

Obesity – A Silent Killer?

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Excess Body Weight and Increased Cancer Risk; International Expert Group Evaluations, IARC (2002) and WCRF (2007)

**“sufficient / convincing”
evidence**

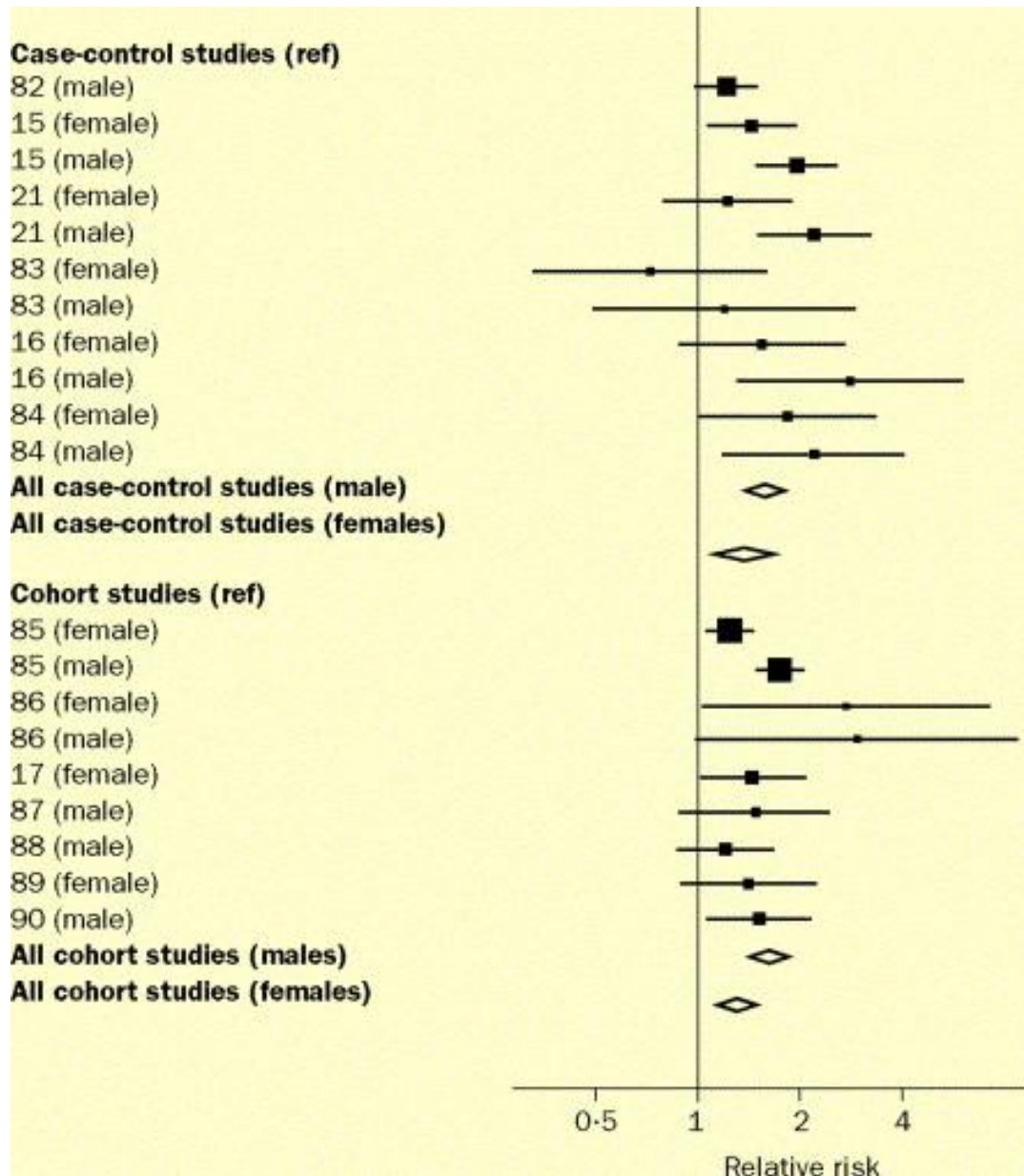
**Colon (not Rectum !)
Breast (postmenopause)
Endometrium
Kidney (renal cell)
Esophagus (adenocarc.)
Pancreas**

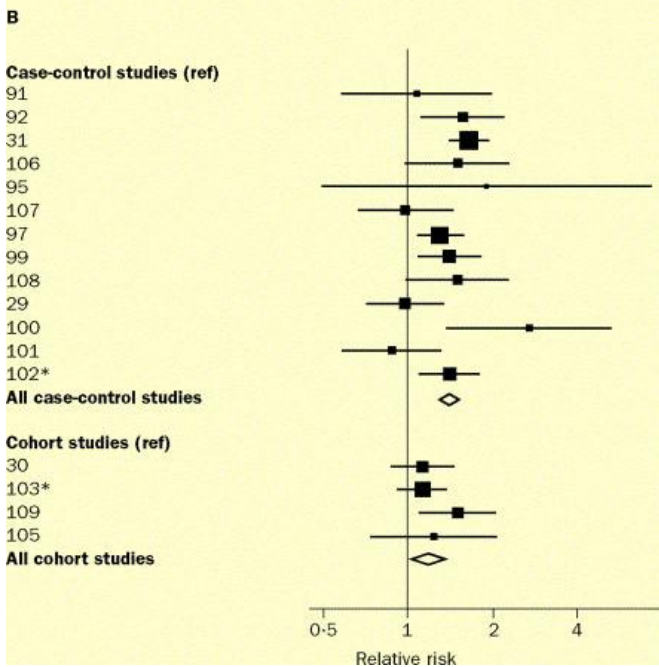
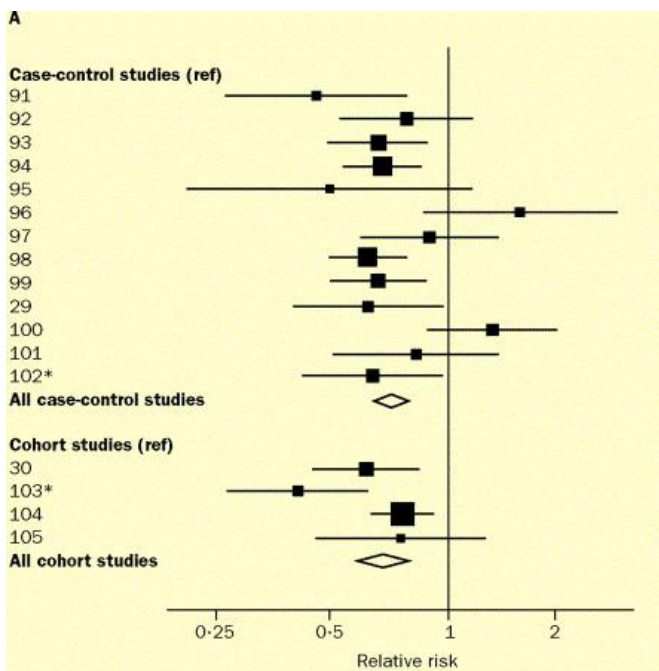
**“limited evidence /
probable relationship”**

**Gallbladder
Thyroid**

BMI and Colon cancer risk; a meta-analysis of epidemiological studies

Bianchini, Kaaks & Vainio,
Lancet Oncol, 2002



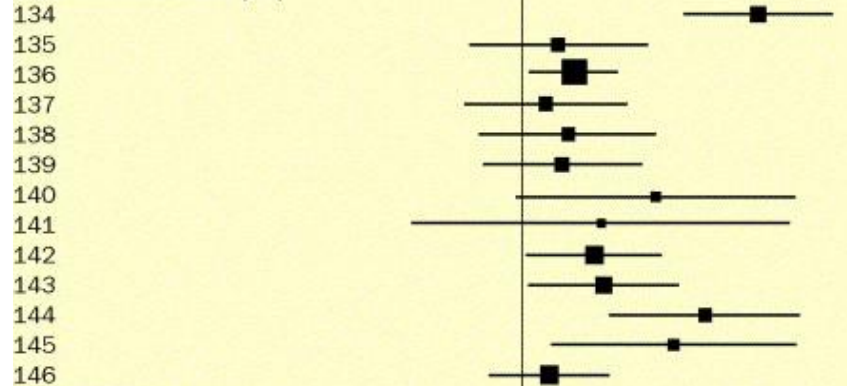


BMI and Breast cancer among pre- and post-menopausal women; a meta-analysis of epidemiological studies

Bianchini, Kaaks & Vainio, *Lancet Oncol*, 2002

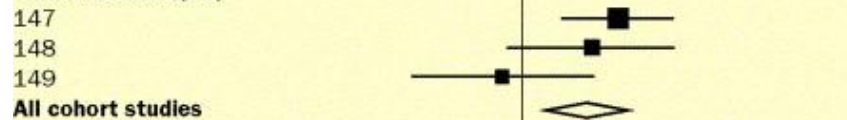
A

Case-control studies (ref)



All case-control studies

Cohort studies (ref)



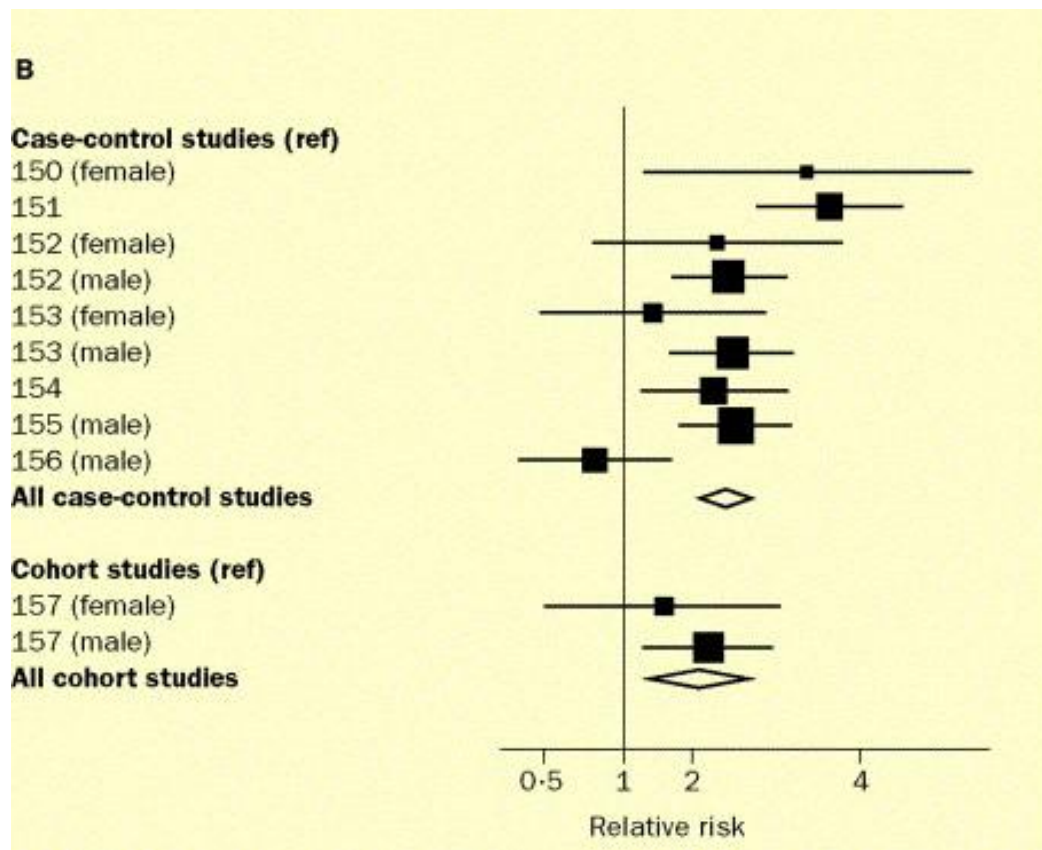
All cohort studies

BMI and risk of Kidney cancer; a meta-analysis of epidemiological studies

Bianchini, Kaaks & Vainio,
Lancet Oncol, 2002

BMI and risk of Adenocarcinoma of the Esophagus; a meta-analysis of epidemiological studies

Bianchini, Kaaks & Vainio,
Lancet Oncol, 2002



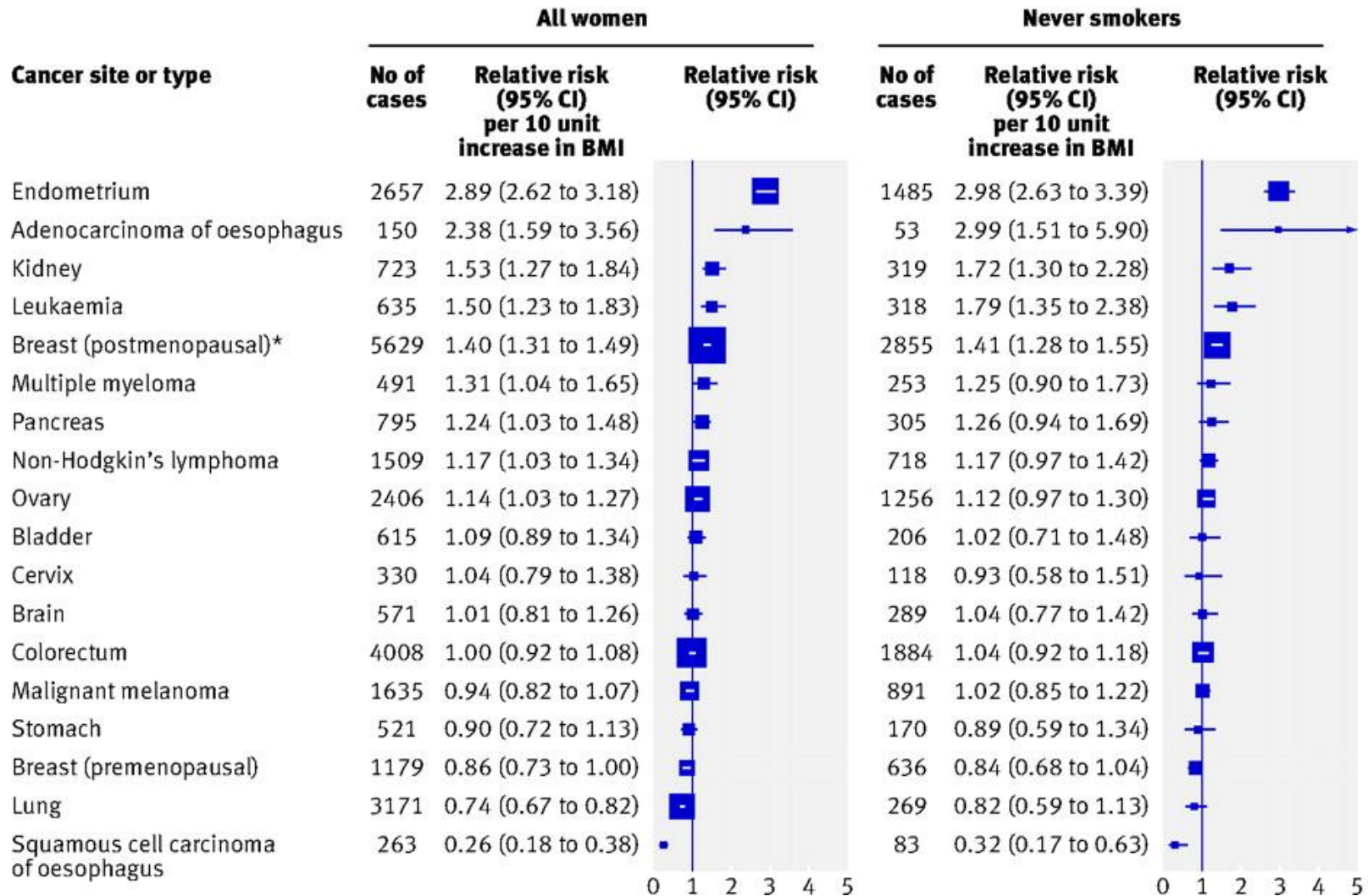
Proportion of cancer cases attributable to overweight and obesity in the USA and the European Union

	25<BMI<30 (overweight)	BMI 30+ (obese)	PAF%	PAF%
	RR	RR	United States	European Union
Breast (post.)	1.3	1.5	22.6	16.7
Endometrium	2.0	3.5	56.8	45.2
Colon, men	1.5	2.0	20.8	14.2
Colon, women	1.2	1.5	22.6	16.7
Gallbladder	1.5	2.0	35.5	27.1
Pancreas	1.3	1.7	26.9	19.3
Renal Cell	1.5	2.5	42.5	31.1

Calle & Kaaks, Nat. Rev. Cancer, 2004

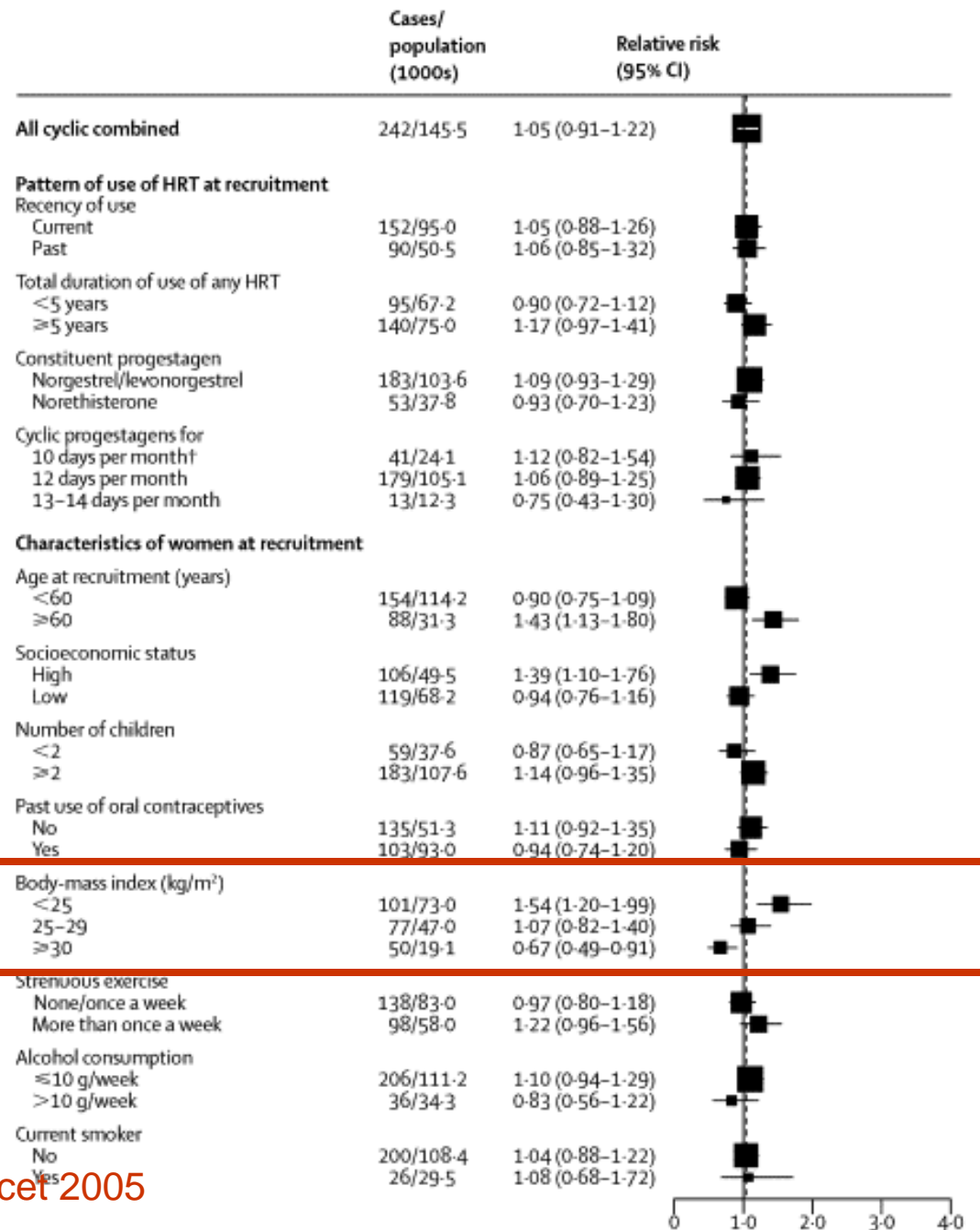
Estimated trend in the relative risk of cancer by type, per 10 unit increase BMI.

*Restricted to never users of hormone replacement therapy



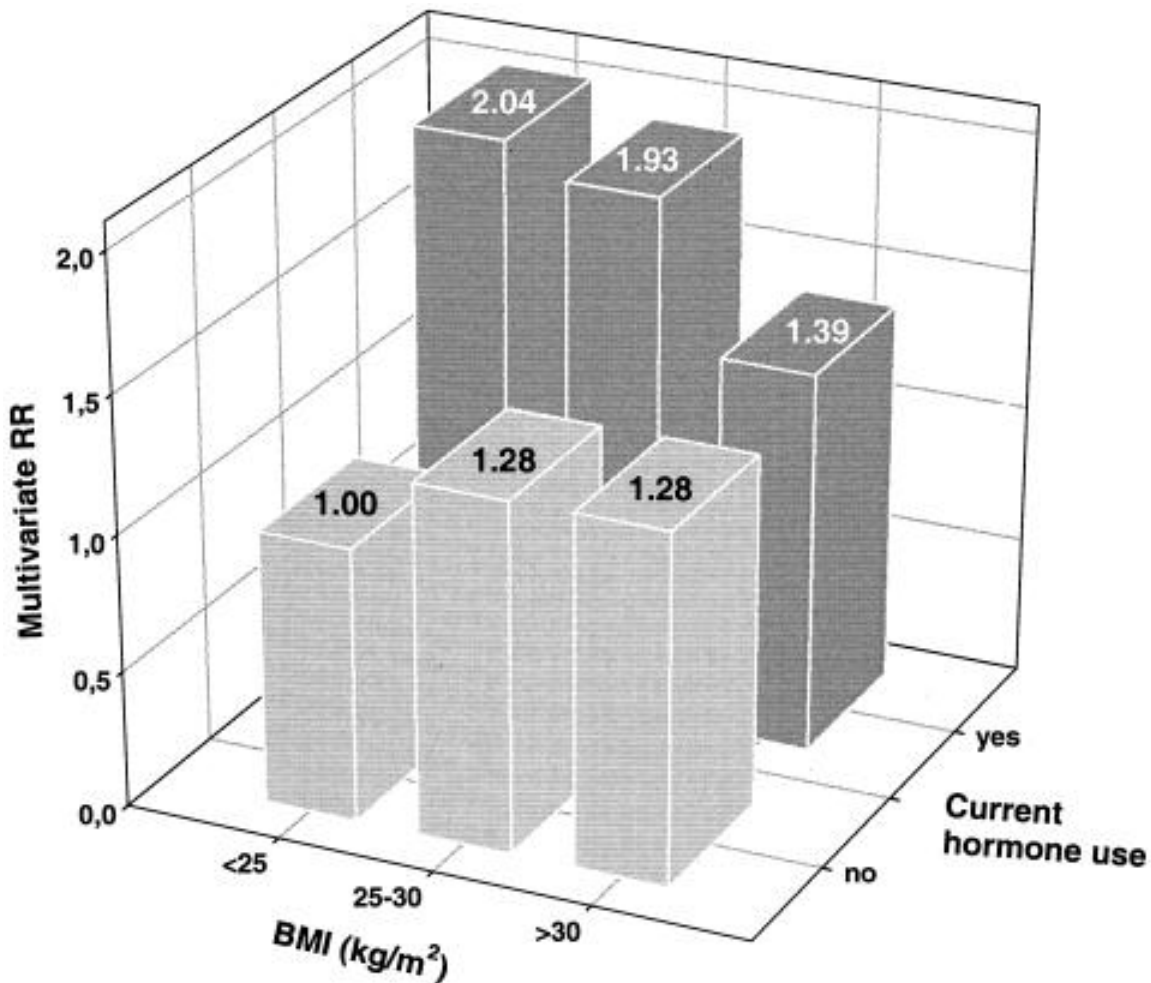
Reeves, G. K et al. BMJ 2007;335:1134

“Million Women” Cohort, UK
Relative risk of endometrial cancer
in women who last used cyclic
combined HRT, by reported
pattern of use of HRT at recruitment
and by various characteristics of
the women studied.



Million Women Study collaborators, Lancet 2005

Relative risk of breast cancer by BMI category and current hormone use among postmenopausal women ($n = 103,344$); the EPIC study.



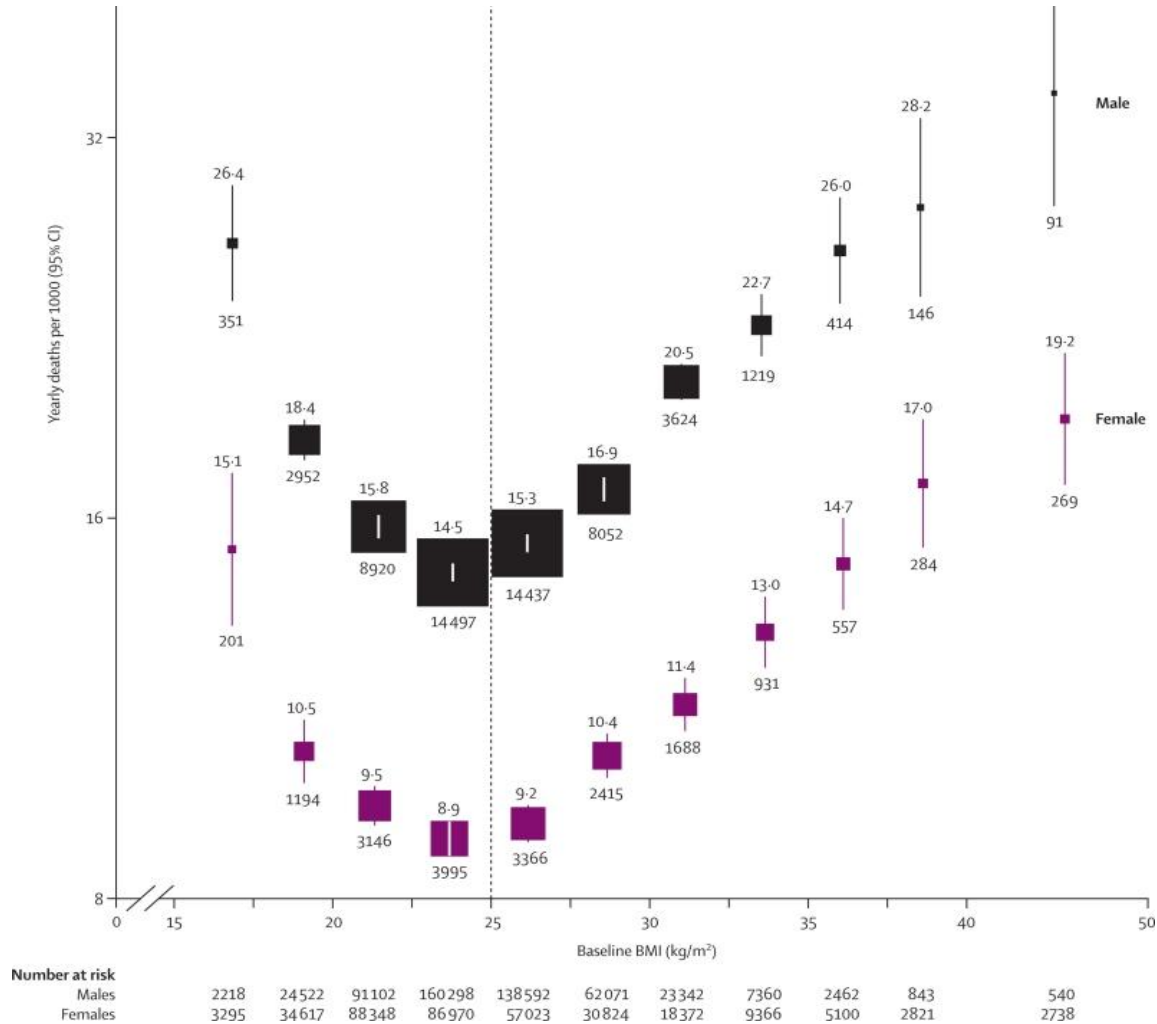
Lahmann et al., Int J Cancer 2006

Conclusions (1)

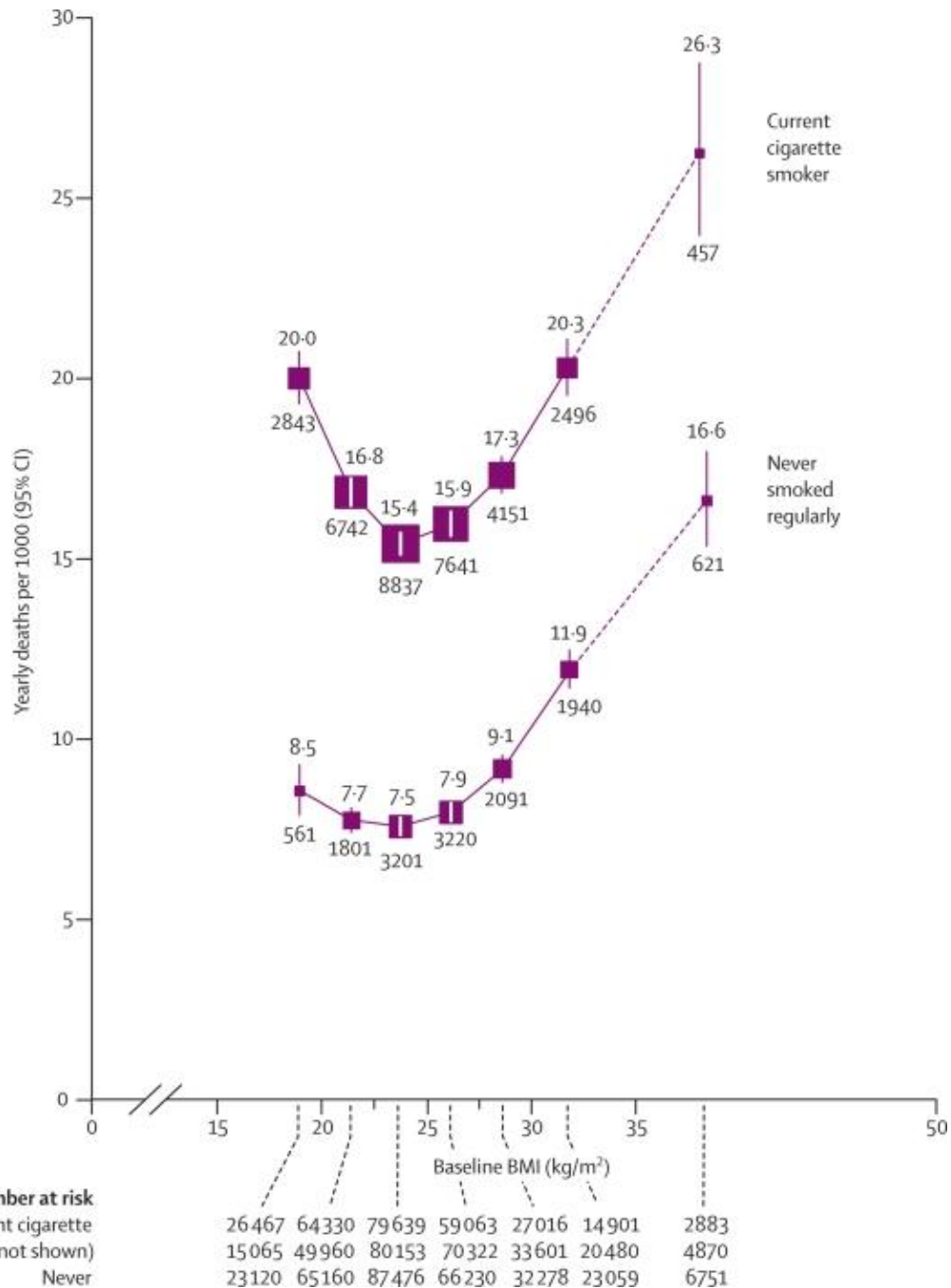
Excess body weight and cancer risk

- Excess body weight has been consistently related to increased risks of cancers of the colon, breast, endometrium, kidney (renal cell), esophagus (adenocarcinoma), and pancreas.
- More recent studies indicate possible increased risks also for leukemias, non-Hodgkin lymphomas, multiple myelomas and ovarian cancer.

All-cause mortality versus Body Mass Index (BMI); a collaborative analysis of 57 prospective studies. (excluding first 5 years of follow-up)



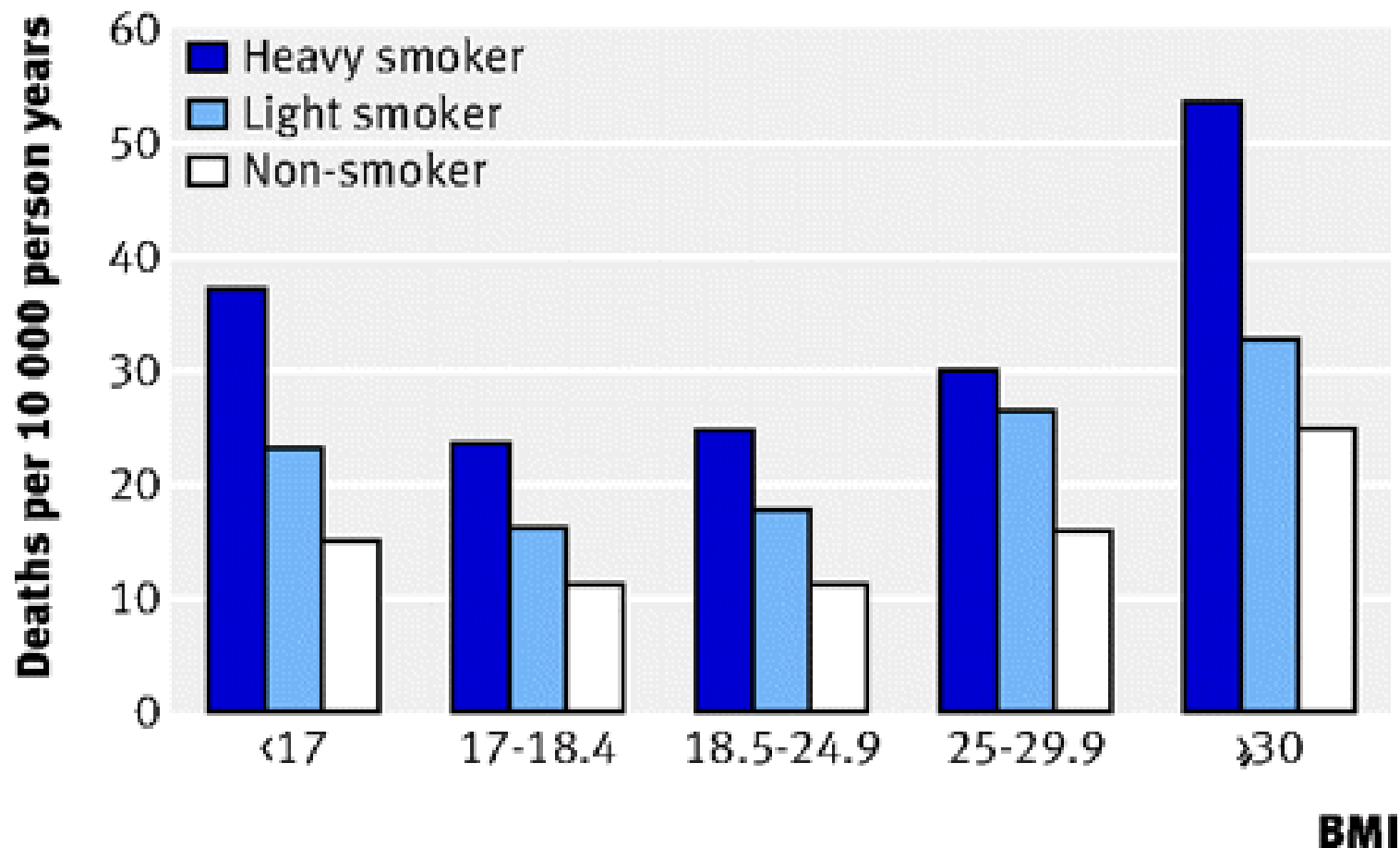
Prospective Studies Collaboration, Lancet, March 2009



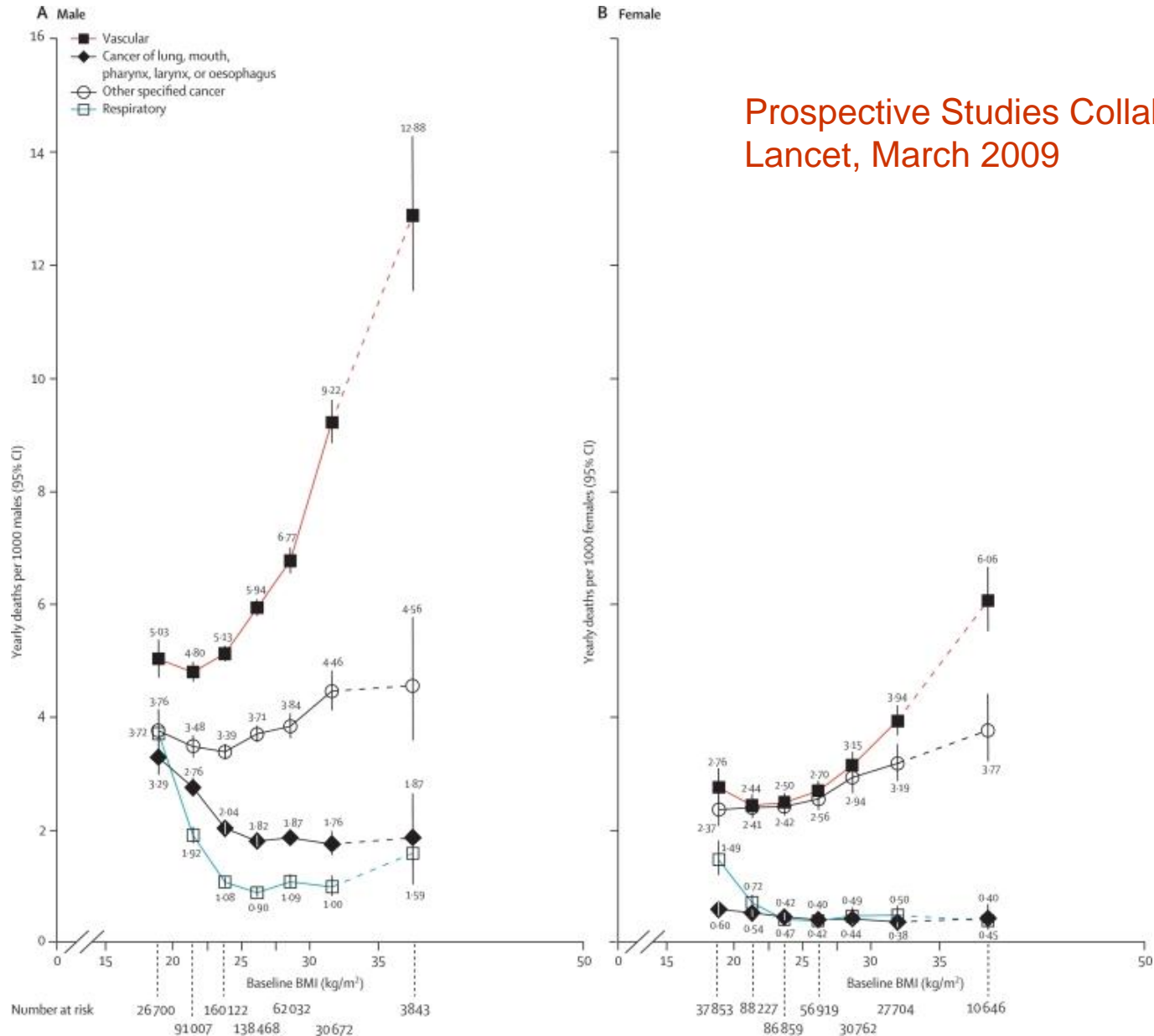
All-cause Mortality in relation to BMI; collaborative analysis of 57 prospective studies.
(excluding first 5 years of follow-up)

Prospective Studies Collaboration,
Lancet, March 2009

Combined effects of BMI and smoking on mortality rates; 45,920 Swedish Men; Nation-wide cohort followed over 38 years.



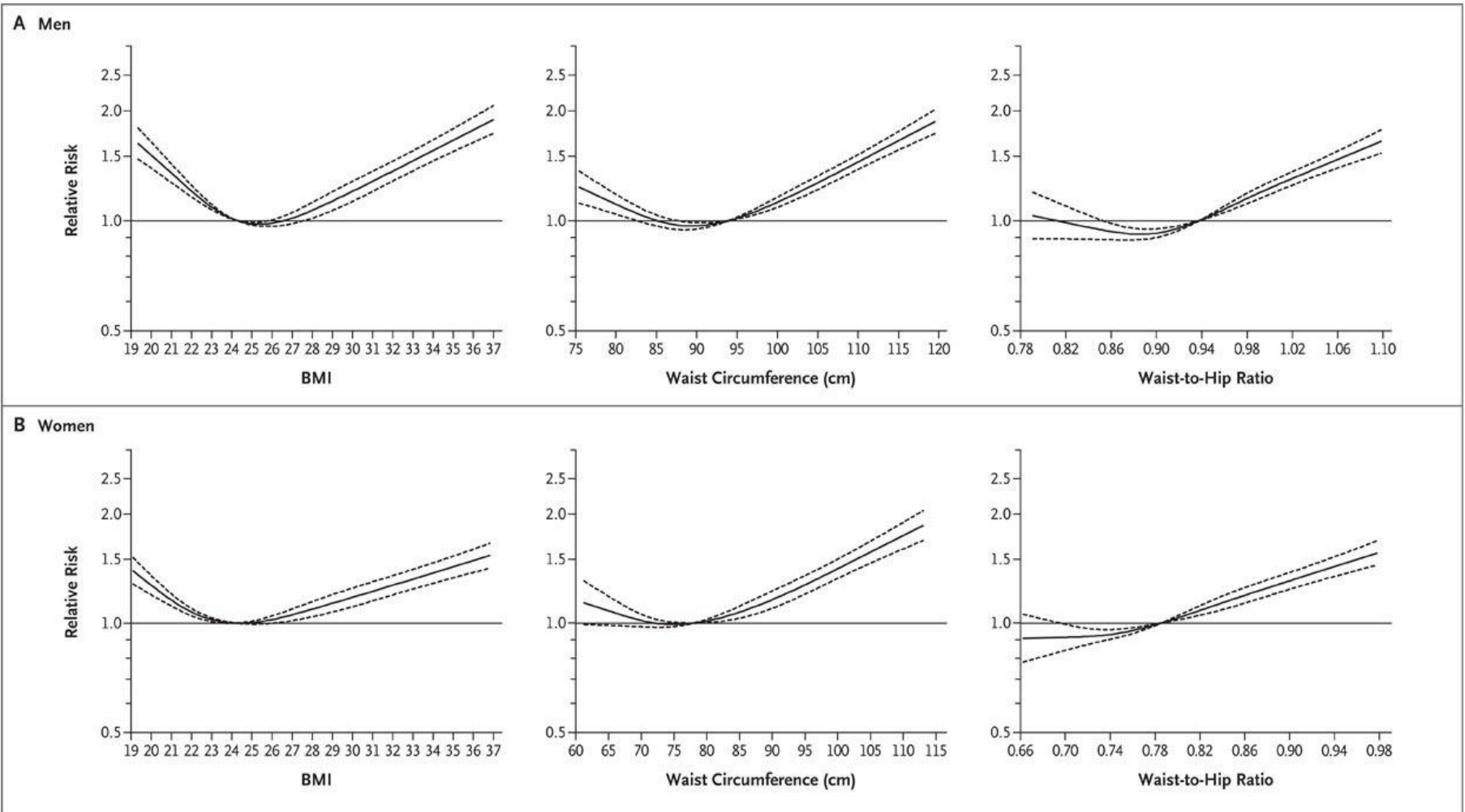
Body Mass Index vs. Mortality rates at ages 35-79 years, for main disease categories vs BMI;



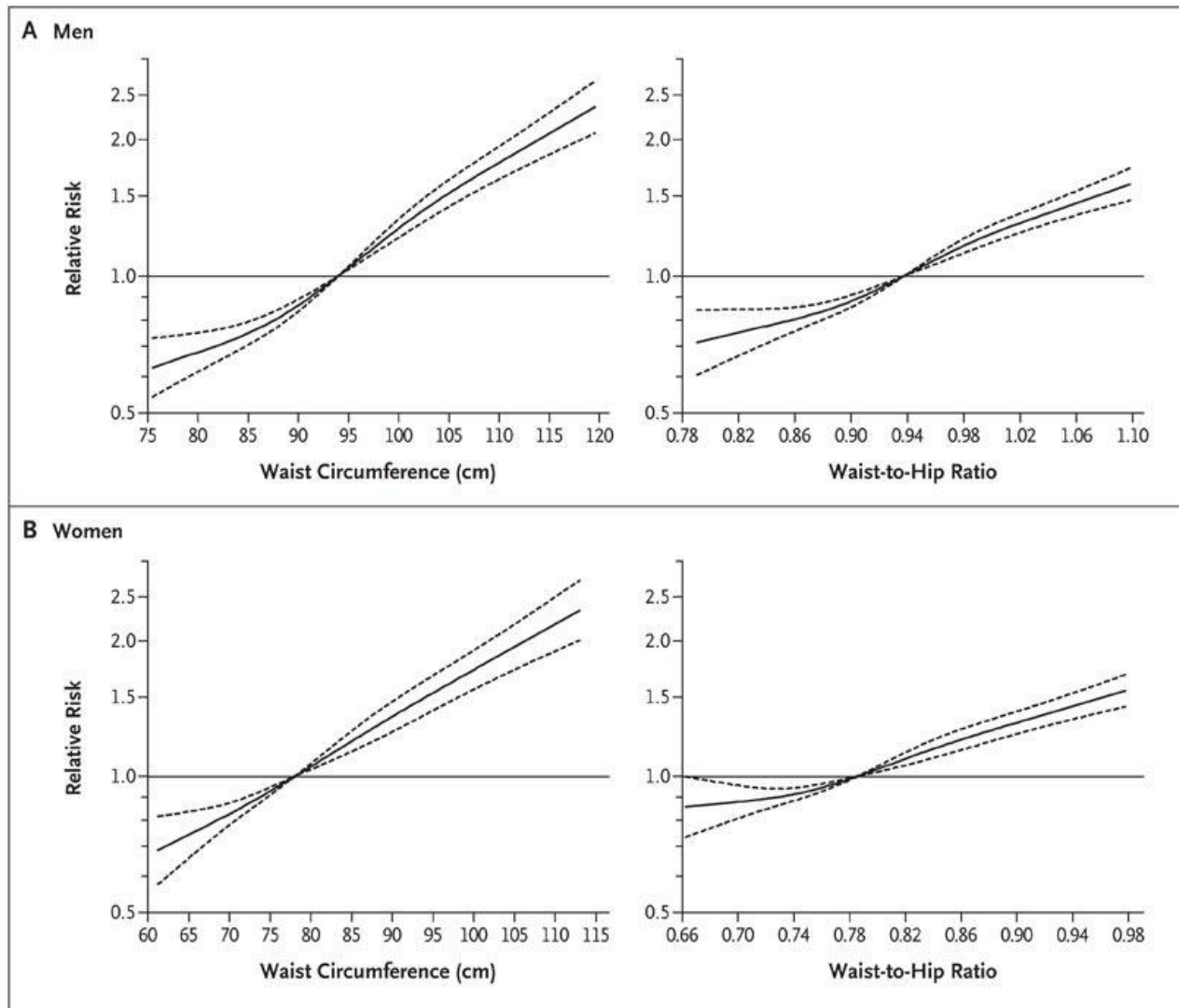
Prospective Studies Collaboration, Lancet, March 2009

Adjusted Relative Risk of Death among Men and Women, According to BMI, Waist Circumference, and Waist-to-Hip Ratio.

European Prospective Investigation into Cancer and Nutrition

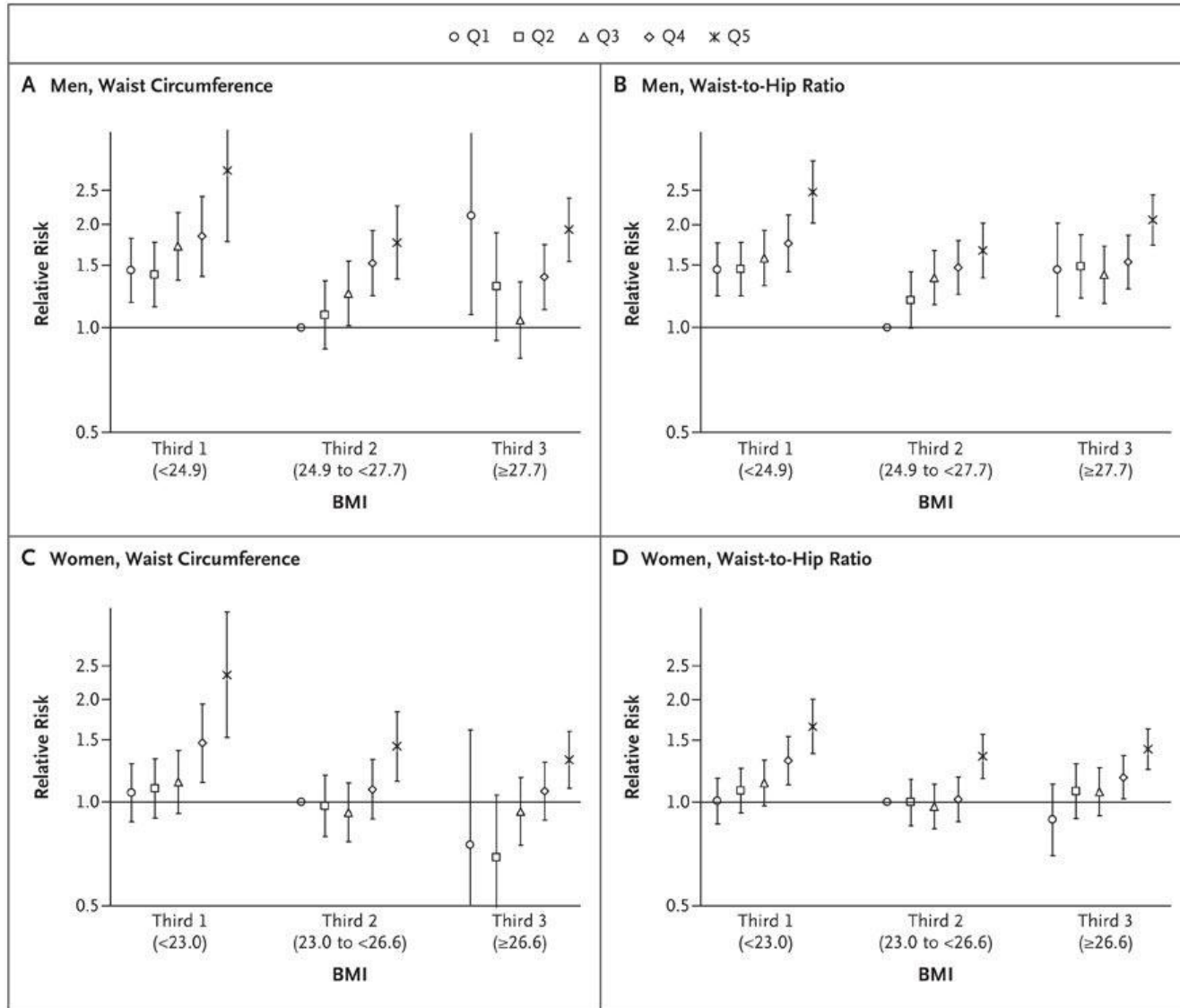


Adjusted Relative Risk of Death among Men and Women, According to Waist Circumference and Waist-to-Hip Ratio after Adjustment for BMI. European Prospective Investigation into Cancer and Nutrition



Adjusted Relative Risk of Death among Men and Women, by tertiles of BMI and quintiles of Waist Circumference or Waist-to-Hip Ratio.

European Prospective Investigation into Cancer and Nutrition



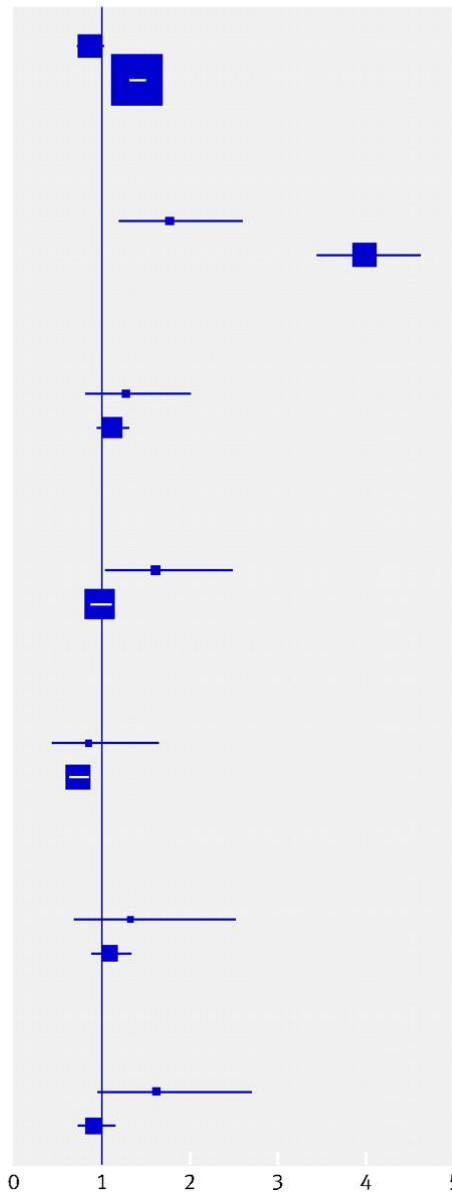
Conclusions (2)

Excess body weight and mortality

- BMI shows a non-linear (“J-shaped”) relationship with overall mortality, as well as with mortality due to broad categories of causes: cancer, cardiovascular disease.
- This non-linear relationship exists among smokers as well as non-smokers.
- Mortality increases with increasing waist circumference – a measure of abdominal obesity – at all levels of BMI
- Waist circumference is more strongly related to mortality in the lower BMI categories.
- Possible reasons for the excess mortality at lower BMI:
 - Higher prevalence of smokers at low BMI
 - Pre-existing illness
 - Ratio of (intra-) abdominal adipose tissue to lean body (particularly muscle) mass.
- Physical activity lowers risk of many chronic diseases and overall mortality, independently of BMI

Thank you for your attention !

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		
Ovary		
Premenopausal	128	1.28 (0.81 to 2.00)
Postmenopausal	982	1.12 (0.95 to 1.31)
χ^2 for heterogeneity=0.3, df=1, P=0.6		
Colorectum		
Premenopausal	136	1.61 (1.05 to 2.48)
postmenopausal	1743	0.99 (0.88 to 1.12)
χ^2 for heterogeneity=4.6, df=1, P=0.03		
Lung		
Premenopausal	64	0.86 (0.45 to 1.65)
Postmenopausal	1351	0.74 (0.64 to 0.86)
χ^2 for heterogeneity=0.2, df=1, P=0.7		
Non-Hodgkin's lymphoma		
Premenopausal	60	1.33 (0.70 to 2.52)
Postmenopausal	627	1.09 (0.89 to 1.34)
χ^2 for heterogeneity=0.3, df=1, P=0.6		
Malignant melanoma		
Premenopausal	98	1.62 (0.97 to 2.70)
Postmenopausal	566	0.92 (0.74 to 1.15)
χ^2 for heterogeneity=4.0, df=1, P=0.05		

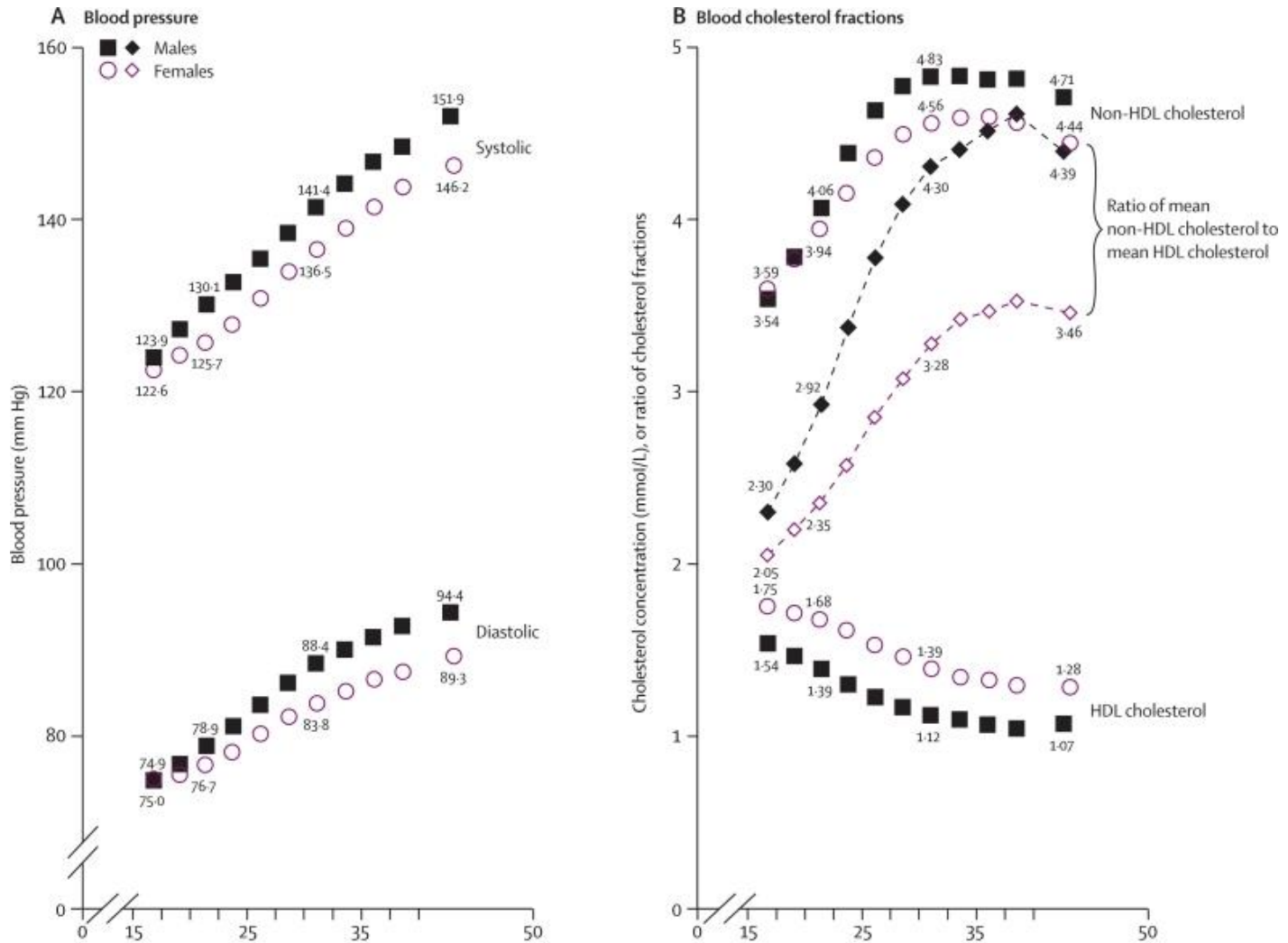


Estimated relative risk of cancer incidence per 10 unit increase in BMI, by menopausal status.

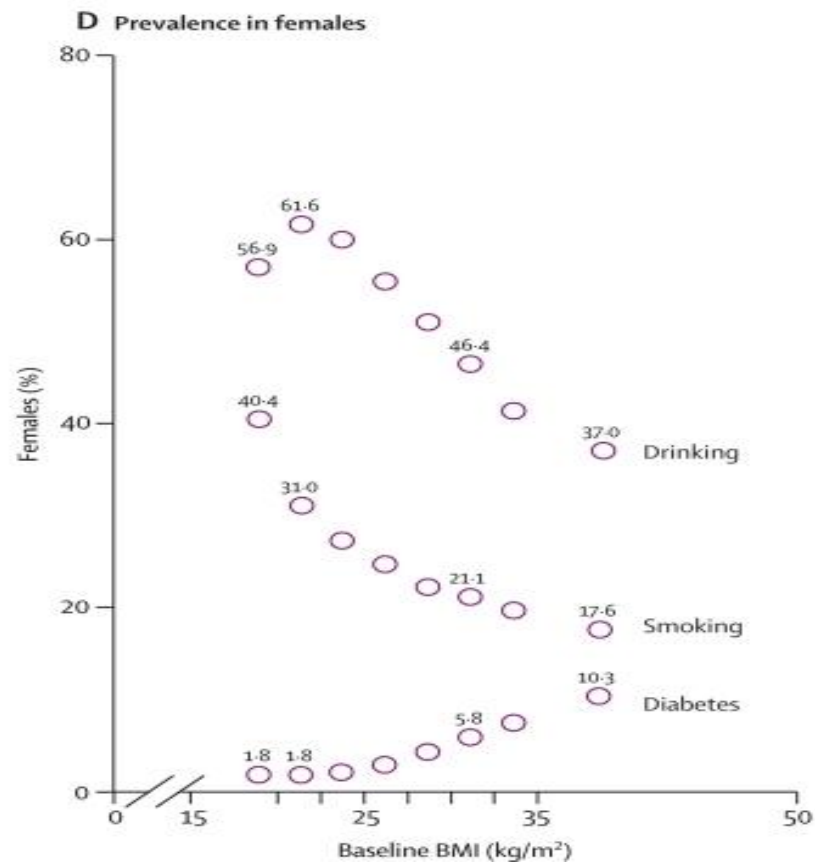
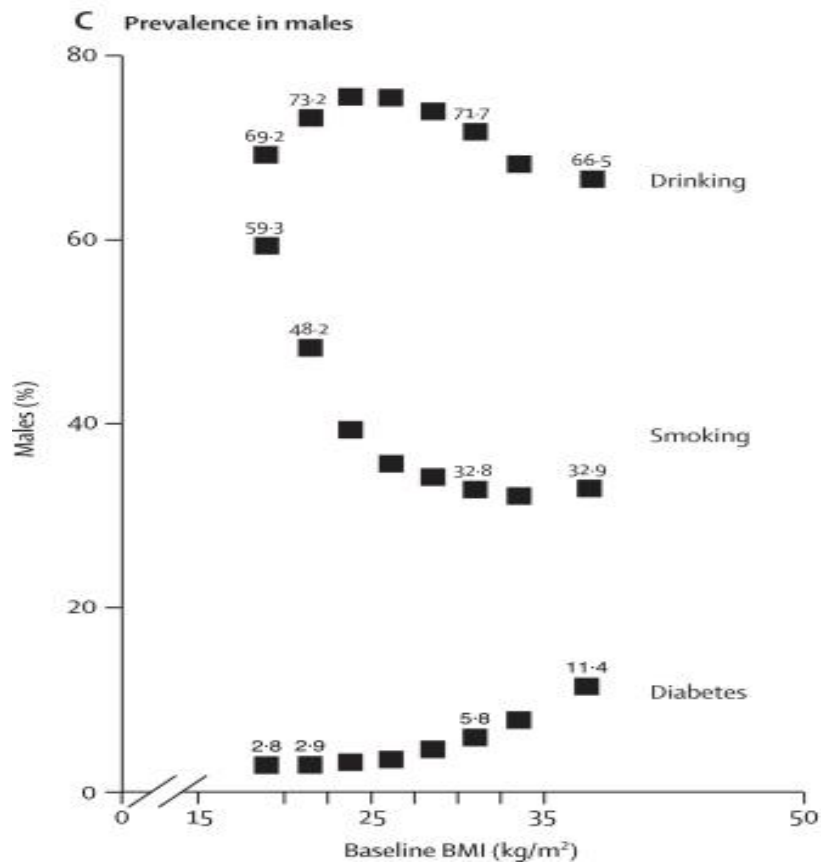
(Adjusted for age, SES, age at first birth, parity, smoking status, alcohol intake, and physical activity)

Reeves, G. K et al. *BMJ* 2007;335:1134

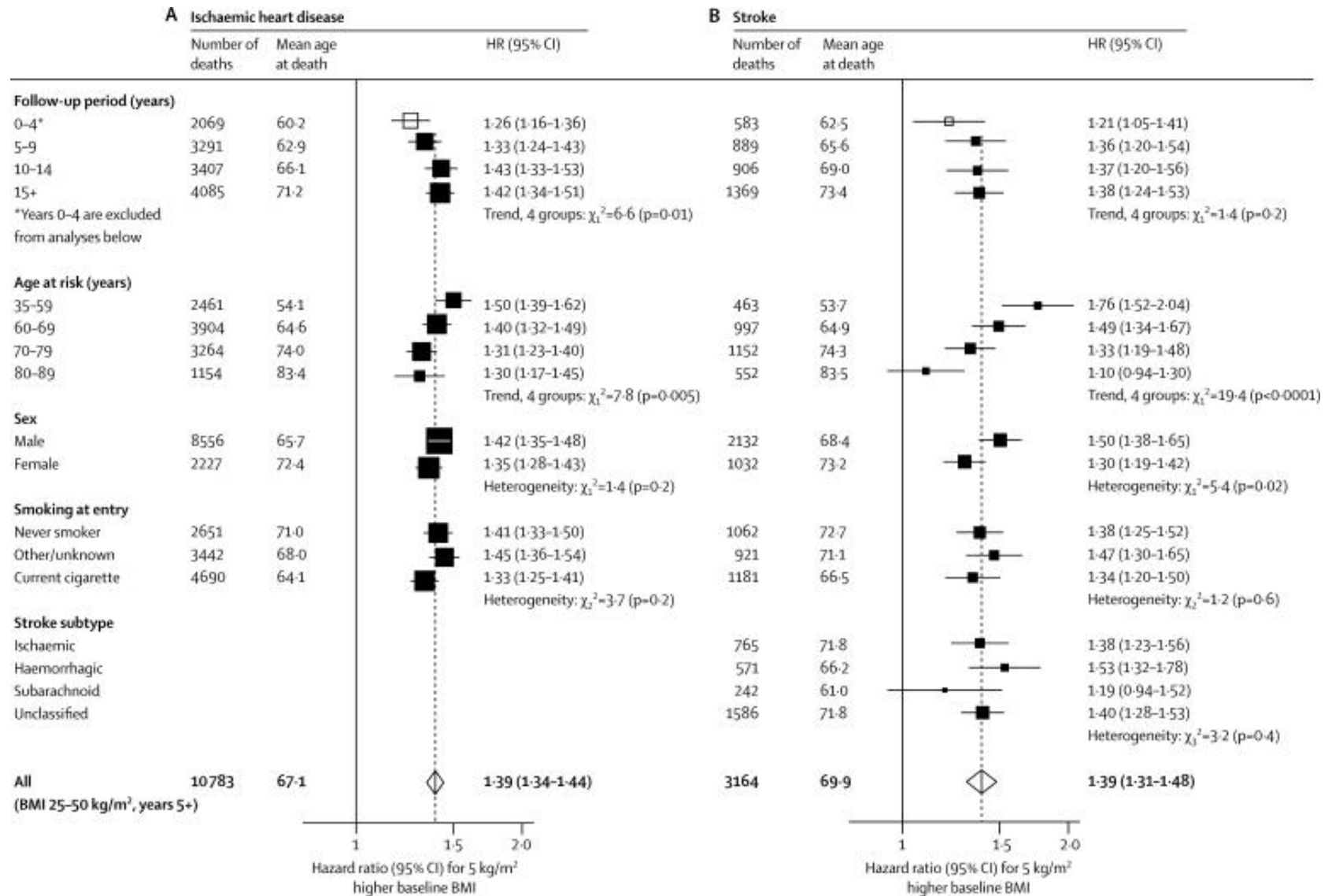
Blood pressure and blood lipid profiles in relation to BMI; a collaborative analysis of 57 prospective studies



Prevalence of alcohol drinking, smoking and type-II diabetes mellitus by category of BMI; a collaborative analysis of 57 prospective studies



Cardiovascular Mortality vs BMI, in the upper BMI range (25-50 kg/m²); (hazard ratios for 5 kg/m² increase in BMI)



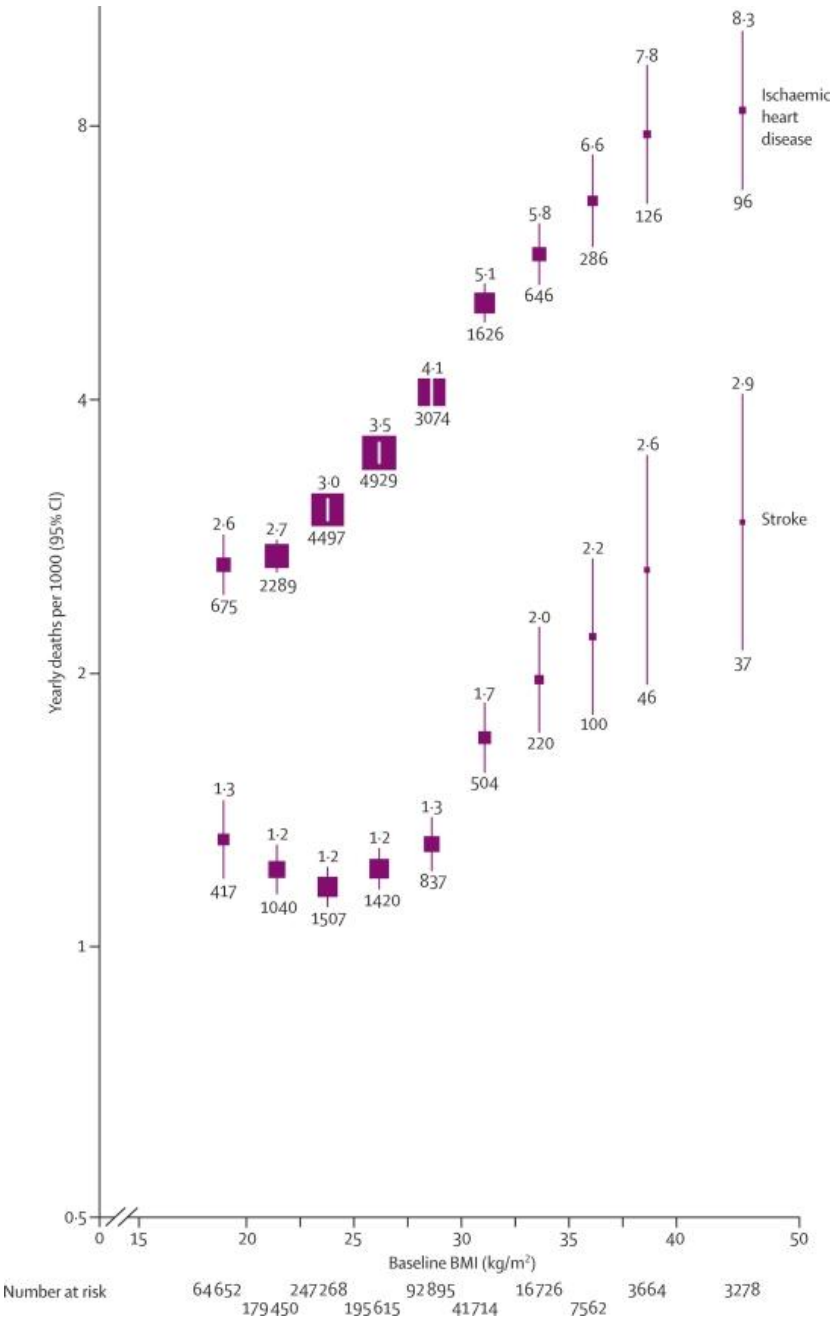
Excess body weight and cancer risk; the European Prospective Investigation into Cancer and Nutrition ("EPIC")

- **Pischon et al., JNCI 2006, colorectal:** waist circumference and WHR directly associated with colon cancer risk; in women only among non-users of HRT.
- **Berrington-de-Gonzalez et al., CEBP 2006, pancreas:** small, non-significant increase in risk with increasing BMI
- **Pischon et al., Int J Cancer 2006, kidney (renal cell);** direct association of BMI and WHR with risk.
- **Friedenreich et al., Cancer Causes Control 2006, endometrium:** increased risk among women with elevated BMI, but after menopause only among non-users of HRT.
- **Britton et al., Haematologie 2008, large B-cell lymphoma:** increased risk among women with high BMI.

Mortality due to Ischaemic Heart Disease and Stroke in relation to BMI;

a collaborative analysis of 57 prospective studies.

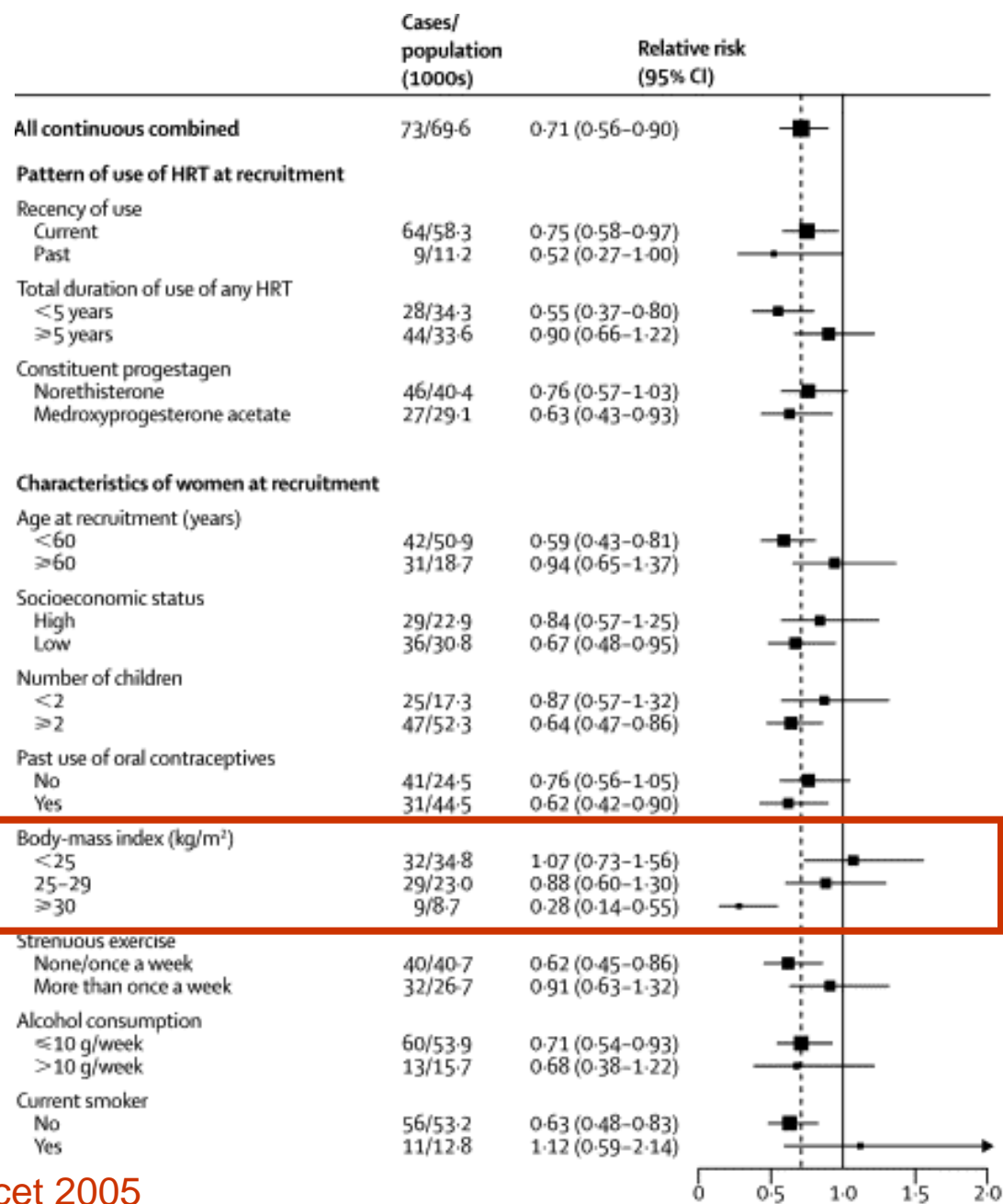
(excluding first 5 years of follow-up)



**Prospective Studies Collaboration,
Lancet, March 2009**

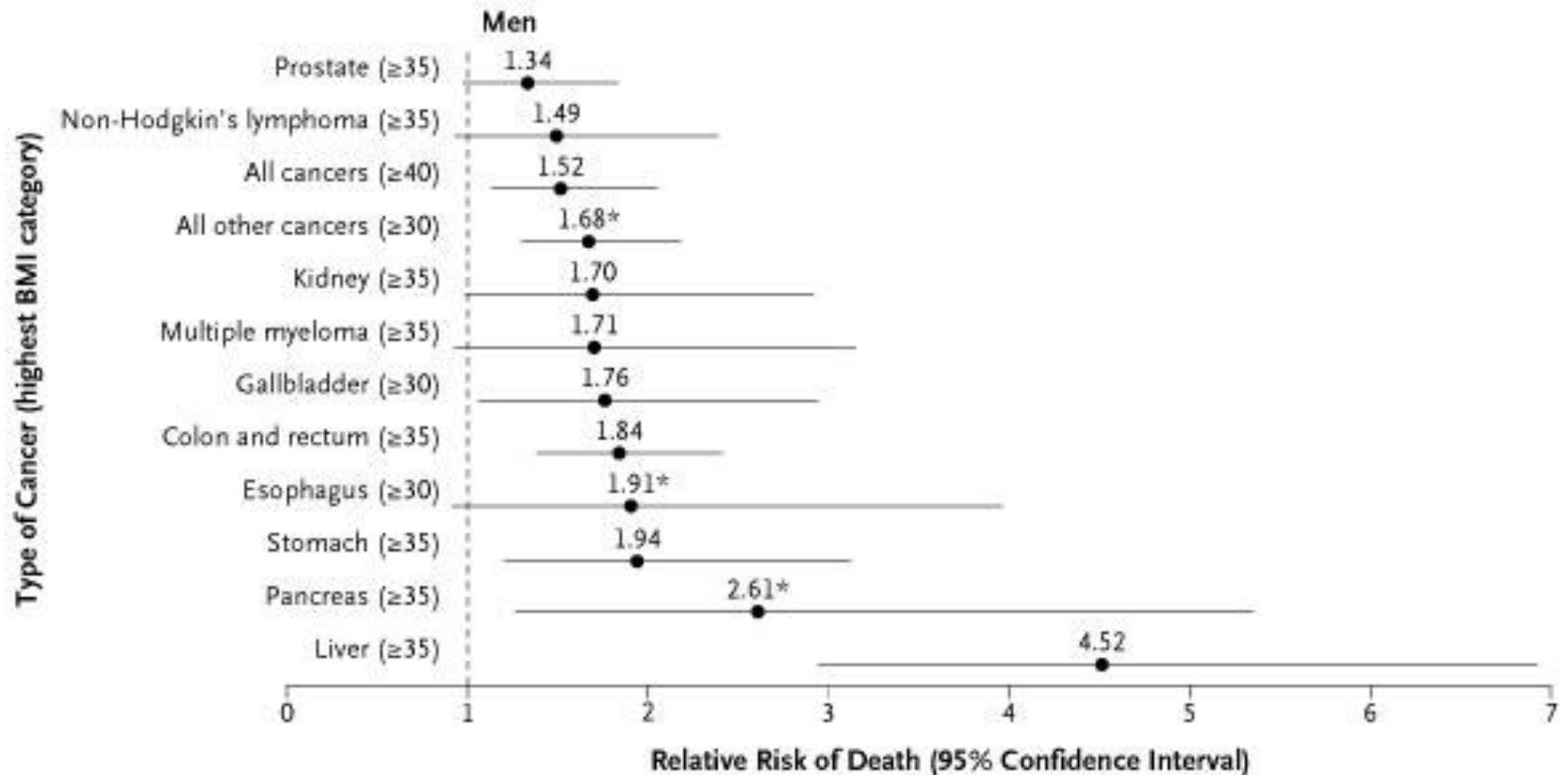
“Million Women” Cohort, UK

Relative risk of endometrial cancer in women who last used continuous combined HRT, by reported pattern of use of HRT at recruitment and by various characteristics of the women studied.



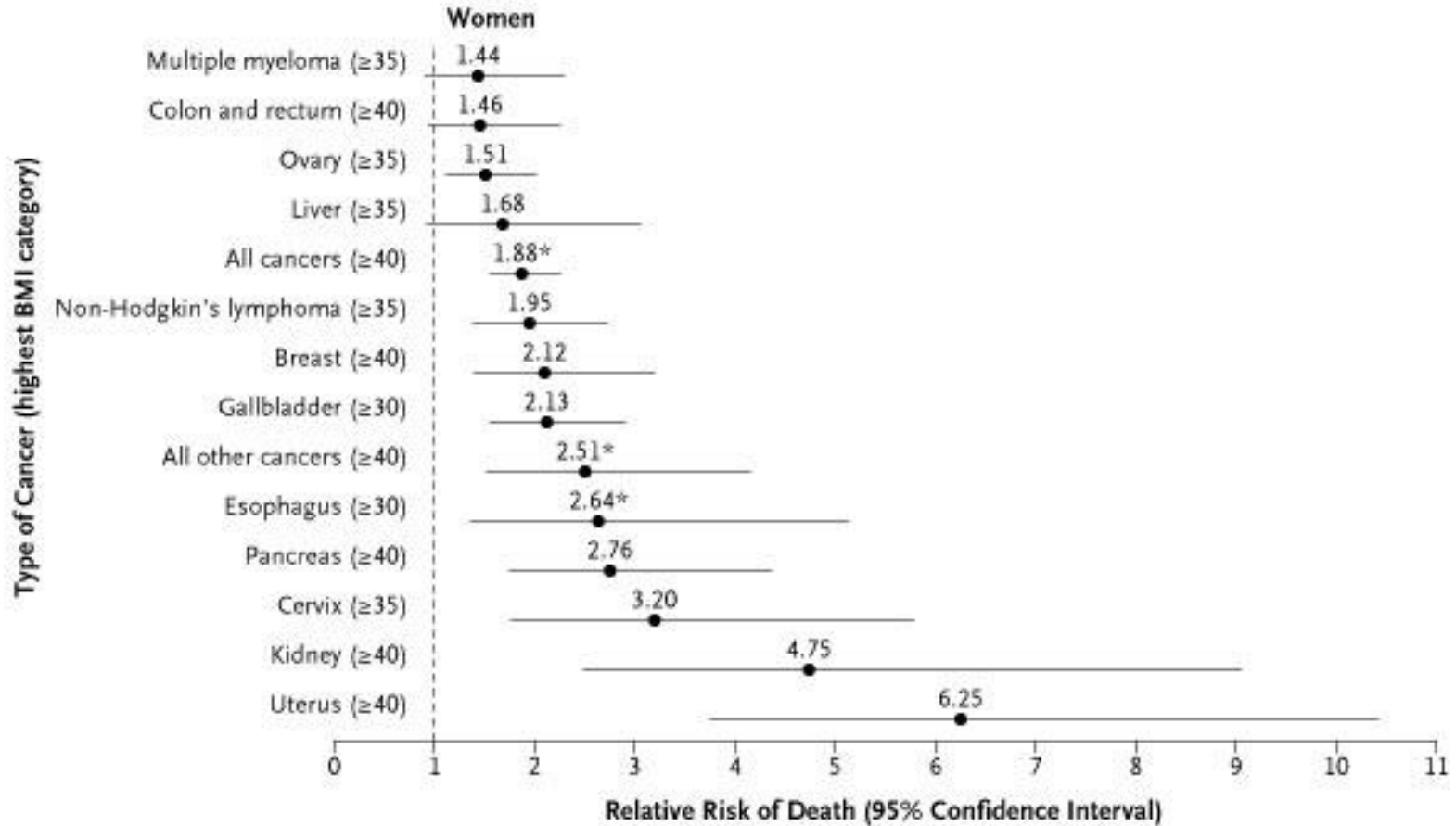
Million Women Study collaborators, Lancet 2005

Cancer Mortality according to BMI, among US Women; Cancer Prevention Study-II (1982-1998) (reference category: BMI 18.5-24.9)



Calle et al., New Engl J Med, 2003

Cancer Mortality according to BMI, among US Men; Cancer Prevention Study-II (1982-1998) (reference category: BMI 18.5-24.9)



Calle et al., New Engl J Med, 2003

Estimated population fraction of cancer mortality attributable to BMI, for US men and women.

Body-Mass Index	Men			Women		
	Prevalence of Exposure	Relative Risk	Population Attributable Fraction	Prevalence of Exposure	Relative Risk	Population Attributable Fraction
	%		%	%		%
All subjects						
25.0–29.9	42.1	0.97	-1.2	28.8	1.08	2.0
30.0–34.9	21.0	1.09	1.8	22.5	1.23	4.5
35.0–39.9	9.2	1.20	1.8	10.7	1.32	3.0
≥40.0	3.6	1.52	1.9	7.9	1.62	4.9
Total population attributable fraction			4.2			14.3
Subjects who never smoked						
25.0–29.9	42.1	1.11	4.0	28.8	1.14	3.3
30.0–34.9	21.0	1.38	6.8	22.5	1.33	6.1
35.0–39.9†	12.8	1.31	3.4	10.7	1.40	3.5
≥40.0				7.9	1.88	7.0
Total population attributable fraction			14.2			19.8

Calle et al., New Engl J Med, 2003