HPV in older people: to vaccinate or not to vaccinate?

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Disclosures

Nothing to declare

EXCEPT…

Clinical epidemiologist

Medically trained but haven't seen a patient for 20 years

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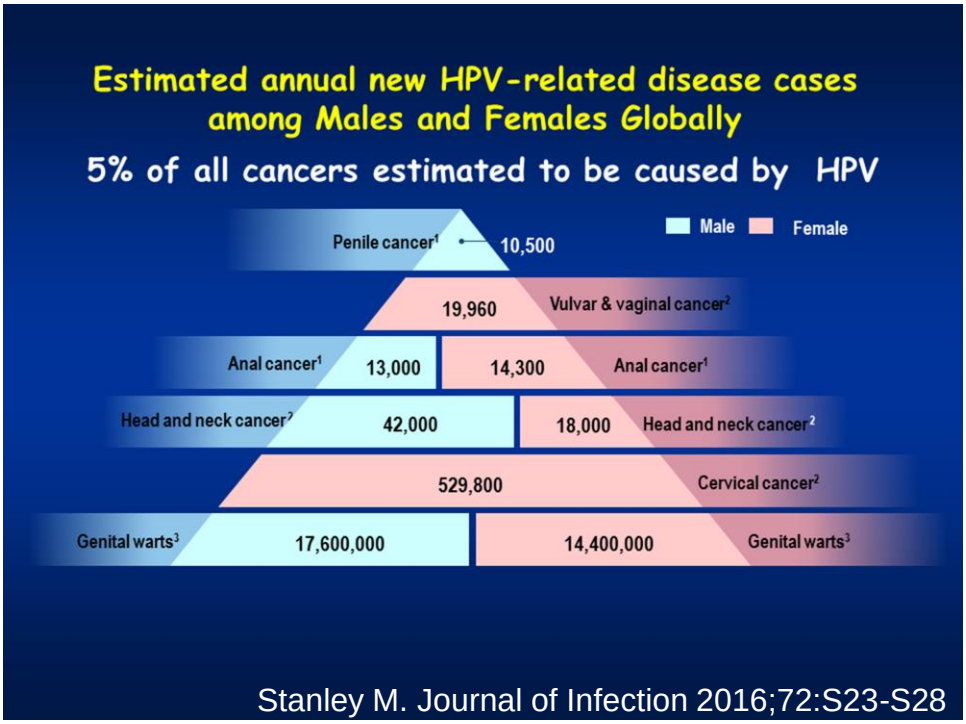
HPV vaccination in older people

Talk outline

- What is HPV and which cancers are associated?
- HPV vaccines
- Current recommendations
- Evidence
- What do clinicians think?
- Pros and cons

HPV – basic facts

- Majority of sexually active individuals acquire ≥1 ano-genital HPV genotype during their lifetime
- Most individuals will clear or control infection within 1-2 years
- Same type HPV infections can reappear among previously exposed individuals (reactivation of latent infections or new infection after successfully clearing type-specific infection)
- 60%–70% of women and 40-50% of men who acquire an HPV infection develop a measurable type-specific serum antibody response
- Offers only some protection –vaccine generates antibody concentrations that are 1-4 logs higher than those in natural infections
- Most HPV-associated cancers appear 10-30 years after infection (shorter in immunocompromised/HIV positive)



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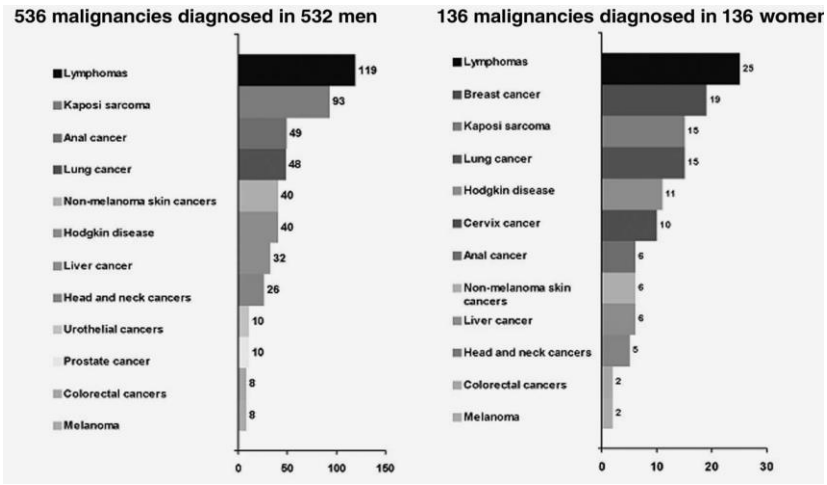
Malignancies in people with HIV



E Lanoy et al, Int J Cancer 2011

Three prophylactic, highly efficacious vaccines available

- First licensed in 2007

- Bivalent vaccine (Cervarix®):

Non-infectious protein antigens for HPV16 and 18

- Quadrivalent vaccine (Gardasil®):

Non-infectious protein antigens for HPV6, 11, 16, and 18

- Nonavalent vaccine (Gardasil 9®):

Non-infectious protein antigens for HPV6, 11, 16, 18, 31, 33, 45, 52 and 58

Pharmaceutical Benefits Advisory Committee recently recommended that Gardasil 9® be used in the school-age program

The Australian Immunisation Handbook 10th Edition (August 2017)

- **Adolescent girls and boys** (aged ~12–13 years) school based program

- **Adults aged ≥19 years**

Vaccination this age group is not routinely recommended due to previous exposure

However, some adult females and males may gain an individual benefit from HPV vaccination. The decision to vaccinate older people should take into account their likelihood of previous exposure to HPV and their future risks of HPV exposure

- **GBM to 26 years**

Recommended

- **Persons who are immunocompromised**

Recommended

The decision to vaccinate should take into account likelihood of previous exposure to HPV, future risks of HPV exposure, and the extent and duration of immunocompromise

USA and UK recommendations

CDC Recommendations (February 2015)

- Essentially same as Australia

The American Cancer Society's recommendations for HPV vaccine use

- As above

HPV vaccines are not approved nor recommended after age 26. While the vaccines are safe, they will not provide much, if any, benefit

UK Joint Committee on Vaccination and Immunisation (JCVI)

- Recommend HPV vaccination for MSM ≤ 40 years attending sexual health services

EVIDENCE FROM CERVICAL HPV TRIALS

Vaccine Efficacy vaccine in Women Previously Exposed to HPV

Phase III PATRICIA trial

- 15-24 years, < 6 lifetime partners, **2vHPV**
- VE in **DNA negative**, regardless of serological status = **88.7%** (85.7–91.1) for 6m persistent infection and **92.4%** (84.0–97.0) for CIN2+
- VE in **DNA neg/seropositive** = **72.3%** (53.0–84.5) for 6m persistent infection and **67.2%** (10.9–89.9) against CIN1+
- No therapeutic effect against prevalent HPV16 or 18 infections

Szarewski et al. Int J Cancer 2012

Phase III VIVIANE trial

- 4407 women > 25 years, 7 years f-up, **2vHPV**
- VE in the **per-protocol population** = 81.1% (52.1–94.0)
- VE in **HPV seronegative** women = 90.5 % (78.6–96.5)
- VE in **HPV seropositive/DNA neg** women at baseline =82.2% (34.2–97.0)

Skinner et al. Lancet 2015; Wheeler et al Lancet ID 2016

Vaccine Efficacy in Women Previously Exposed to HPV

Phase III Future trial

- 24–45 years, 4 years f-up, **4vHPV**
- VE in **per-protocol population** against the combined incidence of persistent infection, CIN/GW = **88.7%** (95% CI: 78.1, 94.8)
- VE for type specific **HPV seropositive/ DNA neg** at baseline = **66.9%** (95% CI: 4.3, 90.6)

Castellsague et al Br J Cancer 2011

EVIDENCE FOR VACCINATION AGAINST ANAL HPV

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HPV vaccination in GBM – impact on anal HSIL

- The 4vHPV vaccine - shown to be safe and immunogenic in men aged 27 to 45
  Giuliano et al Vaccine 2015

- RCT of 4vHPV x 3: efficacious, immunogenic and safe in 602 ≤ 26 yr old GBM with ≤ 5 lifetime partners - 75% effective in reducing anal HSIL associated with vaccine types

Table 2. Vaccine Efficacy against HPV-6, 11, 16, or 18–Related Anal Intraepithelial Neoplasia (AIN) and Anal Cancer in the Per-Protocol Efficacy Population.*

End Point	qHPV Vaccine (N=299)				Placebo (N=299)				Observed Efficacy (95% CI)†
	No. Included in Analysis	No. of Affected Partici-pants	Person-Yr at Risk	Events per 100 Person-Yr at Risk	No. Included in Analysis	No. of Affected Partici-pants	Person-Yr at Risk	Events per 100 Person-Yr at Risk	
									percent
By lesion type									
AIN grade 1	194	4	383.1	1.0	208	16	413.8	3.9	73.0 (16.3 to 93.4)
Condyloma acuminatum	194	0	386.8	0.0	208	6	418.2	1.4	100 (8.2 to 100)
Flat lesion	194	4	383.1	1.0	208	11	416.7	2.6	60.4 (−33.5 to 90.8)
AIN grade 2 or 3	194	3	383.9	0.8	208	13	417.2	3.1	74.9 (8.8 to 95.4)

Palefsky et al NEJM 2011

- Retrospective observational study of HIV negative GBM with previously treated anal HSIL: 4vHPV vaccination halved HSIL recurrence rate c/w unvaccinated patients (p=0.04)
  Swedish et al Clin Infect Dis 2012

Anal 9vHPV incidence (neg, pos, pos) in the SPANC study (GBM > 35 yrs)

	Person-Years	n	Incidence (Per 100 PY)	95% CI
HPV6	205	11	5.4	3.0 -9.7
HPV11	231	5	2.2	0.9 -5.2
HPV16	176	9	5.1	2.7 -9.9
HPV18	221	7	3.2	1.5 -6.6
HPV31	237	7	3.0	1.4 -6.2
HPV33	238	3	1.3	0.4 3.9
HPV45	219	9	4.1	2.1 -7.9
HPV52	221	5	2.3	0.9 -5.4
HPV58	225	9	4.0	2.1 -7.7
9vHPV	252	50	19.8	15.0 -26.2

IM Poynten et al, poster #740, IPV Cape Town 2017

EVIDENCE FOR VACCINATION AGAINST ORAL HPV

NHANES study of effect of HPV vaccination on prevalent oral HPV

- 3 year US cross-sectional study,18-33 years (n = 2,627)
- 18.3% ≥1 HPV vaccine-dose (29% women and 7% men; *P*< 0.001)
- ↓↓ oral 4vHPV types in vaccinated **(0.11% vs 1.61%; p= 0.008)**
- In men… **(0.0% vs. 2.13%; p= 0.007)**
- Prevalence for non-vaccine HPV types similar (4.0% vs. 4.7%; *p*= 0.24)

Gillison et al 2017 ASCO meeting, June 2–6, Chicago (abstract #6003)

EVIDENCE FOR VACCINATION OF HIV POSITIVE PEOPLE

HPV vaccination in older HIV positive populations

2vHPV and 4vHPV vaccines shown to be safe and immunogenic

ACTG5298: RCT of 4vHPV vaccine in HIV + (» 27 yrs)

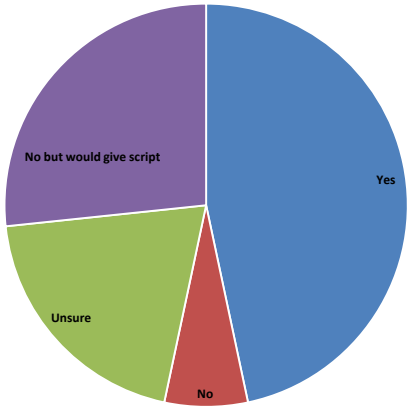
- rate of type-specific anal HPV persistent infection was reduced by a non-significant 25% in HIV + women and GBM
- Trial stopped early with 2.4 years of follow-up – no protective benefit
- Intriguingly (only 9 cases) found that vaccinated men had a lower rate of persistent detection of *oral* HPV (VE 88%, 95% CI 2-98%)

Outcome	4vHPV (n)	Placebo (n)	HR (95% CI)
Persistent anal HPV, or single detection at last visit	26	33	0.75 (0.45, 1.26)
Persistent anal HPV	13	17	0.73 (0.36, 1.52)
Anal HSIL*	46	45	1.0 (0.69-1.44)

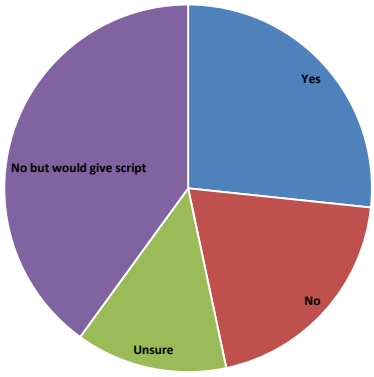
T Wilkin et al, CROI 2016

Straw poll of 15 sexual health clinicians, HIV specialists, GPs

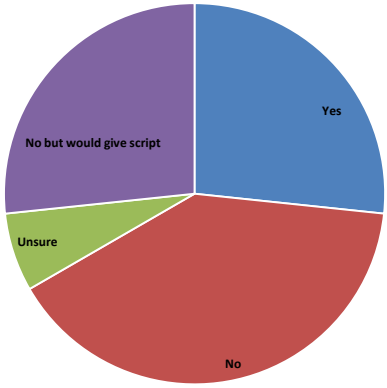
HIV + GBM aged 45, reports > 10 partners per year



HIV - GBM, aged 55, reports > 10 partners per year



HIV - heterosexual woman aged 50, recently single, reports > 2 partners per year



To consider..

PROS	CONS
High burden of HPV-associated cancers concentrated in some groups (GBM, HIV +)	Next to nothing known about HPV natural history in the oropharynx, or vaccination efficacy at this site
Evidence from trials in cervix of efficacy in previous exposed women	Most HPV infection in women occur in adolescence/early 20's
Absence of evidence of efficacy does not mean absence of efficacy	Few women >50 developed CIN2+ lesions
No evidence that vaccination causes harm	Cost of vaccine (~$450)
Can take only 5 to 10 years for cervical cancer to develop in women with untreated HIV infection	Imminent arrival of Gardasil 9
	10 to 30 years for cancer to develop in people with normal immune systems

Summary

- Evidence that vaccination can offer protection to those without current infection or disease, irrespective of previous viral exposure
- There must be ongoing risk for the HPV vaccine to provide any benefit
- With 9vHPV on an individual level, virtually everyone will receive some benefit
- Need more evidence of effectiveness for older GBM, immunocompromised populations

Thank you