Controlling HPV infection: who should be vaccinated?

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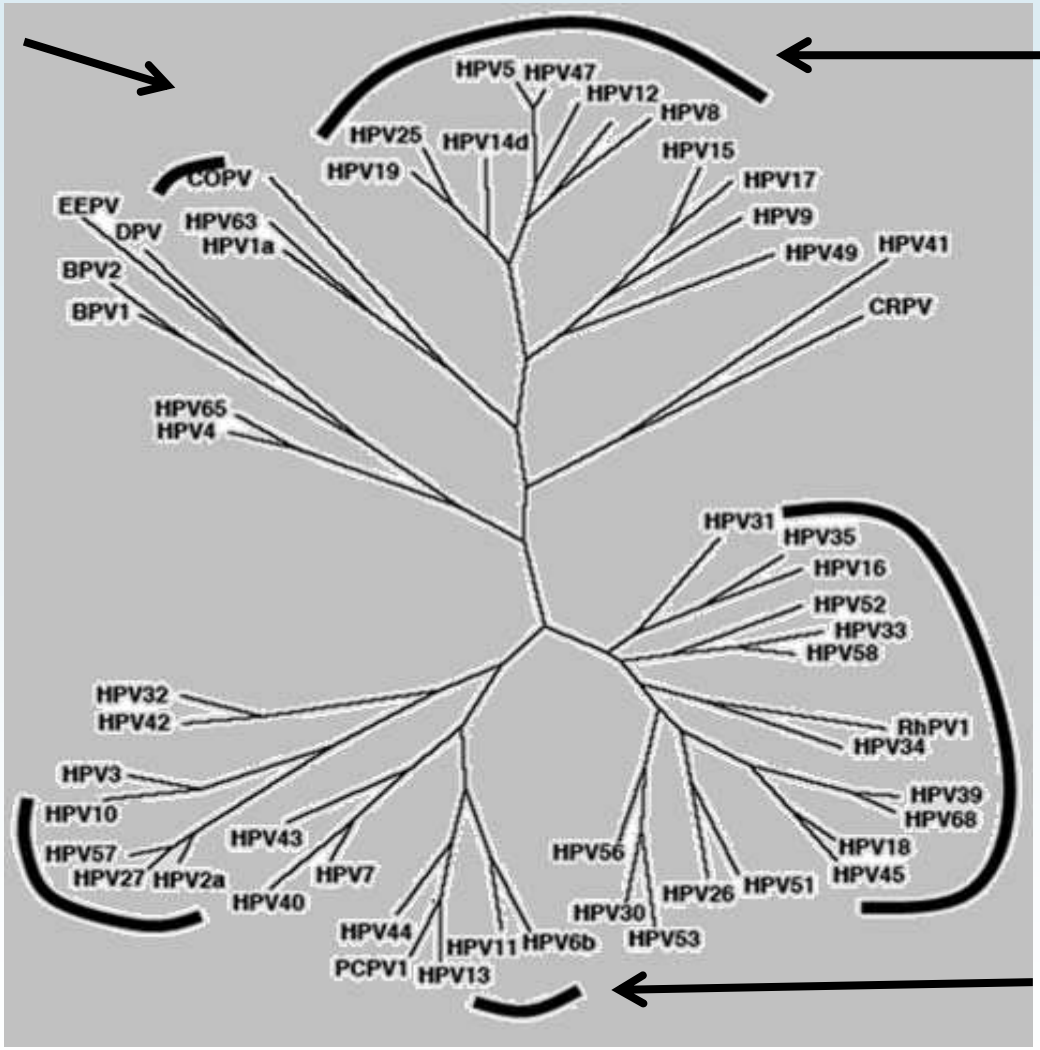
XII Course on HIV Infection and Viral Hepatitis, February 2018

Overview:

- HPV vaccines – background
- HPV vaccination programme: scope and objectives
- HPV vaccination programmes in MSM and HIV positive population
- Future developments

Plantar Warts



Cutaneous (mostly asymptomatic)

Genital mucosa (cancer–associated)

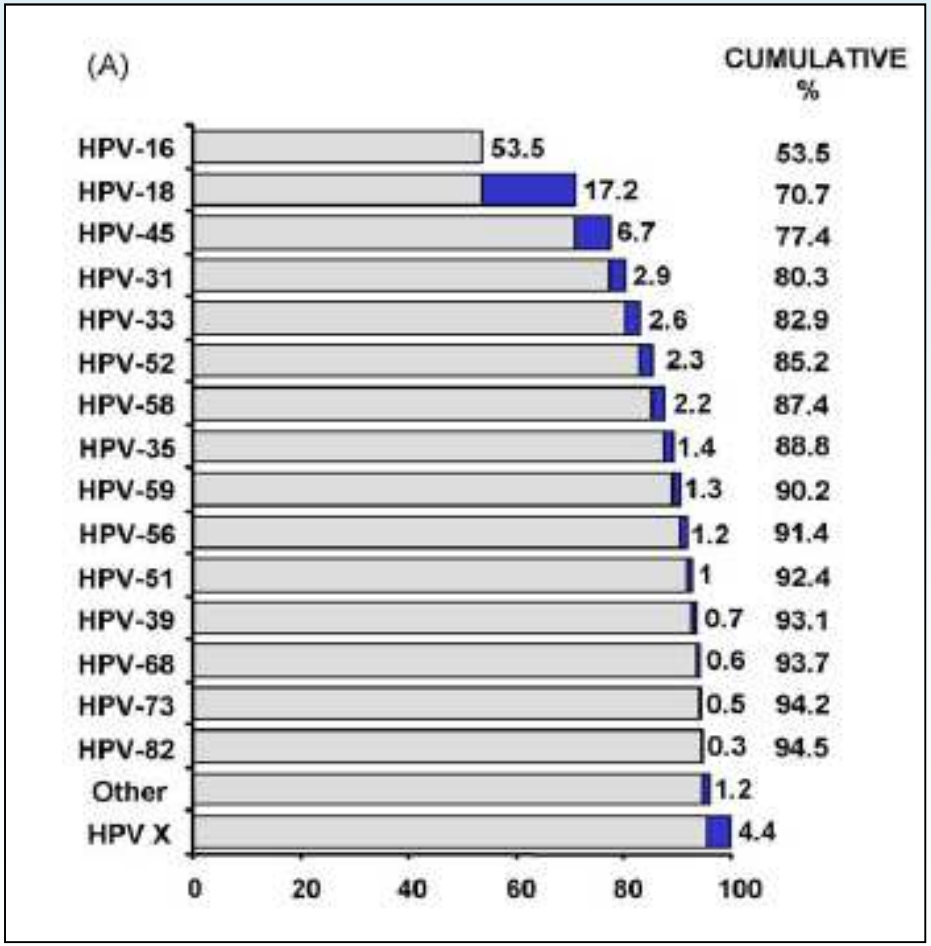
Common and flat warts

External genital warts

De Villiers 2004

Proportion of cervical cancer attributable to type-specific HPV infection

HPV 16 and 18 cause 70% of cervical cancers



Clifford G, et al. Vaccine 2006.

Muñoz N, et al. Int J Cancer, 2004.

HPV vaccines licensed in Europe

	Gardasil®	Cervarix®
Manufacturer	Merck	GlaxoSmithKline
VLP Types	6/11/16/18	16/18
Dose of L1 Protein	20/40/40/20 µg	20/20 µg
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Adjuvant	225 µg aluminum hydroxyphosphate sulfate	500 µg aluminum hydroxide, 50 µg monophosphoryl lipid A
Injection Schedule	0, 2, 6 months	0, 1, 6 months
First EU marketing authorisation	September 2006	September 2007

HPV vaccine – programme implementation

National HPV vaccine programme in the UK

- primary aim – reduce cervical cancer incidence and mortality
- started in UK in September 2008 – bivalent vaccine – HPV16/18
- School-based programme
- girls aged 12 -13
- catch-up programme in young women up to 18 years
- boys not included – not cost-effective unless uptake in girls low

HPV vaccine – programme implementation

National HPV vaccine programme

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Phase 2: Switch to quadrivalent vaccine

- September 2012 - switch to Gardasil - HPV 6/11 (and HPV 16/18)
- protects against genital warts
- 3 doses – 0, 2, 6-12 months

HPV vaccine – programme implementation

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Switch to quadrivalent vaccine

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Phase 3: Switch from 3 dose to 2 doses

- Equivalent immunogenicity for girls under 14/15 years of age only

- 0, 6 months

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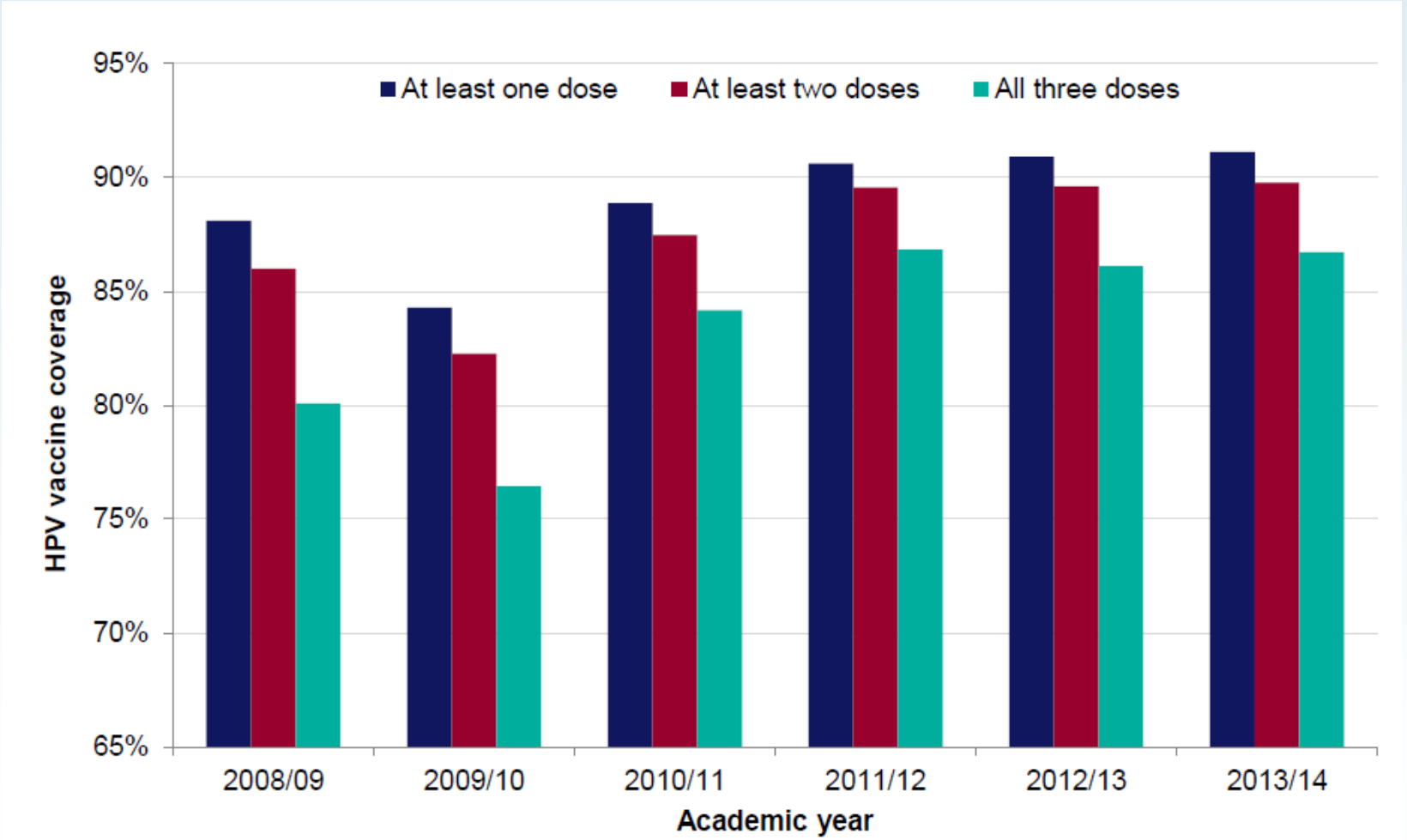
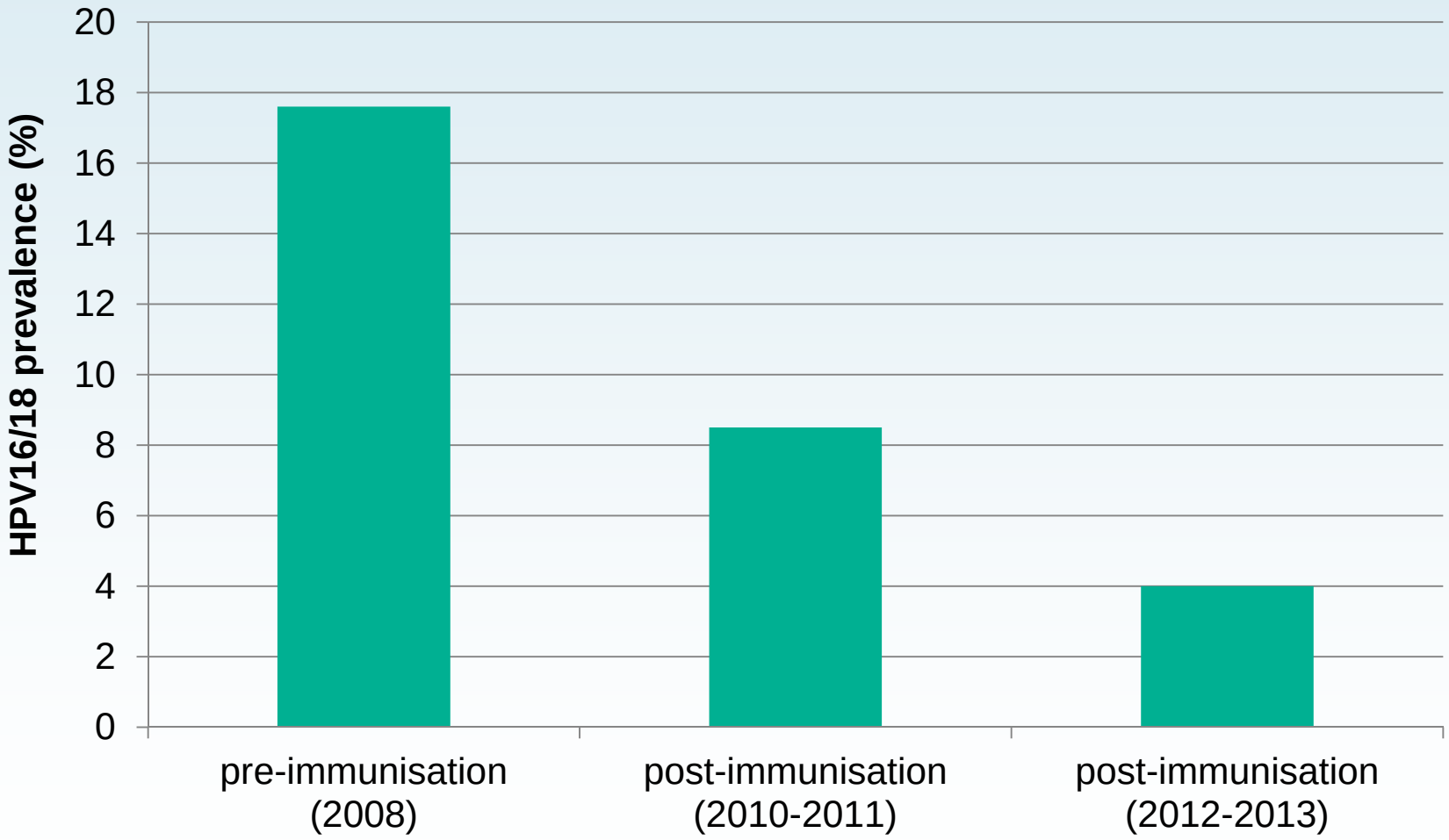
HPV vaccine coverage, school year 8 females



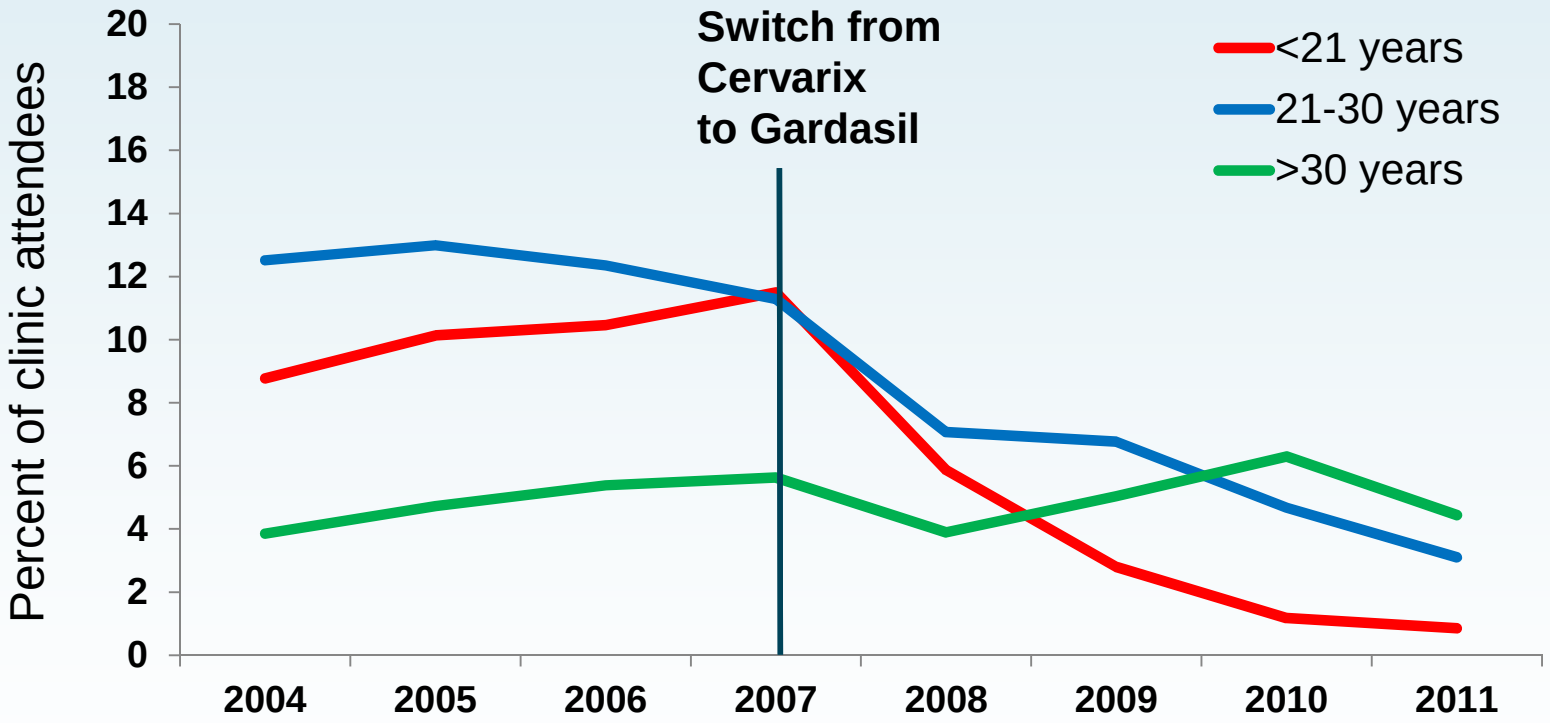
PHE data for England

Prevalence of HPV16/18 among 16-18 year old females



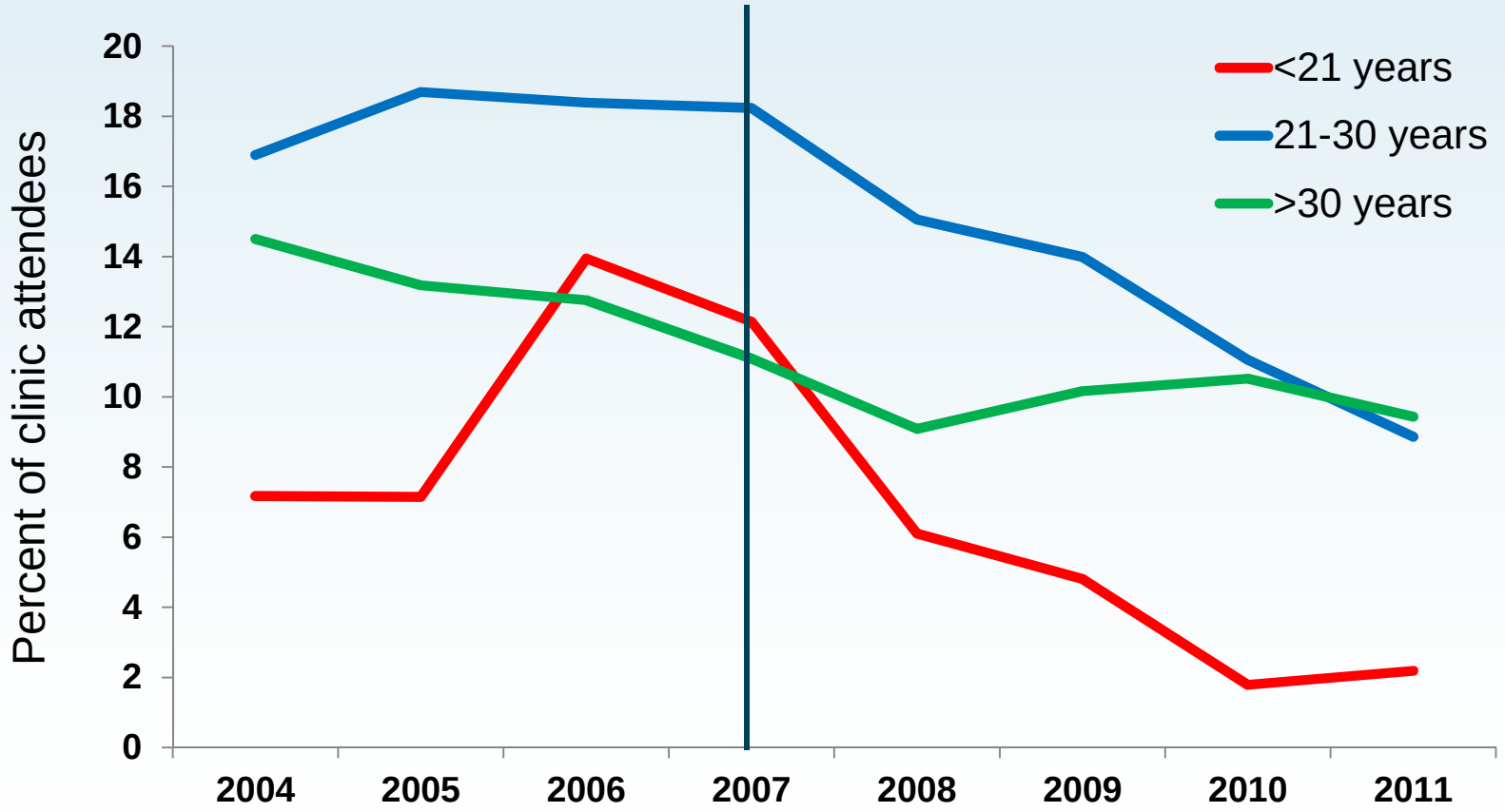
Prevalence estimate from HPV DNA testing of chlamydia screening samples – NCSP/PHE

Proportion of Australian-born women with genital warts by age group, 2004-2011



Ali H etal; Genital warts in young Australians five years into national human papillomavirus vaccination programme: national surveillance data. BMJ 2013;346:

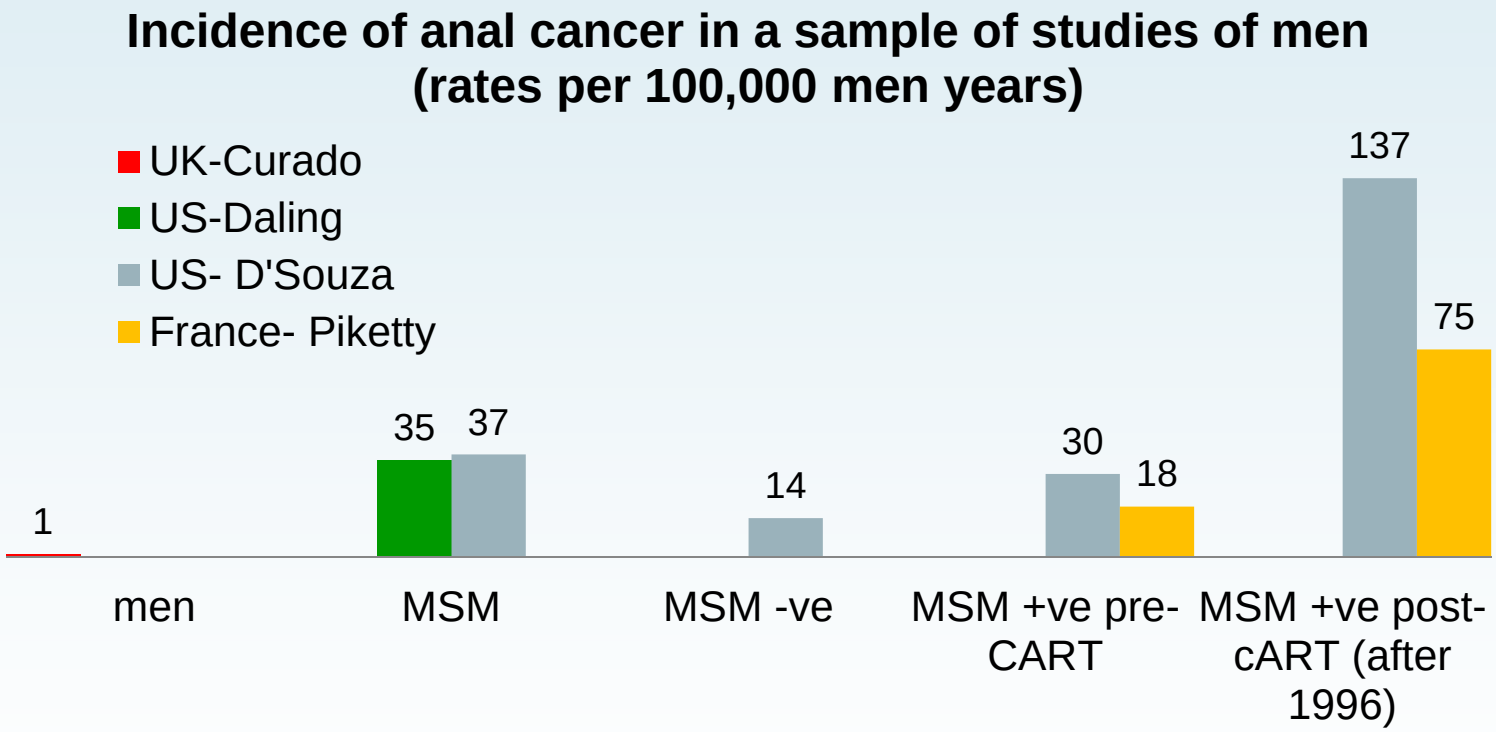
Proportion of Australian-born heterosexual men with genital warts by age group, 2004-2011 (Ali H et al BMJ 2013)



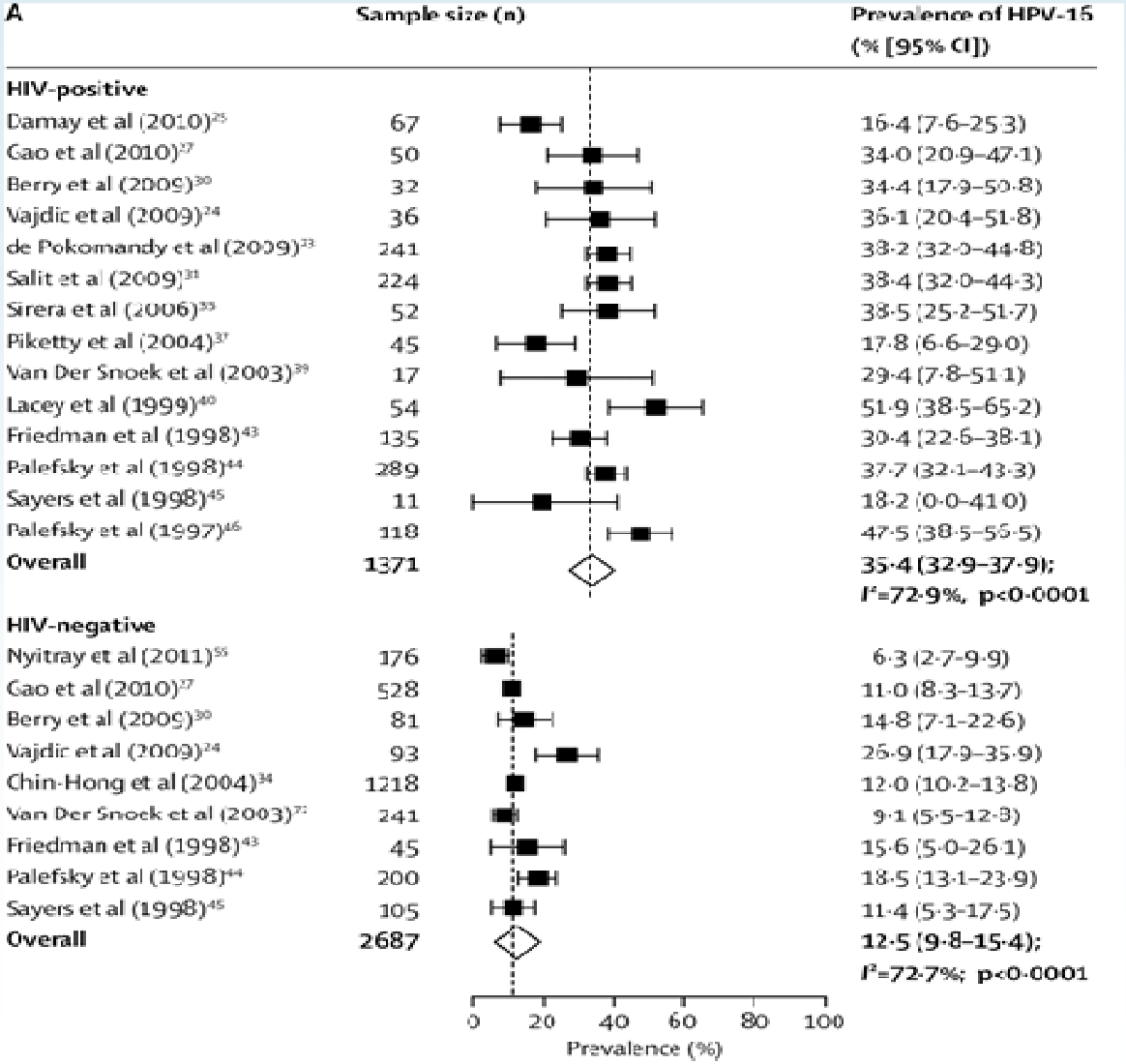
Rationale for targeted vaccination of men who have sex with men (MSM)

- MSM will not derived indirect benefit from vaccination of girls – no herd protection
- MSM who attend sexual health and HIV treatment services
  - high incidence of HPV infection
  - Clinic attendees include more men with high risk sexual behaviour and other STIs
- HPV 16-associated anal cancer is more common in MSM compared to heterosexual men
- Incidence of anal cancer is highest in HIV positive MSM – similar to cervical cancer rates before cervical screening
- MSM would benefit from the direct protective effect of vaccine.

MSM - disproportionate HPV disease burden



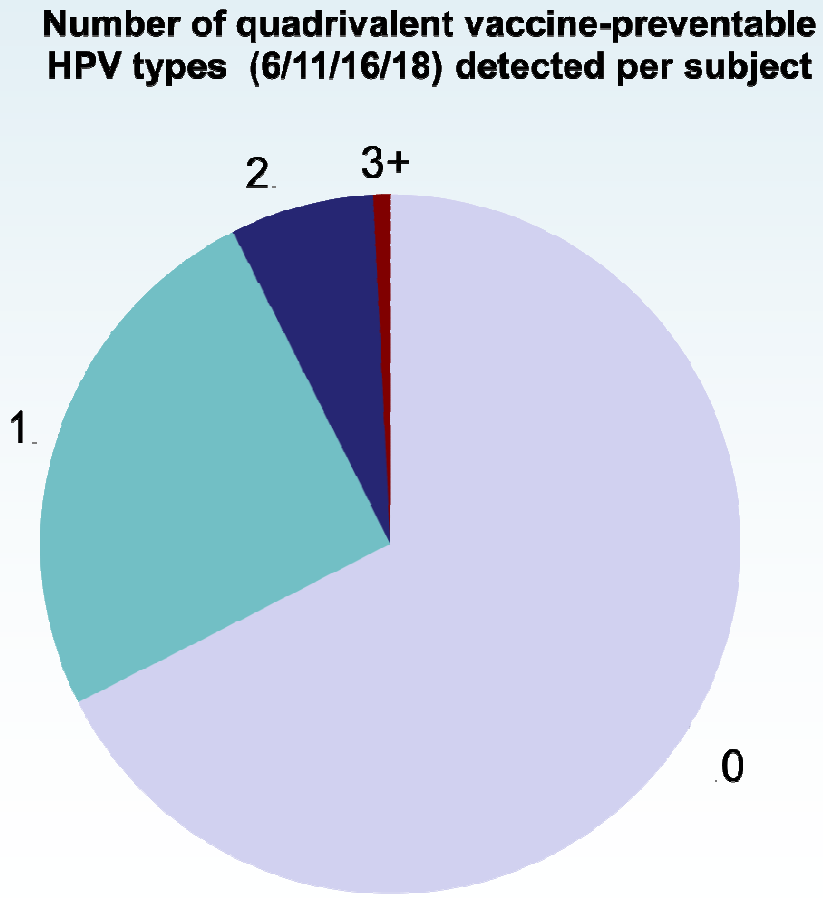
Prevalence of anal HPV 16 in HIV-positive and HIV-negative MSM
(Machalek, et al Sexual Health 2012)



HPV prevalence in MSM attending a sexual health clinic – potential for prevention? (King et al 2014)

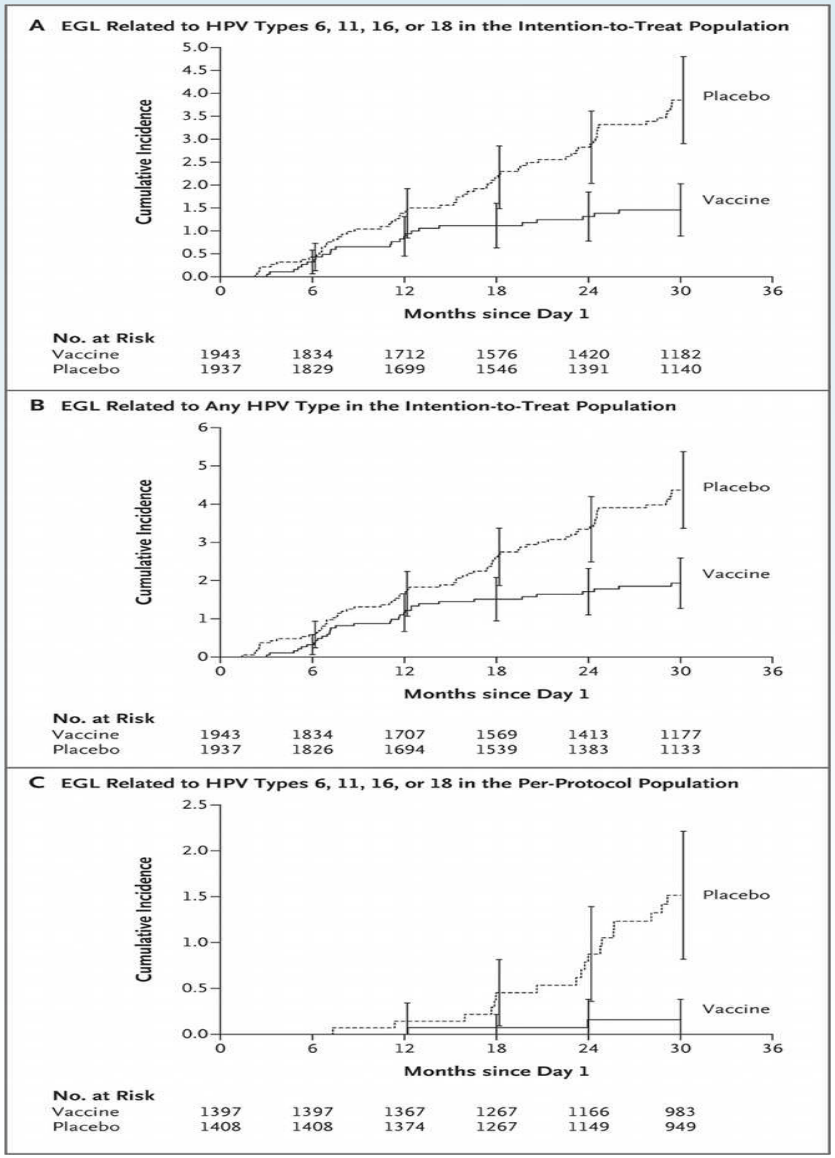
1 type – 25.1%
2 types – 6.7%
3 types – 0.8%
4 types – 0%

No HPV – 67.5%



Analysis of the Time to Appearance of External Genital Lesions in the Intention-to-Treat and Per-Protocol Populations.

Giuliano AR et al. N Engl J Med 2011;364:401-411.

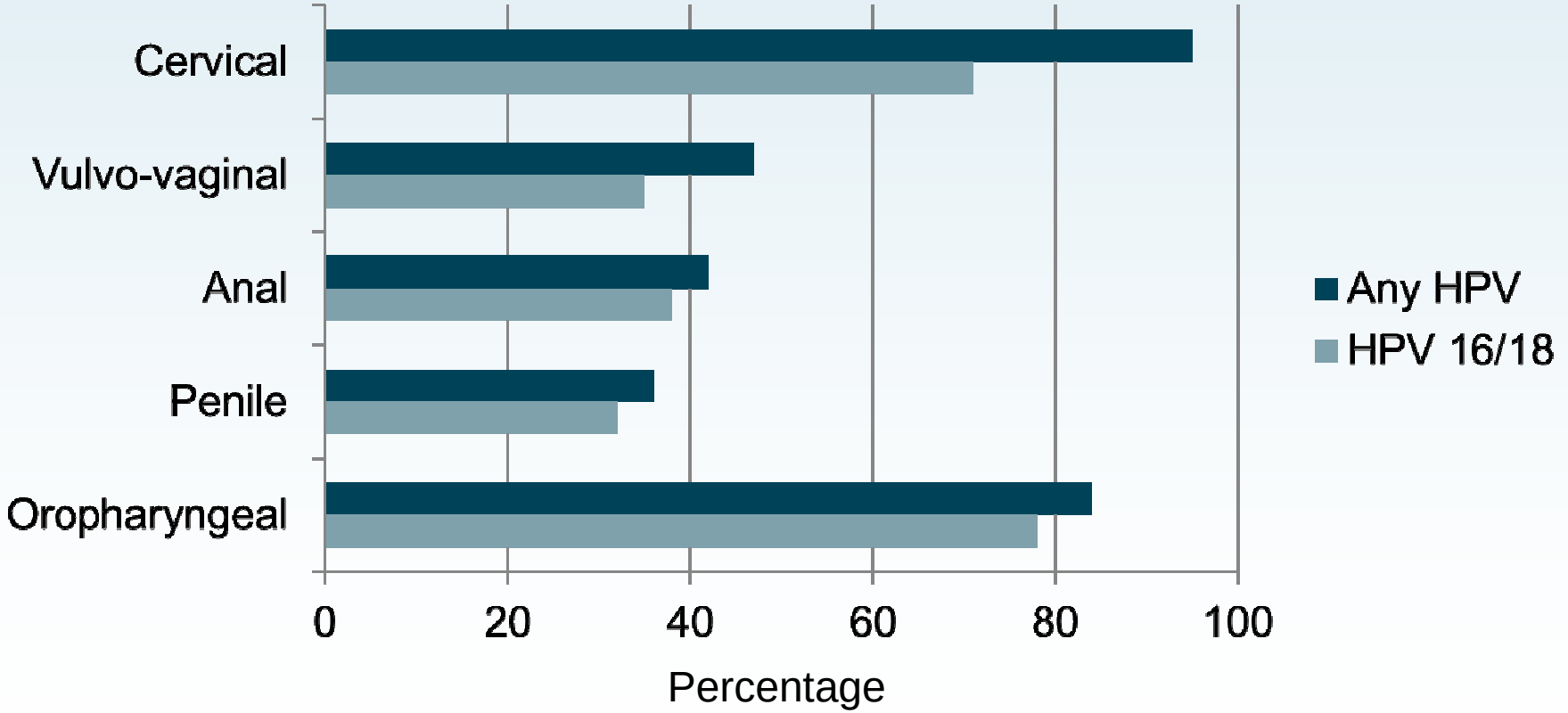


Recommendation for a programme of HPV vaccination in MSM (2015)

- Targeted vaccination of MSM attending sexual health and HIV services.
- Age up to 45
- Quadrivalent vaccine – bivalent not cost effective
- Provided that:
  - Vaccine purchase and delivery feasible
  - Vaccine cost the same or less than the national programme price
  - Delivery cost is low
  - No adverse effect on the girls programme

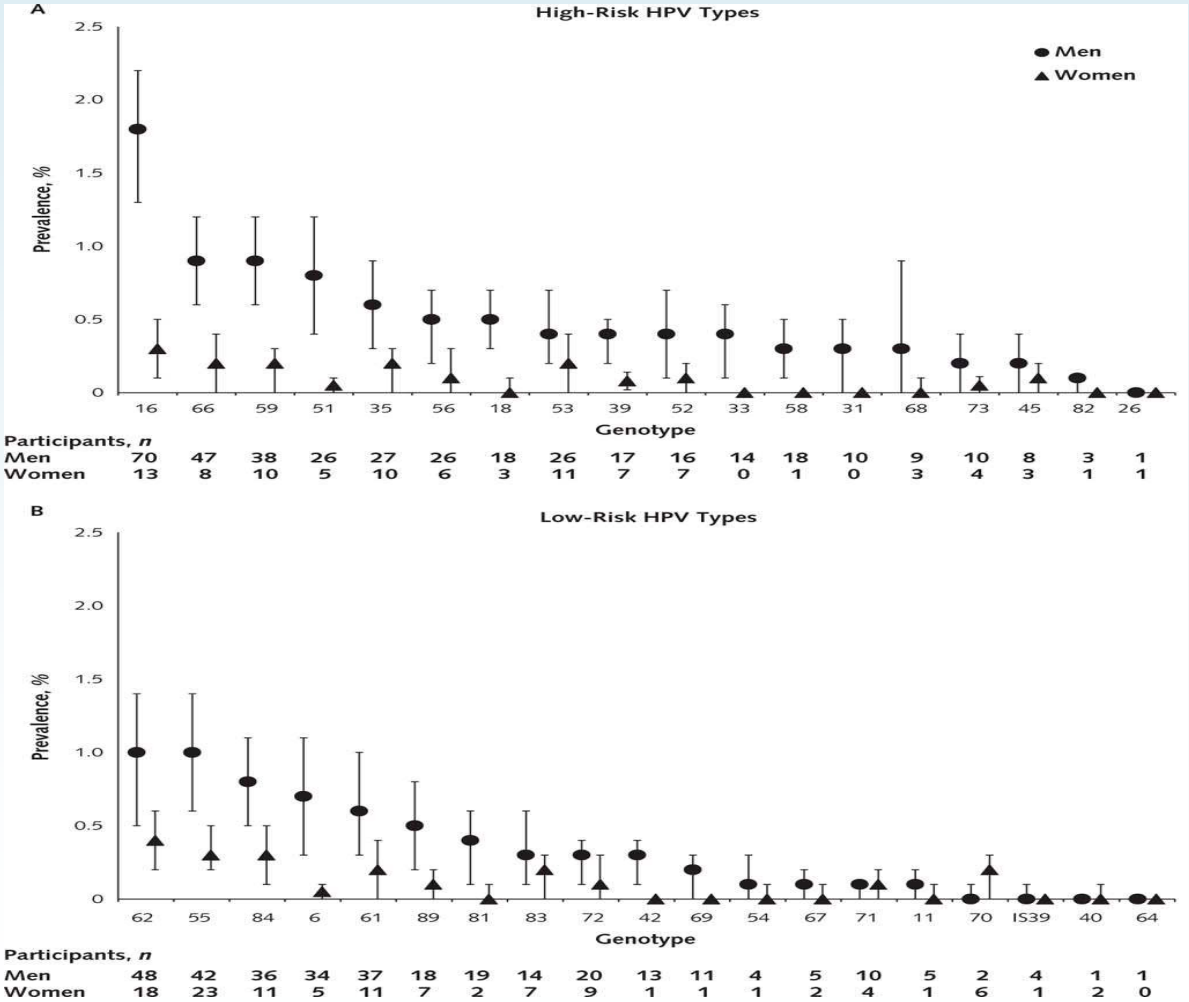
(UK Joint Committee on Vaccination and Immunisation)

HPV – cause of genital and extra-genital cancer



After Jit et al 2011

Type-specific prevalence of oral HPV infection among men and women, NHANES 2011–2014.



Sonawane et al
Ann Int Med 2017

HPV vaccine – programme implementation – next phase?

‘Gender neutral’ vaccination

Vaccination of all boys in parallel with girls at age 12/13

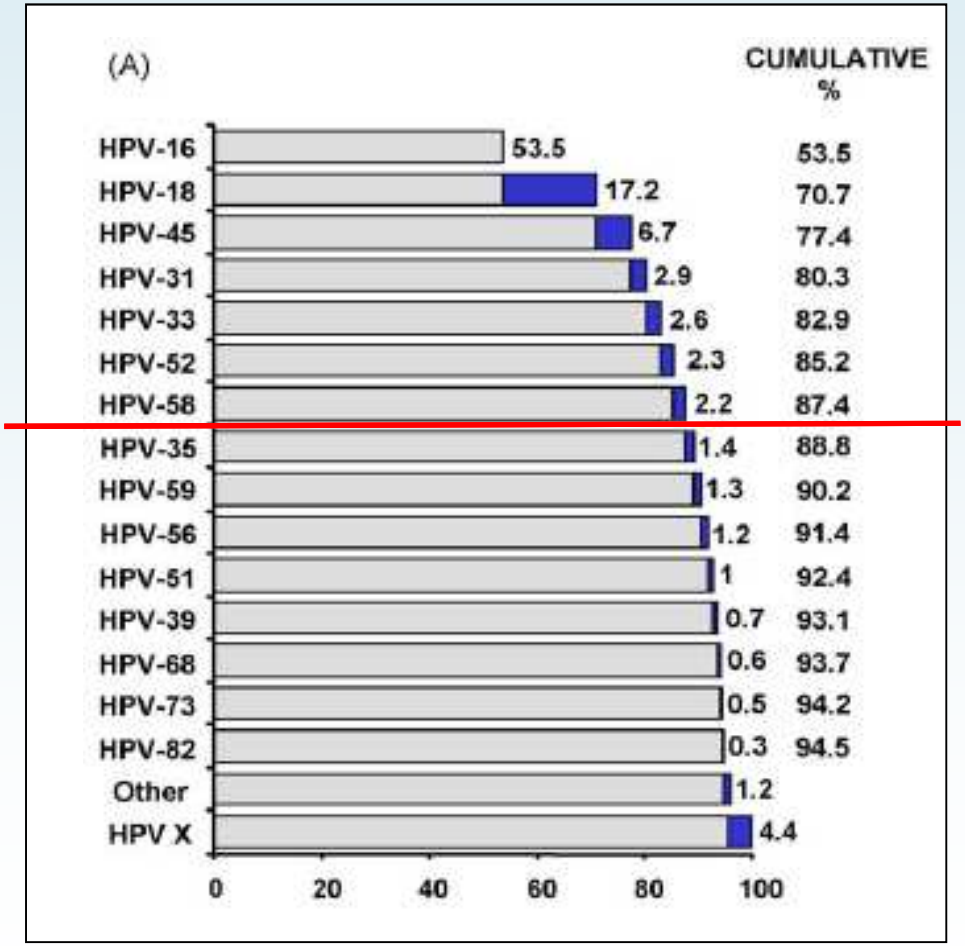
Already implemented – eg in Australia

UK - still under consideration – economic analysis on-going – initial assessment suggests that it is unlikely to be recommended

Strict rules on cost-effectiveness analysis in the NHS

Proportion of cervical cancer attributable to type-specific HPV infection

- HPV 16 and 18 cause 70% of cervical cancers
- 87% of cervical cancer associated with 7 HR HPV types



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Second generation vaccine: Gardasil9

- Extended protection against high-risk types: HPV 31, 33, 45, 52, 58
- Same protection against HPV6/11/16/18 – after adjustment of the antigen dose
- Increases the proportion of cancers prevented
- No additional benefit against genital warts
- Schedule: 3 doses
- Licensed in Europe in 2015

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Adverse reactions to HPV vaccines

Common

- Erythema, pain, swelling at the injection site
- Headache, myalgia, fatigue, and low grade fever.

..usually mild or moderate in intensity

NOT associated with:

•POTS – Postural Orthostatic Tachycardia Syndrome

•CRPS – Chronic Regional Pain Syndrome

HPV immunisation of HIV-positive individuals

- Individuals with HIV infection should be given HPV vaccine regardless of CD4 count, antiretroviral therapy use or viral load.
- Safety – no evidence of any difference.
- Seroconversion following vaccination equivalent
- Antibody levels slightly lower – impact on efficacy unknown – probably not significant
- Always use a 3-dose schedule.

Future

- Next generation vaccines – extended range
- Reduced doses
- Extend the age range
- Programmes in low and middle income countries

Thank you…