

# Efficacia dello screening per l'adenocarcinoma cervice

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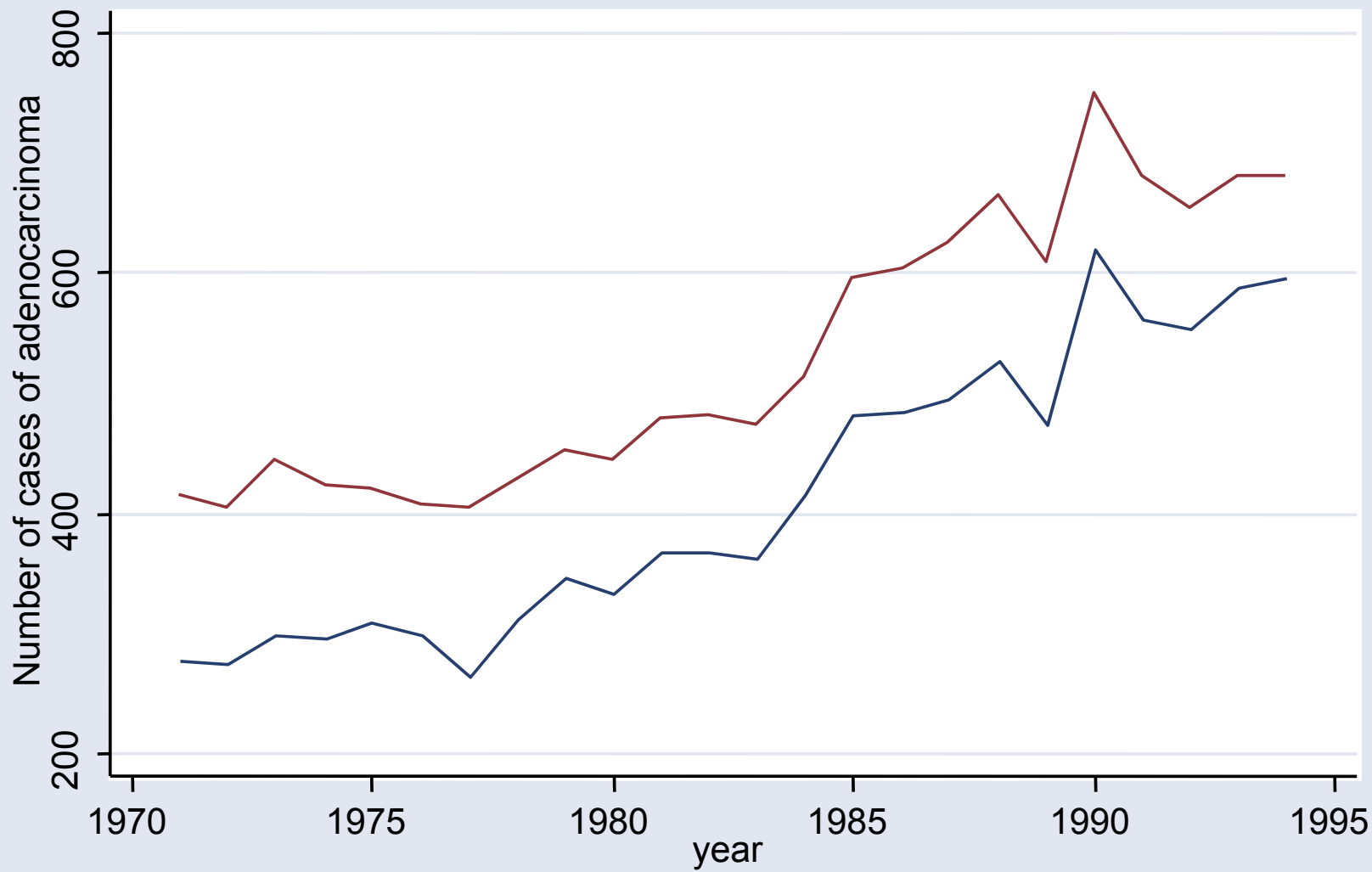
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# Background

- Adenocarcinoma of the cervix is rare, but is becoming more common
  - Approximately 700 cases/year in UK in the 1990s, compared to ~400 in the 1970s
- Squamous cell carcinoma of the cervix is being prevented by screening

# Registered and imputed numbers of adenocarcinoma of the cervix, England 1971-1994



— actual — imputed

# Changing age-specific rates of adenocarcinoma

- Age 30-34:
  - 1971: <0.5 per 100k
  - 1989: >4.5 per 100k
- Age 60-64
  - 1971: ~ 4.0 per 100k
  - 1989: ~ 4.0 per 100k

# Implication of age-specific trends

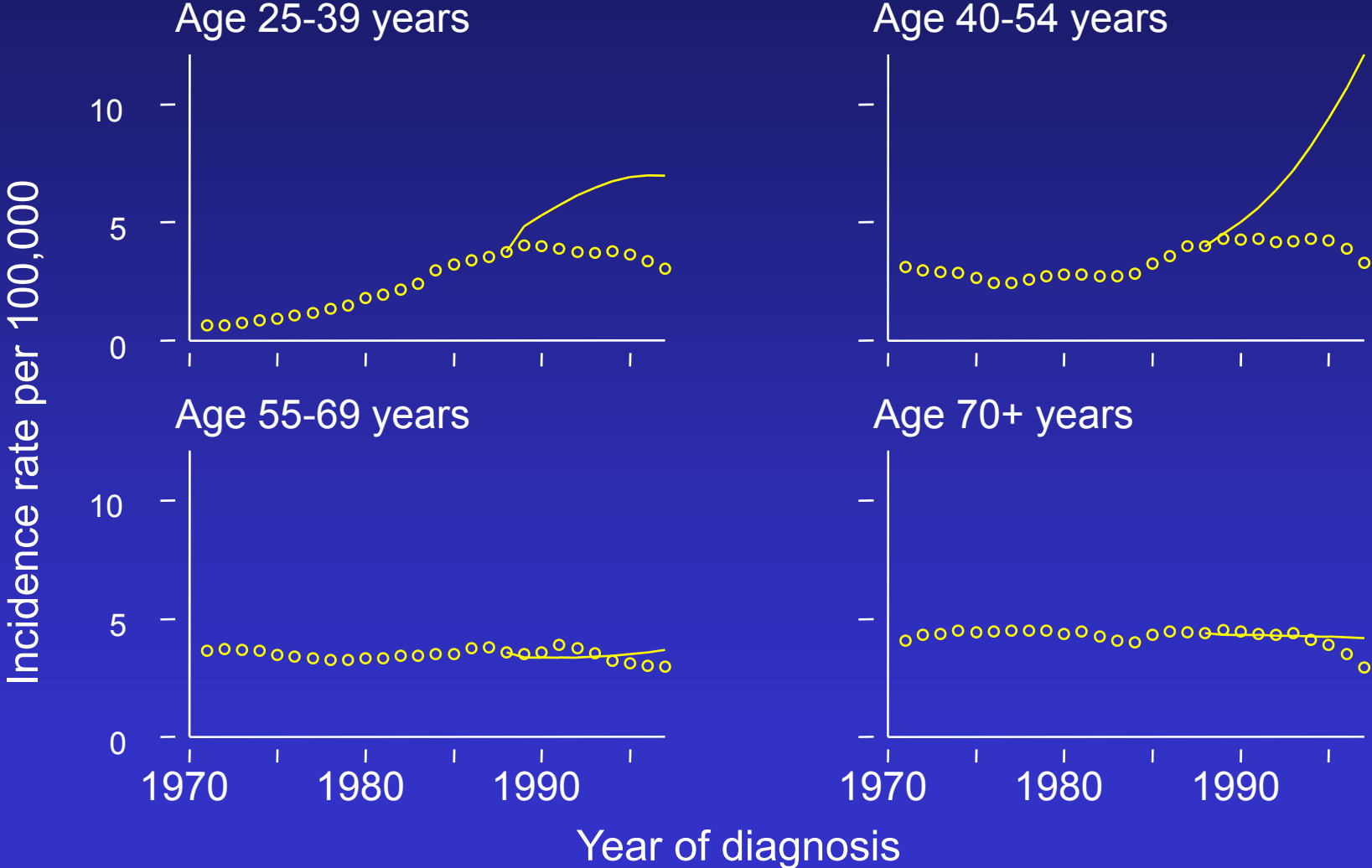
- Increase in adenocarcinoma is unlikely to be primarily an artefact of increased mucin staining and greater awareness

# Trends in England

- Incidence:
  - England 1971-1994
  - 60% of population 1995-1997

Sasieni, Adams. *Lancet* 2001; 357:1490-3

# Comparison of observed and predicted rates

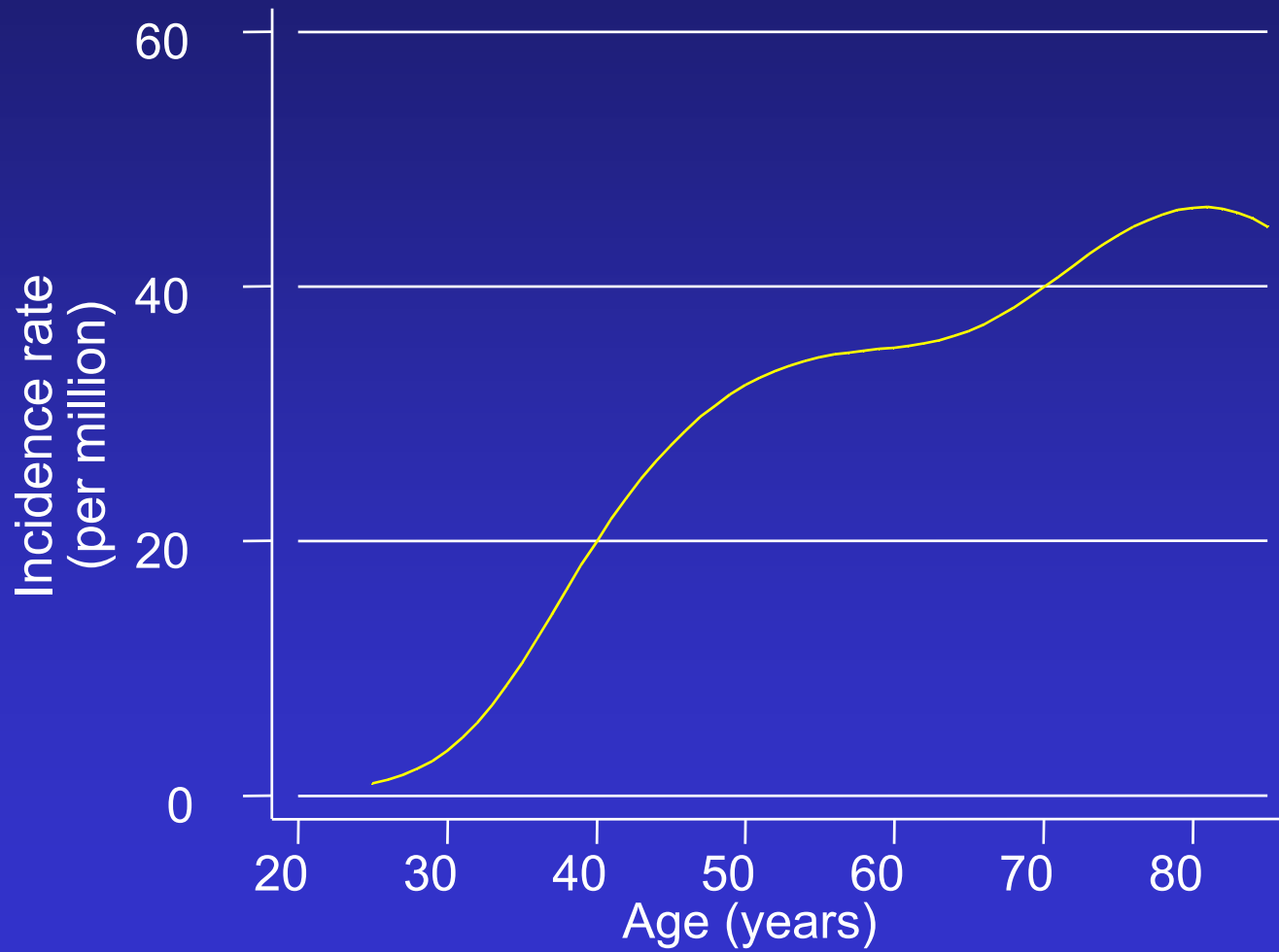


# Model for 1971-1987

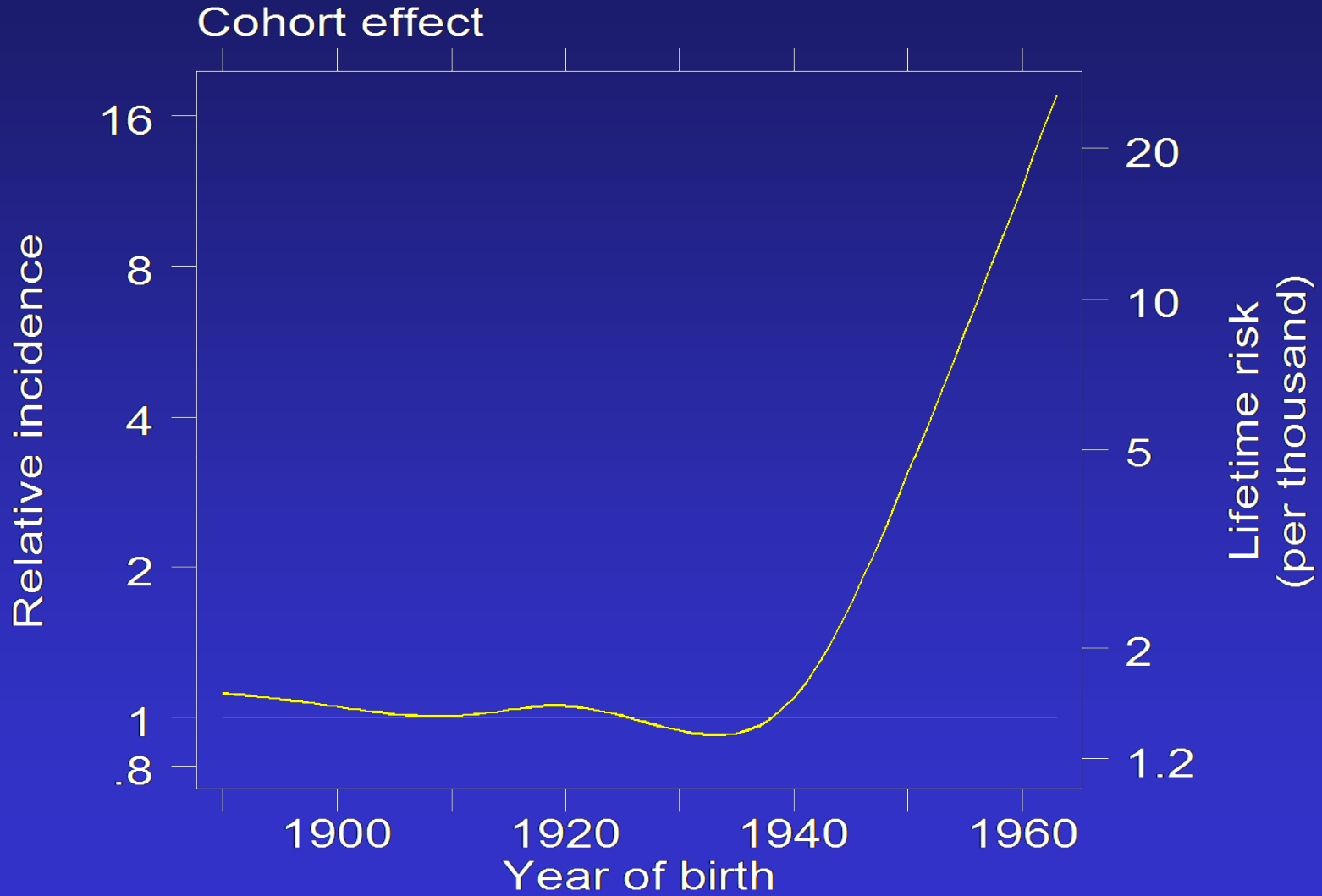
$$\text{Log}(\text{rate}) = f_1(\text{age}) + f_2(\text{cohort})$$

# Age effect

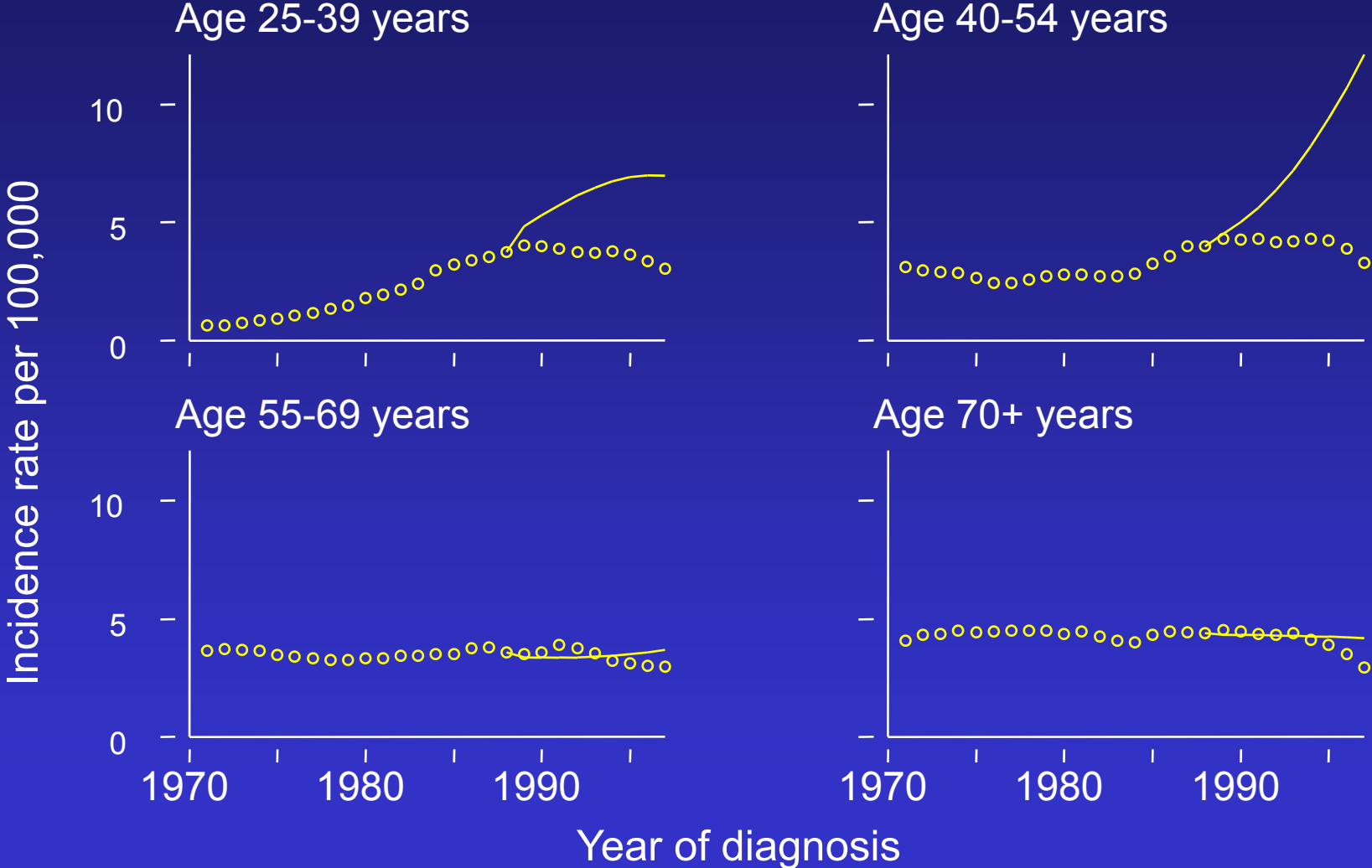
for cohort born in 1924



# Birth cohort effect



# Comparison of observed and predicted rates



# Implication of cohort effect (If you believe the model)

- Women born since 1955 could be as likely to get adenocarcinoma of the cervix as ovarian cancer
- Screening has already prevented a substantial number of adenocarcinomas of the cervix in young women.

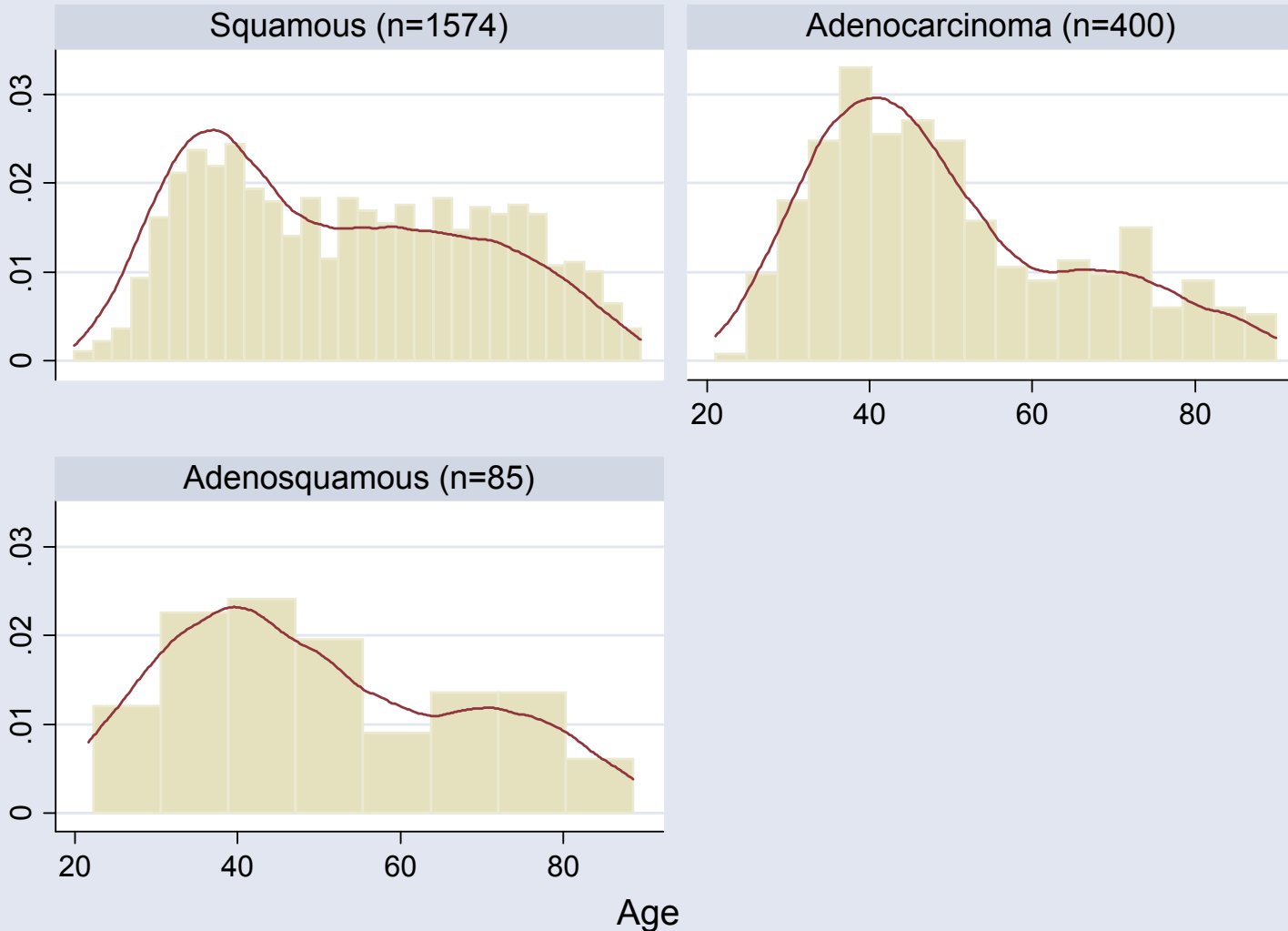
# But ...

- Over reliance on relatively small absolute increases in rates in young women
- Does not take into account of earlier age of coitarche which may shift the age-incidence curve to the left
- Does not allow for screen-detected cancer
  - 50% of adenocarcinoma screen-detected in Southampton (Herbert et al 2001)
  - In our audit 21% were stage 1A and 58% were stage 1.

# UK case-control study

- 456 cases of adeno or adeno-squamous carcinoma diagnosed between 1990 and 1999
- 17% of all invasive cervical cancers
- 2 age-matched controls per case

# Age distribution of different histological types of cervical cancer



# UK audit

## stage 1B+, age 20-69

- 62% had been screened within 5 years of diagnosis:
  - 60% of squamous,
  - 70% of adenocarcinoma.
- 10% diagnosed >6 months after positive cytology.
- 8% of adenocarcinomas (but only 3% of squamous) were diagnosed after two consecutive negative smears.

# Percentage never screened

(except possibly within 6 months of diagnosis)

| Age   | Controls<br>(4385) | All             |                |             | 1B+            |                |             |
|-------|--------------------|-----------------|----------------|-------------|----------------|----------------|-------------|
|       |                    | Squam<br>(1291) | Adeno<br>(341) | A-S<br>(70) | Squam<br>(722) | Adeno<br>(196) | A-S<br>(52) |
| 20-35 | 18%                | 15%             | 15%            | 27%         | 20%            | 10%            | 35%         |
| 35-50 | 13%                | 26%             | 13%            | 33%         | 34%            | 15%            | 38%         |
| 50-65 | 22%                | 46%             | 32%            | 20%         | 55%            | 26%            |             |
| 65-70 | 39%                | 54%             | 47%            |             | 57%            | 53%            |             |

# Effect of screening in previous 6.5 years on all cervical cancer

| Age          | Negative smear          |                         |                         | Adequate smear*  |                   |                  |
|--------------|-------------------------|-------------------------|-------------------------|------------------|-------------------|------------------|
|              | Squamous                | Adeno                   | A-S                     | Squamous         | Adeno             | A-S              |
| <b>20-34</b> | .44<br>(.31-.62)        | .72<br>(.34-1.5)        | .39<br>(.09-1.6)        | 1.2<br>(.82,1.8) | 1.0<br>(.43,2.5)  | .77<br>(.22,2.6) |
| <b>35-69</b> | .21<br>(.17-.25)        | .72<br>(.49-1.1)        | .25<br>(.11-.57)        | .40<br>(.33,.48) | .86<br>(.58,1.3)  | .31<br>(.14,.30) |
| <b>All</b>   | <b>.25</b><br>(.21-.29) | <b>.72</b><br>(.51-1.0) | <b>.28</b><br>(.14-.57) | .49<br>(.42,.58) | .88<br>(.62,1.25) | .41<br>(.21,.78) |

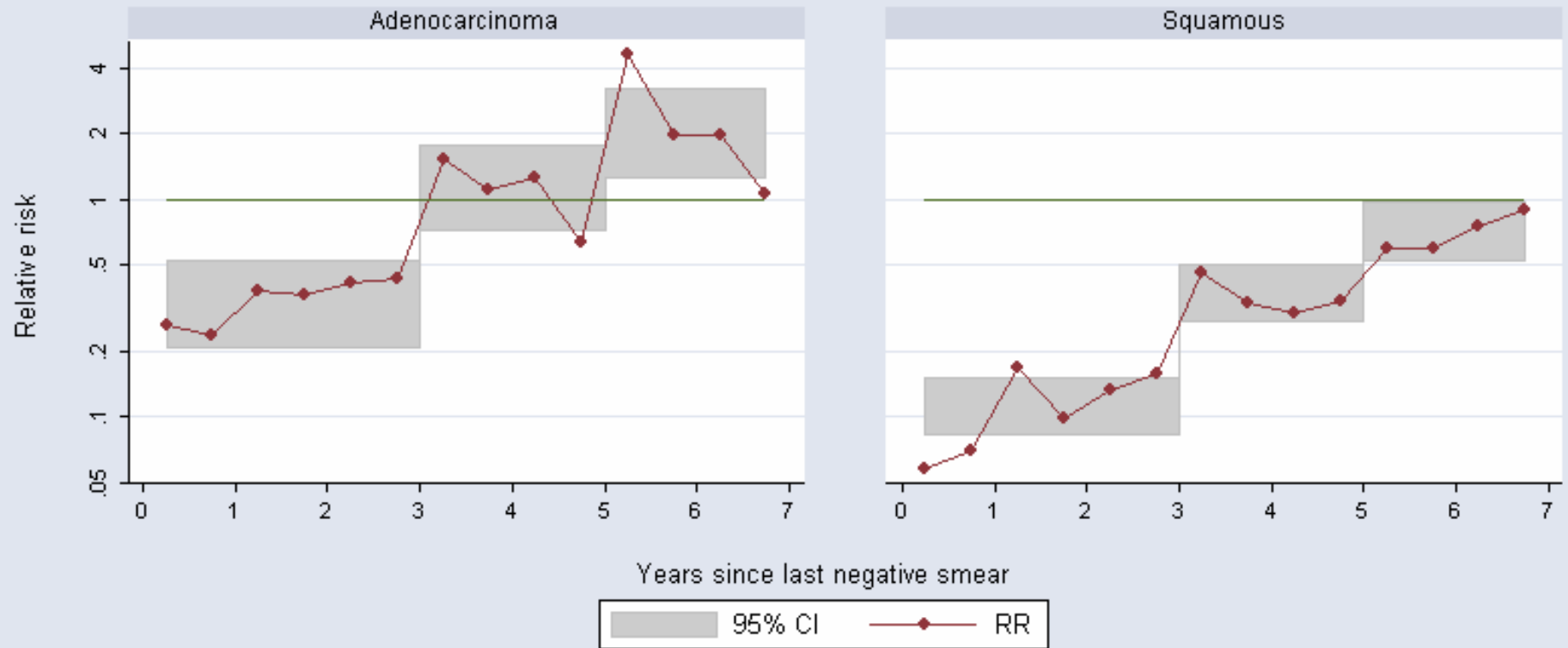
\* Excluding smears within 6 months of diagnosis

## Effect of screening in previous 6.5 years on stage 2+ cervical cancer (Age 20-69)

|                        | <b>Controls</b> | <b>Squamous</b>  | <b>Adeno</b>     | <b>A-S</b>       |
|------------------------|-----------------|------------------|------------------|------------------|
| <b>n</b>               | 4500            | 213              | 25               | 17               |
| <b>% screened*</b>     | 78%             | 38%              | 52%              | 53%              |
| <b>RR screened*</b>    | -               | .17<br>(.11-.26) | .15<br>(.03-.69) | .25<br>(.06-.97) |
| <b>% with negative</b> | 77%             | 31%              | 56%              | 47%              |
| <b>RR negative</b>     | -               | .12<br>(.07-.19) | .07<br>(.01-.56) | .16<br>(.03-.77) |

\*Adequate smear 6 months to 6.5 years before diagnosis

# Time since last negative smear



Graphs by hist

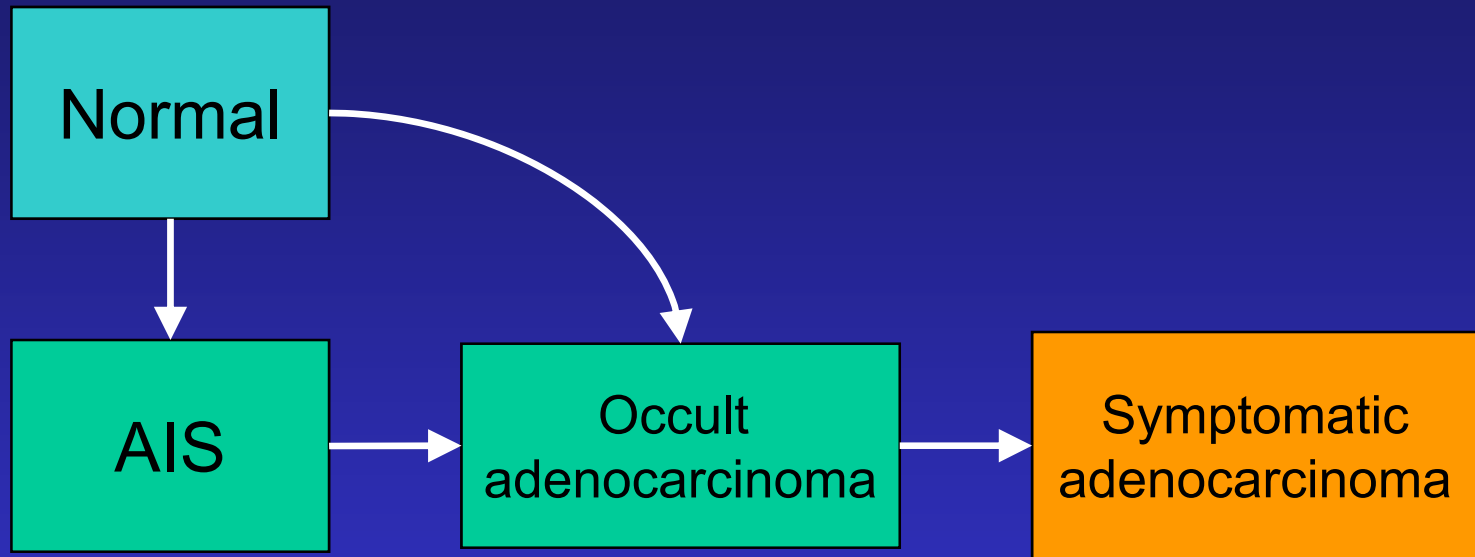
# Why doesn't cervical screening work well?

- Glandular atypia on cervical cytology are rare:
  - About 1 in 2000 smears in England

# Why does cervical screening work at all?

- Preinvasive glandular lesions of the cervix do exist
- Squamous intraepithelial neoplasia must either sometimes be a precursor to adenocarcinoma, or must be a substantial marker of risk
- Invasive adenocarcinoma is often screen detected (50% in Southampton, Herbert et al 2001)

# Natural history of adenocarcinoma



% with glandular cytological abnormality?

% with any cytological abnormality?

# Cytology in women with AIS and HSIL histology

| Cytology                  | % “positive” |
|---------------------------|--------------|
| ≥ Severe glandular atypia | 47%          |
| ≥ Mild glandular atypia   | 64%          |
| ≥ Moderate dyskaryosis    | 70%          |
| ≥ Mild dyskaryosis        | 78%          |

# Conclusions (1)

- Women born in England since 1950 are at greatly increased risk of cervical adenocarcinoma
- Screening reduces the incidence of frank invasive cervical adenocarcinoma, but not to the same extent as for squamous carcinoma

# Conclusions (2)

- Screening has a bigger effect in reducing advanced adenocarcinoma through early detection
- Either
  - Cytology is poor at detecting AIS, or
  - Most adenocarcinoma does not originate from AIS (or only spends a very short time as AIS)

