27th Annual Research Matters Conference
A Conference of the State Academic Centers
Supported by the Maryland Cigarette Restitution Fund

Obesity and Metabolic Syndrome

Jessica Yeh, PhD
Alice Ryan, PhD
Corinne E. Joshu, PhD
Braxton Mitchell, PhD, MPH

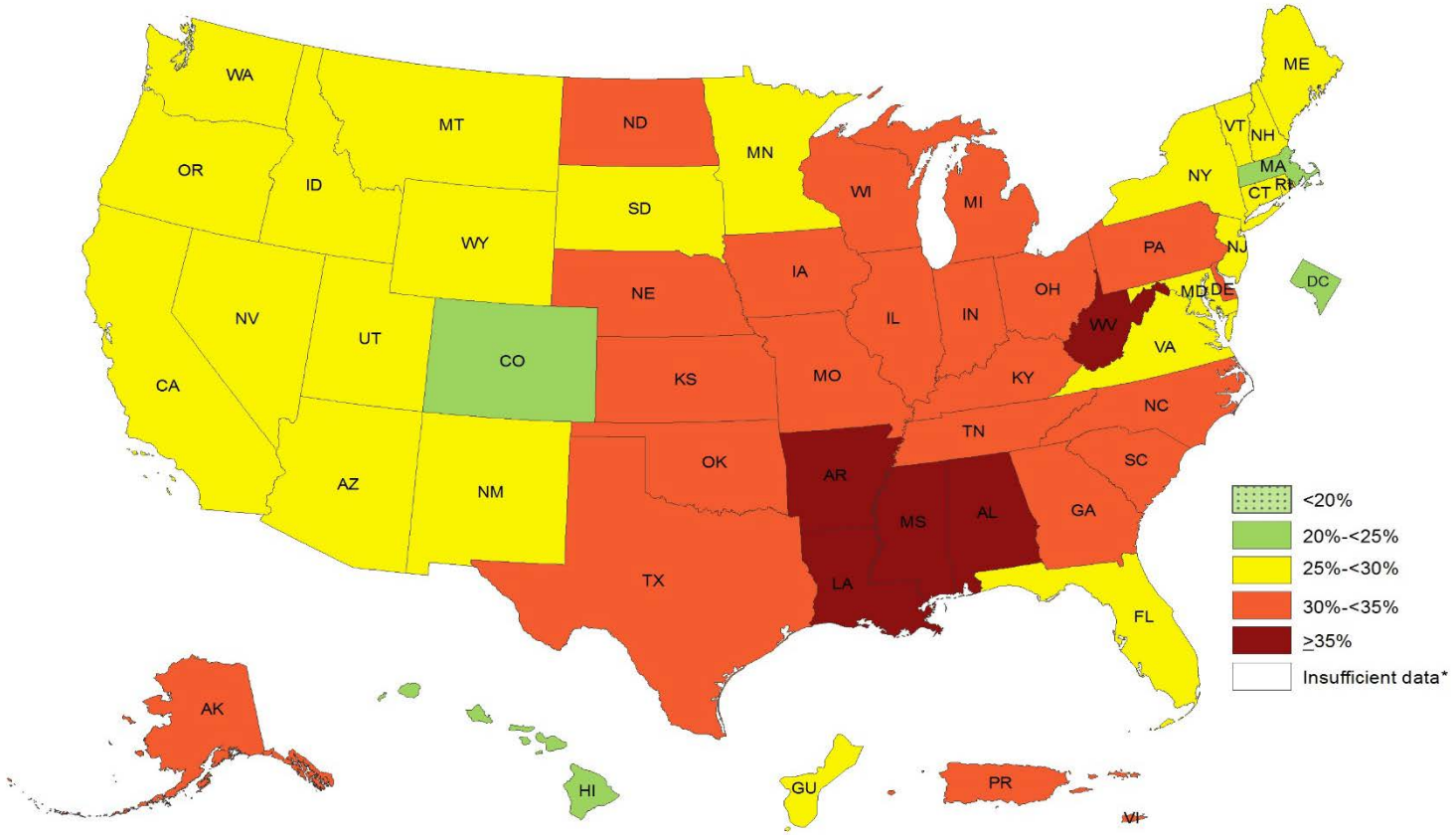
June 7, 2018

Presentations

- **Jessica Yeh, PhD**: Obesity and Cancer: An Epidemiologic Perspective
- **Alice Ryan, PhD**: Survivorship: Weight Loss and Exercise
- **Corinne E. Joshu, PhD, MPH**: Obesity and Cancer in ARIC: Findings for prostate cancer and future opportunities
- **Braxton Mitchell, PhD, MPH**: The Health of the Amish and What we can learn
- **Discussions**

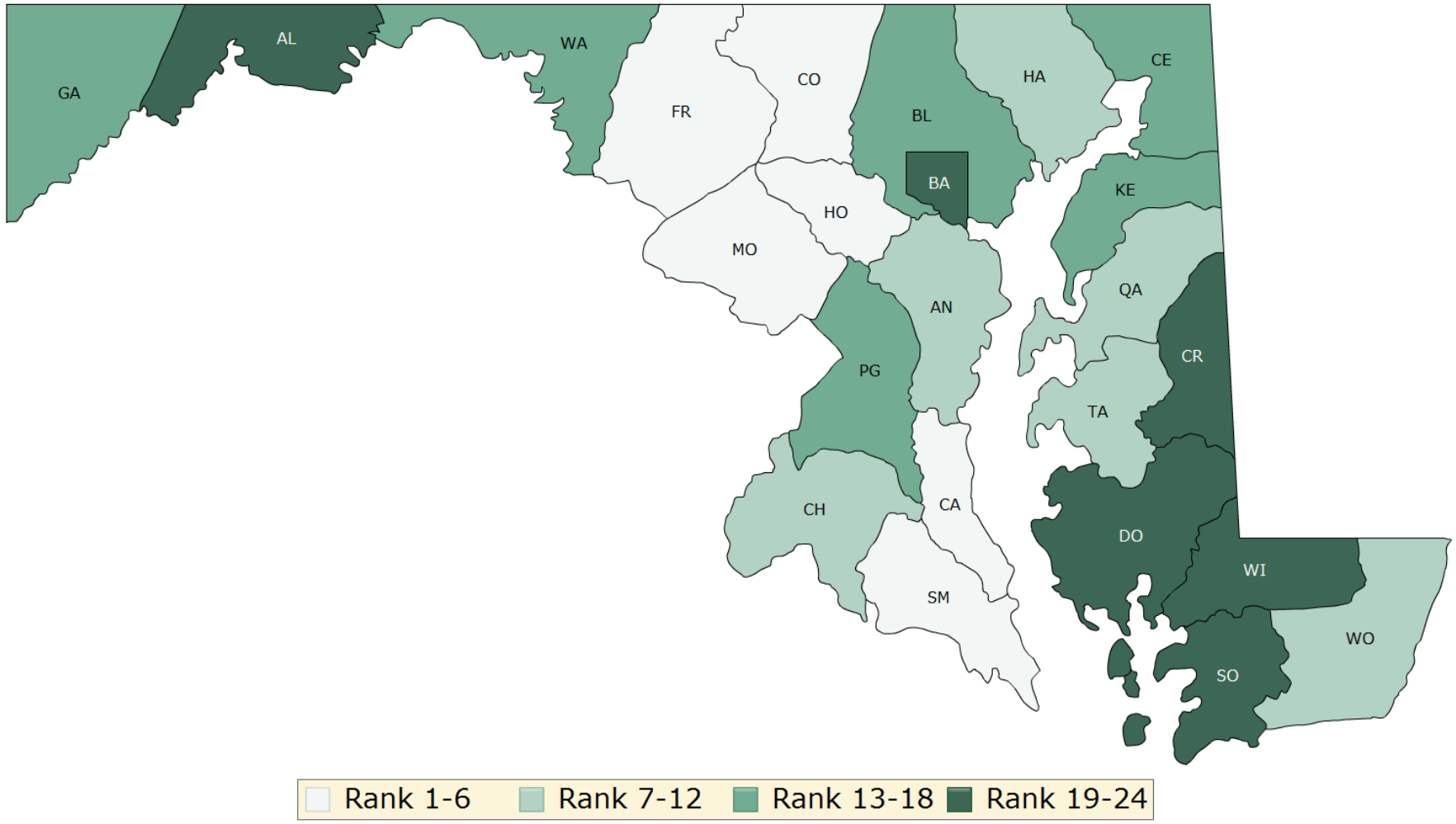
Prevalence¶ of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2016

¶ Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.



***Sample size <50 or the relative standard error (dividing the standard error by the prevalence) ≥ 30%.**

Percentage of Adults that Report a BMI of 30+ in Maryland, 2014



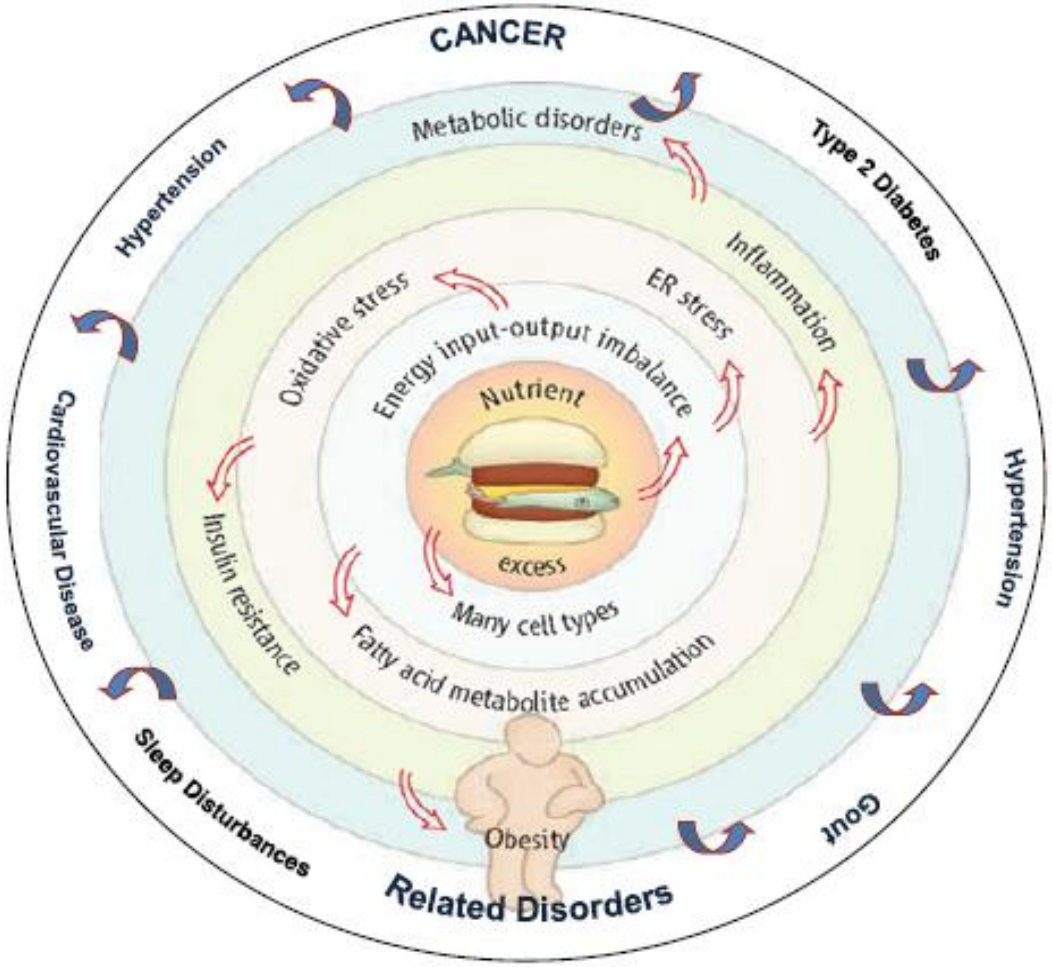
Prevalence of Obesity -Related Unhealthy Behaviors

	MD	US Median	Rank among States and DC (best to worst)
Overweight*	34.7%	35.3%	15th
Obesity*	29.9%	29.9%	27th
Exercise (% None)*	23.2%	23.3%	28th
Fruits (<1 serving per day)**	36.0%	39.7%	9th
Vegetables (<1 serving per day)**	21.3%	22.1%	20th

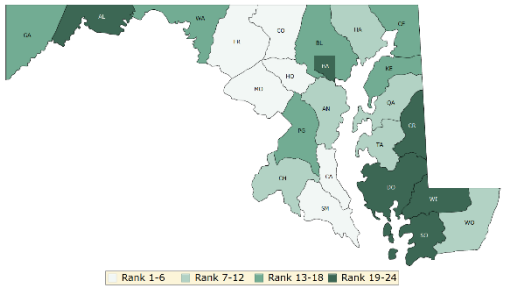
(based on 2015** or 2016* BRFSS data)

Why is Obesity So Bad?

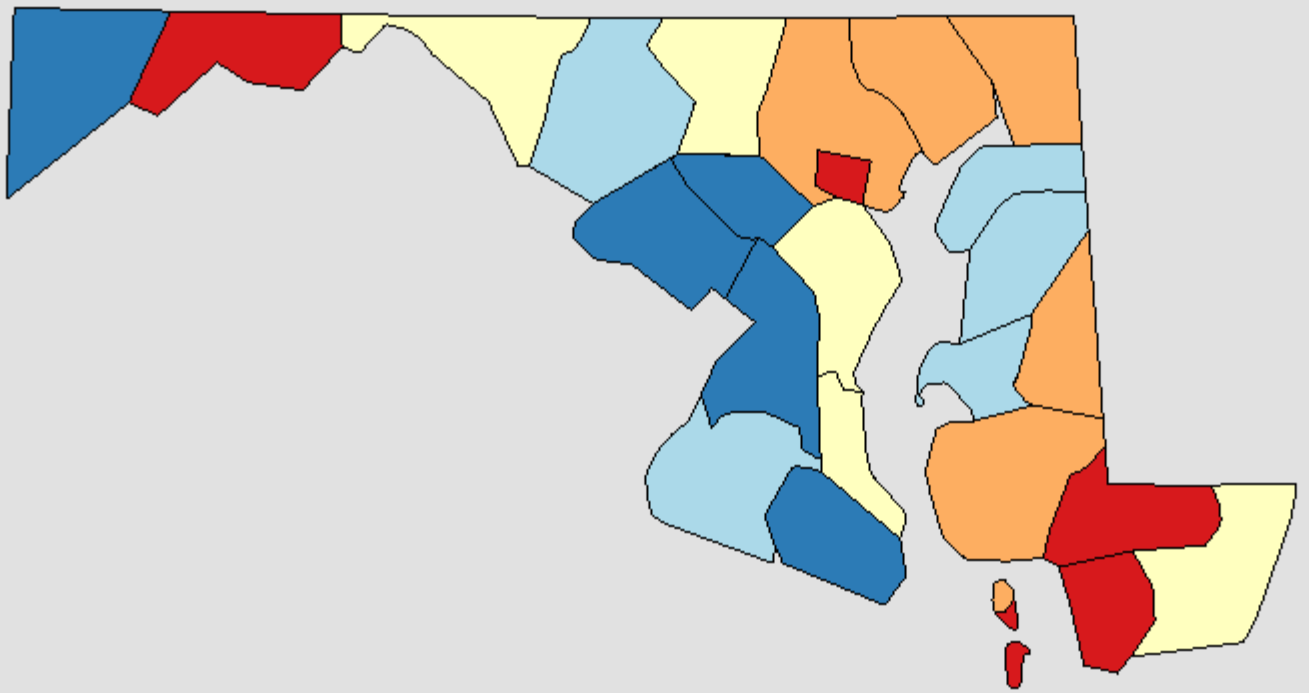
- Adipose tissue is not an “inert storage depot”, but an endocrine organ



The Role of Obesity in Cancer Survival and Recurrence: Workshop Summary. National Academies, 2012



Incidence Rates† for Maryland
All Cancer Sites, 2010 - 2014
All Races (includes Hispanic), Both Sexes, Ages 50+



Age-Adjusted

Annual Incidence Rate

(Cases per 100,000)

Quantile Interval

- 1,143.6 to 1,263.7
- > 1,263.7 to 1,347.3
- > 1,347.3 to 1,421.4
- > 1,421.4 to 1,483.4
- > 1,483.4 to 1,579.1

US (SEER + NPCR)
Rate (95% C.I.)
1341.8 (1340.8 - 1342.8)

Maryland
Rate (95% C.I.)
1354.8 (1347.1 - 1362.5)

Notes:

State Cancer Registries may provide more current or more local data.

Data presented on the State Cancer Profiles Web Site may differ from statistics reported by the State Cancer Registries (for more information).

† Incidence rates (cases per 100,000 population per year) are age-adjusted to the 2000 US standard population (19 age groups: <1, 1-4, 5-9, ... , 80-84, 85+). Rates are for invasive cancer only (except for bladder which is invasive and in situ) or unless otherwise specified. Rates calculated using SEER*Stat. Population counts for denominators are based on Census populations as modified by NCI. The 1969-2015 US Population Data File is used for SEER and NPCR incidence rates.

Data for the United States does not include data from Puerto Rico

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Obesity and Cancer: An Epidemiologic Perspective

Hsin-Chieh "Jessica" Yeh, PhD

Associate Professor, Medicine, Epidemiology, and Oncology

Associate Director, Welch Center for Prevention, Epidemiology, and Clinical research

Johns Hopkins University

June 7, 2018

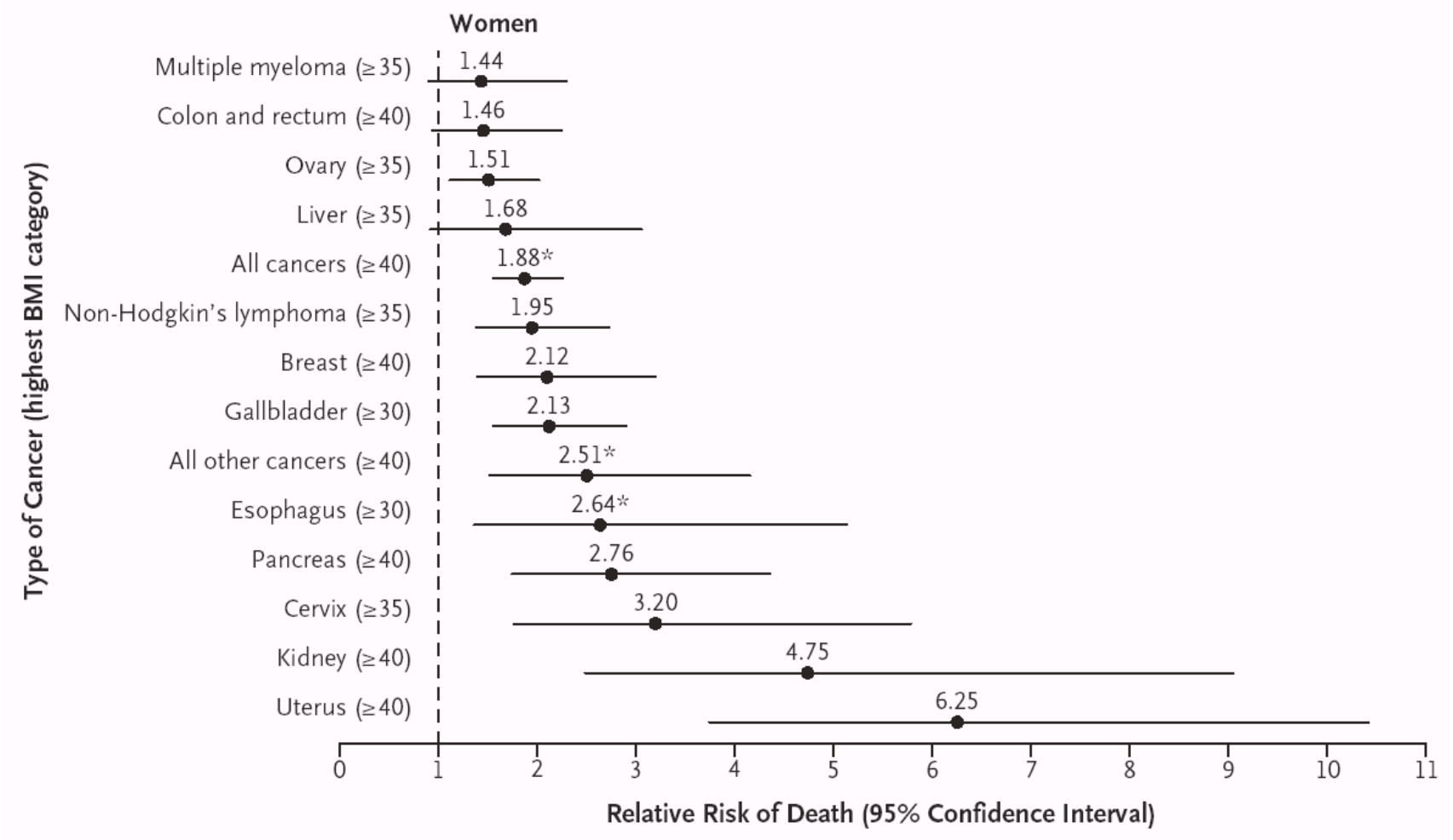
JOHNS HOPKINS
MEDICINE
THE SIDNEY KIMMEL COMPREHENSIVE CANCER CENTER

Molecular Mechanisms in Obesity-Cancer Link

- Obesity is associated with substantial metabolic and endocrine abnormalities,
  - alterations in sex hormone metabolism
  - insulin and insulin-like growth factor (IGF) signaling, and
  - adipokines or inflammatory pathways

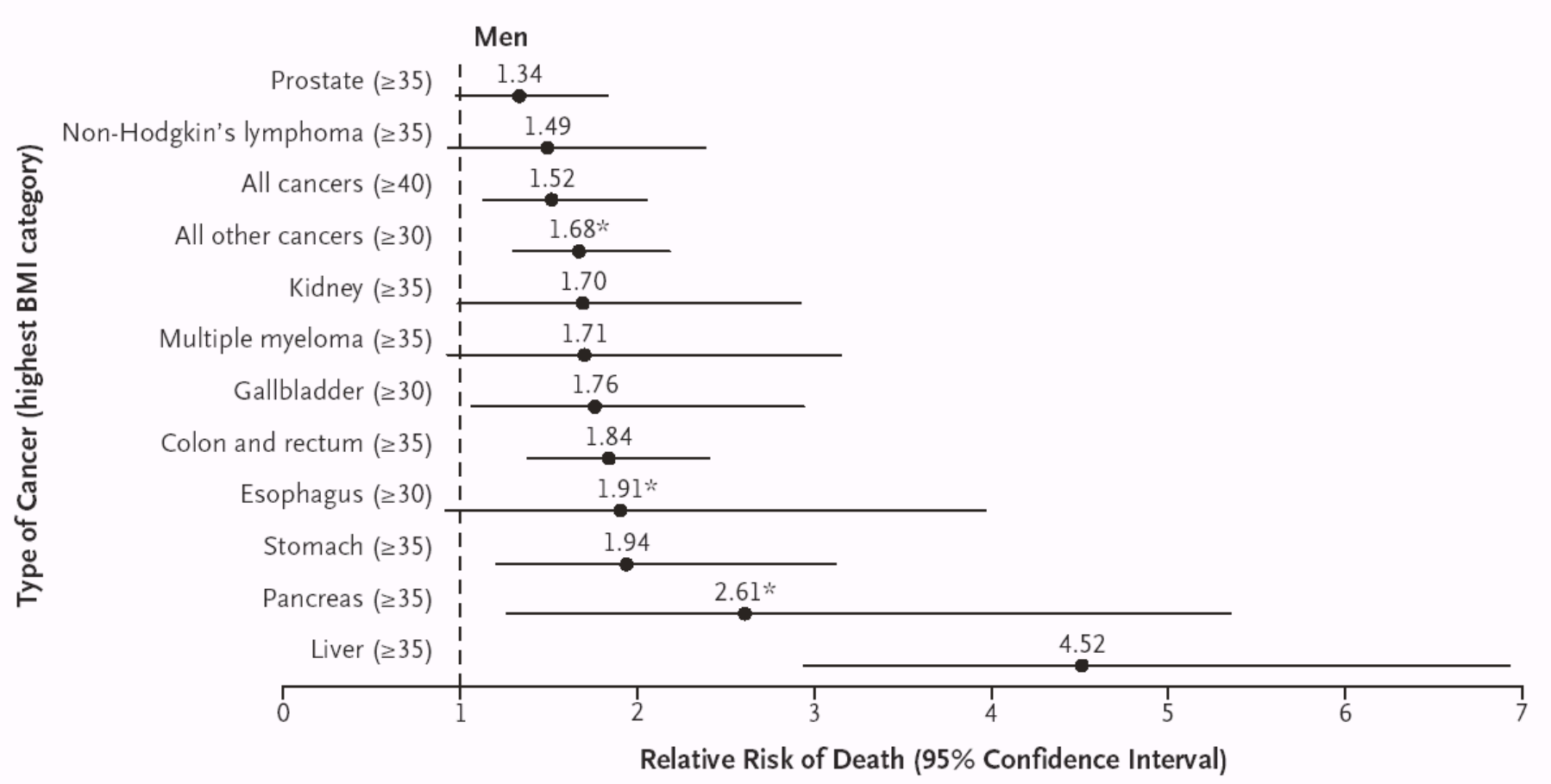
Lauby-Secretan B et al, NEJM 2016

Obesity Increases the Risk of Cancer Death in Women, ACS Cancer Prevention II Cohort



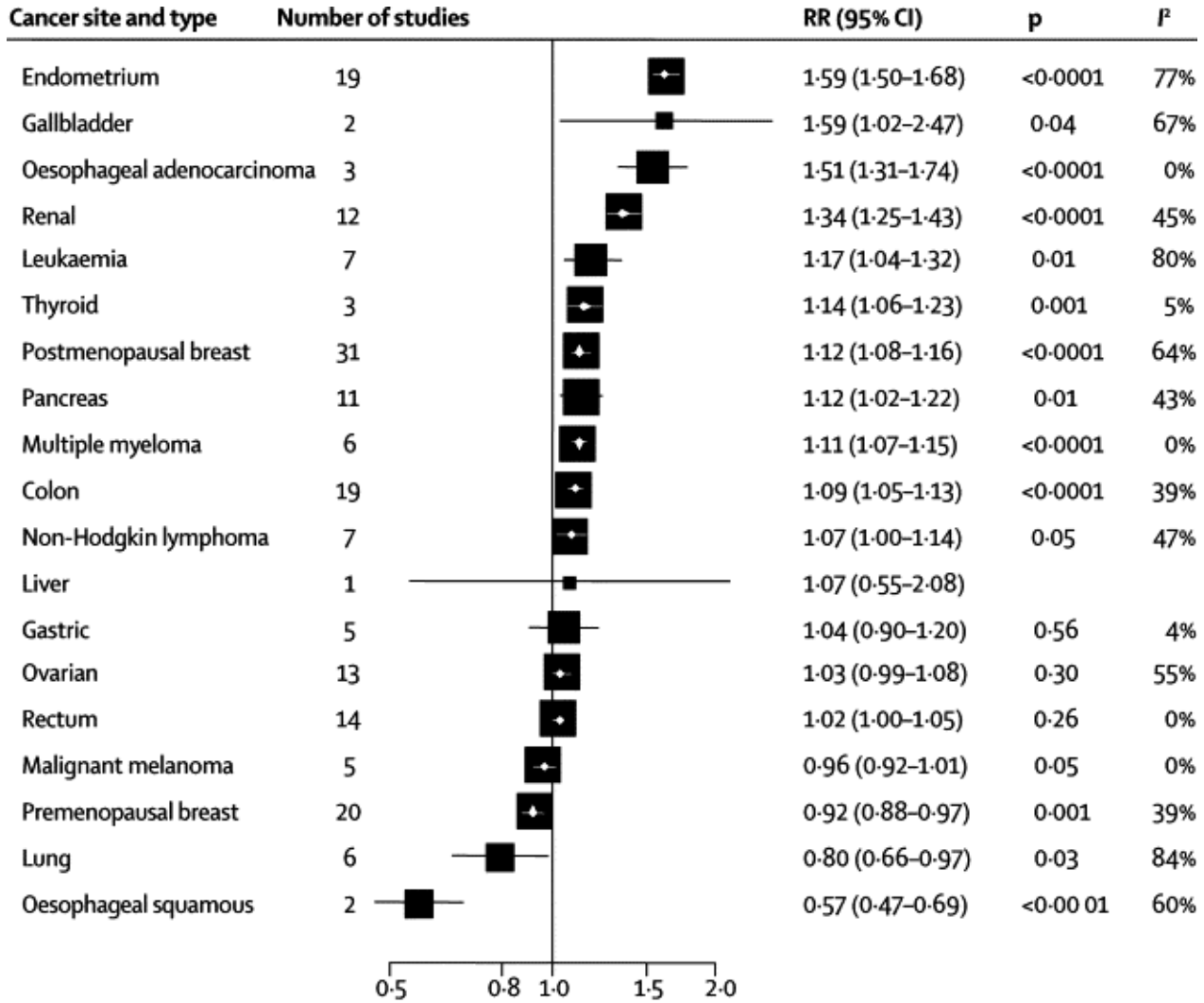
Calle et al. NEJM 2003

Obesity Increases the Risk of Cancer Death in Men, ASC Cancer Prevention II Cohort



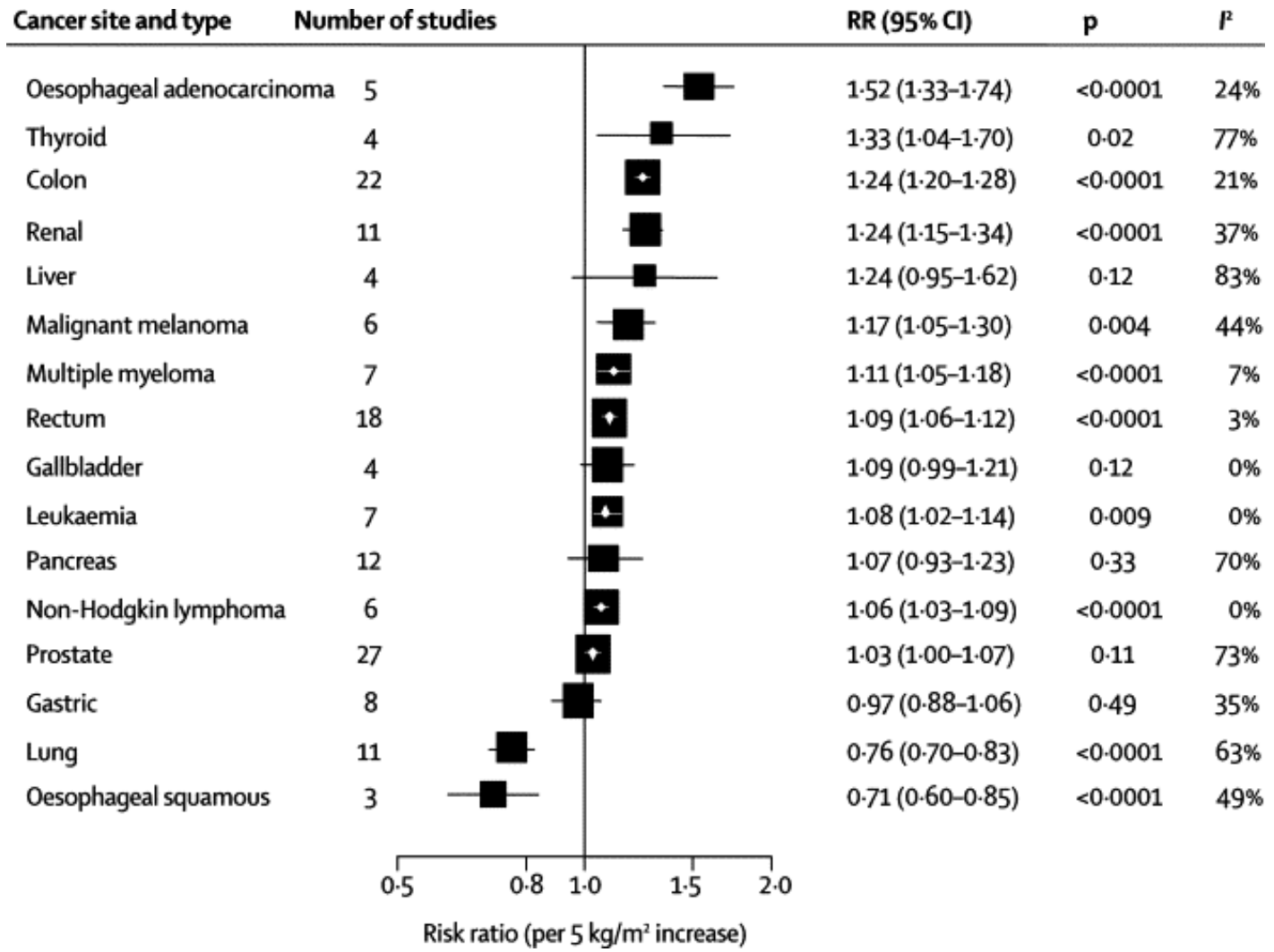
Calle et al. NEJM 2003

Meta-Analysis of BMI (per 5 kg/m2) and Cancer Incidence in Women



Renehan AG et al, *Lancet* 2008

Meta-Analysis of BMI (per 5 kg/m2) and Cancer Incidence in Men



Renehan AG et al, *Lancet* 2008

Association between Treated Diabetes and Cancer Incidence in 18,280 Adults, CLUE II, Washington County, Maryland, 1989–2006

	Diabetes (n=599)		No Diabetes (n=17,681)		
	case	Rate	case	rate	HR
All cancer	116	13.25	2365	10.58	1.22
Men	57	12.36	1143	12.78	1.04
Women	59	13.55	122	9.10	1.33*
Digestive cancers	30	3.17	393	1.76	1.73*
Colorectum	17	1.82	269	1.19	1.41
Pancreas	6	0.67	63	0.28	2.67*
Smoking-related	35	3.90	595	2.72	1.50*

Partly funded by CRF

Yeh HC et al, Diabetes Care, 2012

Association between Treated Diabetes and Cancer Mortality in 18,280 Adults, CLUE II, Washington County, Maryland, 1989–2006

	Diabetes (n=599)		No Diabetes (n=17,681)		
	case	Rate	case	rate	HR
All cancer	51	4.17	856	3.12	1.36*
Men	27	4.73	422	3.84	1.37
Women	24	3.77	434	2.64	1.35
Digestive cancers	23	1.74	181	0.64	2.79*
Colorectum	11	0.83	79	0.28	3.26*
Pancreas	6	0.49	59	0.21	3.42*
Smoking-related	24	1.85	413	1.46	1.44

Yeh HC et al, Diabetes Care, 2012

Partly funded by CRF

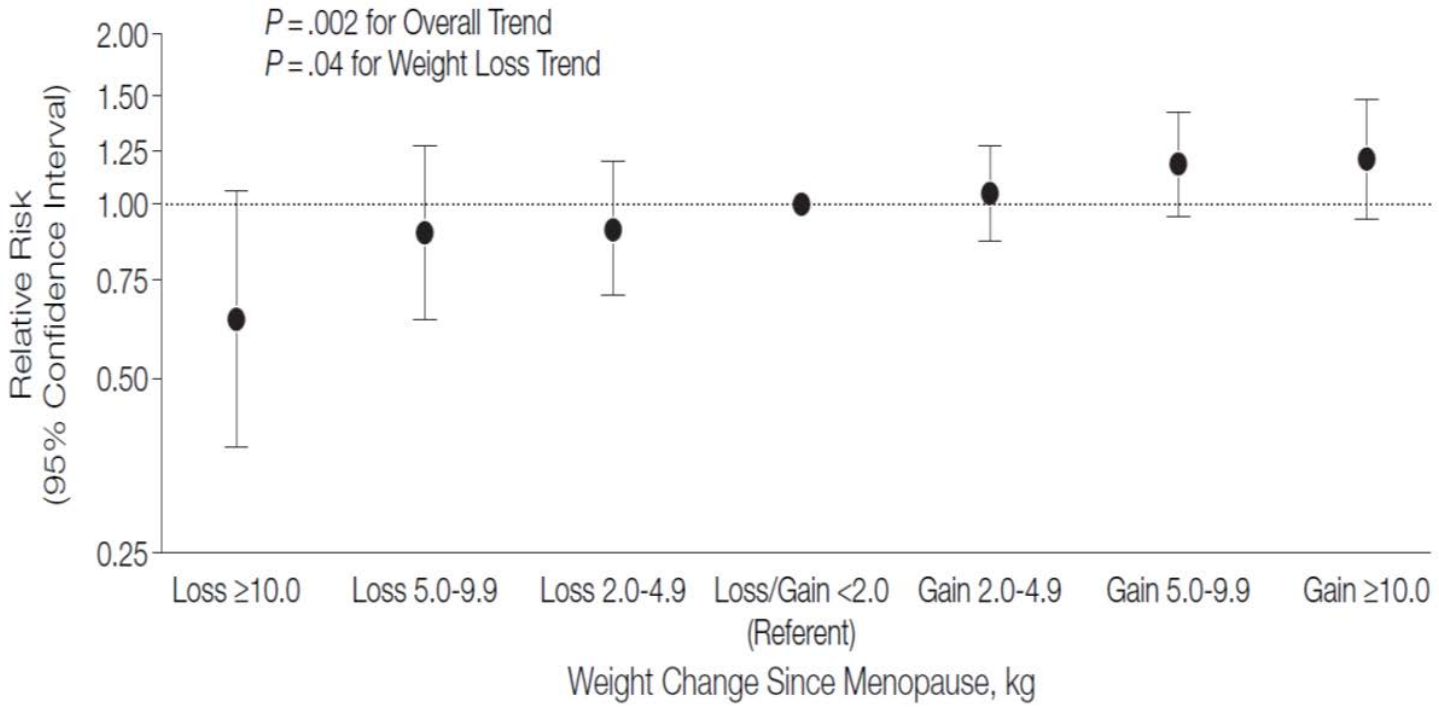
Strength of the Evidence for a Cancer-Preventive Effect of the Absence of Excess Body Fatness

Cancer Site or Type	Strength of the Evidence in Humans†	Relative Risk of the Highest BMI Category Evaluated versus Normal BMI (95% CI)‡
Esophagus: adenocarcinoma	Sufficient	4.8 (3.0–7.7)
Gastric cardia	Sufficient	1.8 (1.3–2.5)
Colon and rectum	Sufficient	1.3 (1.3–1.4)
Liver	Sufficient	1.8 (1.6–2.1)
Gallbladder	Sufficient	1.3 (1.2–1.4)
Pancreas	Sufficient	1.5 (1.2–1.8)
Breast: postmenopausal	Sufficient	1.1 (1.1–1.2)§
Corpus uteri	Sufficient	7.1 (6.3–8.1)
Ovary	Sufficient	1.1 (1.1–1.2)
Kidney: renal-cell	Sufficient	1.8 (1.7–1.9)
Meningioma	Sufficient	1.5 (1.3–1.8)
Thyroid	Sufficient	1.1 (1.0–1.1)§
Multiple myeloma	Sufficient	1.5 (1.2–2.0)

IARC Working Group,
Lauby-Secretan B et al, NEJM 2016

RRs of Postmenopausal Breast Cancer According to Weight Change in 87,143 Women, aged 30 to 55 years: Nurses' Health Study

Figure. Relative Risk of Postmenopausal Breast Cancer Among Women Who Have Never Used Postmenopausal Hormones According to Weight Change Since Menopause



Eliassen AH et al JAMA 2006

Cause of Death in 2,010 Obese Adults Who Underwent Bariatric Surgery and 2,017 Matched Controls Who Did Not

Swedish Obese Subjects (SOS) Study

Table 2. Cause of Death.*

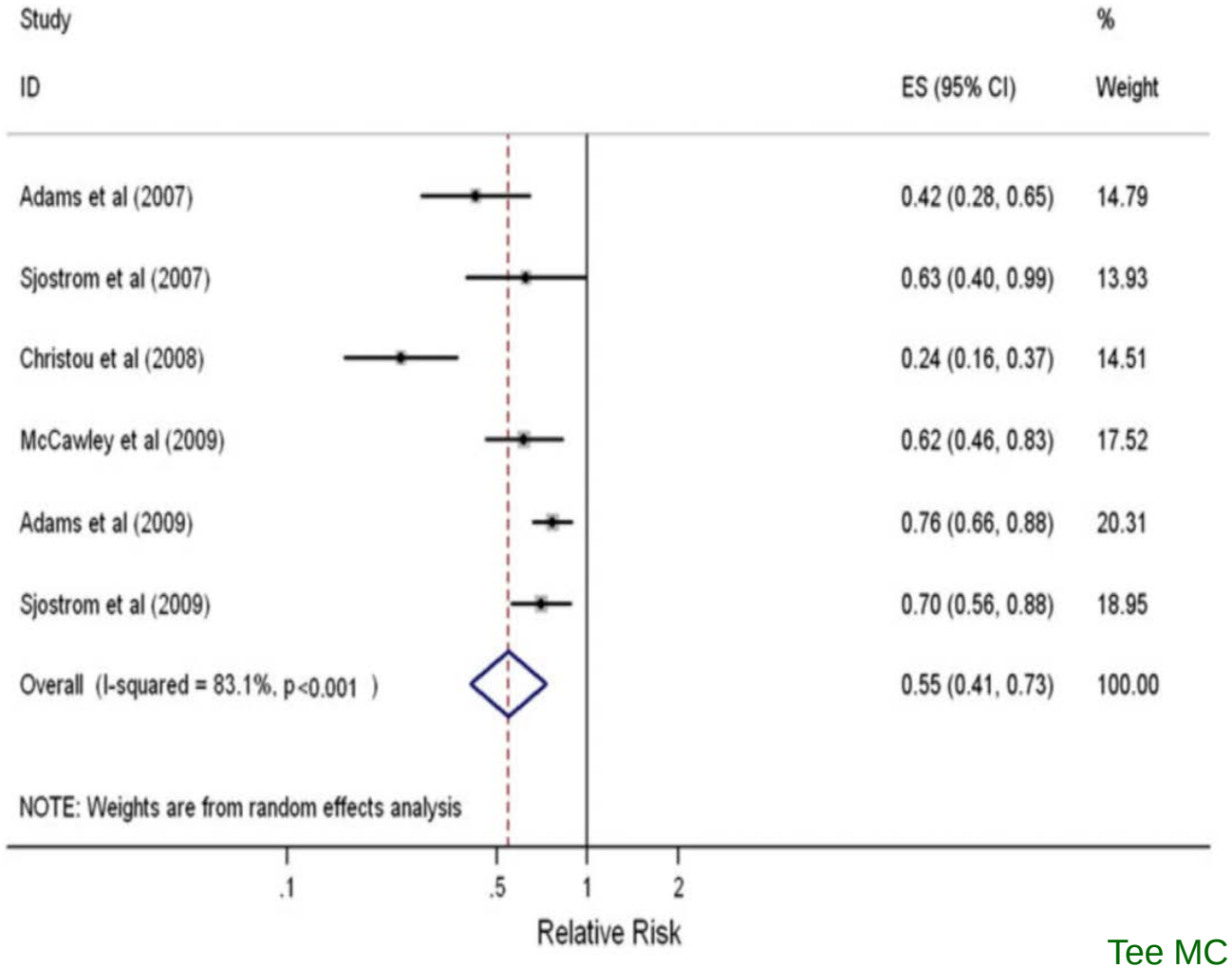
Variable	Surgery Group (N=2010)	Control Group (N=2037)
	no. of subjects	
Cardiovascular condition		
Any event	43	53
Cardiac	35	44
Myocardial infarction	13	25
Noncardiovascular condition		
Any event	58	76
Tumor	29	48
Cancer	29	47
Meningioma	0	1
Infection	12	3
Thromboembolic disease	5	7
Pulmonary embolism	4	7
Vena caval thrombosis	1	0
Other	12	18
Total no. of deaths	101	129

* During the first 90 days after study initiation, there were five deaths in the surgery group (four from peritonitis with organ failure and one sudden death) and two deaths in the control group (one from cancer of the pancreas and one from alcohol-related causes).

38% reduction in risk of Cancer Death

L Sjostrom et al. N Engl J Med. 2007 Aug 23; 357(8): 741-52

Effect of Bariatric Surgery on Cancer Incidence and Mortality



Tee MC et al. Surg Endosc (2013)

Does Weight Loss Improve Cancer Outcomes? Report from ASCO

- Currently no data that provide definitive evidence that weight loss, calorie restriction, or increased exercise will prevent cancer or lower the risk of cancer-specific mortality.

- Hundreds of small trials in patients with cancer evaluated the feasibility and benefits of weight loss and physical activity interventions with regard to intermediate end points and patient-reported outcomes.
  - Most focused on patients with early-stage breast cancer

- These randomized trials have demonstrated that
  - weight loss and physical activity interventions are feasible in cancer survivors
  - can lead to improvements in outcomes such as body composition, physical fitness, body image, fatigue, quality of life, and biomarkers linked to cancer outcomes.

Ligibel JA et al, JCO 2015

Trial of Behavioral Weight Loss and Metformin Treatment to Lower Insulin Growth Factor in Cancer Survivors

SPIRIT
A Research Program for Cancer Survivors

- Objective: Conduct a randomized, 3-arm trial to compare the effects of self-directed weight loss, coach-directed weight loss, and metformin treatment on IGF-1 and the IGF-1 to IGFBP3 ratio
- Population: Participants are cancer survivors – persons who self-report a malignant solid tumor diagnosis and have completed curative intent treatment and have no ongoing or planned active treatment (surgery, radiation therapy or chemotherapy other than chemoprophylaxis).

Jessica Yeh, PhD (PI)
Larry Appel, MD(Co-PI)
Mike Carducci, MD(Co-PI)

Funded by the Maryland Cigarette Restitution Funds and SKCCC

Collaboration with U of Maryland Baltimore

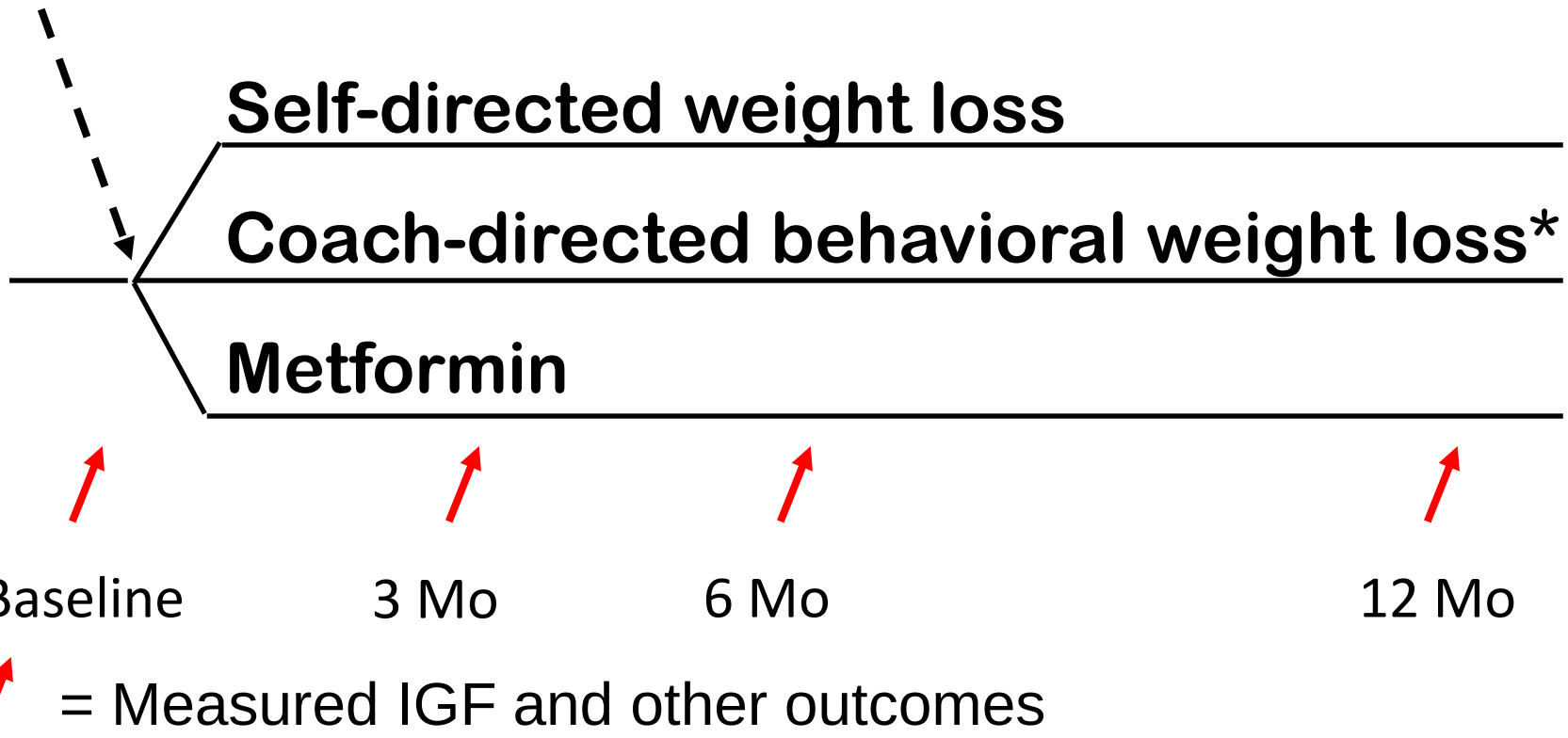
SPIRIT

A Research Program for Cancer Survivors

SPIRIT
A Research Program for Cancer Survivors

Study Design

Randomization (n=121)



= Measured IGF and other outcomes

*Using *Innergy*; delivered by coach through web and phone (Appel L et al, NEJM 2011)

innergy
healthier weight
Welcome back, Taylor
My Account
Help
Logout
Search
Go
Home
Learn
Track
Calendar
Community
Messages
Recipes
Resources
Welcome back, Taylor
Your Progress
Your Weight
Your Activity
Week 159
Tue Sep 29, 2015
STARTING
241.0
POUNDS
CURRENT
241.0
POUNDS
LAST WEEK
0
MINUTES
TOTAL MIN
0
MINUTES
Track Your Food, Weight and Activity
It is important to stay on track!
Track Now
View Progress
Learning Center – Week 157 - 160
Celebrate Your Innergy Journey
Congratulations! You've almost completed two full years of the Innergy program. This is an amazing accomplishment that deserves celebration.
Read More
Your Coach
Coach Arlene
Registered Dietitian
View Coach Profile
Send Message
COACH MESSAGES
no unread messages
See All
NEXT COACHING SESSION
no upcoming sessions
See All

Metformin Treatment

- IND waiver from FDA obtained for the trial

- Oral titration of metformin in an open-label fashion:
  - Start with 500 mg by mouth once daily with breakfast for 7 days or longer if needed for tolerance;
  - Up to 2,000 mg per day

Baseline Characteristics

Number Randomized	N=121
Mean Age	59.7
Mean BMI	35.0
Gender %	
Male	20.7
Female	79.3
Race %	
Non-Black	54.5
Black or African American	45.5
Cancer Type%	
Breast	56.2
Prostate	9.1
Colon	7.4

Community-based Participant Engagement and Translation (CPET) Core

- Provide expert consultation on design and conduct of community-based studies with an emphasis on recruitment and retention of research participants, particularly underrepresented minorities

- Implement and provide expert consultation on the design and conduct of lifestyle interventions; and

- Educate and train investigative teams on protocol development and data collection procedures in community-based studies.

Funded by CRF and NCI

(Co-Directors: Yeh and Appel)

Conclusions

- Obesity is associated with cancer outcomes across the full spectrum -- from cancer development, cancer progression, to death from cancer.

- From a public health perspective, strategies to jointly reduce obesity and cancer are likely to produce much greater reductions in mortality than through initiatives directed at each disease separately.