

Physical Activity, Diet, Obesity and Cancer Risk, Prognosis, and Patient Reported Outcomes

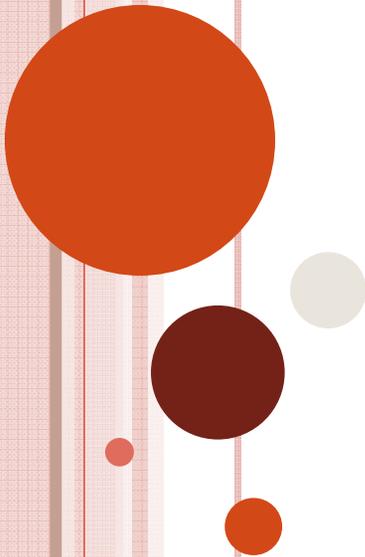
Rachel Ballard-Barbash, MD, MPH
December 2010

Applied Research Program (ARP)
Division of Cancer Control and Population Sciences (DCCPS)
National Cancer Institute (NCI)

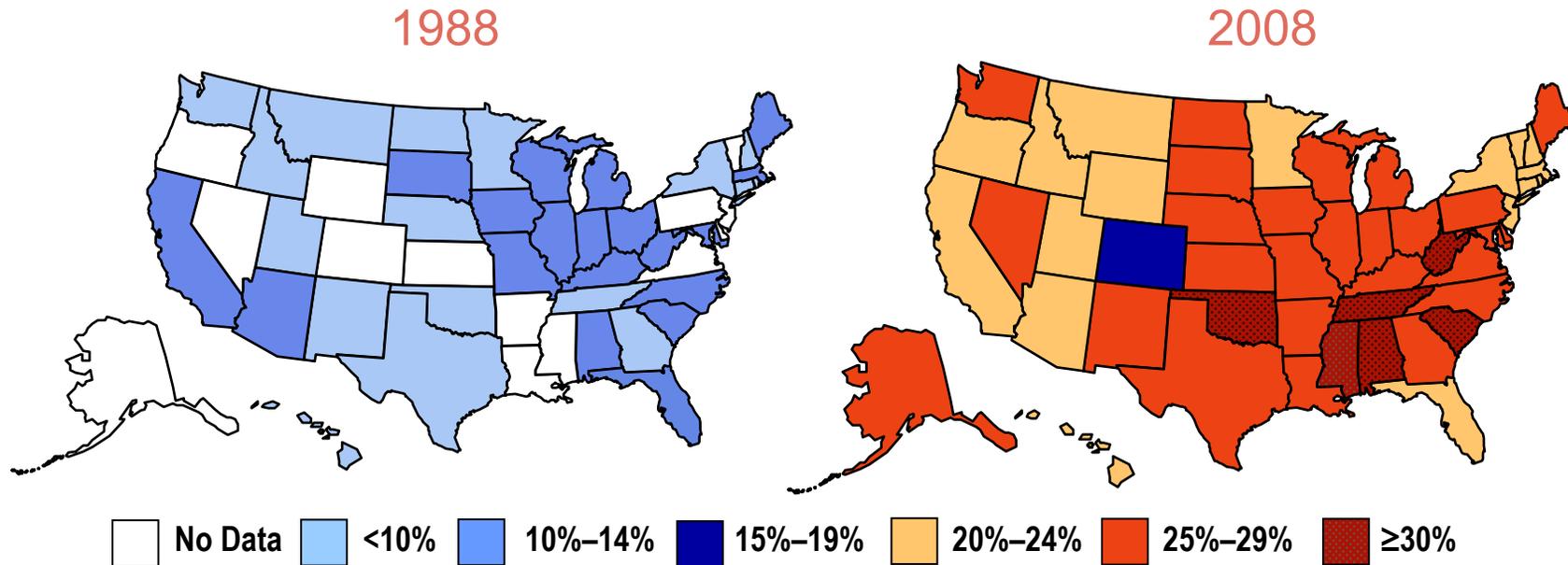


DISCLOSURES

No relevant Financial Relationships with
Commercial Interest



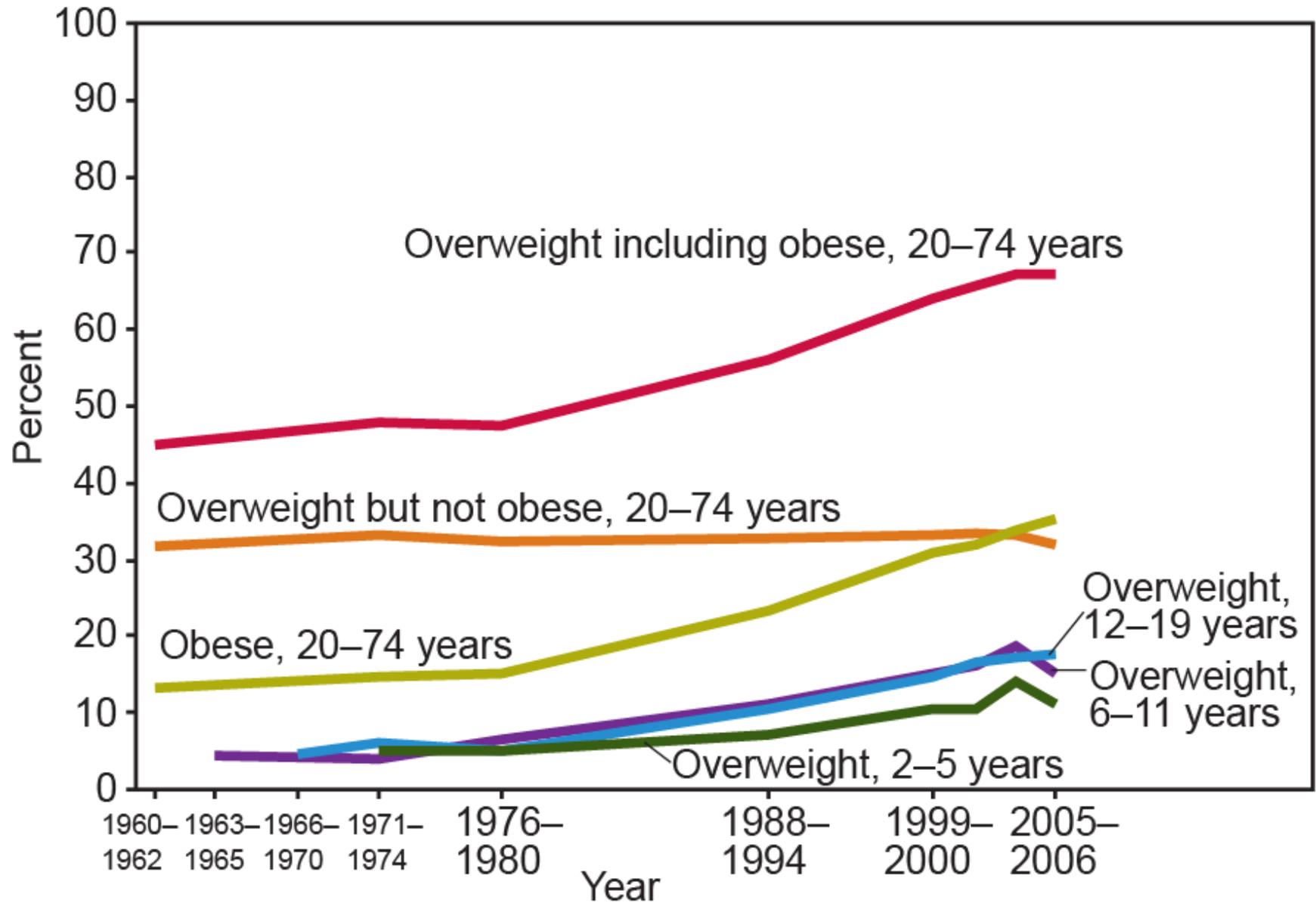
U.S. Obesity Rates Are at Historically High Levels: Adult Obesity Rates by State



Source: Centers for Disease Control and Prevention

- Sharp increase in obesity in US adults in recent decades
- Negative economic and health effects of obesity, including several forms of cancer - obesity-related healthcare costs estimated at \$147Billion annually (Finkelstein et al. 2009)

Overweight and obesity



SOURCE: CDC/NCHS, *Health, United States, 2009*, Figure 7. Data from the National Health Examination Survey and the National Health and Nutrition Examination Survey.

Global Trends in Obesity by Sex, Adults 30+: 2005 vs. 2015 (*projected*)

Males, 2005



Females, 2005



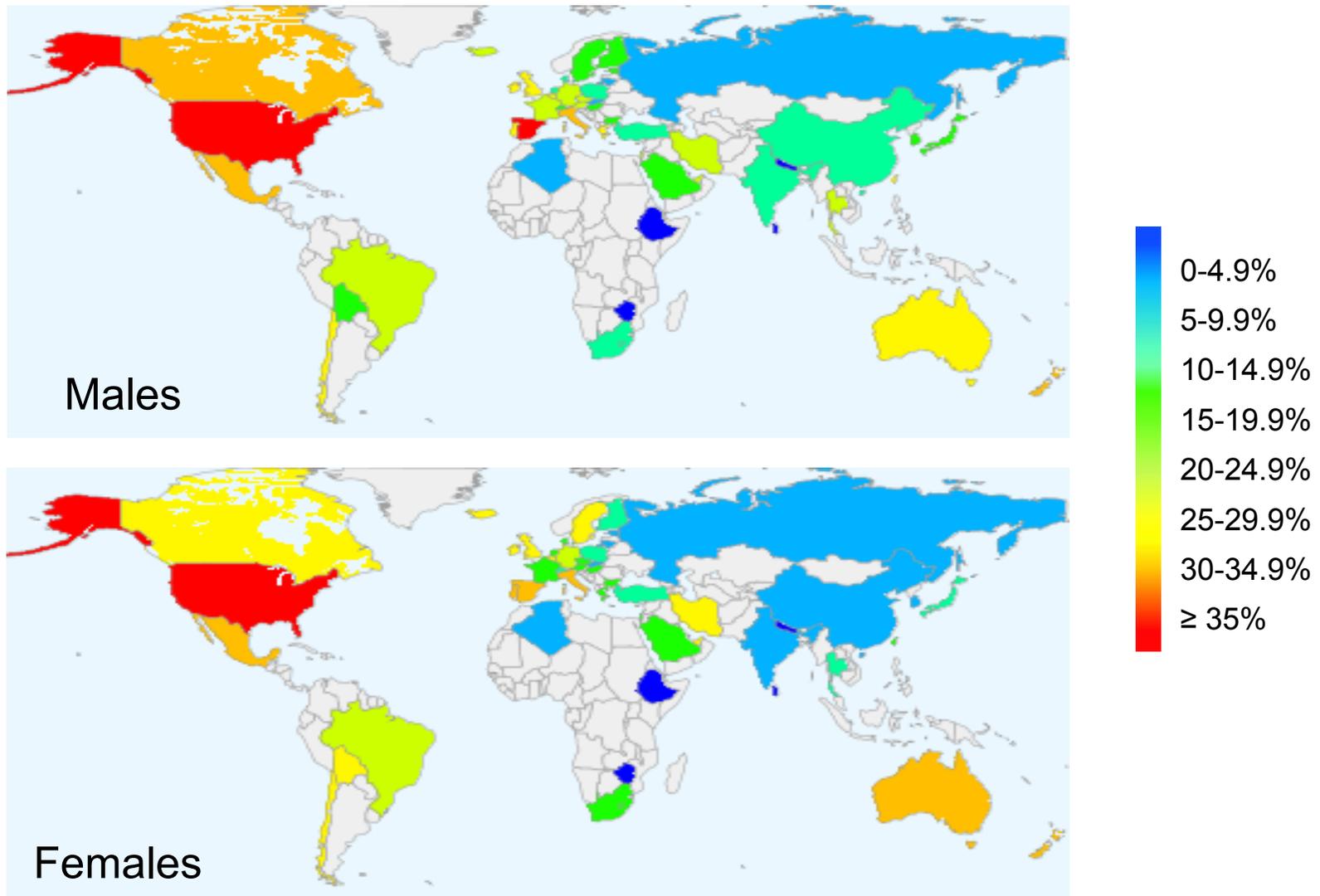
Males, 2015



Females, 2015

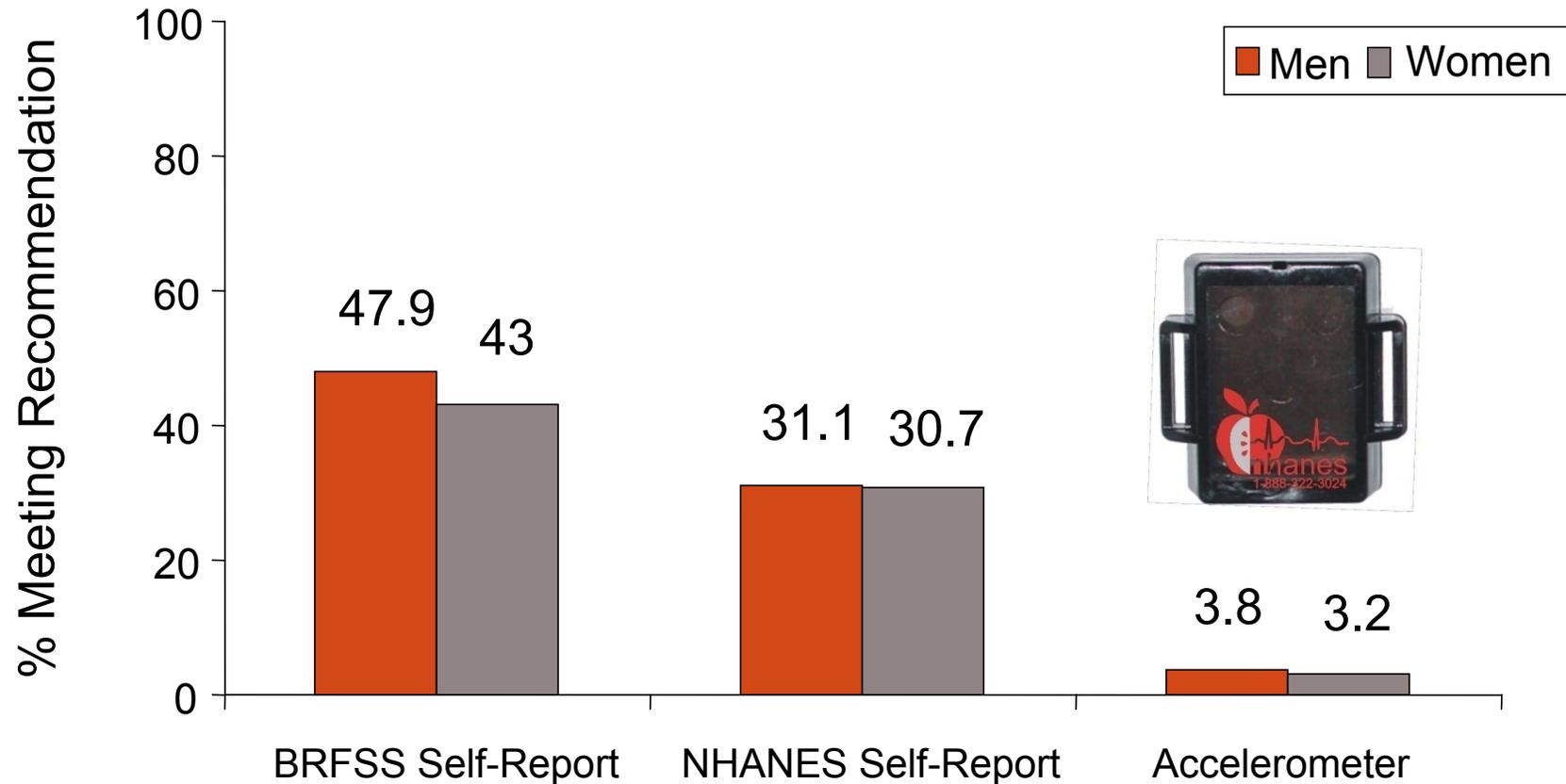


Rates of Overweight in U.S. Children Lead the World: Percentage of Children Meeting Criteria for Overweight



Spruijt-Metz D, J for Research on Adolescence, 2010; in press.

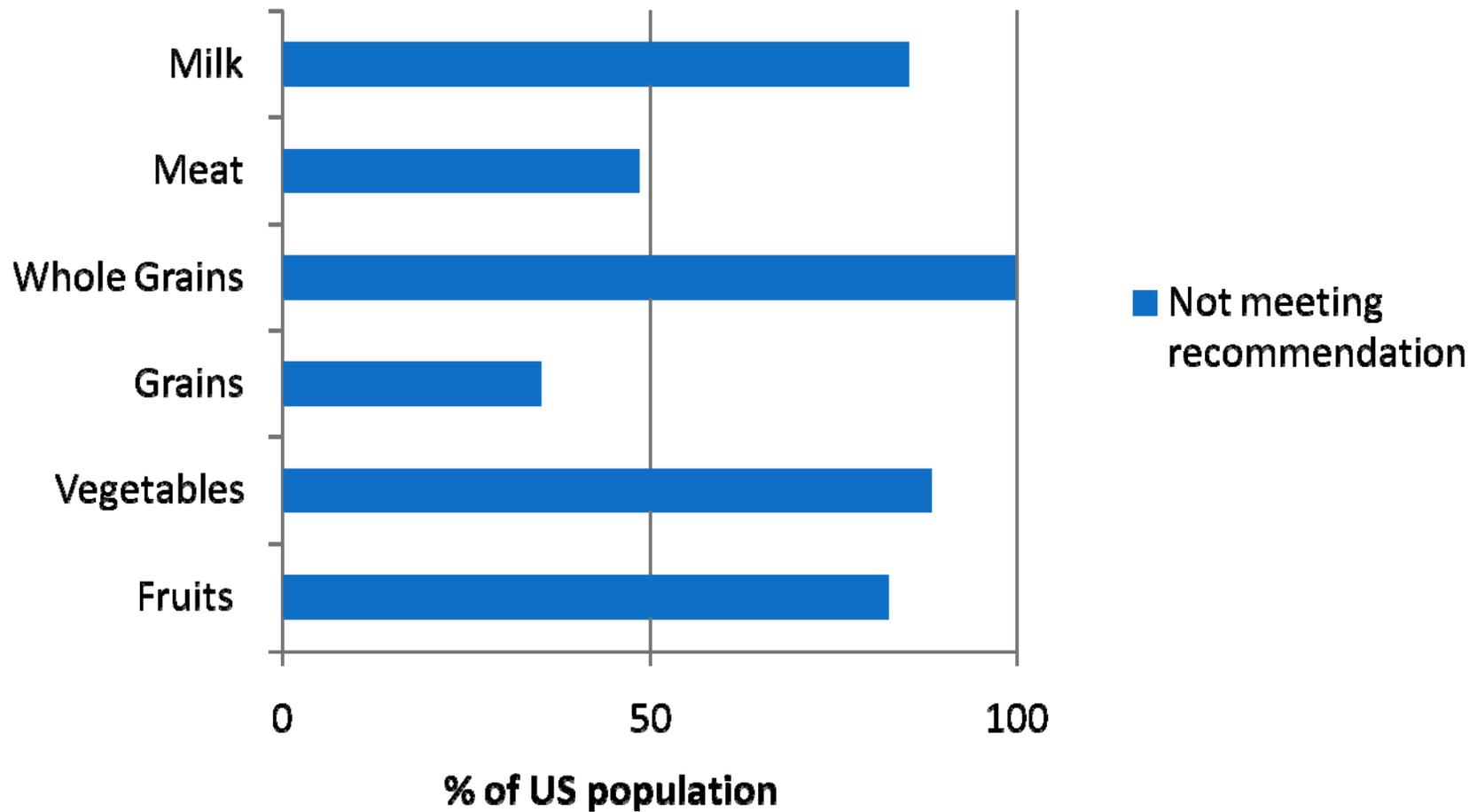
Self Reports of Physical Activity Routinely Over-estimate Amount of Physical Activity, 2003-04



NHANES sample = 6329 individuals with at least one valid day of accelerometer wear

Healthy Eating Index Components

Prevalence of Not Meeting Food Group Guidance

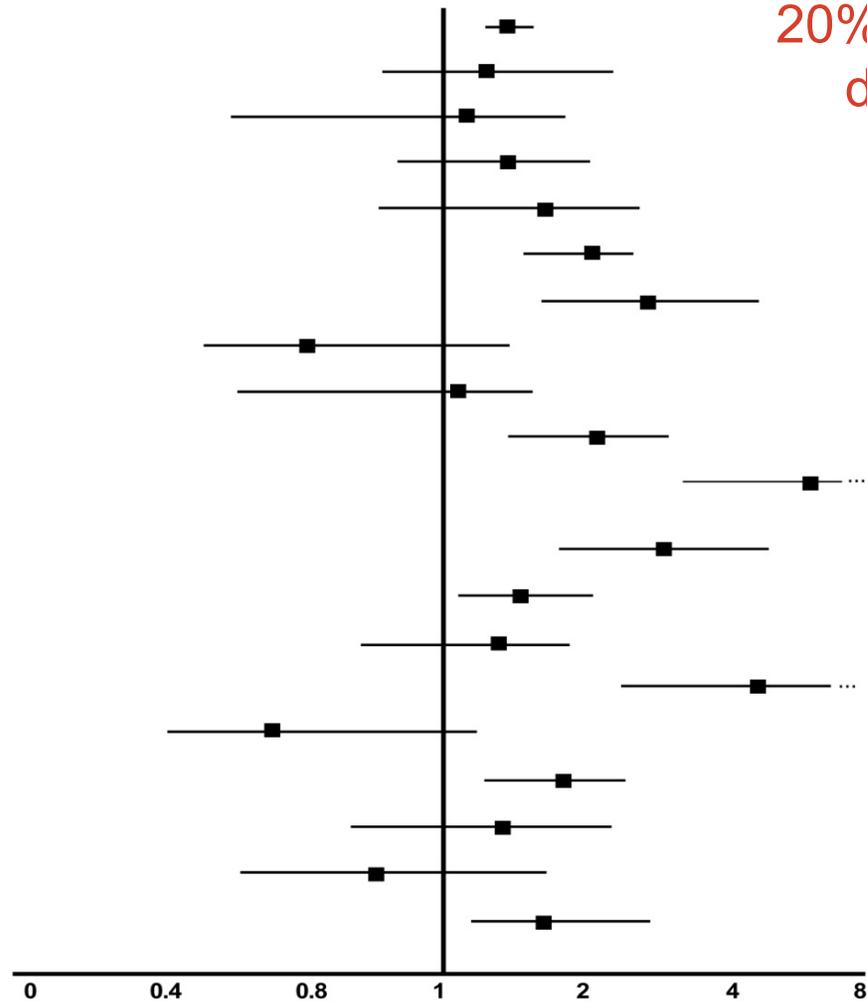


Krebs-Smith, S et al 2009

Body Mass Index and Cancer Mortality: Women

Type of Cancer

- All cancers
- Esophageal cancer
- Stomach cancer
- Colorectal cancer
- Liver cancer
- Gallbladder cancer
- Pancreatic cancer
- Lung cancer
- Melanoma
- Breast cancer
- Cancer of the corpus and uterus, not otherwise specified
- Cervical cancer
- Ovarian cancer
- Bladder cancer
- Kidney cancer
- Brain cancer
- Non-Hodgkin's lymphoma
- Multiple myeloma
- Leukemia
- All other cancers



20% of cancer deaths in women

Obesity and Cancer Risk

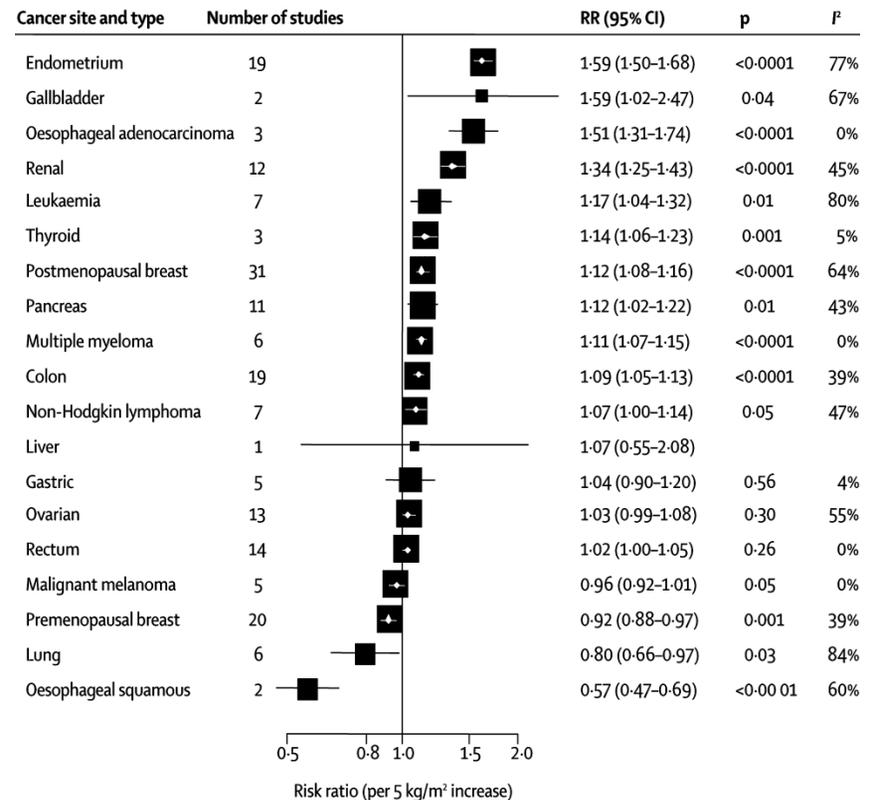
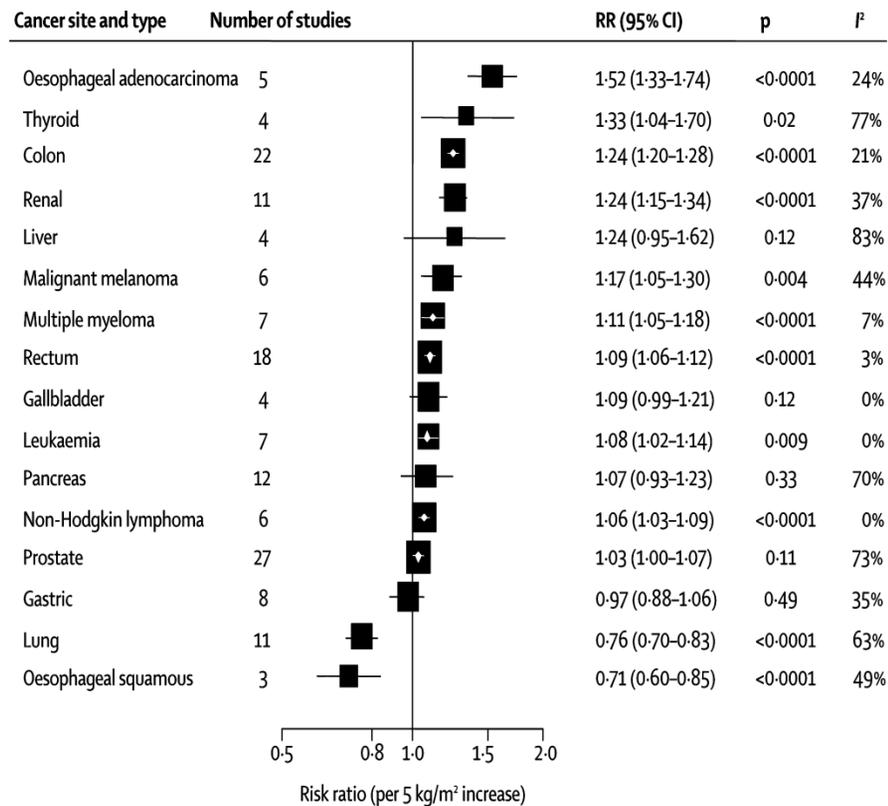
Type of cancer	Relative risk ^a with BMI of 25–30 kg/m ²	Relative risk ^a with BMI of ≥30 kg/m ²
Colorectal (men)	1.5	2.0
Colorectal (women)	1.2	1.5
Female breast (post-menopausal)	1.3	1.5
Endometrial	2.0	3.5
Kidney (renal cell)	1.5	2.5
Esophageal (adenocarcinoma)	2.0	3.0
Pancreatic	1.3	1.7
Liver	ND	1.5–4.0
Gallbladder	1.5	2.0
Gastric cardia (adenocarcinoma)	1.5	2.0

Fair AM, Montgomery K. Methods Mol Biol 472:57-88, 2009.

BMI Associations Vary by Type of Cancer

Men

Women



Physical Activity & Cancer: Epidemiology

Cancer	Number of Studies	Decrease Risk	Countries Involved
Colorectal	50	Yes	N Amer, Eu, Asia, Aus, NZ
Breast	57	Yes	N Amer, Eu, Asia, Aus
Prostate	36	No	N Amer, Eu, Asia
Endometrial	15	Yes	N Amer, Eu, Asia
Lung	21	Yes	US, Eu

Physical Activity, Body Fatness, and the Risk of Cancer



BODY FATNESS, AND THE RISK OF CANCER

In the judgement of the Panel, the factors listed below modify the risk of cancer. Judgements are graded according to the strength of the evidence.

	DECREASES RISK		INCREASES RISK	
	Exposure	Cancer site	Exposure	Cancer site
Convincing			Body fatness	Oesophagus ¹ Pancreas Colorectum Breast (postmenopause) Endometrium Kidney
			Abdominal fatness	Colorectum
Probable	Body fatness	Breast (premenopause)	Body fatness Abdominal fatness	Gallbladder ² Pancreas Breast (postmenopause) Endometrium
			Adult weight gain	Breast (postmenopause)
Limited — suggestive			Body fatness Low body fatness	Liver Lung
Substantial effect on risk unlikely	None identified			

- 1 For oesophageal adenocarcinomas only.
2 Directly and indirectly, through the formation of gallstones.

For an explanation of all the terms used in the matrix, please see chapter 3.5.1, the text of this section, and the glossary.



PHYSICAL ACTIVITY, AND THE RISK OF CANCER

In the judgement of the Panel, physical activity¹ modifies the risk of the following cancers. Judgements are graded according to the strength of the evidence.

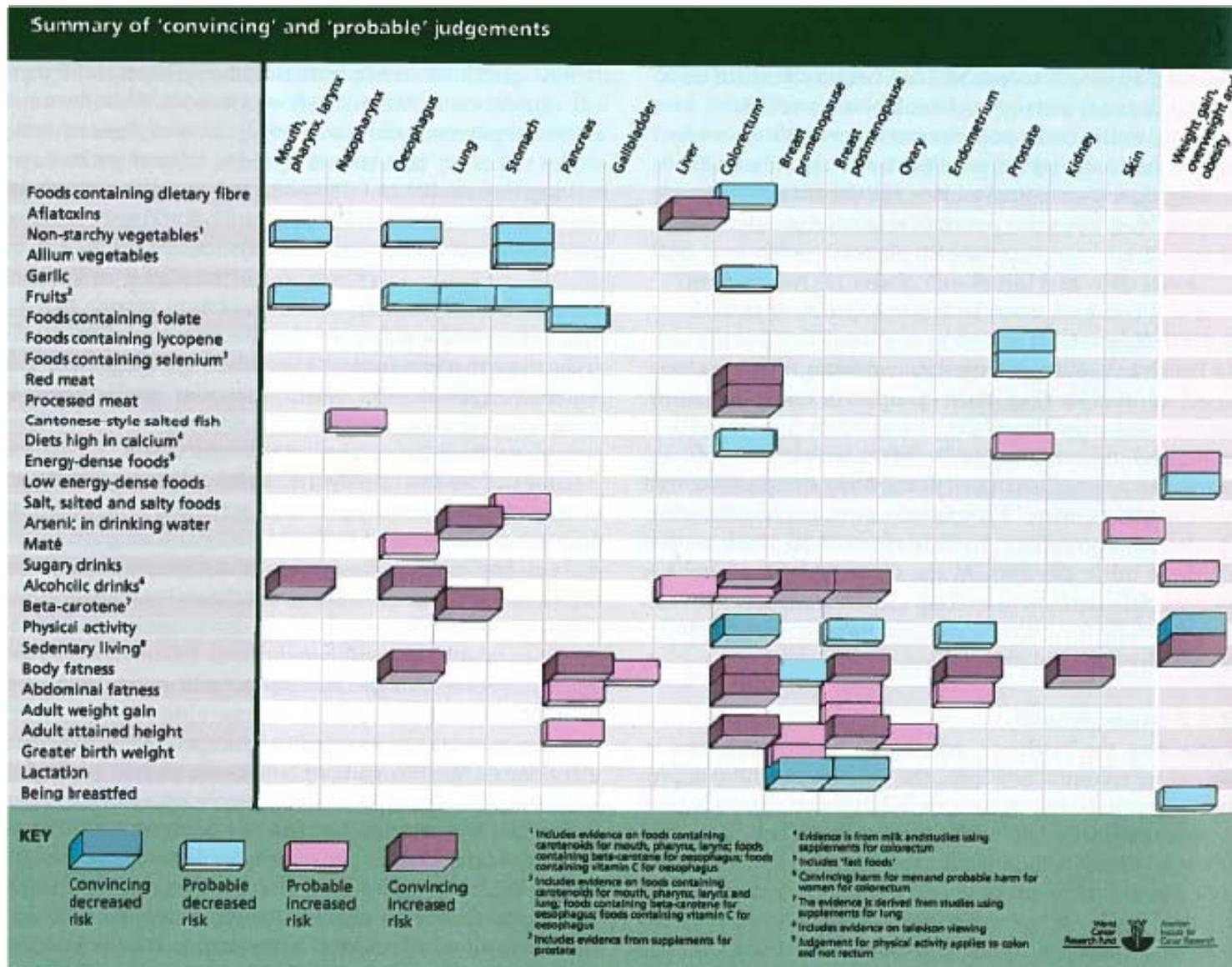
	DECREASES RISK	INCREASES RISK
Convincing	Colon ²	
Probable	Breast (postmenopause) Endometrium	
Limited — suggestive	Lung Pancreas Breast (premenopause)	
Substantial effect on risk unlikely	None identified	

- 1 Physical activity of all types: occupational, household, transport, and recreational.
2 Much of the evidence reviewed grouped colon cancer and rectal cancer together as 'colorectal' cancer. The Panel judges that the evidence is stronger for colon than for rectum.

For an explanation of the terms used in the matrix, please see chapter 3.5.1, the text of this chapter, and the glossary.



Food, Nutrition, Physical Activity, and the Prevention of Cancer



Meta-analysis Evaluating Measures of Adiposity at Breast Cancer Diagnosis and Subsequent Prognosis

	Recurrence at 5 yrs HR (95% CI)	Death at 10 yrs HR (95% CI)
↑ Body Weight	1.78 (1.50-2.11)	1.36 (1.19-1.55)
↑ BMI	1.91 (1.52-2.40)	1.60 (1.38-1.76)

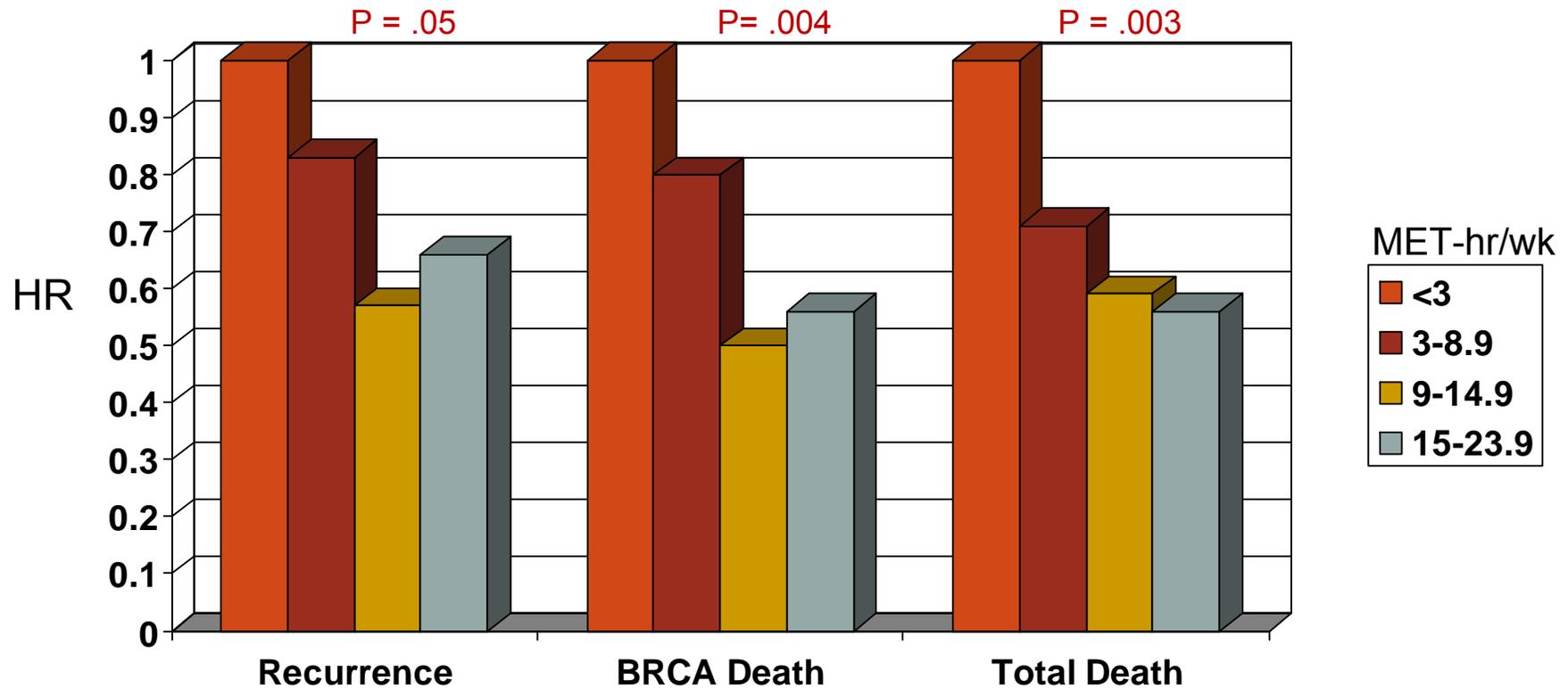
Goodwin, P. In: Psychosomatic Obstetrics and Gynecology, Bitzer J. and Stauber M. (Eds); Monduzzi Editore, International Proceedings Division, Bologna (Italy), p491-496, 1995.

Post Diagnosis Physical Activity and Breast Cancer Survival: Meta-analysis

	Overall HR (CI)	ER status HR (CI)	
		ER+	ER-
All cause mortality	0.59 (0.53-0.65)	0.36 (0.12-1.03)	1.07 (0.58-1.98)
Breast cancer mortality	0.66 (0.57-0.77)	0.50 (0.34-0.74)	0.91 (0.43-1.94)
Breast cancer recurrence	0.76 (0.66-0.87)	N/A	N/A

- Meta-analysis using 6 studies that investigated association between PA and breast cancer outcome
- Includes randomized, case-control, cohort, or observational clinical studies
- Total N = 12,108

Physical Activity After Breast Cancer Diagnosis

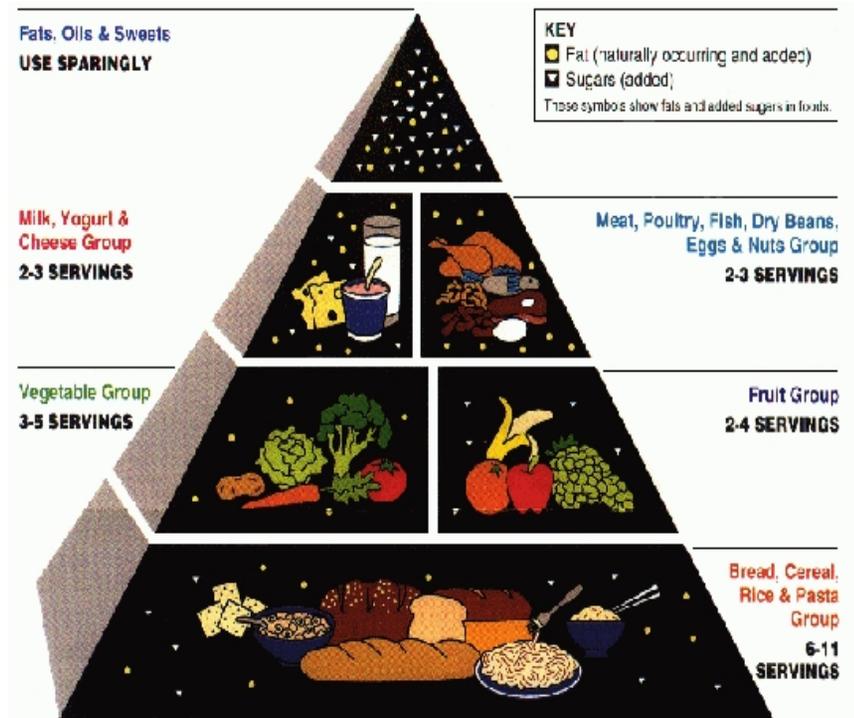


MET is Metabolic Equivalents

9 - 20 MET-hr/wk is about 150 to 225 min walking/wk

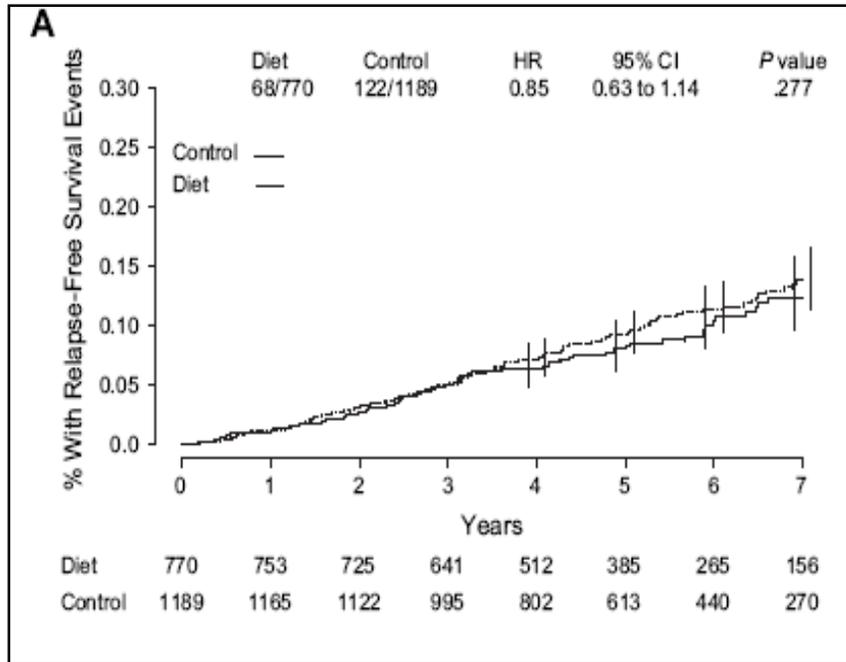
The Women's Interventional Nutrition Study (WINS)

- Randomized 2400 women with early-stage breast cancer to low-fat diet intervention or control group
- Intervention involved one-on-one meetings with dietician, cooking classes
- WINS diet: reduce fat to 15% of total calories

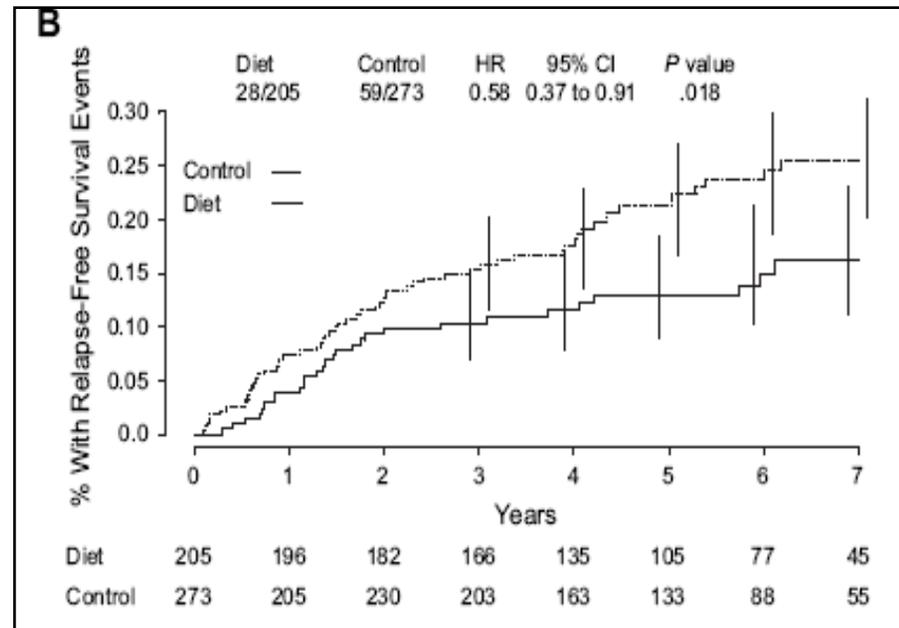


WINS Results by Hormonal Subtype

ER Positive



ER Negative

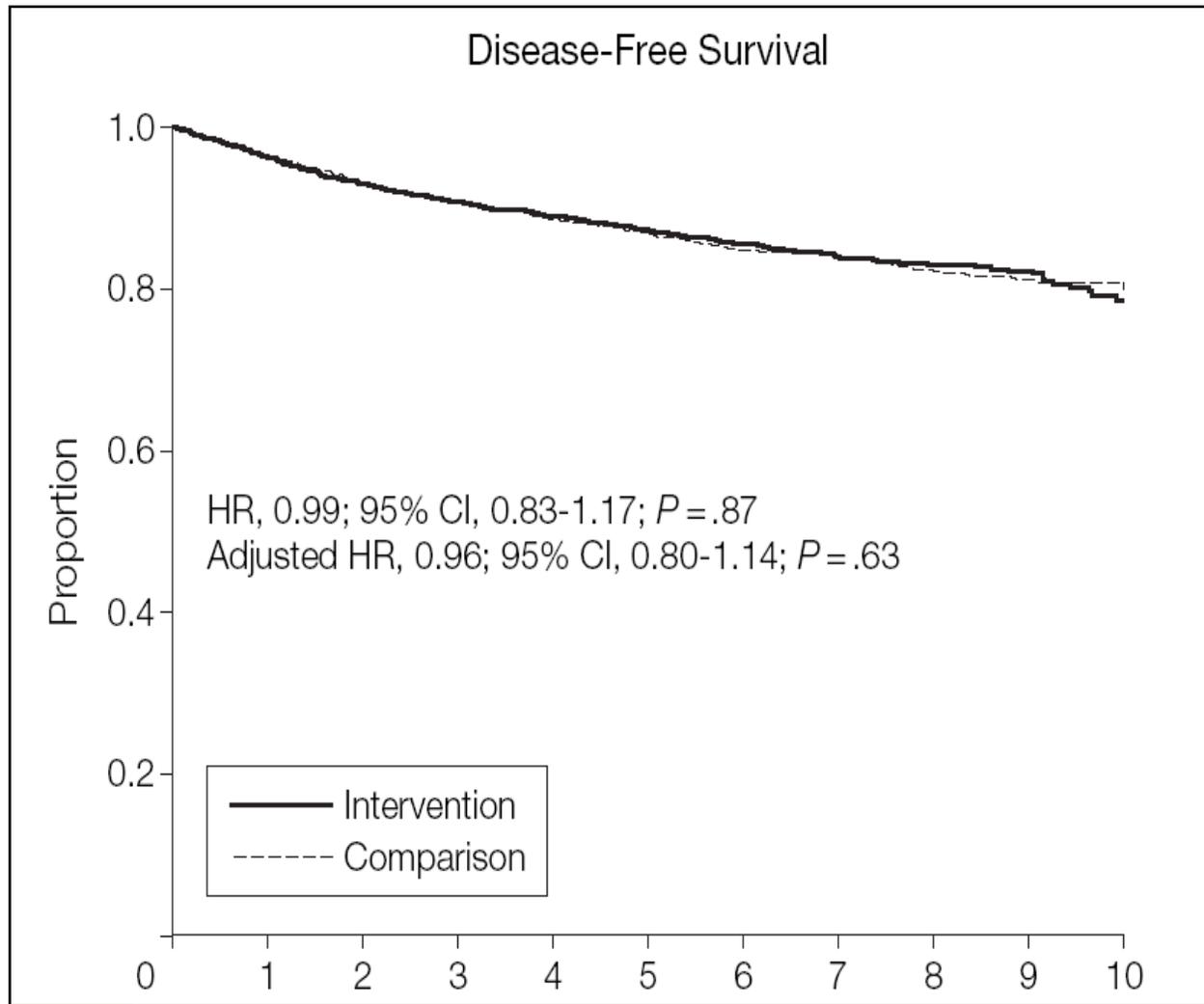


The Women's Healthy Eating and Living Study (WHEL)

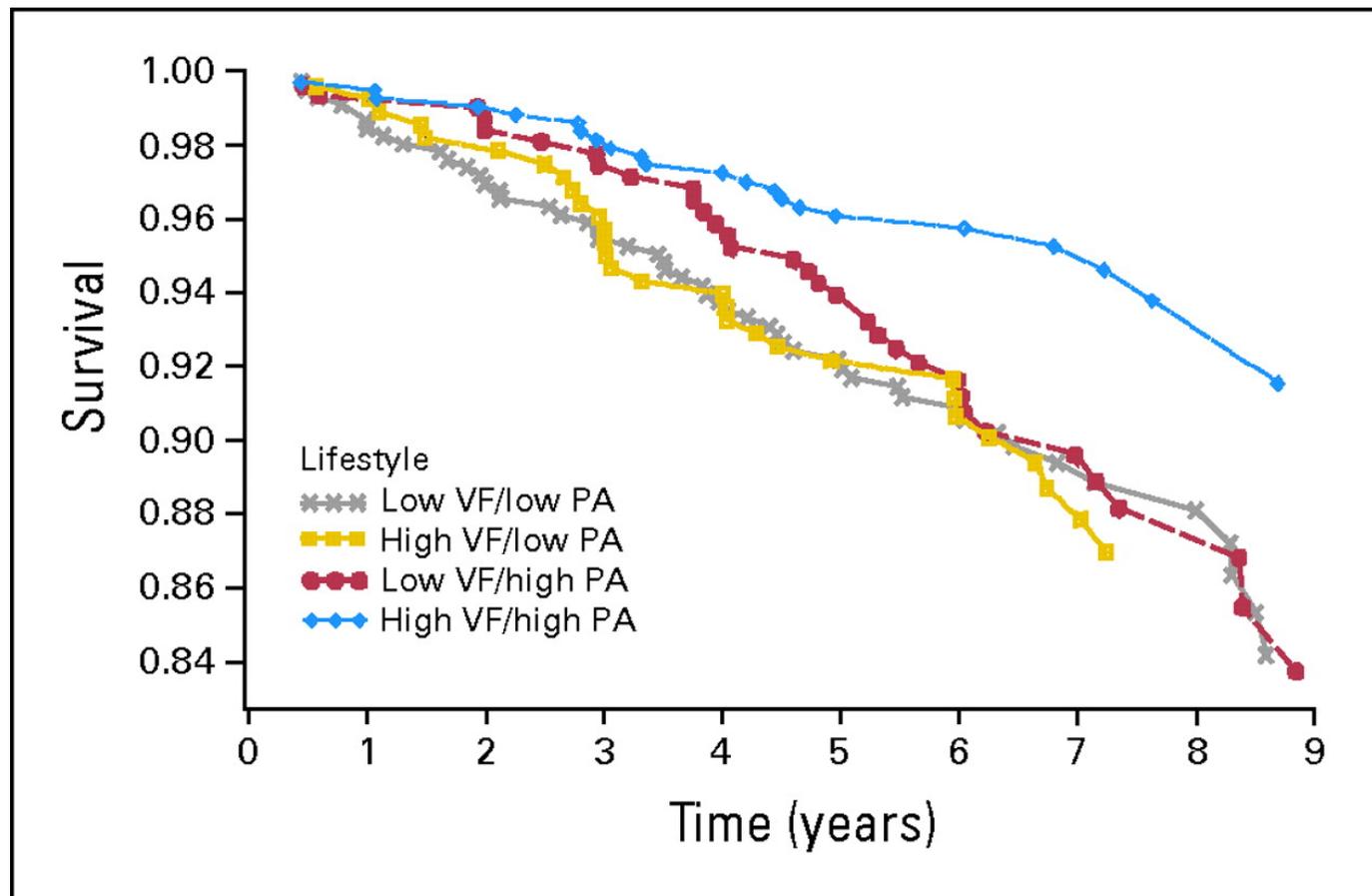
- Included 3088 women with early-stage breast cancer
- Randomized to phone-based diet intervention or control
- WHEL Diet:
 - High fruits and vegetables
 - Low fat
 - High fiber



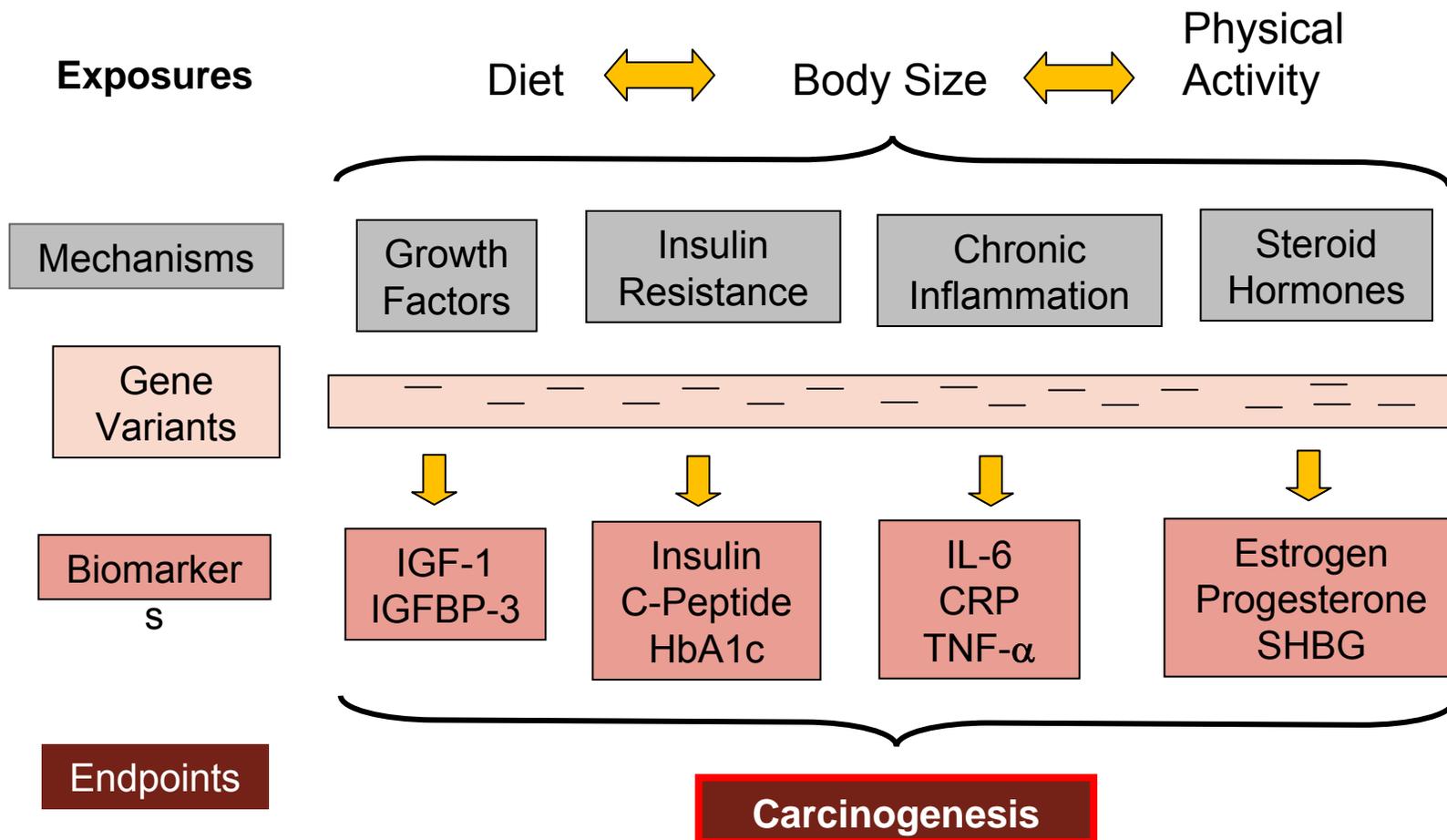
No Impact of WHEL Dietary Intervention on Breast Cancer Disease-Free Survival



Survival after WHEL Study Enrollment by Four Diet & Physical Activity Categories (observational cohort)



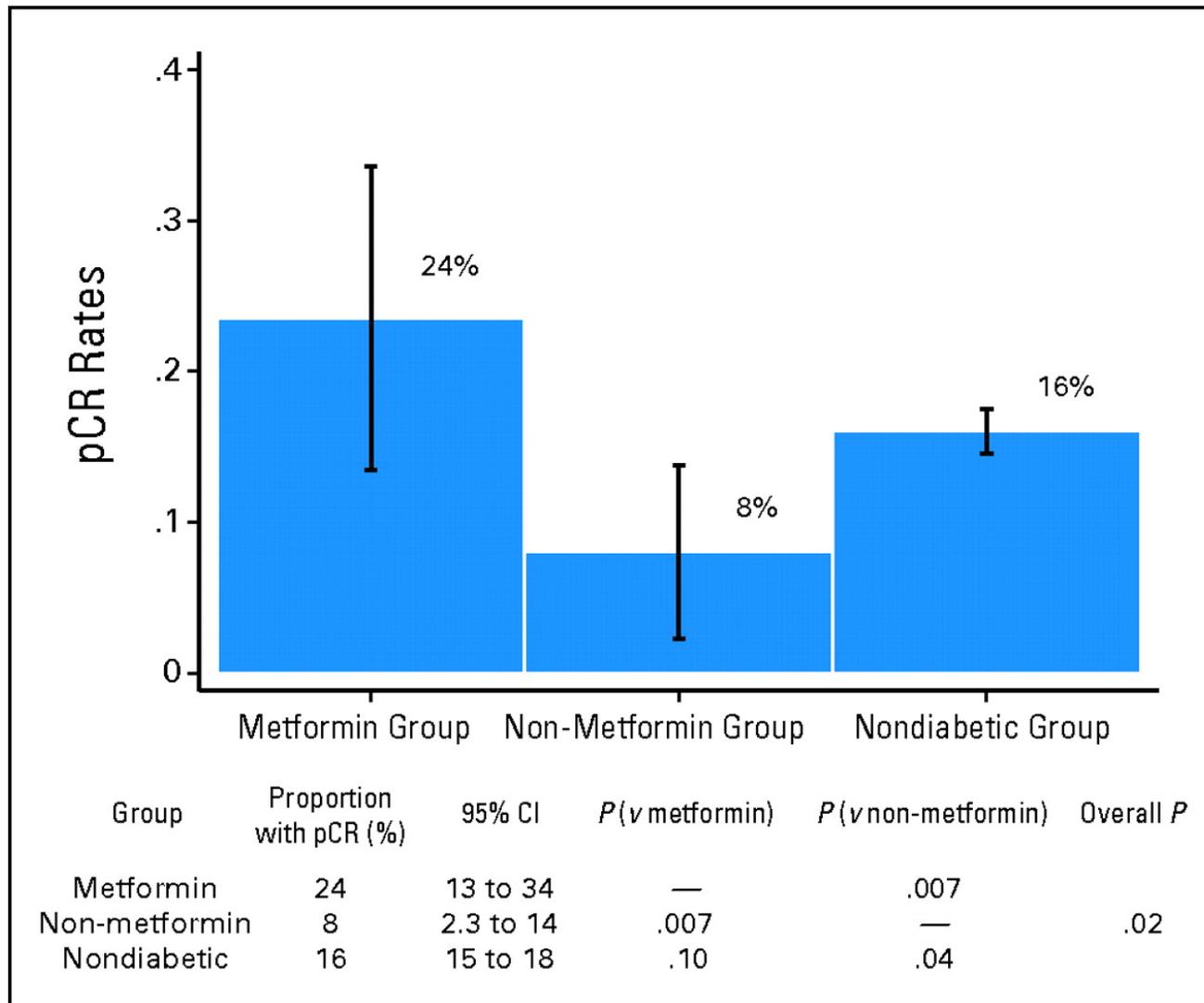
Proposed Mechanisms that Link Energy Balance and Carcinogenesis



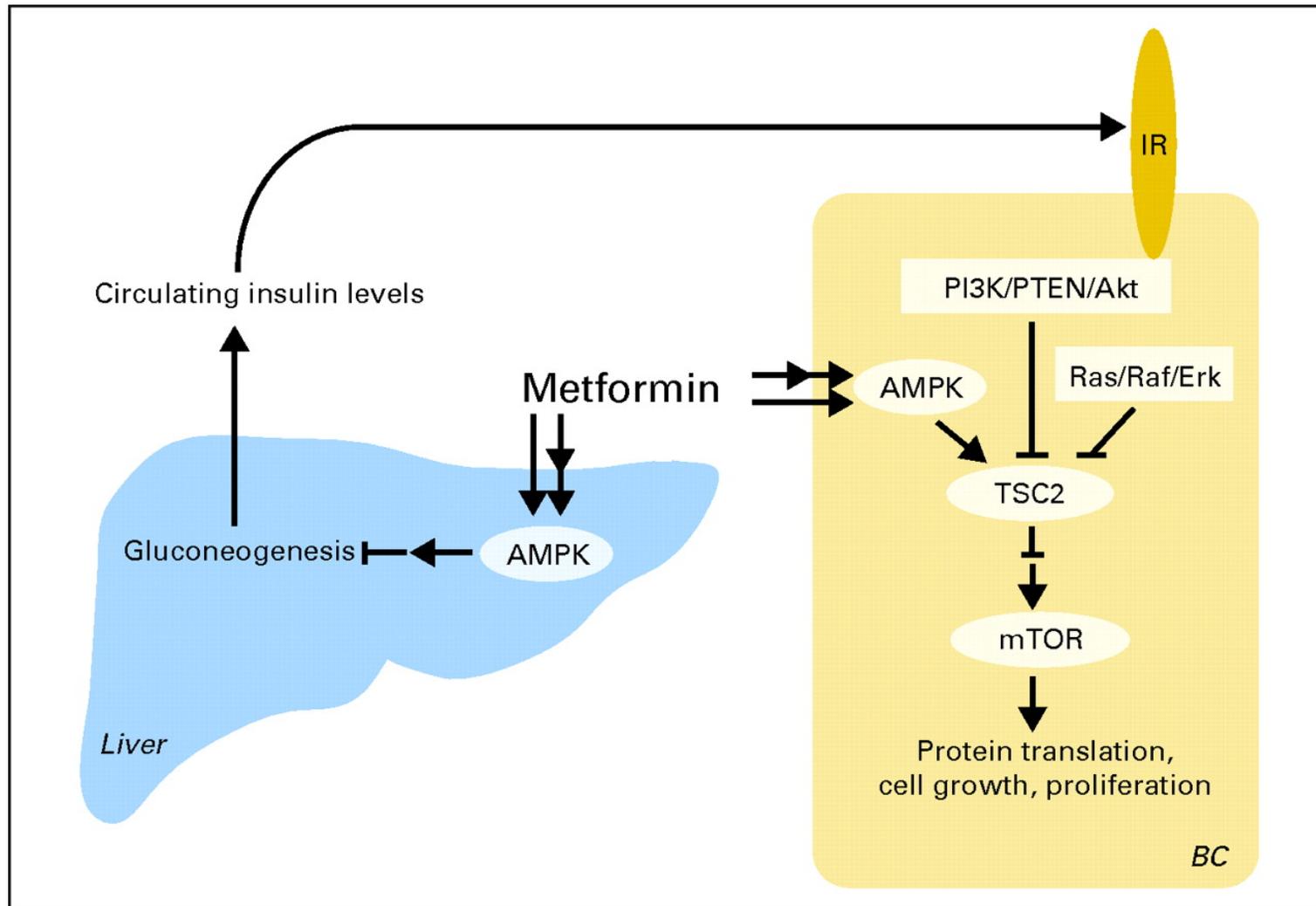
Insulin and Breast Cancer Prognosis

	N	Hormone	Results
Goodwin	312	Insulin	2-fold risk of recurrence and 3-fold risk of death in highest vs. lowest
Pollak	661	C-peptide	Sig. higher risk of recurrence in quartile with highest c-peptide vs. lowest
Pasinisi	110	Metabolic syndrome	3-fold risk of recurrence in women with high glucose and visceral adiposity
HEAL	538	C-peptide and Insulin	2-fold risk of breast cancer death in top vs. bottom tertile

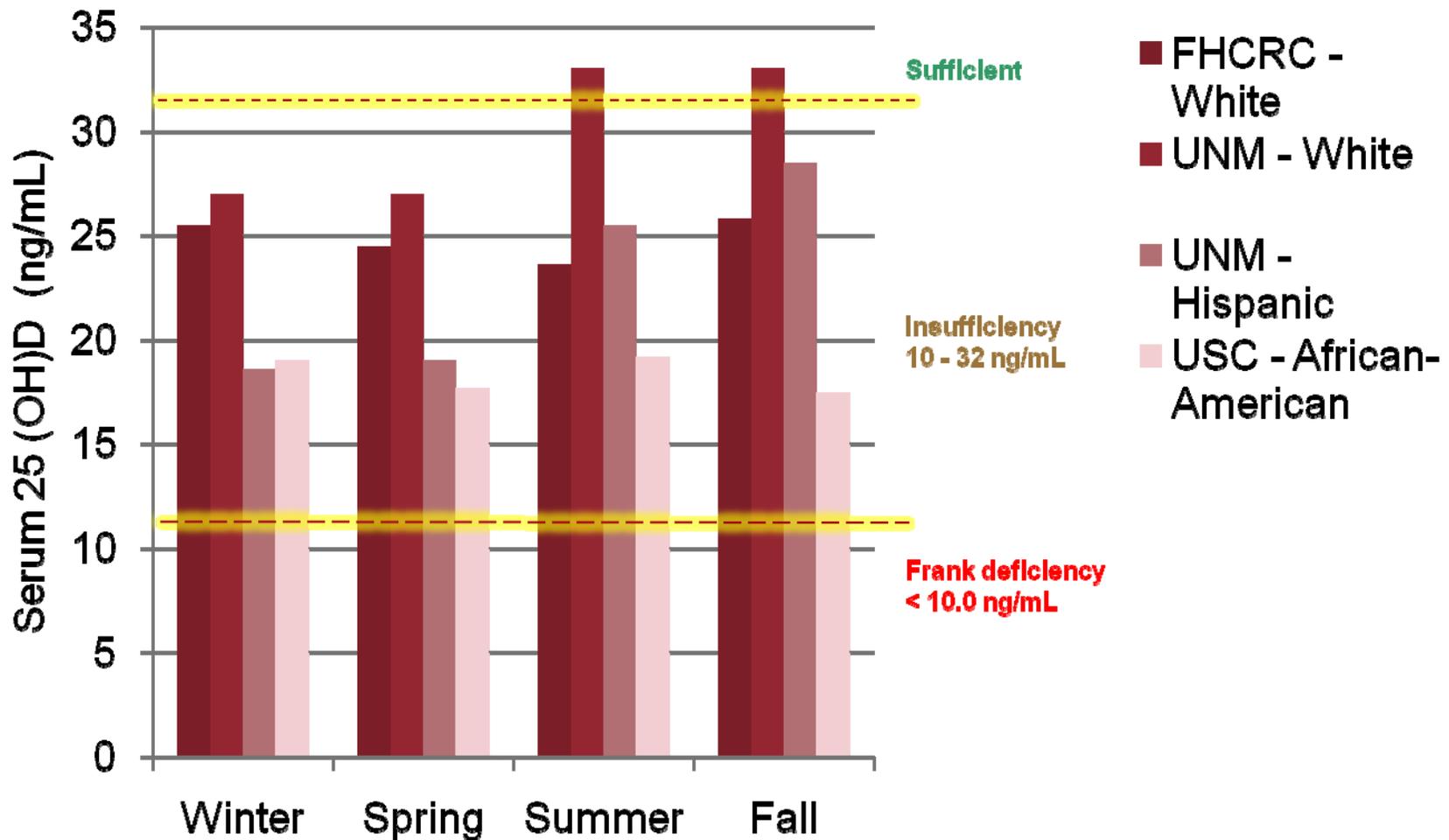
Proportions of Pathologic Complete Response (pCR) between Study Groups of Breast Cancer Patients



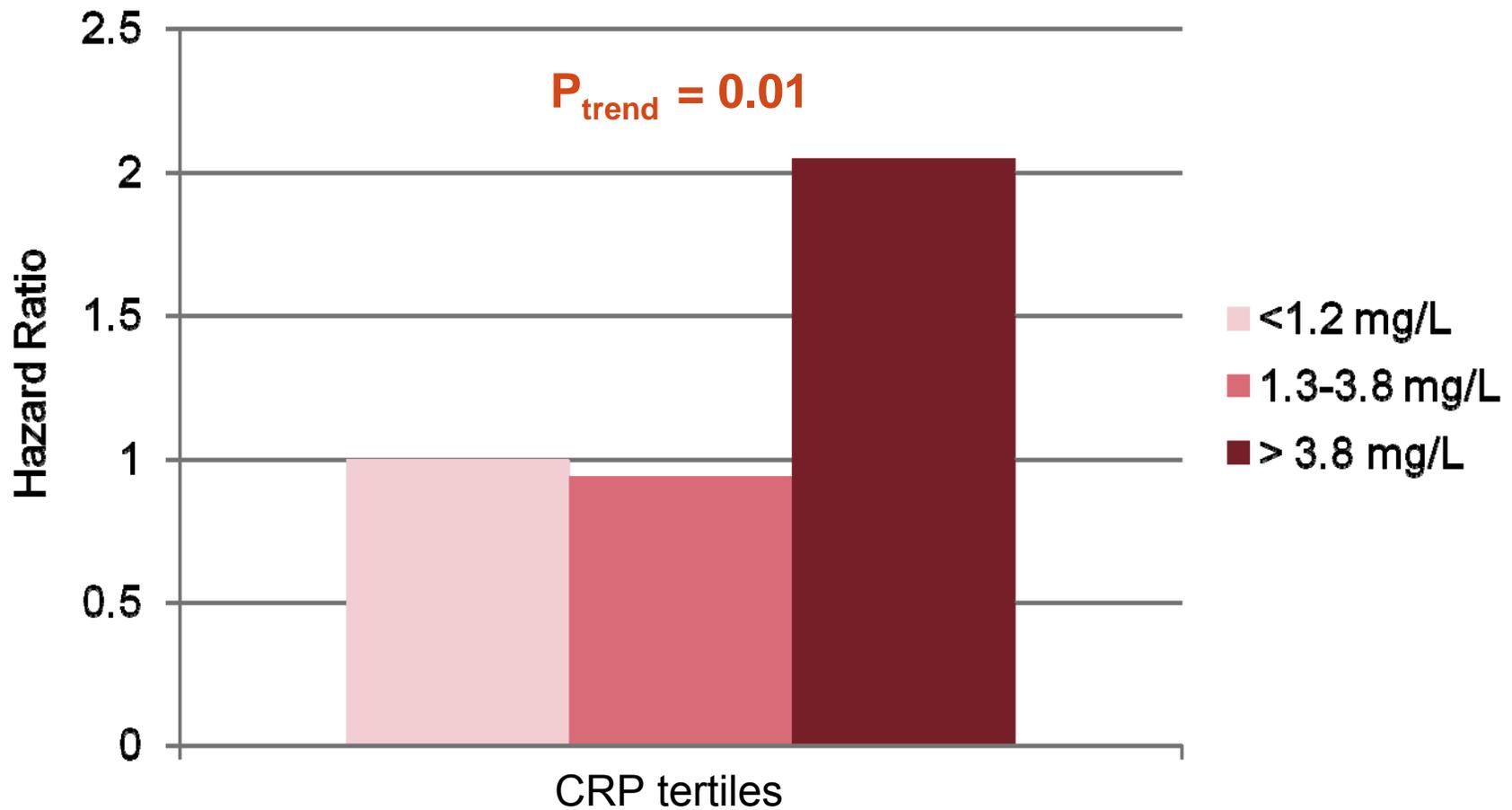
Mechanism of Metformin Action



Serum [25(OH)D] Deficiency in Breast Cancer Survivors



C-Reactive Protein (CRP) and Breast Cancer Mortality



Pierce B, et al. JCO, 2009: HEAL, 734 stage I-IIIa patients, follow up mean of 6 years

Components of the Healthy Eating Index-2005

Healthy Eating Index–2005 components and standards for scoring¹

Component	Maximum points	Standard for maximum score	Standard for minimum score of zero
Total Fruit (includes 100% juice)	5	≥0.8 cup equiv. per 1,000 kcal	No Fruit
Whole Fruit (not juice)	5	≥0.4 cup equiv. per 1,000 kcal	No Whole Fruit
Total Vegetables	5	≥1.1 cup equiv. per 1,000 kcal	No Vegetables
Dark Green and Orange Vegetables and Legumes ²	5	≥0.4 cup equiv. per 1,000 kcal	No Dark Green or Orange Vegetables or Legumes
Total Grains	5	≥3.0 oz equiv. per 1,000 kcal	No Grains
Whole Grains	5	≥1.5 oz equiv. per 1,000 kcal	No Whole Grains
Milk ³	10	≥1.3 cup equiv. per 1,000 kcal	No Milk
Meat and Beans	10	≥2.5 oz equiv. per 1,000 kcal	No Meat or Beans
Oils ⁴	10	≥12 grams per 1,000 kcal	No Oil
Saturated Fat	10	≤7% of energy ⁵	≥15% of energy
Sodium	10	≤0.7 gram per 1,000 kcal ⁵	≥2.0 grams per 1,000 kcal
Calories from Solid Fats, Alcoholic beverages, and Added Sugars (SoFAAS)	20	≤20% of energy	≥50% of energy

¹Intakes between the minimum and maximum levels are scored proportionately, except for Saturated Fat and Sodium (see note 5).

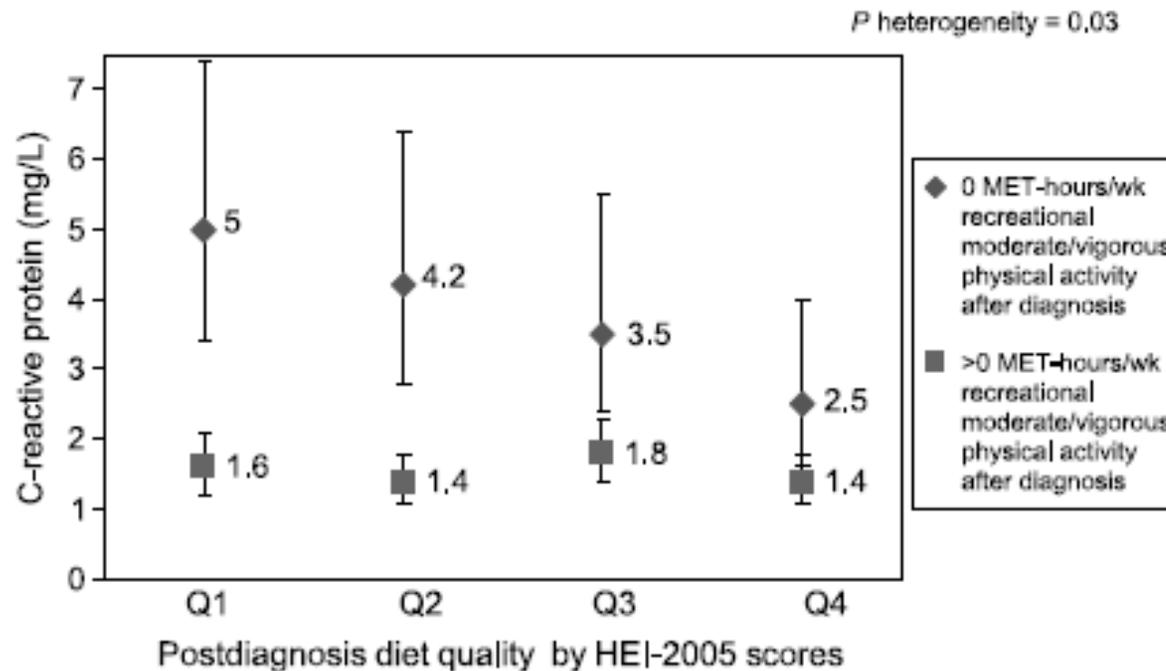
²Legumes counted as vegetables only after Meat and Beans standard is met.

³Includes all milk products, such as fluid milk, yogurt, and cheese, and soy beverages.

⁴Includes nonhydrogenated vegetable oils and oils in fish, nuts, and seeds.

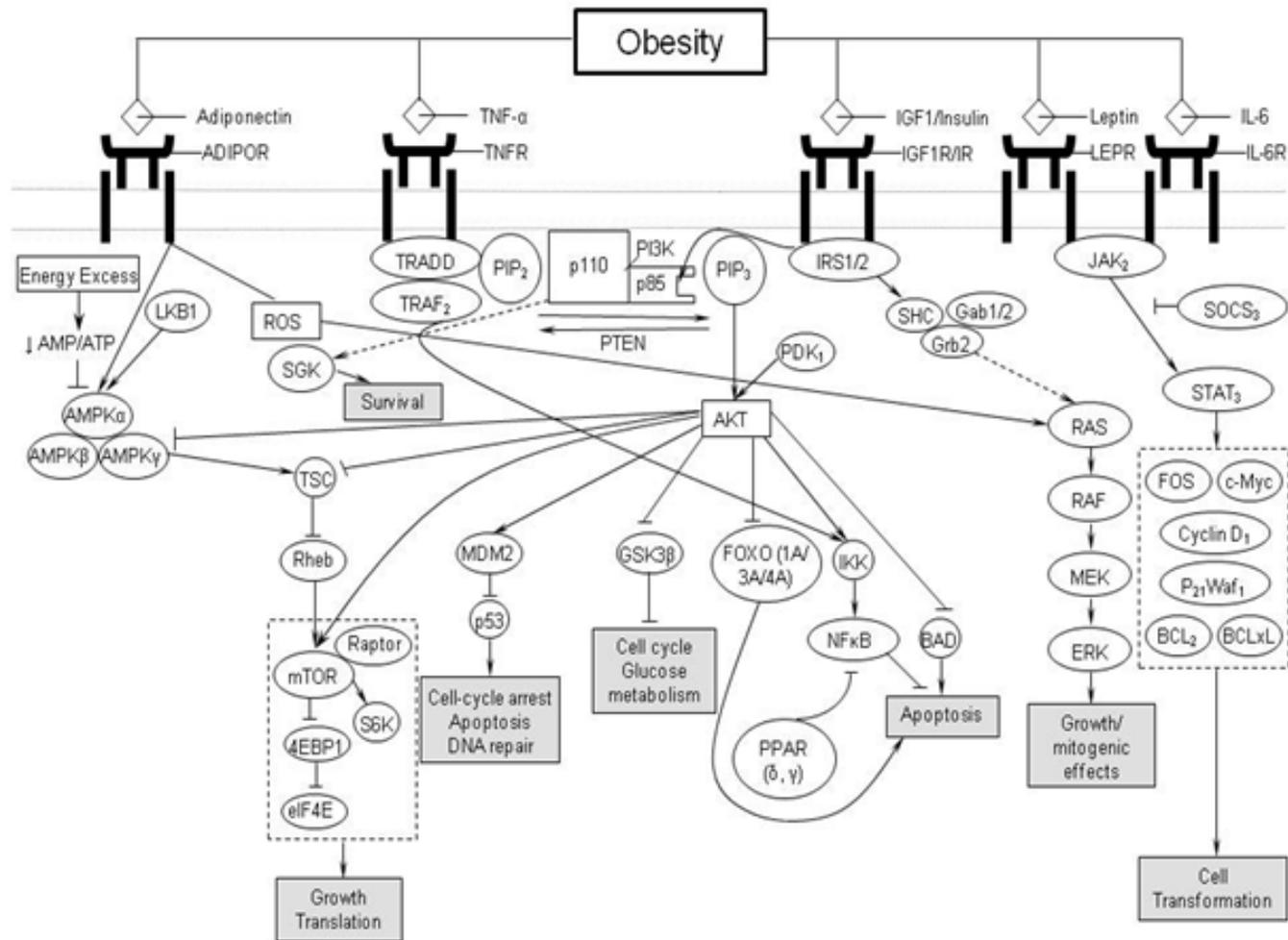
⁵Saturated Fat and Sodium get a score of 8 for the intake levels that reflect the 2005 Dietary Guidelines, <10% of calories from saturated fat and 1.1 grams of sodium/1,000 kcal, respectively.

C-reactive Protein (CRP) by Healthy Eating Index (HEI) and Physical Activity



Adjusted geometric means of CRP

Mechanisms Examined Within Studies of Energy Balance and Carcinogenesis



Sources of Guidance on Health Behaviors and Cancer

U.S. Department of Health and Human Services

HEALTHIER US.GOV

2008 Physical Activity Guidelines for Americans

Be Active, Healthy, and Happy!

www.health.gov/paguidelines

Nutrition and Physical Activity During and After Cancer Treatment: An American Cancer Society Guide for Informed Choices

Colleen Doyle, MS, RD; Lawrence H. Kushi, ScD; Tim Byers, MD, MPH; Kerry S. Courneya, PhD; Wendy Demark-Wahnefried, PhD, RD, LDN; Barbara Grant, MS, RD; Anne McTieman, MD, PhD; Cheryl L. Rock, PhD, RD; Cyndi Thompson, PhD; Ted Gansler, MD, MBA; Kimberly S. Andrews; for The 2006 Nutrition, Physical Activity and Cancer Survivorship Advisory Committee

ABSTRACT Cancer survivors are often highly motivated to seek information about food choices, physical activity, and dietary supplement use to improve their treatment outcomes, quality of life, and survival. To address these concerns, the American Cancer Society (ACS) convened a group of experts in nutrition, physical activity, and cancer to evaluate the scientific evidence and best clinical practices related to optimal nutrition and physical activity after the diagnosis of cancer. This report summarizes their findings and is intended to present health care providers with the best possible information from which to help cancer survivors and their families make informed choices related to nutrition and physical activity. The report discusses nutrition and physical activity issues during the phases of cancer treatment and recovery, living after recovery from treatment, and living with advanced cancer; select nutrition and physical activity issues such as body weight, food choices, and food safety; issues related to select cancer sites; and common questions about diet, physical activity, and cancer survivorship. (*CA Cancer J Clin* 2006;56:323-353.) © American Cancer Society, Inc., 2006.

INTRODUCTION

Over 10 million persons in the United States are cancer survivors.¹ Anyone who has been diagnosed with cancer, from the time of diagnosis through the rest of life, is considered a cancer survivor. Many cancer survivors are highly motivated to seek information about food choices, physical activity, dietary supplement use, and complementary nutritional therapies to improve their response to treatment, speed recovery, reduce risk of recurrence, and improve their quality of life.²

Nutritional needs change for most persons during the phases of cancer survivorship. Although many cancer survivors live with active or advanced disease, a large and growing number live extended, cancer-free lives. Sixty-five percent of Americans diagnosed with cancer now live more than 5 years.¹ The need for informed lifestyle choices for cancer survivors becomes particularly important as they look forward to successful completion of therapy and search for the best strategies to recover from treatment and improve their long-term outcomes. For long-term cancer survivors, an appropriate weight, a healthful diet, and a physically active lifestyle aimed at preventing recurrence, second primary cancers, and other chronic diseases should be a priority. For some, managing nutritional needs while living with advanced cancer becomes a particular challenge.

CA Cancer J Clin 2006;56:323-353

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This article is available online at <http://CAonline.AmCancerSoc.org>

What Is New About the Physical Activity Guidelines?

- **First major science review in more than a decade**
 - Provides guidance for all people age 6 and over by group:
 - Children and adolescents
 - Healthy adults and older adults
 - Pregnant and postpartum women
 - People with disabilities and chronic conditions
 - Provides guidance for non-aerobic activities:
 - Muscle and bone-strengthening, flexibility, balance
- **Identifies health benefits, amounts necessary to get the benefits, and provides bridge to PA promotion**
- **Specifies a total amount of activity per week**
 - People can design own way to meet Guidelines

Major Messages - I

- Regular activity reduces risk of many adverse health outcomes
- Some activity is better than none
- Added health benefits generally occur as amount of activity increases
- Most health benefits require at least 2 hours and 30 minutes (150 minutes) a week of moderate-intensity physical activity
- For fitness benefits, aerobic activity should be episodes of at least 10 minutes

Major Messages - II

- Both aerobic & muscle-strengthening activity are beneficial
- Health benefits apply to people of all types, sizes, and ages
- Health benefits occur for people with disabilities
- Physical activity can be done safely. Benefits far outweigh possible risks.

What May Surprise You About the PA Guidelines

- Can use either absolute or relative aerobic intensity
- More choices on frequency (days / week)
- Muscle-strengthening activities strongly endorsed, but not some features of typical training programs (e.g., no requirement for non-consecutive days)
- Flexibility activities, and warm-up / cool down activities are acceptable, but not a guideline
- Separate guideline to avoid inactivity

More Surprises About the PA Guidelines

- Revised guidelines on PA and healthy weight; PAG did not repeat:
 - “60 minute guideline” for prevention of wt gain and “90 minute guideline” for wt regain
 - Obesity / healthy wt regarded as one of many chronic conditions where “more is better”
- Clear statement that healthy children and adults do **not** need “physician approval” or consultation prior to engaging in PA
- Substantial attention to preventing adverse events

Guidance on Physical Activity and Cancer Survivorship

SPECIAL COMMUNICATIONS

Roundtable Consensus Statement

American College of Sports Medicine Roundtable on Exercise Guidelines for Cancer Survivors

EXPERT PANEL

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Anna L. Schwartz, PhD, FAAN

Early detection and improved treatments for cancer have resulted in roughly 12 million survivors alive in the United States today. This growing population faces unique challenges from their disease and treatments, including risk for recurrent cancer, other chronic diseases, and persistent adverse effects on physical functioning and quality of life. Historically, clinicians advised cancer patients to rest and to avoid activity; however, emerging research on exercise has challenged this recommendation. To this end, a roundtable was convened by American College of Sports Medicine to distill the literature on the safety and efficacy of exercise training during and after adjuvant cancer therapy and to provide guidelines. The roundtable concluded that exercise training is safe during and after cancer treatments and results in improvements in physical functioning, quality of life, and cancer-related fatigue in several cancer survivor groups. Implications for disease outcomes and survival are still unknown. Nevertheless, the benefits

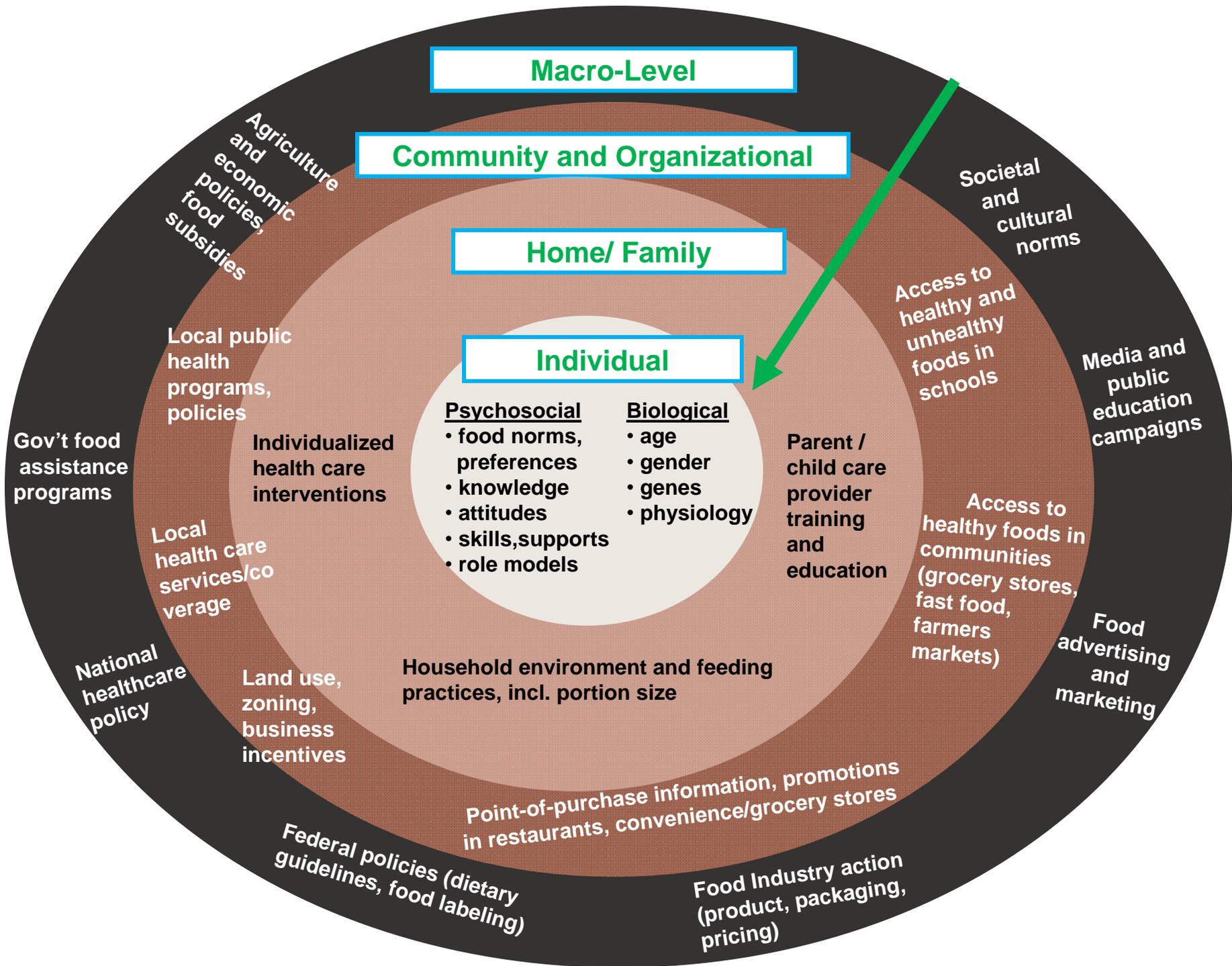
to physical functioning and quality of life are sufficient for the recommendation that cancer survivors follow the 2008 Physical Activity Guidelines for Americans, with specific exercise programming adaptations based on disease and treatment-related adverse effects. The advice to "avoid inactivity," even in cancer patients with existing disease or undergoing difficult treatments, is likely helpful.

In 2009, the American Cancer Society (ACS) estimated that there were nearly 1.5 million new cases of cancer diagnosed in the United States and just more than 500,000 people who died from the disease (76). Currently, there are close to 12 million cancer survivors in the United States, and this number grows each year (66,70,122). Improved prognosis on the basis of earlier detection and newer treatments has created a welcomed new challenge of addressing the unique needs of cancer survivors, which include the sequelae of the disease, its treatment, and conditions predating diagnosis. Cancer is a disease largely associated with aging; most survivors are older than 65 yr (112). Nearly half are survivors of breast or prostate cancer (66). Colon, hematological, and endometrial cancers each account for approximately 10% of survivors (66).

In the last two decades, it has become clear that exercise plays a vital role in cancer prevention and control (25,140). Courneya and Friedenreich (26) proposed a Physical Activity and Cancer Control Framework that highlights specific phases along the cancer continuum where exercise has a logical role (Fig. 1) and identifies two distinct periods before diagnosis and four periods after diagnosis with objectives for exercise programs in each phase. There is a growing body of evidence suggesting that exercise decreases the risk of many of cancers (107,140), and data to support the premise that exercise may extend survival for breast and colon cancer survivors are emerging (68,73,91,92). Our focus here is on the influence of regular exercise on the health,

Physical Activity and Quality of Life in Cancer Patients

- Extensive research - observational and controlled trials
- Most studies have focused on women with breast cancer both during (22) and after (32) adjuvant therapy
- Evidence suggests activity is
 - Safe and feasible during initial treatment
 - Results in significant improvement in cardiorespiratory fitness, physical functioning, fatigue, lymphedema, QOL
 - Nonsignificant changes in body weight but most show decreases in body fat mass, increases in lean body mass and improvements in metabolic parameters
 - May help counter osteopenia and sarcopenia that may occur with some cancer chemotherapies



Questions?