UNIVERSITY OF HAWAI'I

CANCER CENTER

"What Have We Learned from Studies on Overnutrition and Cancer?"

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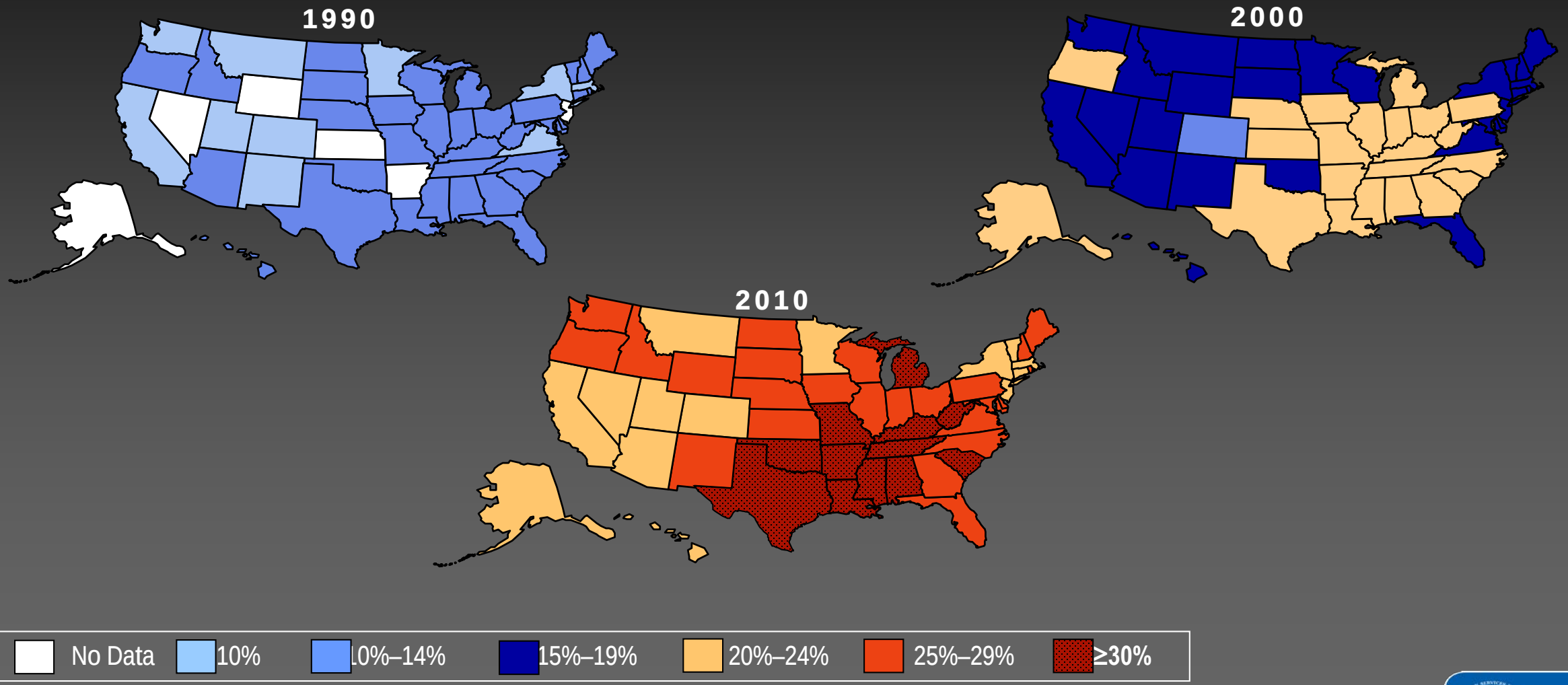
NCI Cancer Center

A Cancer Center Designated by the National Cancer Institute

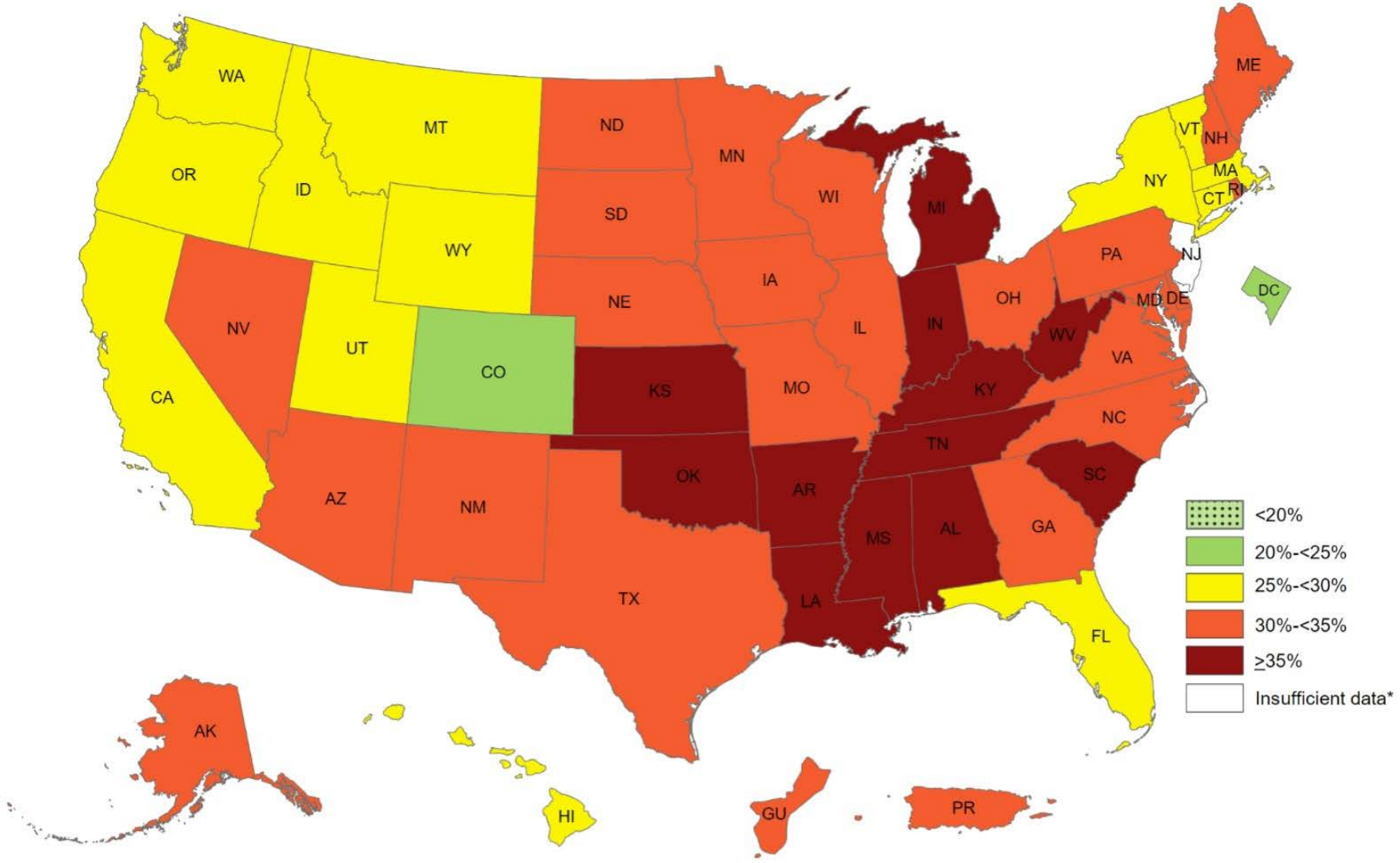
Obesity Trends* Among U.S. Adults

BRFSS, 1990, 2000, 2010

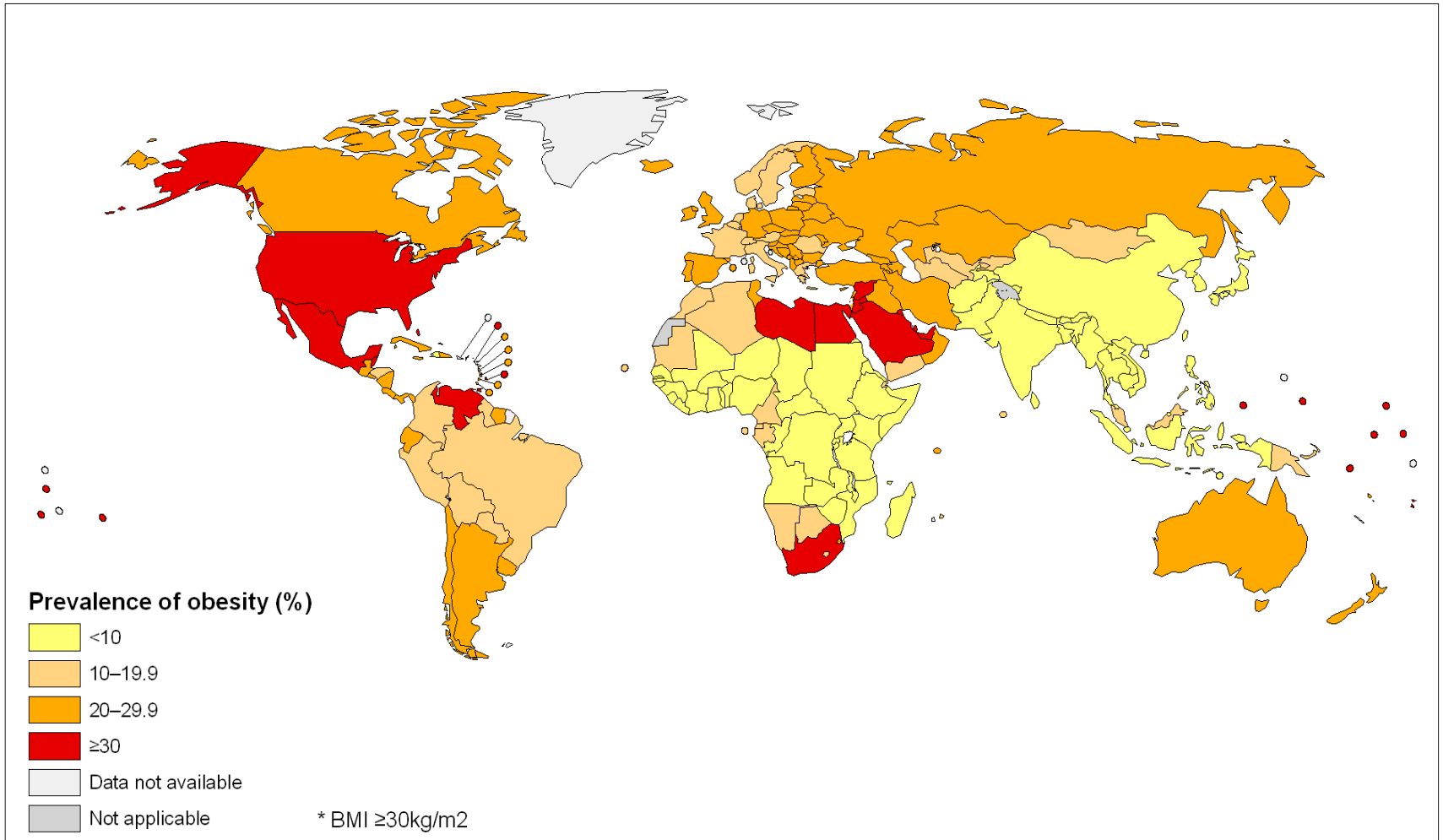
(*BMI ≥30, or about 30 lbs. overweight for 5'4" person)



Prevalence of Obesity Among U.S. Adults by State, 2019



Prevalence of obesity*, ages 20+, age standardized
Both sexes, 2008



Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

Overnutrition → excess body fat

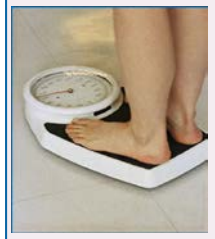
- Overweight and obesity are both chronic conditions that are the result of an energy imbalance over a period of time
- This energy imbalance can be due to a combination of factors that vary from one person to another
- Individual behaviors, environmental factors, and genetics all contribute to the complexity of the obesity epidemic

Weight Gain

Calories Consumed > Calories Used

Weight Loss

Calories Consumed < Calories Used



No Weight Change

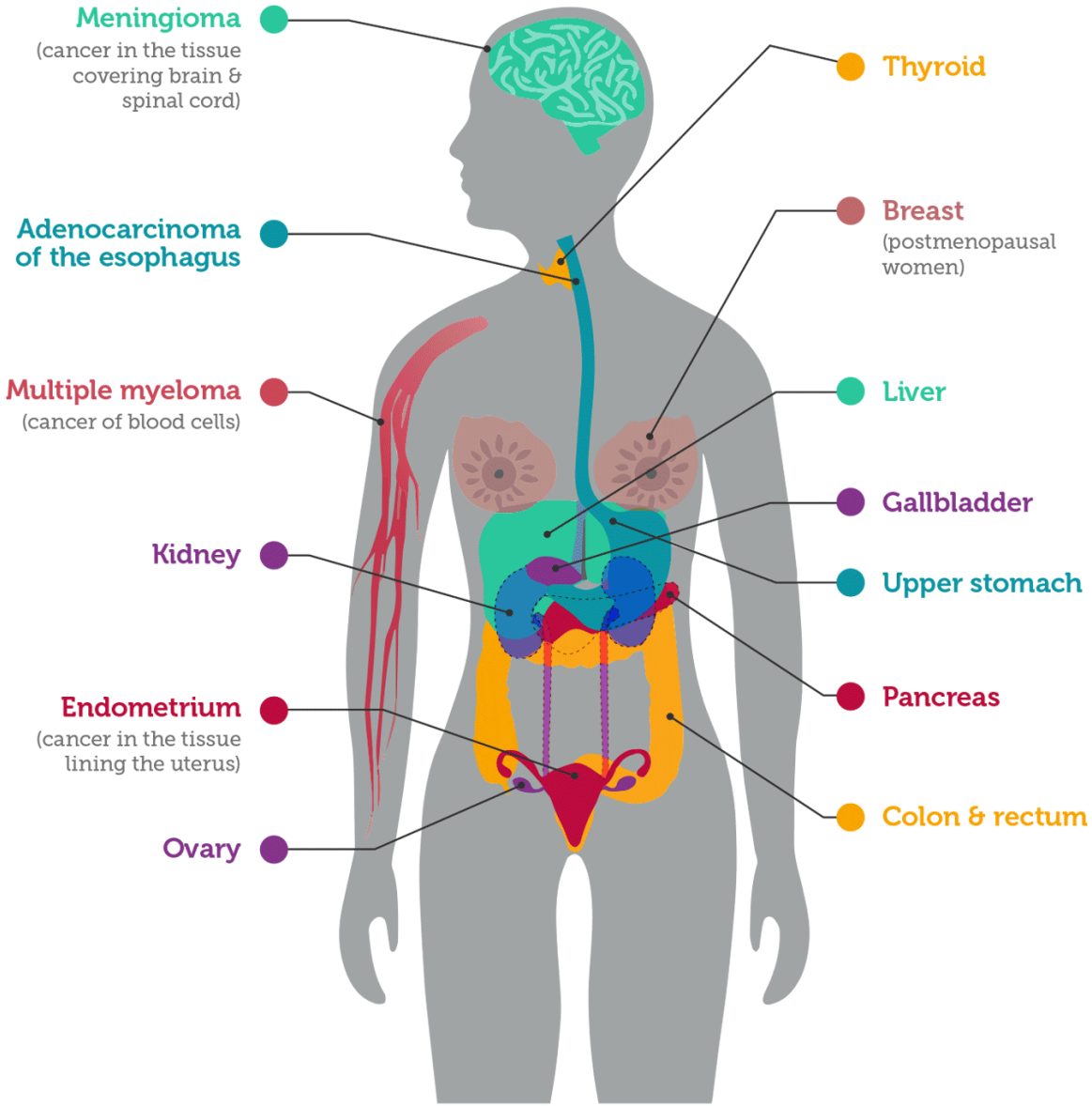
Calories Consumed = Calories Used

Effects of Obesity on Disease Risk

- All-cause mortality
- High blood pressure
- High LDL, low HDL or high levels of triglycerides
- Type 2 diabetes
- Coronary heart disease
- Stroke
- Gallbladder disease
- Osteoarthritis
- Sleep apnea and breathing problems
- 13 types of cancers
- Low quality of life
- Depression, anxiety, and other mental disorders
- Body pain and difficulty with physical functioning

NATIONAL CANCER INSTITUTE

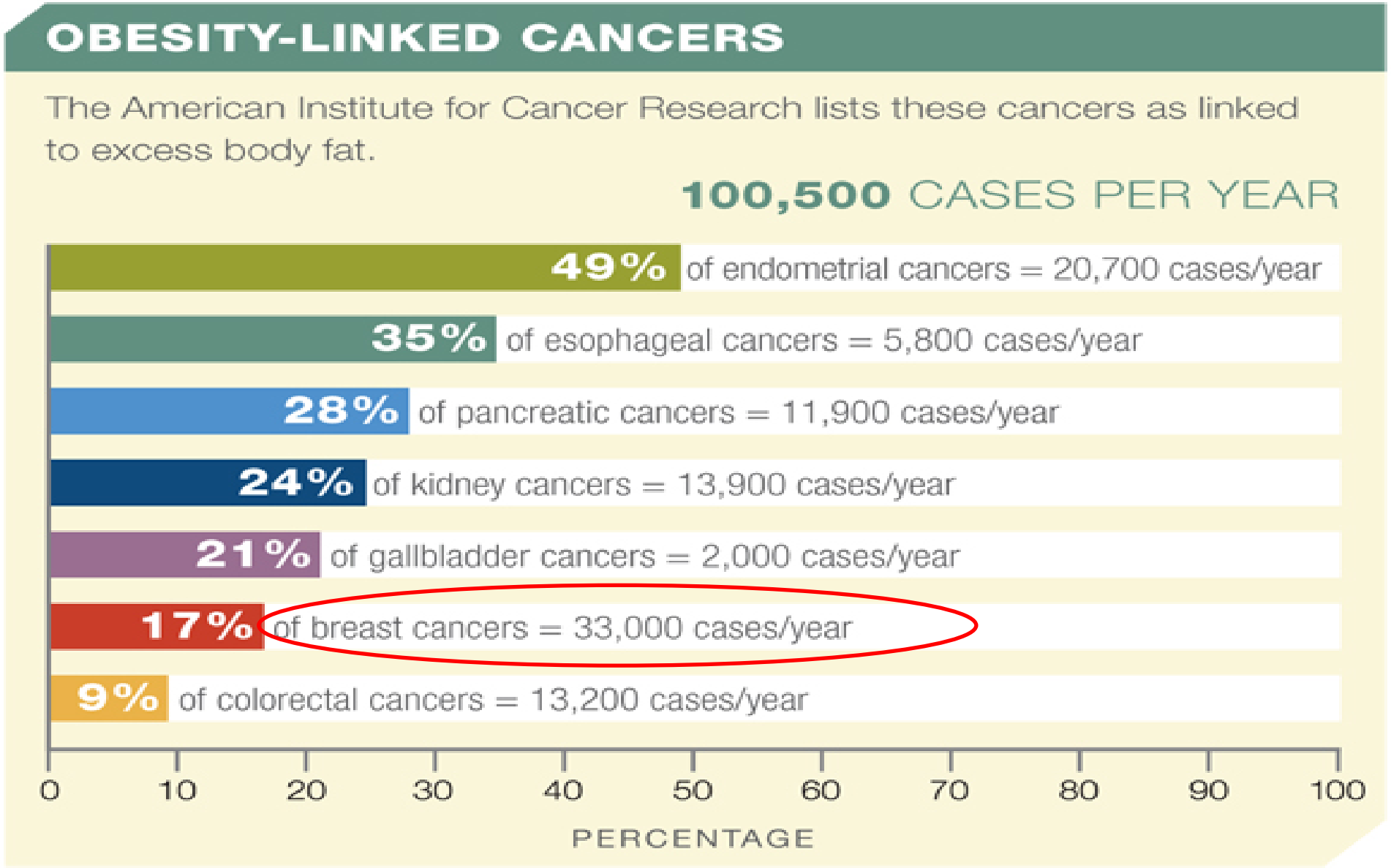
Cancers Associated with Overweight & Obesity



cancer.gov/obesity-fact-sheet

Adapted from Centers for Disease Control & Prevention

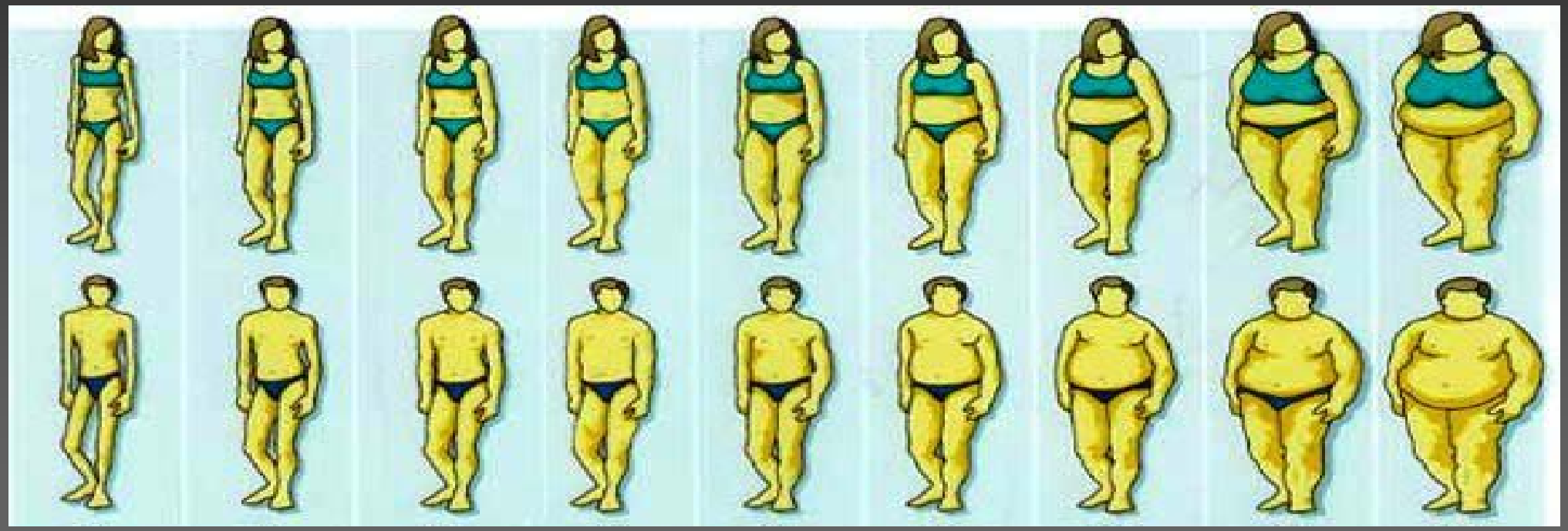
Number of Obesity-Related Cancers in the US



American Institute for Cancer Research (AICR) 2012

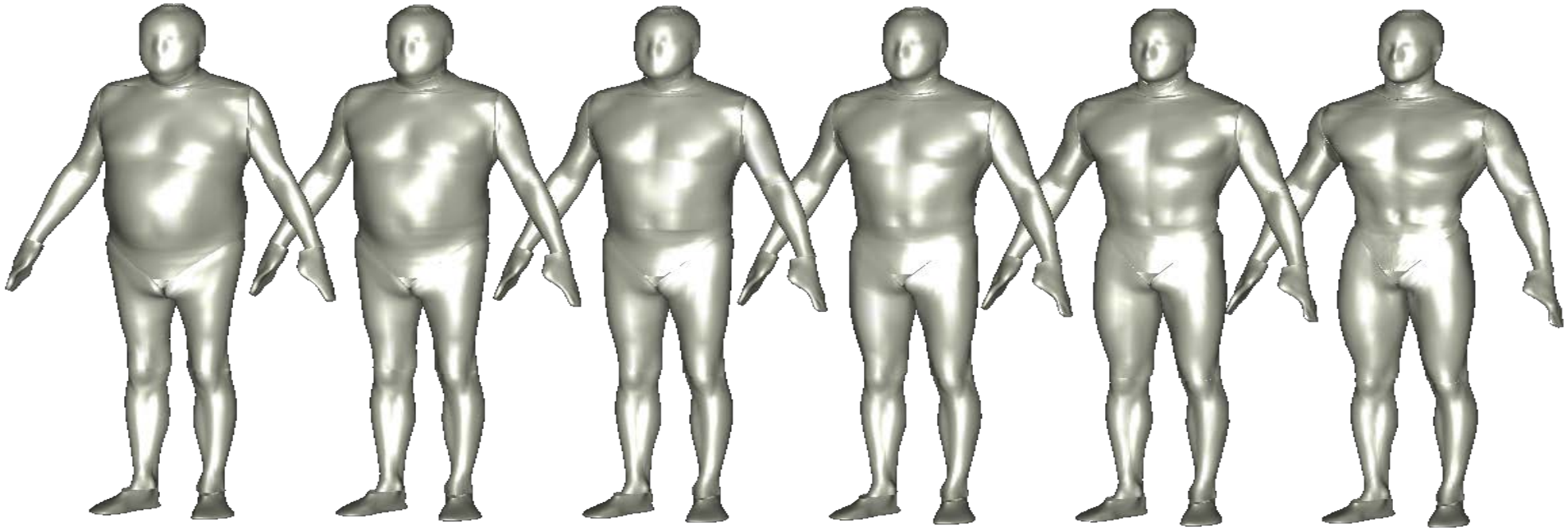
Measure of Obesity

- Body Mass Index = weight (kg) / height (m^2)
- Obesity: BMI $\geq$ 30 kg/m^2



BMI	<20	20 - 25	26 - 29	>30	>40
	Underweight	Normal Weight	Overweight	Obese	Extremely Obese

Which figure has the highest BMI?



BMI lumps body types together

Regional Fat Distribution and Mortality

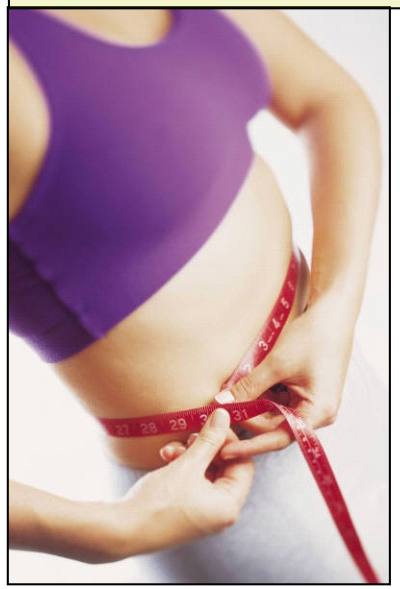
- Regional fat distribution contributes to mortality
- Obese individuals with an android (or apple) distribution of body fat are at a *greater risk* for diabetes and heart disease than those with a gynoid distribution (pear)
- Android fat distribution results in higher free fatty acid levels, higher glucose and insulin levels and reduced HDL levels. It also results in higher blood pressure and inflammatory markers
- Intra-abdominal fat is more “metabolically active” than other fat depots

Higher Risk **Lower Risk**

Endocrinol Metab Clin N Am. 2003; 32: 761-786.

Central Obesity: Waist Circumference & Disease Risk

Men = Greater than 40 inches
Women = Greater than 35 inches

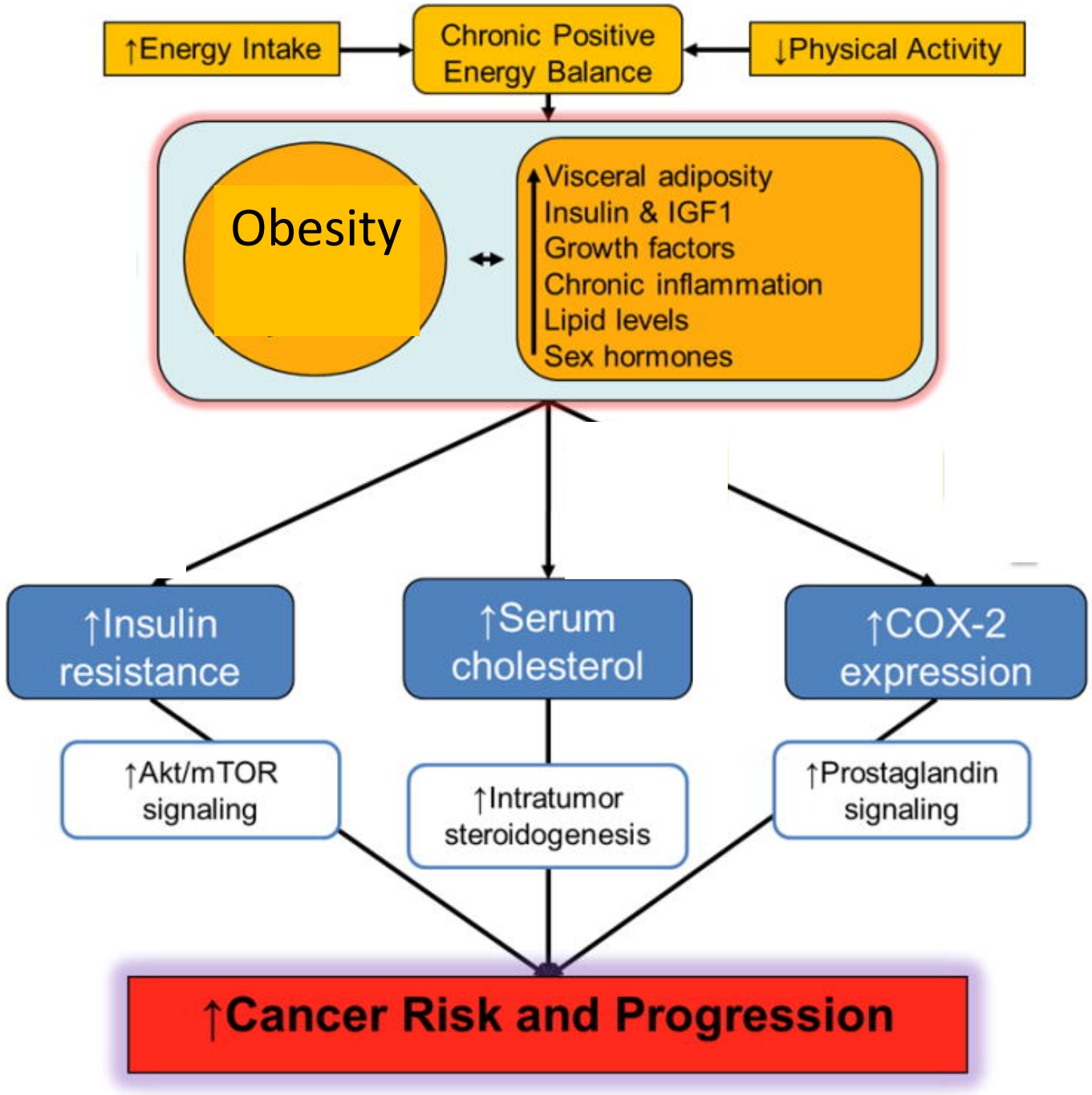


Disease Risk * Relative to Normal Weight and Waist Circumference

	BMI (kg/m^2)	Obesity Class	Men ≤ 102 cm (≤ 40 in) Women ≤ 88 cm (≤ 35 in)	> 102 cm (> 40 in) > 88 cm (>35 in)
Underweight	< 18.5		-----	-----
Normal	18.5 – 24.9		-----	-----
Overweight	25.0 – 29.9		Increased	High
Obesity	30.0 – 34.9 35.0 – 39.9	I II	High Very High	Very High Very High
Extreme Obesity	≥ 40	III	Extremely High	Extremely High

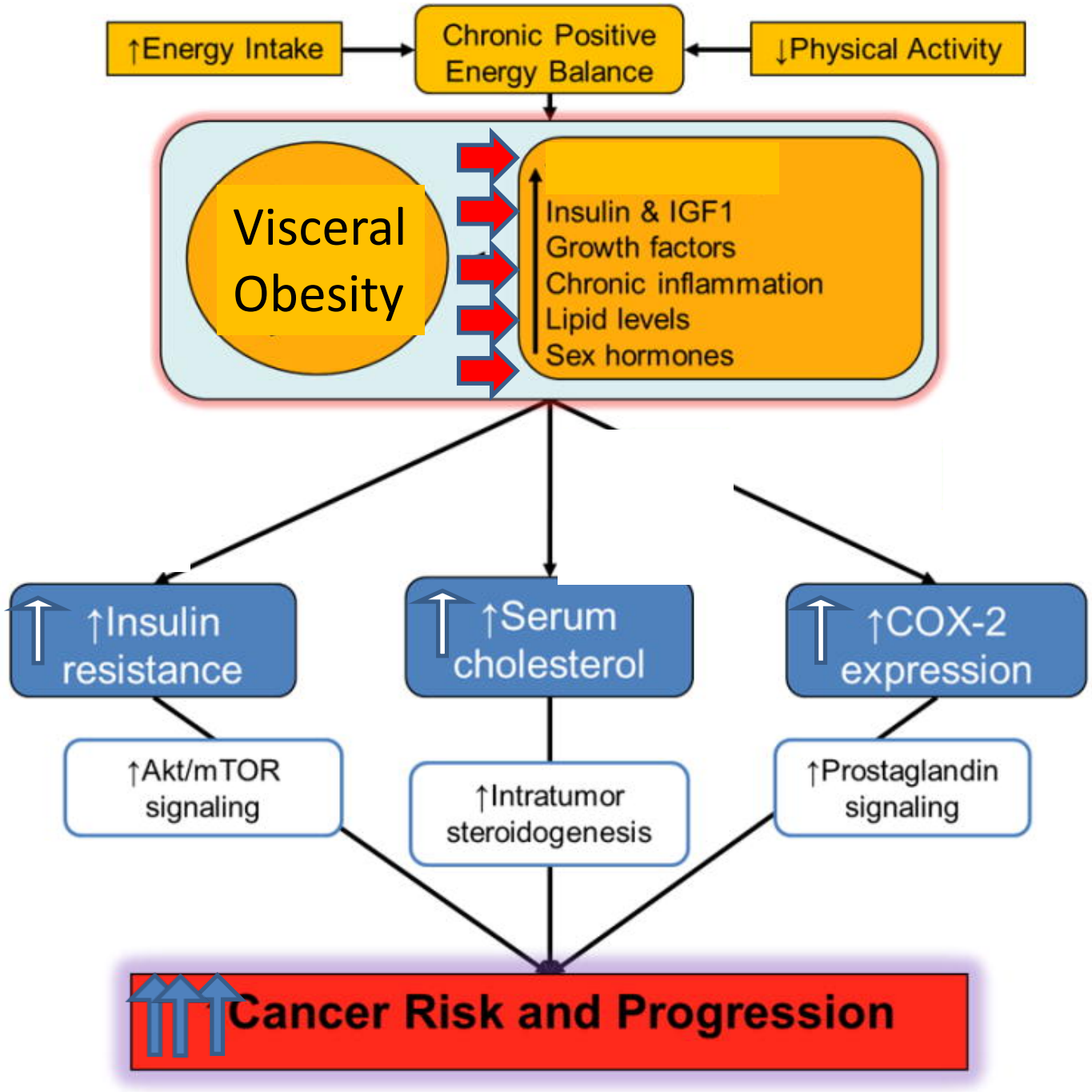
* Disease risk for type 2 diabetes, hypertension, and cardiovascular disease

Putative mechanisms linking obesity with cancer risk and progression

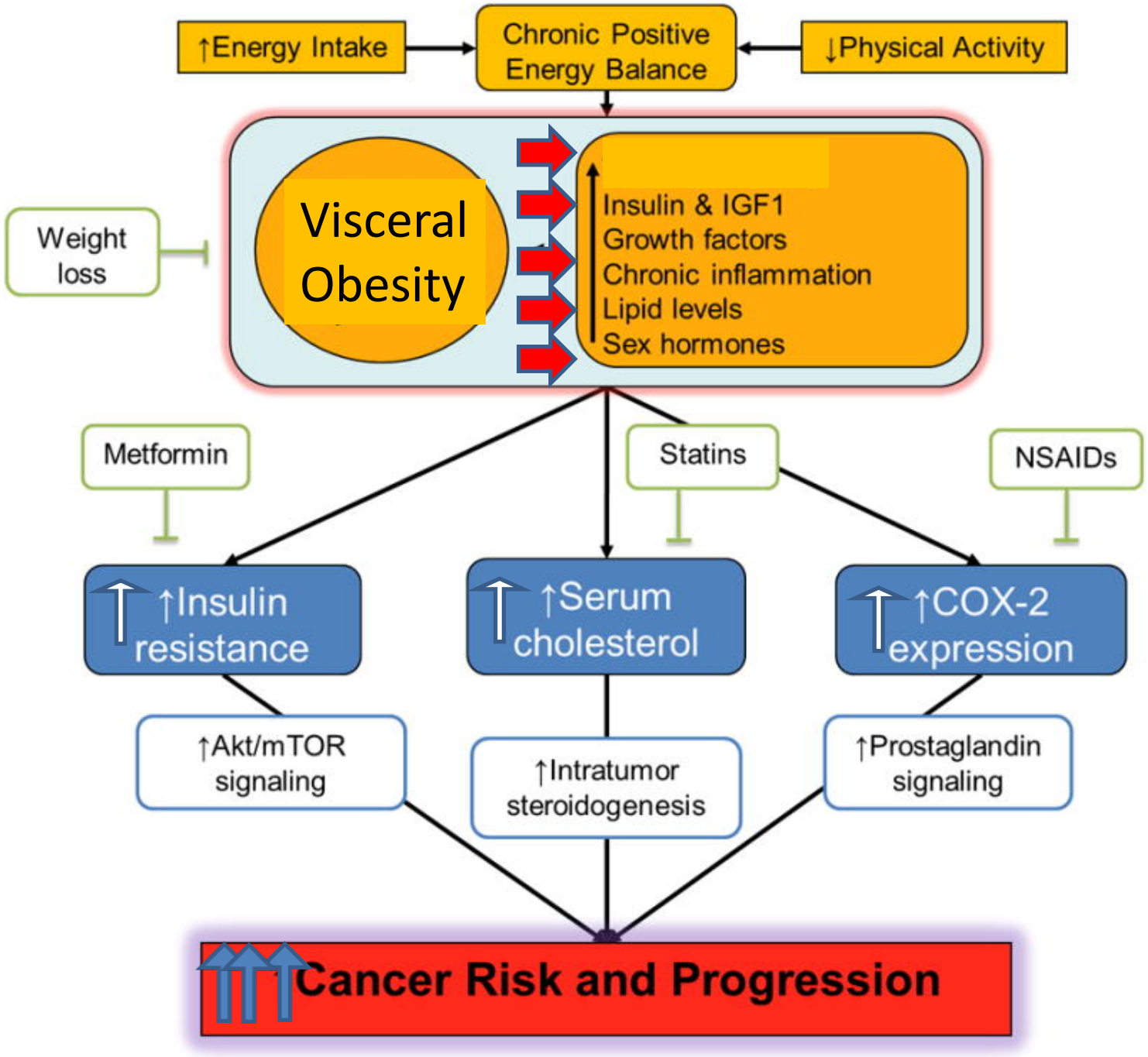


Allott & Hursting, 2015

Putative mechanisms linking obesity with cancer risk and progression



Putative mechanisms linking obesity with cancer risk and progression



Research Hypotheses in MEC

- Fat deposition in various body fat storage compartments carries different risks of cancer
- Amount & distribution of fat vary among the 5 MEC ethnic groups
- These differences contribute to ethnic/racial disparities in cancer rates and survival

Body Fat Distribution Study (N=1,681)

DXA

- **Total fat mass**
- **Trunk fat mass**
- **Lean mass**

Abdominal MRI

- **Visceral fat**
- **Subcutaneous fat**
- **Liver fat**

Top: DXA: dual-energy x-ray absorptiometry; bottom: MRI: magnetic resonance imagi

Visceral vs. Subcutaneous Fat

Lim et al. Nutrition and Diabetes 2011

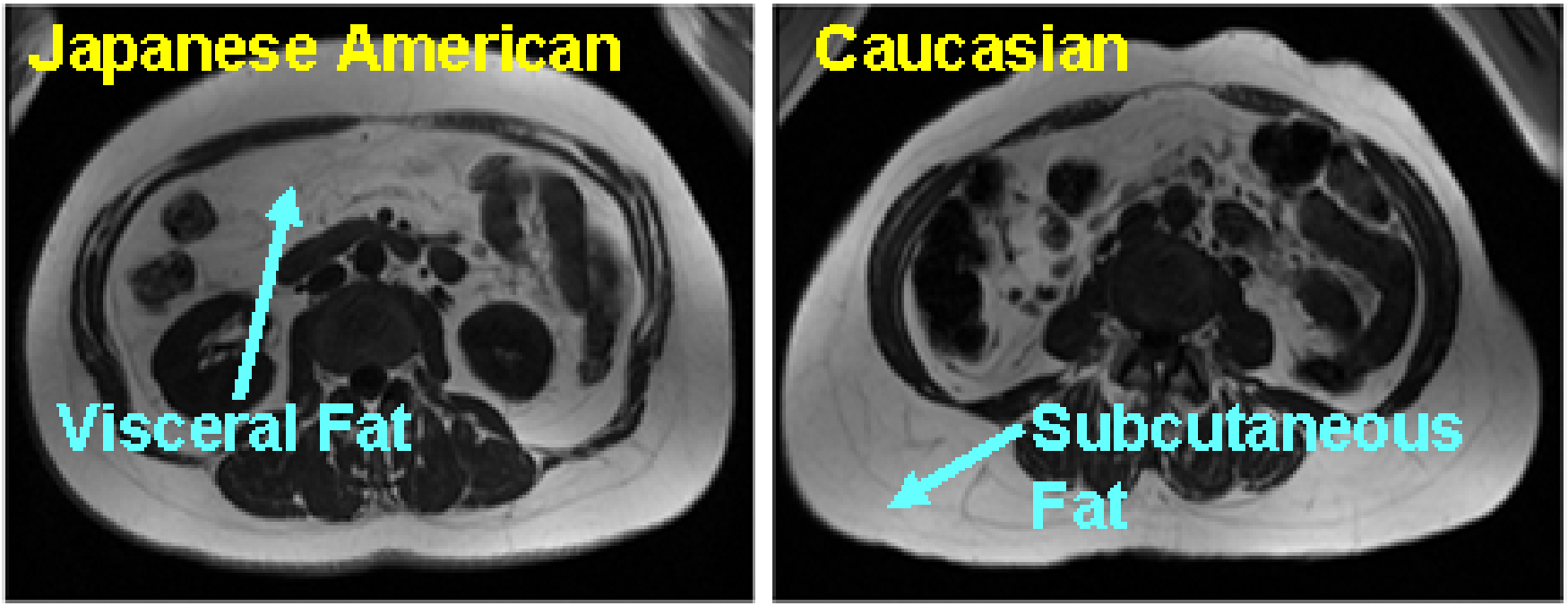
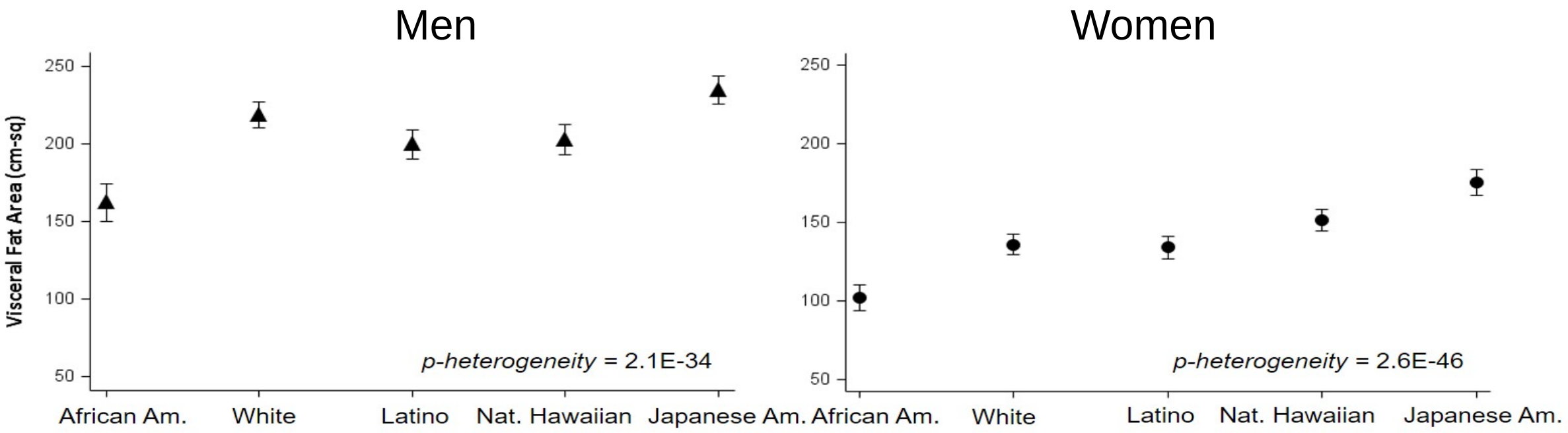


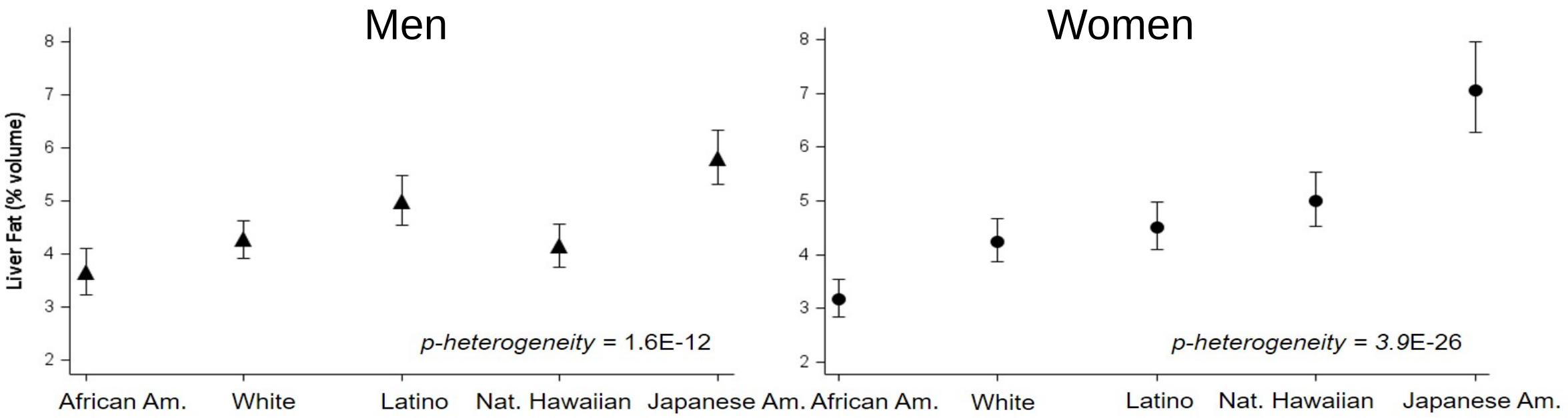
Figure 2. An example MRI scan of L4/L5 vertebral inter-space for visceral and subcutaneous fat

Mean Visceral Fat Adjusted for Total Fat Mass in APS



Lim et al., Gastroenterology, 2018

Mean % Liver Fat Adjusted for Total Fat Mass in APS



Lim et al., Gastroenterology, 2018

Visceral fat score: Blood levels of leptin, adiponectin, HDL, LDL, total cholesterol, triglycerides, insulin, total carotene and SHBG, and BMI, $(BMI)^2$, height and $(height)^2$

Association of Visceral Fat Score and Risk of Postmenopausal Breast Cancer in MEC

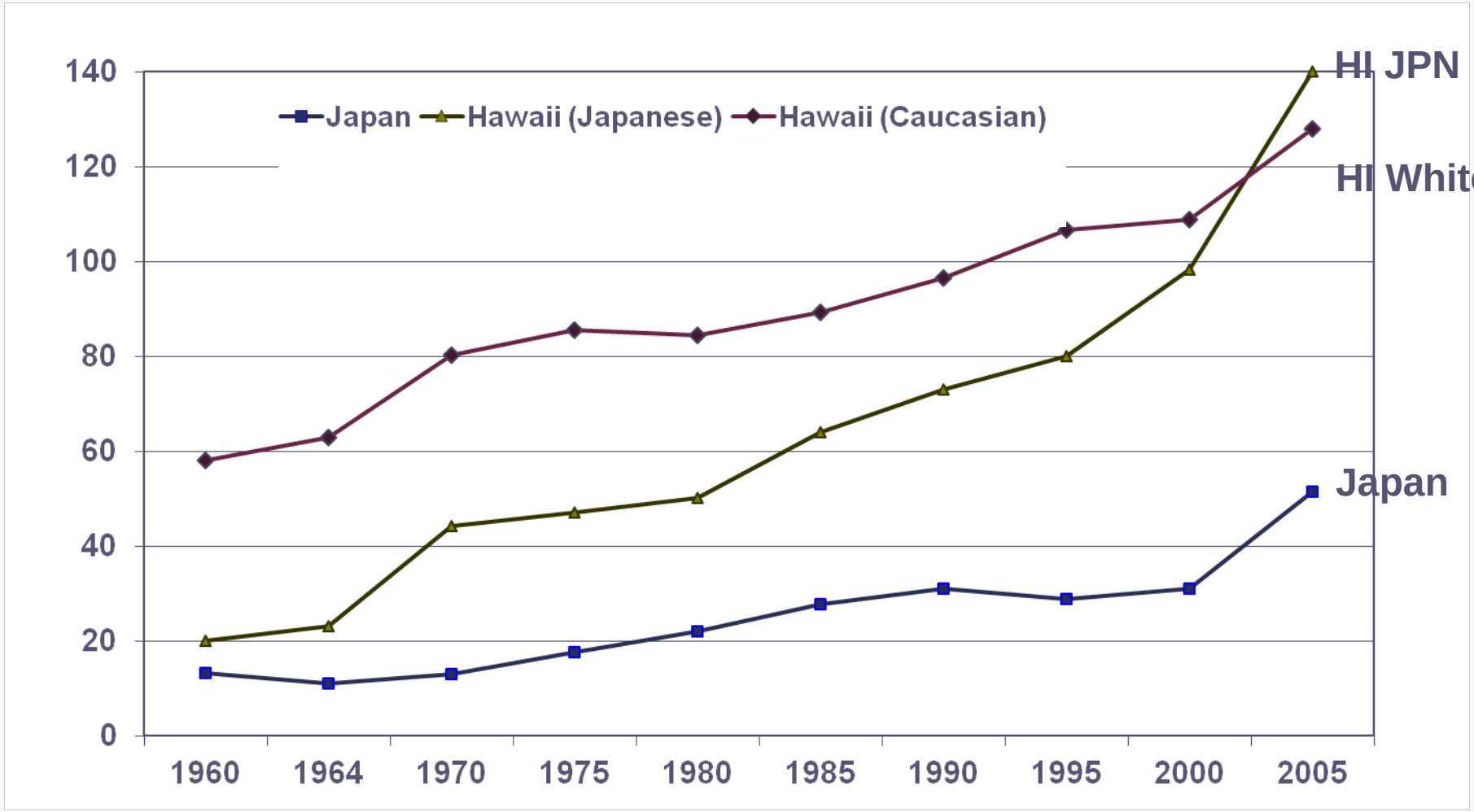
(n=896 cases, 880 controls)

Visceral Fat Score (No. of case/ No. of controls)	Multivariate adjusted	Further Adjusted for BMI
T1 (low) (247/315)	1.00	1.00
T2 (289/302)	1.10 (9.88-1.38)	1.09 (0.86-1.39)
T3 (high) (330/213)	1.45 (1.15-1.82)	1.48 (1.16-1.89)
P for trend	0.002	0.002

*Multivariate model is adjusted for matching factors and age at blood draw, menopausal hormone therapy, pack-years of smoking, moderate to vigorous activity, family history of breast cancer, type and age of menopause, age at first live birth, number of children, ethanol (g/day), and log energy (kcal/day).

Le Marchand et al., CEBP 2020

Breast Cancer Incidence in Hawaii and Japan



Summary on Obesity and Cancer in MEC

- BMI increases risk of several cancers by different amounts across ethnic groups
- Body fat distribution varies by race / ethnicity
- Amount of visceral fat can be predicted by BMI + blood biomarkers
- *Visceral Fat Score* independently predicts risks of breast cancer suggesting a role for intra-abdominal fat, beyond that of total body fat
- This risk increase is likely to be related to visceral fat's greater metabolic activity, suggesting risk lowering approaches for further research (**weight loss**, metformin, NSAID, statin)
- *Next step*: **Intermittent energy restriction** as a means to preferentially reduce intra-abdominal fat

Conclusions on Obesity and Cancer in MEC

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Obesity and cancer collaborators

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