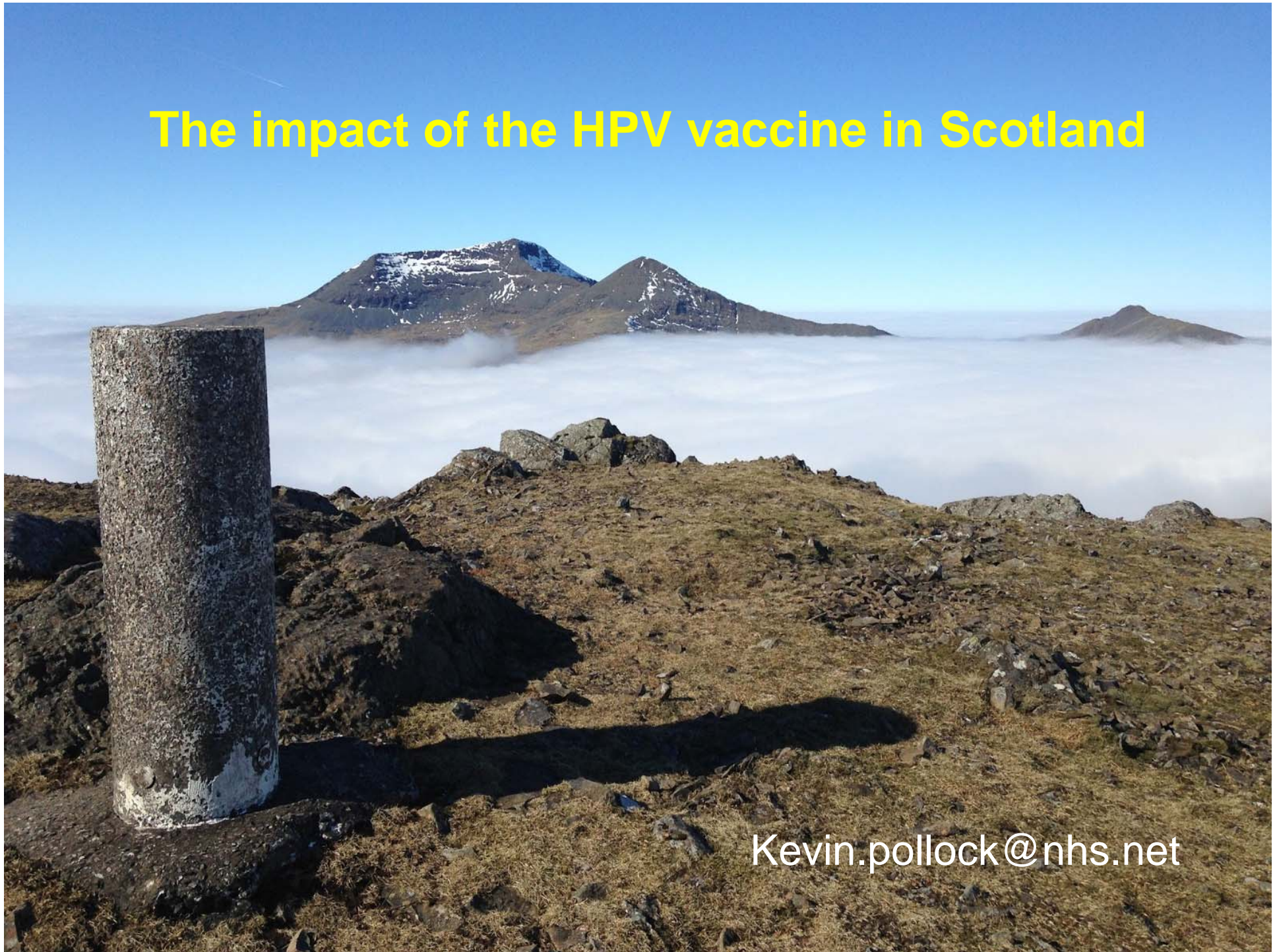


The impact of the HPV vaccine in Scotland



Kevin.pollock@nhs.net

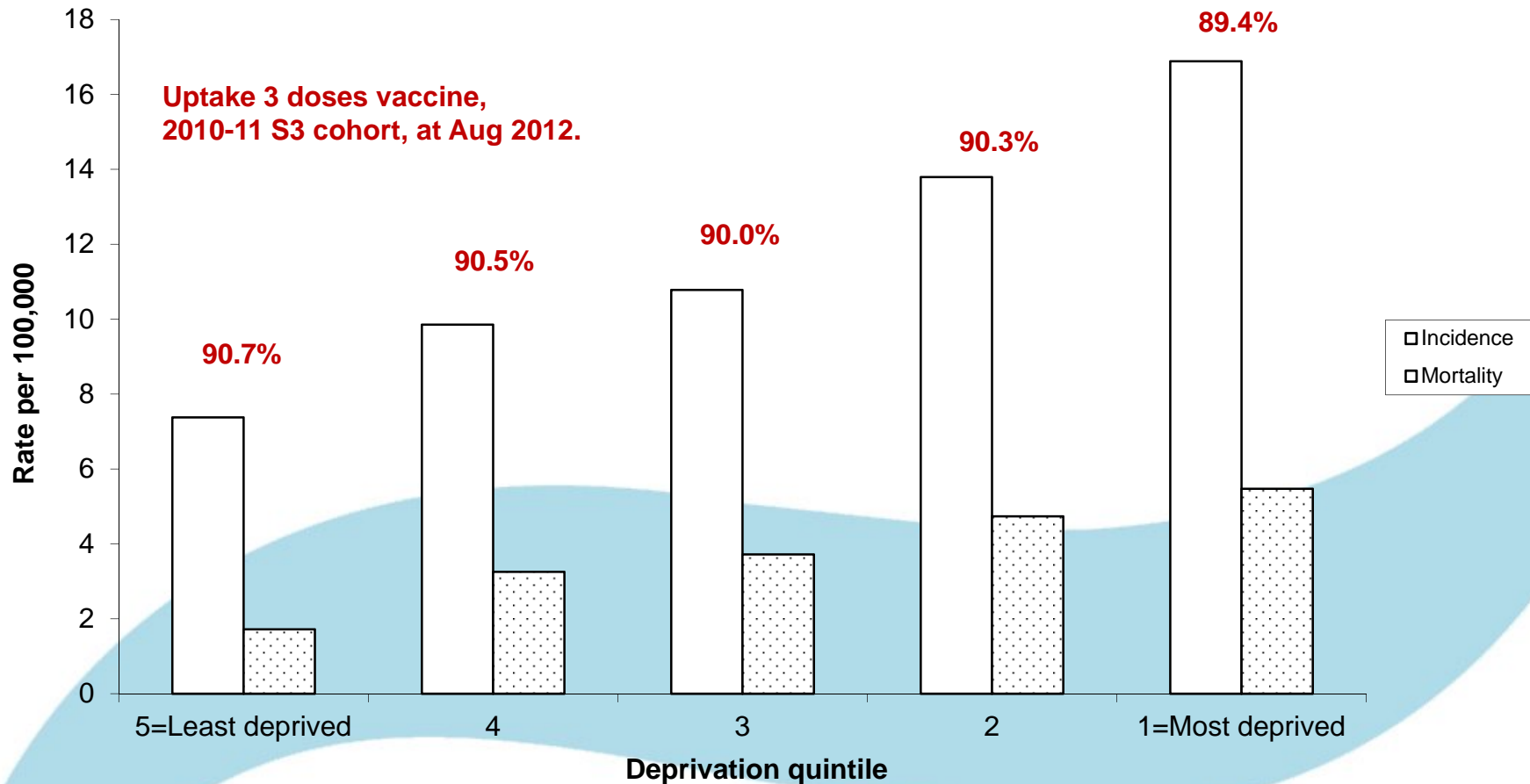


Health
Protection
Scotland

Cervical cancer by deprivation Scotland



Cancer of the cervix uteri (ICD-10 C53)
Age-standardised incidence and mortality rates by SIMD 2012 deprivation quintile



Cervical screening in Scotland

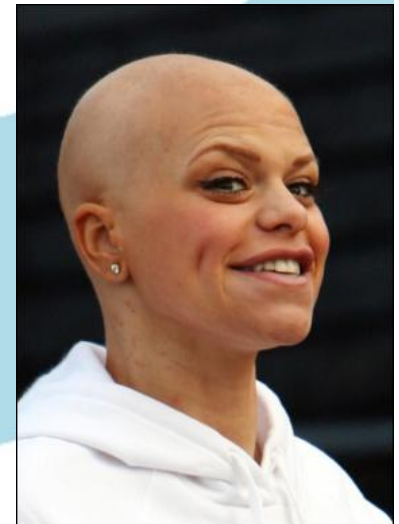
Uptake for Cervical Screening by Health Board: Scotland, 1st April 2006 to 31st March 2016

Percentage uptake of females aged 20-60¹ who had a record of a previous screening test taken within last 3.5 years

NHS Board of Residence	2006-07	2007-08	2008-09	2009-10	2010-11	2011-12	2012-13	2013-14	2014-15	2015-16
Scotland²	76.5	69.7	73.4	73.7	73.6	73.0	71.2	70.7	70.4	69.2
(Former) Argyll & Clyde*	74.8	67.1	72.4	74.2	74.6	74.2	72.7	72.1	71.7	70.7
Ayrshire & Arran	78.3	70.4	75.1	75.6	75.3	74.7	73.0	73.1	72.9	71.8
Borders	84.6	75.8	78.4	78.4	77.9	77.0	75.2	75.0	75.0	73.7
Dumfries & Galloway	83.6	73.8	76.7	76.8	76.6	76.6	76.1	75.5	75.2	74.0
Fife	73.2	71.2	73.8	72.6	72.6	72.1	70.8	70.5	70.4	69.2
Forth Valley	77.5	75.5	76.8	76.2	75.1	75.0	73.0	72.7	72.6	72.0
Grampian	79.7	72.2	75.7	76.1	75.9	75.3	73.5	73.1	72.9	71.6
Greater Glasgow*	73.5	64.2	68.7	70.1	70.1	69.5	67.4	66.3	65.1	63.5
Highland*	81.7	71.4	75.8	76.5	76.4	75.9	74.2	73.8	73.5	72.2
Lanarkshire	76.6	67.9	72.6	74.0	73.9	73.7	72.4	72.1	72.3	71.2
Lothian ³	77.4	70.3	73.1	72.5	72.5	71.3	69.2	68.5	67.9	66.7
Orkney	83.4	75.7	79.0	79.3	80.2	79.9	79.5	78.2	77.6	76.7
Shetland	85.8	77.9	81.4	81.0	80.6	80.1	78.2	78.8	78.2	77.1
Tayside	73.5	72.5	75.0	74.2	74.0	73.3	71.8	71.7	71.6	70.7
Western Isles	79.8	70.8	74.0	74.7	74.7	74.1	72.6	72.8	72.6	71.6

Cervical cancer – incidence and burden

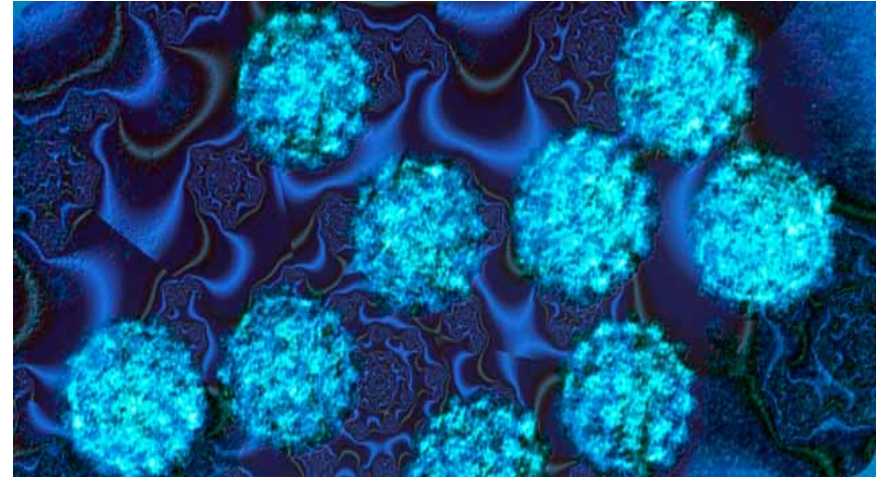
- ~ 3000 UK cases
- ~ 940 deaths a year
- ~ 300,000 cervical abnormalities
- 1 death every 2 minutes, each year worldwide
 - Mortality rates high in developing world
- Risk factors
 - HPV
 - Smoking
 - Socio-economic status



HPV: a necessary but insufficient cause of cervical cancer

- Other co-factors necessary for progression from cervical HPV infection to cancer
 - Established co-factors: tobacco smoking, high parity, long-term hormonal contraceptive use, coinfection with HIV^a
 - Probable co-factors: co-infection with *Chlamydia trachomatis*, herpes simplex virus type-2, immunosuppression, certain dietary deficiencies^a
 - Likely important: genetic and immunologic host factors and viral factors other than type (ie, variants of type, viral load, viral integration^b)
- High number of sexual partners increases acquisition of oncogenic HPV infections^a

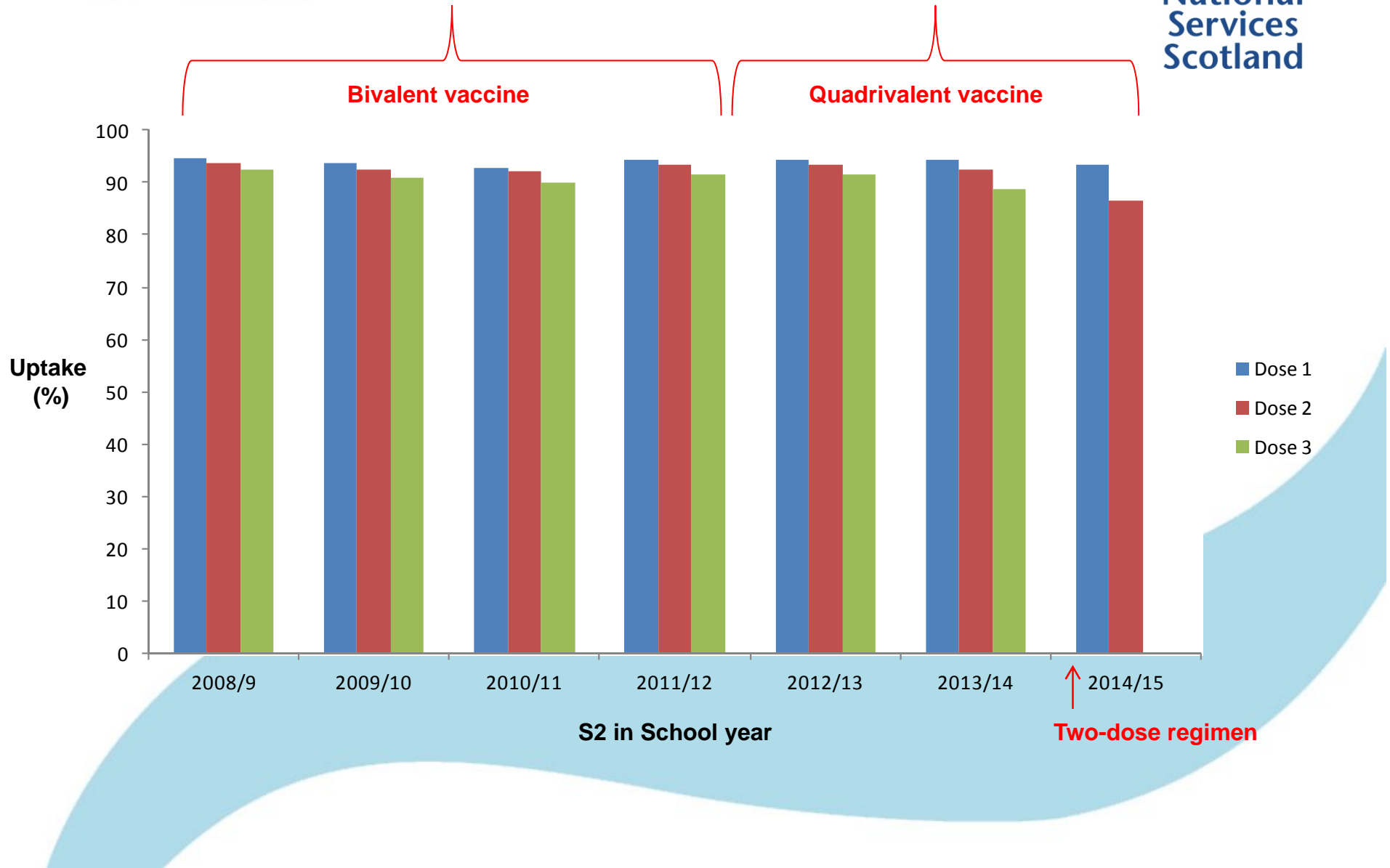
a. ICO HPV Information Centre. Human Papillomavirus and Related Diseases Report. World.; b. Muñoz N, et al. *Vaccine*. 2006;24:1-10



What is HPV?

- Human papillomavirus
- ds DNA genome comprising 8 genes
- Approximately 205 types (<http:pave.niaid.nih.gov>)
- Tropism for epithelial cells
- Extremely diverse
- Cause skin warts, plantar warts, genital condylomas
- Cervical, ano-genital and subset of oropharyngeal cancer

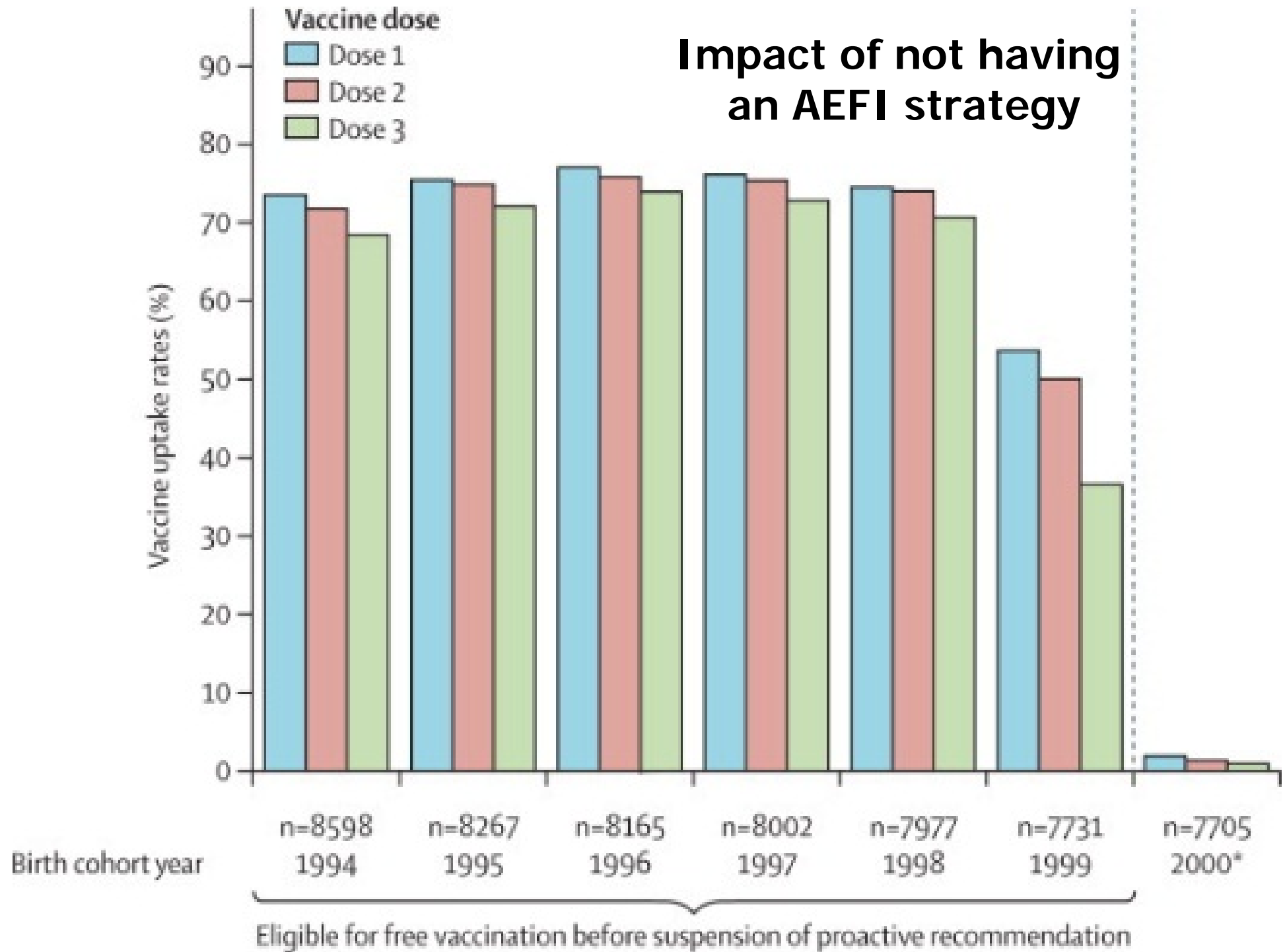
Vaccine uptake; 2008-2015



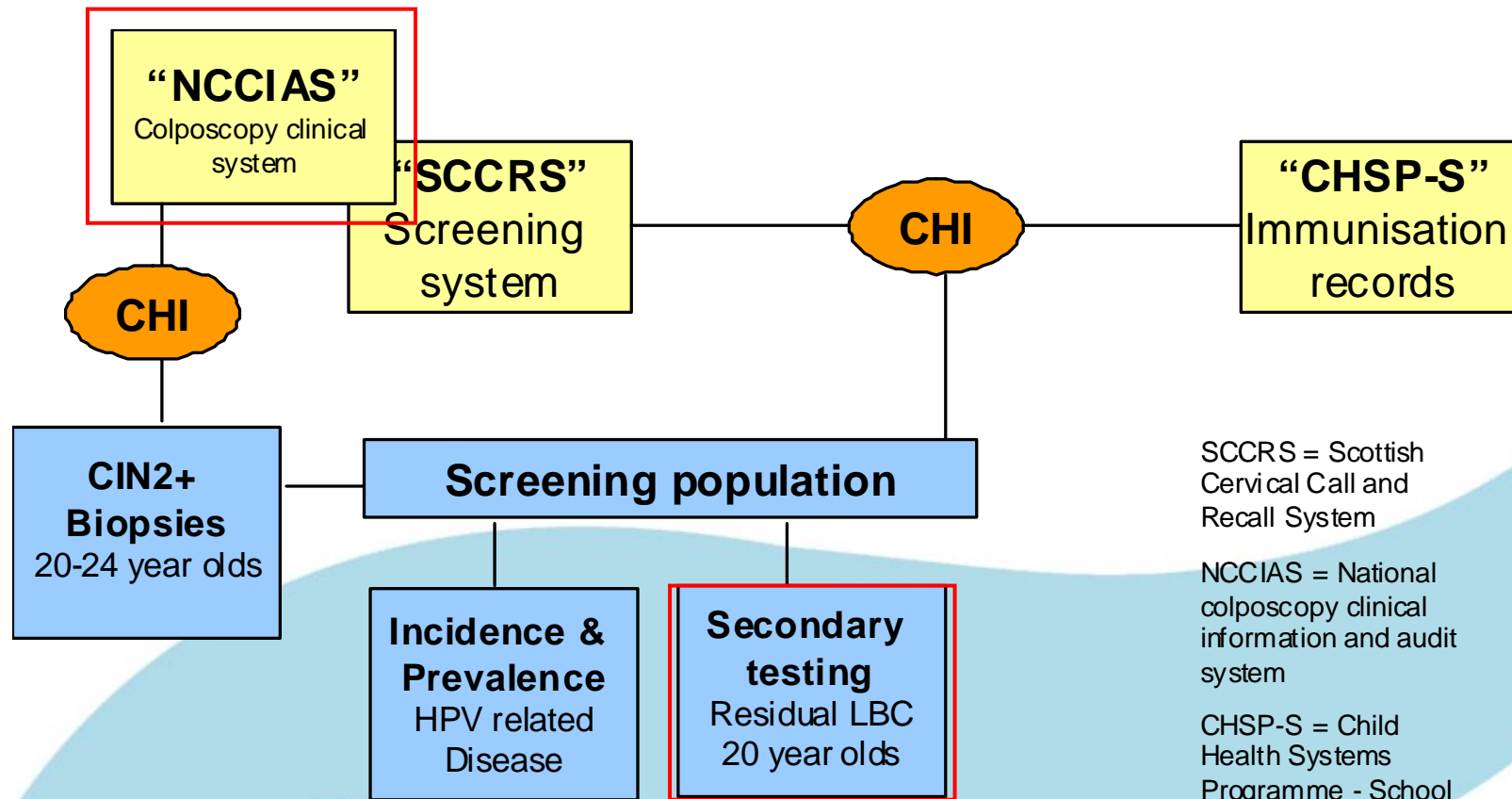
Adverse event monitoring

- Two systems
 - UK - MHRA – yellow card system
 - Scotland – SMR01 system
- ‘Blue hands’
- ‘Pain at injection site’
- No increase in over 60 conditions associated with either vaccine
 - Includes POTS, CFS and other neurological conditions
- Excellent safety profile of both vaccines

Impact of not having an AEFI strategy



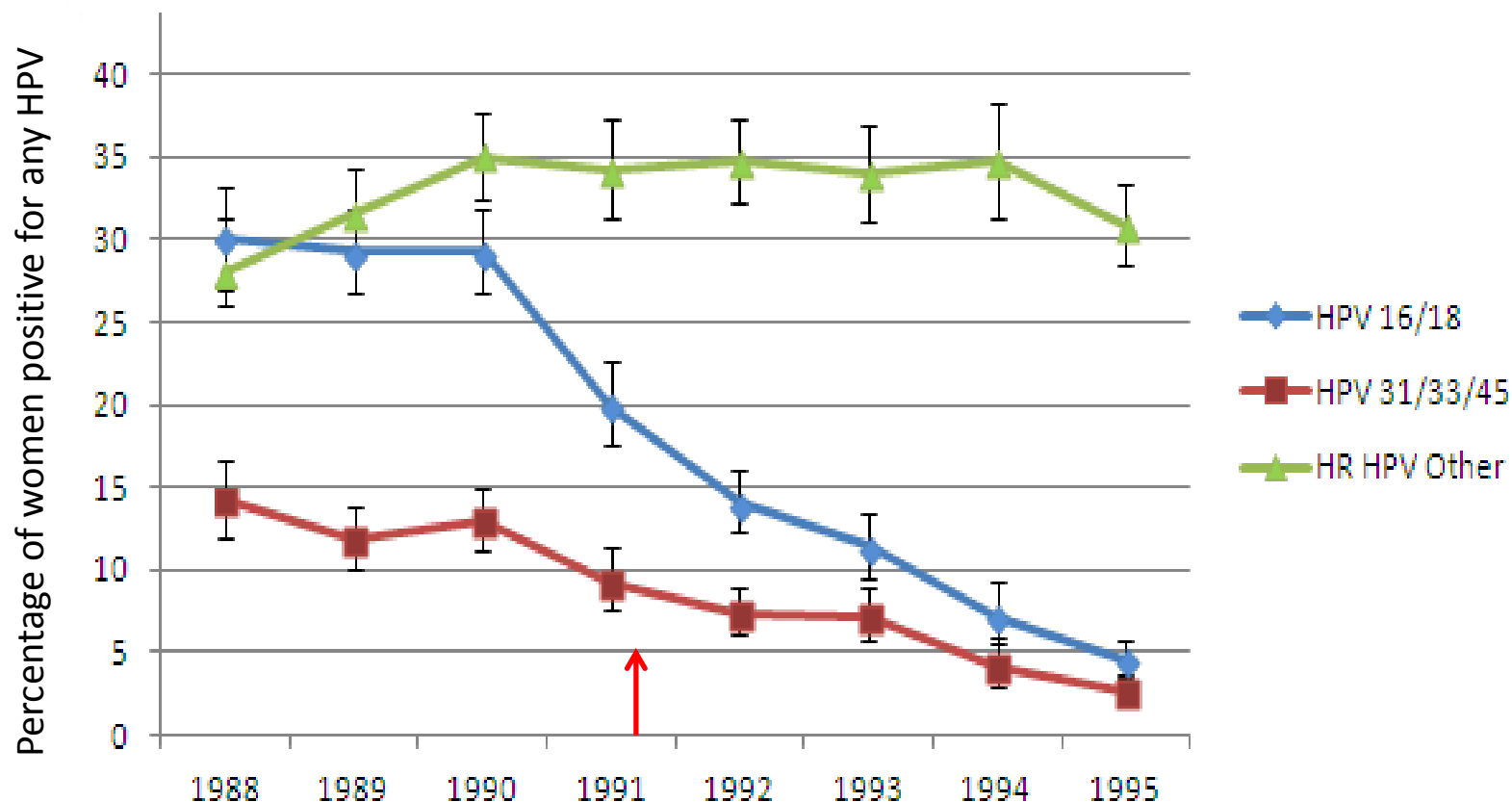
Data linkage ensures robust analyses



Scottish HPV Ref Lab (SHPVRL)

- Women attending their 1st cervical smear appointment (from age 20 in Scotland)
- HPV DNA testing of ~ 1000 anonymised residual liquid based cytology (LBC) samples
- Genotyping data for HPS surveillance since 2009 with current assay
 - High risk or putative high-risk types:
16,18,26,31,33,35,39,45,51,52,53,56,58,59,66,68,73,82
 - Low risk types: 6,11,42,43,44 & 70
 - Generates numeric value for HPV type(s) in sample

Pre- and post-vaccine HPV prevalence in 20 yo females



HPV 16/18 prevalence reduced from **30.0%** (26.9, 33.1%) in **1988 cohort** to **4.5%** (3.5, 5.7%) in the **1995 cohort**

HPV 31/33/45 prevalence reduced from **14.2%** (12-16.7%) in the **1988 cohort** to **2.6%** (95% CI: 1.9-3.6%) in the **1995 cohort**

Other HR-HPV - no significant changes

Kavanagh et al submitted

Vaccine effectiveness (VE) by birth cohort year

Birth cohort	HPV 16/18	HPV 31/33/45
	VE (95% CI)	VE (95% CI)
1990	57.8% (45.7%,67.2%)	54.8% (36.7%,67.7%)
1991	63.4% (53.3%,71.2%)	57.9% (41.7%,69.6%)
1992	72.4% (65.3%,78.1%)	63. % (50. %,72.7%)
1993	78.8% (72.5%,83.6%)	64.7% (51.1%,74.5%)
1994	85.5% (79.9%,89.5%)	77.4% (65.6%,85.2%)
1995	90.7% (87.4%,93.1%)	85.7% (78.7%,90.4%)

- All cross protective types showed significant VE at the individual level

- 1995 cohort

- HPV 31: VE=95.1% (86.4-98.3)

- HPV 33: VE=80.3% (66.8-88.2)

- HPV 45: VE=82.2% (62.6-91.5).

Evidence of herd protection in unvaccinated females

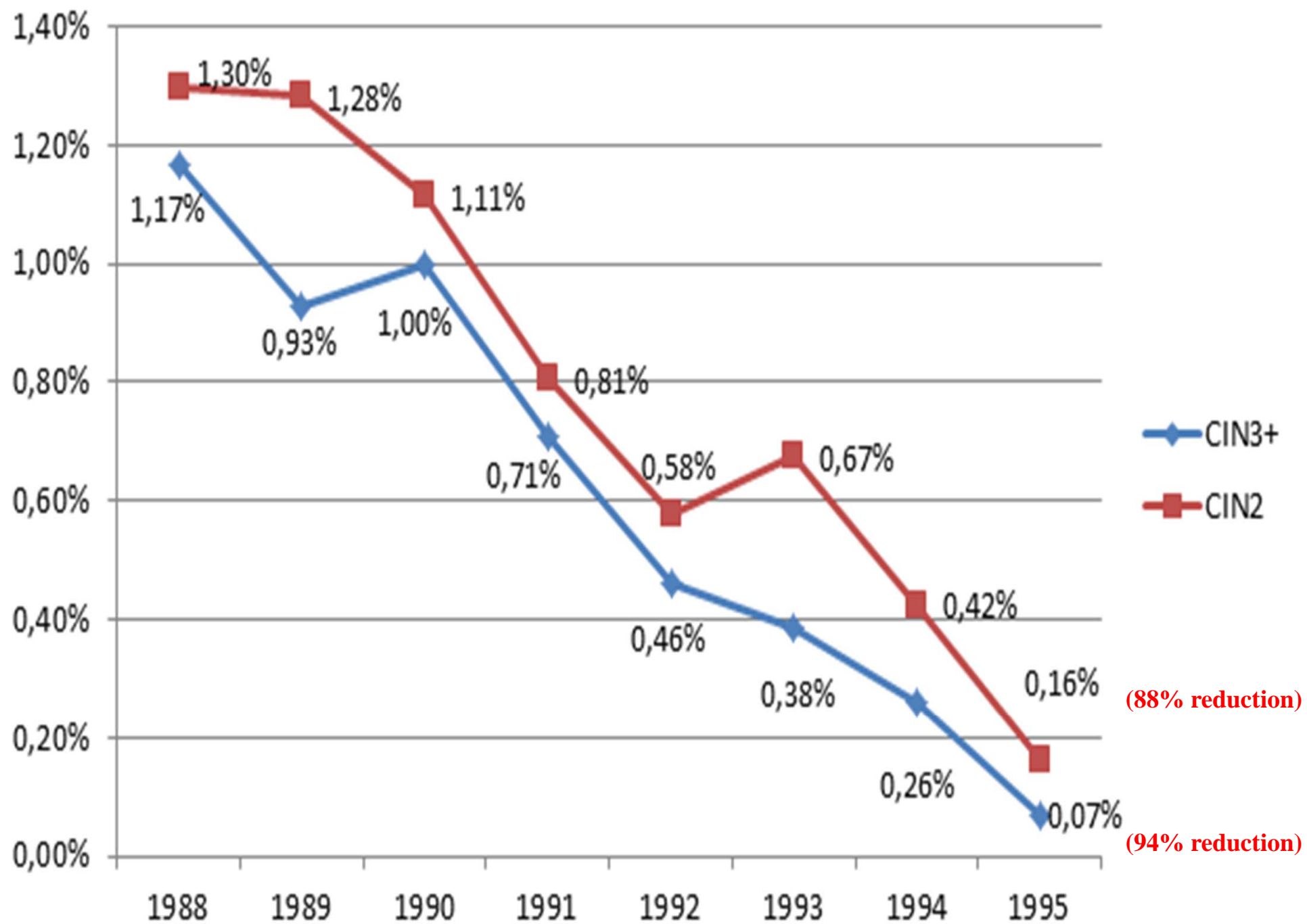
Study year	HPV 16 or 18		HPV31 or 33 or 45	
	OR	95% CI	OR	95% CI
2009	1	-	1	-
2010	1.128	(0.95, 1.339)	1.095	(0.87, 1.379)
2011	1.045	(0.846, 1.291)	0.989	(0.742, 1.32)
2012	1.175	(0.879, 1.57)	0.876	(0.576, 1.333)
2013	0.669	(0.468, 0.956)	0.714	(0.436, 1.171)

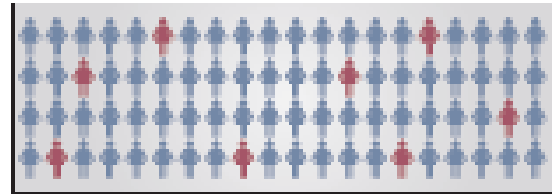
Emerg Infect Dis. 2016 Jan;22(1):56-64.

Human Papillomavirus Prevalence and Herd Immunity after Introduction of Vaccination Program, Scotland, 2009-2013. Cameron RL, Kavanagh K, Pan J, Love J, Cuschieri K, Robertson C, Ahmed S, Palmer T, Pollock KG.

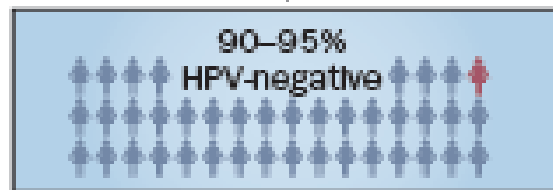
Effect of vaccination on cervical intraepithelial neoplasia (CIN)

- Assessment of screened cohort for women born 1988-1994
 - 1988,1989,1990 – pre-vaccine
 - 1991-95 – vaccine eligible
- Omission of small number of episodes (referred to colposcopy before screening)
- Inclusion of incident abnormal (CIN1-3) cases in 1st year after 1st screen, by cohort year
- Poisson regression model adjustment for birth cohort and deprivation
- **> 4000** individuals censored to December 2015

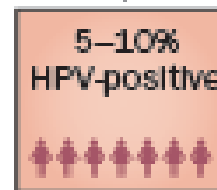




The future of screening?



83%*–90%[‡]
Expected vaccine efficacy in HPV-negative adult women



Triage

Negative
Follow-up until
HPV clearance

CIN2+
Treatment and
follow-up

>90%
Expected protection against invasive disease

'Screen and treat'
protocols

Unknown protection
against
invasive disease

-  Woman without prevalent HPV infection/cervical neoplasia
-  Woman with prevalent HPV infection/cervical neoplasia

Relative risk of genital warts episodes in females adjusted for age and birth cohort

Model 3: Brand effect		Age	15	1	.
			16	2.21 (1.6-3.06)	0.000
			17	3.52 (2.57-4.82)	0.000
			18	7.17 (5.29-9.7)	0.000
			19	9.79 (7.13-13.46)	0.000
Vaccination Status	Bivalent			1	.
	Unvaccinated			0.91 (0.66-1.26)	0.564
	Quadrivalent			0.33 (0.14-0.83)	0.018

Conclusions

Annual HPV vaccine coverage in Scotland exceeds 90%

School-based approach is best – Scottish school nurse

Analysis suggests reduction/ablation in HPV 16 and 18 and other HR HPV types – account for 90% of cervical cancers

Good evidence of herd protection in unvaccinated

Vaccine associated with 88% and 94% reduction in CIN 2 and 3+ at population level

Landscape of cervical disease is changing – screening to evolve due to reduced PPV – opportunity to vaccinate HPV (-) women?

67% reduction in genital warts associated only with 4-valent vaccine



Communicate
via media!

Matthew 5:16
“Let your light so
shine before men,
that they may see
your good works”

Acknowledgements

- School nurses
- Scottish cytology and pathology laboratories
- Colposcopists
- Screening programme co-ordinators
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