Obesity and cardiovascular disease epidemics: a time for reflection

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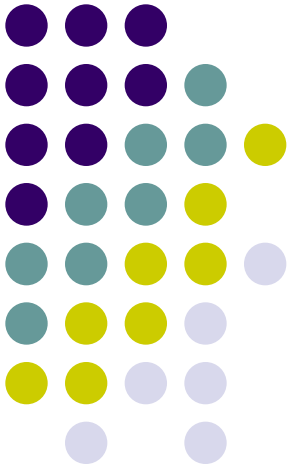
Editor in Chief Maturitas



EUROPEAN MENOPAUSE AND ANDROPAUSE SOCIETY

EMAS

Classifications

- Overweight and obesity are defined as abnormal or excessive fat accumulation that presents a risk to health.
- A person with a BMI of 30 or more is generally considered obese. A person with a BMI equal to or more than 25 is considered overweight.
- http://www.who.int/topics/obesity/en/

BMI	**Classification**
< 18.5	underweight
18.5–24.9	normal weight
25.0–29.9	overweight
30.0–34.9	class I obesity
35.0–39.9	class II obesity
≥ 40.0	class III obesity

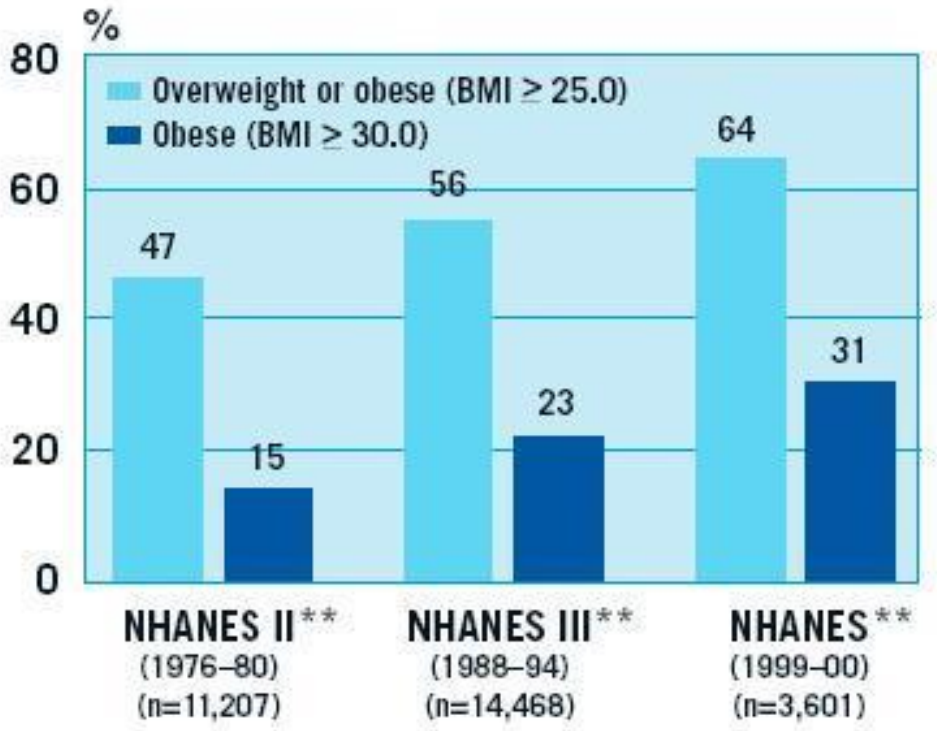
Further classifications

- Any BMI ≥ 35 or 40 is *severe obesity*
- A BMI of ≥ 35 or 40–44.9 or 49.9 is *morbid obesity*
- A BMI of ≥ 45 or 50 is *super obese*

- Asians develop negative health consequences at a lower BMI than Caucasians: the Japanese have defined obesity as any BMI greater than 25

- Sturm R (July 2007). "Increases in morbid obesity in the USA: 2000–2005". Public Health 121 (7): 492–6.
- Kanazawa M, Yoshiike N, Osaka T, Numba Y, Zimmet P, Inoue S (December 2002). "Criteria and classification of obesity in Japan and Asia-Oceania". Asia Pac J Clin Nutr 11 Suppl 8: S732–S737.

Age-adjusted* prevalence of overweight and obesity among U.S. adults, age 20–74 years

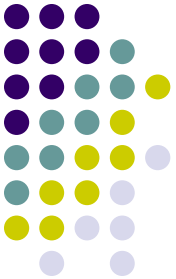


*Age-adjusted by the direct method to the year 2000 U.S. Bureau of the Census estimates using the age groups 20–39, 40–59, and 60–74 years.

**NHANES: National Health and Nutrition Examination Survey

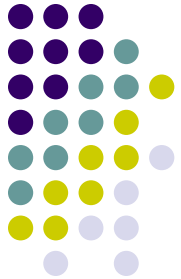
Source: Centers for Disease Control and Prevention

Prevalence and Trends in Obesity Among US Adults, 1999-2008
Katherine M. Flegal; Margaret D. Carroll; Cynthia L. Ogden; Lester R. Curtin
JAMA. 2010;303(3):235-241



- In 2007-2008, the age-adjusted prevalence of obesity was 33.8% overall,
- 32.2% men
- 35.5% women.
- Prevalence estimates for overweight and obesity combined were 68.0% overall
- 72.3% men
- 64.1% women
- the rate of increase for obesity in the U.S. in recent decades may be slowing

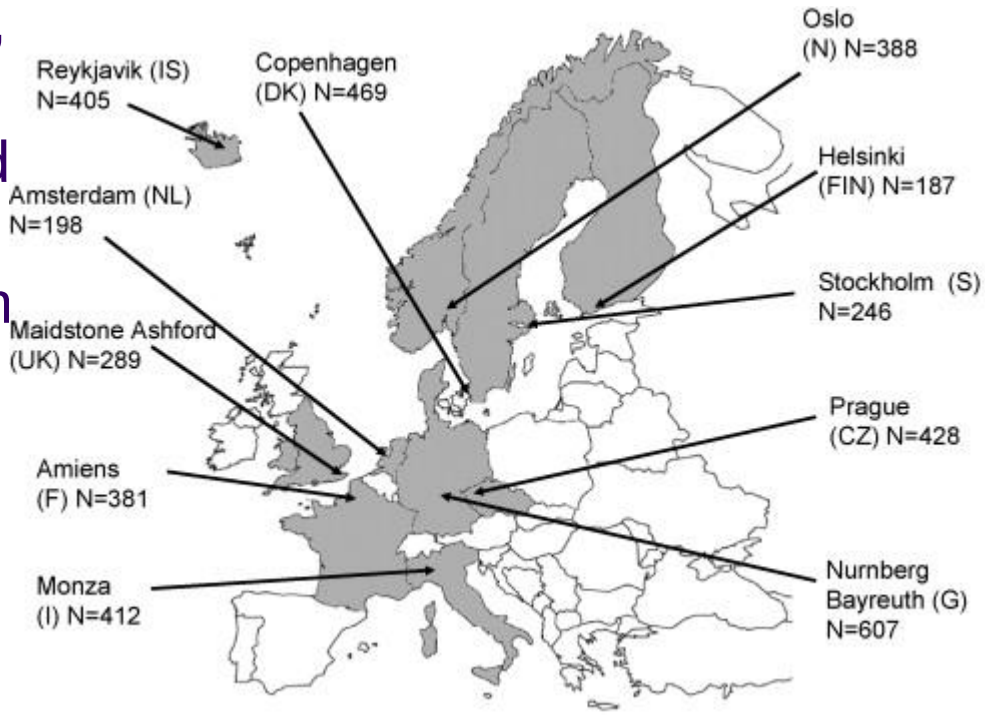
Consequences of obesity



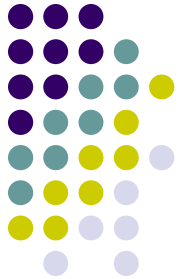
- diabetes
- heart disease
- high blood pressure
- stroke
- cancers
- gall bladder disease
- VTE
- obstructive sleep apnea syndrome
- metabolic syndrome
- reduced mobility
- reduced quality of life
- Depression
- Earlier need of home/residential care

AdHOC database: assessing home care

- Extreme obesity was present in 4.0% of women, who were on average 5 years younger and needed 7 months more of home care provision than women who were not obese
- Sørbye LW et al, Home care needs of extremely obese elderly European women, Menopause Int 2007; 13: 84–87.



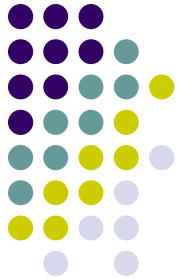
Managing the obese menopausal woman



- Transdermal estrogen delivery because of reduced VTE and gall bladder disease risk risk
- ? Mirena because of increased risk endometrial cancer

- EMAS position statement: managing obese postmenopausal women. Lambrinoudaki I, et al Maturitas. 2010;66:323-6.

HRT and weight gain systematic review



- **Objectives**
- . To assess the likelihood of gaining weight associated with hormone replacement therapy in perimenopausal and menopausal women.
- . To assess the likelihood of a redistribution of body fat from the hips and thighs (gynaecoid) to the abdomen (android) associated with hormone replacement therapy in perimenopausal and menopausal women.
- **HRT definition**
- unopposed oestrogen therapy (E) or oestrogen therapy with combined, cyclic or continuous progestogen therapy (E+P).
- **Parameters examined**
- . The effect of E compared with placebo or no treatment
- . The effect of E+P compared with placebo or no treatment

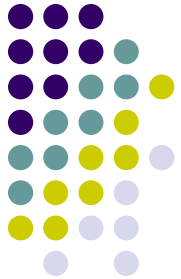
TRIALS

- Nine RCTs of E vs placebo or no therapy with a total of 12,221 women
- Twenty RCTs of E+P vs placebo or no therapy with a total of 18,365 participants

UNOPPOSED OESTROGEN

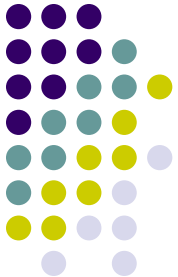
- The use of unopposed oestrogen has no significant effect on weight gain compared to those women not on HRT (0.03kg, CI -0.61, 0.67).
- There was no signicant difference in BMI between women using unopposed oestrogen and non-HRT users (-0.14, CI -0.40, 0.12).
- Insufficient data were available for meta-analysis of waist-hip ratio, and no data were available for analysis of fat mass or skinfold thickness.

COMBINED OESTROGEN + PROGESTOGEN



- The use of a combined regimen of E+P has no significant effect on mean weight gain compared to those women not using HRT (0.04 kg, CI -0.42, 0.50).
- Combined E+P regimens have no significant effect on mean BMI increase compared to those women not on HRT (-0.10, CI -0.27, 0.07).
- Insufficient data exist to enable meta-analysis of waist-hip measurement and skinfold thickness

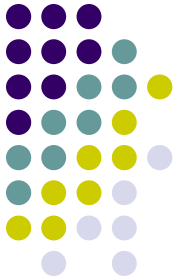
Cardiovascular disease globally 2009 http://www.who.int/mediacentre/factsheets/fs317/en/index.html



- CVDs are the number one cause of death globally: more people die annually from CVDs than from any other cause.
- An estimated 17.1 million people died from CVDs in 2004, representing 29%of all global deaths. Of these deaths, an estimated 7.2 million were due to coronary heart disease and 5.7 million were due to stroke.
- Low- and middle-income countries are disproportionally affected: 82% of CVD deaths take place in low- and middle-income countries and occur almost equally in men and women.
- By 2030, almost 23.6 million people will die from CVDs, mainly from heart disease and stroke. These are projected to remain the single leading causes of death. The largest percentage increase will occur in the Eastern Mediterranean Region. The largest increase in number of deaths will occur in the South-East Asia Region.

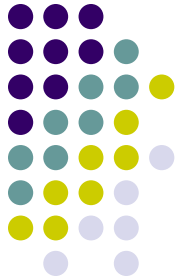
Cardiovascular disease

European Cardiovascular Disease Statistics 2008
http://www.heartstats.org/datapage.asp?id=7683



- Cardiovascular disease (CVD) is the main cause of death in Europe killing over 4.3 million people per year (54% deaths in women and 43% deaths in men).
- CHD accounts for 1.92 million deaths killing 1 in 5 women and men
- Stroke accounts for 1.24 million deaths affecting 1 in 6 women and 1 in 10 men.
- The cost of CVD to the EU economy is estimated at €192 billion per year. Of the total cost of CVD in the EU, 57% is due to direct health care cost, 21% to productivity losses and 22% to the informal care of people with CVD.

Risk factors for CHD



- Smoking
- Diet: fruit and vegetable intake
- Physical activity
- Alcohol
- Blood pressure
- Blood cholesterol
- Overweight and obesity/abdominal fat distribution
- Diabetes

INTERHEART study

- Western Europe 63% heart attacks due to abdominal obesity
- Abdominal obesity doubles risk of myocardial infarction

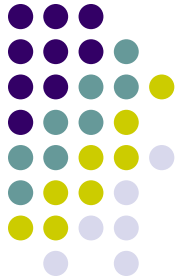
- Yusuf S, et al ; INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet. 2004;364(9438):937-52.

Obesity and stroke

- Stroke is a major cause of long-term disability and death for women in the United States. The lifetime risk of stroke for women aged 55 to 75 years is {approx}20%, which is notably higher than that for men (14% to 17%).
- Stroke rates in midlife women have tripled in the past 2 decades (successive NHANES cohorts between 1988 to 1994 and 1999 to 2004), whereas the rates in men stayed flat.
- Obesity is associated with a >2-fold increased risk of ischemic stroke in women.
- ARIC (Atherosclerosis Risk in Communities) study, degree of obesity, defined by body mass index, waist circumference, or waist-to-hip ratio, was a significant risk factor for ischemic stroke regardless of sex or race.
- Towfighi et al: increased waist circumference was the only independent stroke risk factor explaining the increasing stroke rates among women in the past 2 decades.

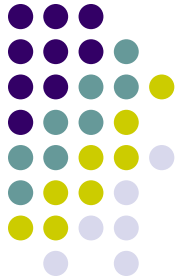
- Rexrode KM. Emerging risk factors in women. Stroke. 2010;41(10 Suppl):S9-11.
- Towfighi A, et al. Weight of the obesity epidemic. Rising stroke rates among middle-aged women in the United States. *Stroke.* 2010; 41: 1371–1375.

Managing the menopause in women at risk of CHD



- Primary prevention
- Timing?
- Secondary prevention
- Symptomatic woman or one with POF with pre-existing CHD.

Coronary heart disease per 10,000 women per year (WHI)



- Combined HRT
- The excess absolute risk at
- 50-59 + 5
- 60-69 +1
- 70-79 + 23

- Oestrogen alone HRT
- The reduced absolute risk at
- 50-59 - 10
- 60-69 years -5
- with an excess risk at 70-79 + 4

Years since menopause and starting HRT

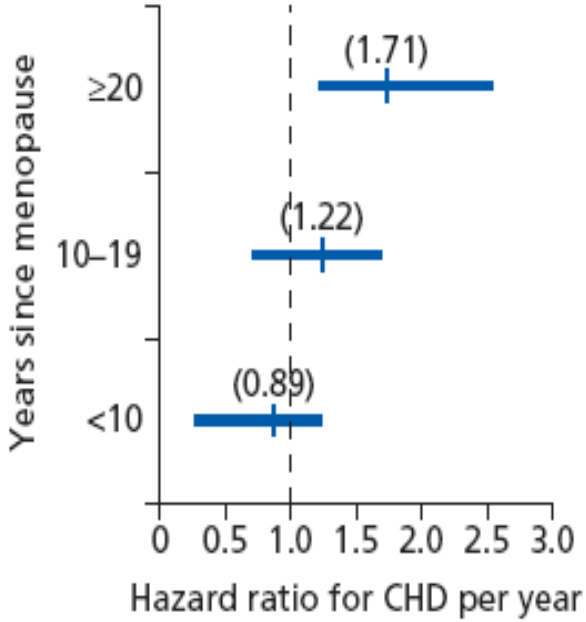
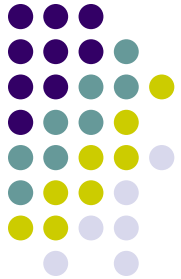


Figure 7.1 Influence of time since menopause on the effect of hormone replacement therapy on coronary heart disease. Adapted from Manson (2003)

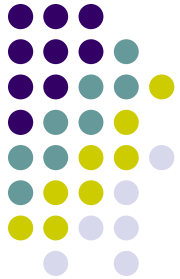
Coronary heart disease per 10,000 women per year WHI combining both arms



- Absolute risk at
- 50-59 -2
- 60-69 -1
- 70-79 + 19

Rossouw JE, et al. Postmenopausal hormone therapy and risk of cardiovascular disease by age and years since menopause. JAMA. 2007;297:1465-77.

Benefits and risks of postmenopausal hormone therapy when it is initiated soon after menopause. Prentice et al Am J Epidemiol. 2009;170:12-23.



- The interpretation is complicated, for several reasons.
- First, there is the multiple testing issue.
- Another reason for a cautious interpretation, and a limitation of the current analyses more generally, is that hazard ratios pertaining to 5 or more years from hormone therapy initiation were derived mainly from the observational study.
- In addition, there were few recently postmenopausal women without prior hormone therapy who were followed in WHI during their early years of hormone therapy use, so corresponding hazard ratios were imprecisely estimated and may have depended on modeling assumptions.

Timing

- Kronos Early Estrogen Replacement Study (KEEPS) is testing the hypothesis that HT when initiated early in menopause reduces progression of atherosclerosis
- Early Versus Late Intervention Trial With Estradiol (ELITE) study is examining the effects of oral 17beta-estradiol on the progression of early (subclinical) atherosclerosis and cognitive decline in healthy postmenopausal women

Randomized controlled trials of HRT as secondary prevention for coronary heart disease.

CEE=conjugated equine estrogens.
MPA=medroxyprogesterone acetate.

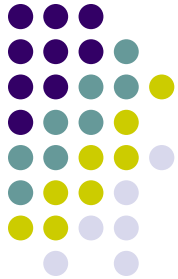
Study	Hormone replacement therapy	Route	Relative risk (95% confidence interval) of acute myocardial infarction	N
HERS (Hulley, 1998)	CEE/MPA	Oral	0.99 (0.8 to 1.22)	2769
PHASE (Clarke, 2002)	17β-oestradiol	Patch	1.29 (0.84 to 1.95)	255
WEST (Viscoli, 2001)	17β-oestradiol	Oral	1.1 (0.6 to 1.9)	664
ESPRIT (Cherry, 2002)	Oestradiol valerate	Oral	0.99 (0.7 to 1.41)	1017

What regimen

- Transdermal oestrogen
- Which progestogen as mainly have data on MPA?
- Observational studies suggest that micronized progesterone or dydrogesterone may have a better risk profile than other progestogens with regard to thrombotic risk

- EMAS position statement:
- Managing the menopause in the context of coronary heart disease
- Karin Schenck-Gustafsson, MD,PhD,FESC,FACC on behalf of EMAS board Maturitas 2011. In Press.

Stroke cases per 10,000 women per year (WHI).

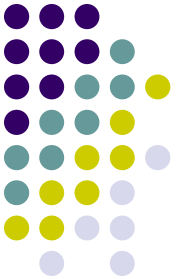


- Combined HRT
- Excess absolute risk at 50-59 + 4
- 60-69 + 9
- 70-79 + 13

- Oestrogen alone HRT
- Excess absolute risk at 50-59 0
- 60-69 +19
- 70-79 +14

Increased risk ischemic but not haemorrhagic stroke

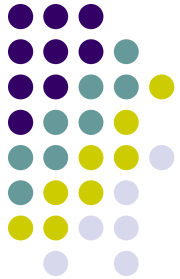
Stroke cases per 10,000 women per year WHI combined trials.



- Hormone therapy increased the risk of stroke (HR, 1.32; 95% CI, 1.12-1.56).
- Risk did not vary significantly by age or time since menopause.

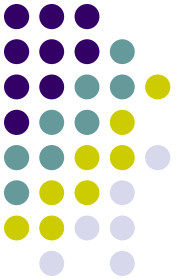
Rossouw JE, et al. Postmenopausal hormone therapy and risk of cardiovascular disease by age and years since menopause. JAMA. 2007;297:1465-77.

Stroke secondary prevention



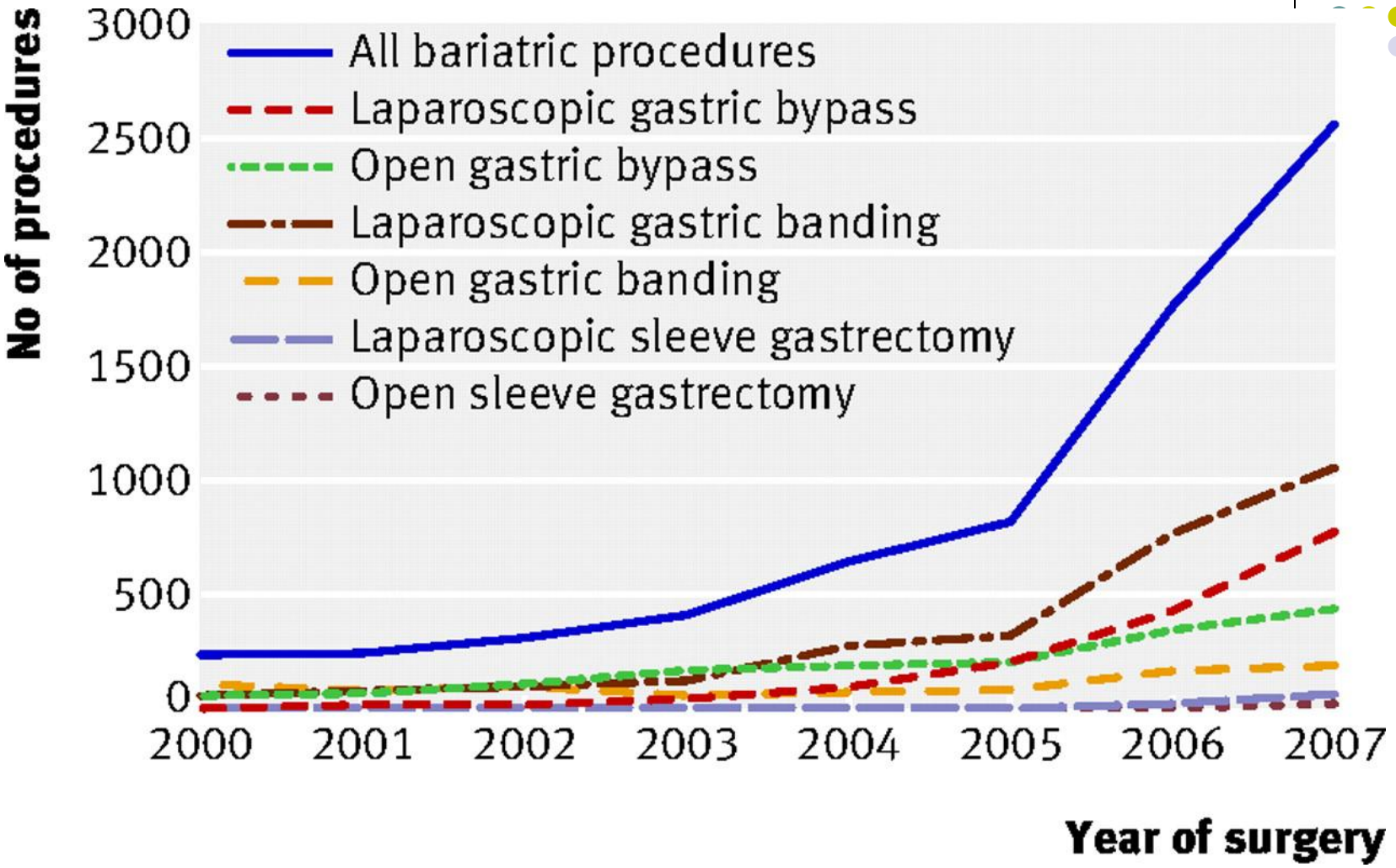
- A randomized, double-blind, placebo-controlled trial of estrogen therapy (1 mg of estradiol-17beta per day) in 664 postmenopausal women (mean age, 71 years) who had recently had an ischemic stroke or transient ischemic attack. Women were recruited from 21 hospitals in the United States and were followed for the occurrence of stroke or death.
- During a mean follow-up period of 2.8 years, there were 99 strokes or deaths among the women in the estradiol group, and 93 among those in the placebo group
- CONCLUSIONS: Estradiol does not reduce mortality or the recurrence of stroke in postmenopausal women with cerebrovascular disease.
- Viscoli CM, et al. A clinical trial of estrogen-replacement therapy after ischemic stroke. N Engl J Med. 2001;345:1243-9.

The U.S. Department of Health and Human Services (HHS) awarded more than $119 million to states and U.S. territories to support public health efforts to reduce obesity, increase physical activity, improve nutrition, and decrease smoking. 2009



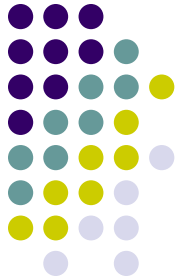
- **Outcome objectives:**
- Decrease prevalence of obesity.
- Increase physical activity.
- Improve dietary behaviors related to population burden of obesity and chronic diseases.
- **Principal target areas:**
- Increase physical activity.
- Increase the consumption of fruits and vegetables.
- Decrease the consumption of sugar sweetened beverages.
- Increase breastfeeding initiation, duration and exclusivity.
- Reduce the consumption of high energy dense foods.
- Decrease television viewing.

Changes in type of operation over time and trends in uptake of laparoscopic surgery.



Burns E M et al. BMJ 2010;341:bmj.c4296

Bariatric surgery



- Not universally available
- Postcode lottery in UK with different interpretations of guidelines
- Obesity patients need to weigh more in order to qualify for NHS-funded weight-loss surgery in North Somerset than they do elsewhere. BBC News 27.10.10
- People with no other health problems need to have a body mass index of 50, compared to 40 in Somerset and Bath and North East Somerset (Banes).
- North Somerset Primary Care Trust (PCT) said the decision to insist on a BMI of at least 50 for gastric bypass or gastric banding operations was made in conjunction with Bristol and South Gloucestershire NHS Trusts.
- But the National Obesity Forum said the trust was failing to follow government guidelines which "should be honoured".
- Surgery in private sector with poor follow up


PA