

Efficacia dello screening per l'adenocarcinoma cervice

Professor Peter Sasieni

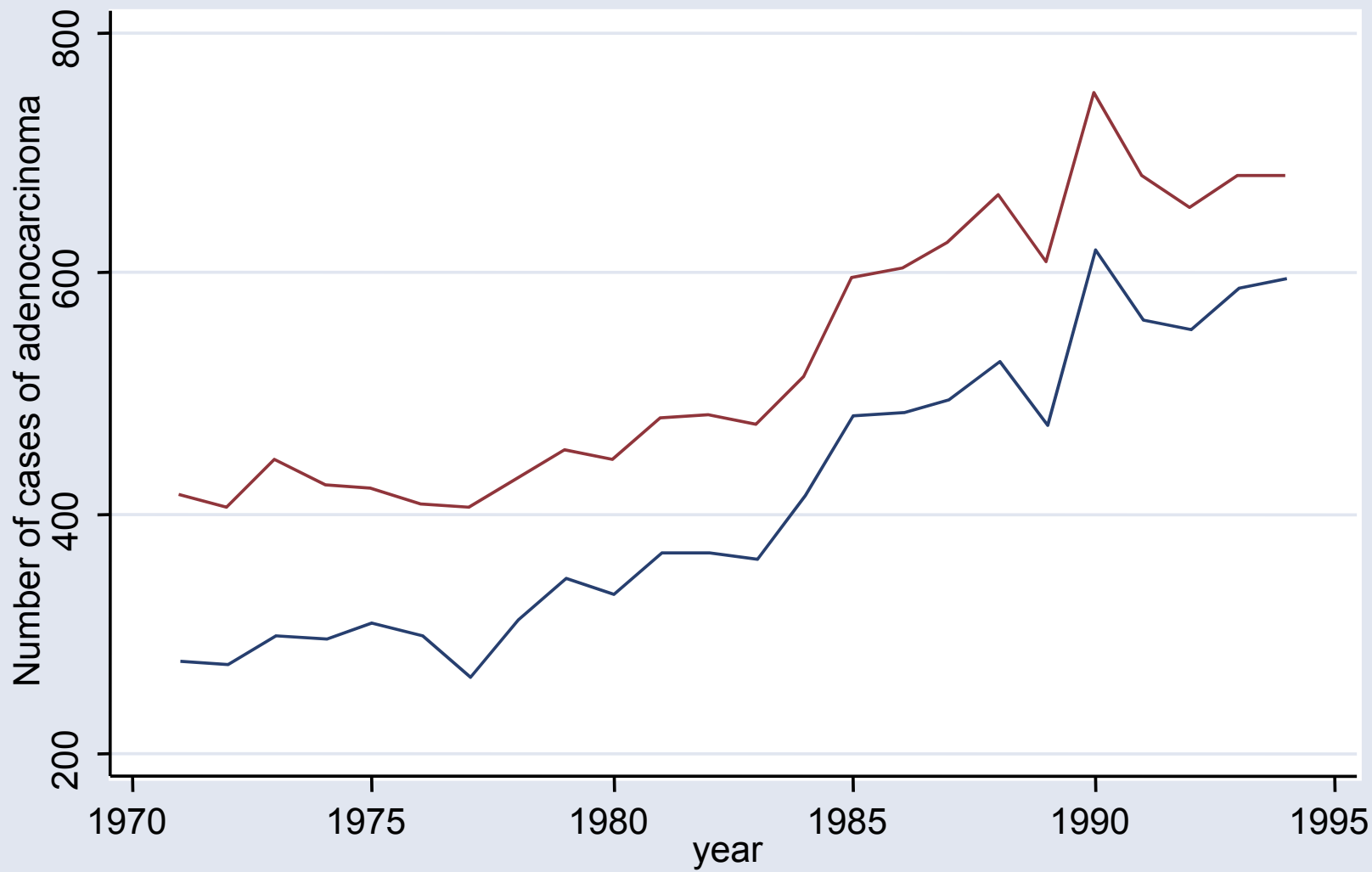
Wolfson Institute of Preventive Medicine
St Bartholomew's Medical School



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

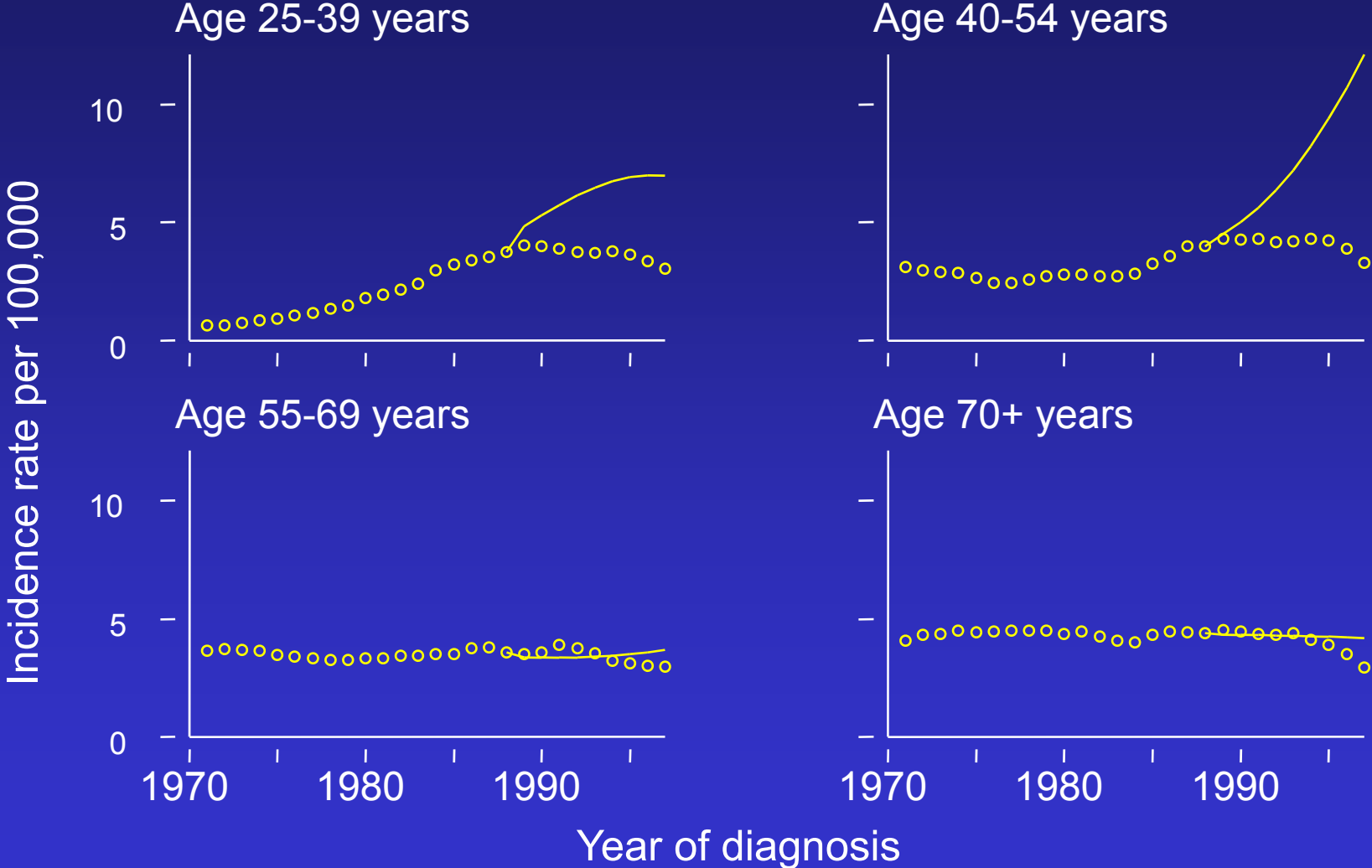
- Increase in adenocarcinoma is unlikely to be primarily an artefact of increased mucin staining and greater awareness

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

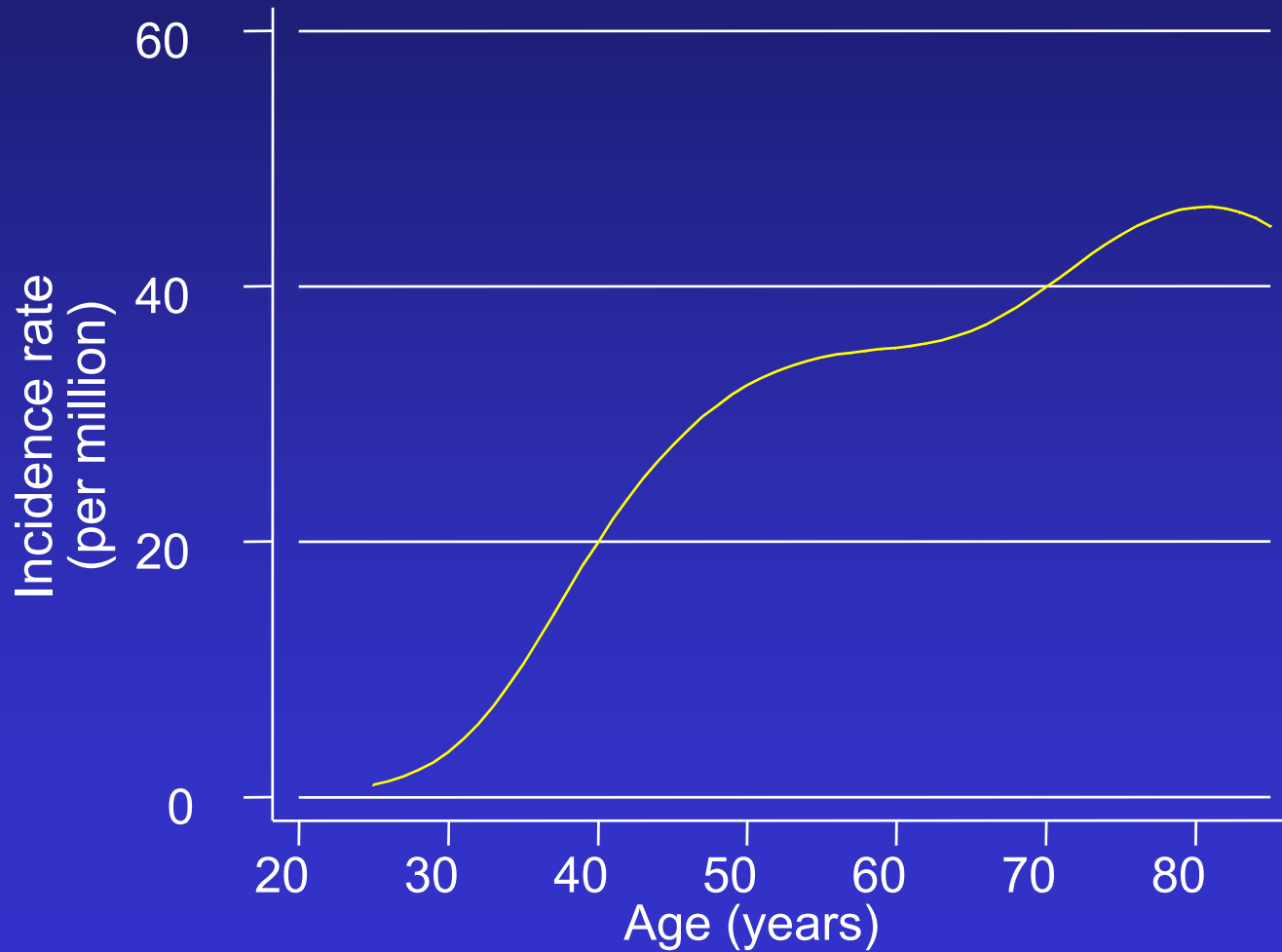


Model for 1971-1987

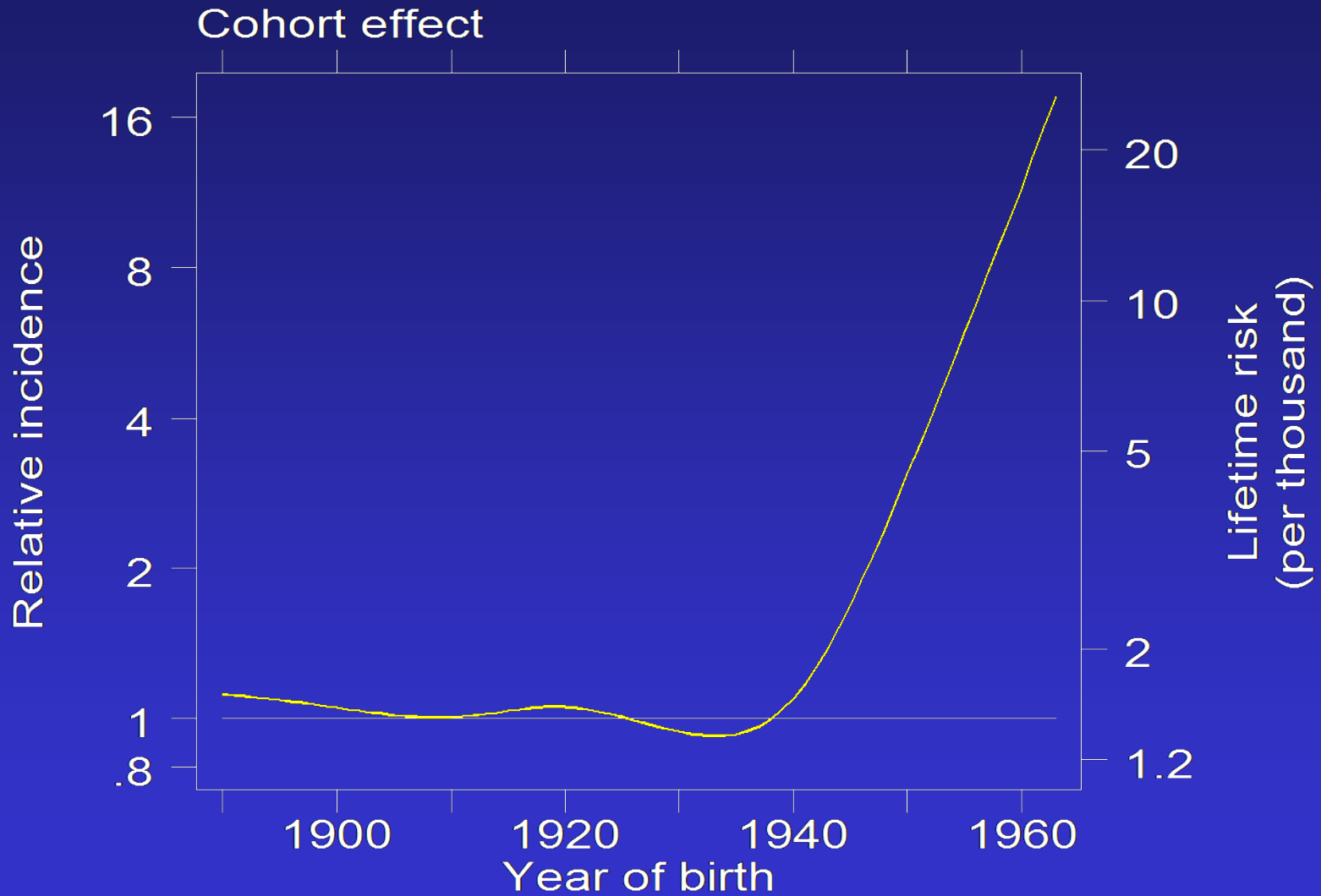
$$\text{Log}(\text{rate}) = f_1(\text{age}) + f_2(\text{cohort})$$

Age effect

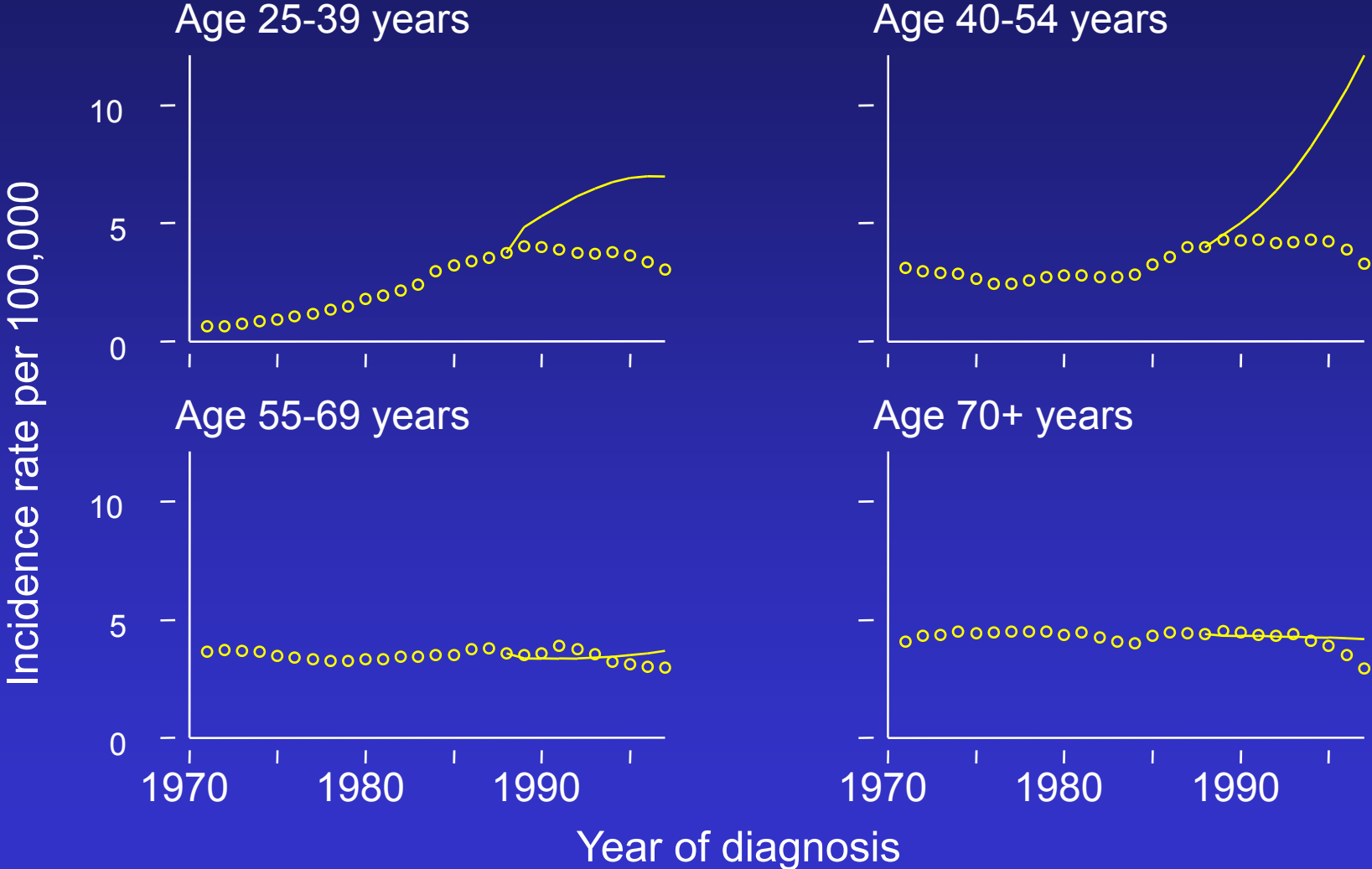
for cohort born in 1924



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.

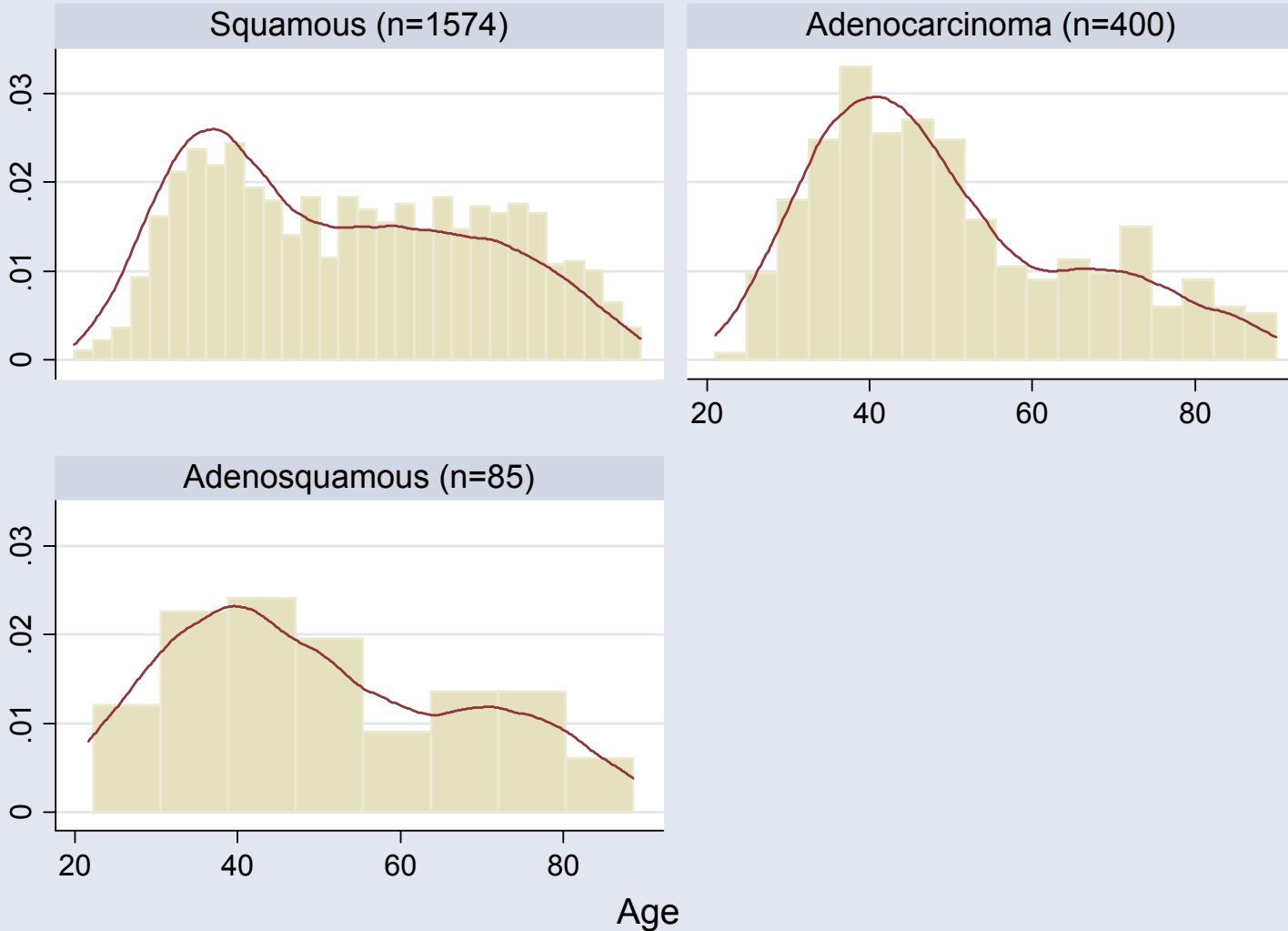
But ...

- 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 (4385)	All			1B+		
		Squam (1291)	Adeno (341)	A-S (70)	Squam (722)	Adeno (196)	A-S (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
20-34	.44 (.31-.62)	.72 (.34-1.5)	.39 (.09-1.6)	1.2 (.82,1.8)	1.0 (.43,2.5)	.77 (.22,2.6)
35-69	.21 (.17-.25)	.72 (.49-1.1)	.25 (.11-.57)	.40 (.33,.48)	.86 (.58,1.3)	.31 (.14,.30)
All	.25 (.21-.29)	.72 (.51-1.0)	.28 (.14-.57)	.49 (.42,.58)	.88 (.62,1.25)	.41 (.21,.78)

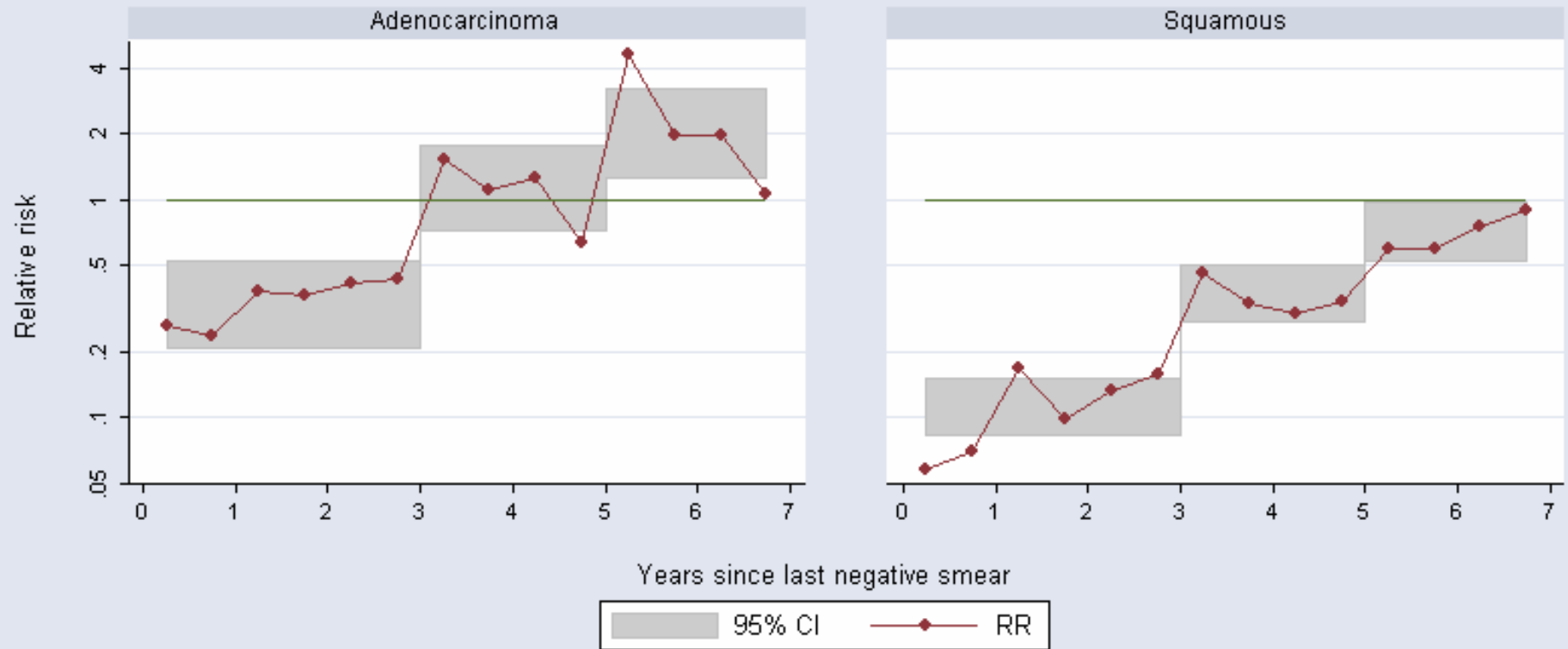
* Excluding smears within 6 months of diagnosis

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

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

*Adequate smear 6 months to 6.5 years before diagnosis

Time since last negative smear



Graphs by hist

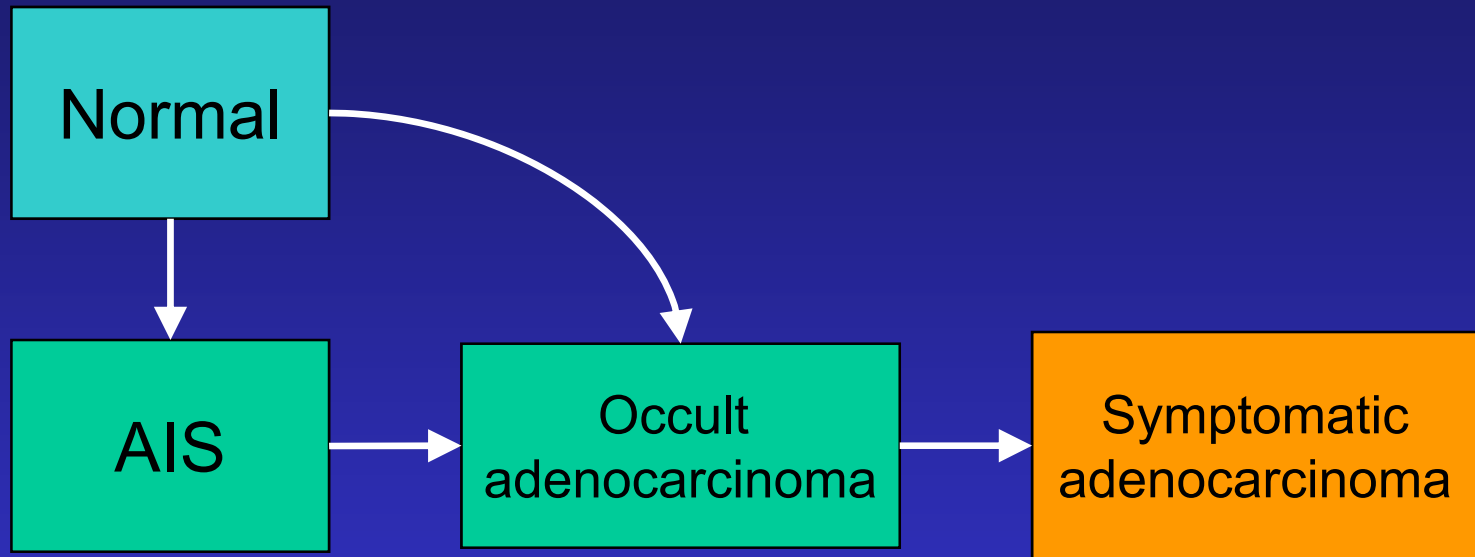
Why doesn't cervical screening work well?

- 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)

