OVERVIEW
The Role of Obesity in Cancer Risk and Progression

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November 2, 2011
The Role of Obesity in Cancer Survival and Recurrence: A Workshop
Hosted by the **National Cancer Policy Forum**

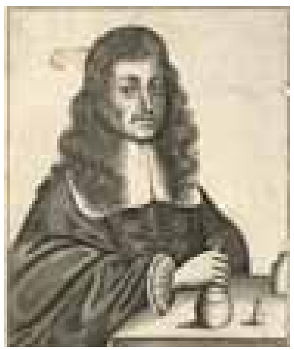
Outline

- **A little history**
- **Anthropometrics and definitions**
- **Trends in obesity and causes**
- **Obesity and general health/mortality**
- **Obesity and cancer risk**
  - Breast and endometrial
  - Prostate
  - Colorectal
- **Summary**

A Little History

Hippocrates of Kos (460 BC- 370 BC)
Father of Medicine
http://www.platos-academy.com/archives/hippocrates.html

Among the first to recognize the dangers of obesity



Venner, Tobias (1577–1660),
Physician and medical writer
http://www.europeana.eu/portal/record/oo401/1007E048

Recognized as the first to use the term obesity

Robert Thomas (1753-1835)
In 1811, wrote: "…*in women of a full plethoric habit, such persons should be careful to confine themselves to a more spare diet than usual; they should likewise take regular exercise,. . . Should any scirrhous or cancerous affection of the uterus take place…all that can be done in such a case is to have recourse to palliatives, such as opium, hyoscyamus…*"

Anthropometric Measures

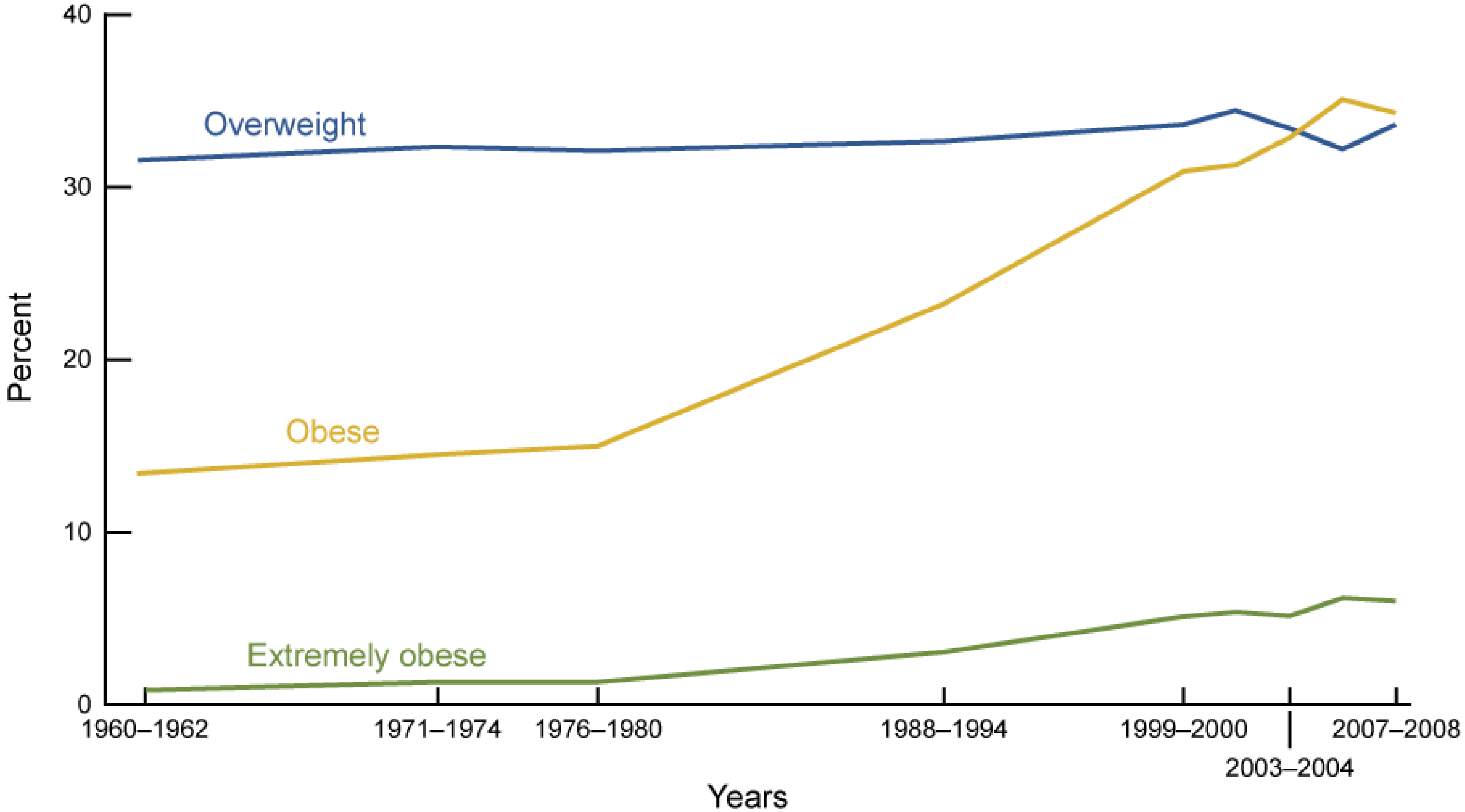
- **Percent body fat**
- **Waist and hip circumference**
- **Weight and height**
- **Body Mass Index**
  - (BMI): weight (kg)/height squared (m^2)
  - A single measure that can be compared across studies and populations
  - Gained favor in the 1970's
  - Corr = 0.6-0.9 with densitometry estimates of body fat

WHO Criteria for Overweight and Obesity

- Underweight = BMI < 18.5 kg/m^2
- Normal weight = BMI 18.5-24.9 kg/m^2
- Overweight = BMI 25.0-29.9 kg/m^2
- Obese = BMI 30+ kg/m^2

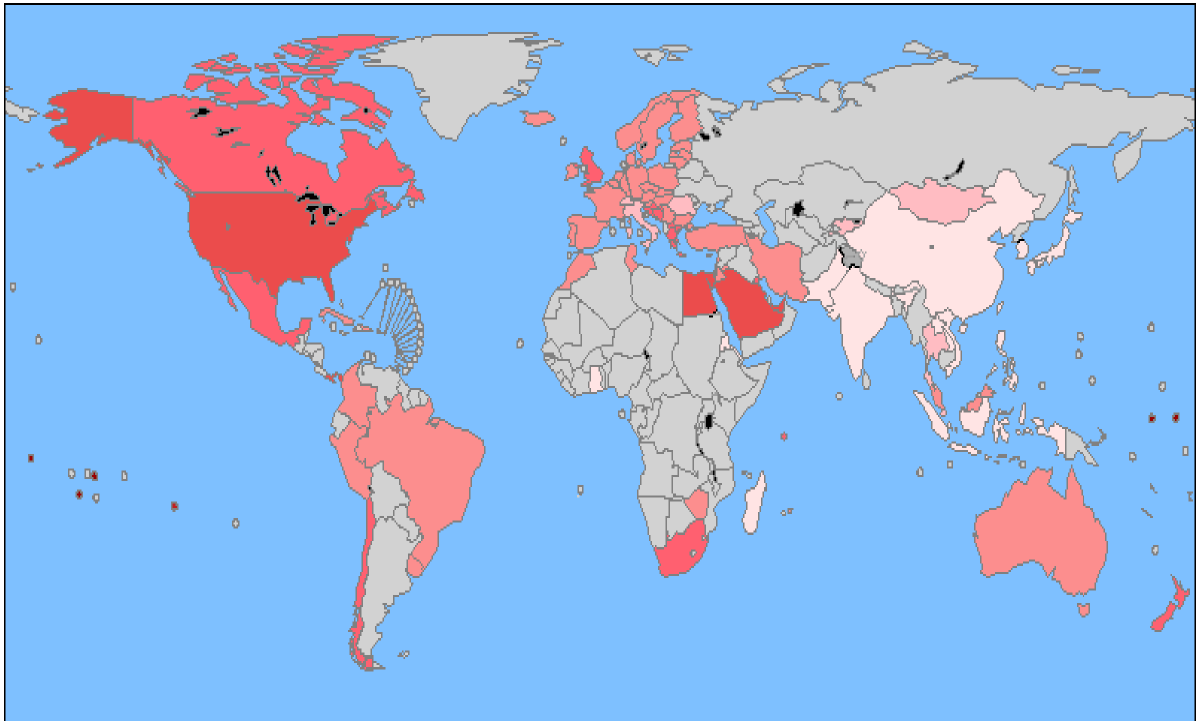
http://www.who.int/mediacentre/factsheets/fs311/en/

U.S. Trends in Overweight* Prevalence (%), Adults 20-74 yrs



NOTE: Age-adjusted by the direct method to the year 2000 U.S. Census Bureau estimates, using the age groups 20–39, 40–59, and 60–74 years. Pregnant females were excluded. Overweight is defined as a body mass index (BMI) of 25 or greater but less than 30; obesity is a BMI greater than or equal to 30; extreme obesity is a BMI greater than or equal to 40.
SOURCE: CDC/NCHS, National Health Examination Survey cycle I (1960–1962); National Health and Nutrition Examination Survey I (1971–1974), II (1976–1980), and III (1988–1994), 1999–2000, 2001–2002, 2003–2004, 2005–2006, and 2007–2008.

Global Variation in Overweight/Obesity



World Health Organization (WHO) 2008 estimates:

- 1.5 billion adults overweight
- ~ 500 million obese

http://www.who.int/mediacentre/factsheets/fs311/en/

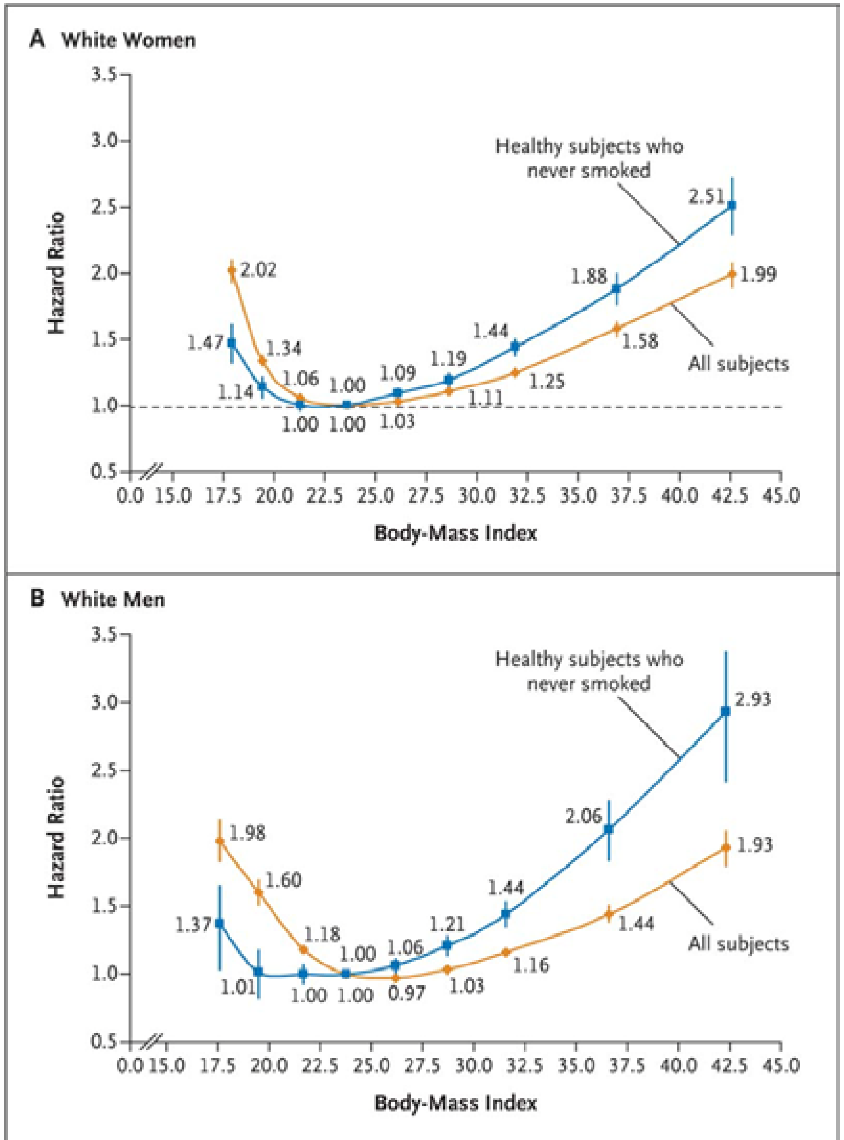
Causes of the Obesity Epidemic

Hippocrites - "*It is very injurious to health to take in more food… when at the same time one uses no exercise to carry off this excess.*"
Hippocrates 400 BC De Priscina Medicina

- Increased intake of energy-dense foods that are high in fat and carbohydrates
- Decrease in physical activity and increasein sedentary nature of many forms of work, changing modes of transportation, and increasing urbanization.

http://www.who.int/mediacentre/factsheets/fs311/en/

Obesity and Mortality



The NEW ENGLAND JOURNAL of MEDICINE

Berrington de Gonzalez et al. 2010;363:2211-9.

Obesity and Cause Specific Mortality

Table 3. Estimated Hazard Ratios for Death from Specific Causes among Healthy Subjects Who Never Smoked, According to Body-Mass Index.*

Cause of Death	Body-Mass Index								
	15.0–18.4	18.5–19.9	20.0–22.4	22.5–24.9	25.0–27.4	27.5–29.9	30.0–34.9	35.0–39.9	40–49.9
Cancer									
No. of deaths	140	400	1933	3099	2948	1755	1851	520	207
Hazard ratio (95% CI)	1.09 (0.92–1.29)	0.96 (0.87–1.07)	0.95 (0.90–1.01)	1.00	1.05 (1.00–1.10)	1.12 (1.06–1.19)	1.34 (1.27–1.42)	1.47 (1.34–1.61)	1.70 (1.48–1.96)
Cardiovascular disease									
No. of deaths	151	301	1222	2075	2334	1557	1697	604	267
Hazard ratio (95% CI)	1.50 (1.27–1.77)	1.15 (1.02–1.30)	0.96 (0.90–1.03)	1.00	1.19 (1.12–1.26)	1.43 (1.34–1.53)	1.80 (1.69–1.93)	2.63 (2.40–2.88)	3.56 (3.12–4.04)
Other causes									
No. of deaths	182	372	1570	2241	2093	1255	1288	503	261
Hazard ratio (95% CI)	1.88 (1.61–2.19)	1.30 (1.17–1.45)	1.12 (1.05–1.19)	1.00	1.00 (0.94–1.06)	1.07 (1.01–1.15)	1.24 (1.16–1.33)	1.91 (1.73–2.11)	2.96 (2.60–3.38)

* Participants were considered healthy if they had no cancer or heart disease at baseline. Hazard ratios were calculated with age as the underlying time scale, stratified by study, and adjusted for sex, alcohol consumption (grams per day), educational level, marital status, and overall physical activity.

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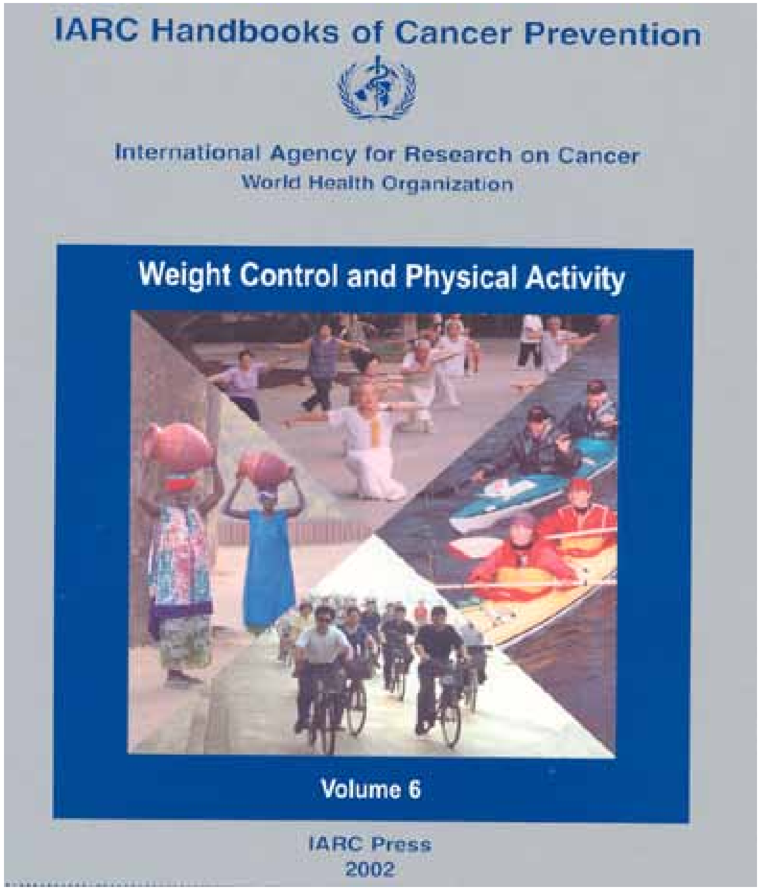
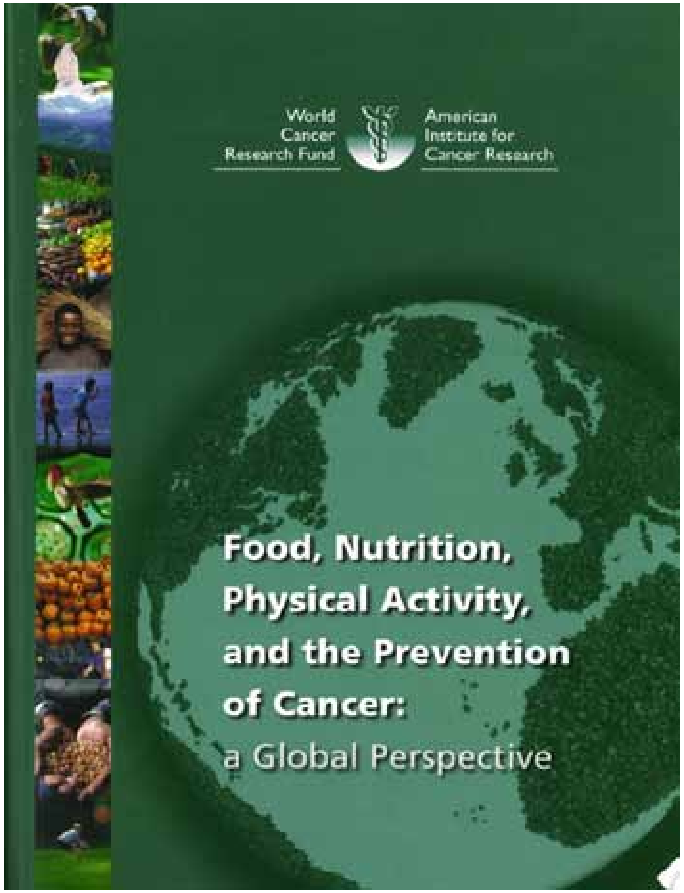
Berrington de Gonzalez et al. 2010;363:2211-9.

Health Consequences of Adult Obesity

- **Type 2 diabetes**
- **Cardiovascular Disease**
  - Coronary Heart disease
  - Stroke
- **Cancer**
- **Fatty liver**
- **Gall stones**
- **Osteoarthritis**
- **Psychosocial**

Obesity and Cancer





Growing List of Cancers Associated with Obesity

	Men	Women
IARC 2002, evidence is "Sufficient"	Colon Esophagus (adeno) Kidney	Endometrium Postmenopausal breast Colon Esophagus (adeno) Kidney
WCRF/AICR 2007, evidence is "Convincing"	Colorectum Kidney Esophagus (adeno) Pancreas	Endometrium Postmenopausal breast Colorectum Kidney Esophagus (adeno) Pancreas
WCRF/AICR 2007, evidence is "Probable or Limited"	Gallbladder Liver	Gallbladder Liver

Accumulating evidence: Non-Hodgkin's lymphoma,
Ovarian (women)
Aggressive prostate (men)

http://www.dietandcancerreport.org/downloads/summary/english.pdf

Obesity and Site Specific Cancer Mortality

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 24, 2003 VOL. 348 NO. 17

Overweight, Obesity, and Mortality from Cancer in a Prospectively Studied Cohort of U.S. Adults

Eugenia E. Calle, Ph.D., Carmen Rodriguez, M.D., M.P.H., Kimberly Walker-Thurmond, B.A., and Michael J. Thun, M.D.

Obesity and Site Specific Cancer Mortality: MEN

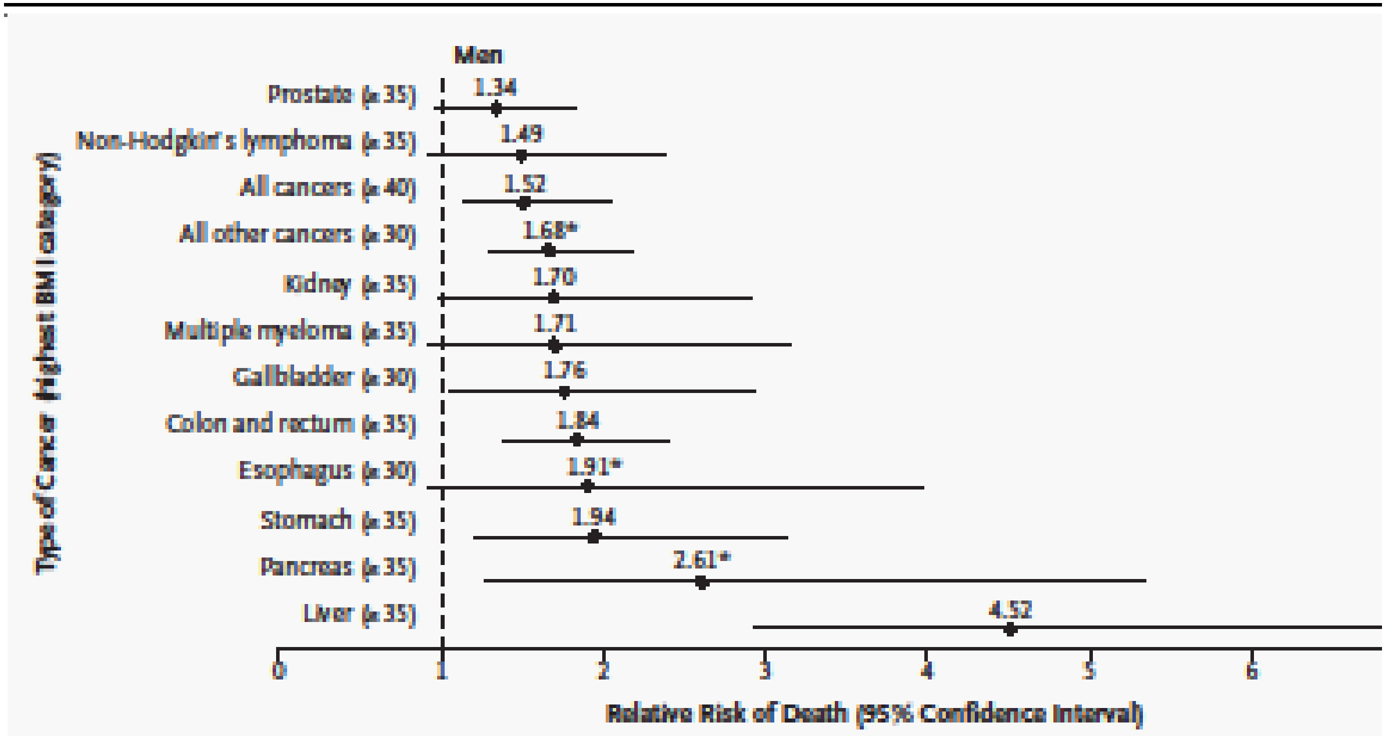


Figure 1. Summary of Mortality from Cancer According to Body-Mass Index for U.S. Men in the Cancer Prevention Study II, 1982 through 1998.

For each relative risk, the comparison was between men in the highest body-mass-index (BMI) category (indicated ir rentheses) and men in the reference category (body-mass index, 18.5 to 24.9). Asterisks indicate relative risks for m who never smoked. Results of the linear test for trend were significant (P≤0.05) for all cancer sites.

Calle, et al; NEJM, 2003

Obesity and Site Specific Cancer Mortality: WOMEN

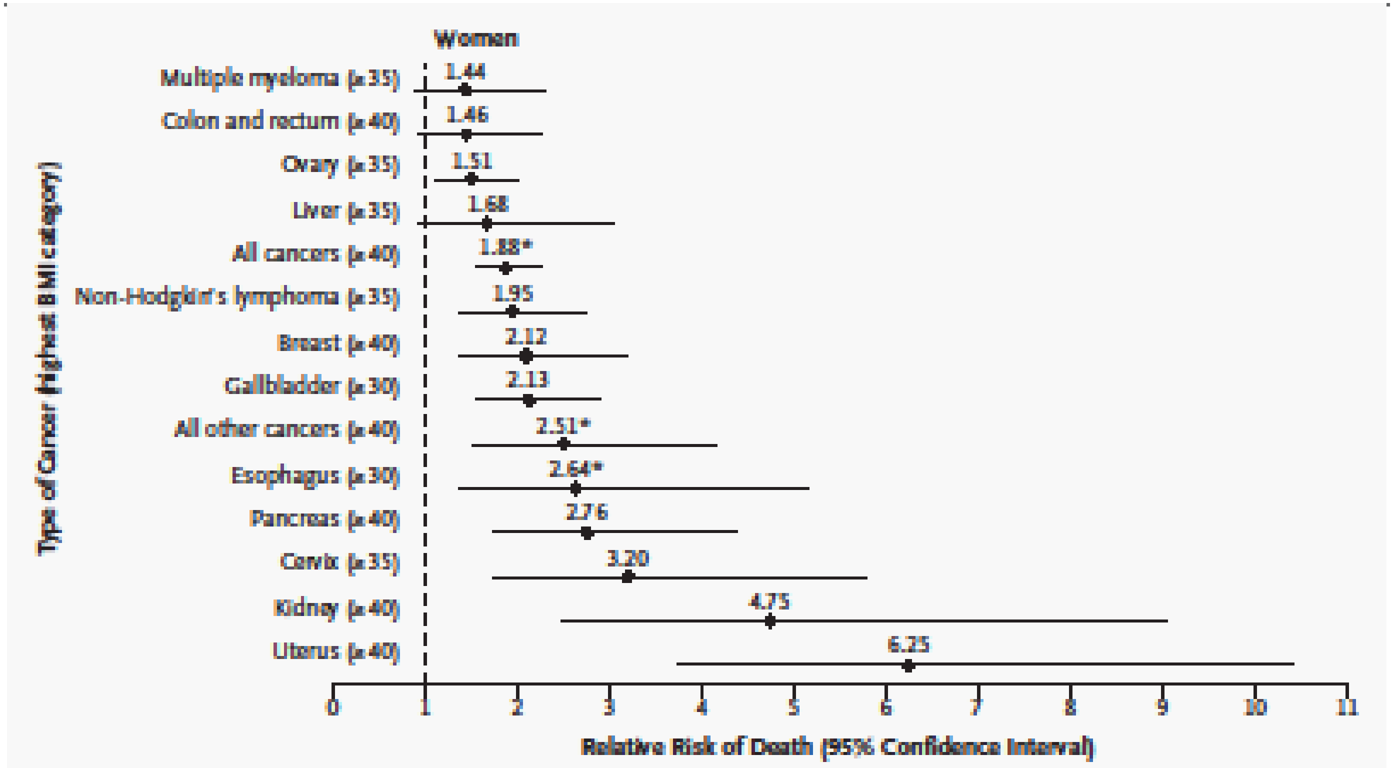


Figure 2. Summary of Mortality from Cancer According to Body-Mass Index for U.S. Women in the Cancer Prevention Study II, 1982 through 1998.

For each relative risk, the comparison was between women in the highest body-mass-index (BMI) category (indicated in parentheses) and women in the reference category (body-mass index, 18.5 to 24.9). Asterisks indicate relative risks for women who never smoked. Results of the linear test for trend were significant ($P \leq 0.05$) for all cancer sites.

Calle, et al; NEJM, 2003

BMI & Breast Cancer Incidence

Pooled analysis: 7 studies; 337,819 women; 4,385 incident invasive

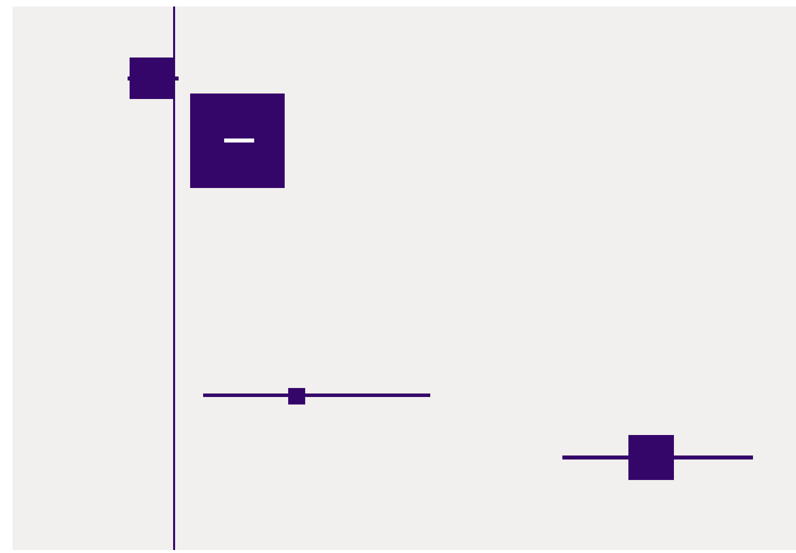
BMI (kg/m^2)	Pre RR	Post RR
< 21	1.0	1.0
21 -< 23	1.24	1.14
24 - < 25	1.03	1.15
25 - < 27	1.08	1.26
27 - <29	0.97	1.43
29 - <31	0.96	1.21
31 - <33	0.55	1.29
≥ 33	0.58	1.27
(p-trend)	(0.007)	(0.001)

Am J Epidemiol 2000;152:514–27.

BMI and Breast & Endometrial Cancer

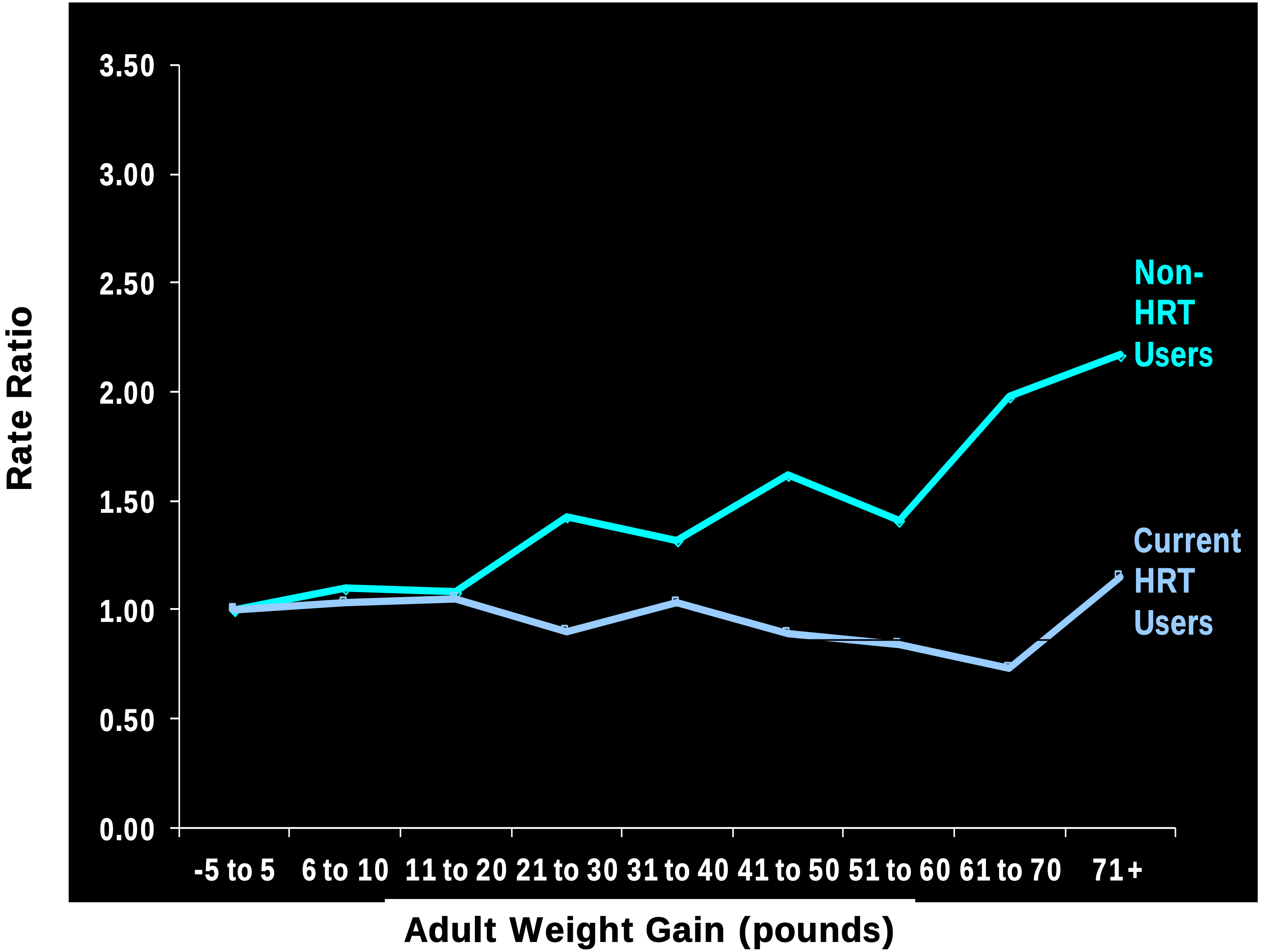
Cancer site or type	No of cases	Relative risk (95% CI) per 10 unit increase in BMI
Breast		
Premenopausal	1179	0.86 (0.73 to 1.00)
Postmenopausal	5629	1.40 (1.31 to 1.49)
χ^2 for heterogeneity=31.6, df=1, P<0.0001		
Endometrium		
Premenopausal	164	1.77 (1.20 to 2.60)
Postmenopausal	1149	3.98 (3.44 to 4.61)
χ^2 for heterogeneity=14.8, df=1, P=0.0001		

Relative risk (95% CI) per 10 unit increase in BMI



UK Million Women Study, Reeves et al. *BMJ* 2007

Weight Gain and Postmenopausal Breast Cancer

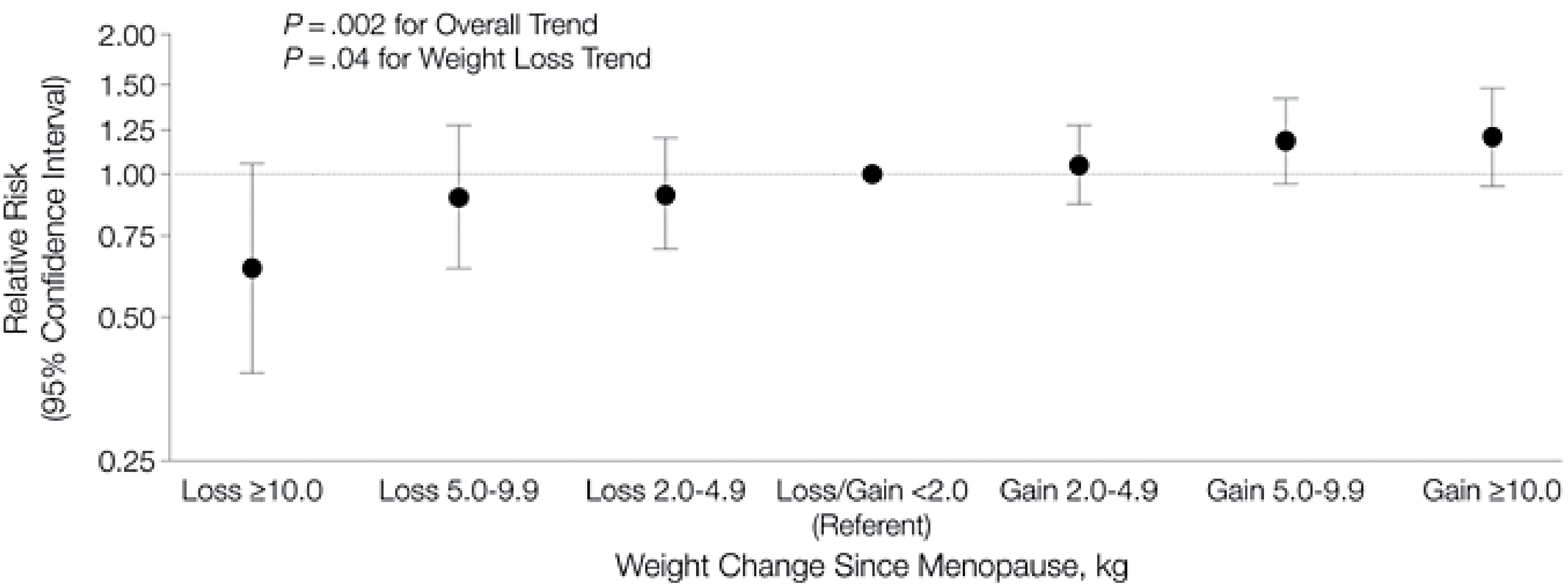


Feigelson, et al. *Cancer Epid Biom Prev* 2004;13:220-4

Weight Loss and Breast Cancer

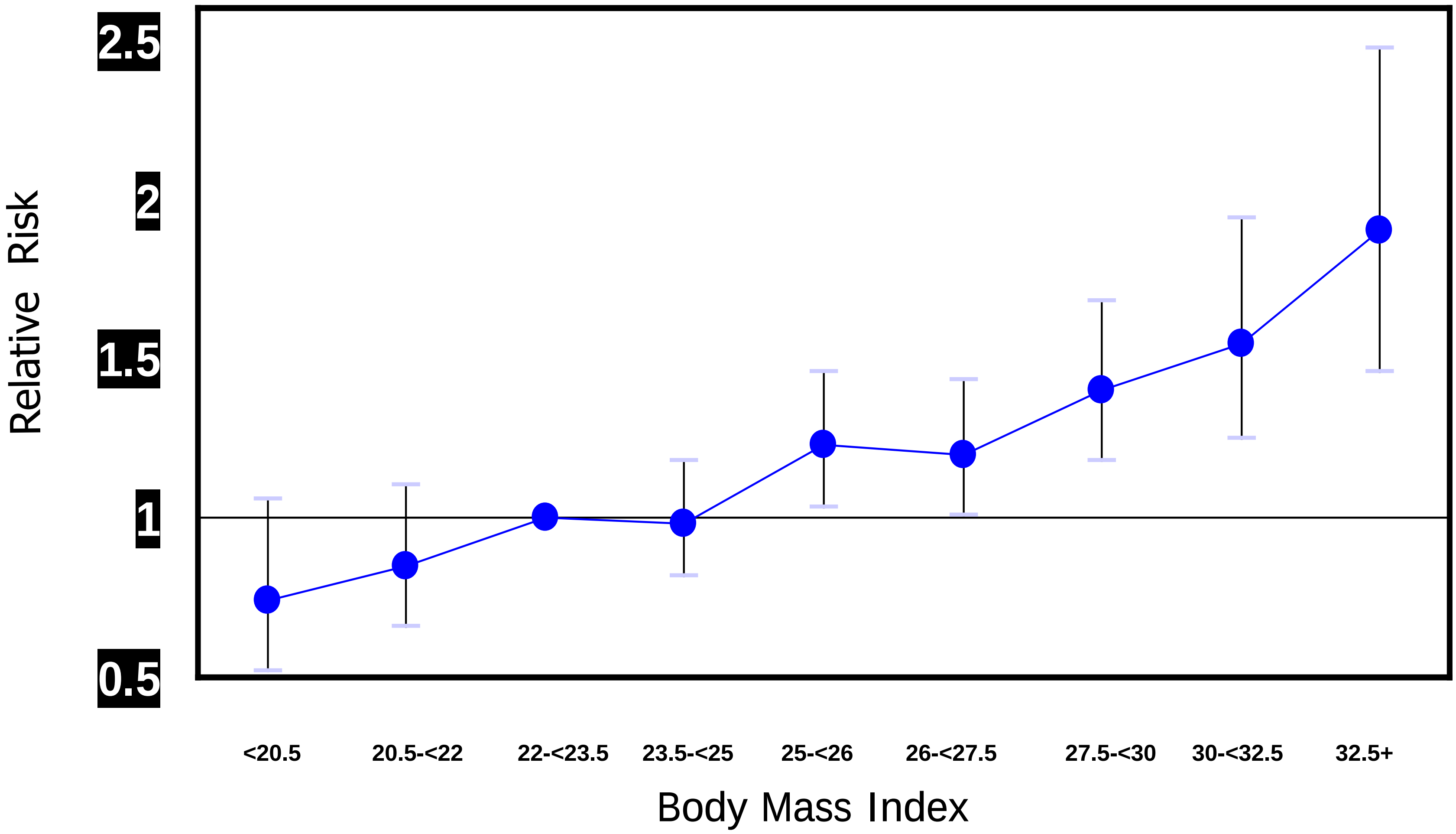
- Bariatric surgery studies suggest inverse association between weight loss & cancer
- In non bariatric surgery studies, two studies suggest that ***sustained*** weight loss must be considered.

Relative Risk of Postmenopausal Breast Cancer Among Women Who Have Never Used Postmenopausal Hormones According to Weight Change Since Menopause in the Nurses' Health Study, 1976.



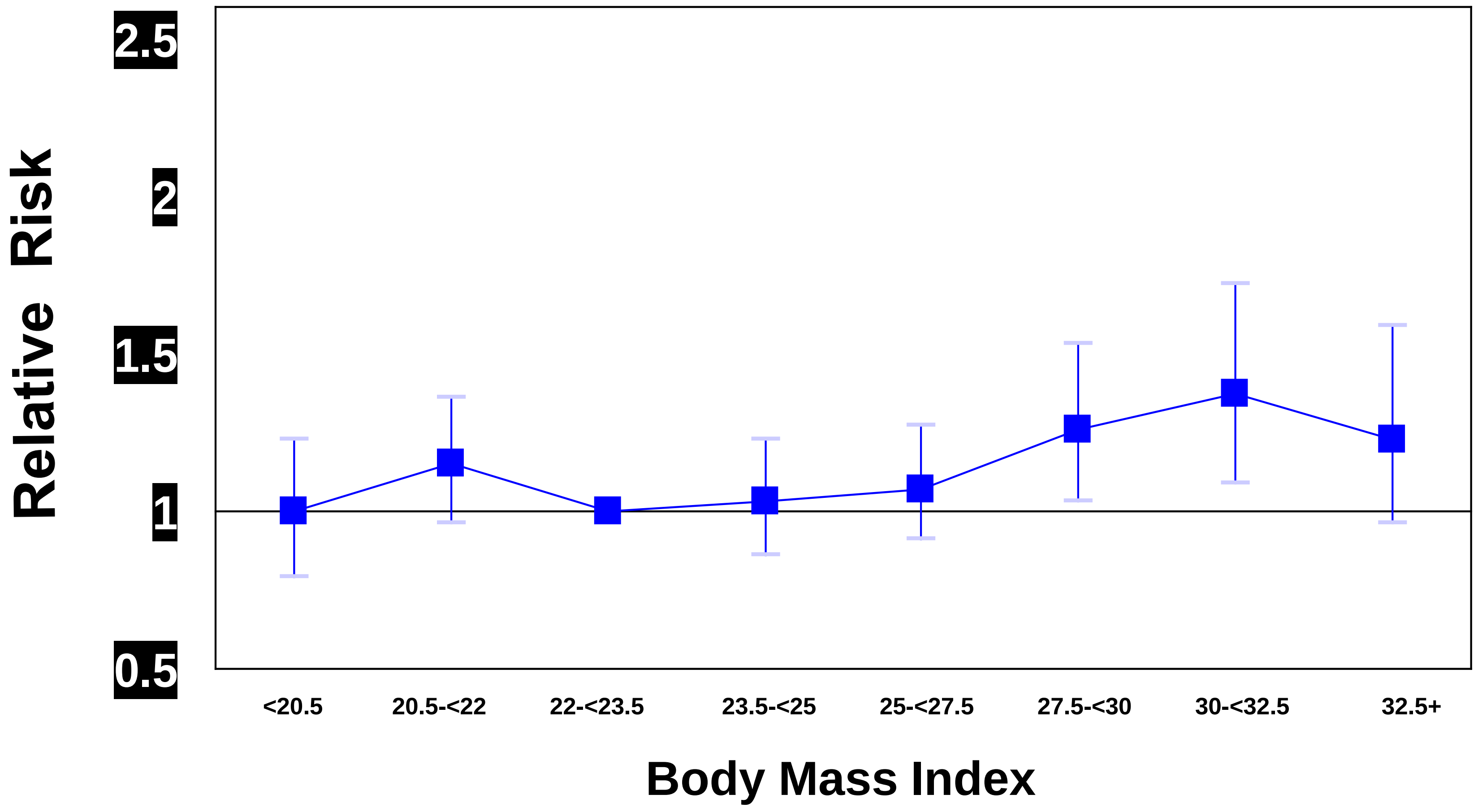
Eliassen, A. H. et al. JAMA 2006;296:193-2

BMI and Colon Cancer Mortality: MEN



Murphy et al. ***Am J Epidemiol*** **2000;152:847-54**

BMI and Colon Cancer Mortality: WOMEN



Murphy et al. ***Am J Epidemiol*** **2000**

BMI and Colon Cancer

Possible reasons for gender differences:

BMI is a better surrogate of central obesity in men than in women

There is an offsetting beneficial effect of obesity (due to estrogen) among women (HRT associated with reduced risk of colon cancer in postmenopausal women)

Obesity & Prostate Cancer MORTALITY:

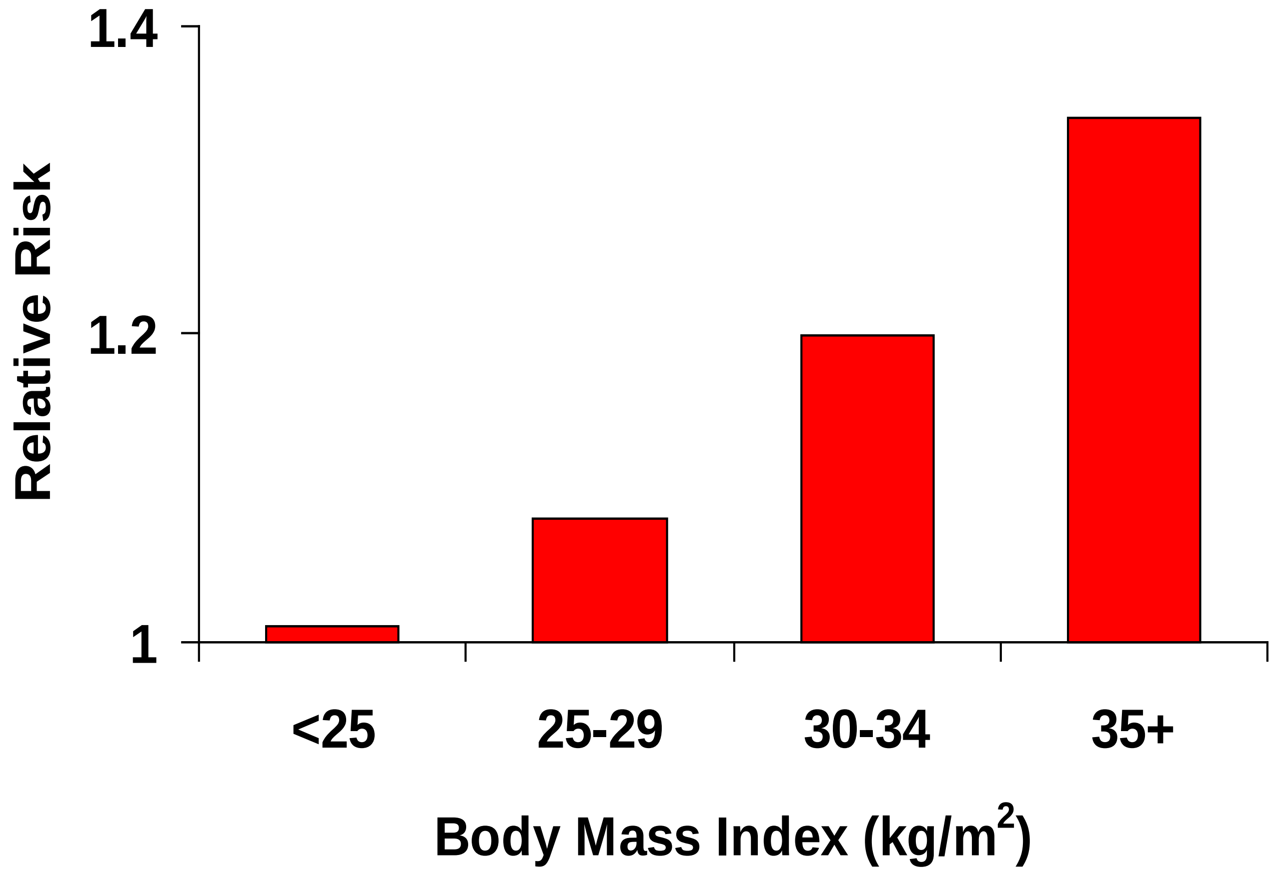
Early Cohort Studies

Reference	No. deaths		RR (95% CI)
Snowdon *et al*., Seventh Day Adventist, US 1984	84	Percent of desirable weight 130–249 vs. 90–109	2.4 (1.3–4.5)
Andersson, *et al*., Sweden, 1997	708	BMI (kg/m^2) >26.2 vs. < 22.2	1.40 (1.09–1.81)

BMI & Prostate Cancer Incidence: Cohort Studies

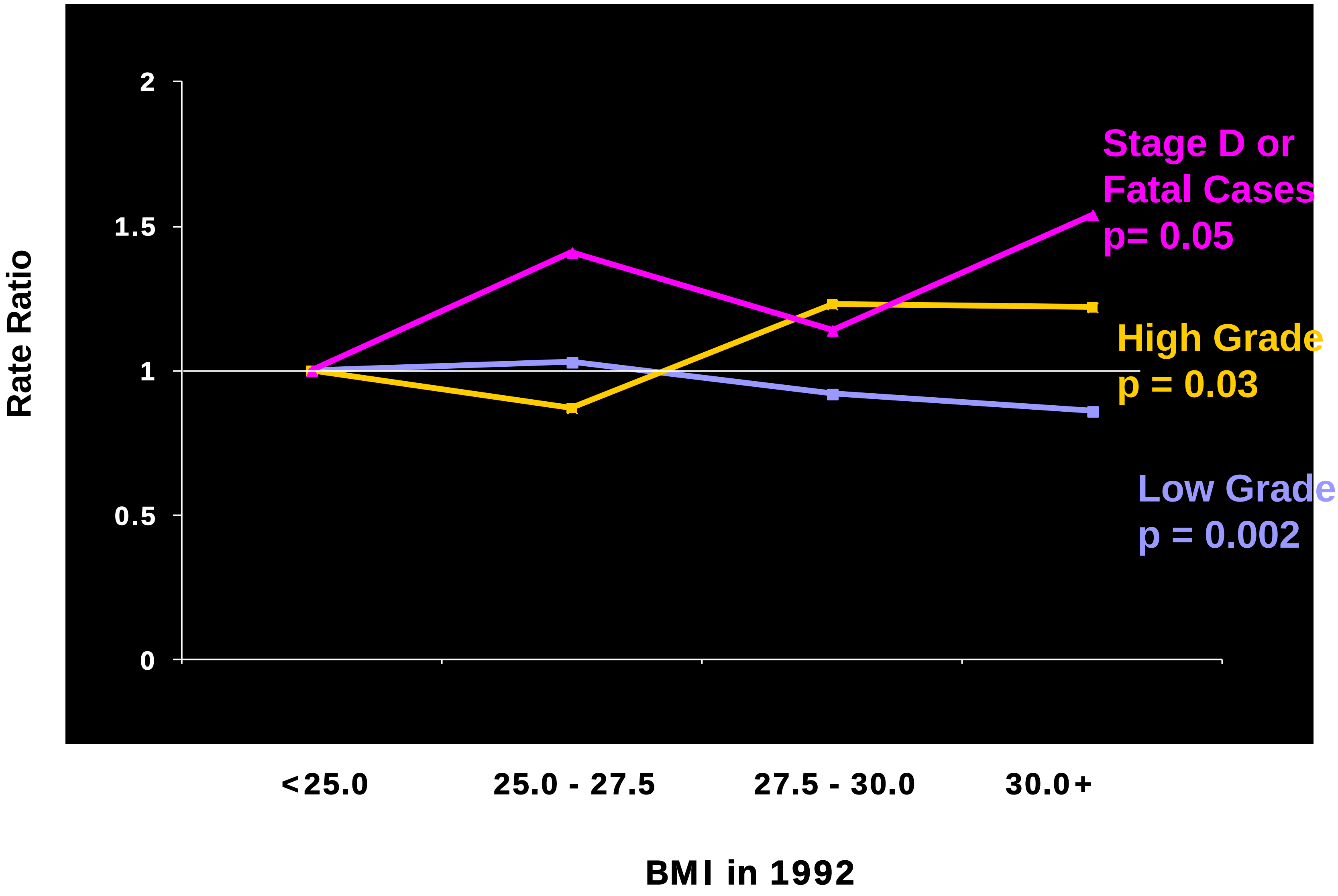
Reference	No. of cases	BMI kg/m^2	RR (95% CI)
Thune *et al*., Norway, 1994		per 1 kg/m^2	1.25 (1.05–1.50)
Gronberg *et al*., Sweden 1996	406	> 29 vs. < 23	1.80 ($p < 0.05$)
Andersson *et al*., Sweden 1997	2368	>26.2 vs. < 22.1	1.13 (0.99–1.29)
Severson *et al*., Hawaii (Japanese men) 1988	174	25.00 vs. <22.49	1.33 (0.92–1.92)
Thompson *et al*., Rancho Bernardo, 1989	54	per 2.92 kg/m^2	1.1 (0.9–1.4)
Cerhan *et al*., Iowa rural, 1997	69	>27.8 vs. < 23.6	1.7 (0.8–3.3)
	17 reg/distant	>27.8 vs. < 23.6	3.1 (0.7–14)
Lund Nilsen *et al*., Norway, 1999	642	> 28.2 vs. <23.0	1.0 (0.8-1.3)
Mills *et al*., Seventh Day, 1989	180	25.8 vs. < 23.2	1.17 (0.79–1.72)
Giovannucci *et al*., US 1997	1369	29 vs. <23	0.90 (0.71–1.15)
	407 advanced	29 vs. <23	1.19 (0.79–1.82)
LeMarchand *et al*., Hawaii 1994	198	>26 vs. <22	0.7 (0.5–1.2)
Schuurman, A.G. *et al*., Netherlands 1999	681	>28 vs. < 22	0.89 (0.58–1.37)

Obesity and Prostate Cancer Mortality



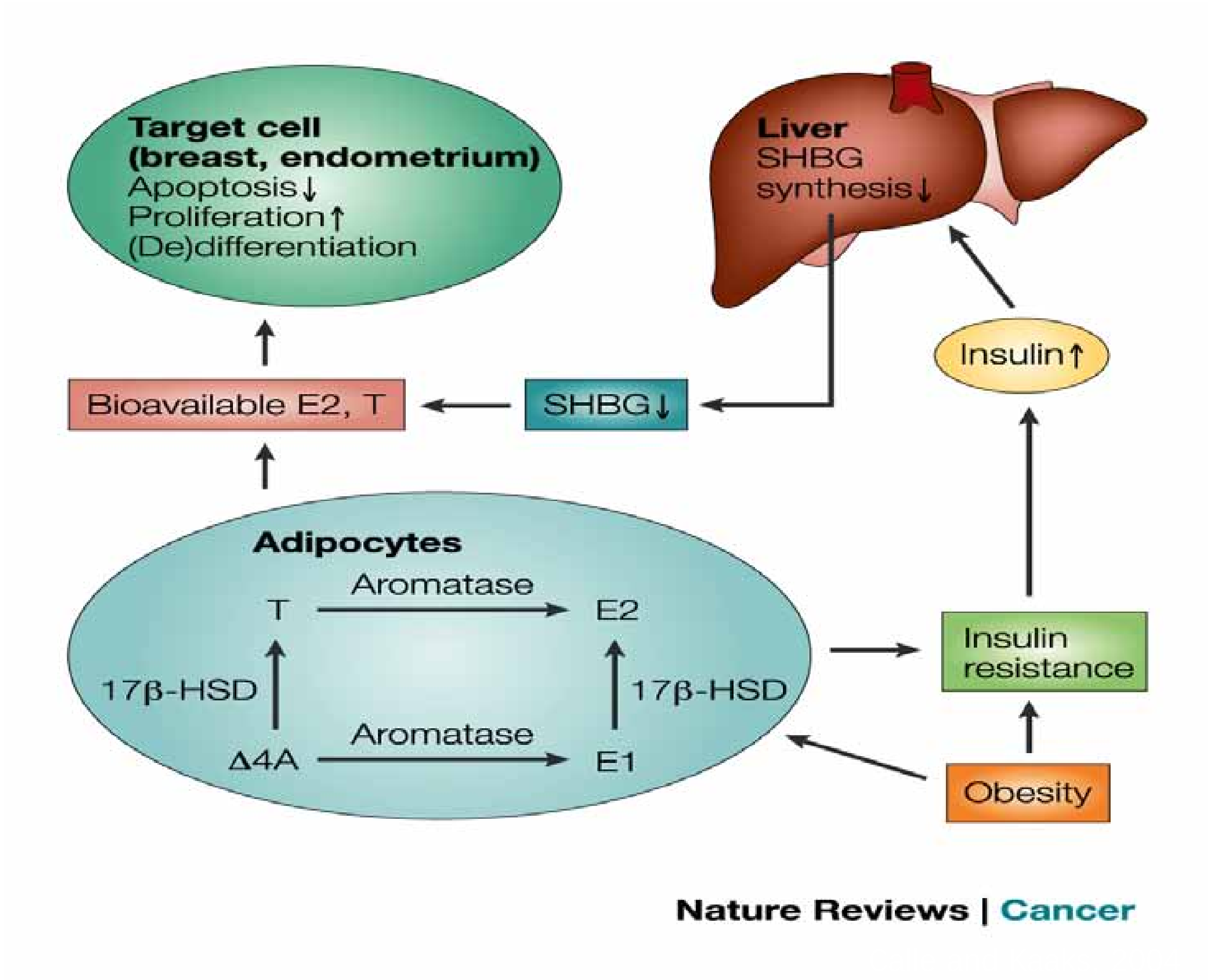
ACS CPSII Cohort n=404,576 n=4,004 deaths
Adapted from Calle et al, NEJM, 2003

BMI and Prostate Cancer Incidence



Rodriguez et al, CEBP, 2007)

Obesity and Hormone Production



Summary and Future Directions

- There is growing evidence that obesity increases risk of cancer at many organ sites
- Hormones, growth factors and inflammation are likely the major mechanisms
- Important Public Health Implications: Obesity is the second (to tobacco) leading risk factor for cancer
- Future research should focus on how risk is affected by successful (sustained) weight loss

What Does the Future Hold?

We don't completely understand the health effects of a ***lifetime*** *of being obese!*

Newsweek Cover Image June 2000 http://www.cdc.gov/EXCITE/images/overweight_newsweek.jpg