

From HPV vaccination to cervical cancer elimination: What the evidence tells us

Peter Sasieni CBE FMedSci

HPV and Cervical Cancer

Protection is strongest before HPV exposure

Randomised trials in adult women

83–89% efficacy in HPV-naïve participants

30–43% efficacy in the whole cohort

Age at vaccination is a proxy for the probability of prior HPV exposure.

Public-health priority: vaccinate early

HPV Vaccination in the UK

School based vaccination introduced in September 2008

- Routine cohorts: Females aged 12-13 (based on school year)
- Catch-up cohorts
 - 2008-09: Females aged 17-18
 - 2009-10: Females aged 14-17

Observed impact of vaccination

Reduced infection → reduced CIN3 → reduced cancer → reduced mortality

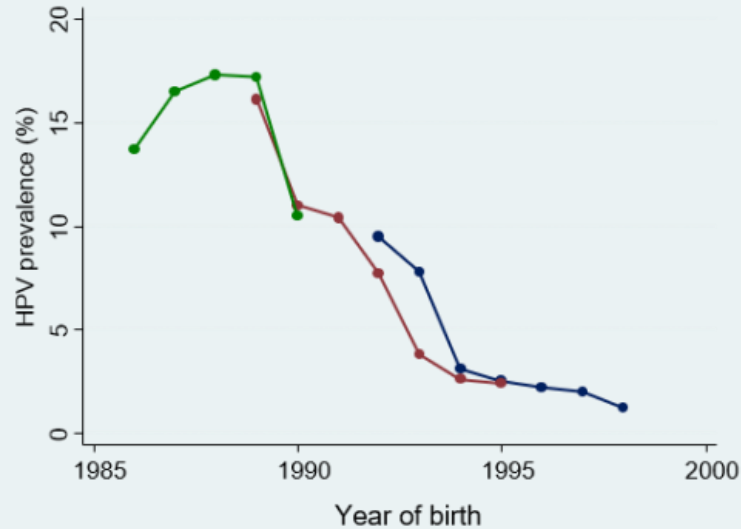
HPV in 15,429 chlamydia screening samples

HPV prevalence by year of birth

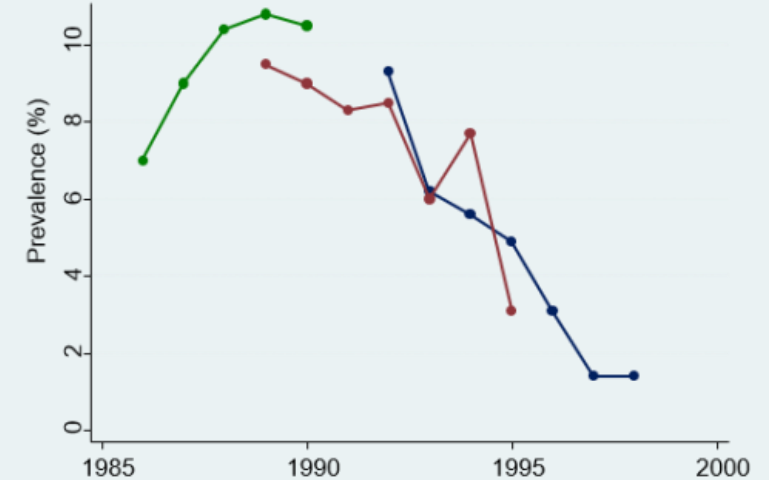
Adapted from Mesher et al *J Infect Dis* 2018 2018

Women born before 1990 were not offered vaccination.
Women born since 1994 had high uptake of HPV vaccination.

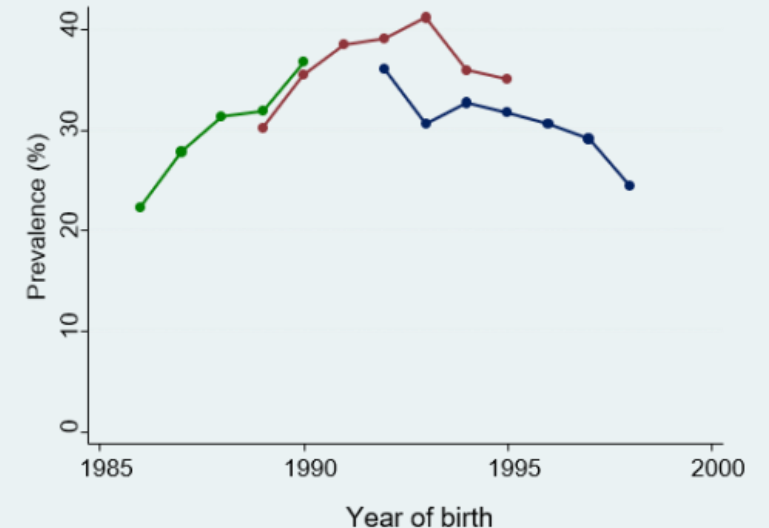
HPV16 and/or HPV18



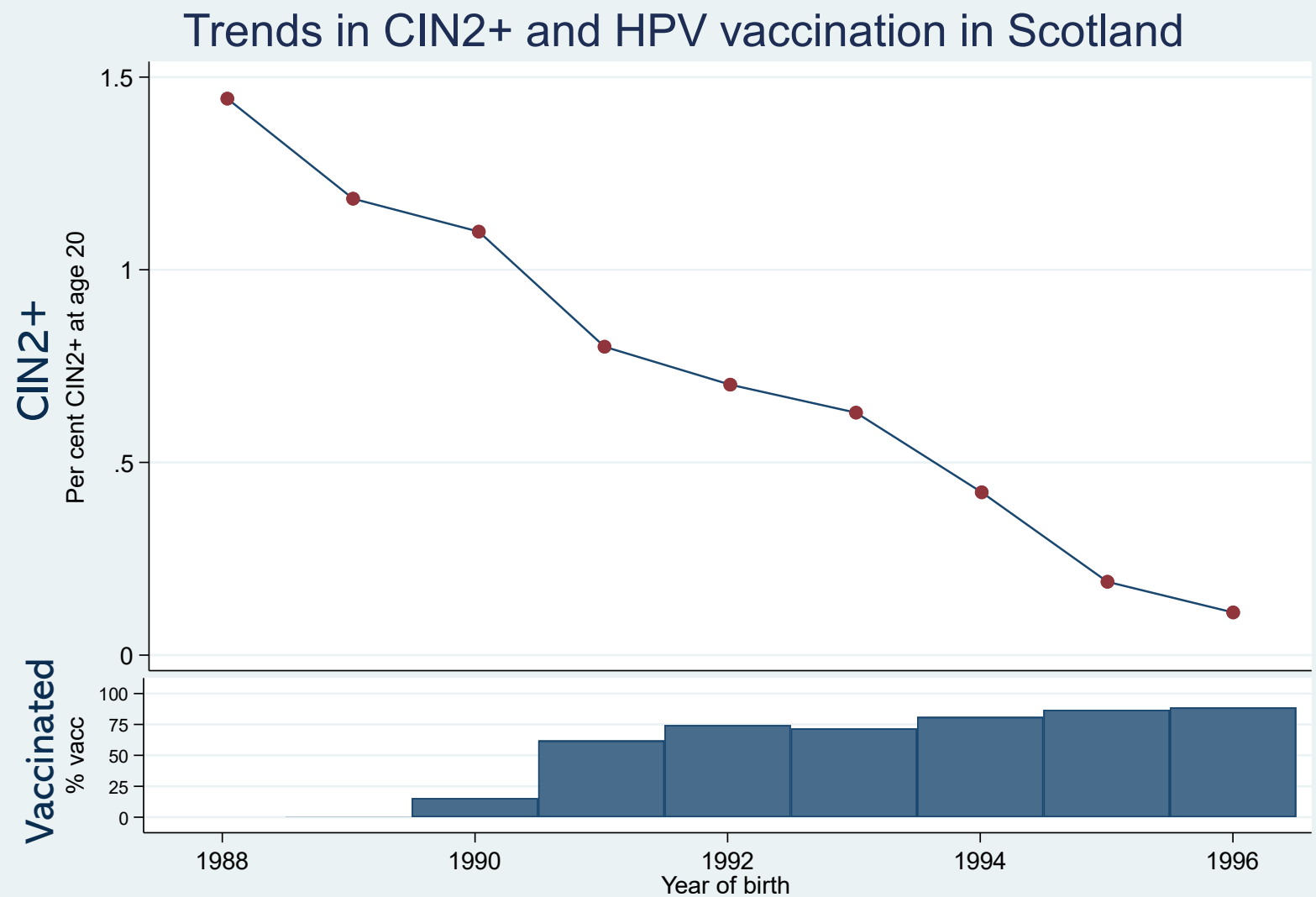
HPV31, HPV33 and/or HPV45



Other HR HPV types



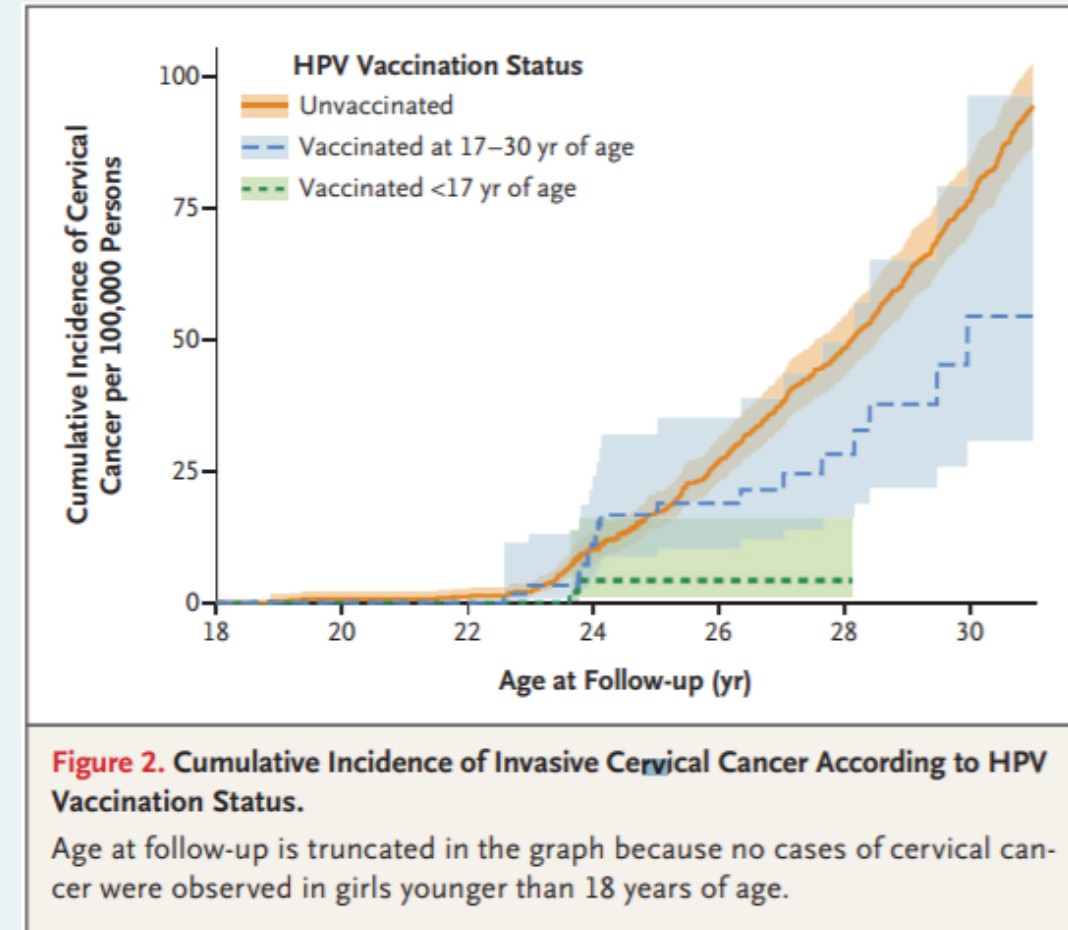
Decline in CIN2+ in 20-year-old women in Scotland



Data from Palmer et al BMJ 2019

HPV Vaccination and the Risk of Invasive Cervical Cancer in Sweden

- 1.6 million women aged 10-30 between 2006 & 2017
 - 557 cervical cancers
- Link to HPV vaccination (quadrivalent vaccine)
- Cumulative incidence of cervical cancer
 - Not vaccinated **94** per 100,000
 - Vaccinated **47** per 100,000
- Adj rate ratio by age at vaccination
 - **Aged 17-30** **0.47 (95%CI 0.27-0.75)**
 - **Aged 12-16** **0.12 (0.01-0.34)**



Impact of the HPV Vaccination Programme on Cervical Cancer Incidence in England

Exposure and endpoint measures

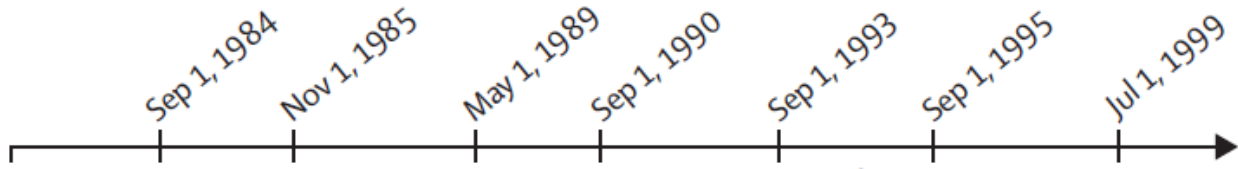
Falcaro et al *Lancet* 2021

Exposure

- Birth cohort
 - Defined by school year
 - Coverage 3 doses, ≥ 1 dose

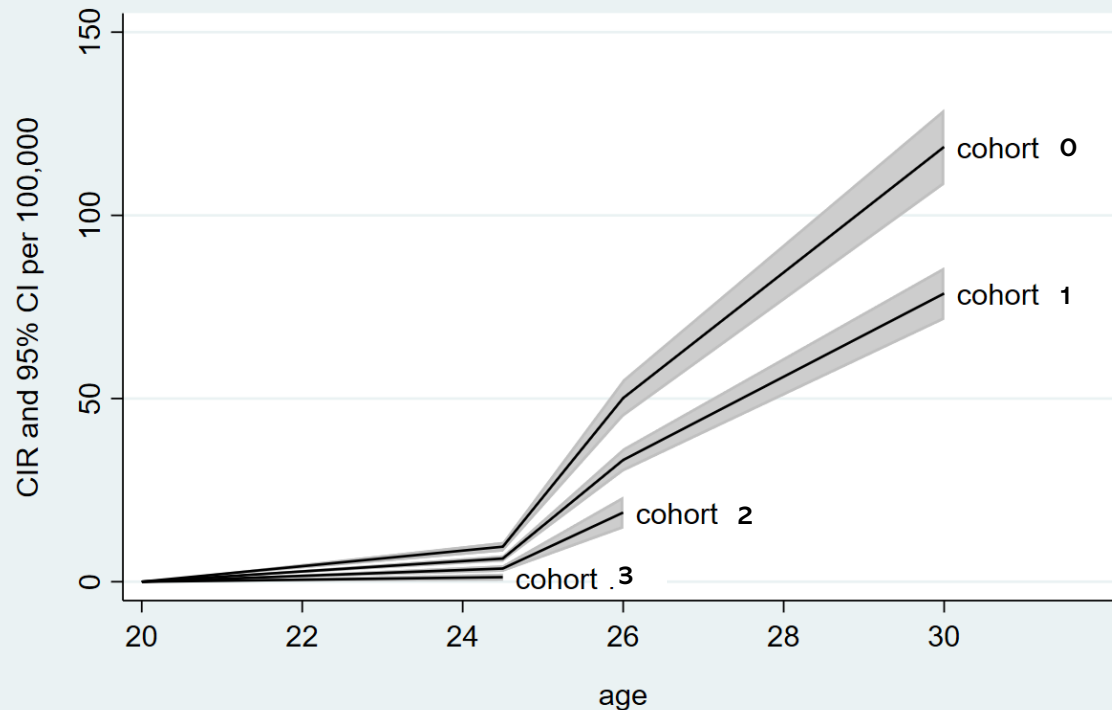
Endpoints

- Cancer registration
 - Invasive cervical cancer (C53)
 - CIN3 (D06)

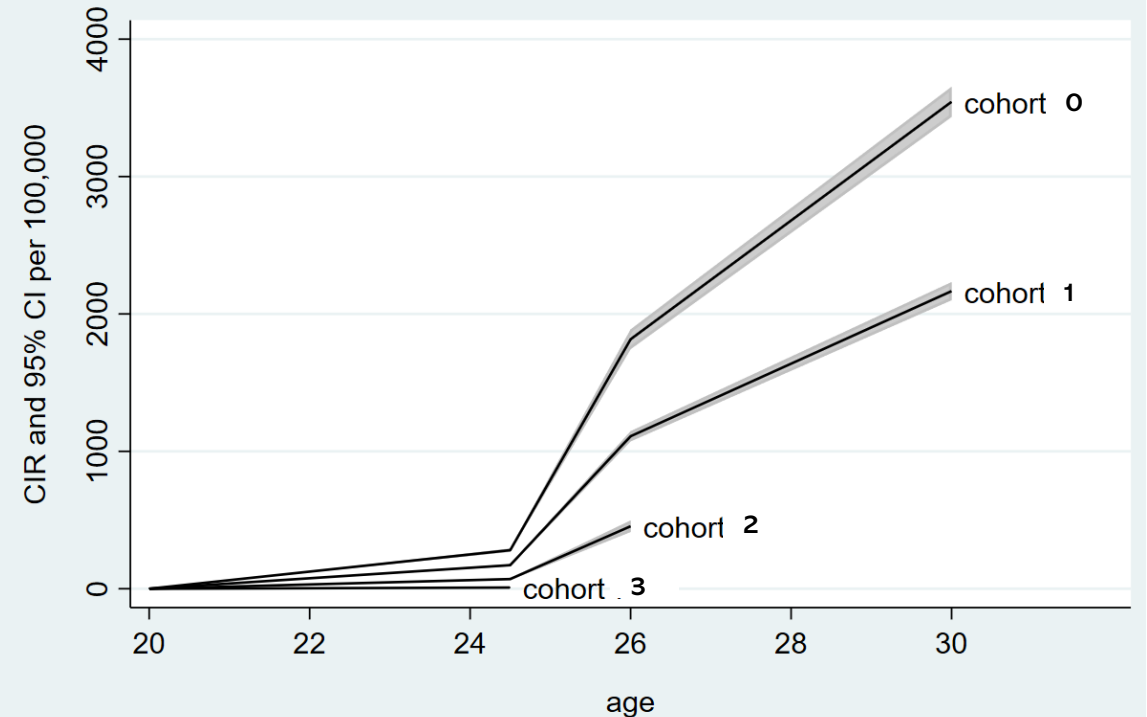
	Date of birth						
							
Birth cohort	1	2	3	4	5	6	7
Age at first invitation to screening (years)	20	20 or 25	25	24·5	24·5	24·5	24·5
Offer of HPV vaccination	No	No	No	No	Yes	Yes	Yes
School years					12–13	10–11	8
Age (years)					16–18	14–16	12–13
Coverage*							
At least 1 dose					60·5%	80·1%	88·7%
3 doses					44·8%	73·2%	84·9%

Dramatic reduction in cumulative incidence in vaccinated birth cohorts

Invasive Cervical Cancer



CIN3



- Cohort 0: Unvaccinated
- Cohort 1: Offered vaccination aged 16-18
- Cohort 2: Offered vaccination aged 14-16
- Cohort 3: Offered vaccination aged 12-13

HPV Vaccination and the Risk of Invasive Cervical Cancer in England

New Data (with additional 12 months) - Cancer

Birth Cohort	Age vaccinated	Vaccine uptake (1 dose)	Vaccine efficacy (95% CI) Cervical Cancer	
			≤ June 2019	> June 2019
1	16-18	60%	33% (24-40%)	47% (34-58%)
2	14-16	80%	63% (52-71%)	81% (72-87%)
3	12-13	89%	87% (72-94%)	84% (64-93%)

Cancers prevented by June 2020: By deprivation

	Predicted No. of diagnoses		No. prevented: A–B
	A: counterfactual	B: factual	
Index of multiple deprivation			
Invasive cervical cancer			
1st (most deprived)	463	271	192
2nd	369	170	199
3rd	271	127	144
4th	212	120	92
5th (least deprived)	155	94	61
Total	1469	782	687

Impact of the HPV Vaccination Programme on Cervical Cancer Mortality in England

Exposure and endpoint measures

Data

- Cervical cancer deaths
 - In 5-year age-groups
 - In each calendar year

Exposure

- Mean (1 dose) HPV vaccine coverage in each 5-year age-group in each calendar year
- Calculated from uptake in each school-year-based birth cohort

Age 20–24 years		Year of death
Deaths	Women-years (millions)	
25		2000*–04
16		2005–09
27		2010–14
5		2015–19
0		2020–24

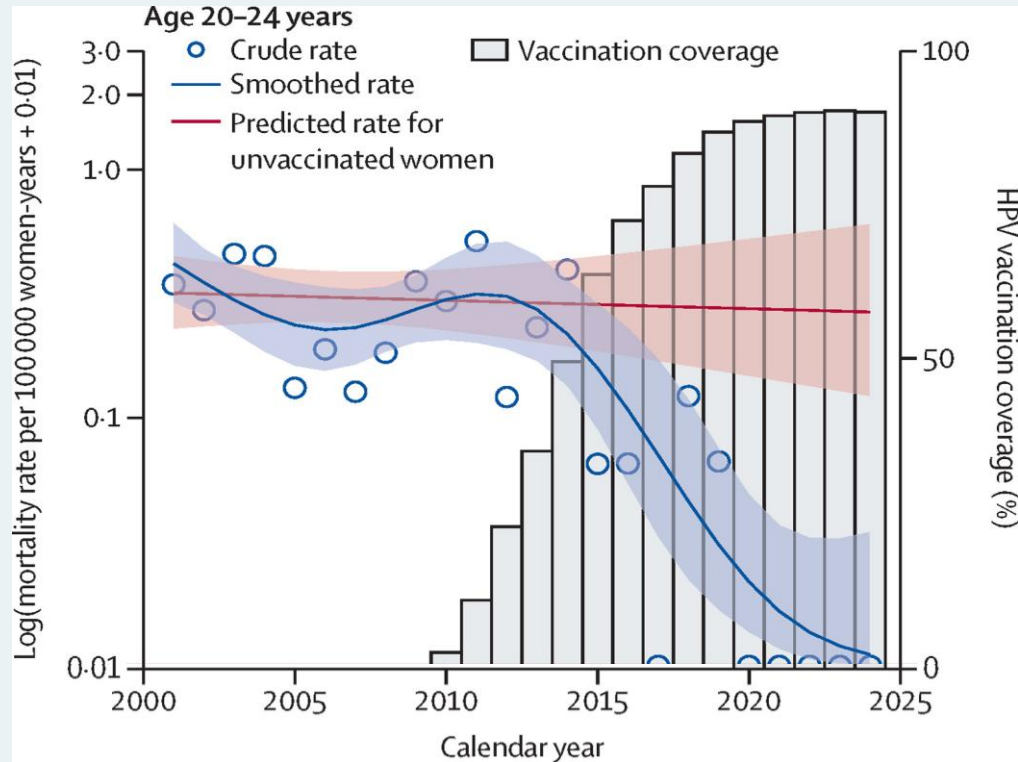
Vaccination coverage	Year of death
None	2000*–04
1–50%	2005–09
51–87%	2010–14
88–91%	2015–19
	2020–24

Age 20–24 years

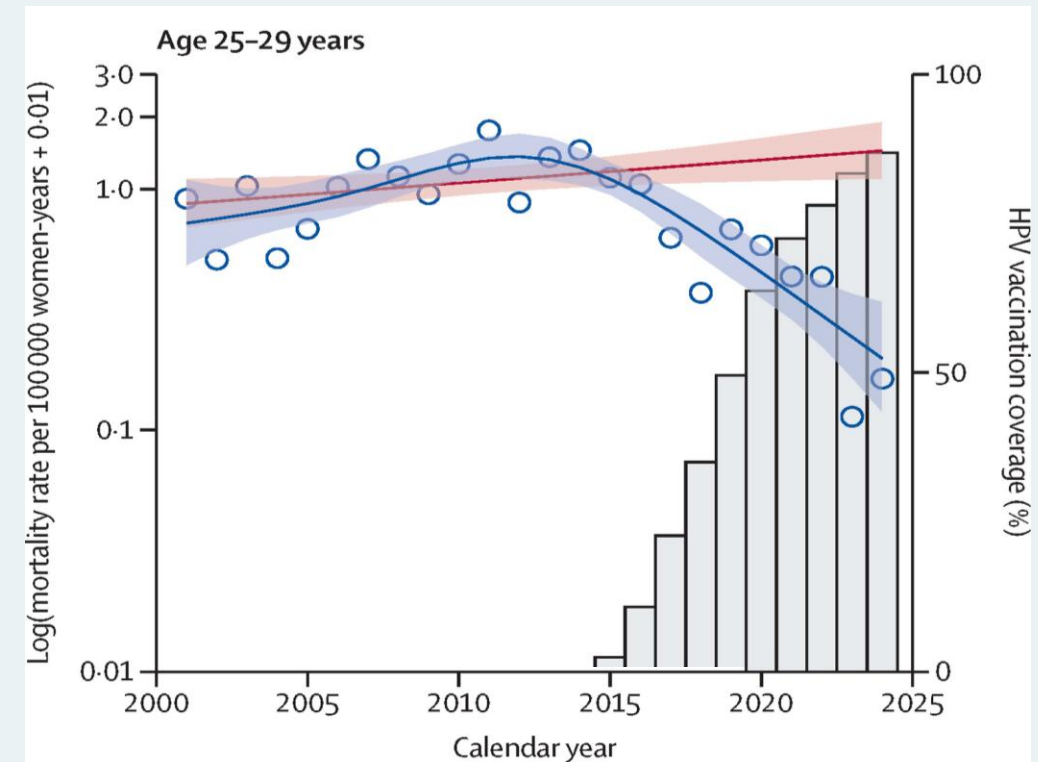
Deaths	Women-years (millions)	Rate per 100 000 women-years	Rate per 100 000 women-years
25	7.72	0.32	1.78
16	8.49	0.19	1.65
27	8.95	0.30	1.60
5	8.95	0.06	1.44
0	8.54	0.00	1.27

Decline in mortality closely mirrors vaccine uptake

Age 20-24



Age 25-29



Estimated relative cervical cancer mortality rates reduction in HPV vaccinated women assuming no herd immunity

- Age 20-24: 100% (**81** to 100%)
- Age 25-29: 100% (**89** to 100%)
- Age 30-34: 63% (-13% to 100%)

Sasieni, Falcaro *Lancet* 2026

Conclusion

- Cervical cancer in England is being 'eliminated' in women born between September 1993 and August 2007

But ...

Declining HPV vaccine uptake and growing heterogeneity across London

Maximal HPV vaccine uptake at end of Y8, Y9 and Y10,
by year of birth: Females

