

# Correlations of Obesity, Comorbidity and Treatment: Implications for Survival Analysis and Interpretation

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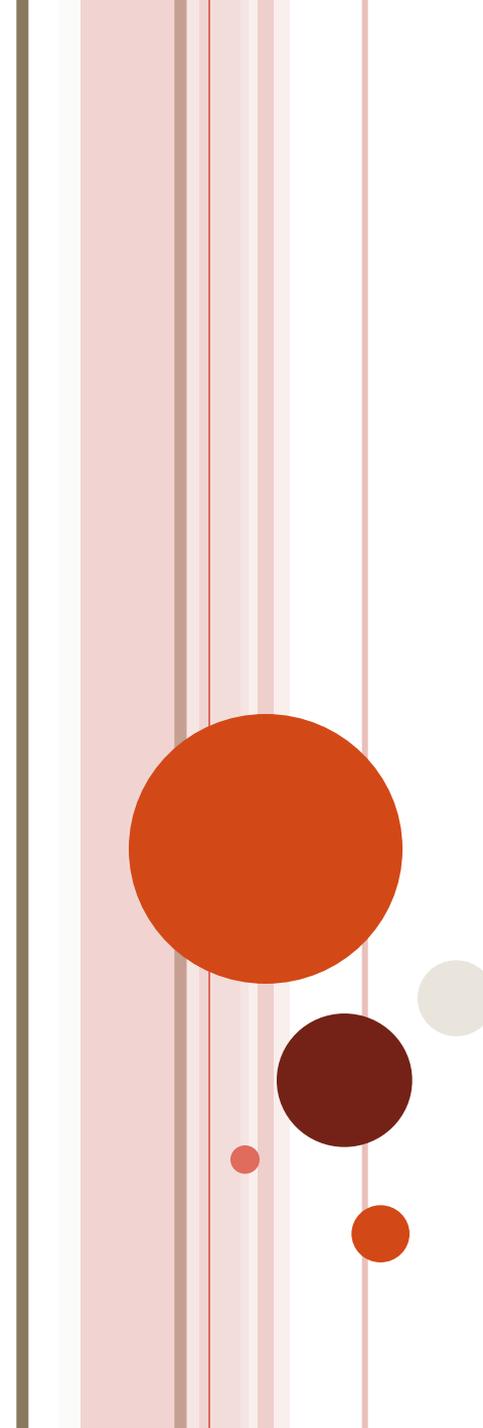
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Institute of Medicine

The Role of Obesity in Cancer Survival and Recurrence

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**Disclosure Information:  
IOM meeting on Role of Obesity in  
Cancer Survival and Recurrence**

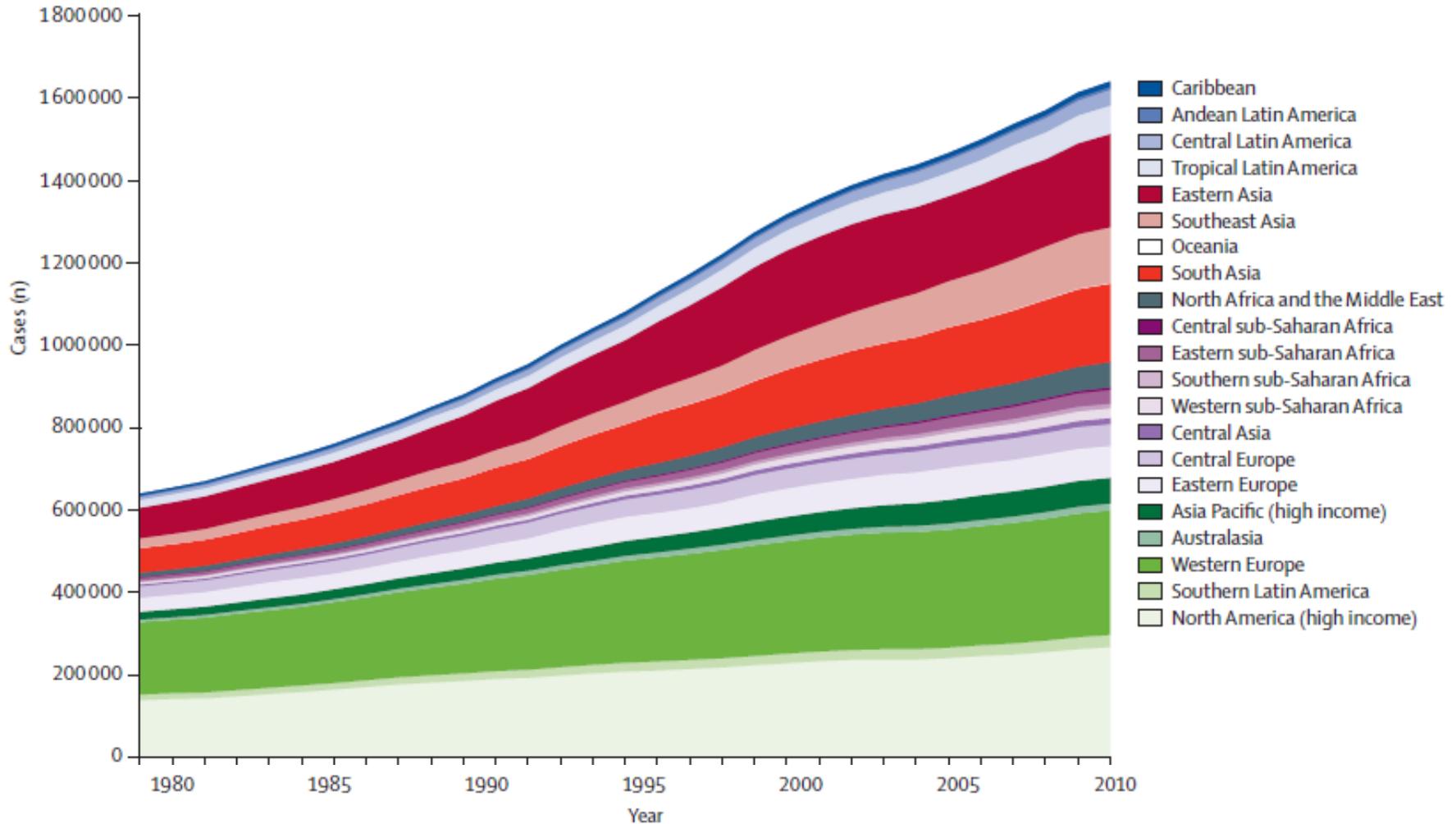
**Rachel Ballard-Barbash**

I have no financial relationships to disclose  
I will not discuss off label use and/or  
investigational use in my presentation

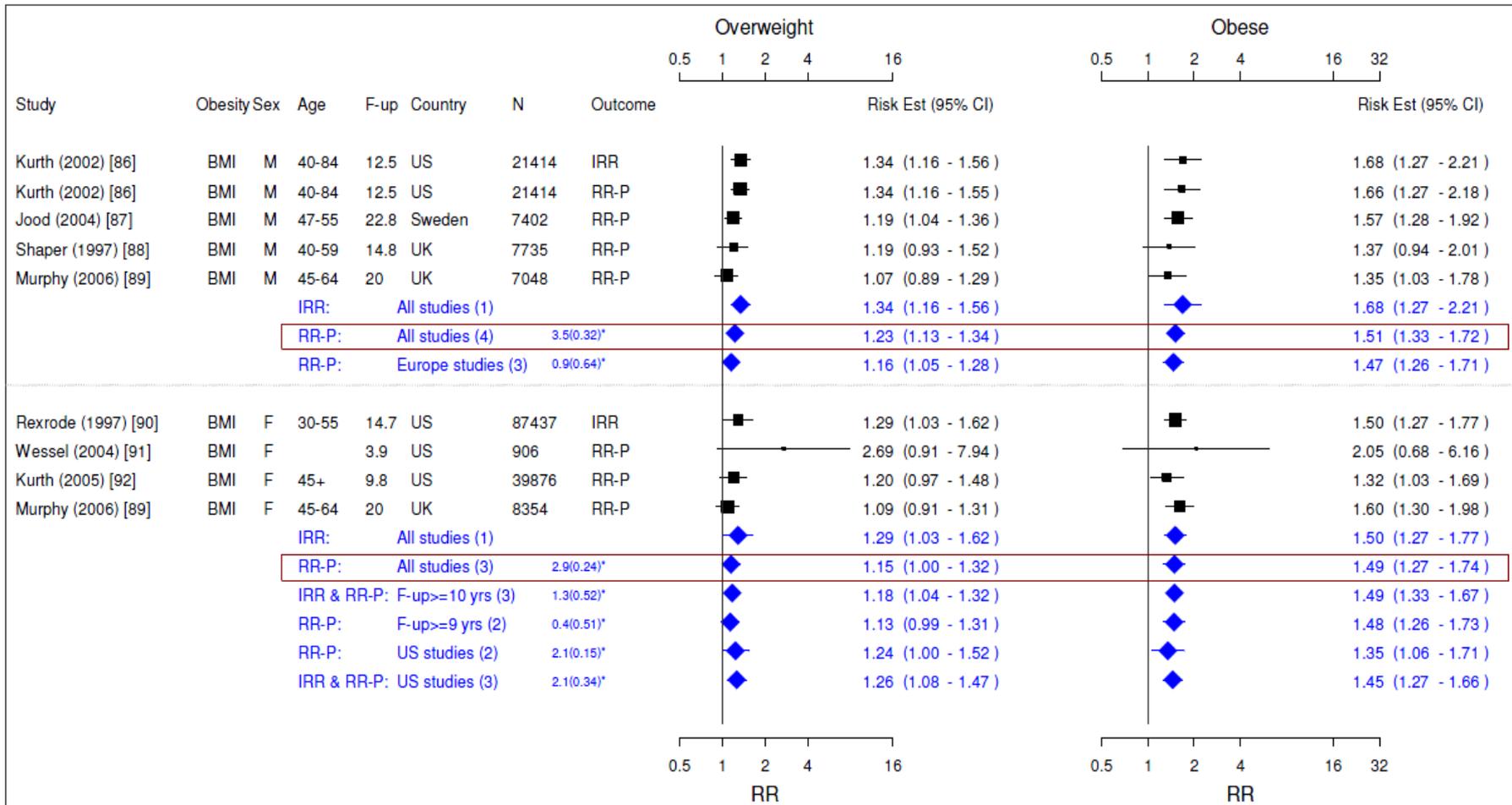
# Simulation Model Estimates of Health and Economic Consequences of Obesity: USA, UK

- § Continued increase in obesity anticipated with aging populations and increased burden of CVD, DM, CA
- § By 2013 – Obesity: 65 M more in US; 11 M more in UK
- § By 2030 – Increased combined health burden in adults
  - Diabetes Mellitus: 6-8.5 Million more cases
  - CVD and stroke: 5.7 – 7.3 Million more cases
  - Cancer: 492,000 – 669,000 more cases
  - 26 – 55 Million QALYs foregone
- § By 2030 – Combined medical costs for treatment
  - Increase by \$48-66 billion/year in the US and 1.9 – 2 billion L/year in the UK

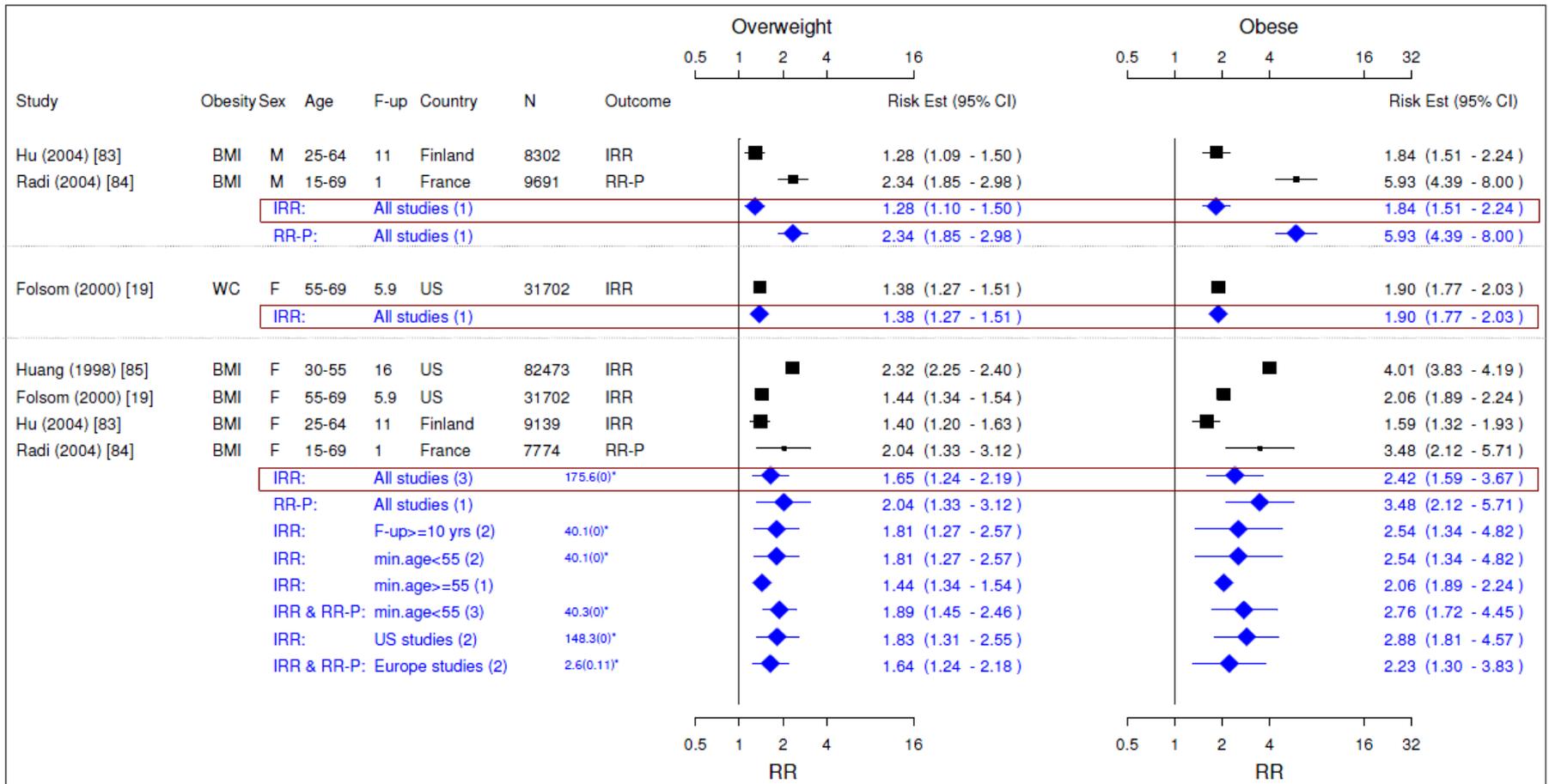
# Breast cancer trends 2008-2010



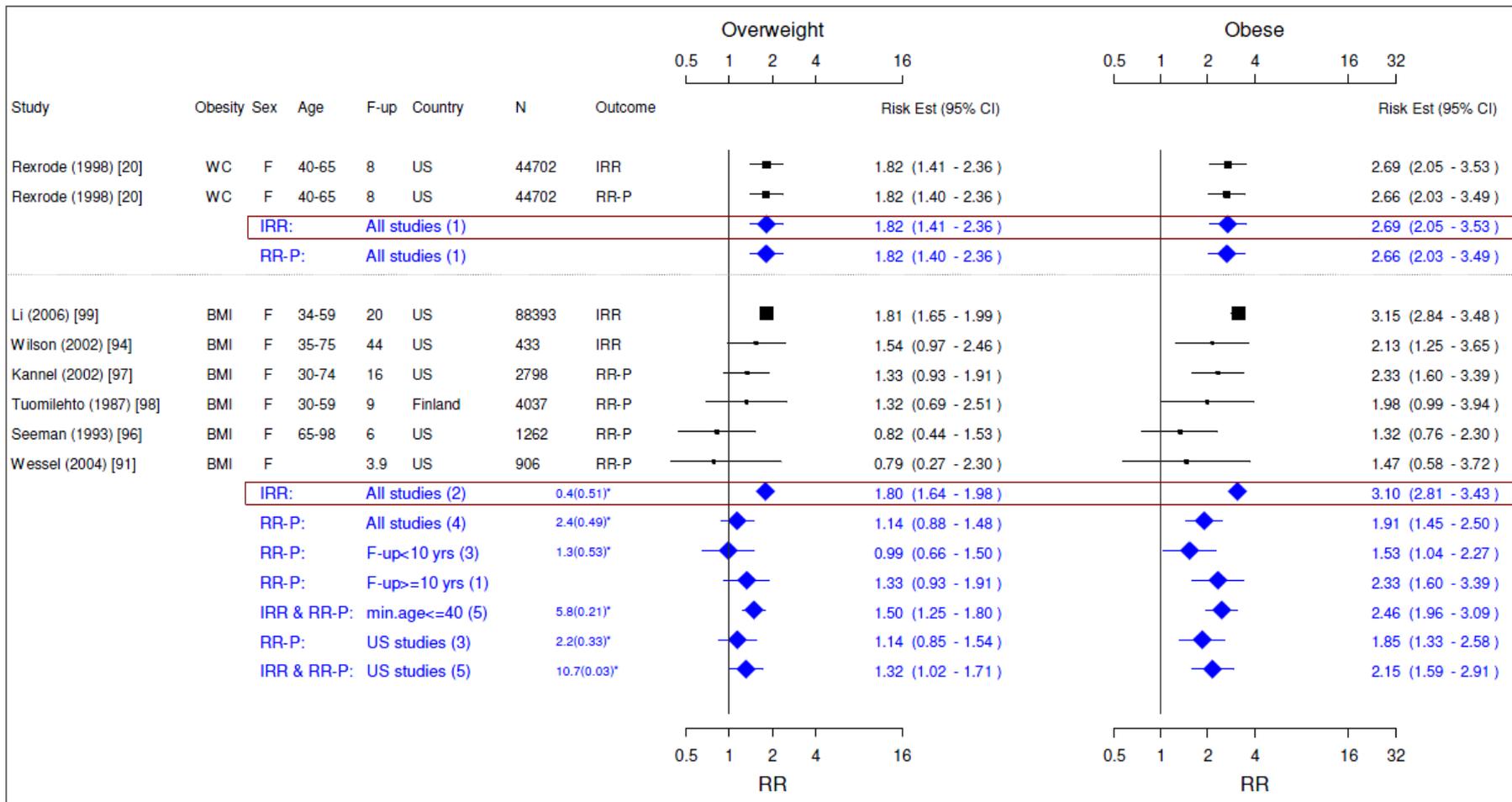
# BMI and Stroke



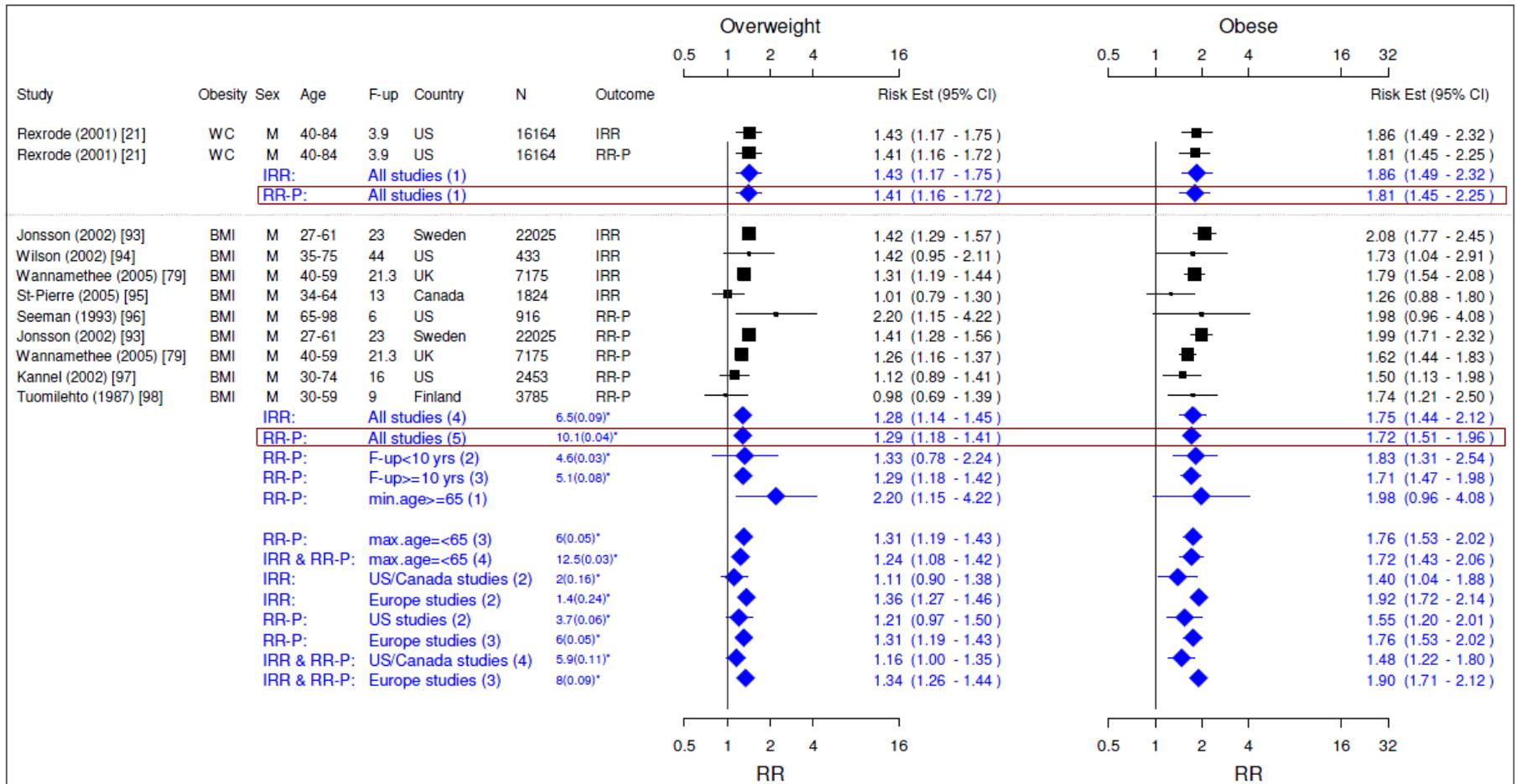
# BMI and Hypertension



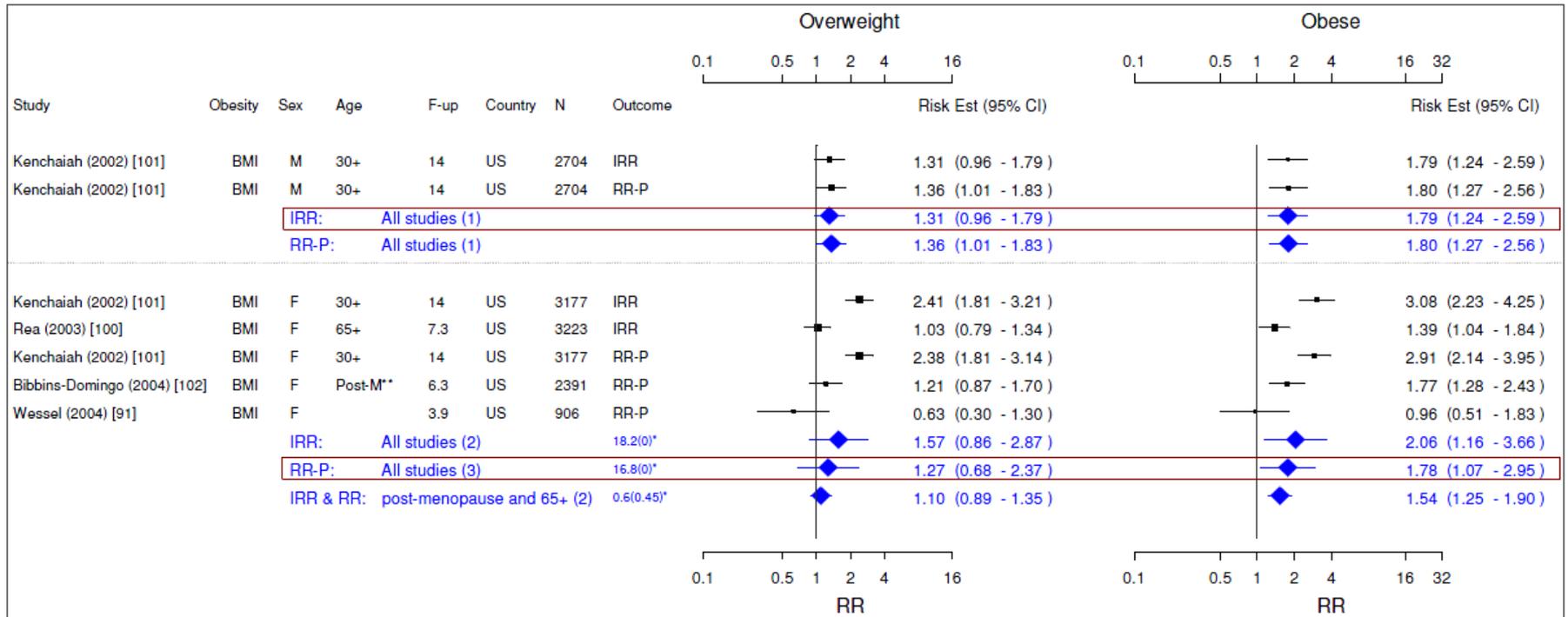
# BMI and Coronary Heart Disease in Women



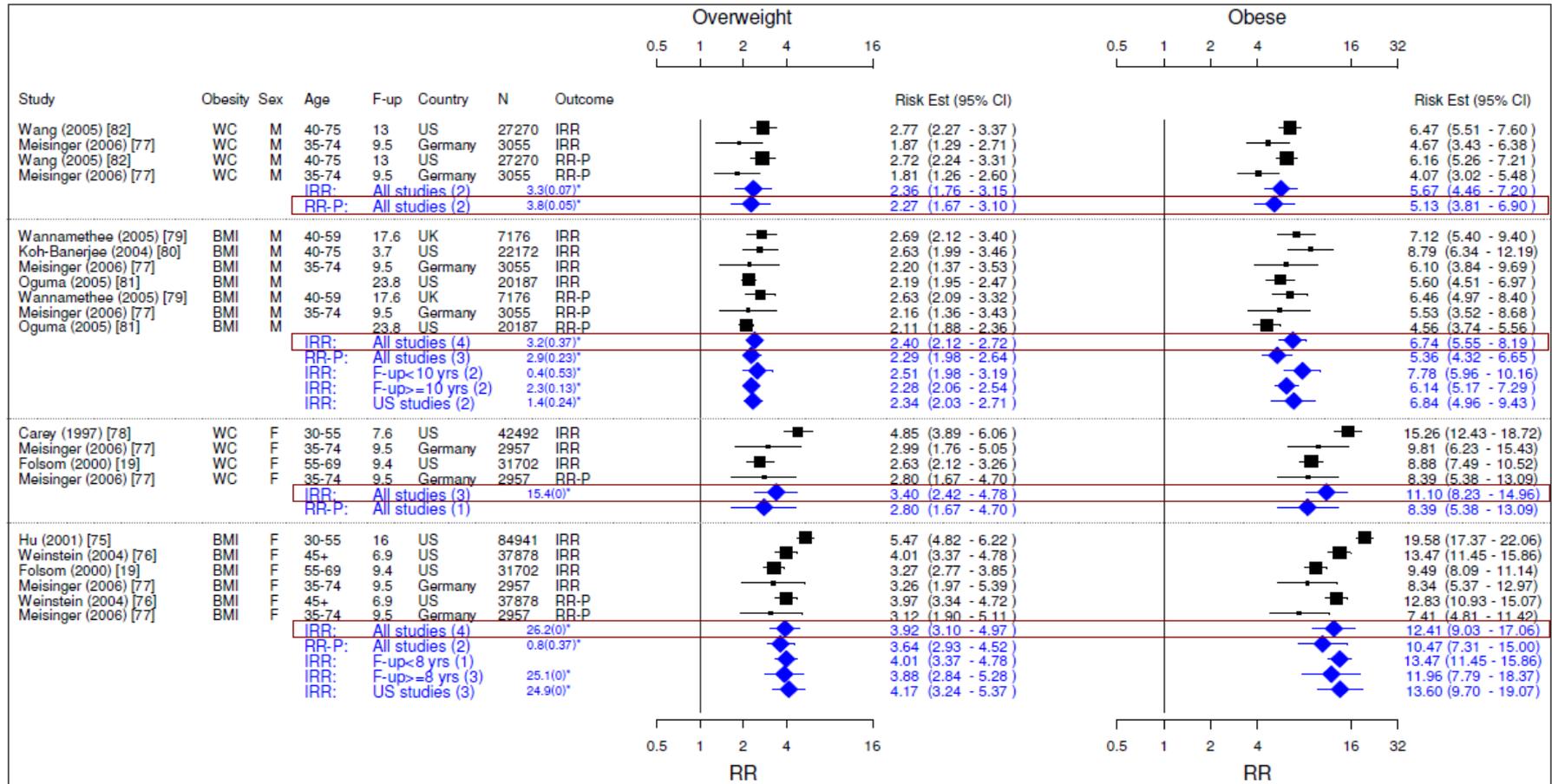
# BMI and Coronary Heart Disease in Men



# BMI and Congestive Heart Failure



# BMI and Type 2 Diabetes Risk



# Diabetes and Cancer Risk by Cancer Site

Cancer site	RR (95% CI)		
	Summary	Case-control Studies	Cohort Studies
Endometrial	2.1 (1.7 – 2.5)	2.2 (1.8 – 2.7)	1.6 (1.2 – 2.1)
Pancreatic	1.8 (1.6 – 1.8)	1.9 (1.5 – 2.4)	1.7 (1.5 – 1.8)
Colorectal	1.3 (1.2– 1.4)	1.3 (1.2– 1.5)	1.2 (1.1– 1.4)
Breast	1.2 (1.1– 1.2)	1.1 (1.0– 1.3)	1.2 (1.1– 1.3)
Prostate	0.8 (0.7 – 0.9)	0.8 (0.7 – 1.1)	0.8 (0.7 – 0.9)

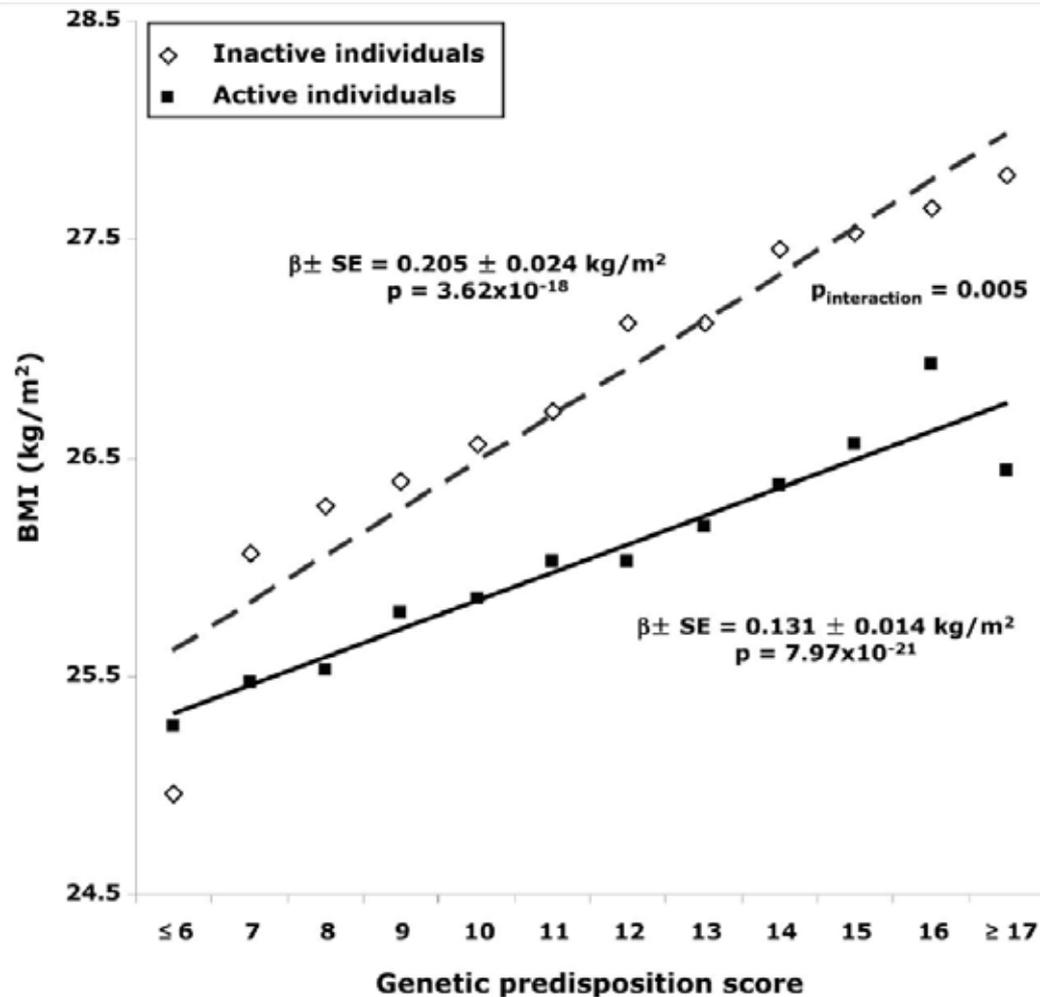
# Prevalence of Common Comorbidities among Patients with the Three Most Common Cancers, Medicare Data

Condition	All claims (%)			
	Breast	Prostate	Colorectal- female	Colorectal- male
Chronic pulmonary disease	7.2	16.2	4.7	4.8
Diabetes	10.2	17.4	6.4	5.4
Congestive heart failure	5.7	9.8	5.1	3.6
Cerebrovascular disease	3.6	7.4	2.4	2.2
Peripheral vascular disease	2.1	4.6	1.5	1.5
Old myocardial infarction	0.8	2.9	0.5	1.0

# Risk of Death Varies by Comorbidity for Patients with the Three Most Common Cancers

Condition	Hazard Ratios (HRs)		
	Breast n=13,247 (841 non-CA deaths)	Prostate n=26,766 (2,122 non-CA deaths)	Colorectal n=16,829 (1,756 non-CA deaths)
Mod./severe renal disease	3.28	1.97	2.63
Congestive heart failure	2.33	2.40	2.16
Dementia	3.29	2.17	1.92
Chronic pulmonary disease	1.60	2.06	1.40
Cerebrovascular disease	2.04	1.30	1.41
Paralysis	1.23	1.48	1.65
Diabetes	1.57	1.27	0.99

# BMI by Genetic Predisposition Score in Inactive versus Active Individuals



# Comorbid Conditions and Guideline Therapy

## § Patterns of Care Insurance Study

- Included 11 cancer sites
- Adjusted for:
  - ⌚ Cancer site
  - ⌚ Stage
  - ⌚ Number of positive nodes
  - ⌚ Type of medical insurance
  - ⌚ Charlson score

§ Guideline-based care was reduced among patients with Charlson Score of 1+

# Increased Number of Comorbid Conditions or Higher Charlson Score Associated with Less Treatment

## § Less guideline consistent care

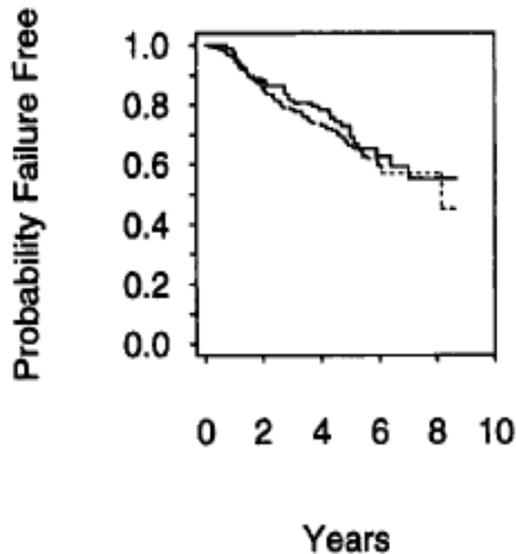
- Colon Stage III and rectal Stage II/IV Patients
- Ovarian Cancer patients

## § Less surgery in pancreatic cancer patients

## § Less likely to have radical nephrectomy in kidney cancer patients

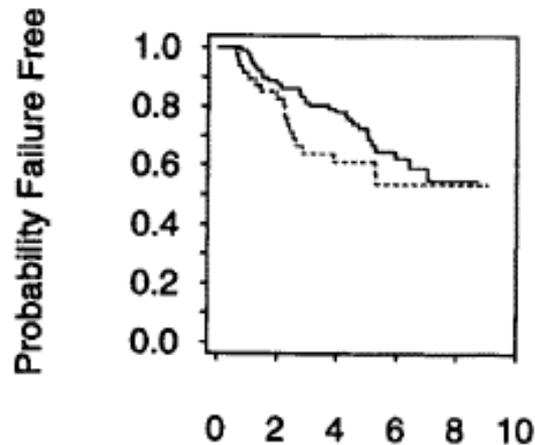
## § Decreased intravesical chemotherapy in bladder cancer patients

# Relationship of Obesity and Dose-intensity with Disease Recurrence in CALGB 8541



Risk of Recurrence in obese vs. non-obese who received full dose treatment:

**RR 1.02 (95% CI 0.83-1.26)**



Risk of recurrence in obese who received full dose treatment vs. <95% dose

**RR 0.73 (0.53-1.00)**

# BMI and Quality of Dosing for Breast Cancer Adjuvant Chemotherapy

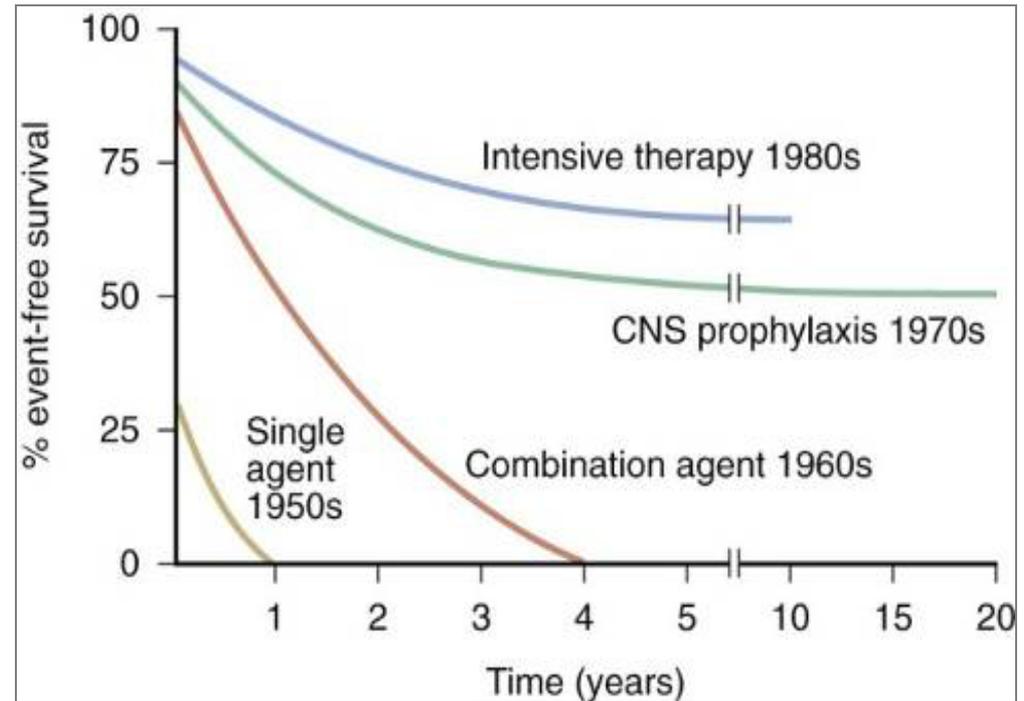
**Table 4.** Multivariate Analysis of Initial Chemotherapy Dose < 85% of Standard (N = 737)

Characteristic	Odds Ratio	95% CI	P	
Age, years	1.01	0.98 to 1.05	.49	
CCI $\geq$ 1	1.16	0.60 to 2.25	.67	
<b>BMI</b>				
Normal	1.00			
Overweight	1.18	0.74 to 1.87	.65	<b>.0004</b>
Obese	<b>2.47</b>	<b>1.36 to 4.51</b>	<b>.003</b>	
Severely obese	<b>4.04</b>	<b>1.46 to 11.19</b>	<b>.007</b>	
Median household income, \$ (in thousands)	1.02	0.85 to 1.22	.81	
Education less than high school	<b>3.07</b>	<b>1.57 to 5.99</b>	<b>.001</b>	
Non-white race	1.30	0.49 to 3.47	.60	
<b>Region</b>				
Northeast	1.00			
Central	1.67	0.43 to 6.44	.46	<b>&lt; .0001</b>
West coast	0.90	0.26 to 3.18	.87	
South	<b>5.58</b>	<b>2.20 to 14.14</b>	<b>.0003</b>	

# Diet-induced Obesity Influences on Acute Lymphoblastic Leukemia and Therapeutic Response

## § Burden of Leukemia:

- Most common childhood cancer
- 10<sup>th</sup> most common adult cancer
- Relapsed leukemia is the 4<sup>th</sup> most common childhood cancer

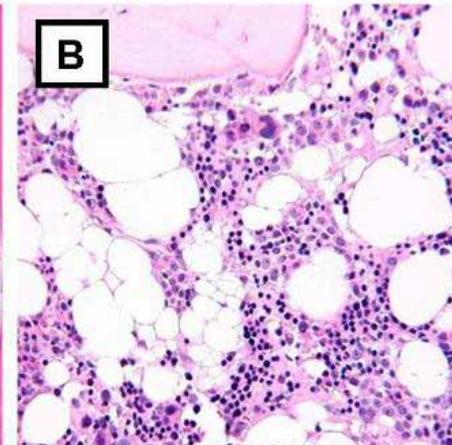
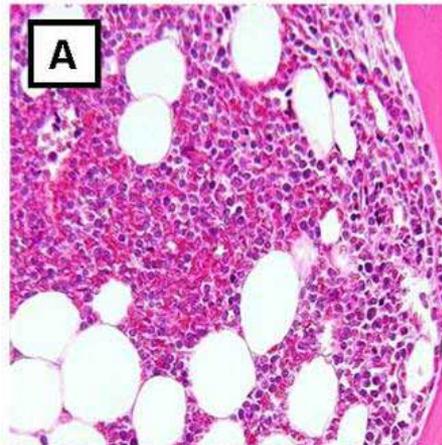


# Adipocytes Occupy a Large Proportion of the Bone Marrow Microenvironment

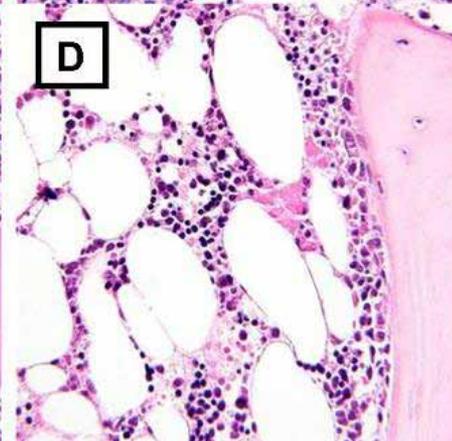
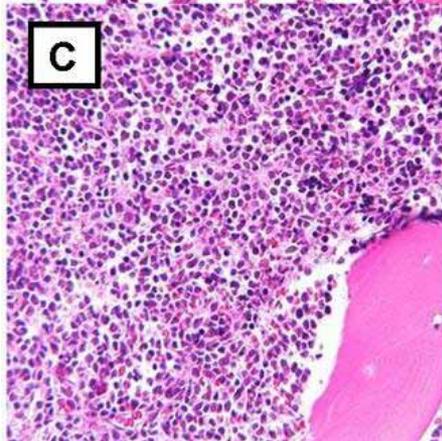
At ALL  
Diagnosis

After Induction  
Chemotherapy

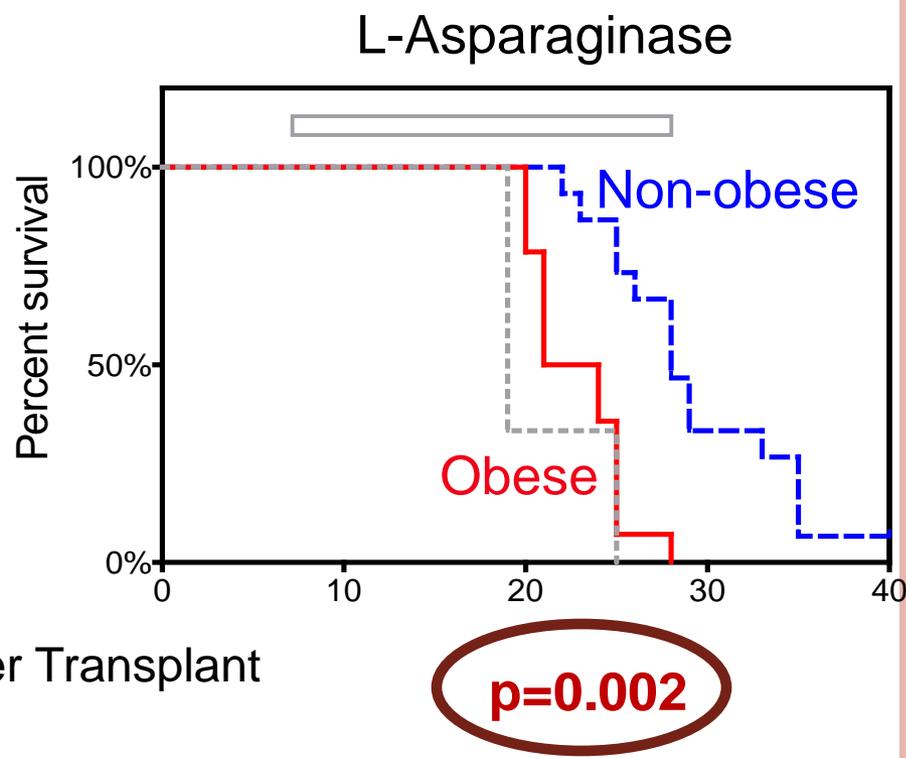
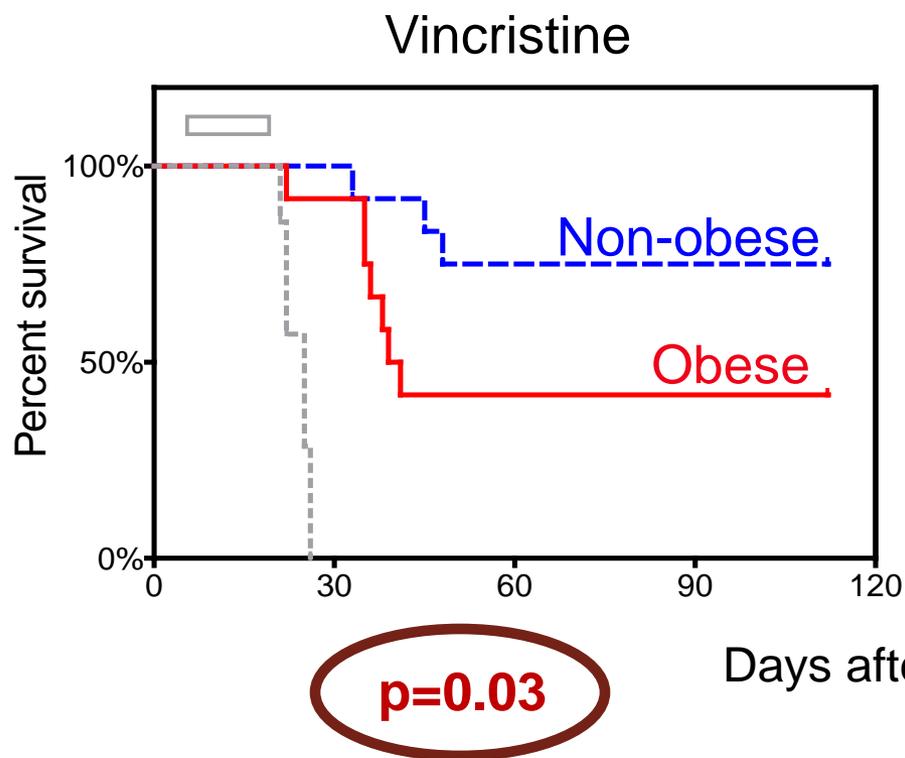
Obese Patient



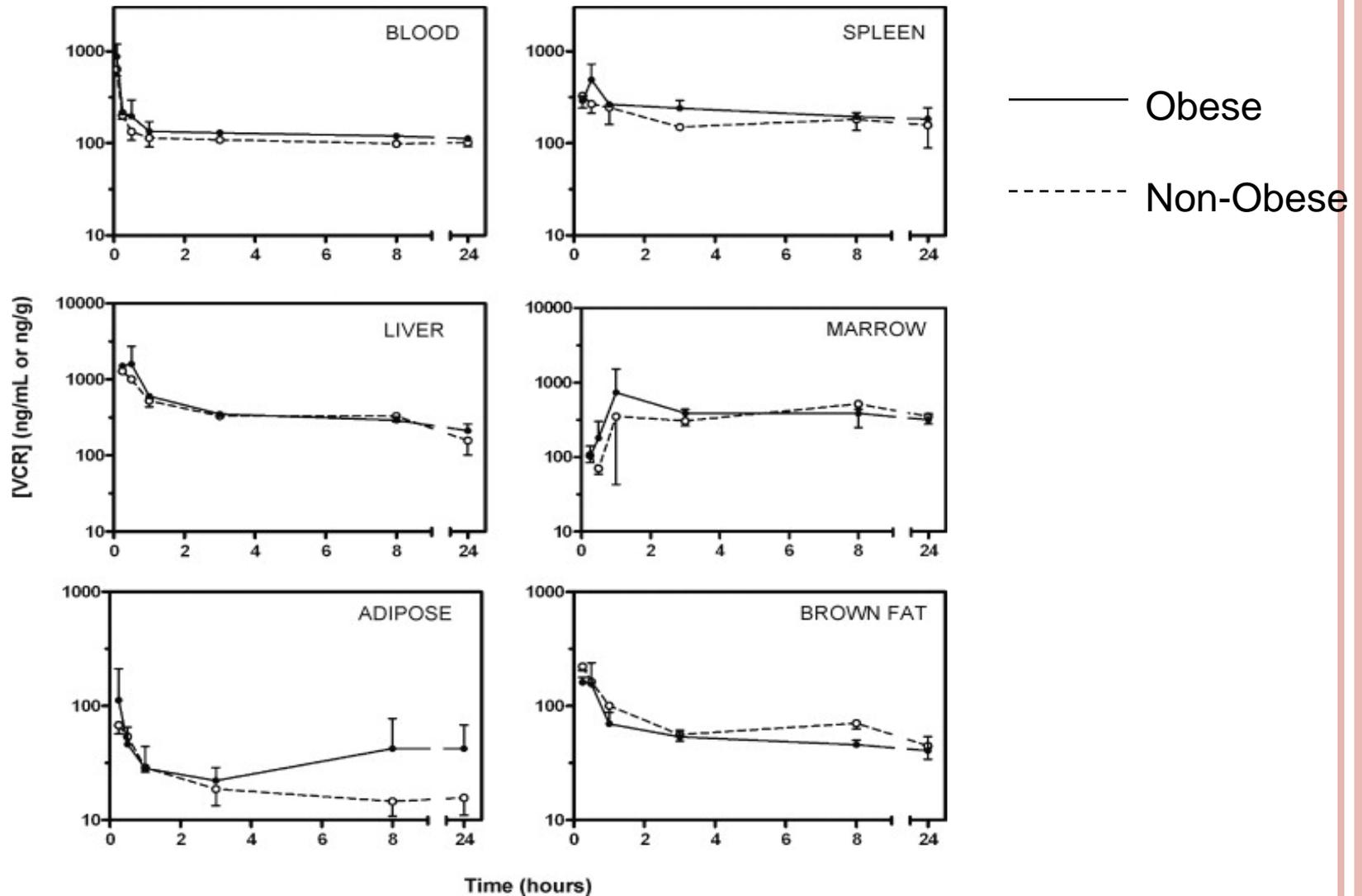
Lean Patient



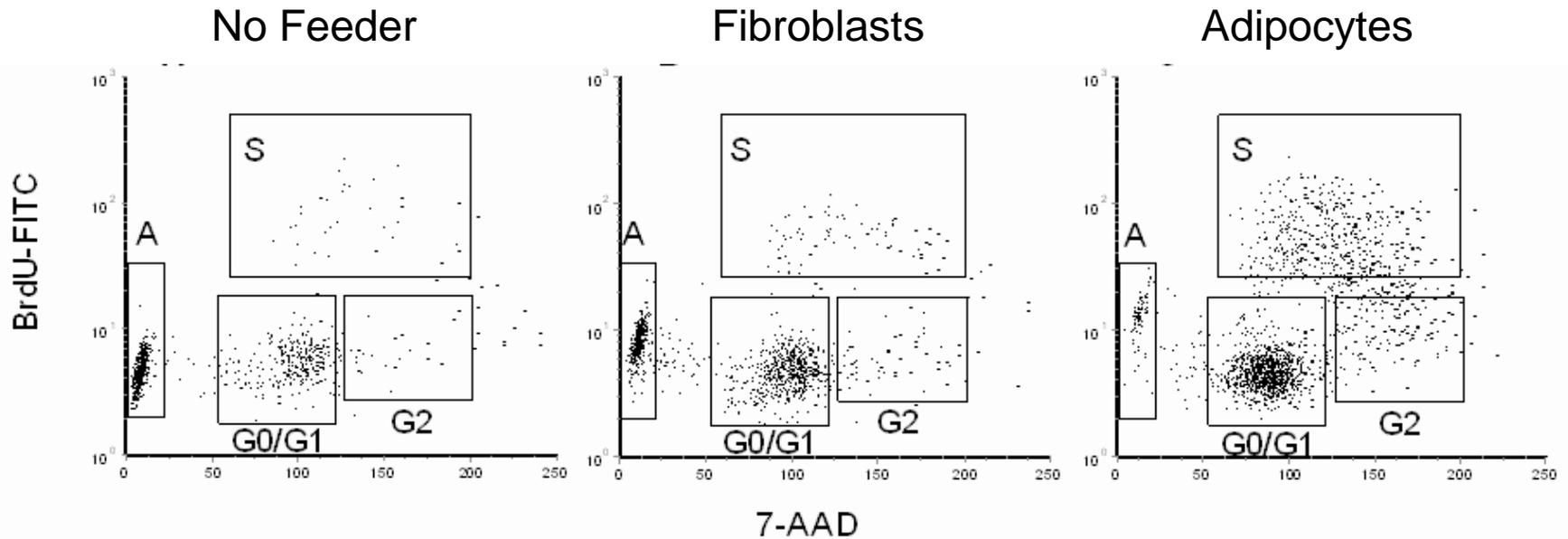
# Obese Mice with ALL Demonstrate Resistance to Chemotherapy Despite Dosage Proportionate to Weight



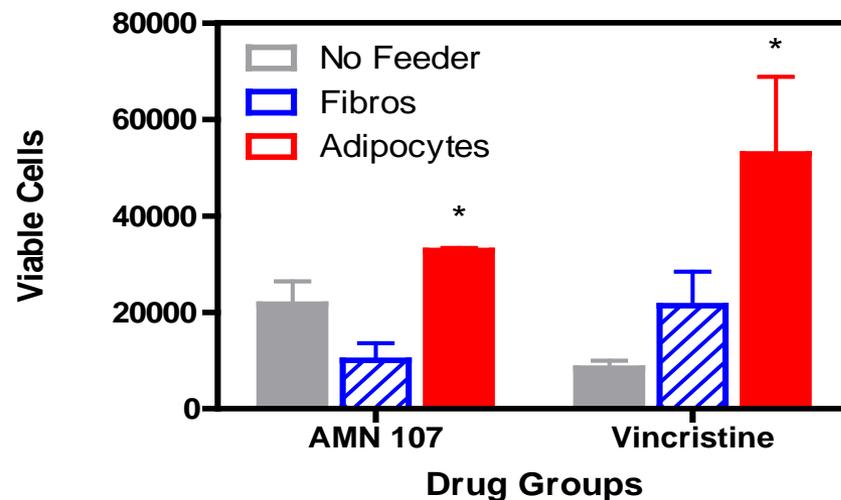
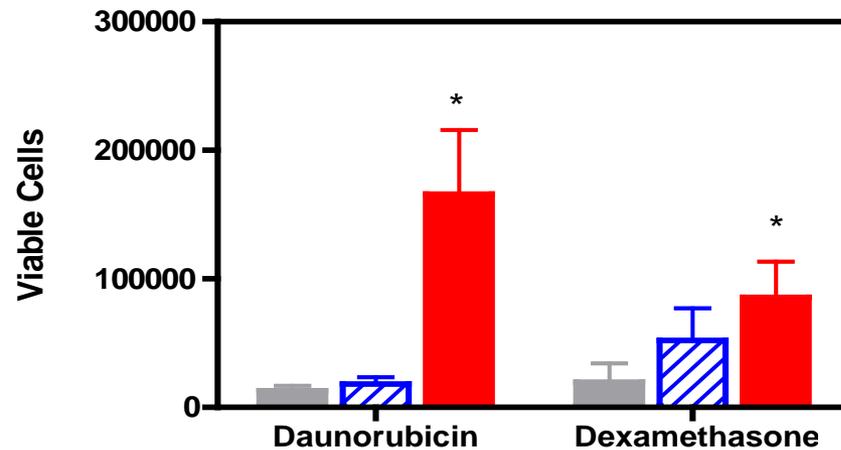
# Vincristine Blood & Tissue Levels Not Altered by Obesity



# Adipocytes Prevent Vincristine-induced Apoptosis



# Adipocytes in ALL Cell Culture Limit Effects of Chemotherapeutic Agents



# Cancer Incidence (I) and Mortality (M) Rates Between Bariatric Surgical and Nonsurgical Obese Groups

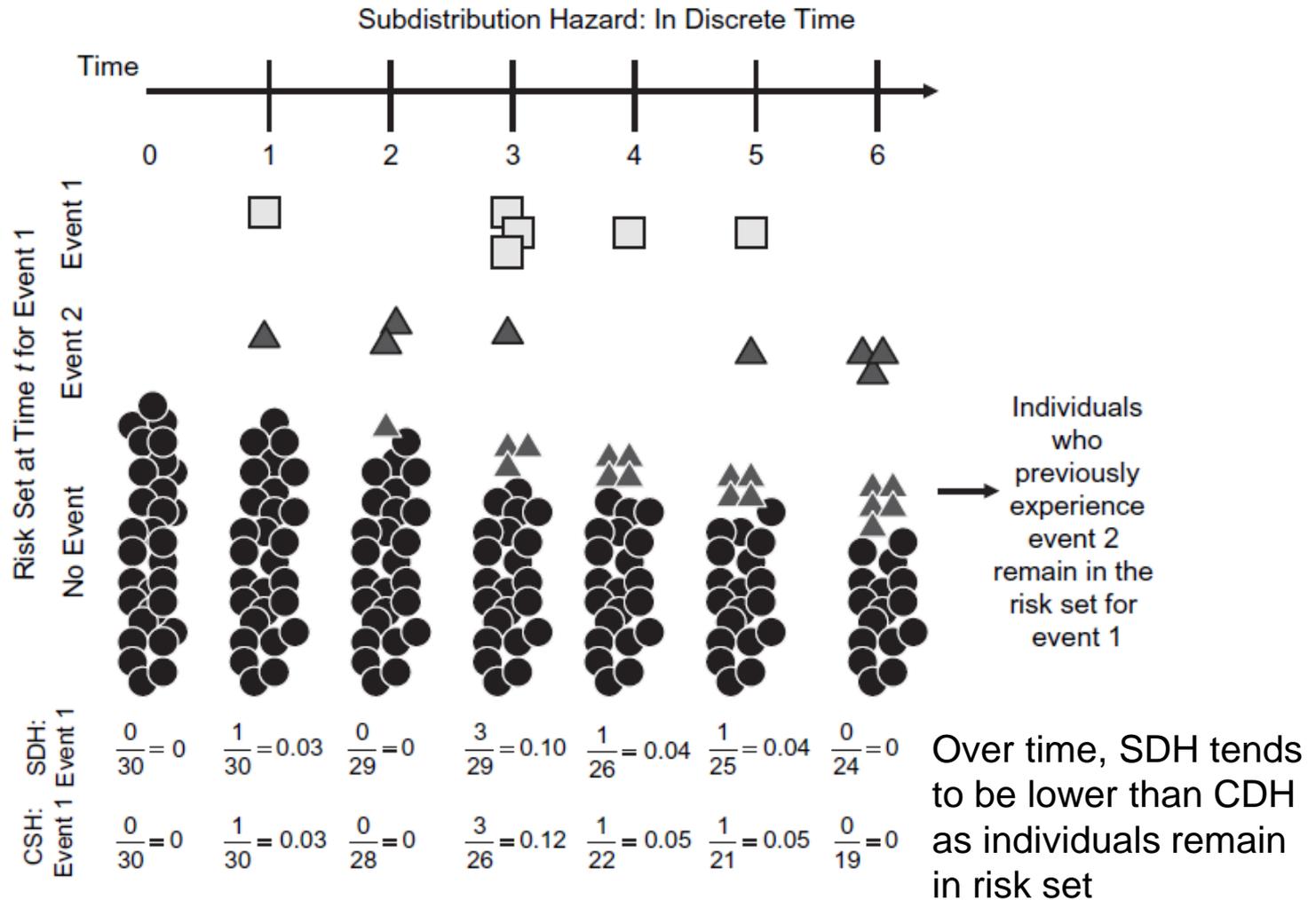
## Men

Author	N	Surgical Obese Cancer Rate	Nonsurgical Obese Cancer Rate	Reduction in Cancer RR
Adams, 2009	942	I = 4.14% M = 1.06%	I = 4.14% M = 1.53%	I = No change M = 30%
McCawley, 2009	Not Studied			
Sjostrom, 2009	590	I = 6.4%	I = 6.6%	I = 3%

## Women

Author	N	Surgical Obese Cancer Rate	Nonsurgical Obese Cancer Rate	Reduction in Cancer RR
Adams, 2009	5654	I = 3.8% M = 0.55%	I = 5.23% M = 1.05%	I = 27.3% (p<0.05) M = 47.6% (p<0.05)
McCawley, 2009	1482	I = 3.6%	I = 5.8%	I = 38% (p<0.05)
Sjostrom, 2009	1447	I = 5.56%	I = 8.98%	I = 38% (p<0.05)

# Competing Risk Regression Analysis



# Conclusions

- § Obesity related comorbid conditions are common among cancer patients and likely to increase in the future
- § Treatment may be less intensive among people who are older, obese, and have comorbid diseases – many of which are increased with obesity, physical inactivity and poor diet
  - May be an issue when analyzing and interpreting outcomes in samples with a very wide age range
  - Possible analytic approaches:
    - ⌘ Competing risk regression
    - ⌘ Age at diagnosis as the time metric
- § Most existing observational studies of BMI and survival do not have detailed treatment data (such as dosage data), few adjust for comorbid disease, or use age as the time metric

Questions?