bernard Harris and Sok Chul Hong

" The health and nutrition of one generation contributes, through mothers and through infant and childhood experience, to the strength, health and longevity of the next generation; at the same time, increased health and longevity enable the members of that next generation to work harder and longer to create the resources which can then, in their turn, be used to assist the next, and succeeding, generations to prosper."

Height is associated with decreased overall and cardiovascular mortality



Age-adjusted rate of mortality (per 100,000 person-years) from all causes and specific causes, by height, South Korea, 1994–2004.

Song Y , Sung J Am. J. Epidemiol. 2008;168:497-505

Dutch men revealed as world's tallest

The nations with the tallest men in 2014 (1914 ranking in brackets):

1.Netherlands (12)
2.Belgium (33)
3.Estonia (4)
4.Latvia (13)
5.Denmark (9)
6.Bosnia and Herzegovina (19)
7.Croatia (22)
8.Serbia (30)
9.Iceland (6)
10.Czech Republic (24)

37.US (3)

The nations with the tallest women in 2014 (1914 ranking in brackets):

1.Latvia (28)
2.Netherlands (38)
3.Estonia (16)
4.Czech Republic (69)
5.Serbia (93)
6.Slovakia (26)
7.Denmark (11)
8.Lithuania (41)
9.Belarus (42)
10.Ukraine (43)

42. US (4)

Tall people: 1) Longer life expectancy
2) Reduced risk of heart disease
3) Greater overall longevity
4) Greater socioeconomic status
5) Increased cancer risk (colorectal, post-menopausal breast, ovarian cancers

The Other Side of the Energy Equation- **Adult Weight Gain and Obesity**

Energy Balance across the Life Course

- Excess calorie intake and reduced calorie burning (activity)

Childhood Energy Imbalance

- In pregnancy (maternal diet) and early childhood

→ *Increase in childhood growth in height*

Adult Energy Imbalance

- In adolescence and adulthood

→ *Increase in body weight, obesity*

Overweight, Obesity, and Mortality from Cancer in a Prospectively Studied Cohort of U.S. Adults

OBESITY

- **CANCER MORTALITY**
- BIOLOGY
- METABOLIC SYNDROME

Eugenia E. Calle, Ph.D., Carmen Rodriguez, M.D.,M.P.H., Kimberly Walker-Thurmond, B.A. and Michael J. Thun, M.D.

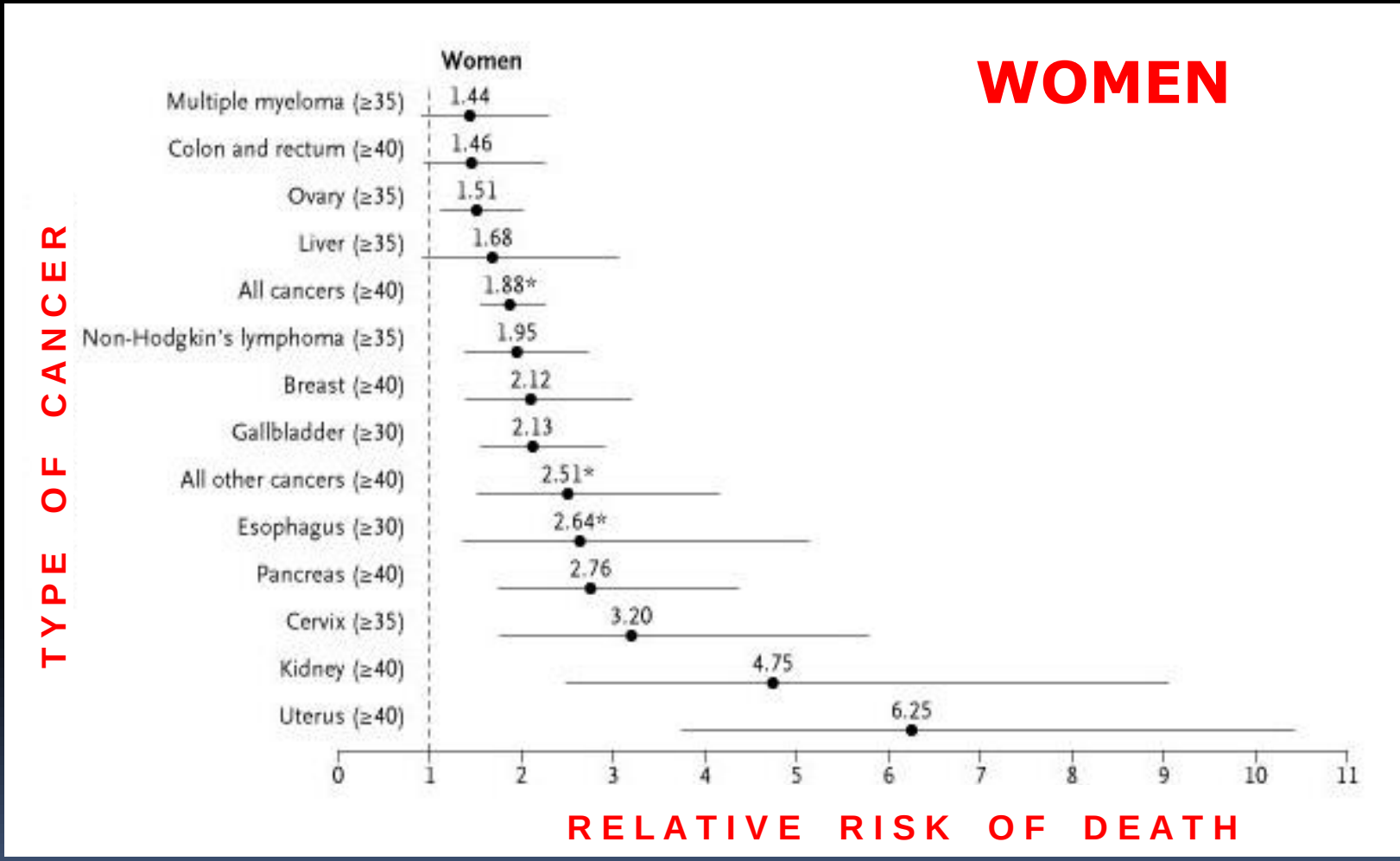
Volume 348;17:1625-1638
April 24, 2003

Summary of Mortality from Cancer According to Body-Mass Index*

U.S. Women in the Cancer Prevention Study II, 1982 through 1998

OBESITY

- **CANCER MORTALITY**
- BIOLOGY
- METABOLIC SYNDROME



*Highest body BMI category

Summary of Mortality from Cancer According to Body-Mass Index*

U.S. Men in the Cancer Prevention Study II, 1982 through 1998

OBESITY

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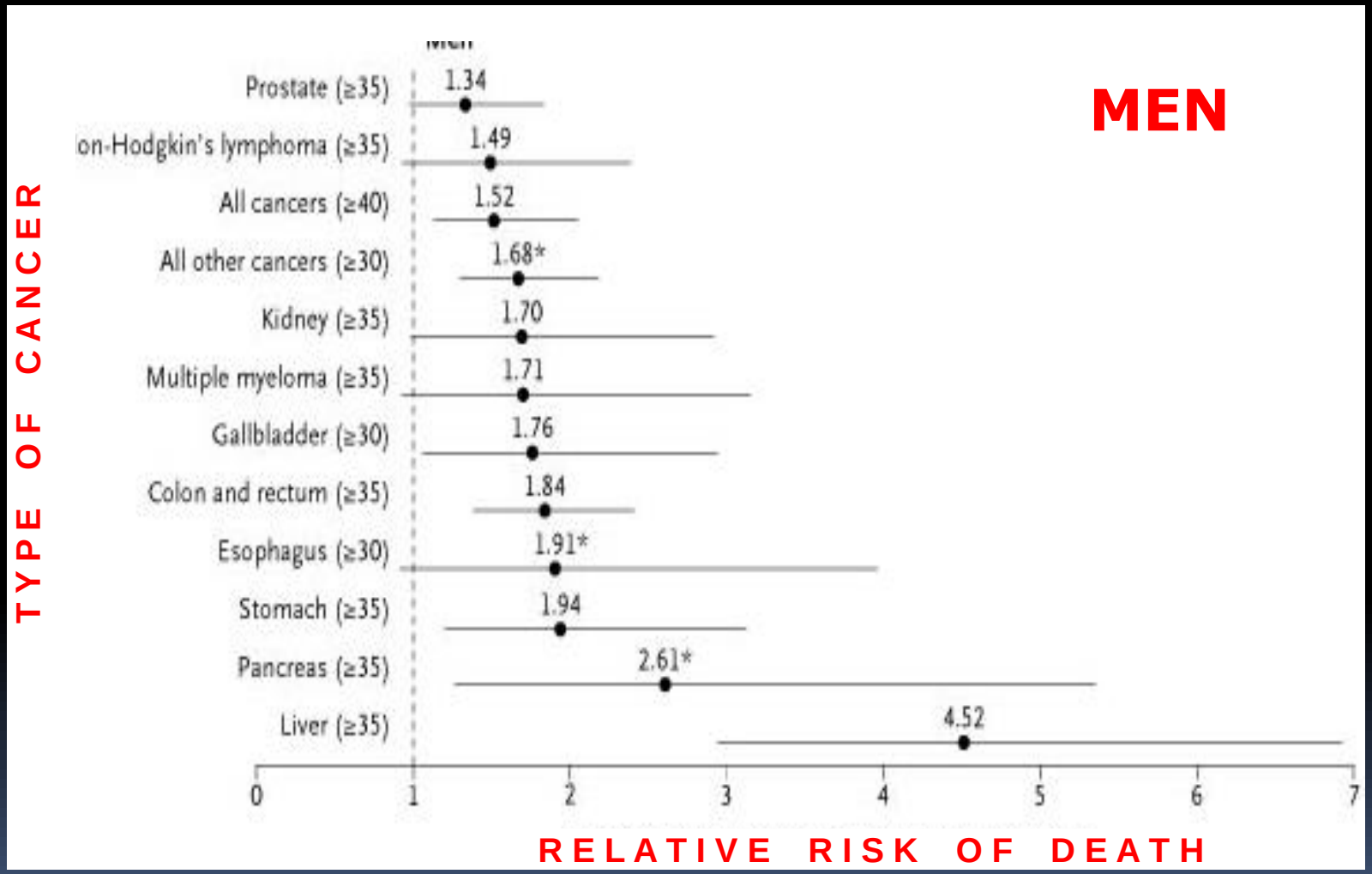
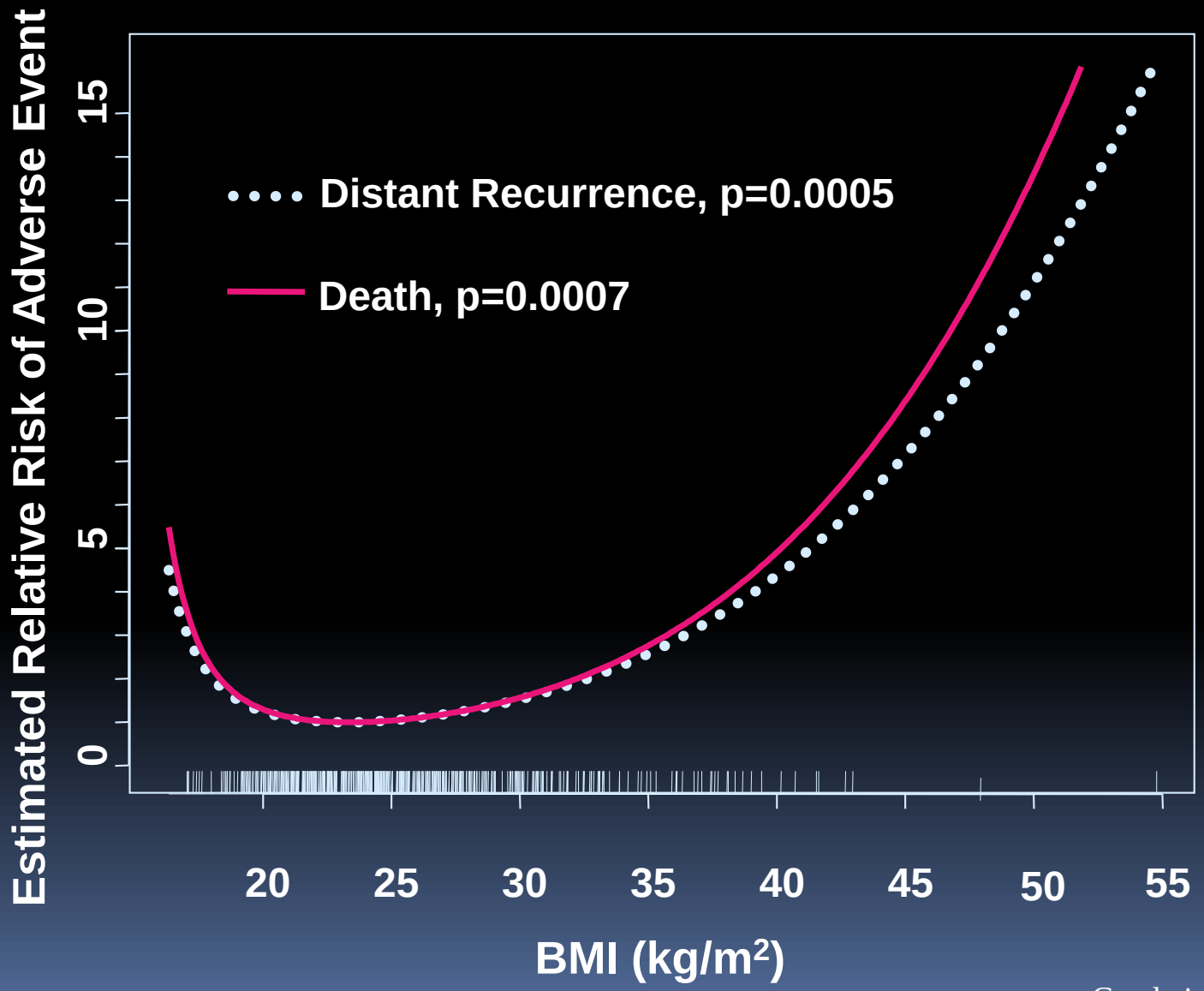


*Highest body BMI category

Weight and Survival in Early-Stage Breast Cancer



Goodwin et al, JCO 2002

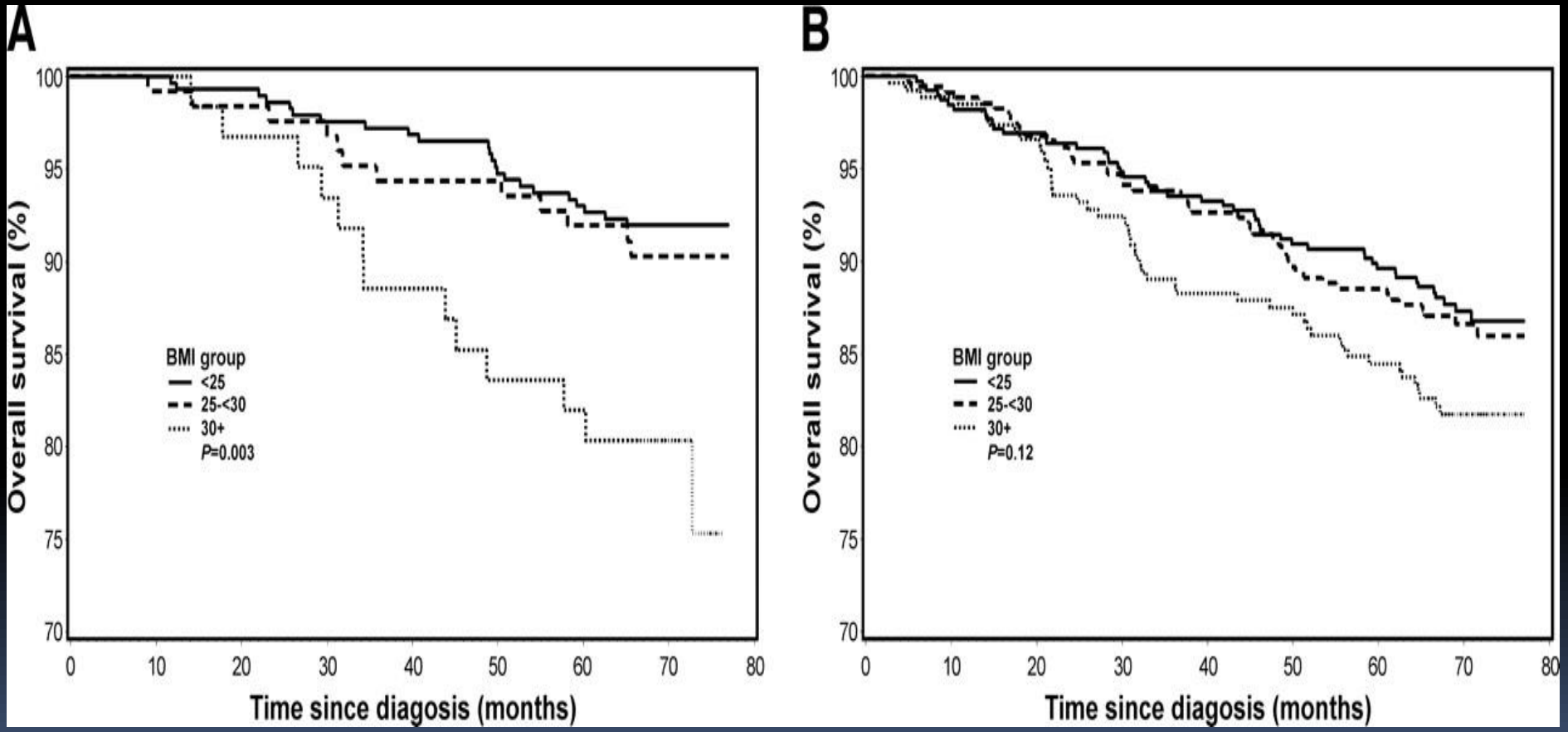
Weight, Weight Gain and Breast Cancer Survival

- Weight at diagnosis may increase recurrence risk
- Weight gain often occurs with adjuvant treatment, including chemotherapy
- Post-treatment weight gain may influence recurrence risk

Survival curves for mortality due to all causes after breast cancer diagnosis, stratified by BMI group

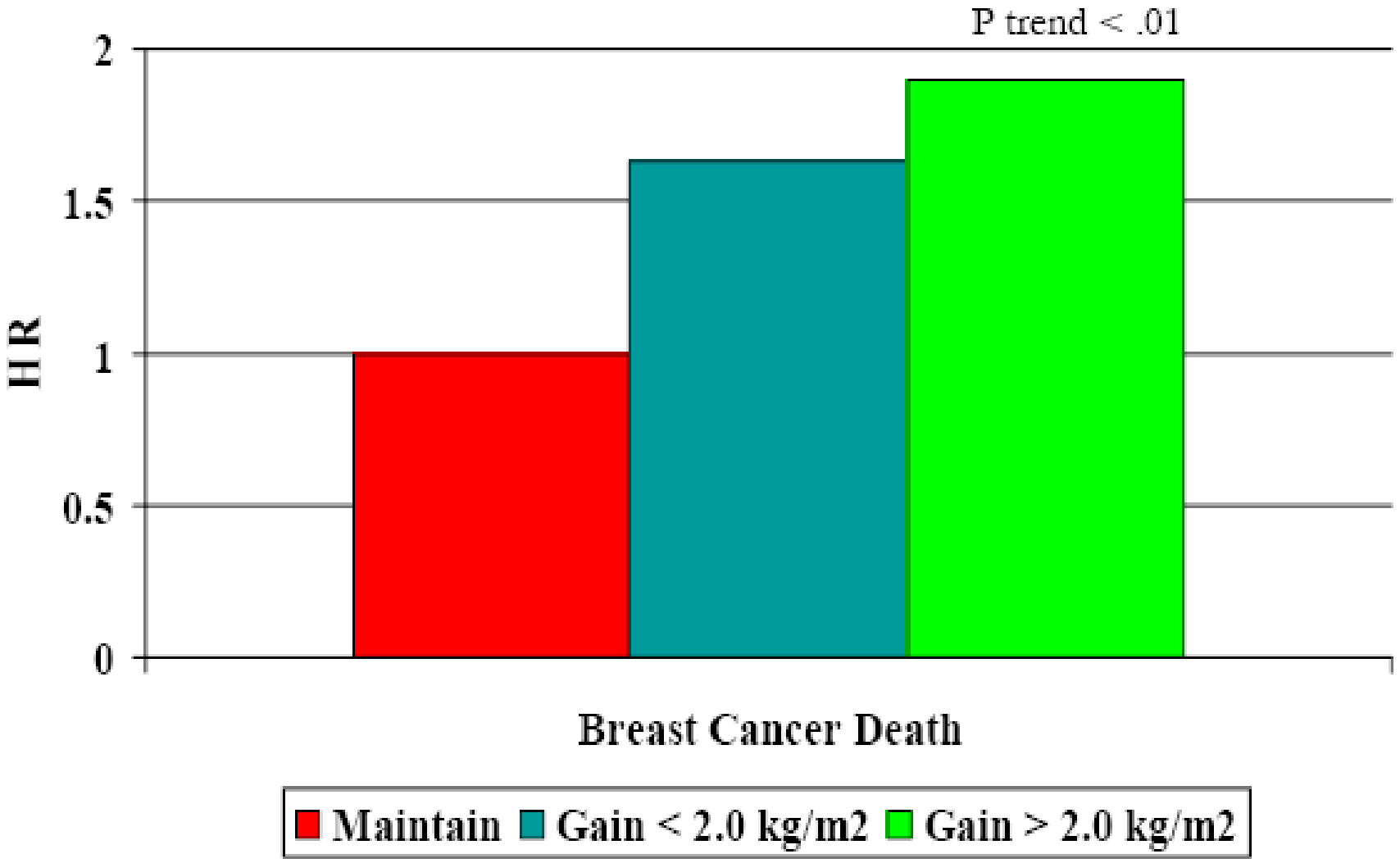
A. Premenopausal breast cancer diagnosis.

B. Postmenopausal breast cancer



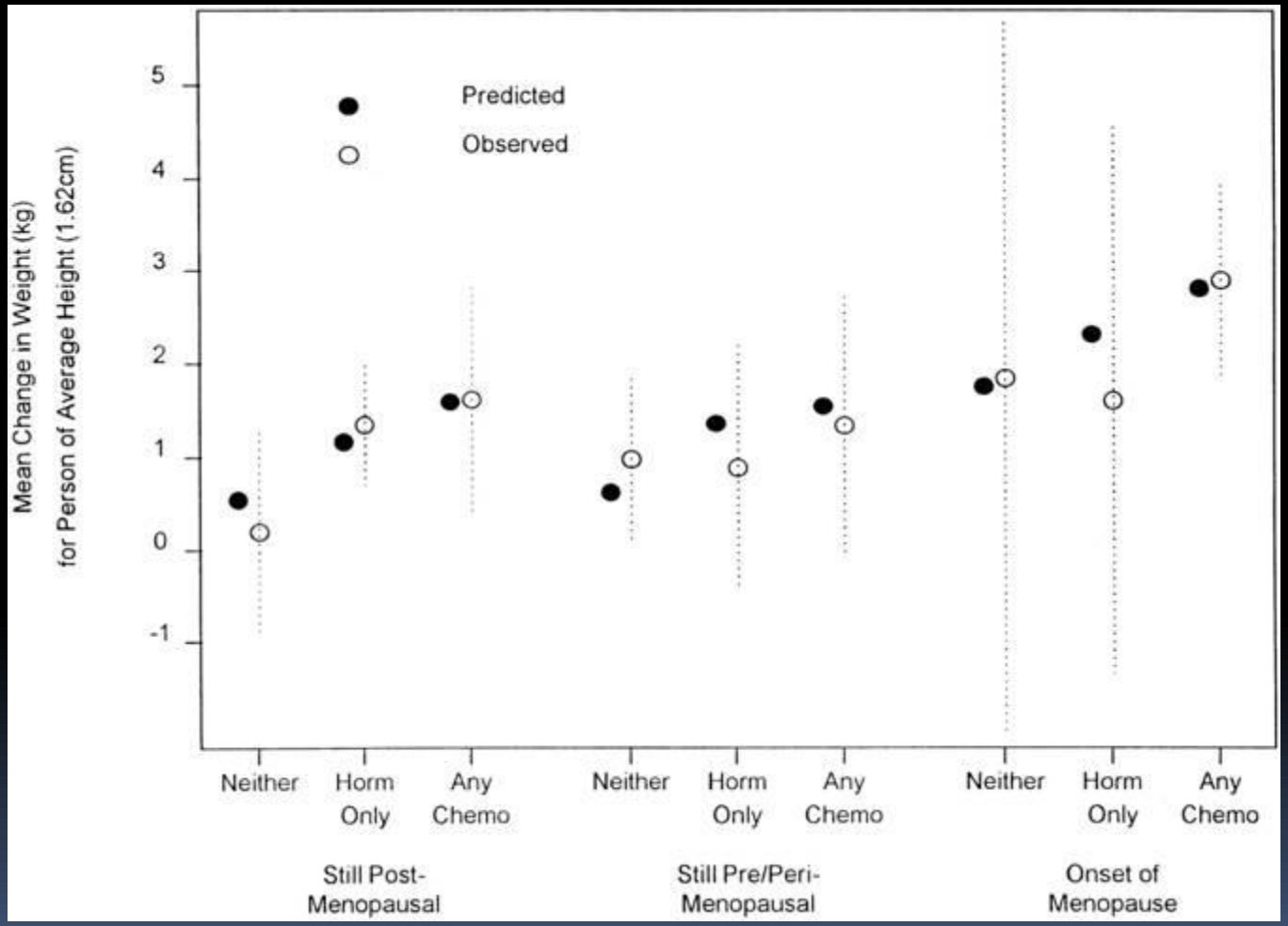
Cleveland R J et al. Cancer Epidemiol Biomarkers Prev 2007;16:1803-1811

Post – Diagnosis Weight Gain and Breast Cancer Mortality In Women with BMI < 25 at diagnosis



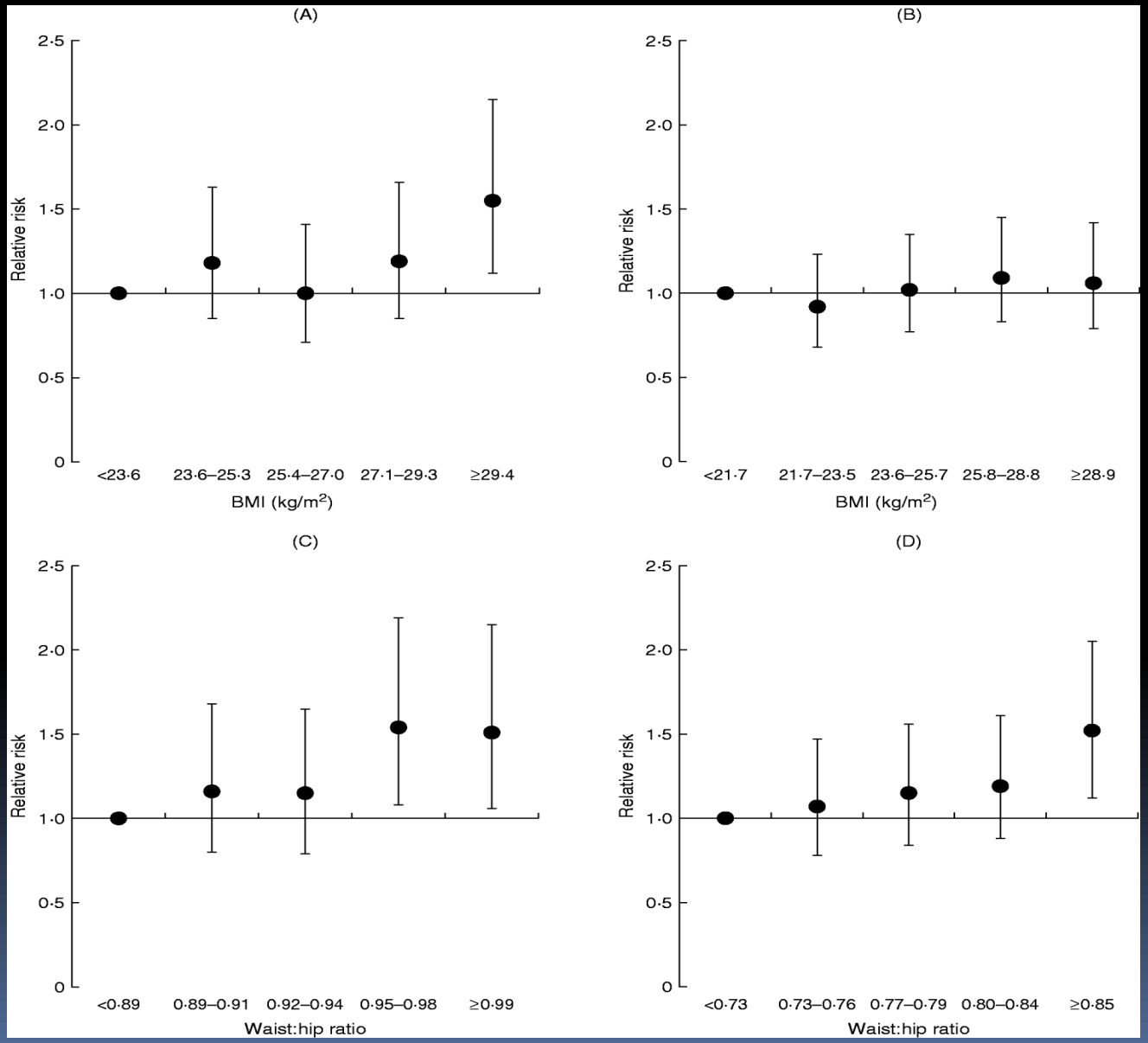
Kroenke C JCO 2005

Chemotherapy → Weight Gain



Goodwin PJ, J Clin Oncol 1999; 17:120

Obesity and Colorectal Cancer Mortality



Obesity and Adiposity

OBESITY

- CANCER MORTALITY
- **BIOLOGY**
- METABOLIC SYNDROME

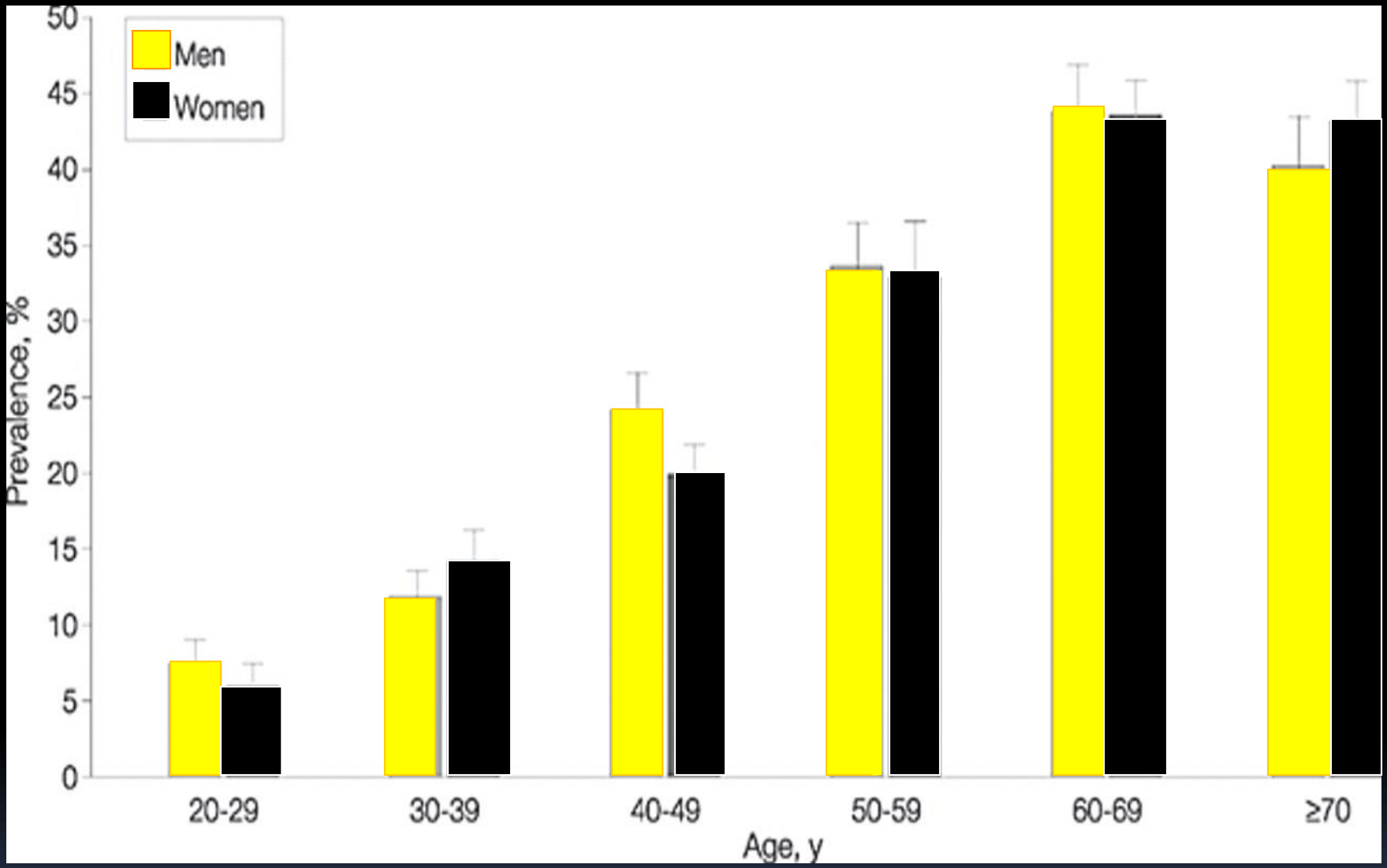
- Adipose tissue as *an endocrine organ*
- Adipose tissue and *systemic inflammation*
- Adipose tissue and the *metabolic syndrome*

Metabolic Syndrome (Syndrome X)

OBESITY

- CANCER MORTALITY
- BIOLOGY
- **METABOLIC SYNDROME**

- Linked to progressive *abdominal/visceral obesity*
- Peripheral *insulin resistance & high insulin*
- Hyperlipidemia - high VLDL, triglycerides
- Rising incidence 40%+ in adults over 40 yrs
- Excess energy intake, reduced activity
- Risk - Diabetes Mellitus II, CAD, Hypertension
- *Rising incidence late 20th century parallels rising incidence of epithelial cancers*

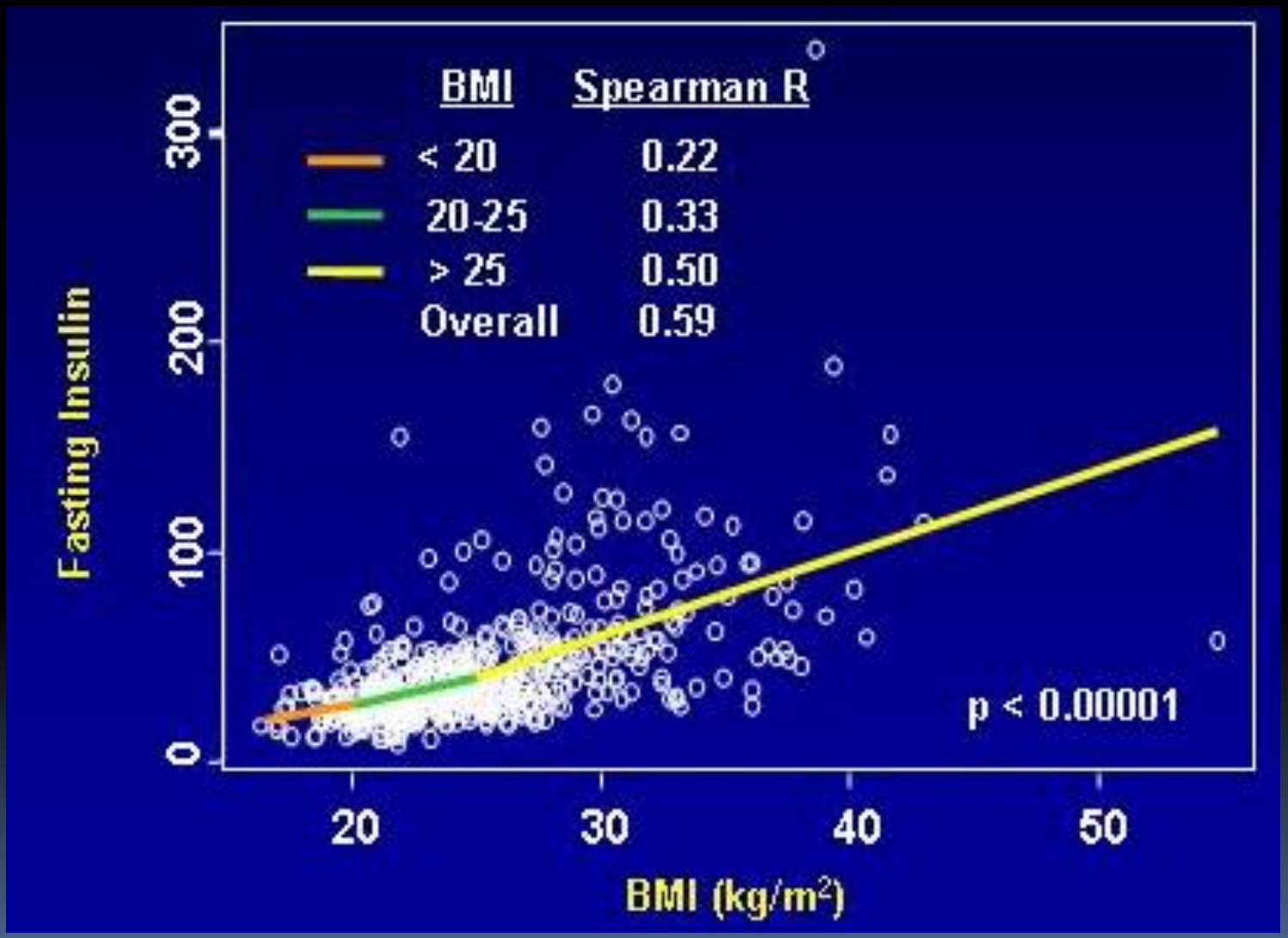


Age-Specific Prevalence of the Metabolic Syndrome Among 8814 US Adults Aged at Least 20 Years, by Sex, National Health and Nutrition Examination Survey III, 1988-1994

BMI and Fasting Insulin

BREAST CANCER PROGNOSIS

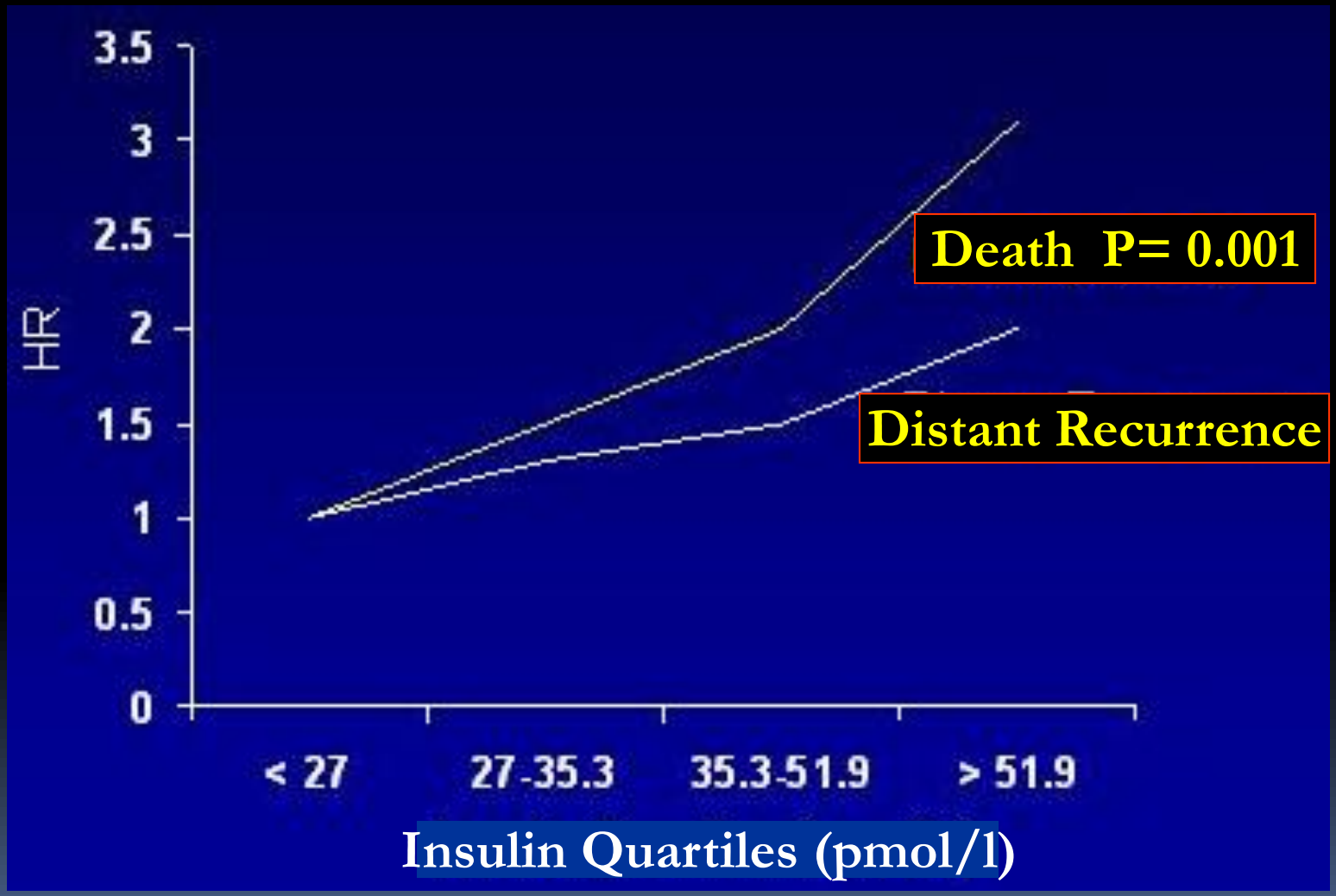
- GENERAL
- **NEW CONCEPTS**



Insulin and Breast Cancer Prognosis

BREAST CANCER PROGNOSIS

- GENERAL
- **NEW CONCEPTS**



Goodwin P J Clin Oncol 20 (1): 42-51, 2002

Can Low Dietary Fat Reduce Breast Cancer Recurrence?

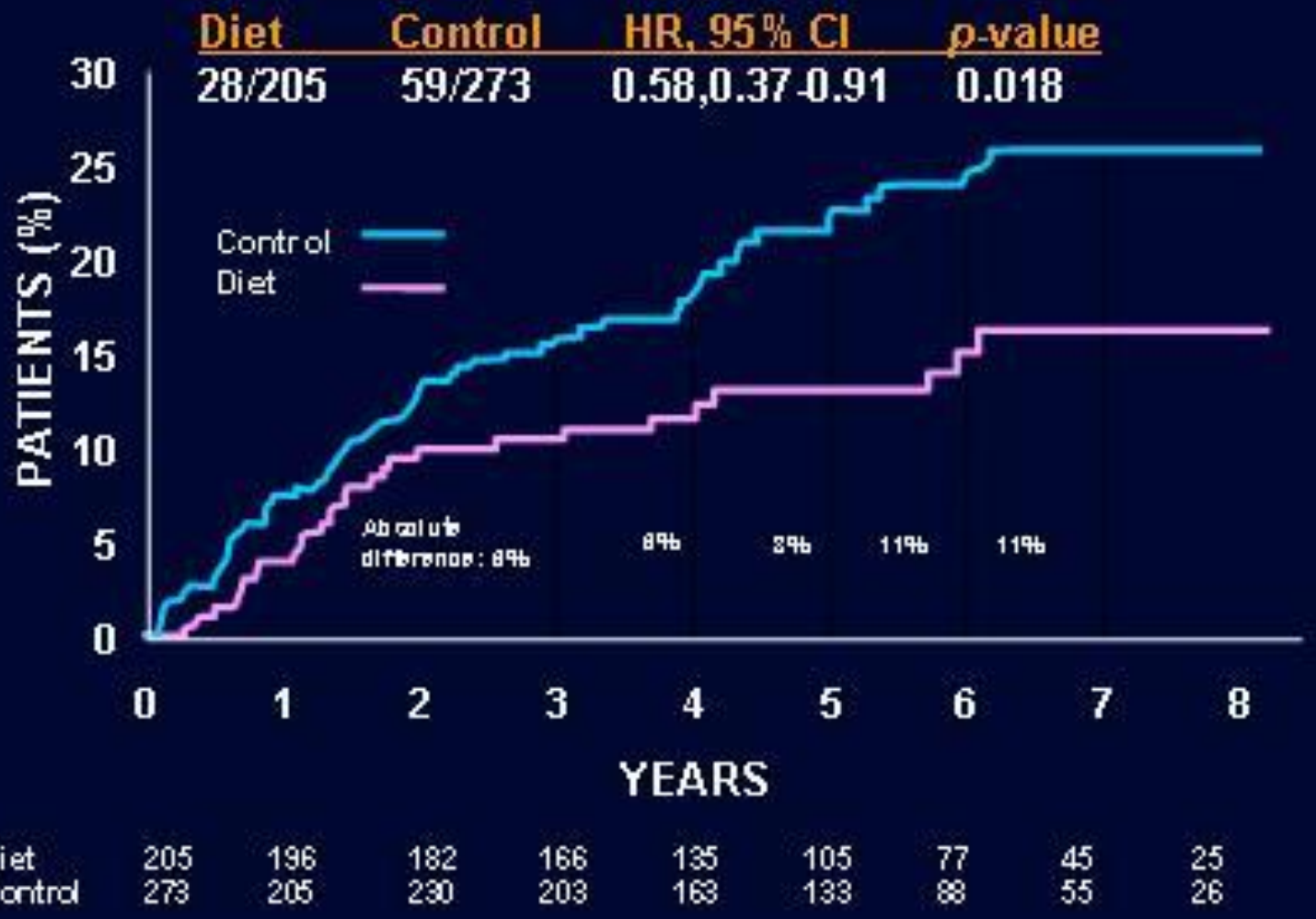
ASCO Plenary Session, 2005

Phase III Randomized Clinical Trials of Diet Change with Breast Cancer Recurrence

Women's Intervention Nutrition Study (WINS)
Adjuvant Breast CA Trial
2,437 randomized

Women's Health Eating Lifestyle (WHEL)
Adjuvant breast cancer trial
3000 randomized

WINS: Relapse Events in ER Negative Patients



ER – Risk Reduction – 42%

Chlebowski, R. T. et al. J Clin Oncol; 22:4507-4513 2004

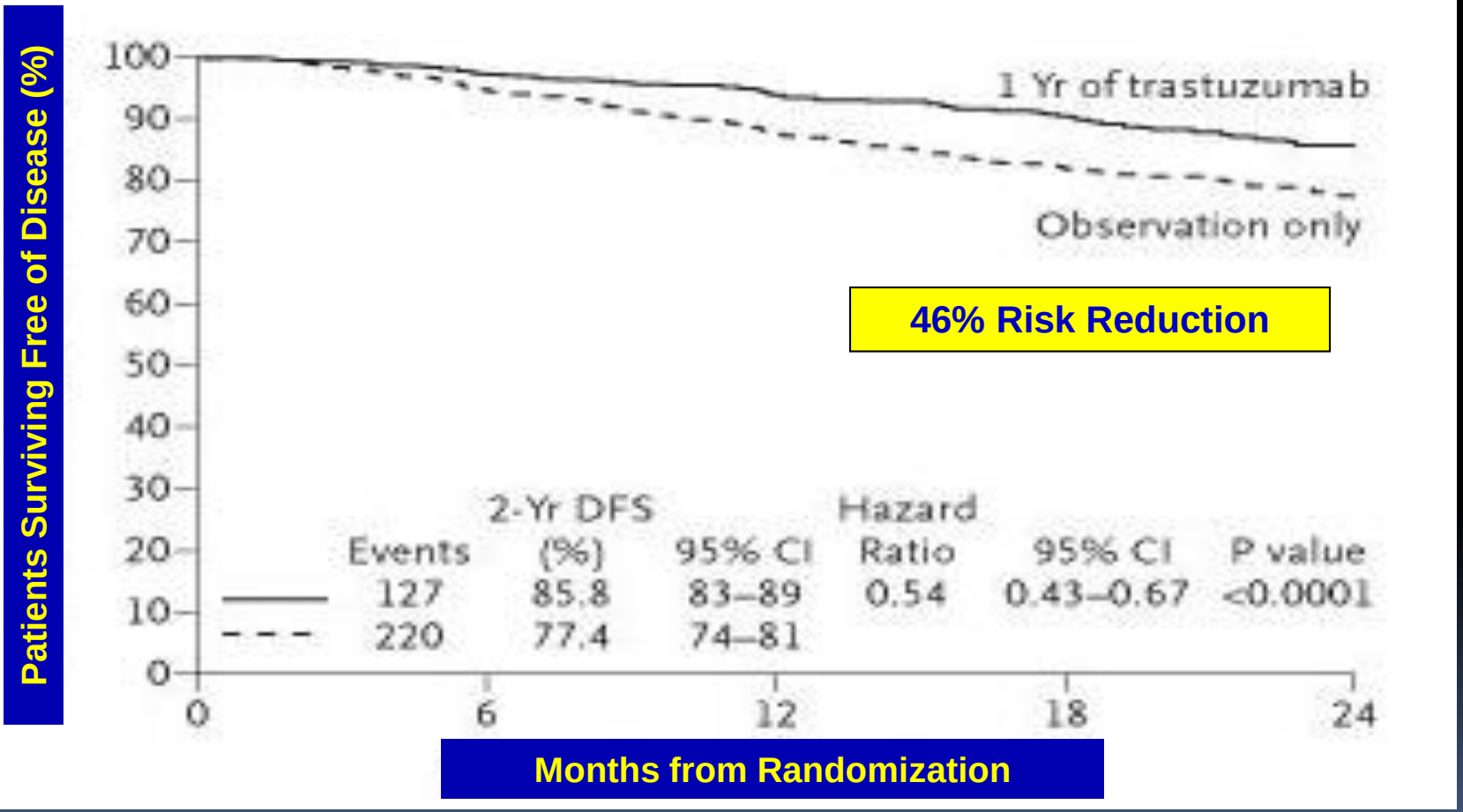
The Washington Post

Diet May Cut Risk Of Cancer Recurring; Eating Less Fat Found to Ward Off New Breast Tumors

May 17, 2005

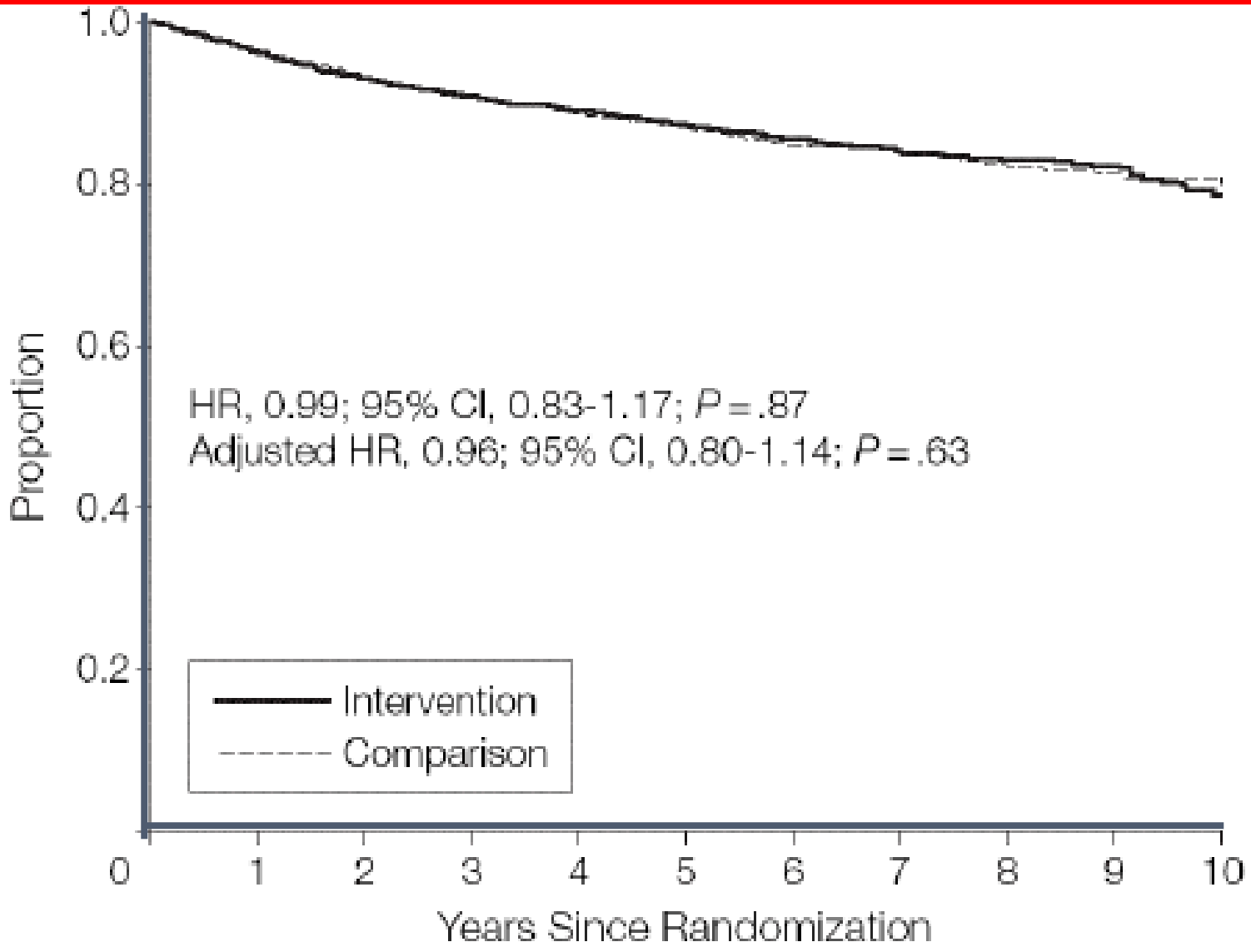
The Washington Post - Washington, D.C.

Herceptin Reduces Breast Cancer Recurrence
ASCO, Plenary Session 2005



Women's Healthy Eating & Living Trial

Disease-Free Survival (Pierce et al., JNCI 2006)



From The TimesJuly 18, 2007

Eating fruit and veg does not boost chances of beating breast cancer

Eating very large amounts of fruit and vegetables does not improve the survival chances of women with breast cancer, scientists have found.

Dietary Intake and Body Weight Change During WINS and WHEL Intervention

	WHEL	WINS
% Energy from fat		
Baseline	→ 28.5 ± 0.18	→ 29.6 ± 7.1
1 Yr	22.7 ± 0.20	20.3 ± 7.8
4 Yrs	27.1 ± 0.24	22.6 ± 8.5
6 Yrs	→ 28.9 ± 0.25	→ 23.0 ± 9.2
Body Weight (kg)		
Baseline	→ 73.5 ± 0.42	→ 72.7 ± 15.9
1 Yr	73.0 ± 0.45	70.6 ±15.2
4 Yrs	74.2 ± 0.51	71.2 ± 14.9
6 Yrs	→ 74.1 ± 0.54	→ 69.4 ± 13.9

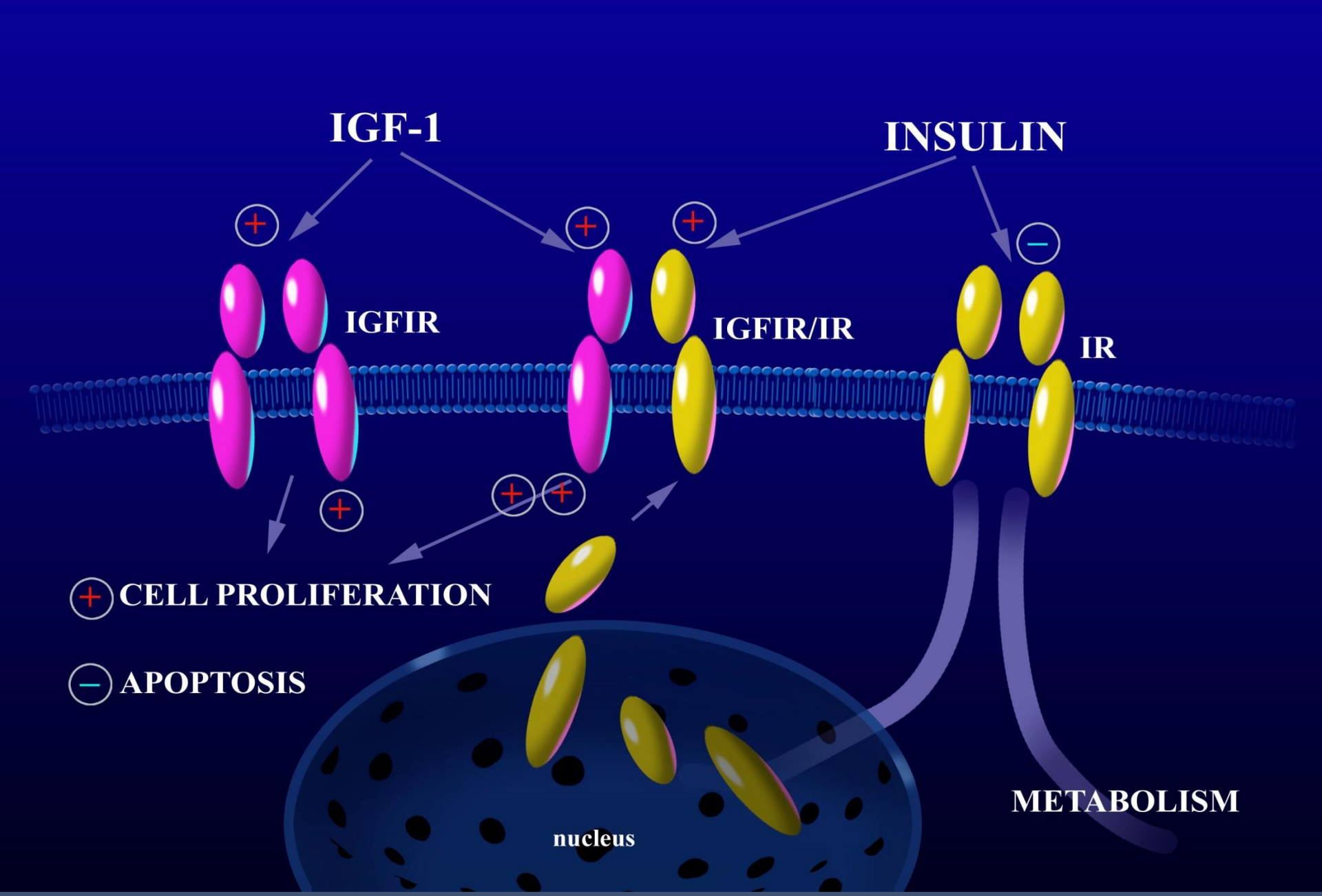
Can a 8-10 lb weight loss really influence cancer via insulin?
The Diabetes Prevention Project

Fasting Insulin Levels decline with Weight Loss in Early Diabetes

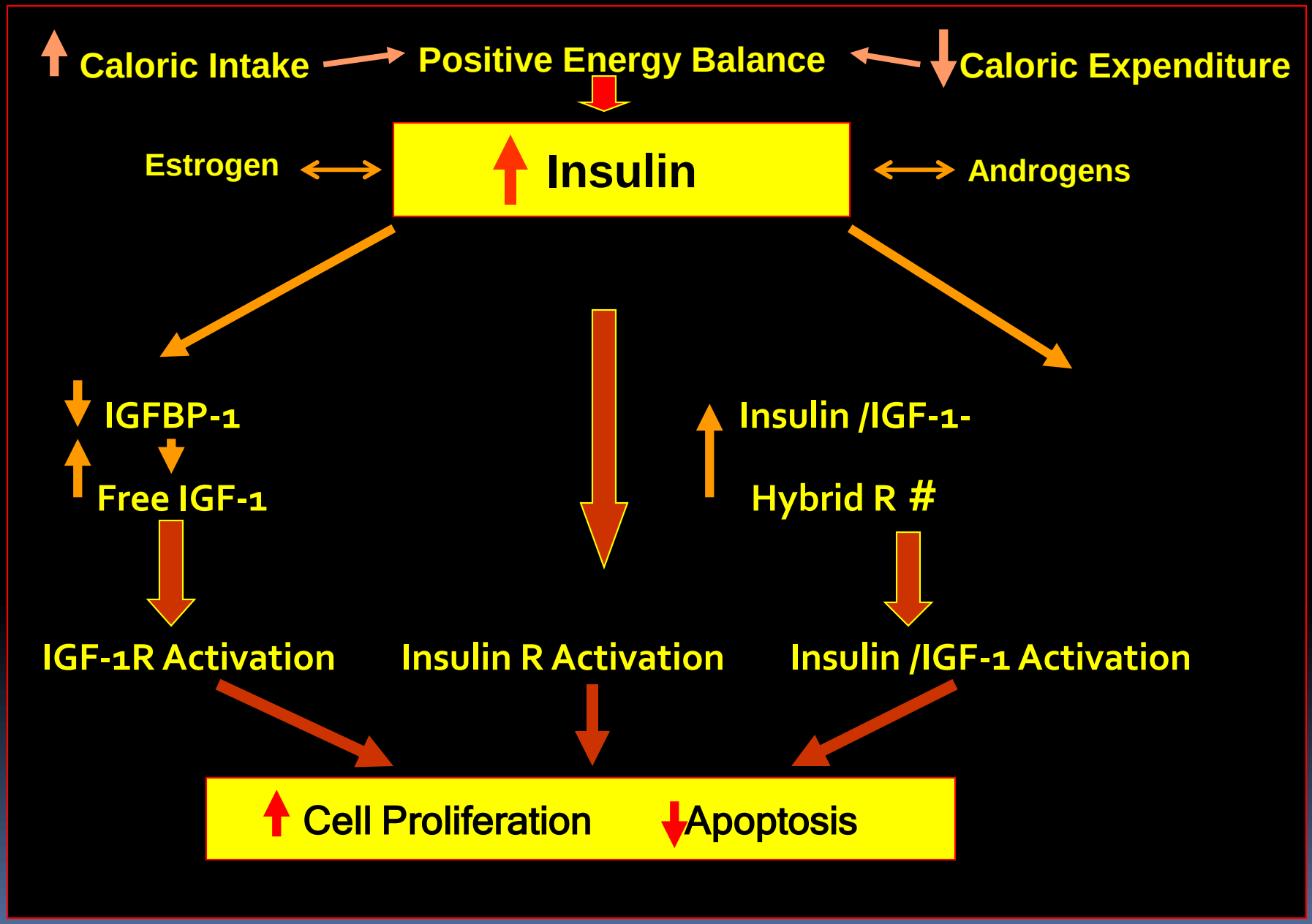
**** 5 to 15 lb weight loss → 50% decrease in insulin***

*P<0.01 vs before.

Wing et al. *Arch Intern Med* 1987;147:1749.


IGF-1
INSULIN
IGFIR
IGFIR/IR
IR
CELL PROLIFERATION
APOPTOSIS
nucleus
METABOLISM

How does Insulin influence tumor progression?



Risk of breast cancer recurrence associated with carbohydrate intake and tissue expression of IGF-1 receptor

- Nested Case Control study: form WHEL Cohort
  - 265 Post-menopausal breast cancer survivors
  - Primary Breast tumor stained for IGF-1R
  - Change in carbohydrate intake- from diagnosis to 1 year post-diagnosis
  - Assess breast cancer recurrence risk after change
  - Carb Intake Change: < - 22 gr/d = *Reduced* vs. -22 gr/d to +26.8, >26.8 + gr/d = *Stable to Increased*

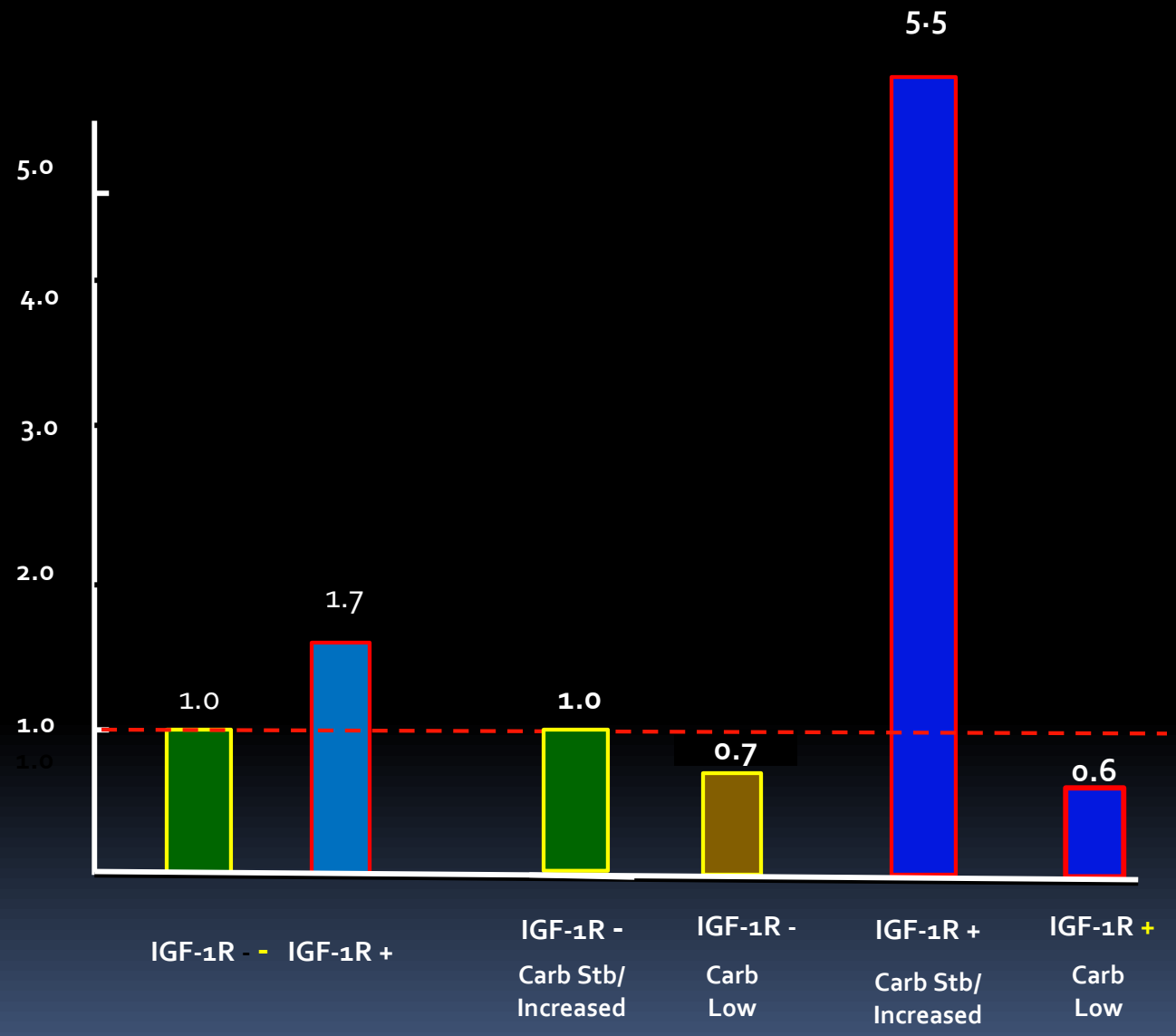
- Results:
  - 50% tumors – IGF-1R +
  - Recurrence risk (RR)- Increased in IGFR-1R + vs. IGFR-1R - patients (HR=1.7)
  - Higher carbohydrate - Increased Recurrence (HR=2.0)
  - Carbohydrate intake - No change Recurrence in IGF-1R negative tumors
  - ***Higher carbohydrate*** - ***Marked increase Recurrence*** *in IGF-1R* + *(HR=**5.5**)* ***550%*** ↑
  - ***Lower carbohydrate*** - ***Decreased recurrence*** *in IGF-1R* + (HR=**0.6**) ***40%*** ↓

Role of insulin/ IGF system in determining metabolic response of tumor to diet

Personalize dietary guidelines based on tumor molecular features

JA Emond Cancer Epidemiol Biomarkers Prev. 2014 Jul;23(7):1273-9.

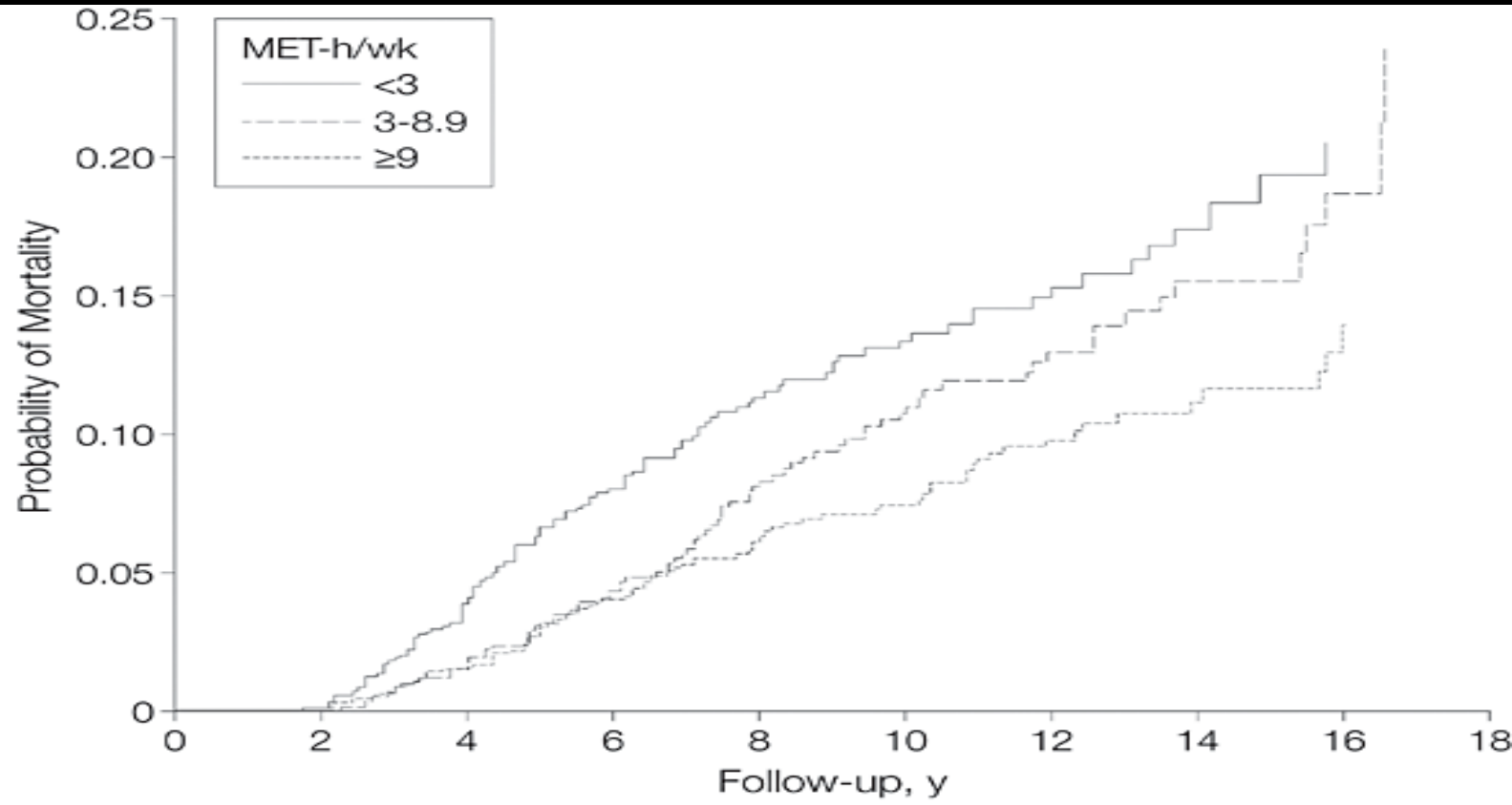
Risk of breast cancer recurrence associated with carbohydrate intake and tissue expression of IGFI receptor



J A Emond. Cancer Epidemiol Biomarkers Prev. 2014 Jul;23(7):1273-9.

Can Physical Activity Influence Cancer Prognosis?

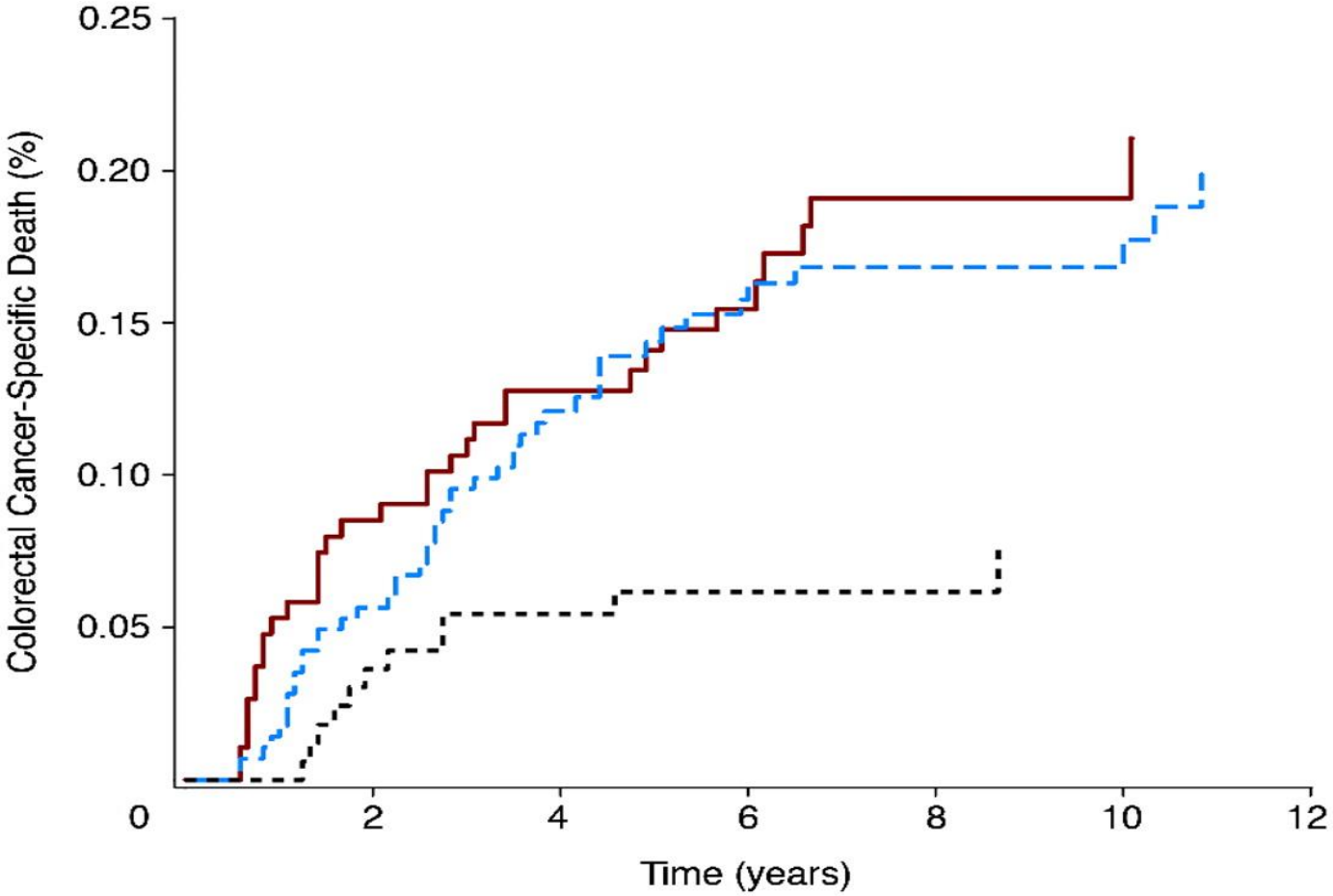
Breast Cancer Mortality is Reduced by Physical Activity



No. at Risk

Physical Activity, MET-h/wk									
<3	959	957	809	573	407	286	222	83	43
3-8.9	862	862	767	569	489	372	184	84	31
≥9	1166	1166	1066	773	692	449	290	164	86

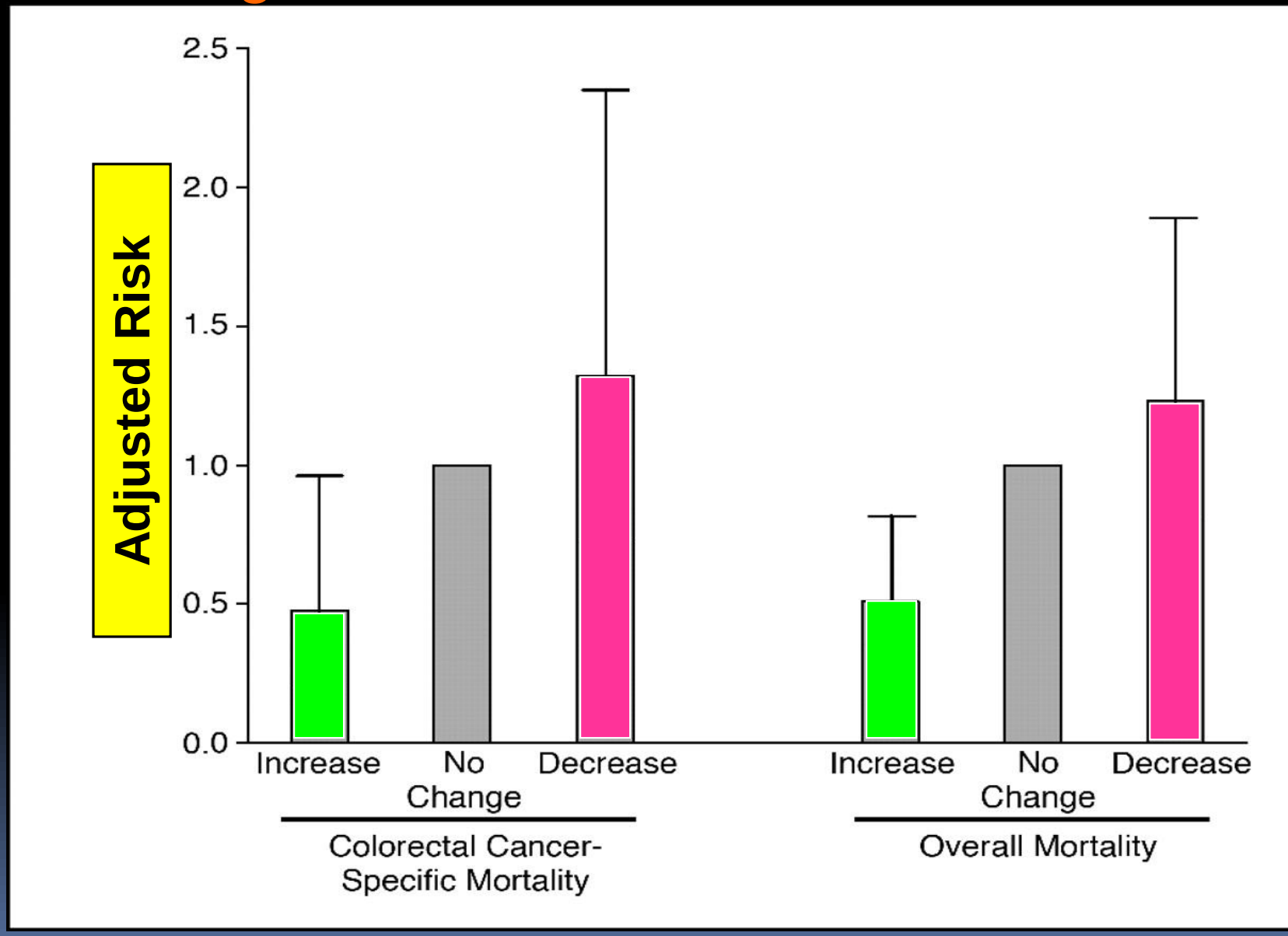
Exercise (18 met-hrs) Reduces Colorectal Mortality



No. at risk:	2 Years	5 Years	10 Years
< 3 MET-hours/week	172	128	41
3-18 MET-hours/week	267	188	93
> 18 MET-hours/week	159	130	46

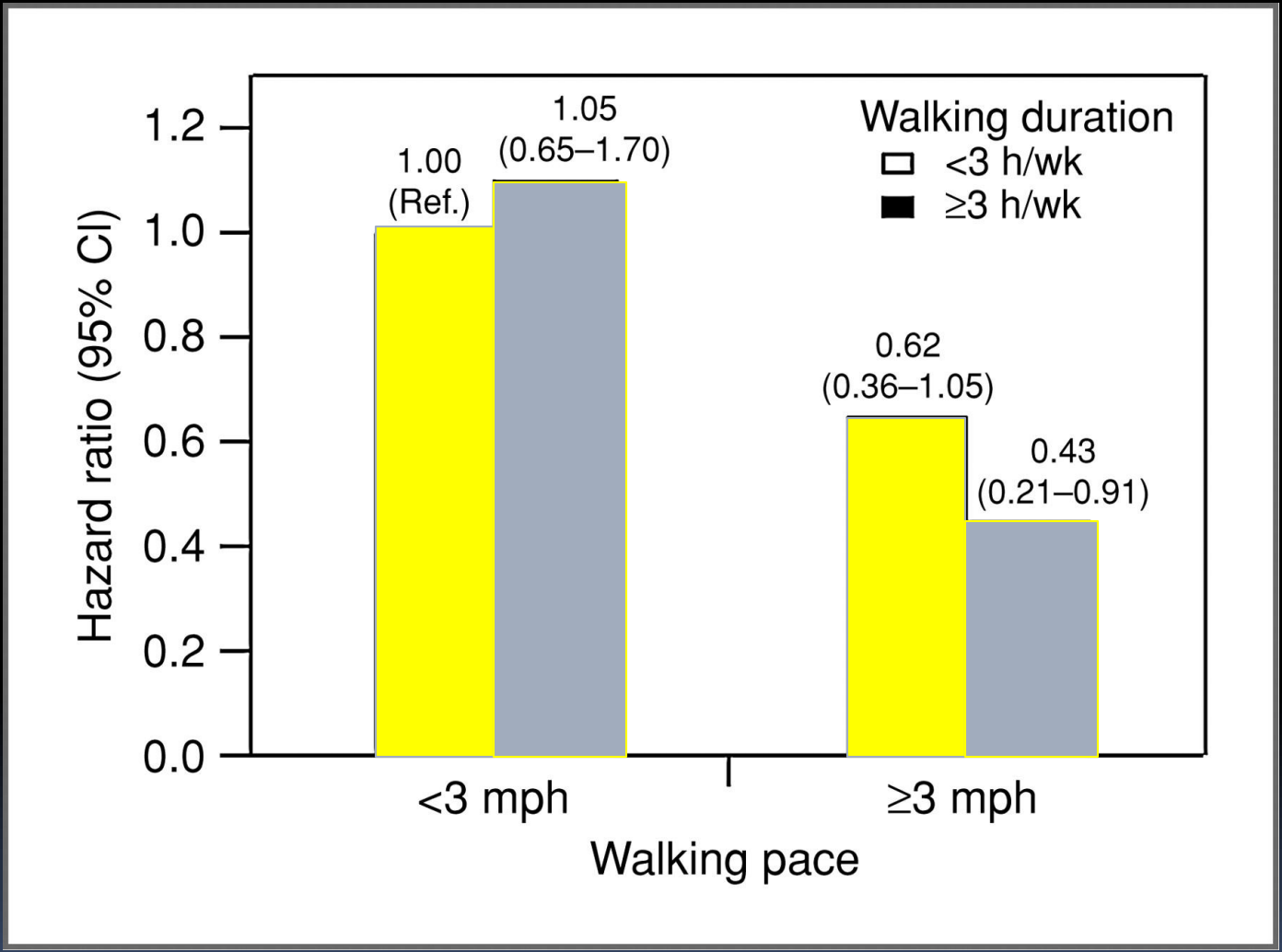
Meyerhardt, J. A. et al. J Clin Oncol; 24:3527-3534 2006

Physical Activity Begun *After* Colon Cancer Diagnosis Reduces Risk >50%



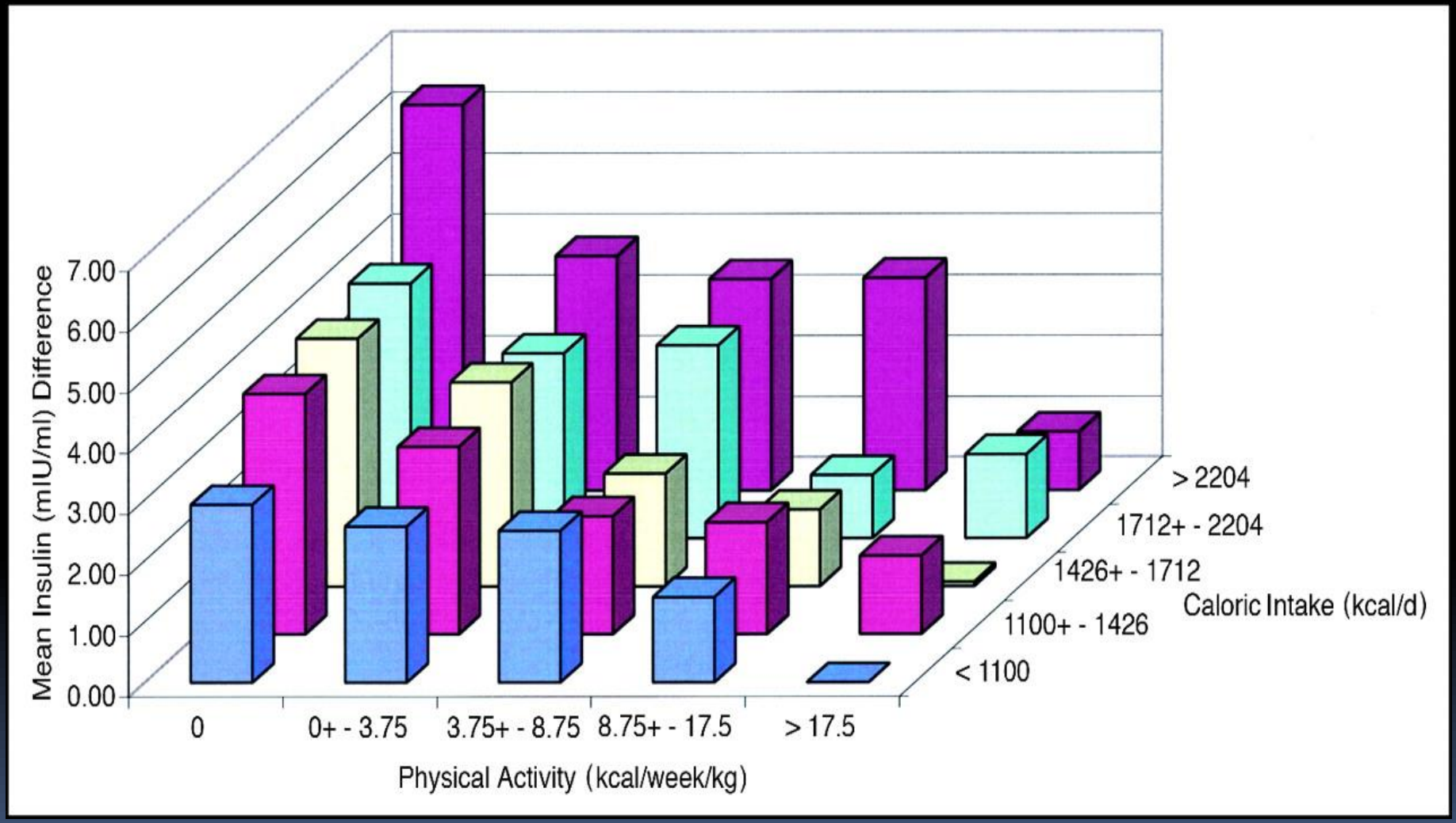
Meyerhardt, J. A. et al. J Clin Oncol; 24:3527-3534 2006

Post-diagnostic walking duration, walking pace, and risk of prostate cancer progression



Richman E L et al. Cancer Res 2011;71:3889-3895

Differences in fasting insulin levels as mean values by quintiles of physical activity and caloric intake



Chlebowski, R. T. et al. J Clin Oncol; 22:4507-4513 2004

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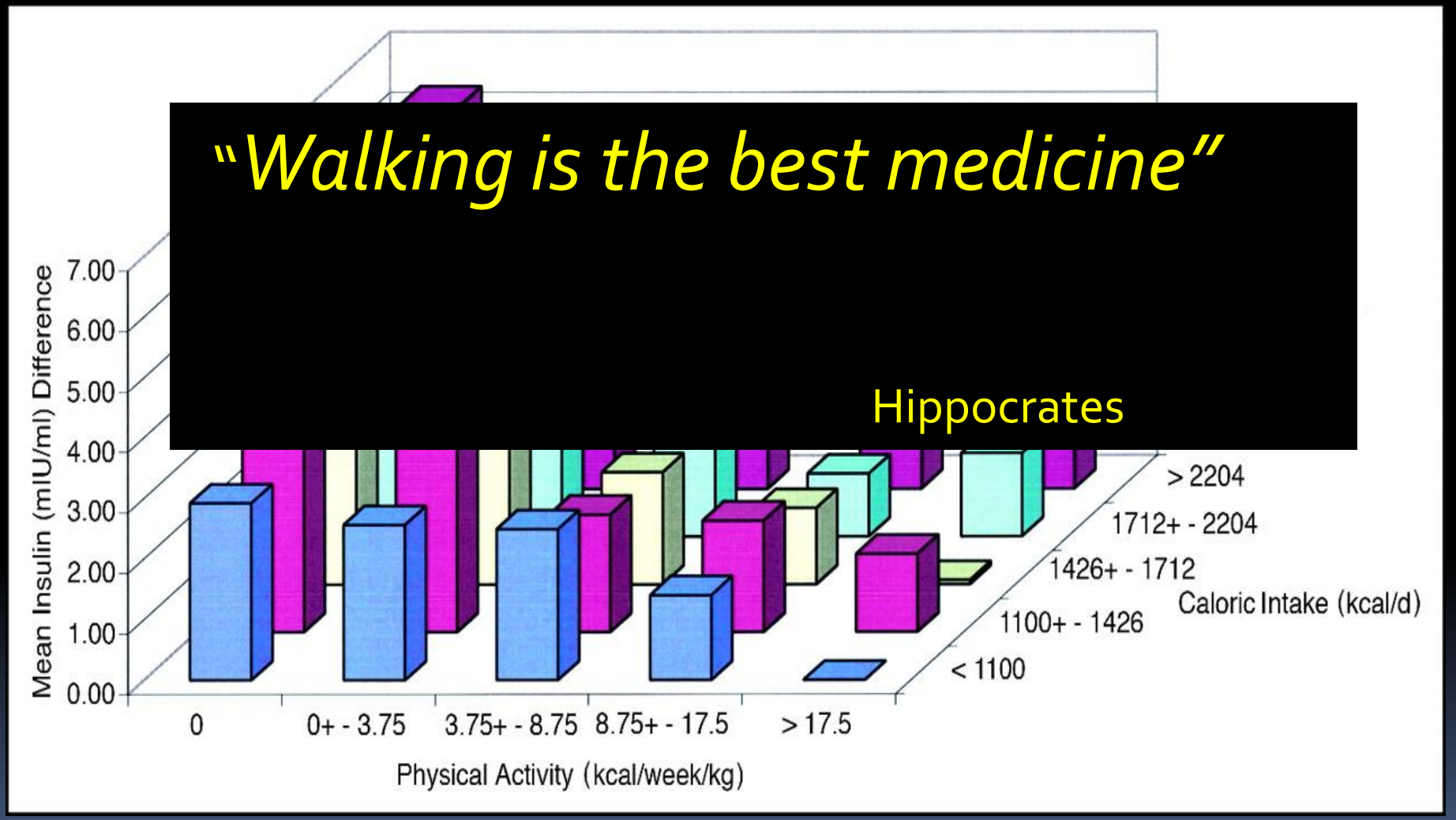
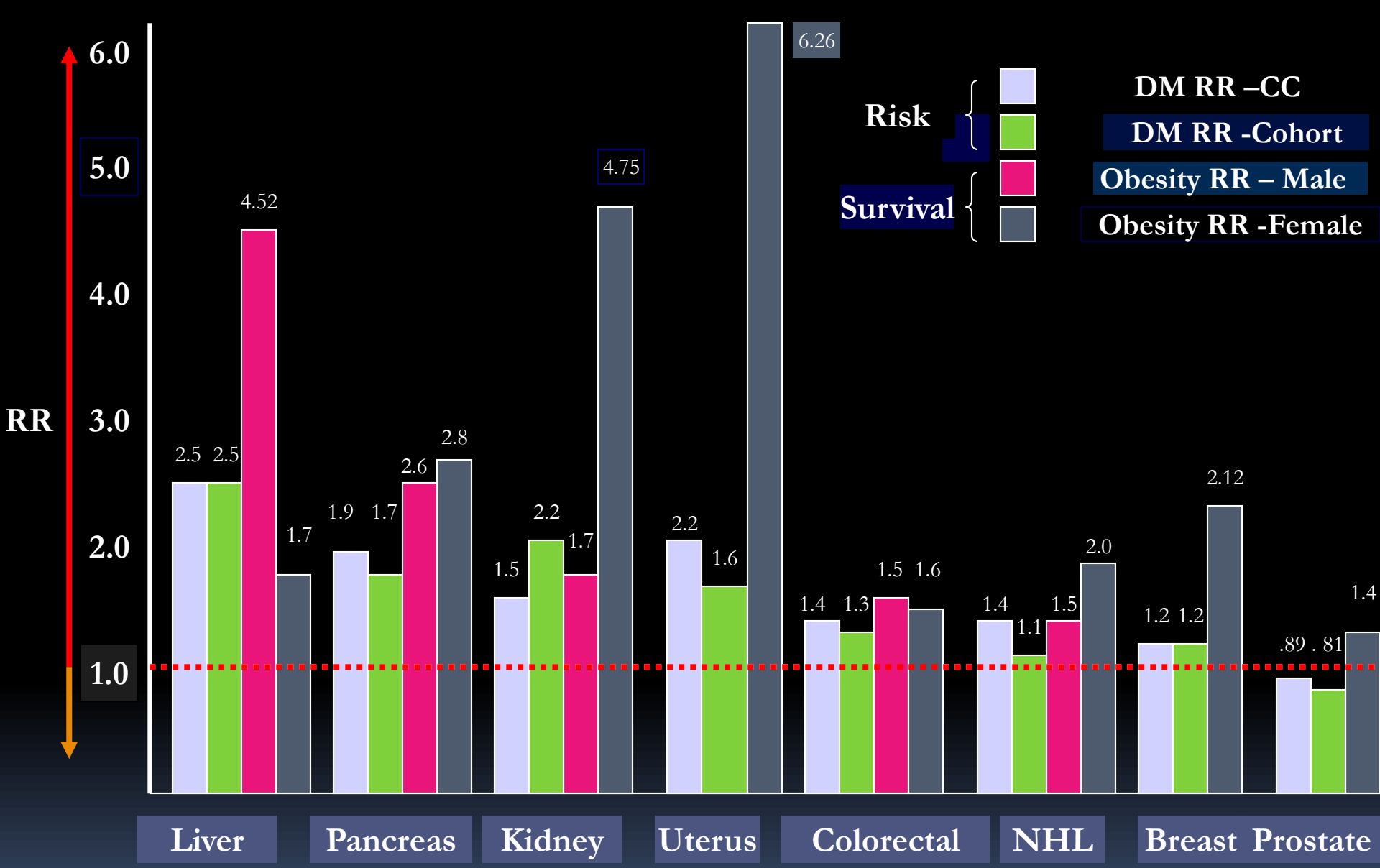


Chlebowski, R. T. et al. J Clin Oncol; 22:4507-4513 2004

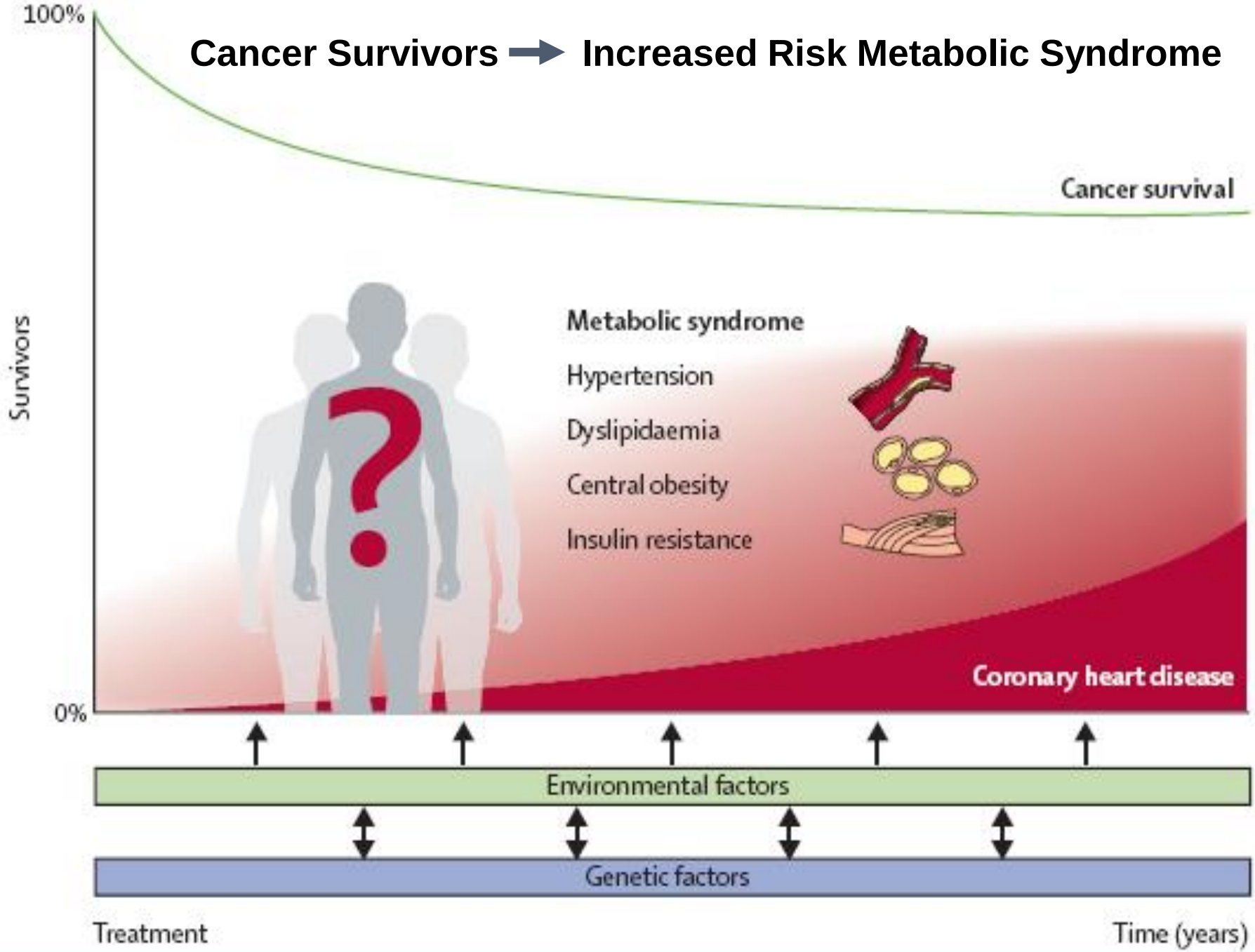
What cancers may benefit from lifestyle interventions?

- Express hormone receptors
  (IR-A, IR-B, IGF-1R, ER, PR, etc.)
- Exercise influences risk
- Weight, weight gain linked to risk and outcome
- Metabolic Syndrome/Insulin Resistance linked to risk
- Tumor differentiation status may influence responsiveness to interventions

(Responsiveness to growth signals, PI3K- Akt activation)



Relative Risk of Cancer/ Mortality
Diabetes Mellitus/ Obesity


Cancer Survivors → Increased Risk Metabolic Syndrome
100%
Cancer survival
Survivors
Metabolic syndrome
Hypertension
Dyslipidaemia
Central obesity
Insulin resistance
Coronary heart disease
0%
Environmental factors
Genetic factors
Treatment
Time (years)

Metabolically Obese, Normal Weight Individuals

Metabolically Obese Normal Weight (MONW)

High Visceral Fat
Low BMI
High Fat mass
Low Lean Body Mass
Low Insulin Sensitivity
High Liver Fat
High Triglycerides

Metabolically Healthy

Low Visceral Fat
Low BMI
Low Fat mass
High Lean Body Mass
High Insulin Sensitivity
Low Liver Fat
Low Triglycerides

Karelis, A. D. et al. J Clin Endocrinol Metab 2004;89:2569-2575

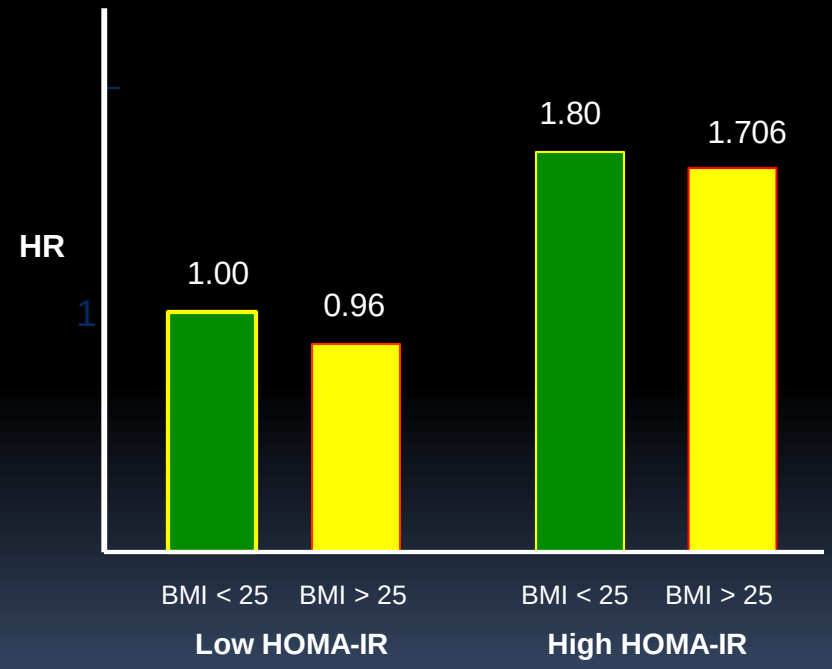
Metabolism vs. BMI: The role of insulin in ER + breast cancer

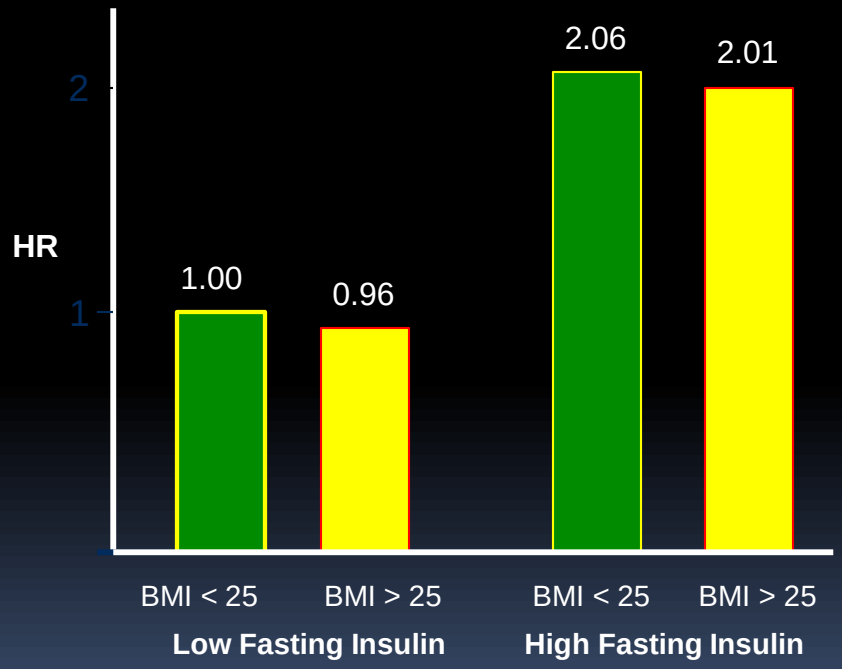
Breast Cancer Risk in Metabolically Healthy but Overweight Postmenopausal Women

- Prior Research : Insulin mediates **- 65%** ; estrogen - **28 %** of postmenopausal Br Ca risk
- Prospective case cohort study from 2 WHI cohorts
- Breast cancer risk vs IR (HOMA-IR, fasting insulin and wt.)

Incident Breast cancer pts (N=497) and WHI participants (N=2,830)

Risk in overweight (BMI > 25Kg/m2) and normal weight vs. insulin resistance





Being metabolically "unhealthy" increases risk independent of BMI

Gunter MJ et al Cancer Res;75(2):270-274

Metabolic Syndrome in Long Term Cancer Survivors

Pediatric cancer survivors- post-treatment (RT,CT)

High risk of MS/IR and premature CVD, DM

eg. ALL, CNS Tumors, Lymphomas, Testicular Ca

Adult cancer survivors

Obesity/ Insulin resistant linked to risk and outcome

Survivors at higher risk- recurrent cancer, second Ca, CVD, DM, other illness

Treatment- increased weight gain, metabolic syndrome

Integrative Medicine- Opportunity to bring together "divorced disciplines" Oncology, CV Medicine, Endocrinology, Nutritional Medicine, CAM practitioners in care of cancer survivors in 21st Century

Lifestyle Intervention Behavior

Cancer Survivors' Adherence to Lifestyle Behavior Recommendations : *ACS SCS-I* Blanchard, C. et al JCO 26:2198- 2204, 2008

9,105 survivors, 9 different cancers

Physical Activity, Diet Recommendations, Smoking

Results: *5 %* meeting recommendations

Diet ("five a day") - 14 – 19 %

PA (60 min /week) - 29 – 47%

Smoking Cessation - 82 – 91%

Adjuvant Chemotherapy / Hormonal Therapy (Breast, Colorectal Cancer) Guidelines

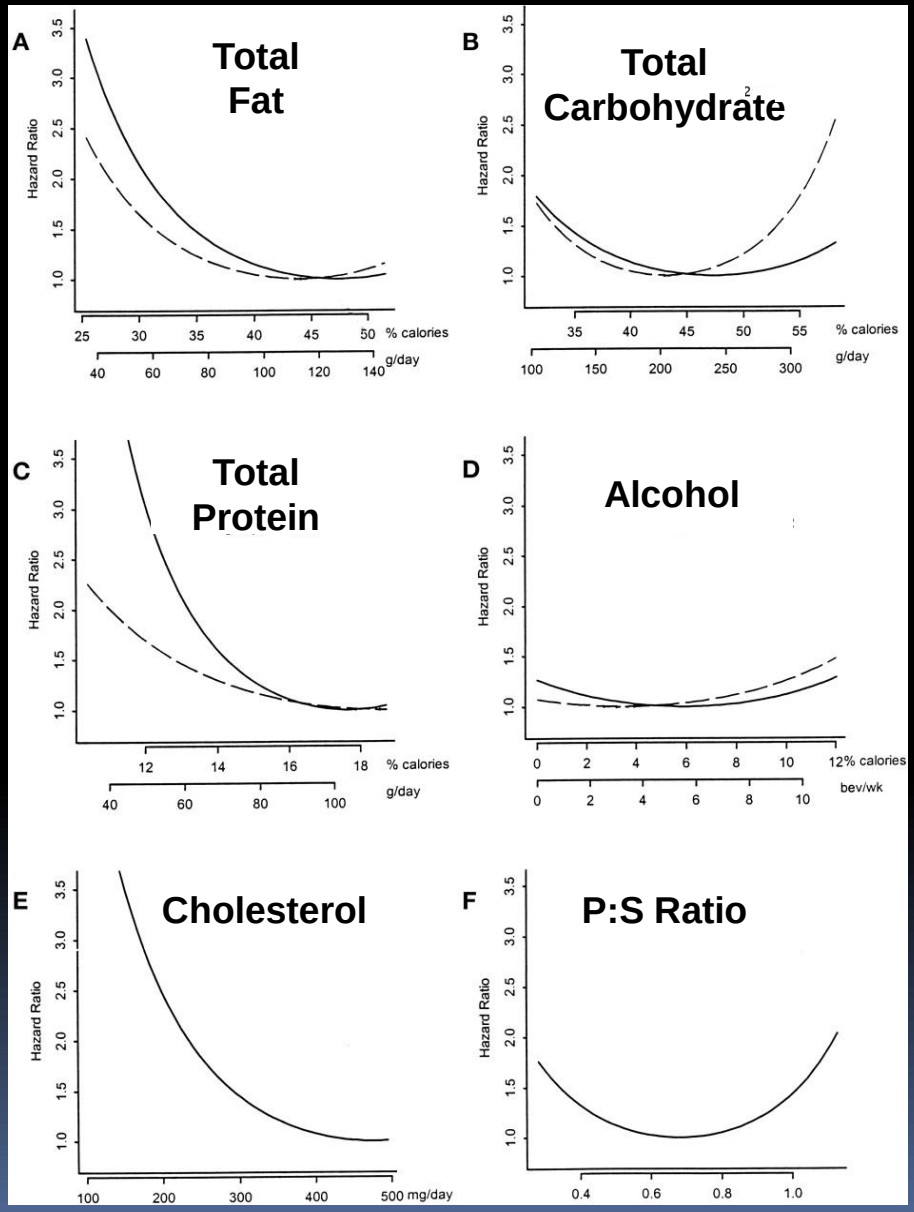
Results: *85 -98 %* meeting recommendations

Phenotypic Modulation of Cancer

- **Lifestyle Modifications to influence promotional effects on early stage cancers: breast, prostate, colorectal can change outcomes !!**
- ***Will this apply to other cancers, i.e., Lung, Ovarian, Renal, Endometrial, Liver, NHL , Myeloma ??***
- **Target:**
- Metabolism is key! Insulin, estrogen
  - → **Insulin resistance-related inflammatory state**
  - → ***Prevent treatment-related Weight Gain***
- **Intervention:**
  - → **Diet- Low Fat , Low Glycemic**
  - → **Exercise**
  - → **Stress Reduction**

Diet and Breast Cancer : Evidence that Extremes in Diet Are Associated With Poor Survival

Prognostic association of selected dietary variables



Goodwin, P. J. et al. J Clin Oncol; 21:2500-2507 2003

Association of Dietary Patterns with Cancer Recurrence and Survival in Patients with Stage II Colon Cancer

Meyerhardt JAMA, 8/2007

Prospective Observational Study- 1009 Pt, St III

Colon Ca (CALGB 89803) 1999-2001

2 Dietary Patterns:

Western- "Meat and Potatoes"

Prudent- Poultry, Fish, Fruits & Vegetables

Recurrence Risk Western 3.25 x > Prudent Diet

Overall Survival Western 2.32 x < Prudent Diet

Western Diet Significantly reduced disease-free and Overall Survival in Stage III Colon Cancer

Prudent Diet → Low "C-Peptide Score"

→ Lower weight/ lower "glycemic index"

CALGB Non-Interventional Study of Colorectal Cancer

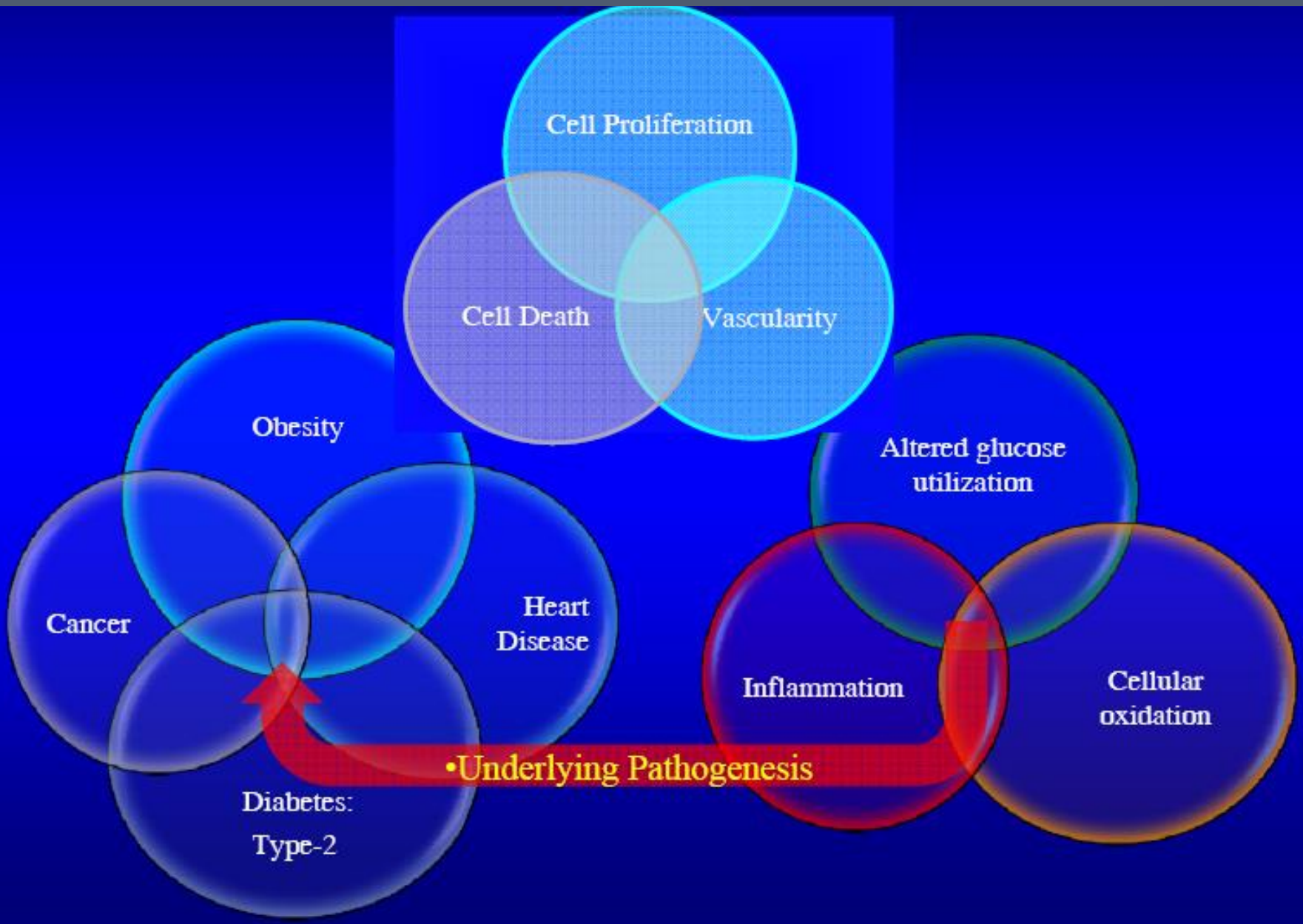
Foods / Food Groups Correlated with Diet Patterns

(Meyerhardt et al., JAMA 2007)

Western Diet Pattern	
Food	**r**
High-fat dairy	0.67
Low-fat dairy	0.64
Refined grains	0.60
Red meat	0.53
Sweets and desserts	0.53
Condiments	0.51
Margarine	0.50
Processed meat	0.45
Potatoes	0.45

Prudent Diet Pattern	
Food	**r**
Vegetables	0.72
Leafy vegetables	0.71
Yellow vegetables	0.67
Cruciferous vegetables	0.65
Legumes	0.56
Fruit	0.55
Light salad dressing	0.48
Tomatoes	0.46
Fish	0.46

Common Alterations Underlying the Pathogenesis of Modern Chronic Diseases



Hiding in plain view: the potential for commonly used drugs to reduce breast cancer mortality

Holmes M, Chen W. Breast Canc Res 2012,14:216

- **Many medications developed for other purposes have other activity**
- **Increasing evidence that many non-cancer drugs have potential impact on breast cancer survival**
- **Evidence for both OTC and generic medications**

  Aspirin and other NSAIDS

  Blood Pressure Medications (b-blockers, ACE-I)

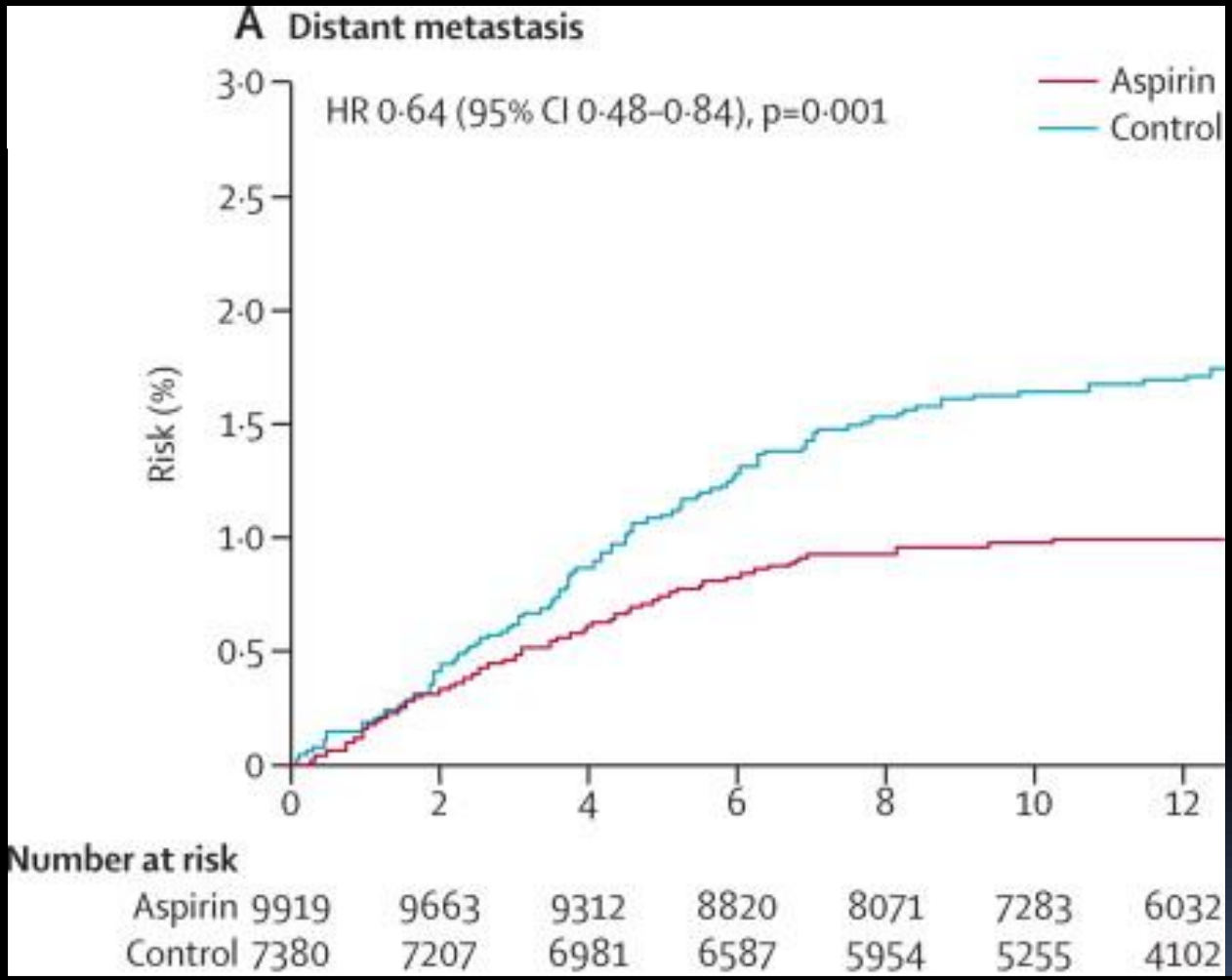
  Lipid lowering agents (Statins)

  Diabetic medications (metformin)

- **Benefit potentially significant**
  Metformin (50%), ASA (50%), Statins (30%) b-Blockers- (50+% in TNBC)

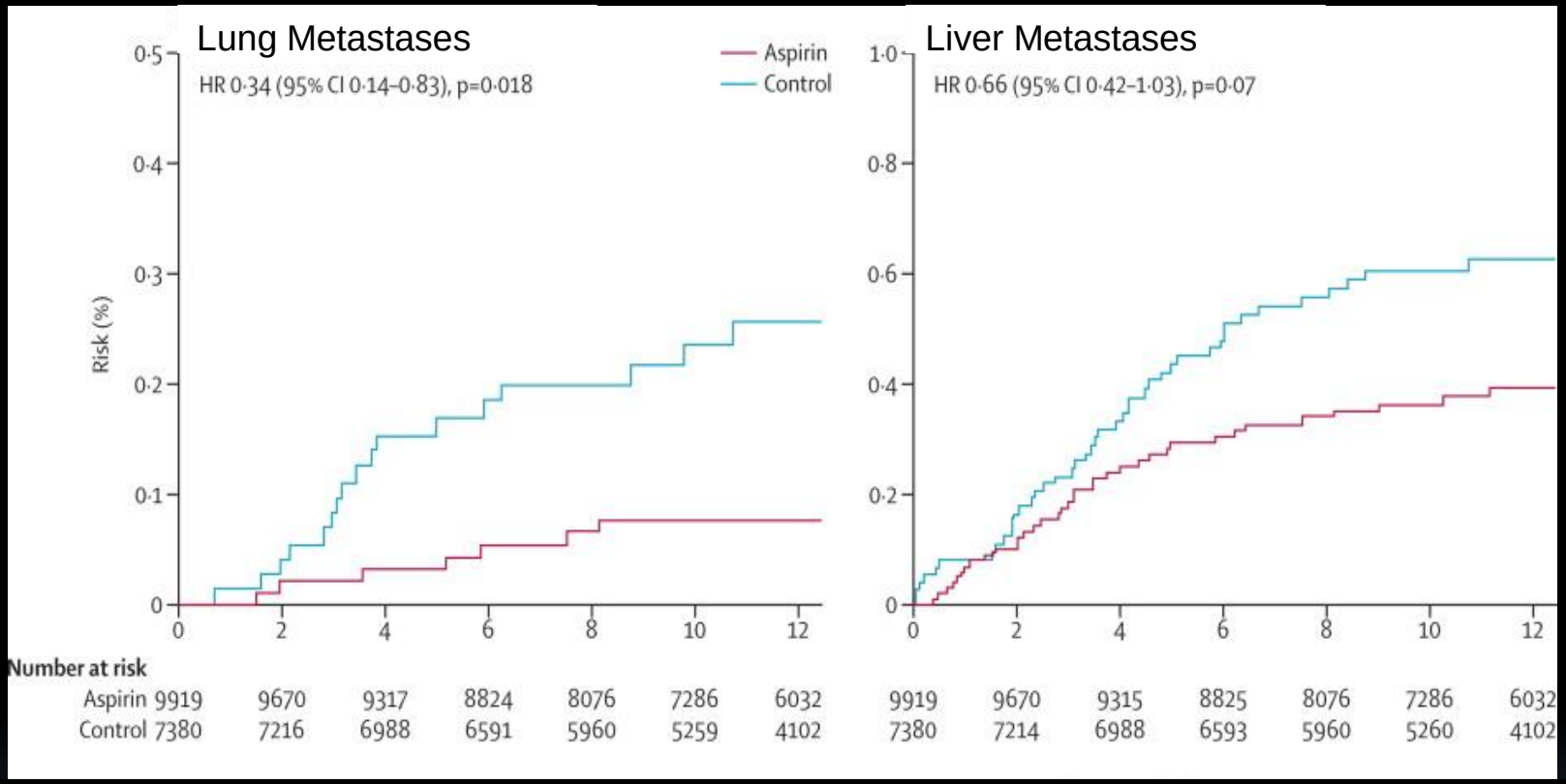
"We advocate that confirmation of these findings in randomized trials be considered a high research priority, as the potential impact on human lives saved could be immense"

Risk Reduction of Metastases by Aspirin

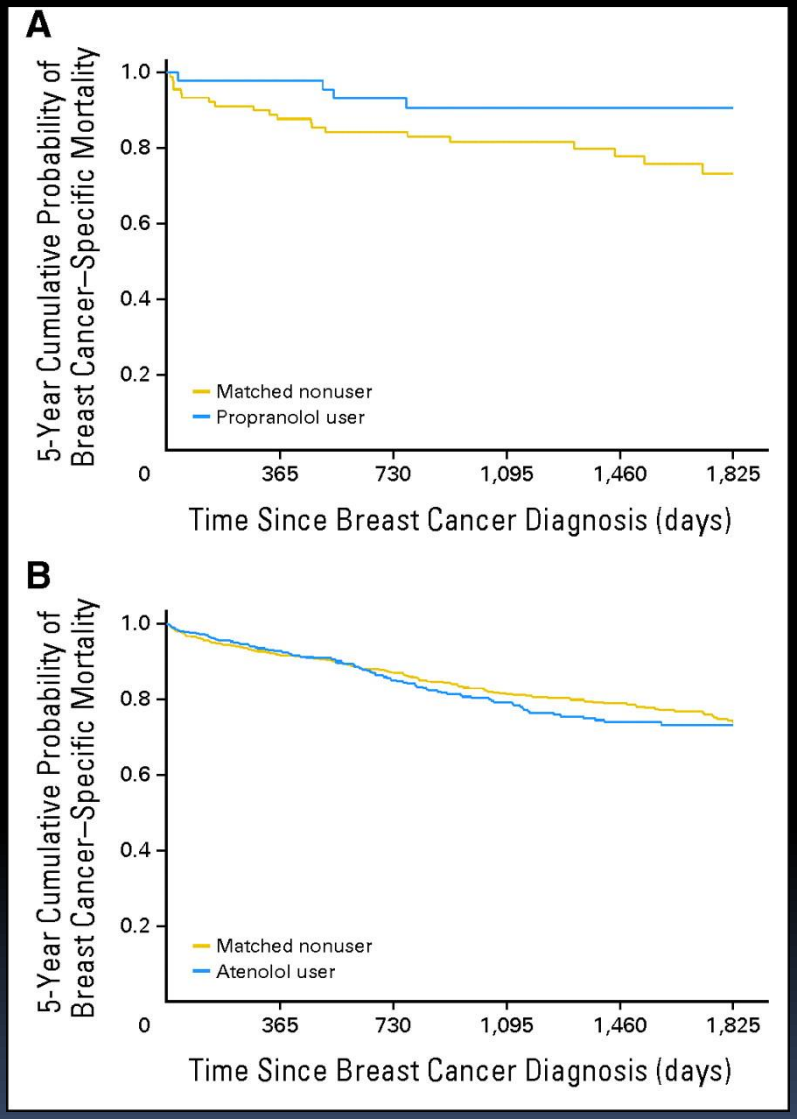


The effect of aspirin on risk of metastasis due to any incident cancer diagnosed during five trials of aspirin versus control Analysis is based on time from randomization to diagnosis of metastasis during or after the trials.
Part A shows definite site-specific distant metastasis

Risk Reduction of Metastases of Aspirin, by Site - I



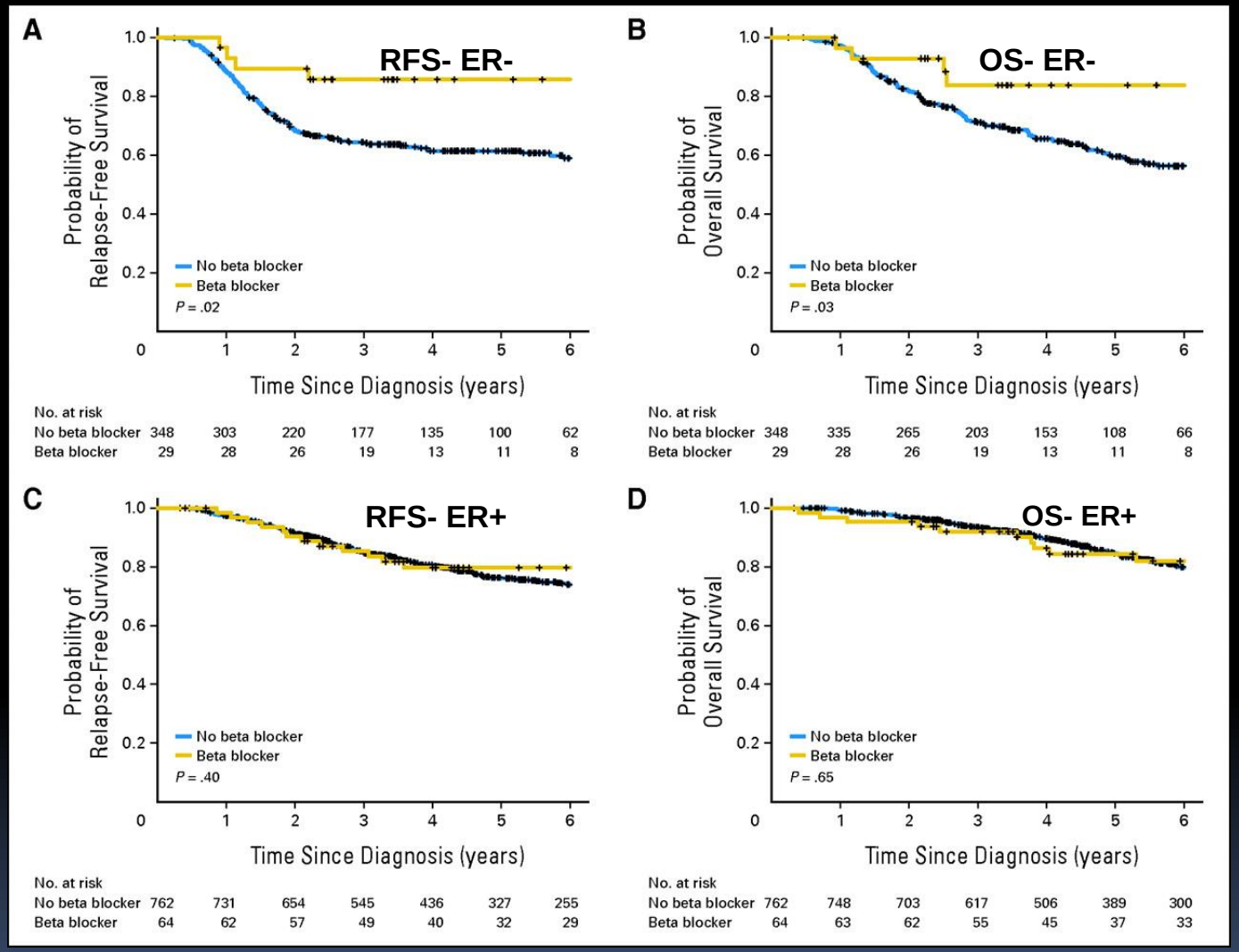
Beta-Blockers Reduce Breast Cancer Mortality



Five-year cumulative probability (unadjusted) of breast cancer–specific mortality in propranolol users (A) or atenolol users (B) versus matched nonusers.

Barron T I et al. JCO 2011;29:2635-2644

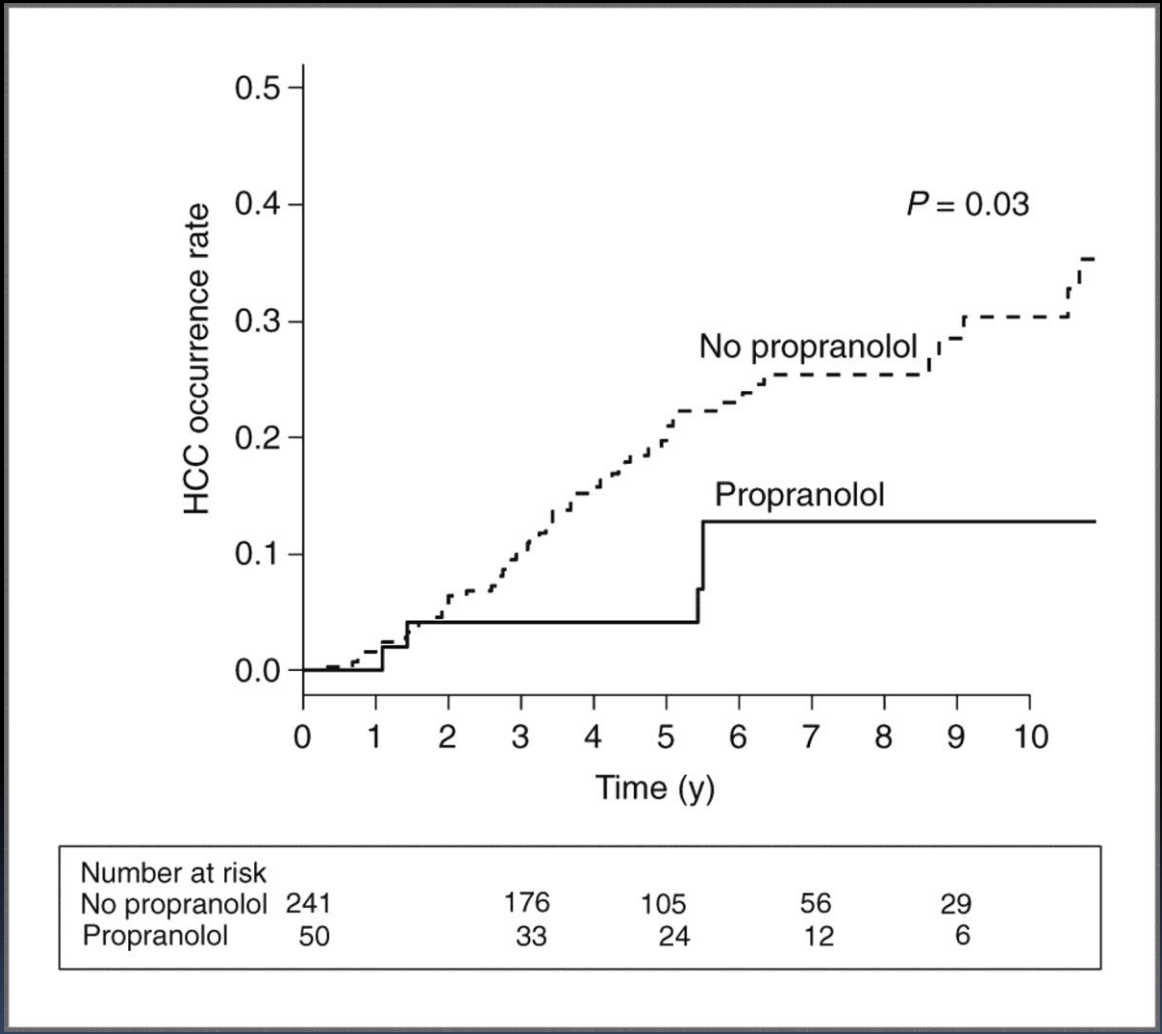
Beta-Blocker Use Is Associated With Improved Relapse-Free Survival in Patients With Triple-Negative Breast Cancer



(A) Relapse-free survival (RFS) and (B) overall survival (OS
(B) in patients with triple-negative breast cancer.
and with estrogen receptor–positive breast cancer

Melhem-Bertrandt A et al. JCO 2011;29:2645-2652

Long-term Propranolol Treatment Reduces Hepatocellular Carcinoma Incidence in Patients with HCV-Associated Cirrhosis



The 3- and 5-year HCC incidence was 4% and 4%; and 10% and 20% in patients treated and not treated by propranolol, respectively (Gray test, P = 0.03).

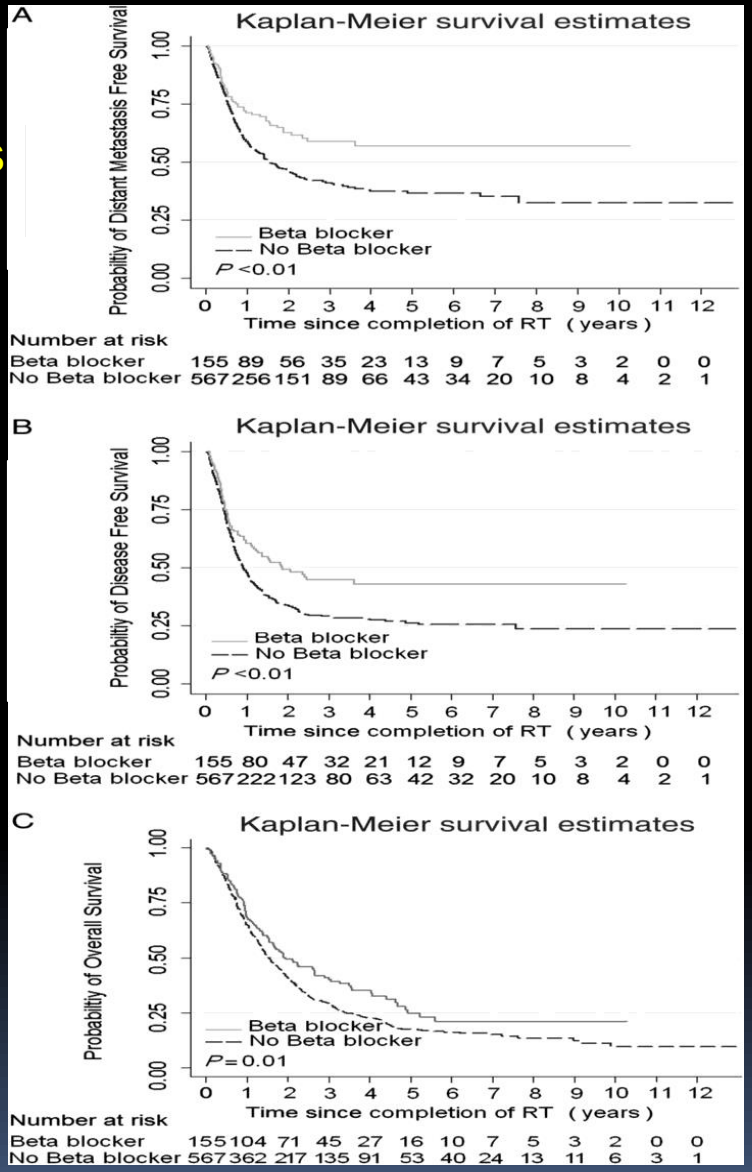
Nkontchou G et al. Cancer Prev Res 2012;5:1007-1014

Beta- Blockers Improve Survival in NonSmall Cell Lung Cancer

DMFS

DFS

OS



Comparison of (A) distant metastasis-free survival (DMFS), (B) disease-free survival (DFS), and (C) overall survival (OS) in patients with non-small-cell lung cancer (NSCLC) who were or were not taking beta-blockers during definitive radiation therapy. **Wang H M et al. Ann Oncol 2013**

Metabolic Syndrome and Risk Reduction

At Risk:
Childhood and Adult Cancer Survivors

↓

CV / Metabolic Risk Assessment
- Fasting Lipid Profile
- Smoking history
- Family HX- Ca & DM/CVD
- Blood Pressure
- BMI
- FBS,HgBA1C
- Physical Activity Hx

↓

At Risk Profile
- BMI > 30
- BMI < 30 + MS
  - FBS>100,HgBA1C->5.8%,
  - TG>150, HDL<45-55)
- BP elevated/ on meds
- Low PA history

↓

Lifestyle Prescription (Diet, Activity, Stress Reduction)
Pharmacologic (Metformin,etc)
Surgical ?

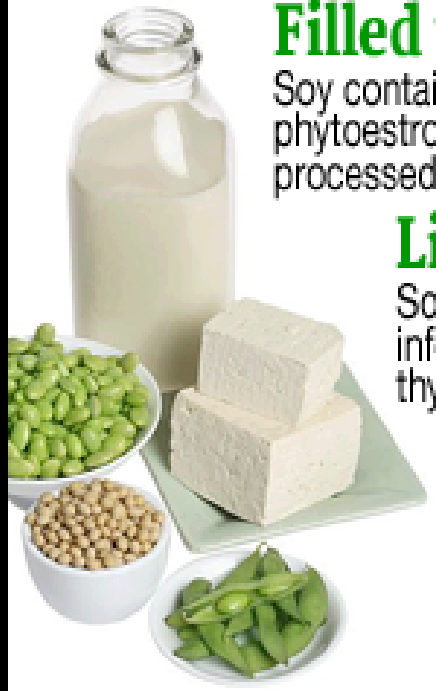
Dietary and Lifestyle Goals

- Prudent plant-based ***dietary pattern*** reduces weight gain,improves metabolic status and disease risk and daily physical activity
- Its not individual food items alone
- Limit calorie-dense foods linked to obesity and metabolism
  - Red meat, High fat dairy (butter, whole milk)
  - Limit calorie dense carbohydrates
    - Sugar, FBCS foods, high calorie soda, fruit juices
    - Whites- (potatoes, white pasta, white bread)
  - Emphasize whole grains high in fiber, nutrients
  - Increase intake of diverse plant based foods Soy *NOT* a risk
- Limit Alcohol – Increases Br Ca Risk but ***? Recurrence Risk***
  - Balance modest CV benefit for light intake
- Avoid high dose supplements: Remember the U-shaped Curve

Vitamin D3 2000-4000 IU daily (>30 but <50ng/ ml) : Daily Multivitamin

What about Soy?

The Truth About Soy



Filled with Anti-Nutrients

Soy contains high levels of phytic acid and phytoestrogens which withdraw nutrients when processed by your body.

Linked to Multiple Cancers

Soy has been linked to endocrine disruption, infertility, breast cancer, hypothyroidism and thyroid cancer

Harmful for Children

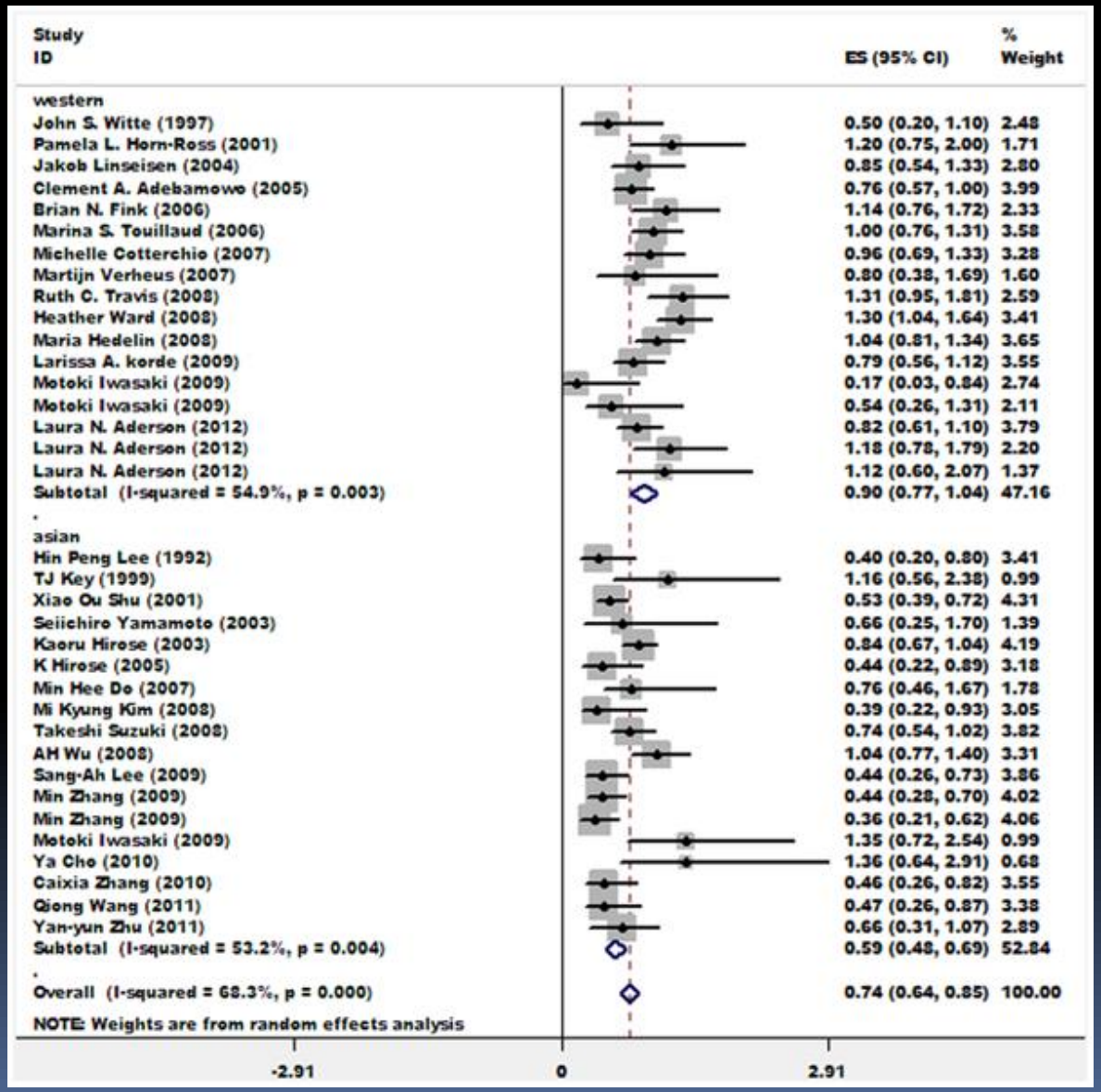
Diets high in phytic acid can cause growth problems in children. Soy Formula has been linked to autoimmune thyroid disease in infants. 50% of Female embryos exposed to soy estrogen had

Infants on soy formula receive the estrogen equivalent of 5 birth control pills a day

healthy surprise

Source: Primal Body, Primal Mind N.Gedgaudas CNS CNT

Association between Soy Isoflavone Intake and Breast Cancer Risk for Pre- and Post-Menopausal Women: A Meta-Analysis of Epidemiological Studies



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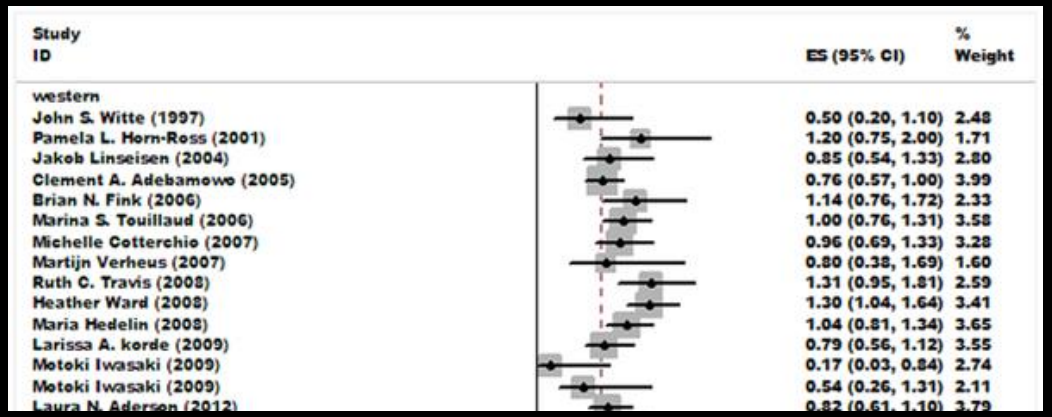
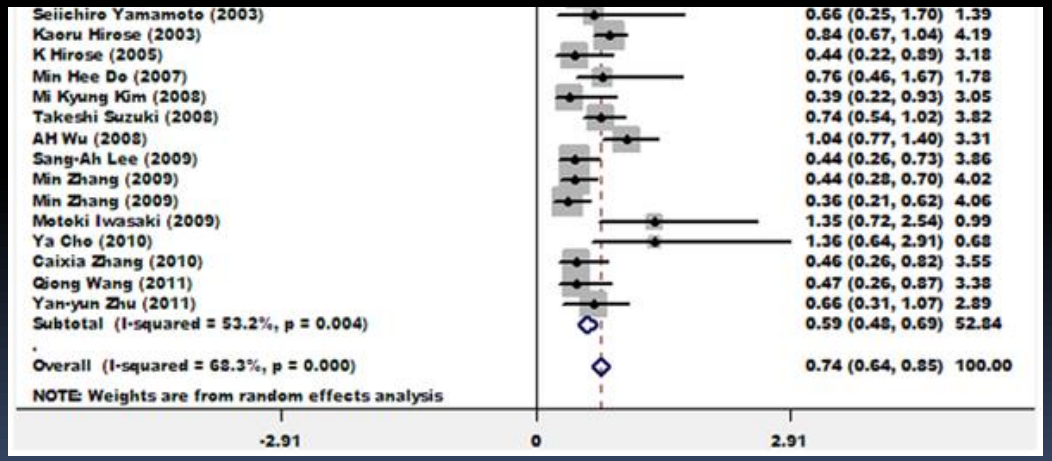
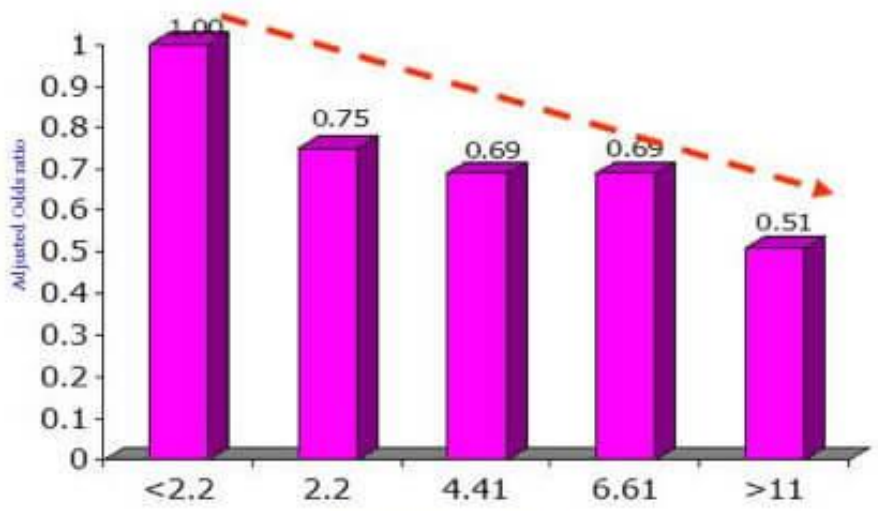


Soy isoflavone intake is protective against breast cancer in both pre- and post-menopausal women



Soy reduces Breast Cancer Risk



Shanghai Women's Health Study

J Nutr 133: 2874, 2003

(Shanghai: 1459 cases, 1556 control)

Results: pre/post, x age 47.
Other legumes not protective.

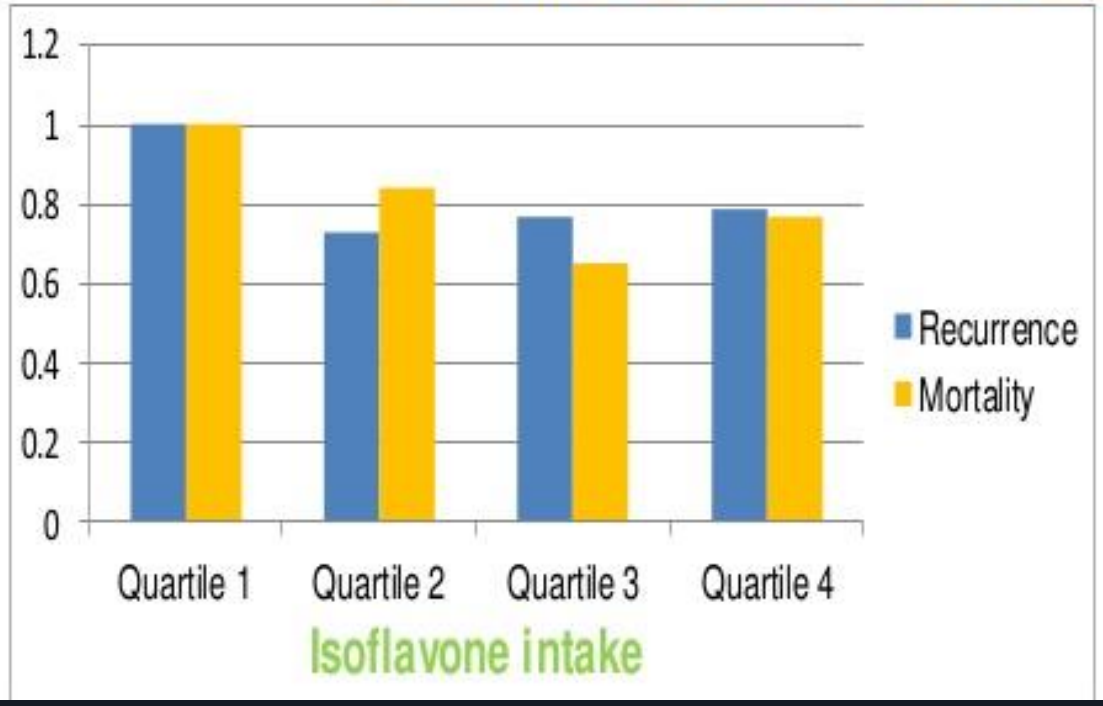
> 11 grams Soy Protein Daily
=
~ 50 % Decrease in Breast Cancer Risk

The protective effects likely due to the multiple protective properties of soy isoflavones: -

Anti-angiogenesis, Anti-Mitotic, Anti-estrogenic, Protein Tyrosine Kinase Inhibition and Free Radicals Scavenging

Soy and Breast Cancer Survival

The Shanghai Breast Cancer Study

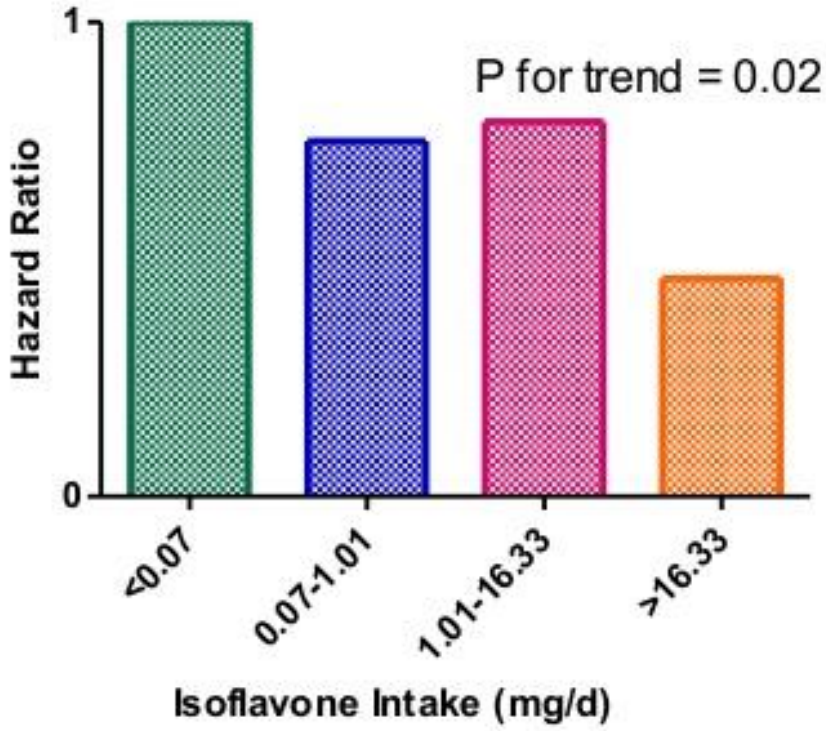


High Soy Intake throughout life

Largely Dietary Soy

Soy and Breast Cancer Survival

Soy and Cancer Recurrence or Mortality- The WHEL Study

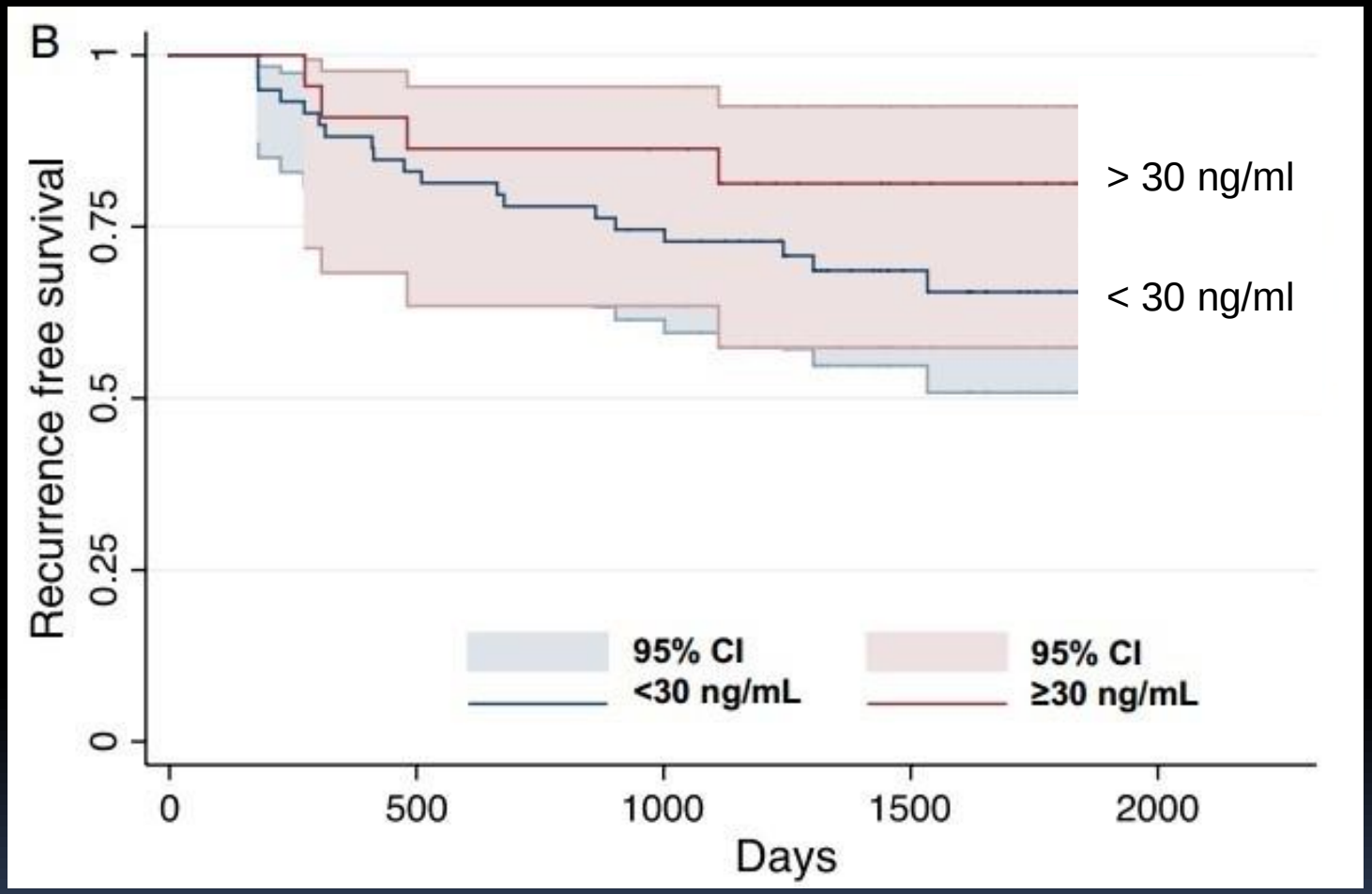


Caan BJ. Cancer Epidemiology, Biomarkers, & Prevention. 2011;20:854-8.

What about Vitamin D ?

Pretreatment vitamin D level and response to neoadjuvant chemotherapy in women with breast cancer on the I-SPY trial

Clark AS et al. Cancer Med. 2014 Jun;3(3):693-701



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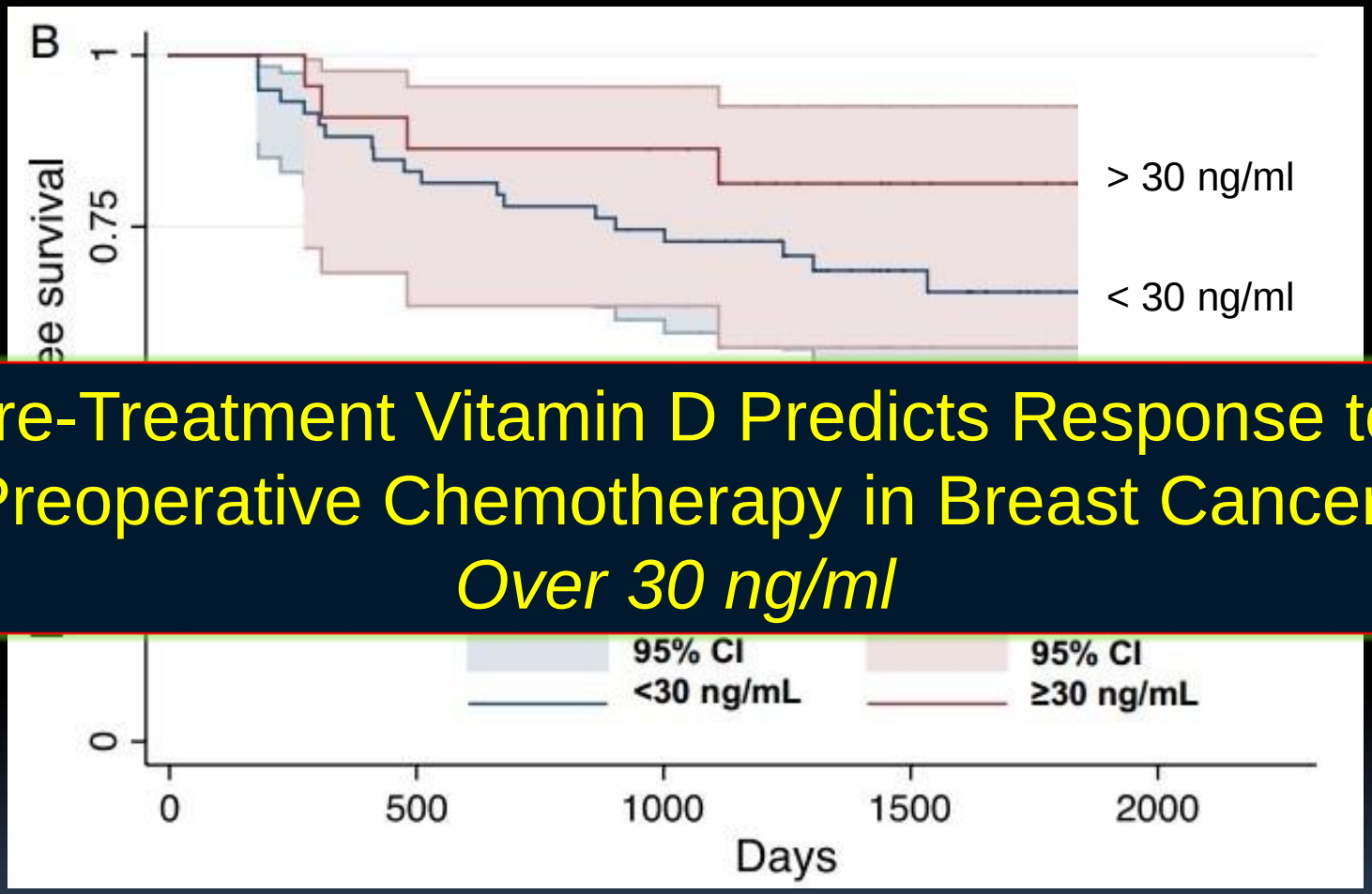
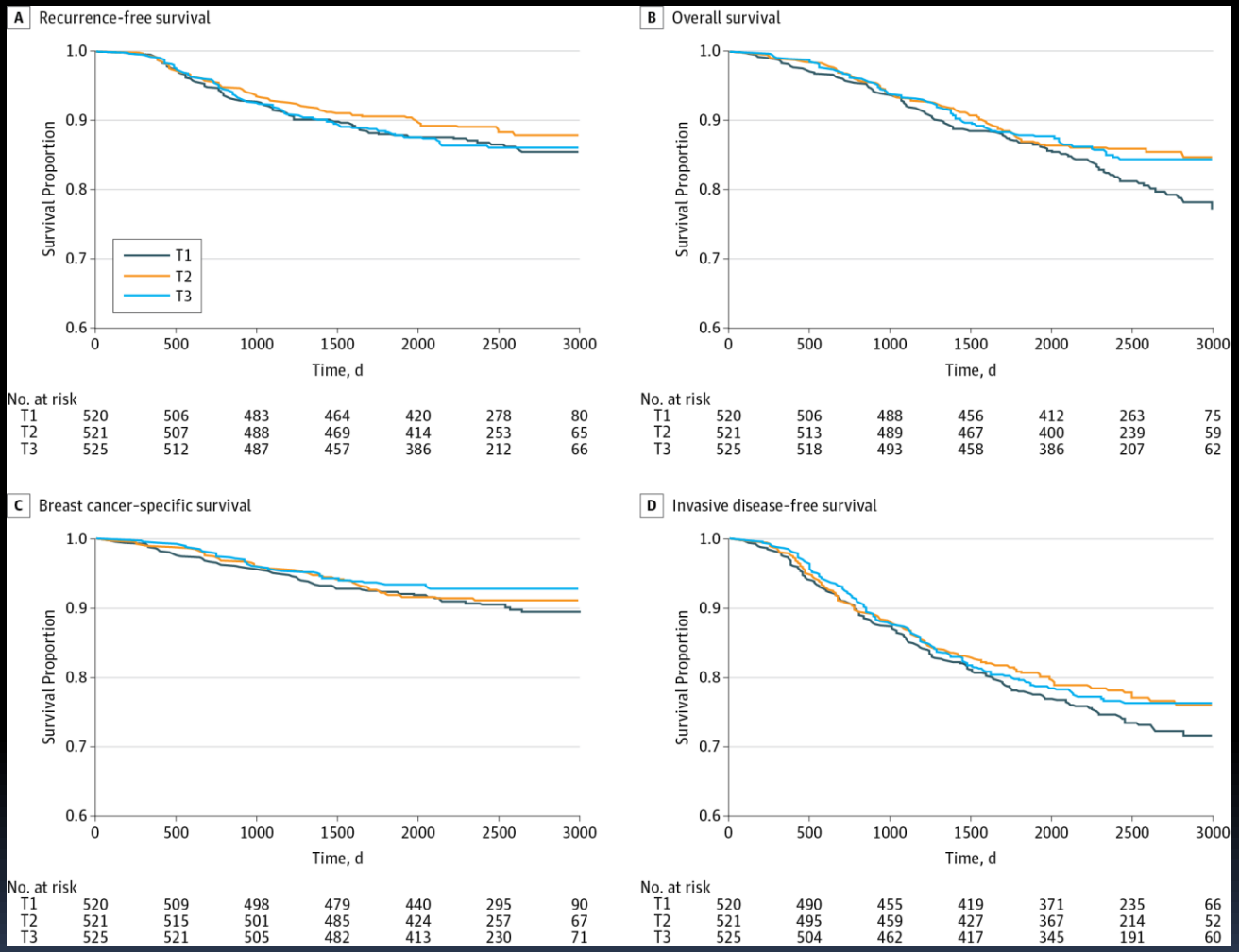


Pre-Treatment Vitamin D Predicts Response to Preoperative Chemotherapy in Breast Cancer

Over 30 ng/ml

Association of Serum Level of Vitamin D at Diagnosis With Breast Cancer Survival: A Case-Cohort Analysis in the Pathways Study

Song Yao, PhD, Marilyn L. Kwan, PhD, Isaac J. Ergas, MPH; et al JAMA Oncol. 2017;3(3):351-357



Cohort study of 1666 women with breast cancer, higher serum 25-hydroxyvitamin D levels were independently associated with better outcomes, including overall survival.

Women in the highest third of Vitamin D (>28 ng/ ml) had reduced hazards of all-cause death
Associations were stronger in premenopausal women

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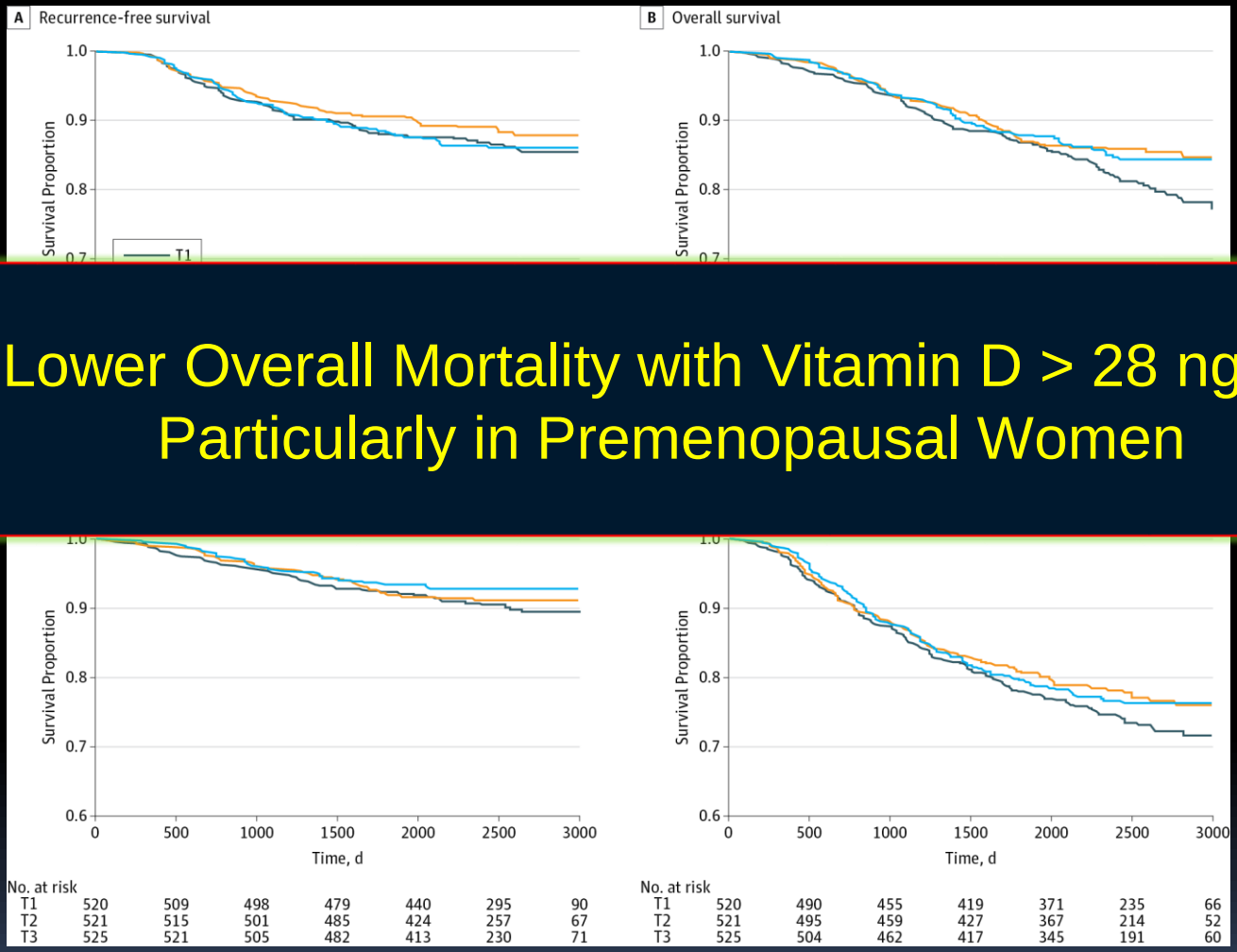

Lower Overall Mortality with Vitamin D > 28 ng/ ml Particularly in Premenopausal Women

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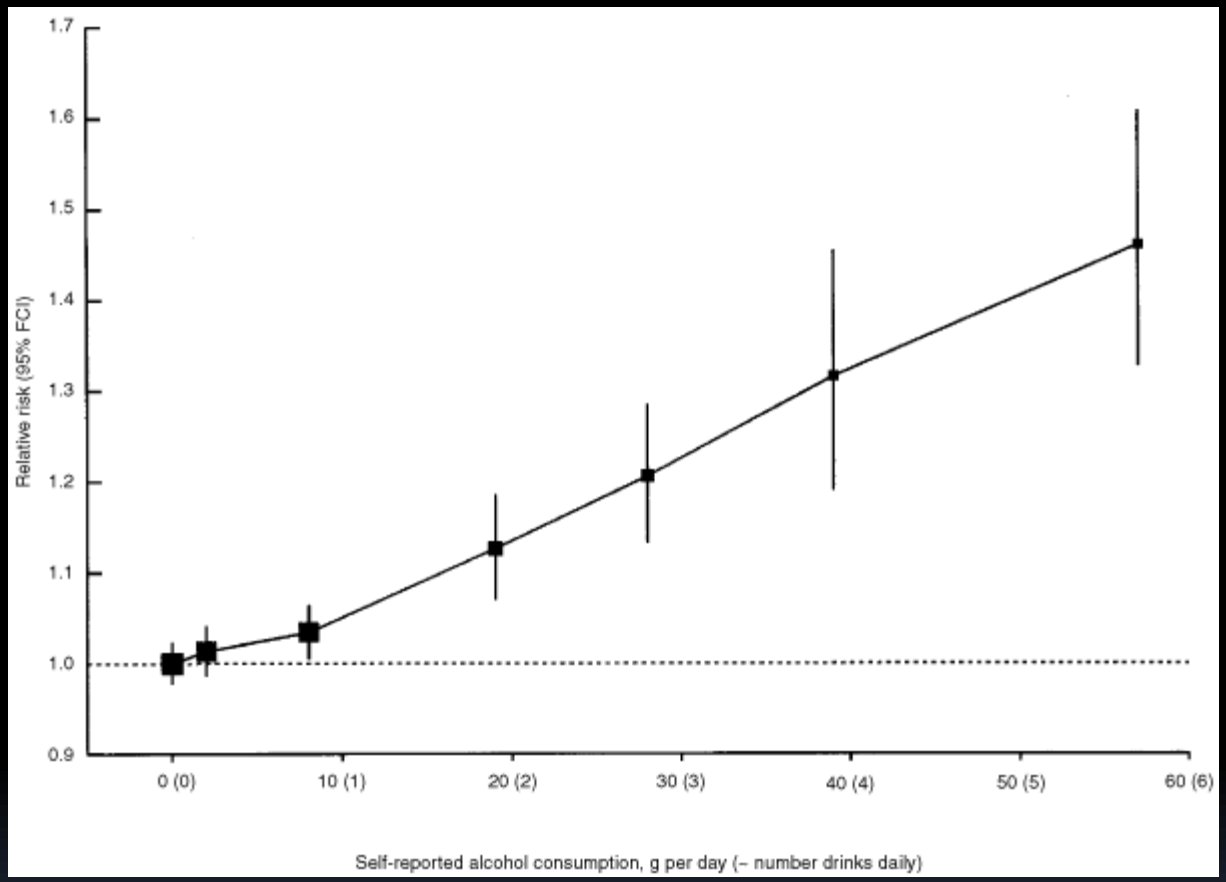
Associations were stronger in premenopausal women

Alcohol & Breast Cancer Risk

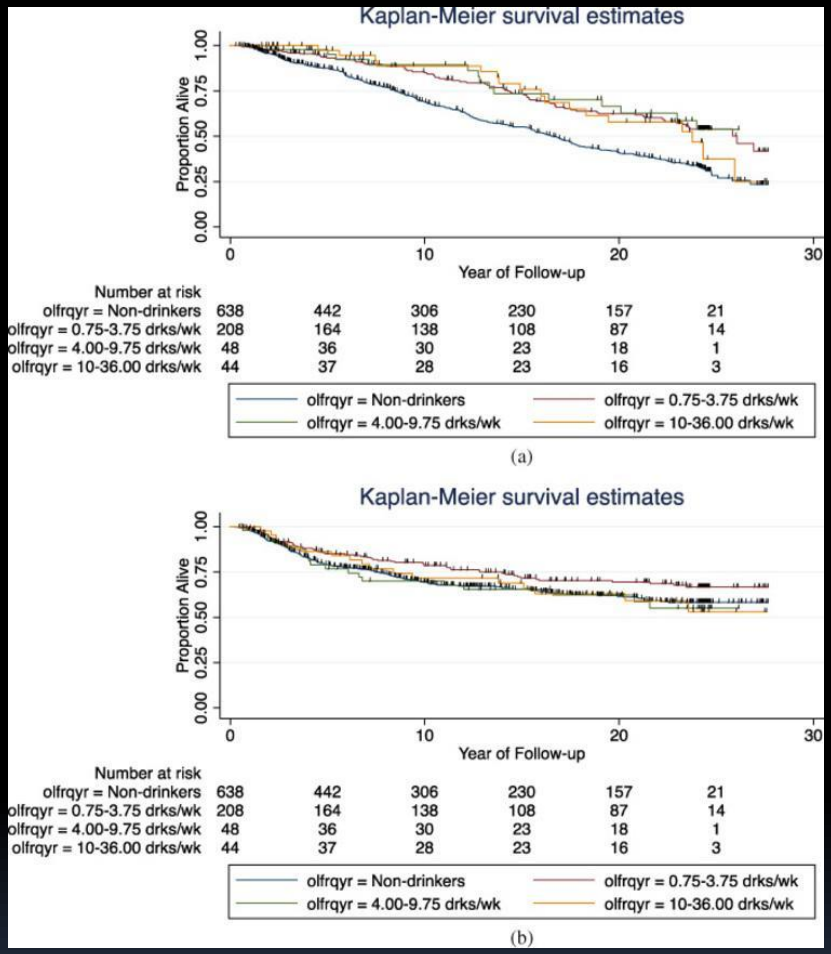


Relative risk of breast cancer in relation to reported intake of alcohol

Alcohol, tobacco and breast cancer – collaborative reanalysis of individual data from 53 epidemiological studies, including 58 515 women with breast cancer and 95 067 women without the disease .Collaborative Group on Hormonal Factors in Breast Cancer.

British Journal of Cancer(2002)87,1234–1245

Alcohol consumption and mortality after breast cancer diagnosis: The health and functioning in women study



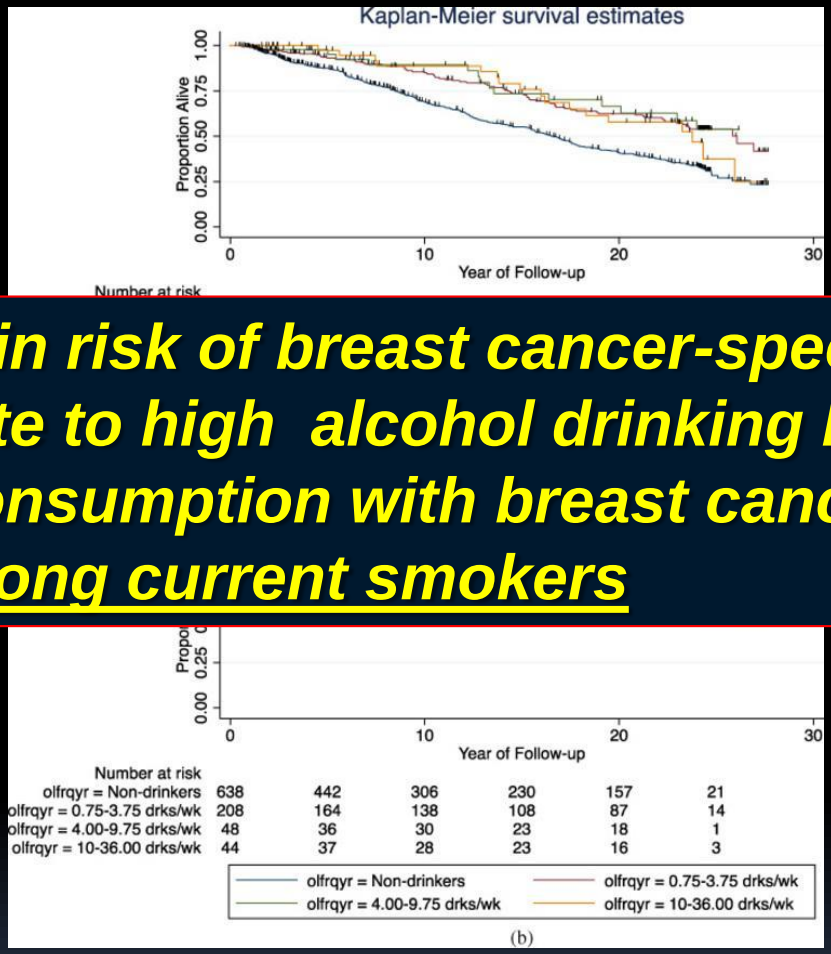
Prospective cohort study, regular consumption of 0.75–36.00 alcoholic drinks per week during the year prior to breast cancer diagnosis
Associated with:

A reduction in other-cause mortality

No increase in risk of breast cancer-specific mortality with moderate (4.00–9.75 drinks/week) and high (10.00–36.00 drinks/week) alcohol drinking in the overall cohort

A positive association of alcohol consumption with breast cancer-specific mortality among current smokers

Alcohol consumption and mortality after breast cancer diagnosis: The health and functioning in women study



No increase in risk of breast cancer-specific mortality with moderate to high alcohol drinking but association of alcohol consumption with breast cancer-specific mortality among current smokers

Prospective cohort study, regular consumption of 0.75–36.00 alcoholic drinks per week during the year prior to breast cancer diagnosis
Associated with:

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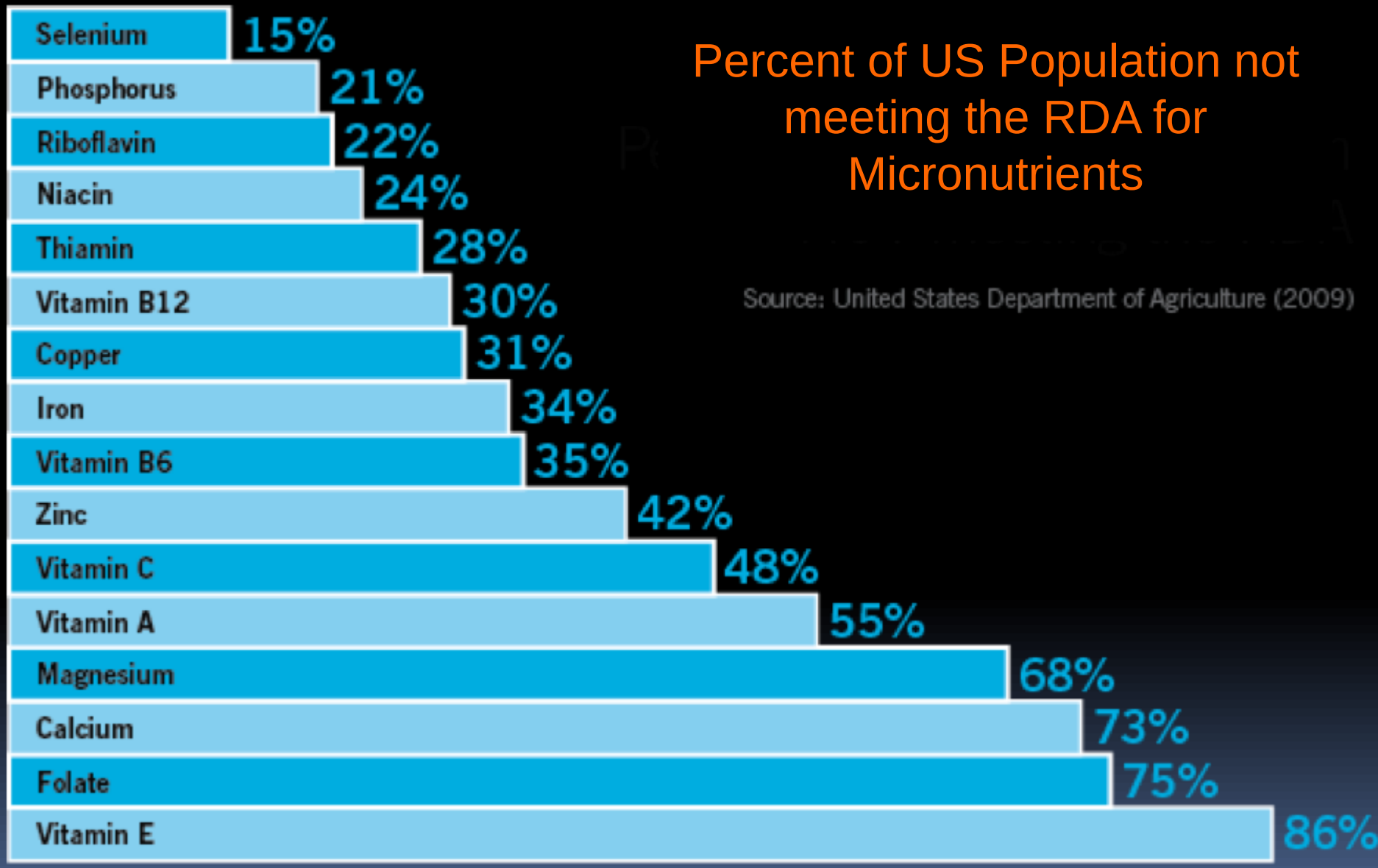
A positive association of alcohol consumption with breast cancer-specific mortality among current smokers

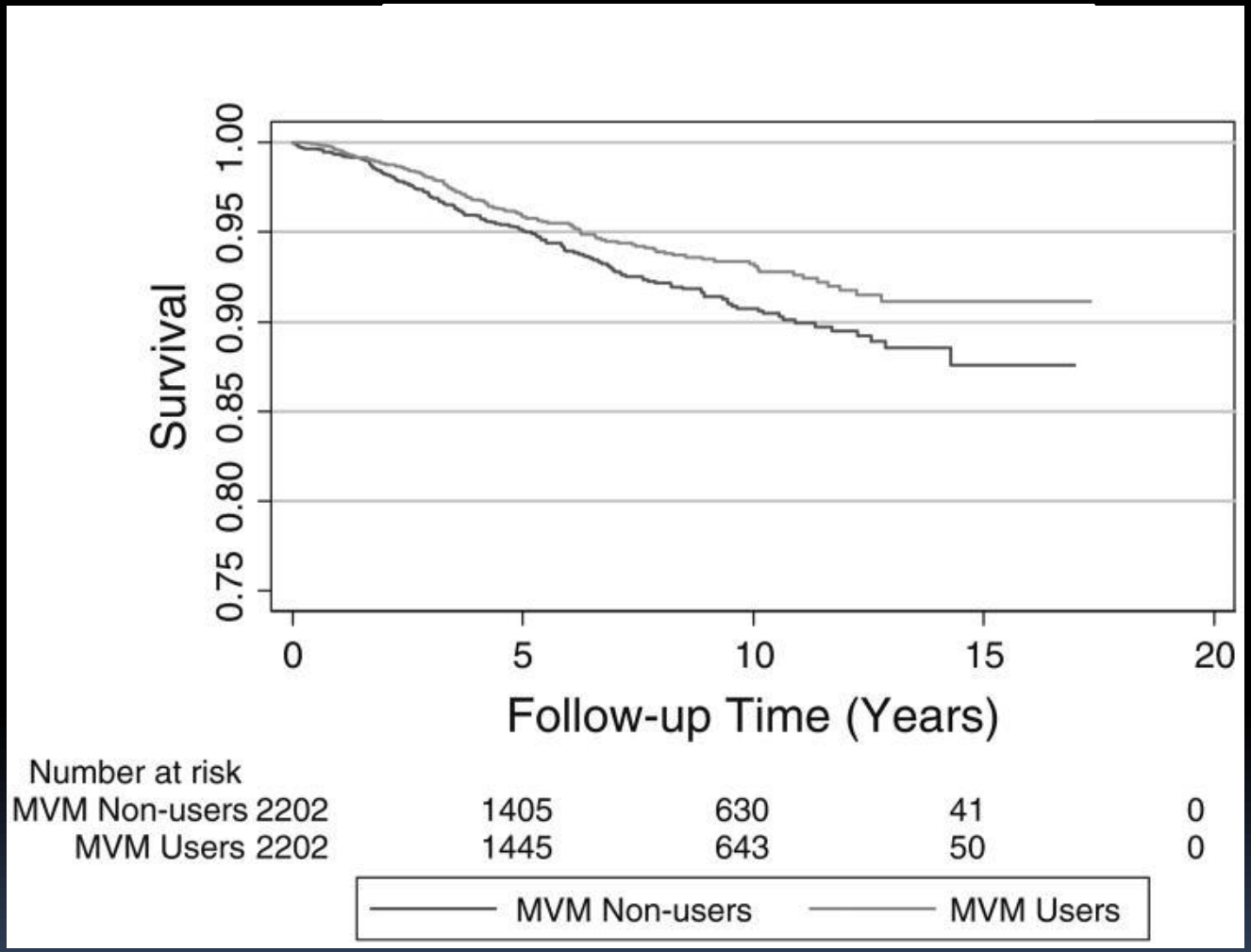
Percent of US Population not meeting the RDA for Micronutrients



Source: United States Department of Agriculture (2009)

Multivitamin and mineral use and breast cancer mortality in older women with invasive breast cancer in the women's health initiative (WHI)

S.Wassertheil-Smoller et al. Breast Cancer Res Treat. 2013 Oct; 141(3): 495–505



7,728 women aged 50–79 at enrollment in the women's health initiative (WHI) in 40 clinical sites across the United States diagnosed with incident invasive breast cancer during WHI, followed for a mean of 7.1 years after breast cancer diagnosis.

Breast cancer mortality was 30 % lower in MVM users as compared to non-users (HR = 0.70)

"Money isn't everything, but it is important"
Socioeconomic Determinants of Health,
Stress and the Biology of Inequality

Brunner, E. BMJ 314:1472-1488,1997

"The available evidence already urges medical oncologists to incorporate dietary habits and lifestyle attitudes as a prominent component of their breast cancer adjuvant treatment strategy."

"A not-only-drug approach to the science and practice of medical oncology has come of age"

Puntoni M et al J Clin Oncol 27: 323-325, 2009

D B Boyd, MD,MS

Contact Information

Yale Smilow Subspecialty Group

Bendheim Cancer Center

Greenwich Hospital – Yale Health

203-863-4610 (office)

barry.boyd@yale .edu