The Million Women Study

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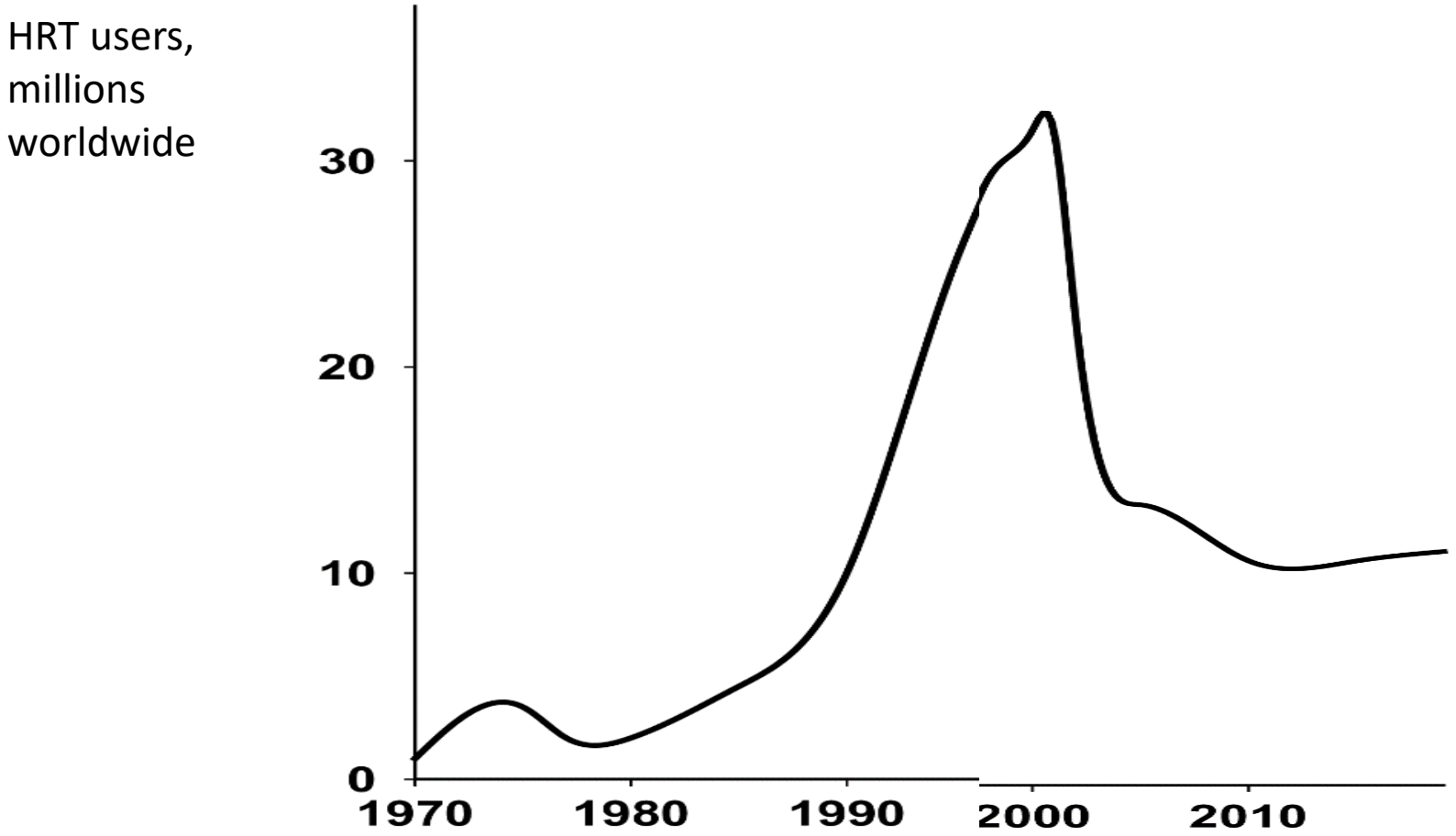
The Million Women Study

- **Why we did the study**
- **What we do**
- **What we have found – breast cancer, smoking, alcohol**
- **Now and the future – dementia, osteoporosis**
- **Changing research- opportunities and challenges for a long term study**

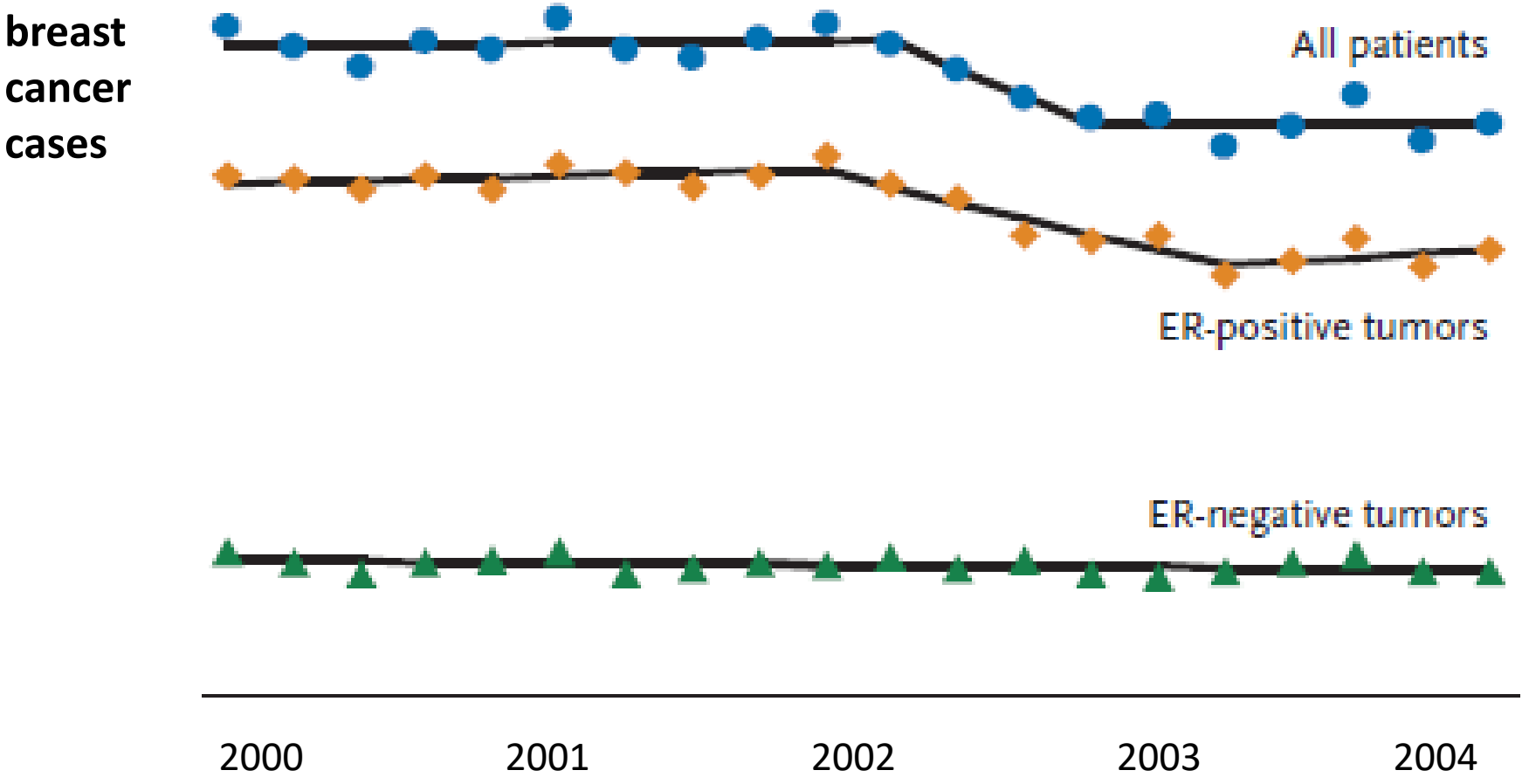
HRT use rose rapidly in the 1980s and 1990s

Europe, USA: by 2000 up to 1 in 3 postmenopausal women taking HRT

lack of evidence risks (breast cancer?) and benefits (bones, heart?)



Fall in cases of breast cancer with fall in HRT use- estimated tens of thousands of cases avoided worldwide



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Recruitment

- 1996-2001, from NHS Breast Screening Programme
- Questionnaire in invitation to routine screening: HRT use, demographics, lifestyle and health
- 1.3 million women, average age 56
- 1 in 4 UK women born in 1935-1950

Follow-up

- Repeat questionnaires and link to NHS records
- 20 year record; women aged 78; only 1.5% lost to follow-up; 1.1 million still alive

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Prospective cohort study [longitudinal study]

Recruit a cohort of people, collect information on exposure factors at start, and follow health of whole cohort over time

See which factors are associated with development of disease – eg compare breast cancer in women taking or not taking HRT

UK NHS: well placed and linkage allows complete, cheap, follow-up.

: breast screening: could recruit screened women at low cost

: funders with vision

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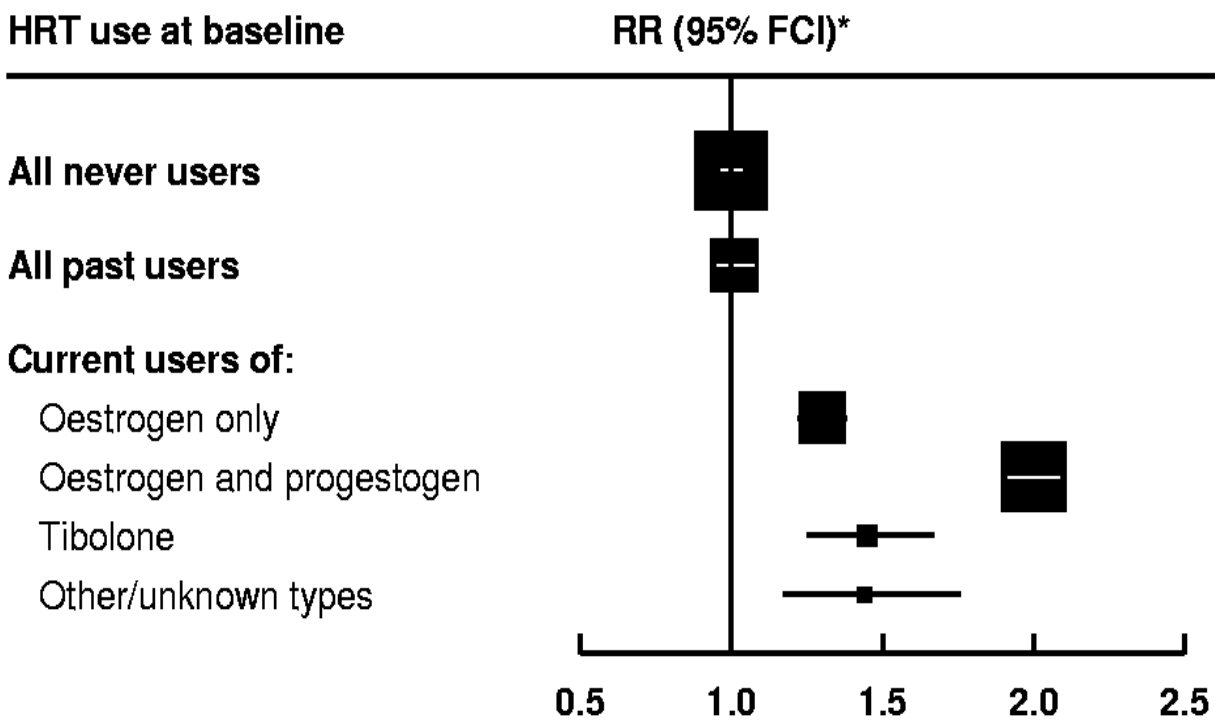
Cohort study

- Unlike a trial- can study many different outcomes and different exposures, and change focus over time- not only for HRT and cancer
- Minimises biases due to selective recall and selective response

- Observational: associations not causation
- WHI USA trial is complementary

Women taking HRT have higher risk of breast cancer

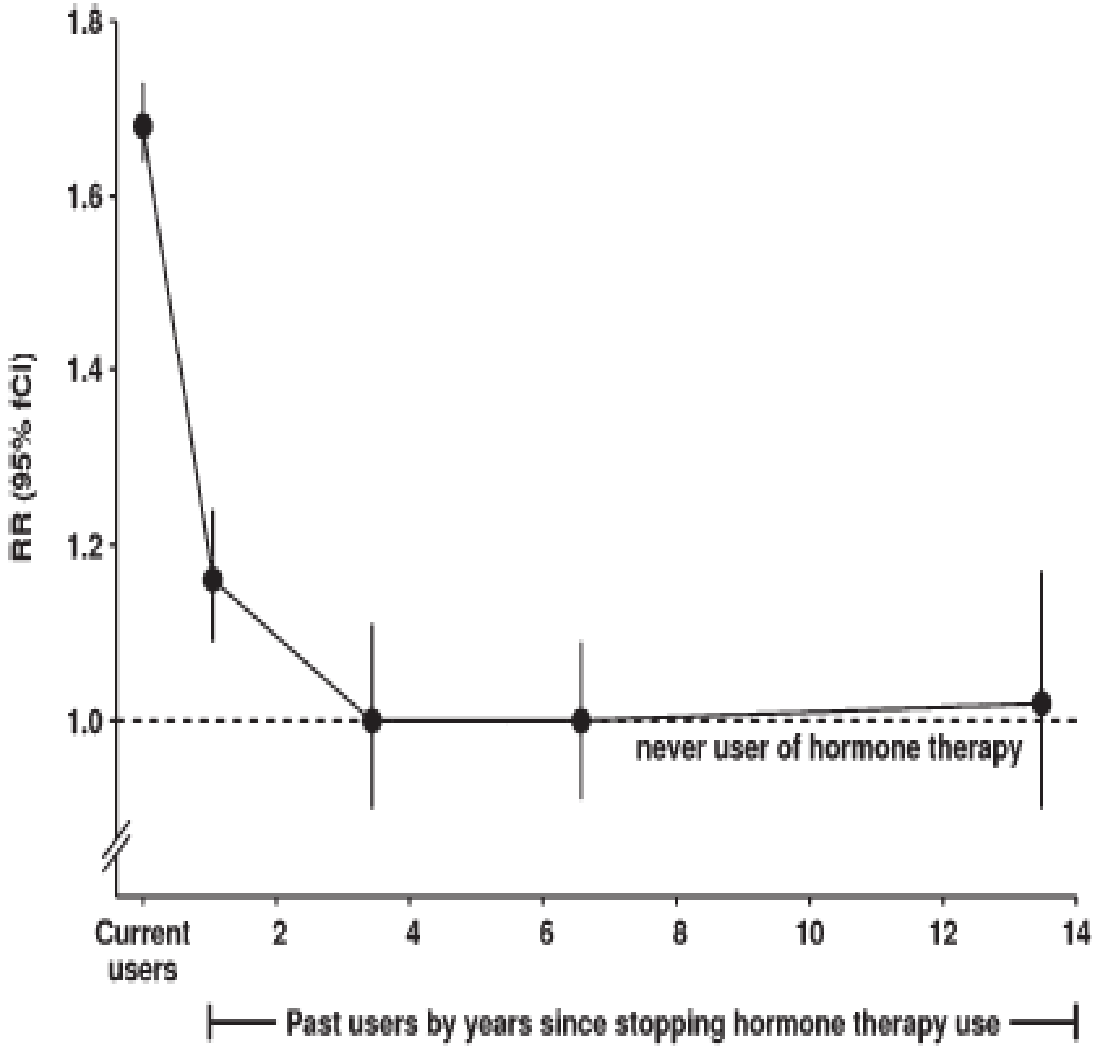


Risk almost all in current users

Risk greater for combined oestrogen-progestogen HRT

Similar pattern for mortality

Risk falls rapidly once stop taking HRT



Risk of breast cancer with HRT varies:

- By duration of use- longer use, higher risk
- By timing of use: lower risk if start age 60+ [few do now]
- By body size: fatter women have a higher risk without HRT, and HRT does not add much additional risk

Thin woman taking combined HRT for 10 years: 2.5 fold risk
Fat woman taking oestrogen-only HRT for 1 year: no extra risk

Never user: breast cancer 6 in 100 women @ 50–69 years
Combined HRT from 50 for 5 years: +2 cases per 100 women
Oestrogen-only from 50 for 5 years: + 0.5 cases per 100 women

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Smoking

- Richard Doll/ Richard Peto: effects of lifetime smoking in men
- Women in UK did not start to smoke in great number until WW2
- First study with data on lifetime smoking in UK women

- Smoke like men, die like men
- But good news on benefits of stopping even in middle age

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All-cause mortality in 60s and 70s

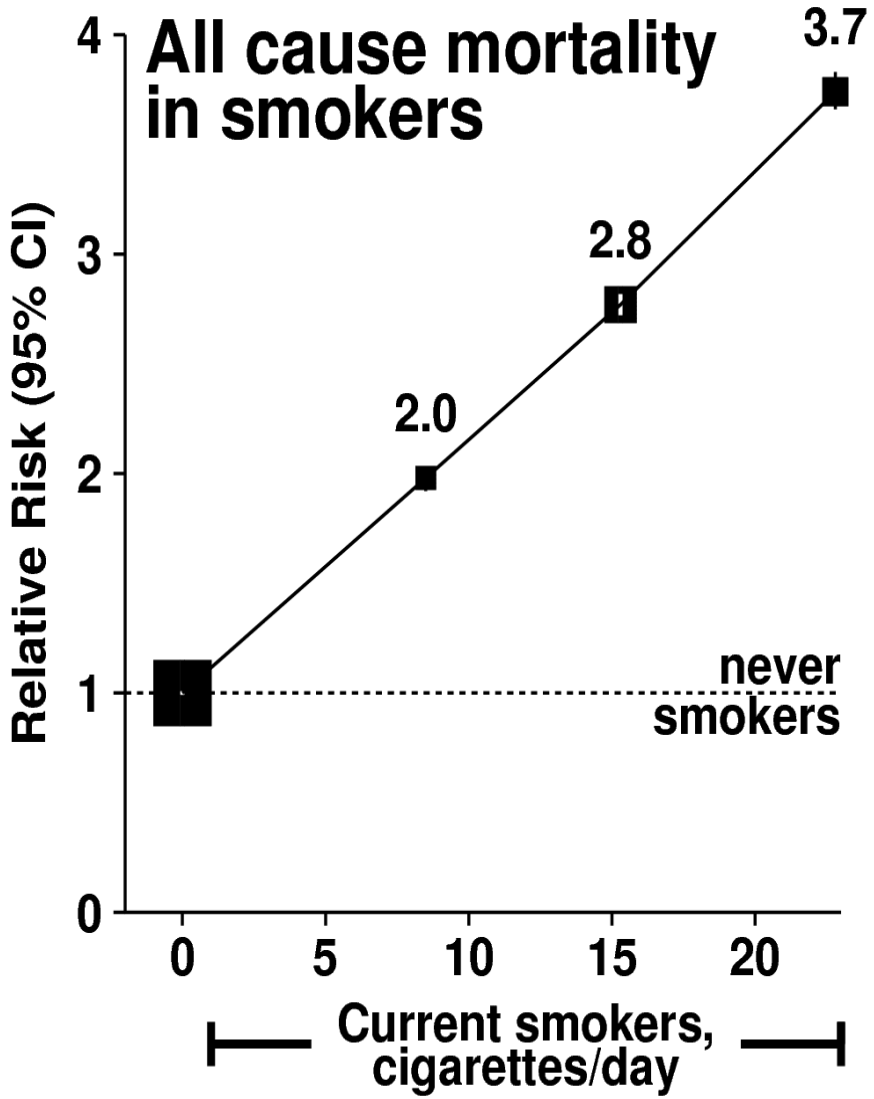
Smokers die earlier than non-smokers

Heavy smokers die earlier than light smokers

Risks are similar to those in men:

2/3 of deaths in smokers are due to smoking

11 years of life lost



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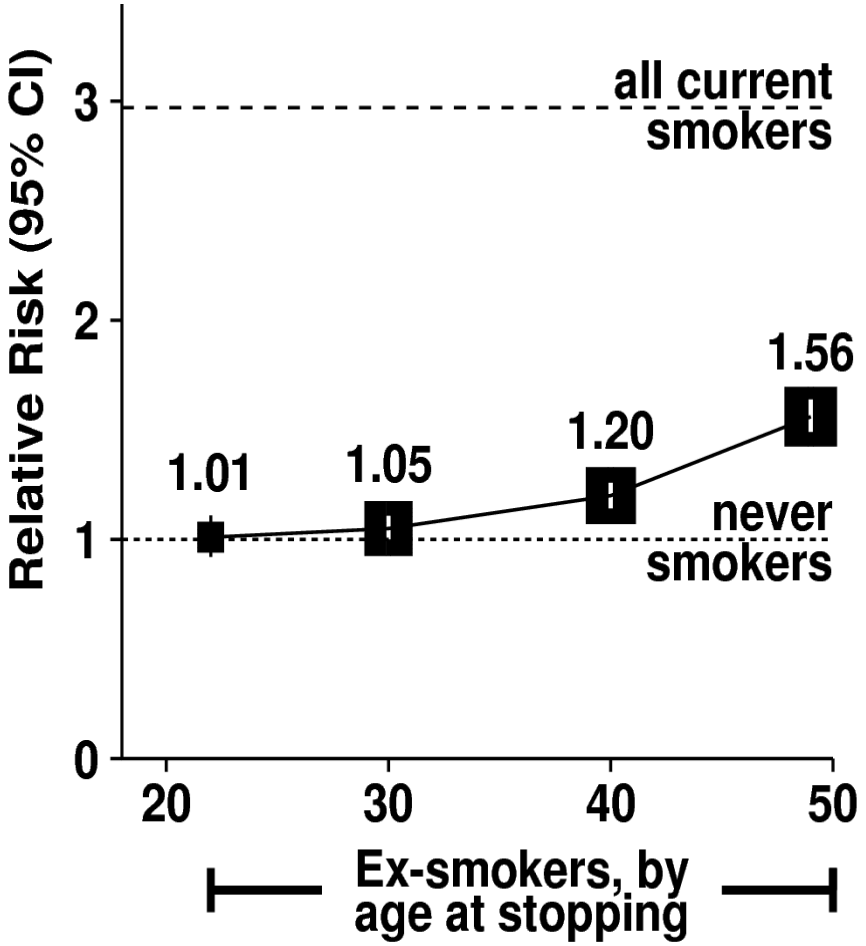
All-cause mortality

in ex-smokers, risk is much lower than if continue to smoke – even if give up in middle age

Stop before 40- avoid 90% excess risk in 60s/70s

Stop at 50- avoid 2/3 of excess risk



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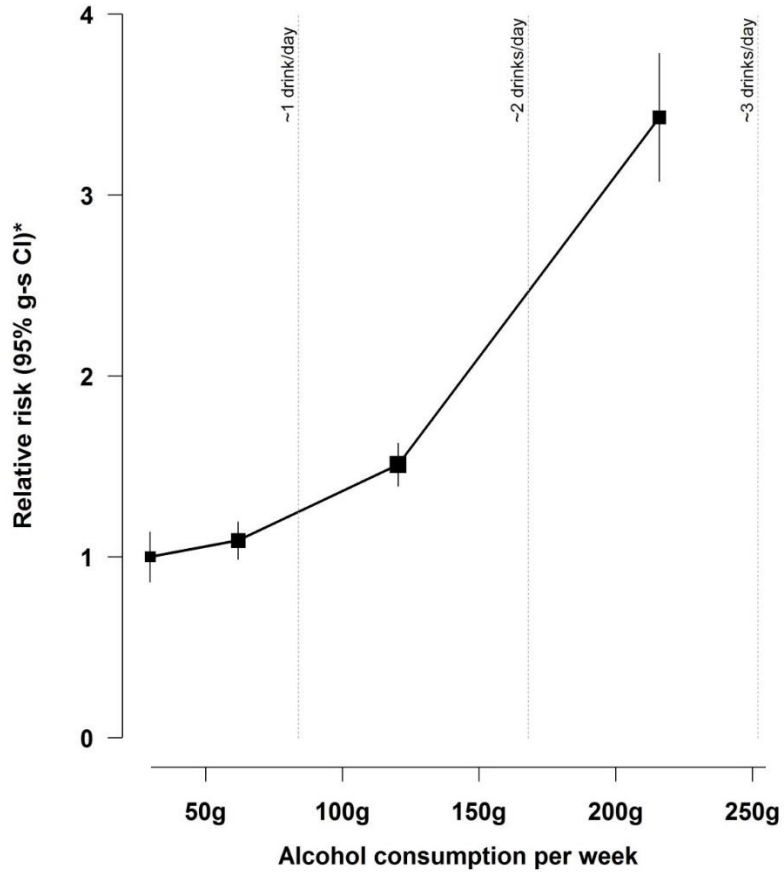
Alcohol

Not just how much,
but when and how
you drink matters

Risk of liver cirrhosis



1 drink/day **3 drinks/day**

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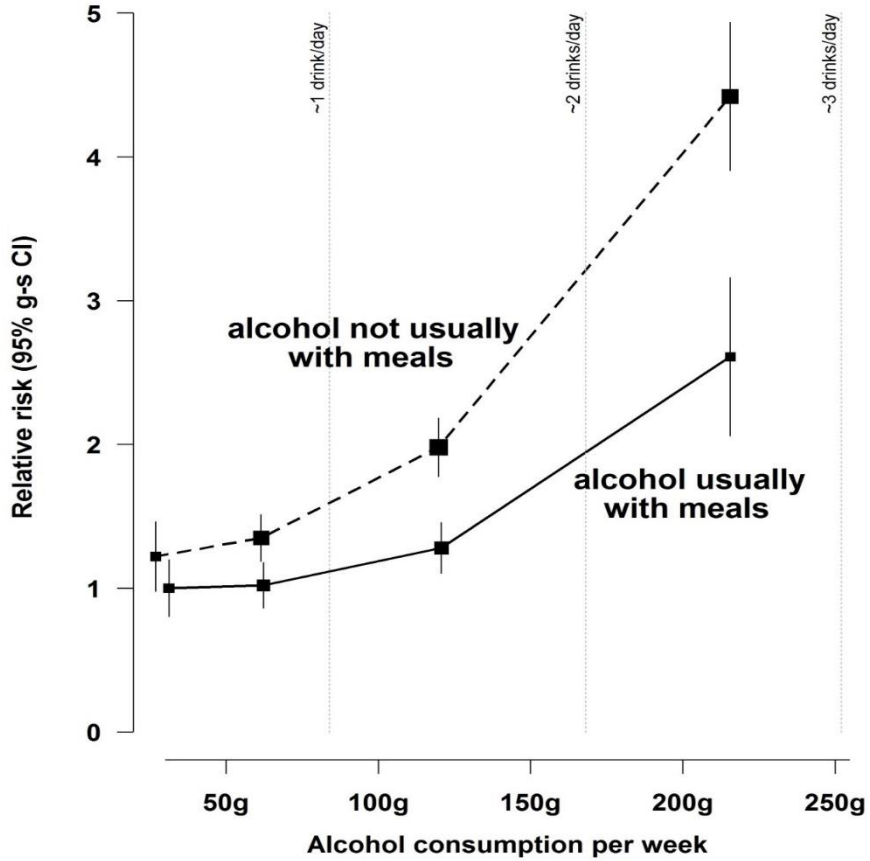
Alcohol

For a given amount, lower risk if drunk with meals

Risk of liver cirrhosis



1 drink/day **3 drinks/day**

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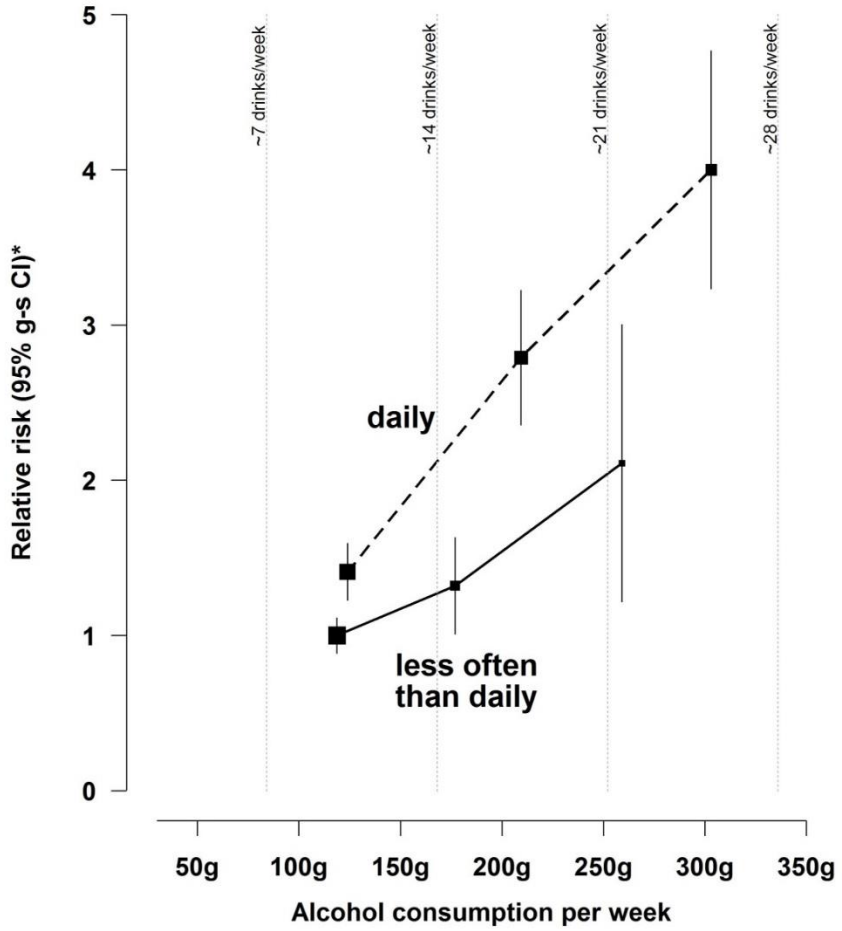
Alcohol

For a given amount, lower risk if don't drink daily

Risk of liver cirrhosis



1 drink/day **3 drinks/day**

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The next 20 years

- cohort now on average aged 78 years (from 69 to 85)
- 20y+ virtually complete follow-up
- Wealth of data: and more data becoming available

modifiable factors in midlife affecting risks in older age

by 85y: breast cancer 1 in 10, dementia 1 in 5, hip fracture 1 in 10

Retirement and changes in lifestyle
Caring and disability

The Million Women Study: dementia

Most common cause of death in UK women

Lifetime risk for women 1 in 5

Distressing and costly

No treatment

Little evidence on causes

MWS: 45,000 cases and 20+ year follow-up

Does health behaviour affect risk?

UK coordinated research: Dementias Platform UK

The Million Women Study: dementia

Suggested – and widely accepted- ‘risk factors’:

Early life - education

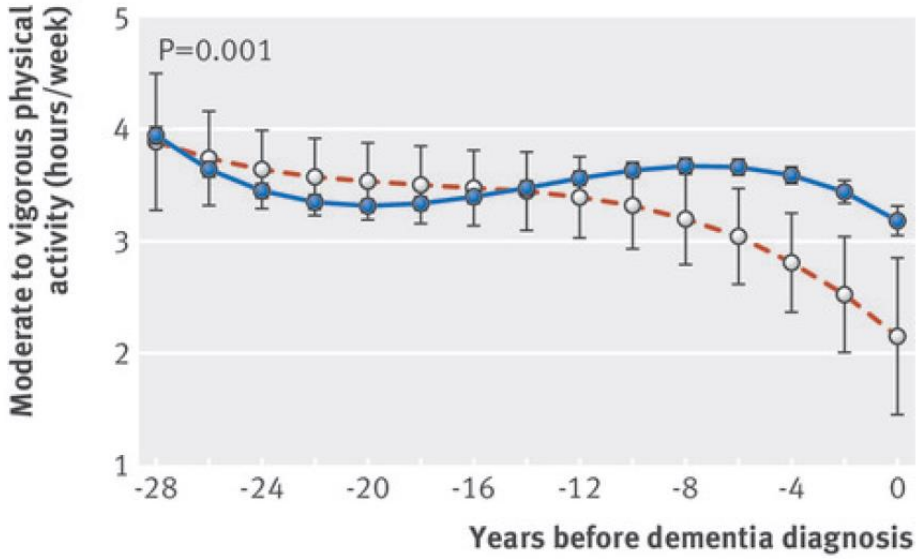
Midlife - hypertension, obesity, and hearing loss

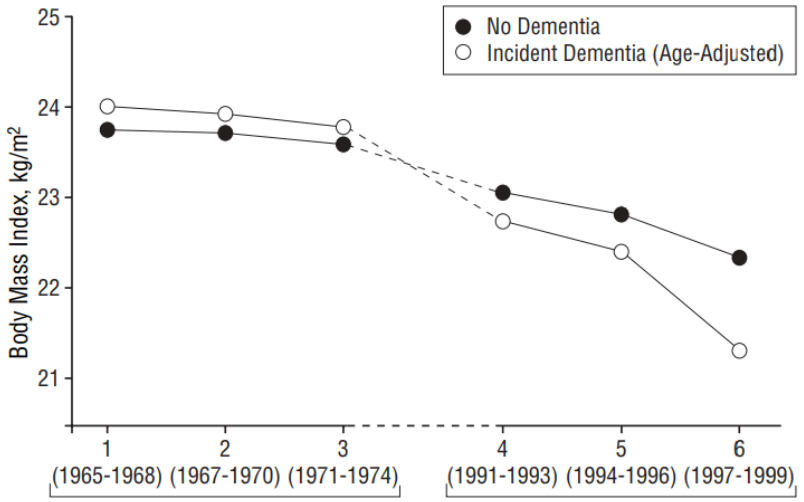
Old-age - smoking, depression, physical inactivity, diabetes, social isolation.

These are associations – but which comes first? Behaviour may change because of disease, long before the disease is diagnosed.

The Million Women Study: dementia

We can see this for physical activity, and for weight loss



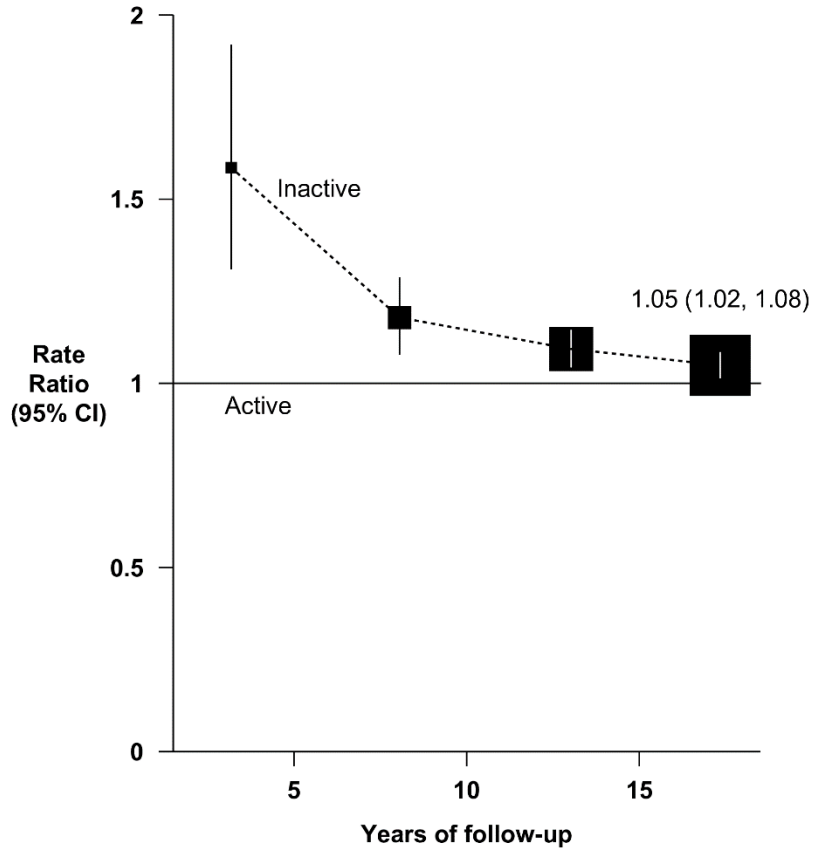


If we compare physical activity just before diagnosis, those with subsequent dementia will have lower levels of activity- activity appears protective. 20 years before diagnosis, no association

The Million Women Study: dementia

and this is exactly what we find

looking at risk in **inactive women** compared with active women, at varying times between report of activity and dementia diagnosis



First 5 years
inactive higher risk
activity close to diagnosis

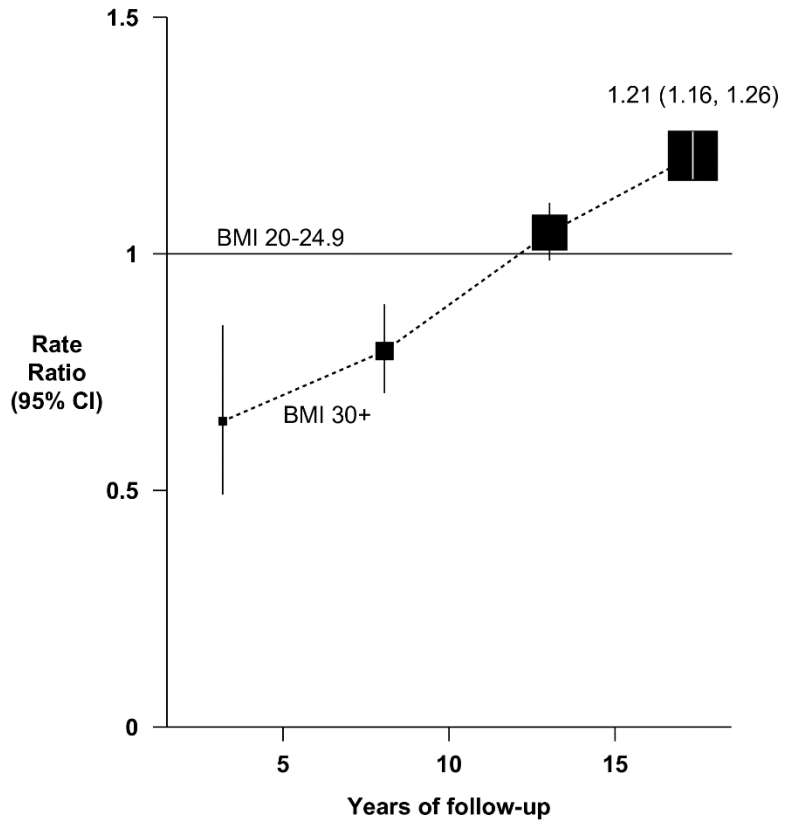
15+ years
no difference in risk
activity long before diagnosis

The Million Women Study: dementia

For obesity, the picture is different

Comparing BMI 30+ with BMI 20-25

Increased risk seen with longer follow-up



First 5 years
Obese lower risk

15+ years
obese higher risk

The Million Women Study: dementia

We find persistent associations, possibly causal, for

- Obesity
- Smoking
- High blood pressure
- Education

We find that associations with other factors do not persist and may be a result, not a cause, of dementia

- Physical activity
- Low BMI/low caloric intake
- Social interaction
- Cognitive activities

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Challenges and opportunities for a long-term health study

- 25 years' investment of time, effort and public money
- Value as mature long-term prospective cohort
- Includes information not available through routine NHS data collection
- Contributor to collaborative research world-wide
- Direct relevance to public health

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- Consent and participant involvement
- Funding
- Data linkage
- Data sharing
- Genetics- feedback of results
- Academic-commercial partnerships

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Consent and participant involvement

Consent to re-contact and to use NHS records; confidentiality; use for medical research only

Consent at recruitment 20+ years ago; no mention of data sharing

Consent is not the legal basis on which we process data (public interest) but for fair processing of sensitive data we need to show that it is reasonable to assume that participants know what we are doing.

- Regular mailings/website/publications/media; ‘no surprises’
- Participant panel

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Funding

Data linkage

Critical to study design and value

UK opportunities with NHS system

Complex and inconsistent governance of access to NHS data: immensely time-consuming

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Data sharing

- With other researchers- by collaboration, or by providing data from our study for them to analyse

- Pressures to share: ethical (maximise use of public data for public good) ; related to this, funders now unwilling to pay for data not freely available to scientific community (ethical and financial arguments).

- Concerns: lack of explicit consent; data security; study reputation

- Practical challenges: NHS linked data onward sharing; resources

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Data sharing

25 years ago

Our study- our time, initiative effort, reputation

No discussion of data sharing with participants or funders

No explicit consent for data sharing

Now

Publicly-funded research data are a public good, and should be openly available to the maximum extent possible

‘an ethical and scientific imperative’

‘an integral part of the research process’

‘not sharing data may be seen as research misconduct’

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Academic and commercial research partnerships

- technology- genetic sequencing- biomarkers
- Crucial to much research now- adds value
- Hugely expensive, and cutting edge development is commercial
- Mutual benefit from shared working- company tests product, scientists/public can afford technology
- not something we had to consider 25 years ago
- are examples of good practice with safeguards for scientific integrity

No wholly commercial use: medical research only

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A cohort among cohorts

A data resource

A mature study with unique potential

Economic as well as directly scientific

Public health in widest sense

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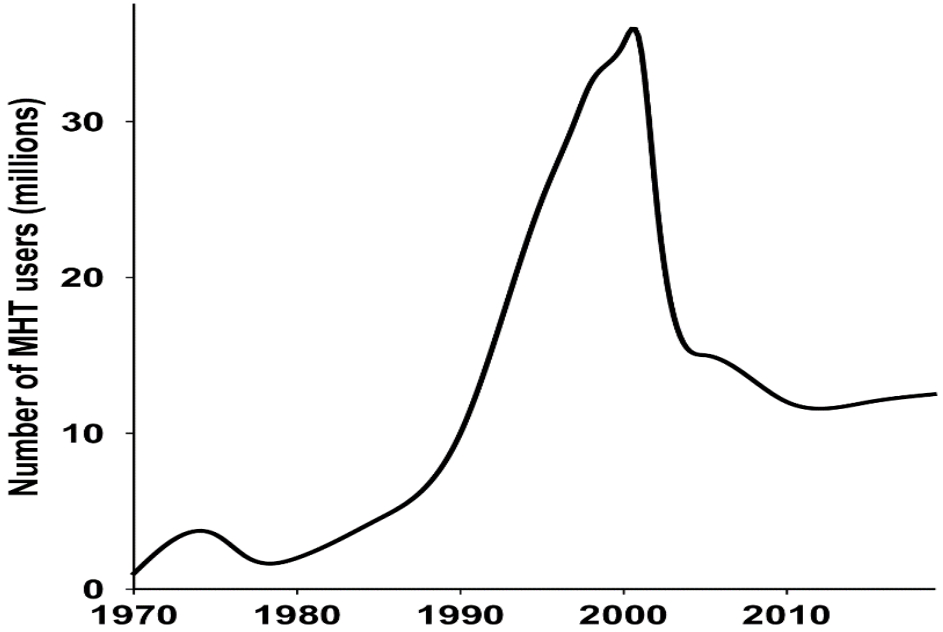
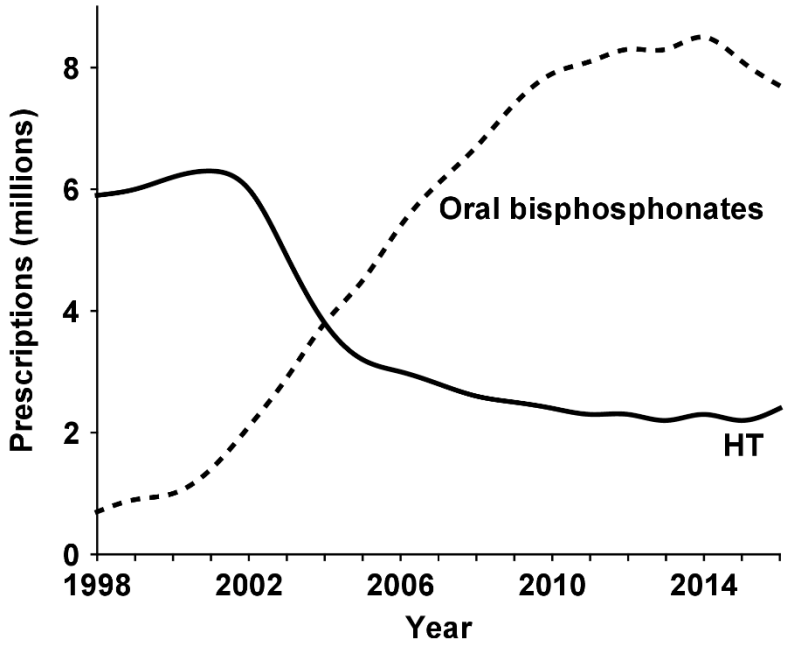
back to the figure



Rise and fall in HRT use



As HRT use fell, use of **bisphosphonates** rose

and of course- COVID-19

Million Women Study Acknowledgements

- 1.3 million participants
- Collaborators from 66 NHS Breast Screening Centres
- GP practices
- MWS co-ordinating centre staff
- MWS Advisory Committee
- NHS data providers
- Funding: Cancer Research UK, MRC, NHS, HSE