

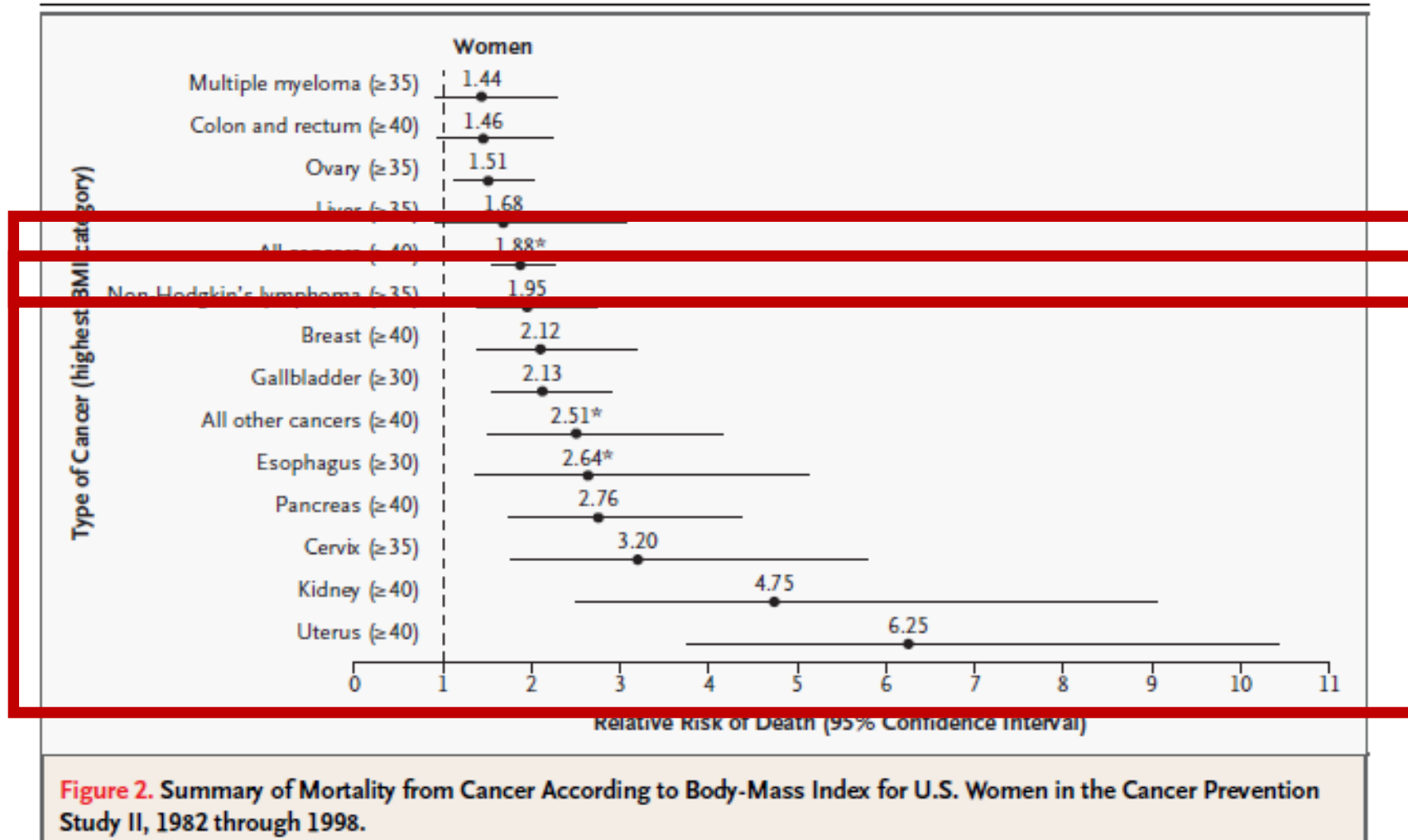


Hot Topics Symposium:

Modifiable Host Factors and the Immune Response

Jennifer Ligibel, MD

Modifiable host factors associated with cancer risk



Strong link between obesity and cancer risk

THE NEW ENGLAND JOURNAL of MEDICINE

SPECIAL REPORT

Body Fatness and Cancer — Viewpoint of the IARC Working Group

- Reviewed more than 1000 studies evaluating the relationship between body weight and cancer risk
- Identified 13 malignancies for which there was sufficient evidence that excess weight led to increased cancer risk

Lauby-Secretan et al. NEJM 2016

Table 2. Strength of the Evidence for a Cancer-Preventive Effect of the Absence of Excess Body Fatness, According to Cancer Site or Type.*

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)
Male breast cancer	Limited	NA
Fatal prostate cancer	Limited	NA
Diffuse large B-cell lymphoma	Limited	NA
Esophagus: squamous-cell carcinoma	Inadequate	NA
Gastric noncardia	Inadequate	NA
Extrahepatic biliary tract	Inadequate	NA
Lung	Inadequate	NA
Skin: cutaneous melanoma	Inadequate	NA
Testis	Inadequate	NA
Urinary bladder	Inadequate	NA
Brain or spinal cord: glioma	Inadequate	NA

Emerging evidence that weight loss could reduce cancer risk from bariatric surgery studies

Meta-analysis of cancer risk and bariatric surgery in controlled studies

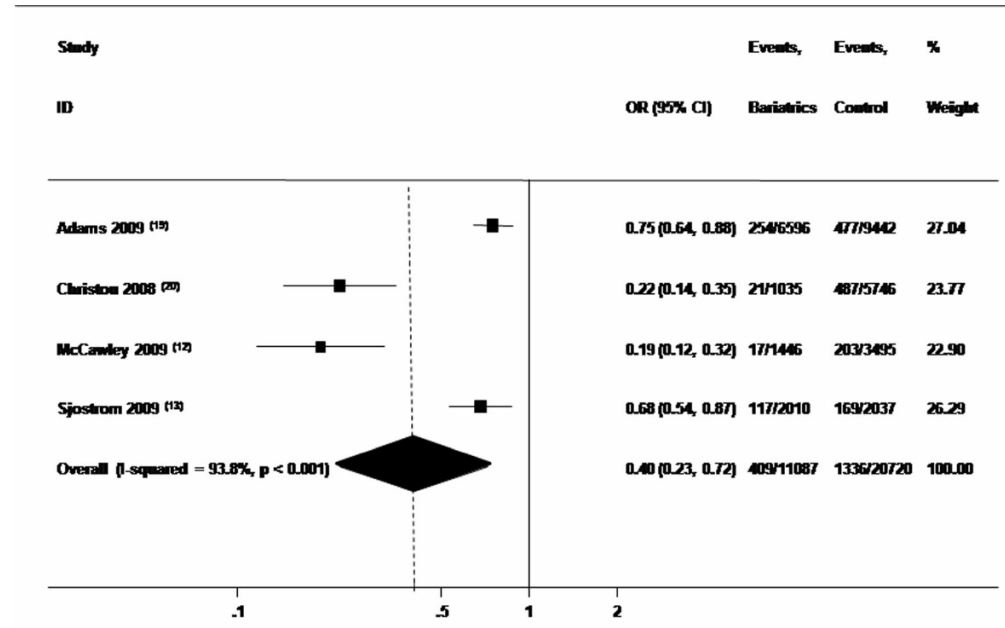
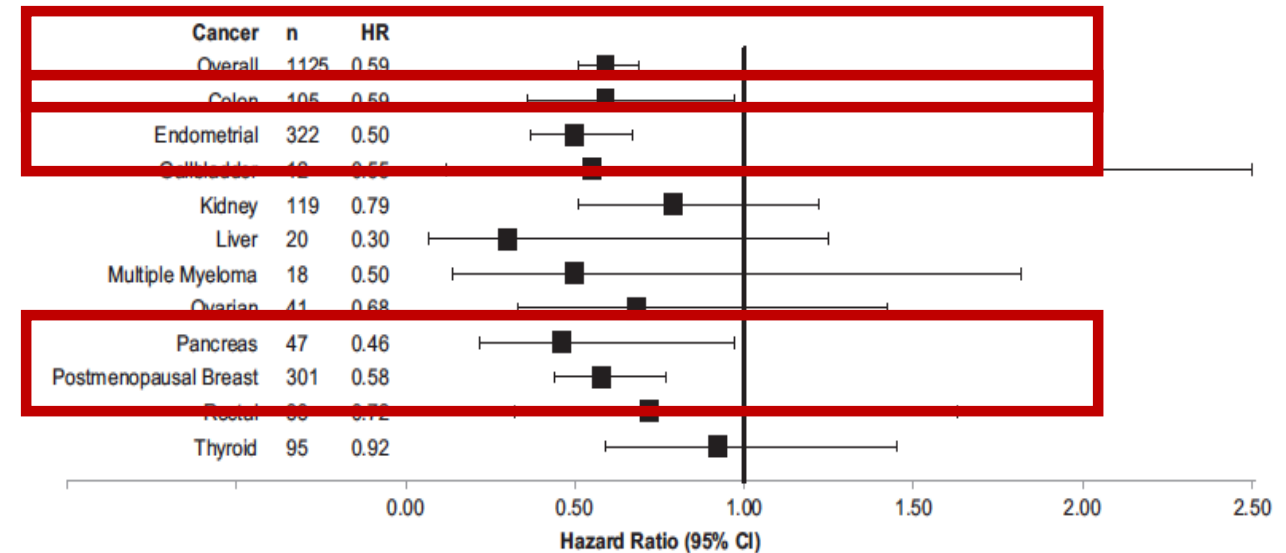


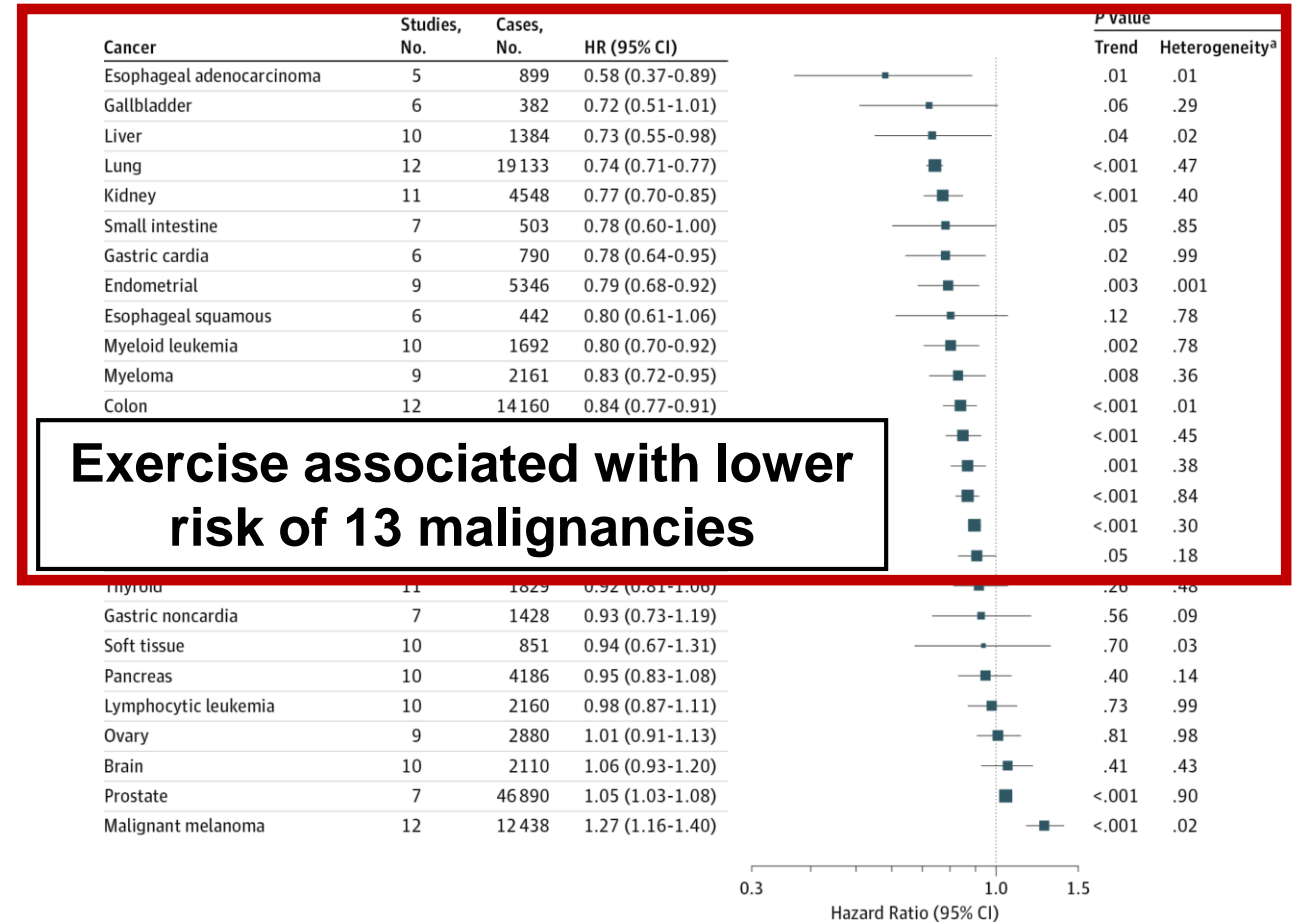
Fig. 2 Association between cancer risk and bariatric surgery in controlled studies

Cancer risk in 22,000 bariatric surgery patients vs. 66,000 matched controls

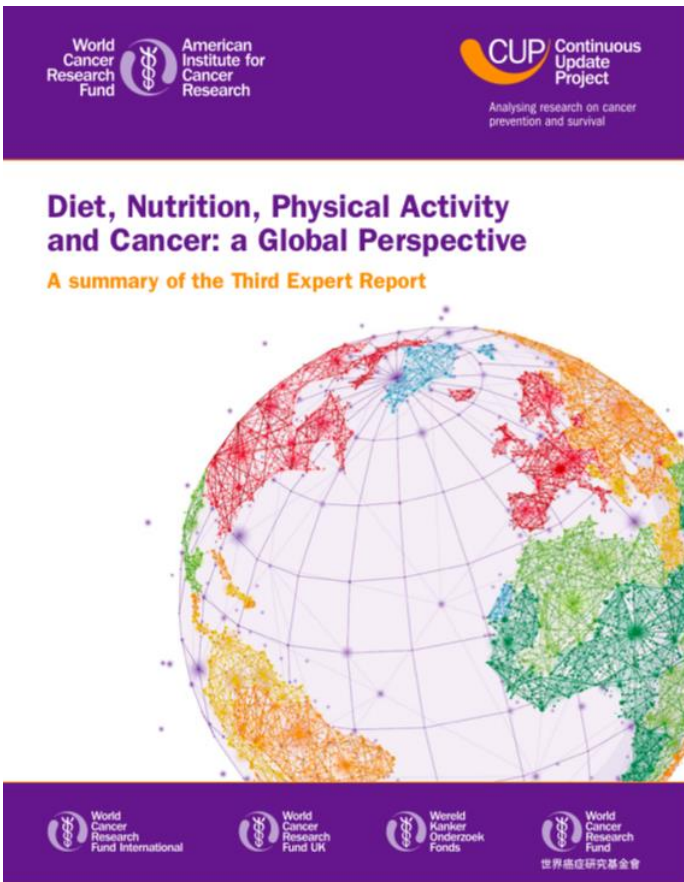


Pooled analysis of leisure-time physical activity and cancer risk

- 12 US/European cohorts, including 1.44 million individuals
- 186,932 cancers diagnosed, 11 years median follow up
- PA assessed through self report
- Multivariate models:
 - Adjustment for BMI modestly attenuated association in several cancers, 10/13 still sig
 - Adjustment for smoking attenuated association for lung



Dietary factors linked to increased cancer risk



- Alcohol
- Red meat
- Processed meat

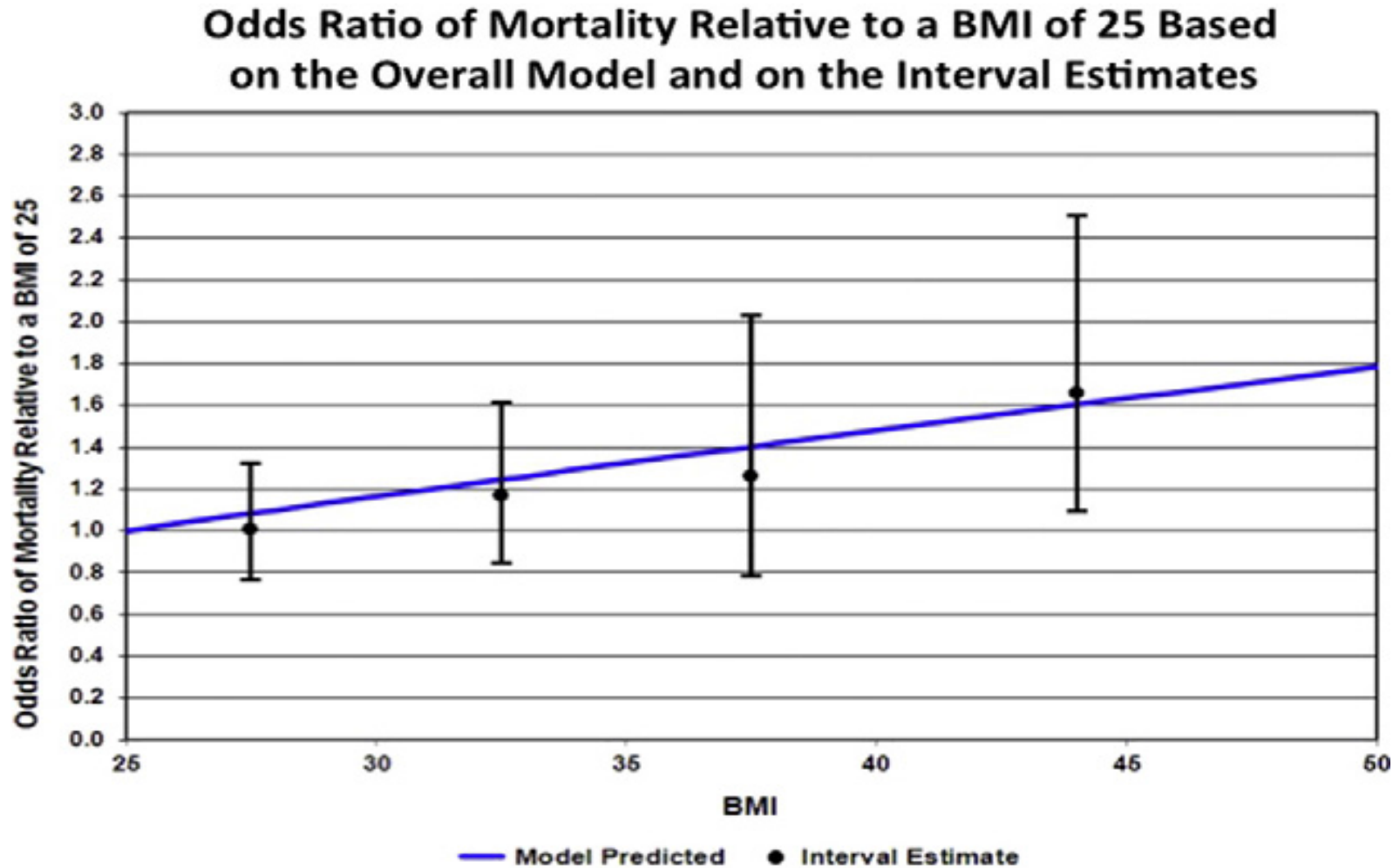
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Host factors also linked to cancer prognosis

Meta-analysis of 82 studies looking at obesity and survival in breast cancer

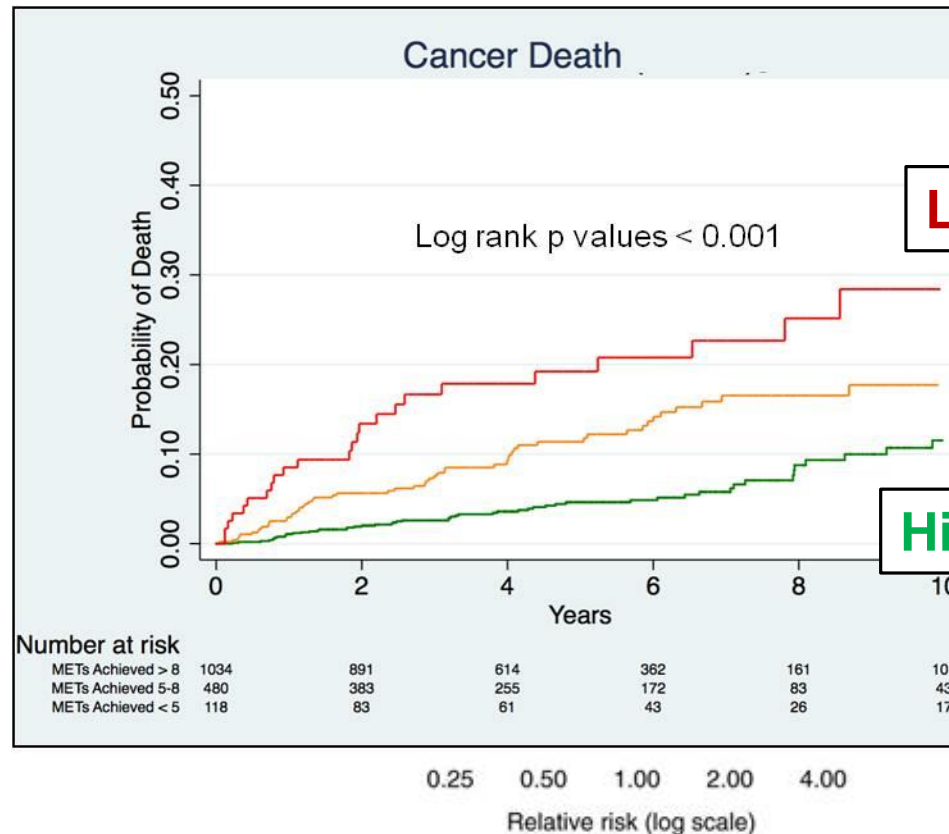
	Breast Cancer-Specific HR [95% CI]	Overall HR [95% CI]
All patients	1.35 [1.24-1.47]	1.41 [1.29-1.53]
Premenopausal		1.75 [1.26-2.41]
Postmenopausal		1.34 [1.18-1.53]

Endometrial cancer: Association of BMI with mortality



Cardiorespiratory fitness (CRF) and physical activity linked to cancer outcomes

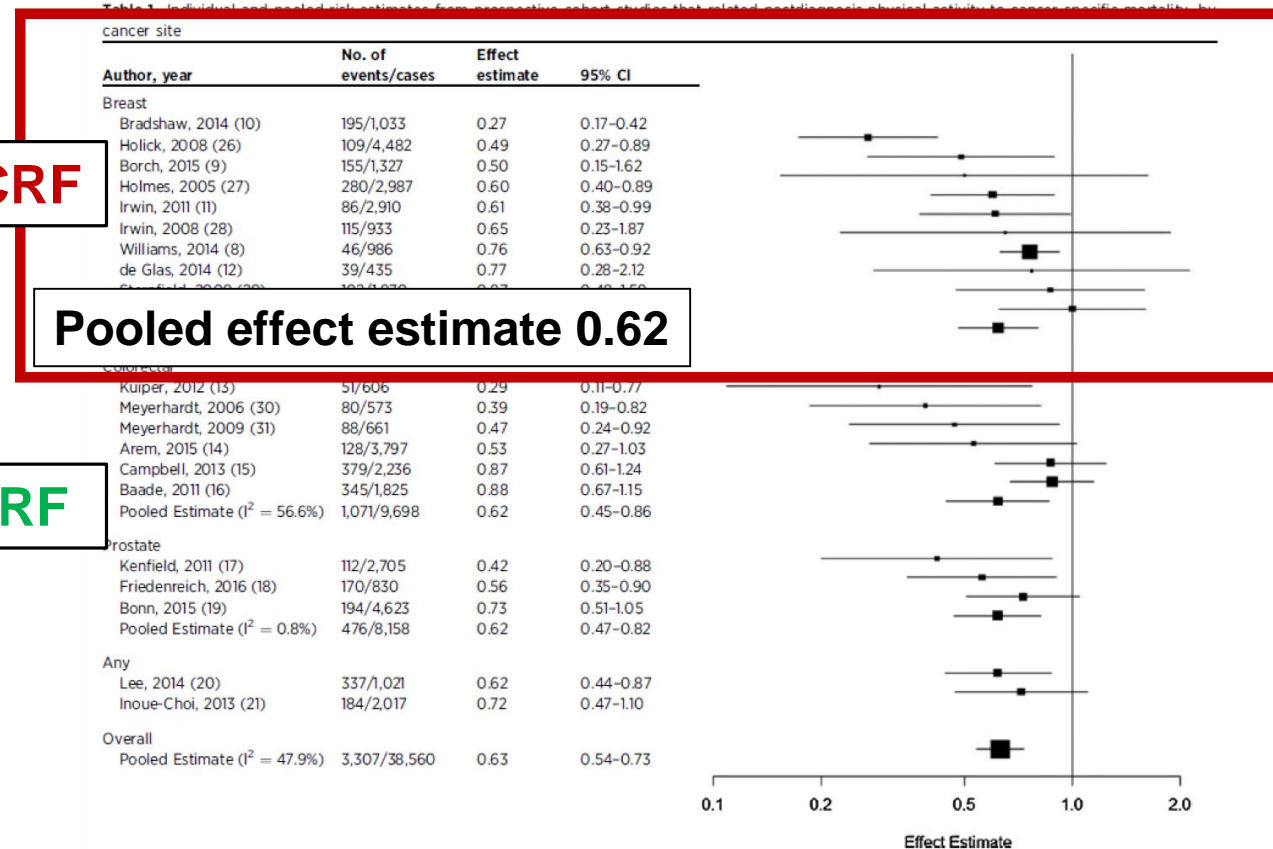
CRF and cancer-related mortality



Low CRF

High CRF

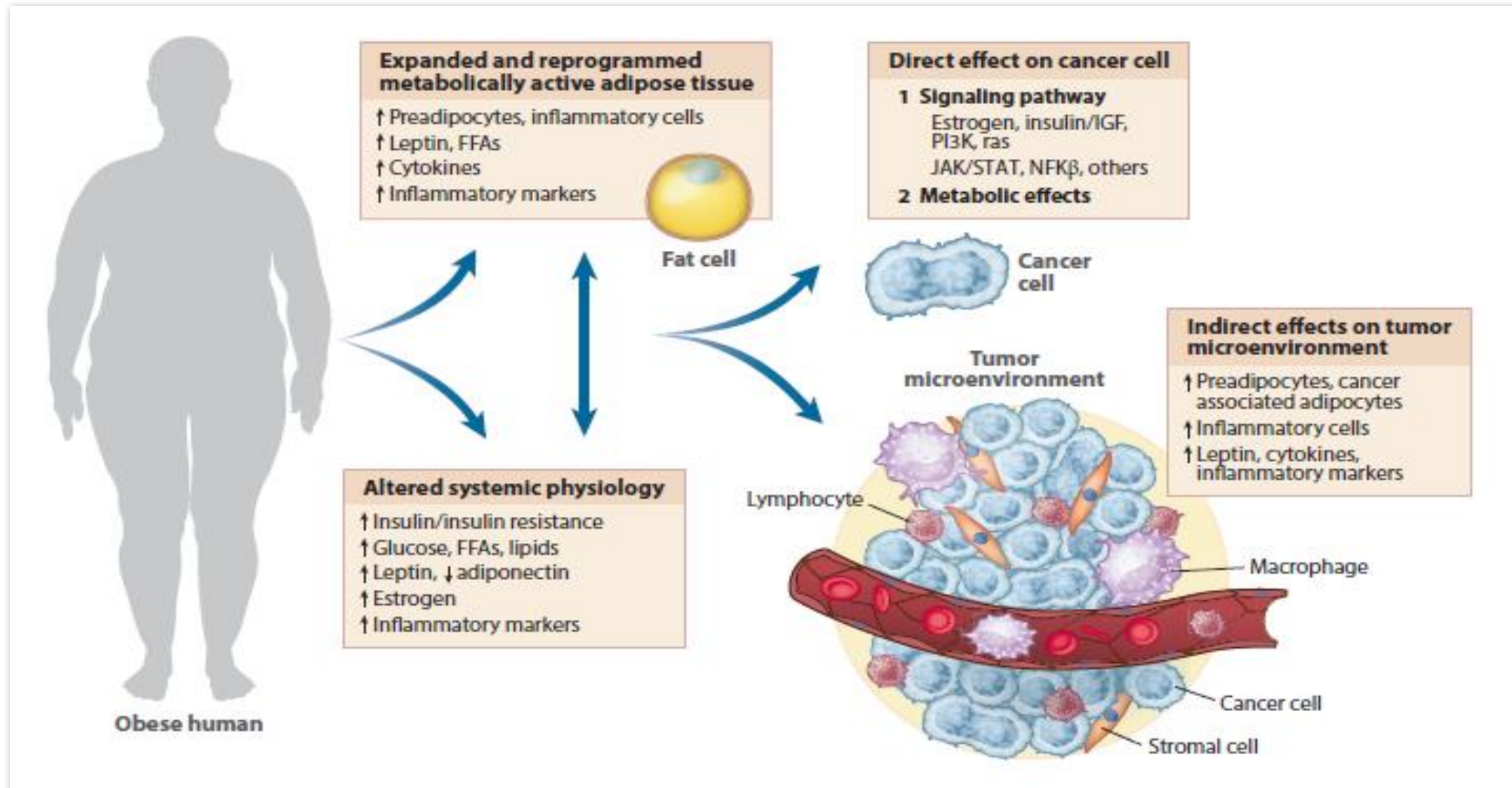
Post-dx PA and cancer mortality



On-going RCT's testing impact of lifestyle change on cancer recurrence/ mortality

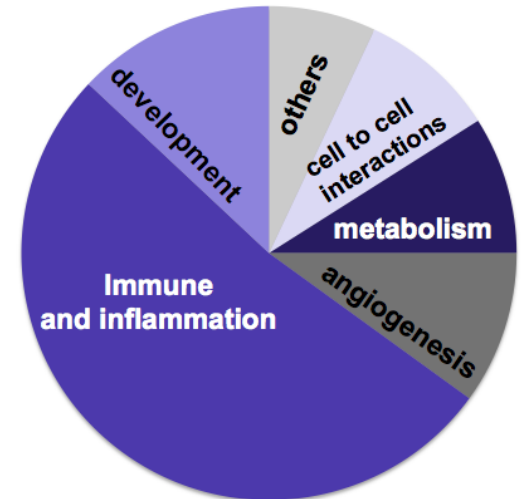
	BWEL	CHALLENGE	DIANA 5	GAP4	LIVES	SUCCESS C
N	3136	962	1241	866	1040	~1400
Disease	Breast	Colon	Breast	Prostate	Ovarian	Breast
Stage	II-III	II-III	I-III	IV	II-IV	II-III
Intervention	2-yr Weight loss	3-yr Ex	4+ yr Med diet + Ex	2-yr Ex	2-yr Diet + Ex	2-yr Weight loss
1° End point	IDFS	DFS	IDFS	OS	PFS	DFS
Correlative	Blood Tissue	Blood	Blood	Blood	Blood	Blood

Mechanistic hypotheses to date have largely focused on sex steroid, metabolic and inflammatory pathways



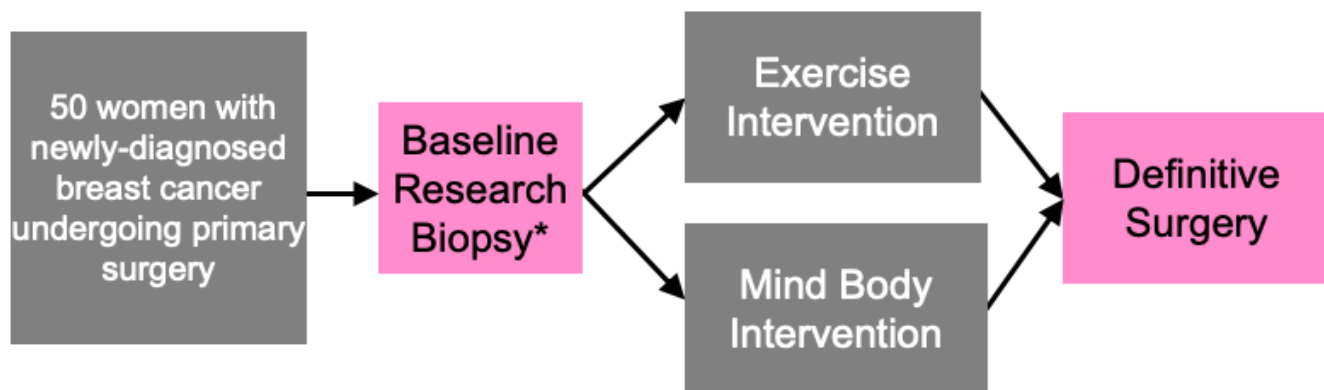
Emerging evidence suggests hosts factors impact tumor immunity

- Animal models show that exercise reduces cancer incidence and suppresses tumor growth
 - Sprague-Dawley rats injected with 1-methyl-1-nitrosurea that were randomized to voluntary wheel running were 32% less likely to develop breast cancer compared to sedentary controls ($P=0.004$).
- Mechanistic studies suggest that exercise leads to upregulation of immune and inflammatory pathways in murine models

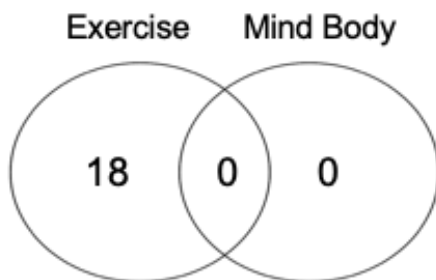


PreHAB

Pre-Operative Health and Body Study

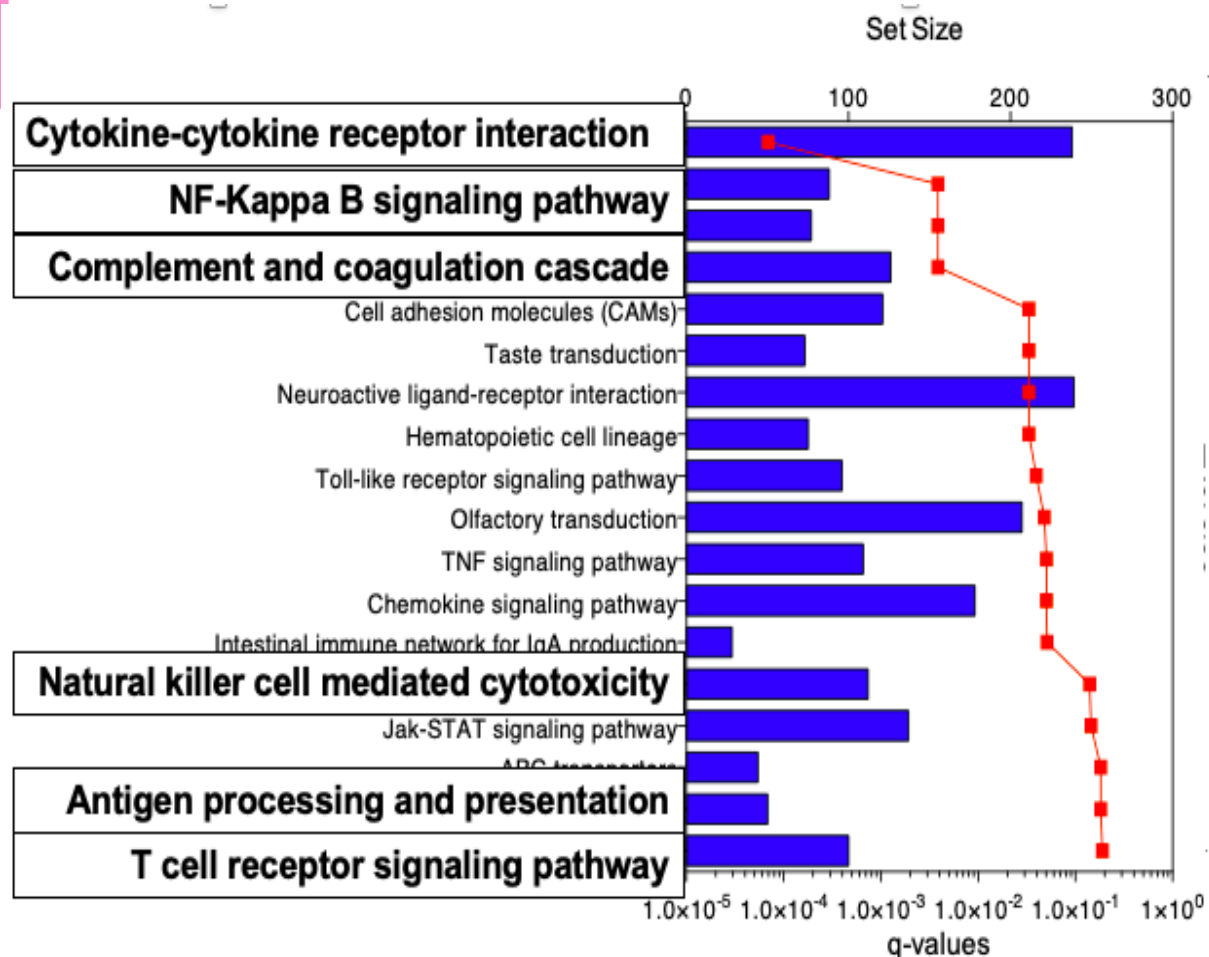


Significantly* Up
Regulated
Pathways



*adjusted p value < 0.1 (q-value)

Pathways Analysis



Hot Topics Symposium

- **Fiber and the Microbiome:** Jennifer McQuade, MD, MS, MA, Lac – *The University of Texas MD Anderson Cancer Center*
- **Obesity:** William J. Murphy, PhD – University of California, Davies
- **Exercise:** Connie J. Rogers, PhD, MPH – The Pennsylvania State University
- **Panel Discussion**