



Decrease in breast cancer and HRT

Pr A.Gompel
University Paris Descartes

Disclosure of interest

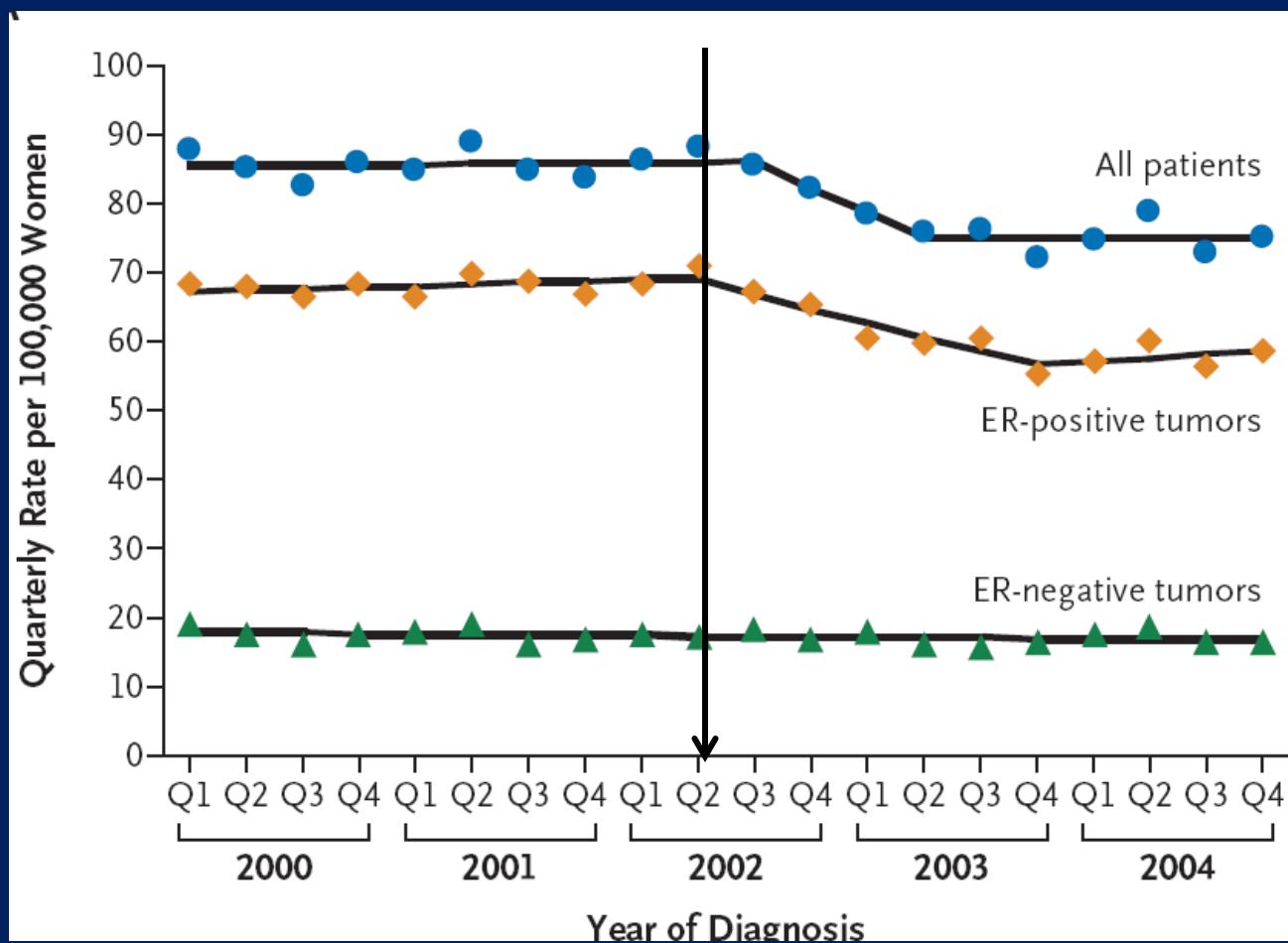
- Member of the Advisory council for EURAS- HRT sponsored by BAYER
- Member of the Steering Committee of CASHMERE sponsored by Pfizer
- Member of the Advisory Committee on Firazyr Shire
- Research grants from:
 - Organon AZKO
 - Panterhei Biosciences
 - Besins
 - Novartis
 - HRA-Pharma

Ravdin: decrease in breast cancer incidence

(NEJM 2007)

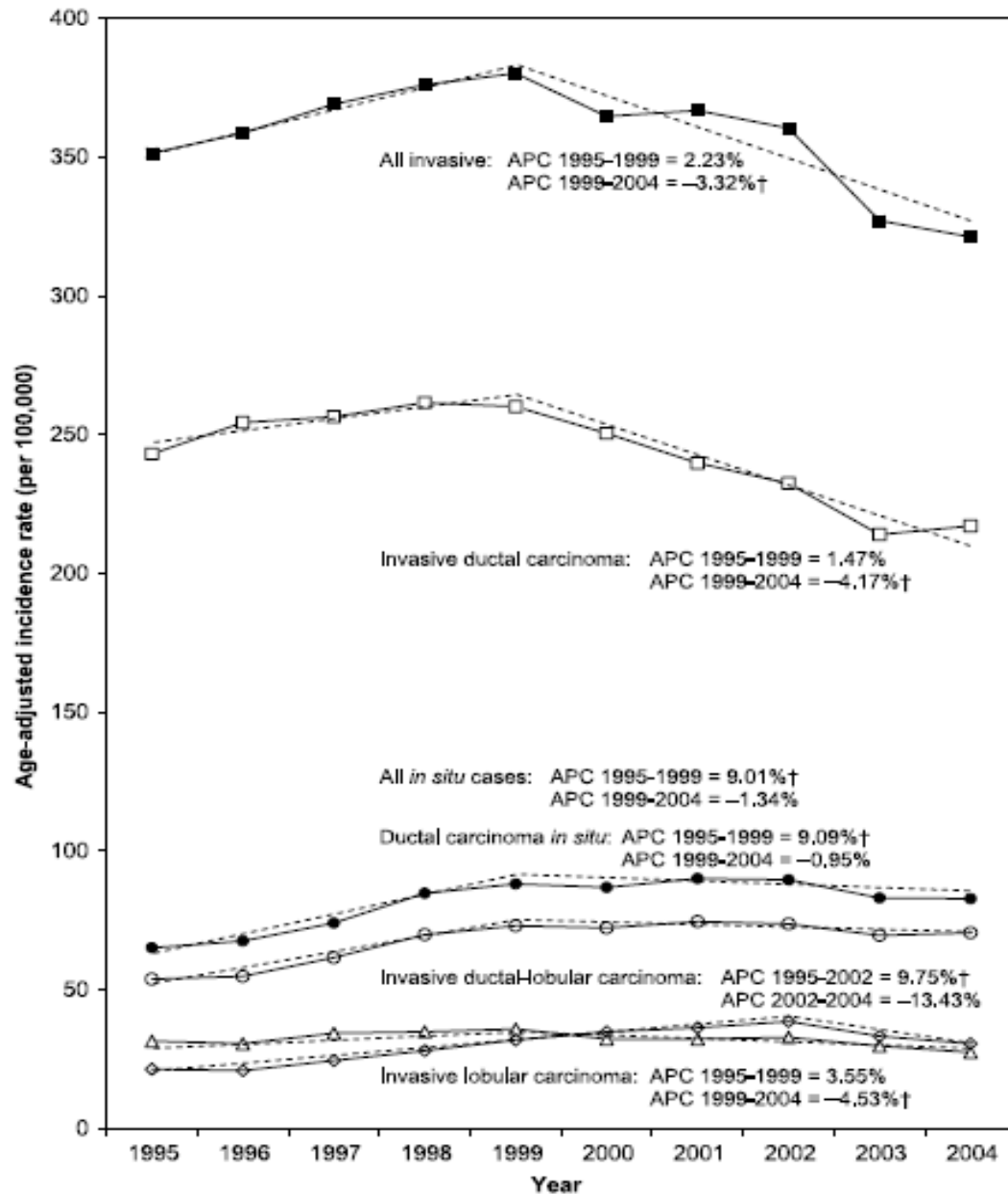
Decrease was evident only in women who over 50 years of age -11.8% 50 and 69 years, - 11.1% >70 years of age

- Mainly ER positive tumors



Li (USA Registries)

(Cancer Epidemiol Biomarkers Prev 2007)



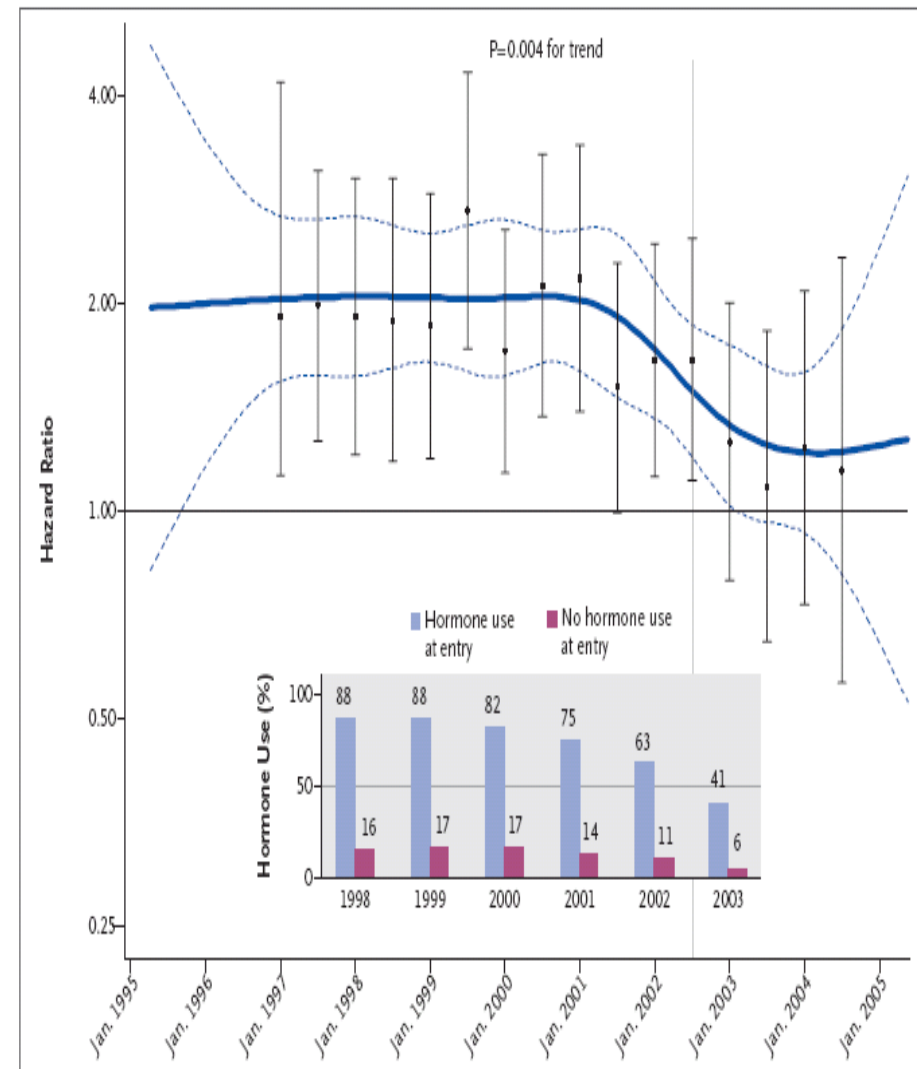
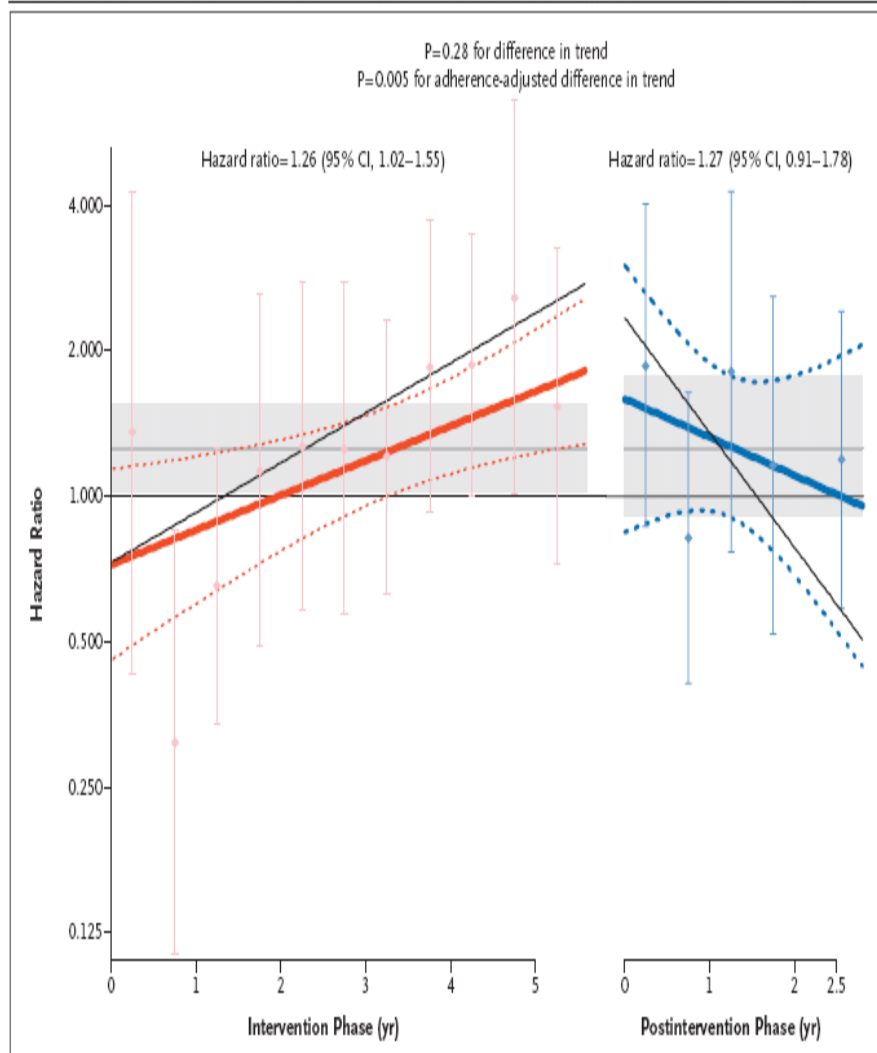
The majority of these declines began around **1998** and all began **before 2002**

Question of

- Causality
- Ecological Epidemiology

WHI: RCT & Observational

(Cheblowski et al N Engl J Med 2009)



Epigenetic
MicroRNA
Tumor
suppressor genes

**Number of cancer
cells**

10^{12}
(1 kg)

10^9

Initiators

promoter

treatment

**Genetic
suceptibility**

transformed cells occult cancer diagnostic death age

PREVENTION

SCREENING

TREATMENT

50-100days X30-35 doubling to get 1cm:
→ i.e. > 4y-10y

“same decrease”

- In Australia
- New Zealand
 - France
- Germany
- England
- Not in
- Norway,
- Sweden,
- Scotland,
 - NDL
 - Italy

Are these observations plausible
and why the differences between
countries?

Incidence may vary with

- **Screening programs**
 - Compliance: increase or decrease
 - Efficiency: saturation effect:
increase in situ vs invasive
- **Risk factors**
- Existence of registries
- Different HRT regimen/products

Norway

Typical effect of initiation of screening

(Zahl & Maehlen, NEJM 2007)

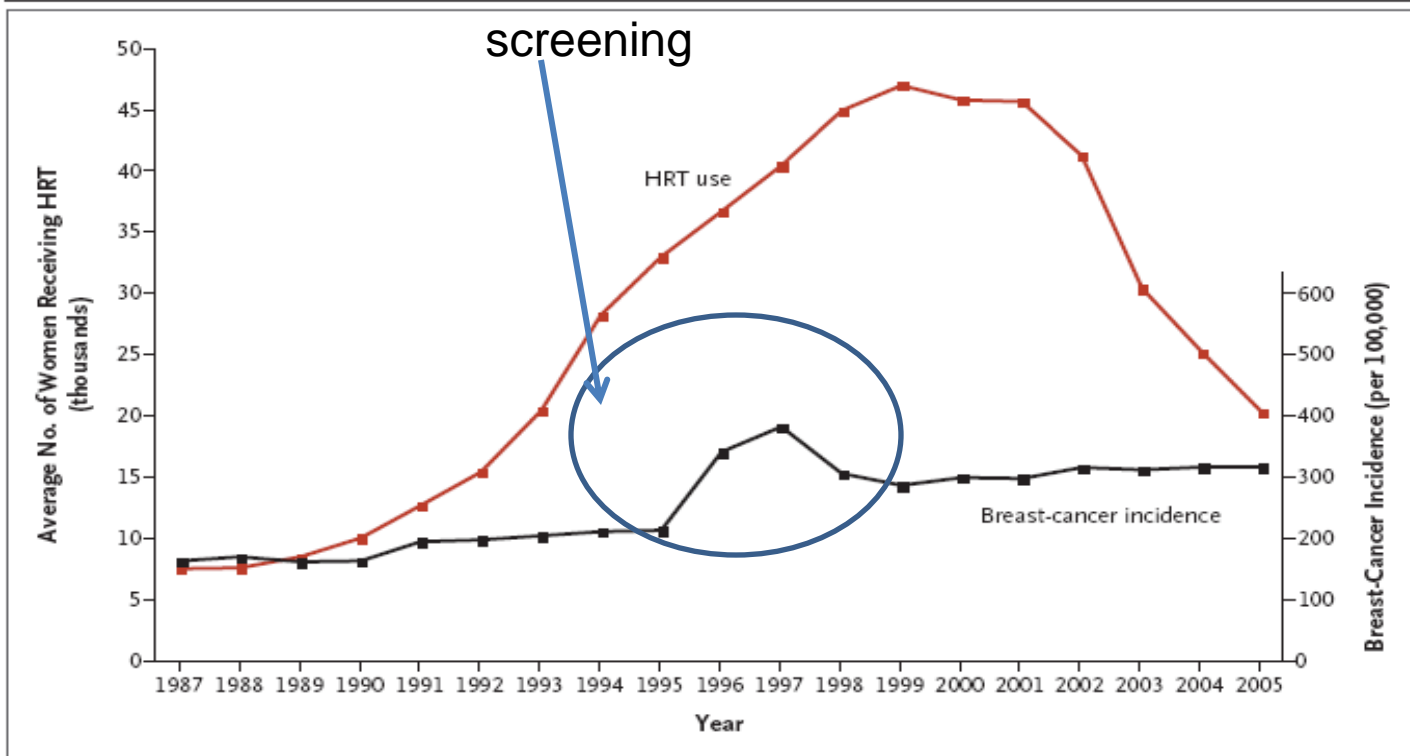


Figure 1. Hormone-Replacement Therapy (HRT) and Breast-Cancer Incidence among Women between the Ages of 50 and 69 Years in Four Norwegian Counties.

The population of the four counties represented in the graph constitutes 40% of the 4.6 million people living in Norway. The red curve indicates the average number of women receiving HRT per year, based on the sales of defined daily doses of HRT divided by 365 days. The black curve shows the breast-cancer incidence. Mammographic screening was introduced in 1996–1997 in this population.

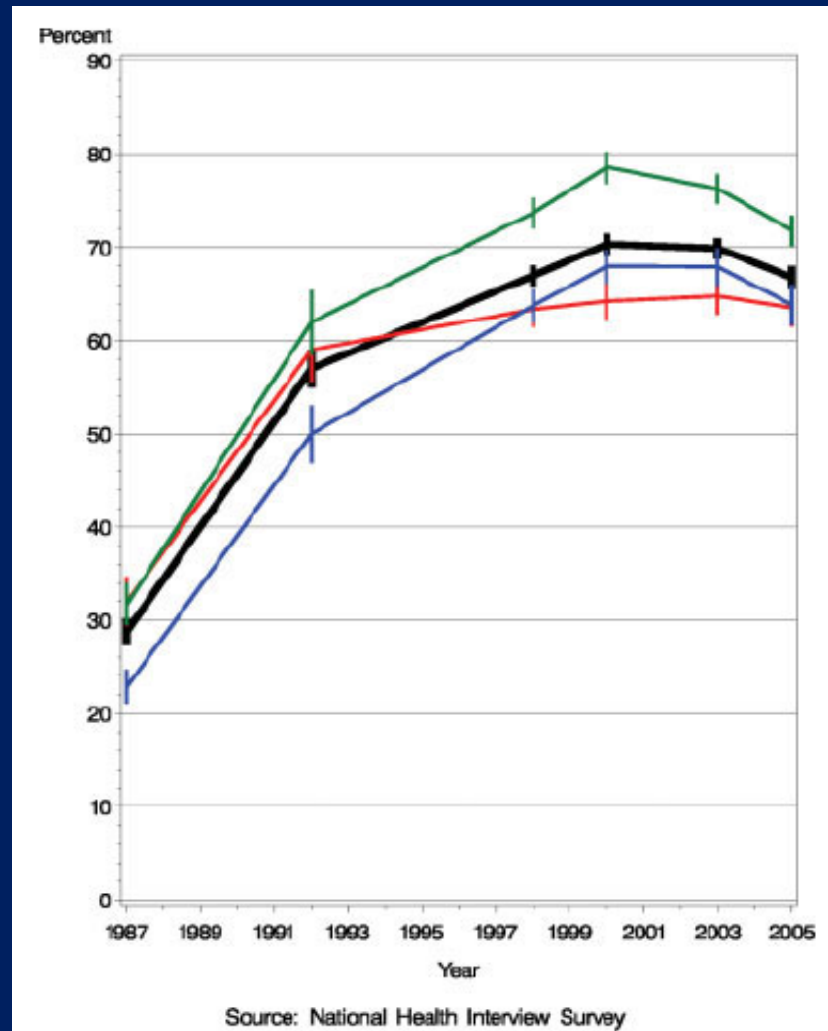
Stable rate of breast cancers and screening

Screening in the USA

Decrease in screening compliance

reported in
The Kaiser
Permanente
(Glass et al, JNCI,
2007,99,1152)

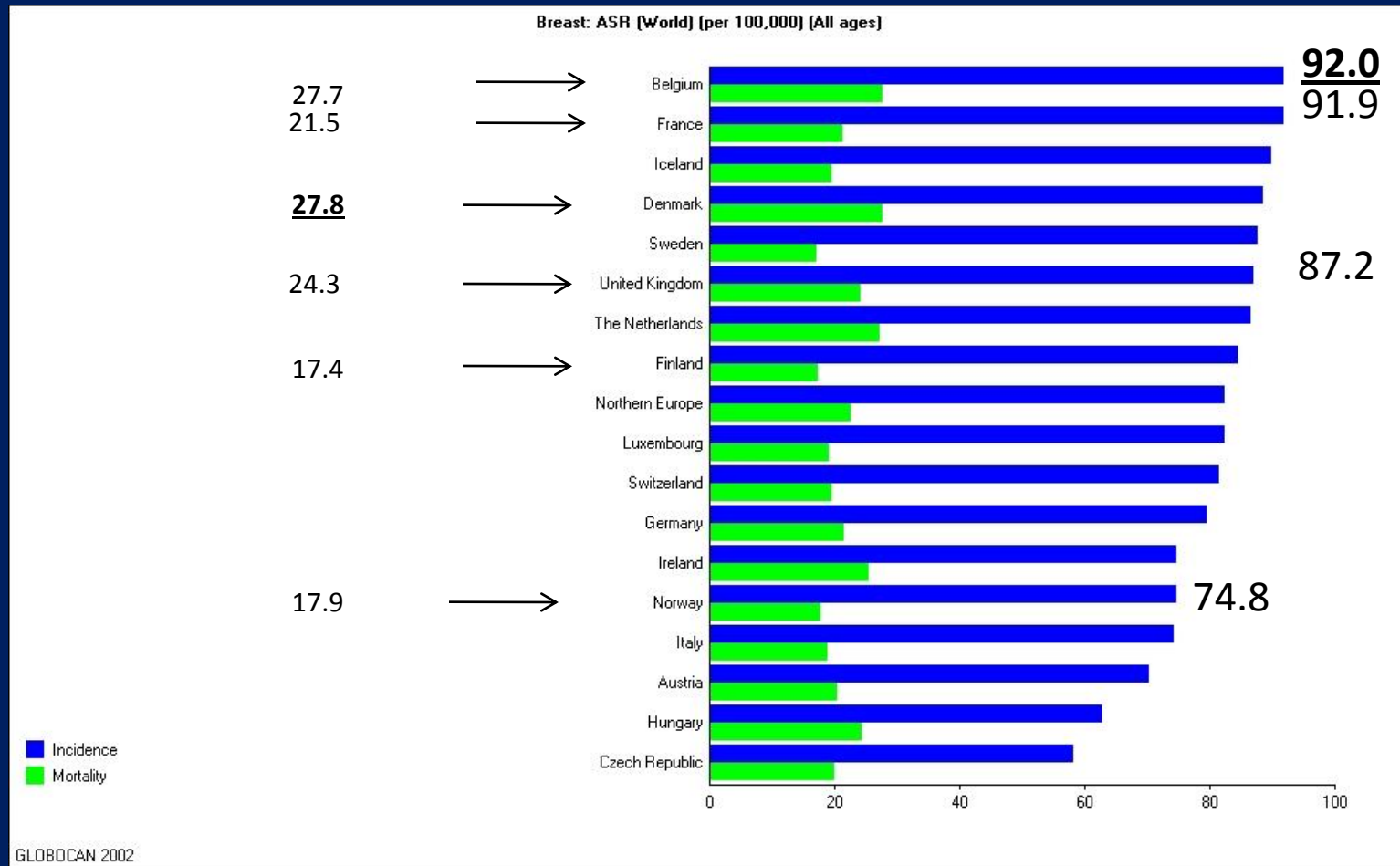
But also in the NHIS



Breen et al, Cancer 2007

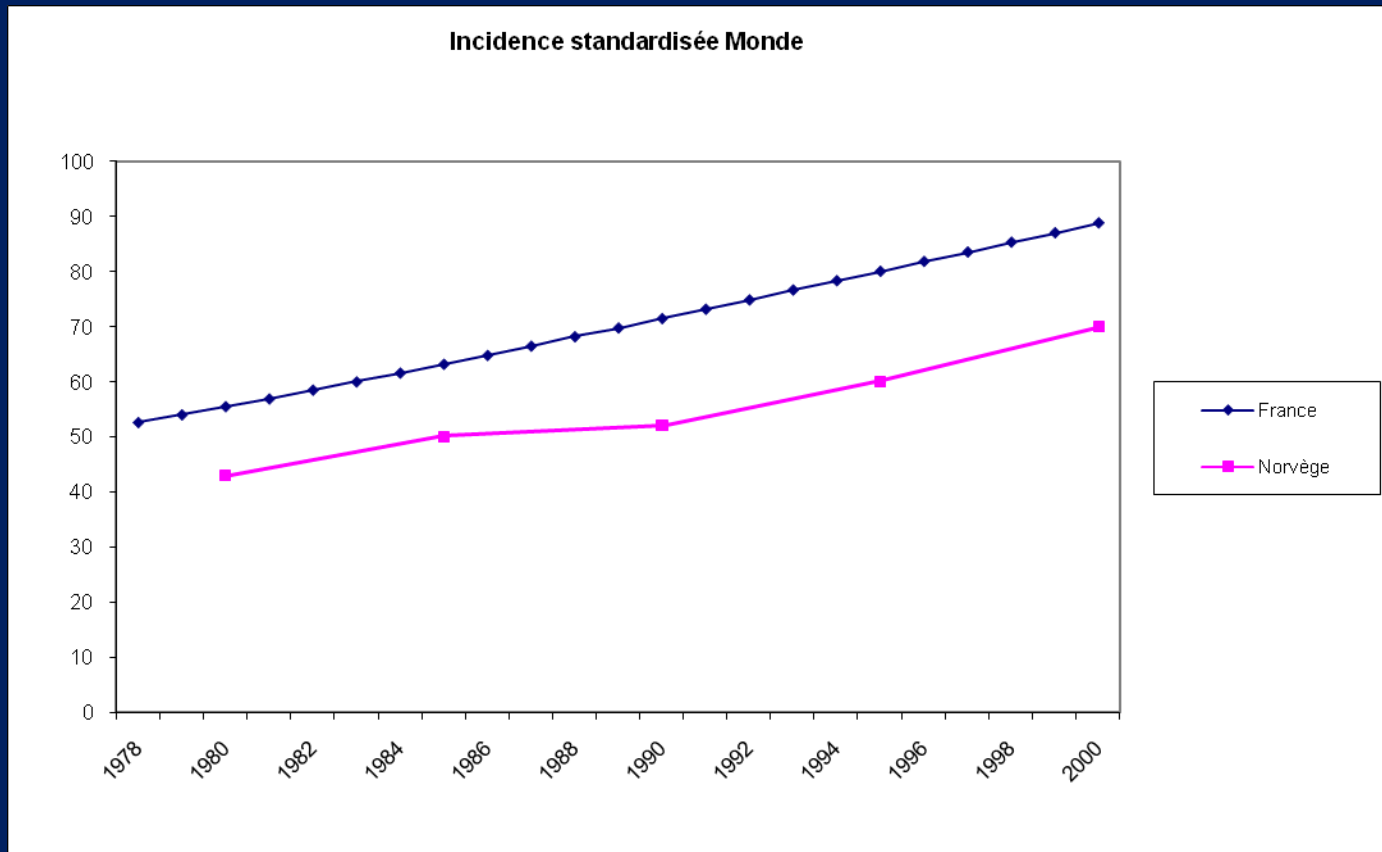
Risk factors

Incidence and mortality in Europe



France and Norway:

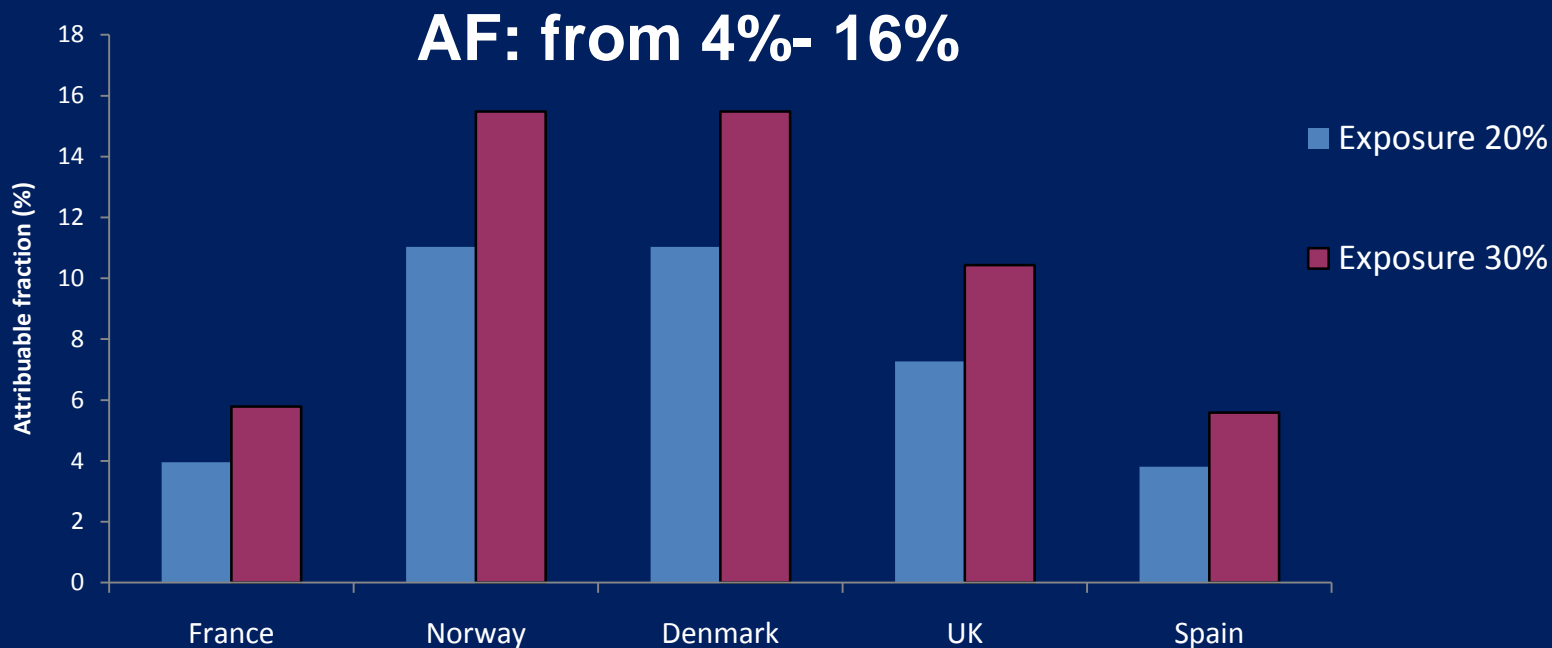
low and high incidence but parallel increase during the last decades



Thus no simple explanation of the variation in BC incidence : risk factors are not similar

→ how much HRT has impacted ?
Increase in HRT use is recent: end of the 1990s

Attributable fraction of breast cancer to HT use with different hypothesis



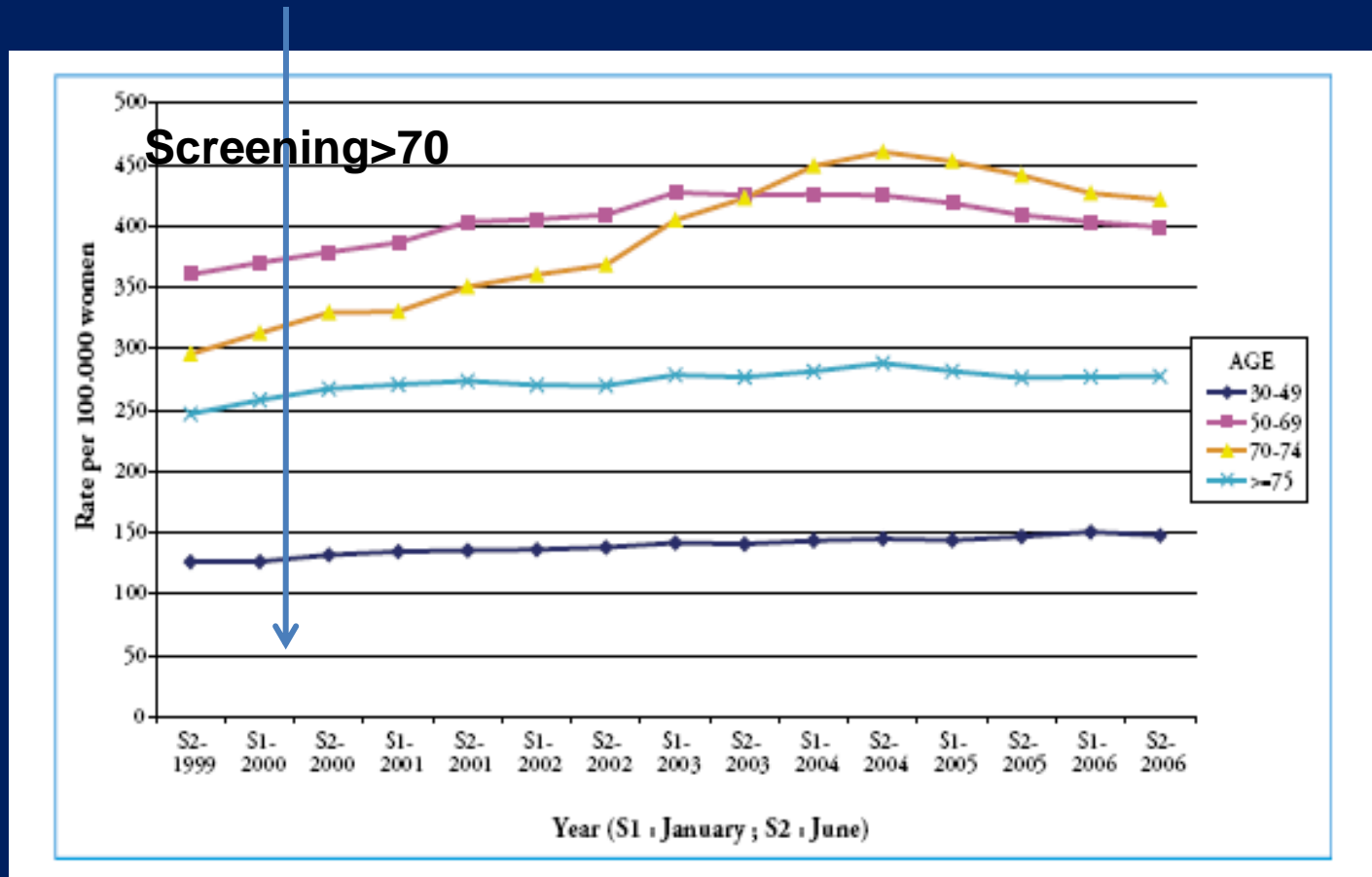
RR BC :
France : 1.26 based on E3N
Norway : 1.8 based on Lund et al
Denmark : 1.8 based on publications
UK : 1.5 MWS
Spain : 1.26 hypothesis close to France

AF calculate using RR and exposition from the available literature

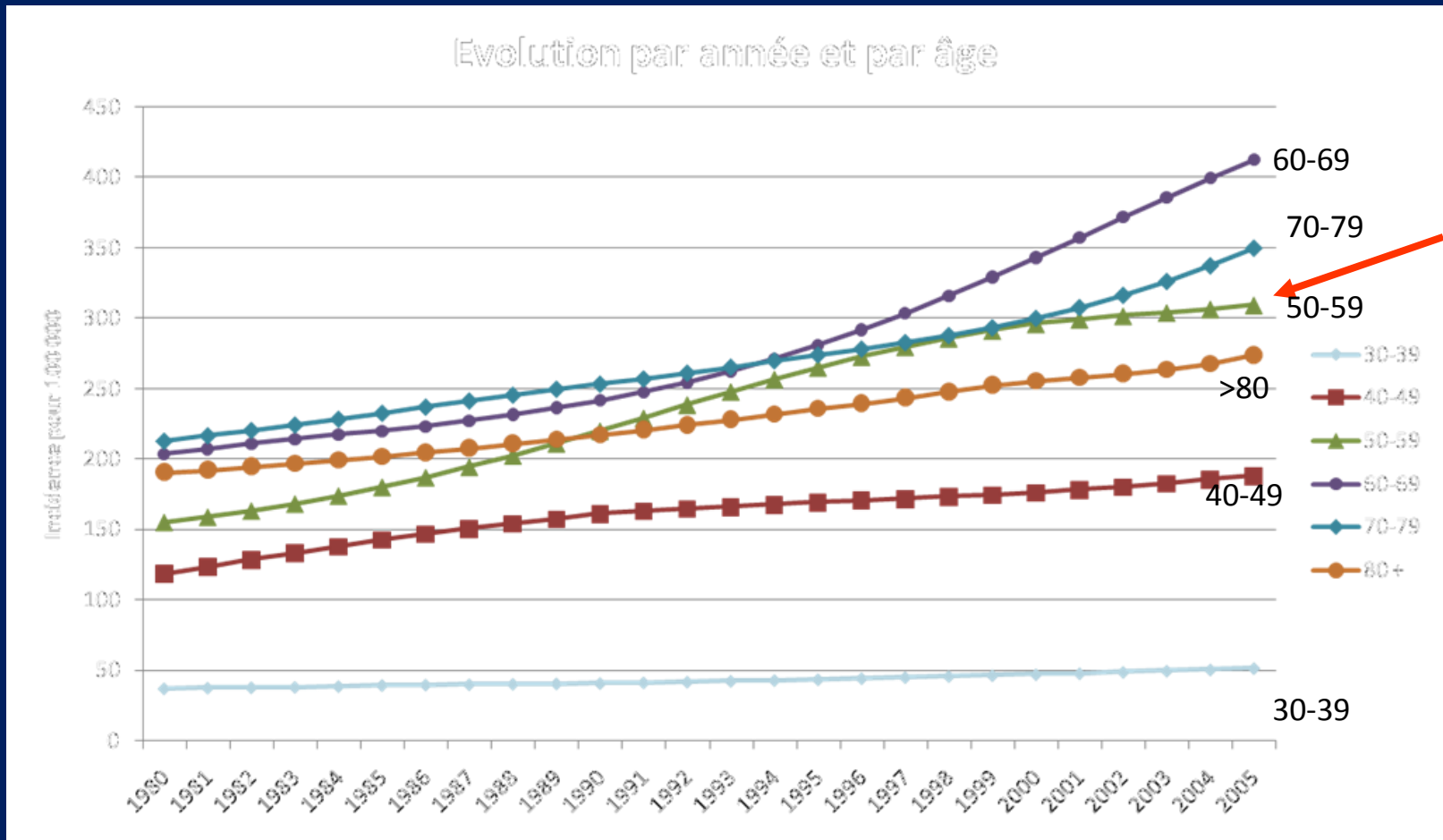
Plu-Bureau and Gompel

France: by chronic disease

65-70% of women have regular screening and 10% new?

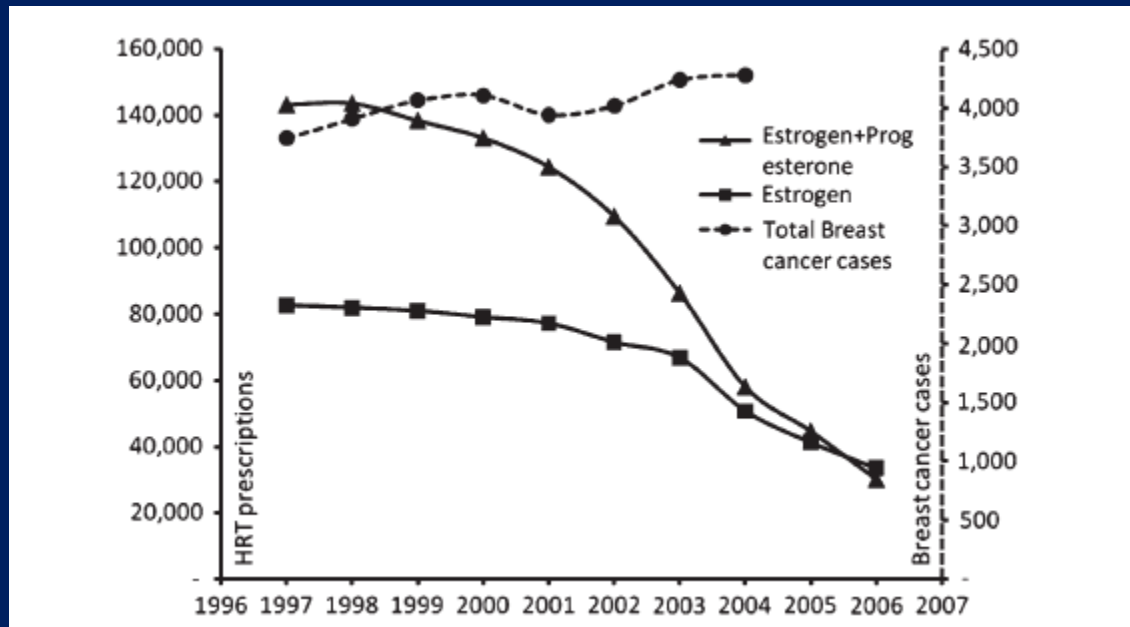


France: by registries



Scotland

Screening since 1983-88, stable, 30% of HRT use UK



(VAIDYA JS, JNCI 2008,8;297)

No decrease in women >50y

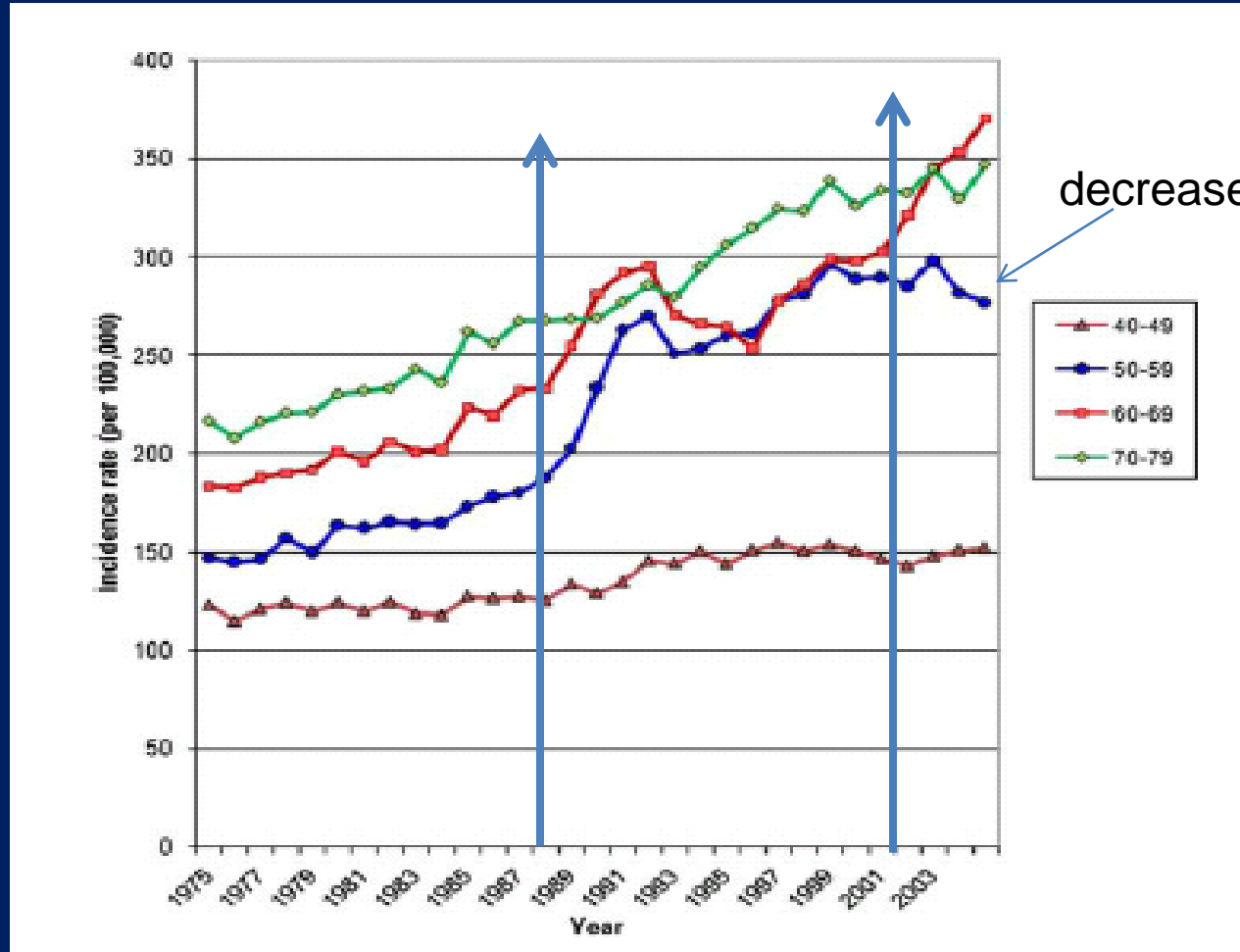
Screening started

1988: 50-64 years

2002: 65-69 years

England

(Parkin ,Eur J Cancer,2009)



DIFFERENTIAL EFFECT ON HISTOLOGY?

LOBULAR

→ MORE RAPID GROWTH

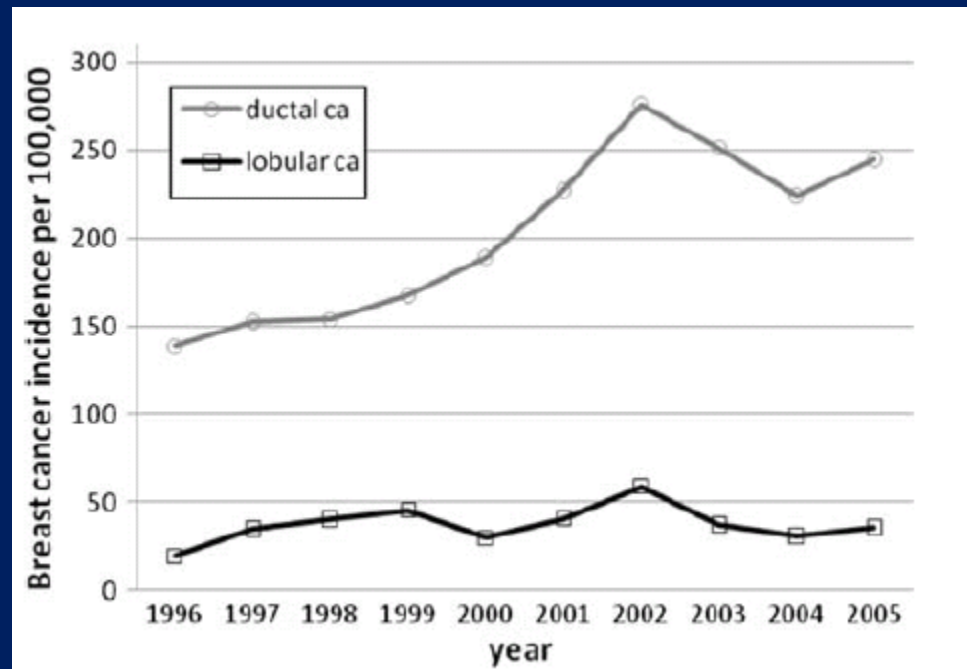
→ LESS INCREASE WITH TIME

MWS ERT (Lancet 2006)

Li & Daling (CEBP 2008)

Cancer Prevention Study II Nutrition Cohort (Calle et al Cancer, 2009)

Decrease in lobular and ductal in Flamish Belgium (Limburg)

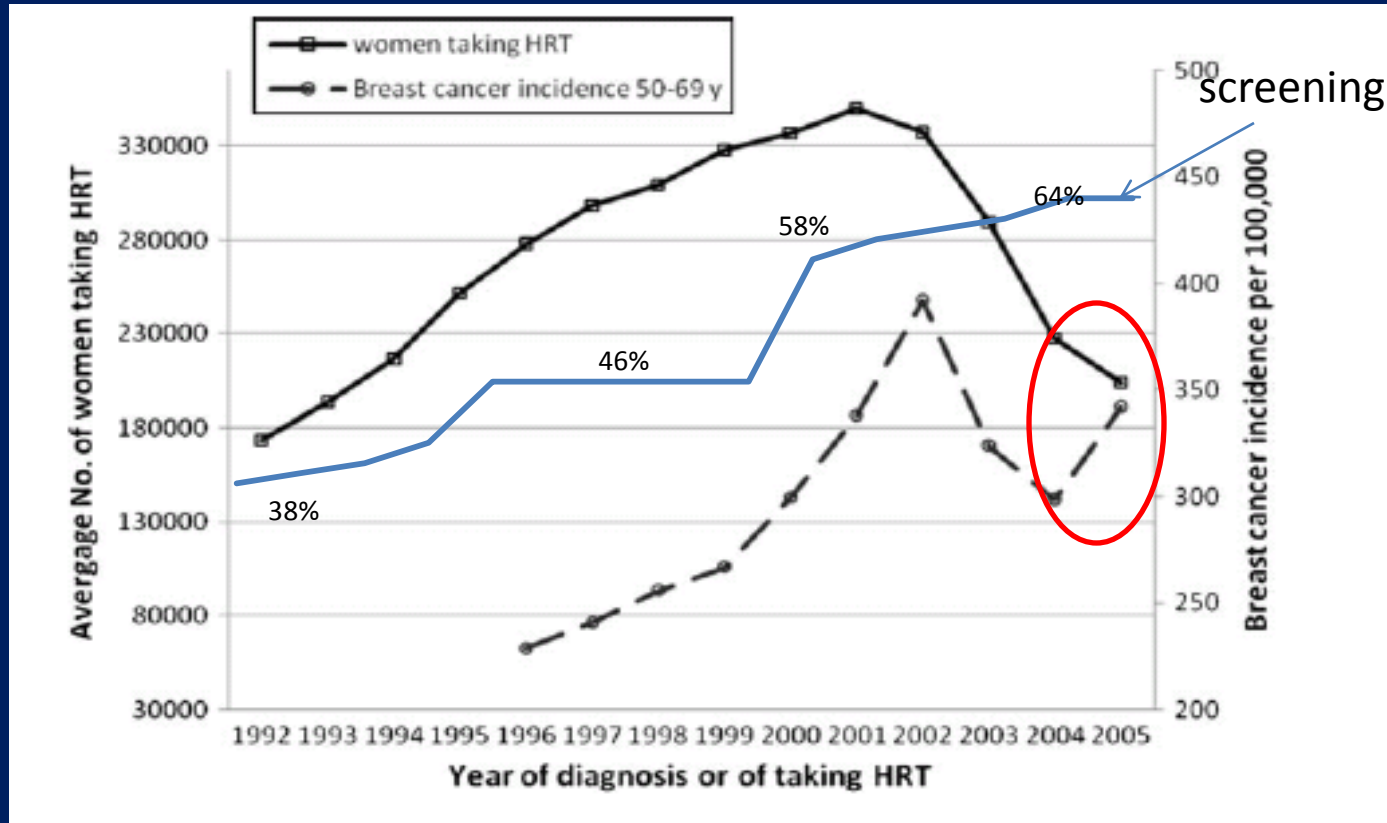


(Vankrunkelsven et al, Breast cancer Res
Treat 2009)

**DECREASE IN INCIDENCE?
DELAY IN DIAGNOSTIC?**

Breast cancer incidence and HRT use in Flamish Belgium (Limburg)

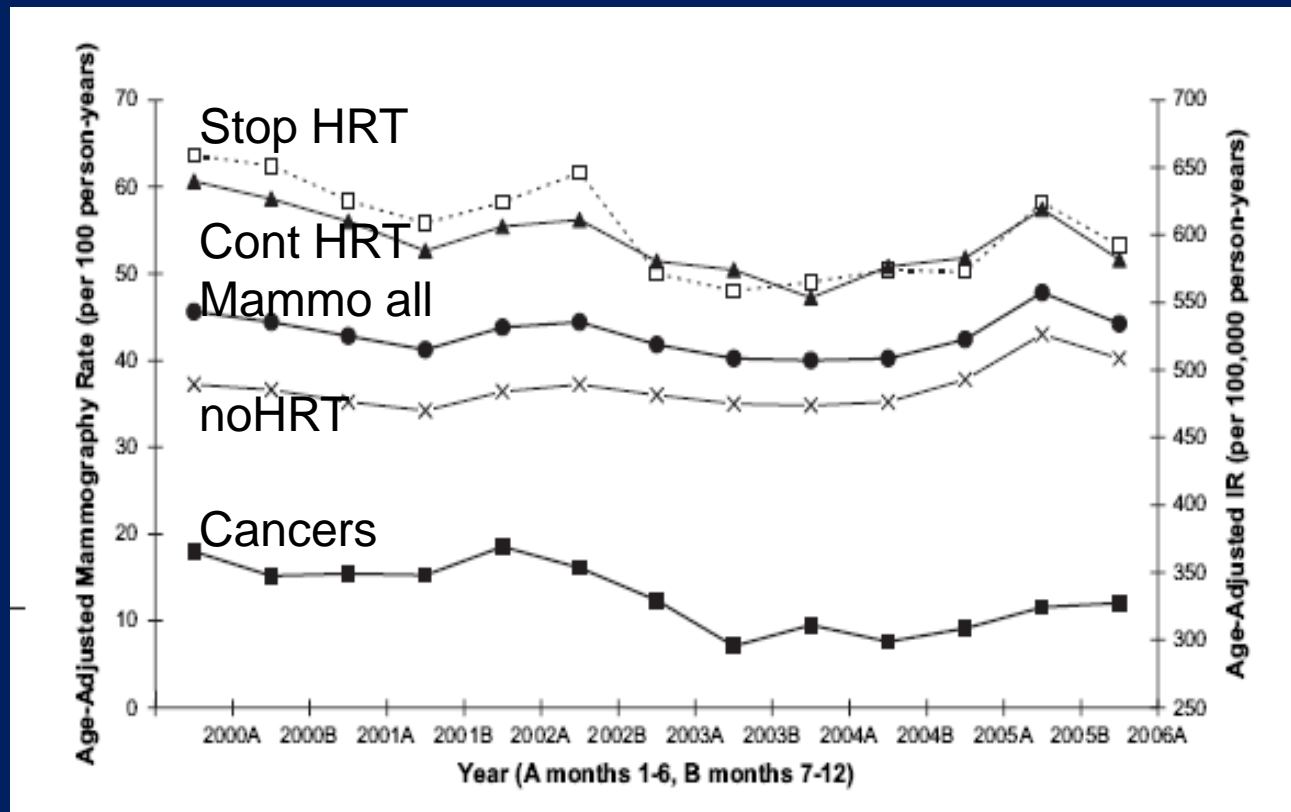
(Vankrunkelsven et al, Breast cancer Res treat 2009)



As a consequence of less HRT: less mammograms

(Caan et al JNCI 2008;8;297)

In the USA



Conclusions

- Despite growing risk factors decrease in breast incidence ...
- Factors vary between countries
- Part of HRT stop in the recent decrease?
- Major factor: screening