HPV AND CERVICAL SCREENING

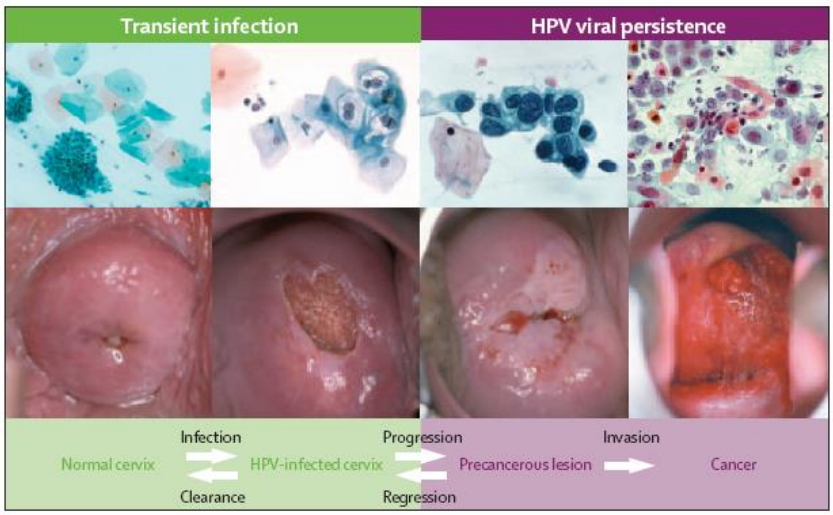
Assoc Prof Julia Brotherton
Medical Director, VCS Population Health

Honorary Principal Fellow
School of Population and Global Health
University of Melbourne

THE UNIVERSITY OF MELBOURNE

Centre of Research Excellence in Cervical Cancer Control

VCS FOUNDATION
eliminating cervical cancer

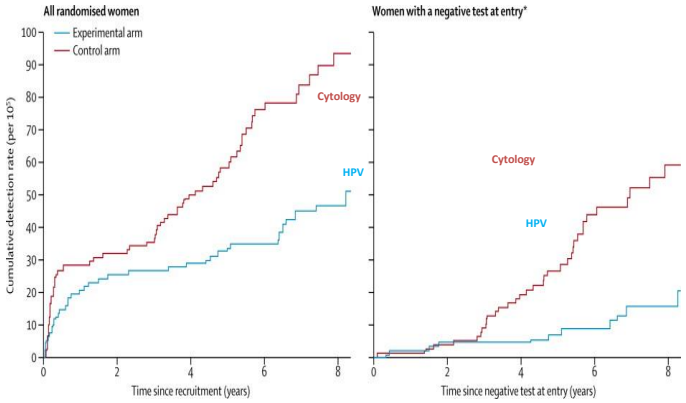


Schiffman et al ***Lancet 2007; 370: 890–907***

VCS FOUNDATION

Primary HPV screening:

Pooled data on invasive cervical cancer outcomes from four European trials - 176,000 women



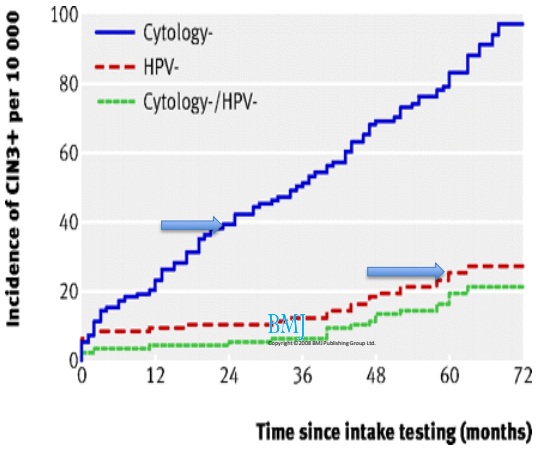
"At longer intervals HPV-based screening provides 60—70% greater protection against invasive cervical carcinomas compared with cytology"

Ronco et al, Lancet 2014

VCS FOUNDATION

Primary HPV screening

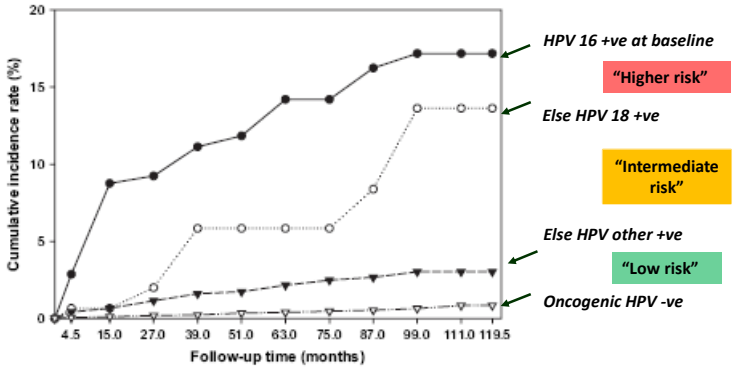
Longitudinal results for screen-negative women



Dillner, J. et al. Joint European Cohort Analysis. BMJ 2008;337:a1754

VCS FOUNDATION

Longitudinal outcomes:
HPV positive women



Cumulative CIN3+ in 20,514 women (median age 34 years)

Khan MJ, Castle PE, et al. The elevated 10-year risk of cervical precancer and cancer in women with human papillomavirus (HPV) type 16 or 18 and the possible utility of type-specific HPV testing in clinical practice. JNCI 2005

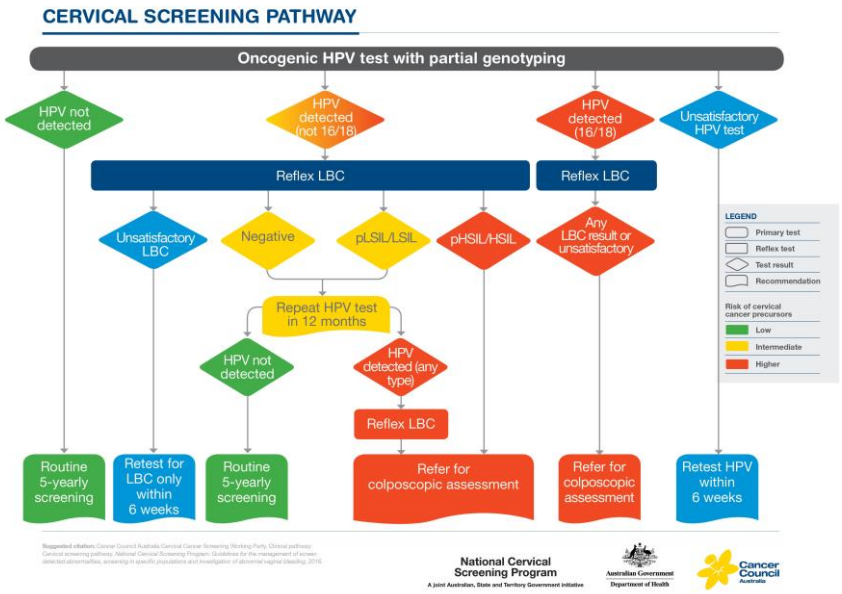
VCS FOUNDATION

MSAC RECOMMENDATIONS

Cervical Screening Test (CST)

- HPV test with partial genotyping (16/18)
- Reflex Liquid Based Cytology (LBC) triage
- Five year screening interval
- Start at age 25 years
- Exit at 70–74 years
- All sexually active women-HPV vaccinated or not
- Self collection: never-screened and under-screened
- Invitation & reminders to screen: National Register

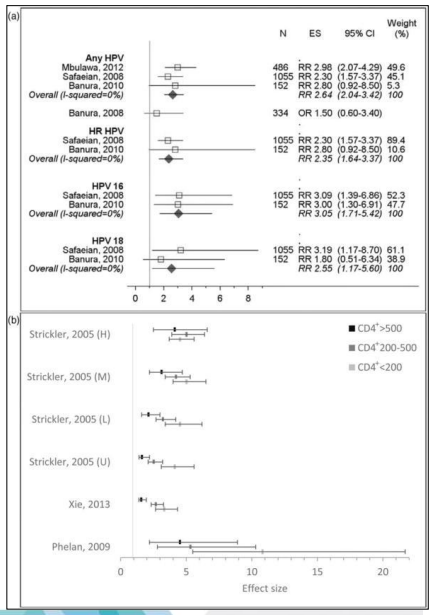
VCS FOUNDATION



HIV-positive women have higher risk of human papillomavirus infection, precancerous lesions, and cervical cancer.

Liu, Gui; Sharma, Monisha; Tan, Nicholas; Barnabas, Ruanne. AIDS. 32(6):795-808, March 27, 2018.

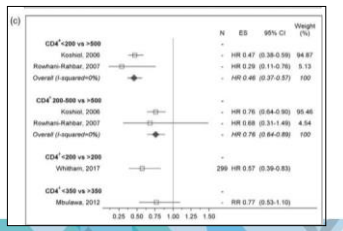
Figure: **HPV incidence among HIV-positive women compared with HIV-negative women**

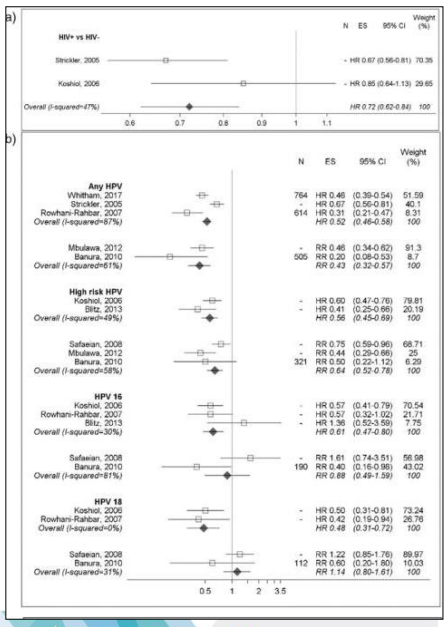


HIV-positive women have higher risk of human papillomavirus infection, precancerous lesions, and cervical cancer.

Liu, Gui; Sharma, Monisha; Tan, Nicholas; Barnabas, Ruanne. AIDS. 32(6):795-808, March 27, 2018.

Figure: **Clearance of newly detected and prevalent human papillomavirus infections by HIV status and CD4+ cell count**



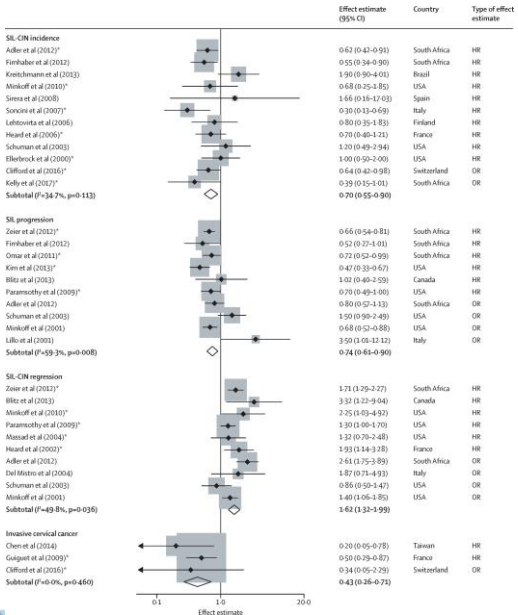


VCS FOUNDATION

Association of antiretroviral therapy with high-risk human papillomavirus, cervical intraepithelial neoplasia, and invasive cervical cancer in women living with HIV: a systematic review and meta-analysis

Kelly H, Weiss HA, Benavente Y et al. The Lancet HIV
Volume 5, Issue 1, Pages e45-e58 (January 2018)

Meta-analysis of cervical lesion incidence, progression and regression, and invasive cervical cancer incidence among ART users compared with ART-naive

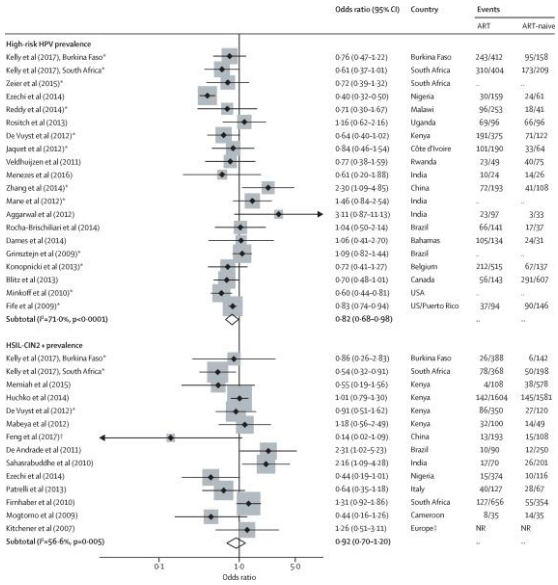


VCS FOUNDATION

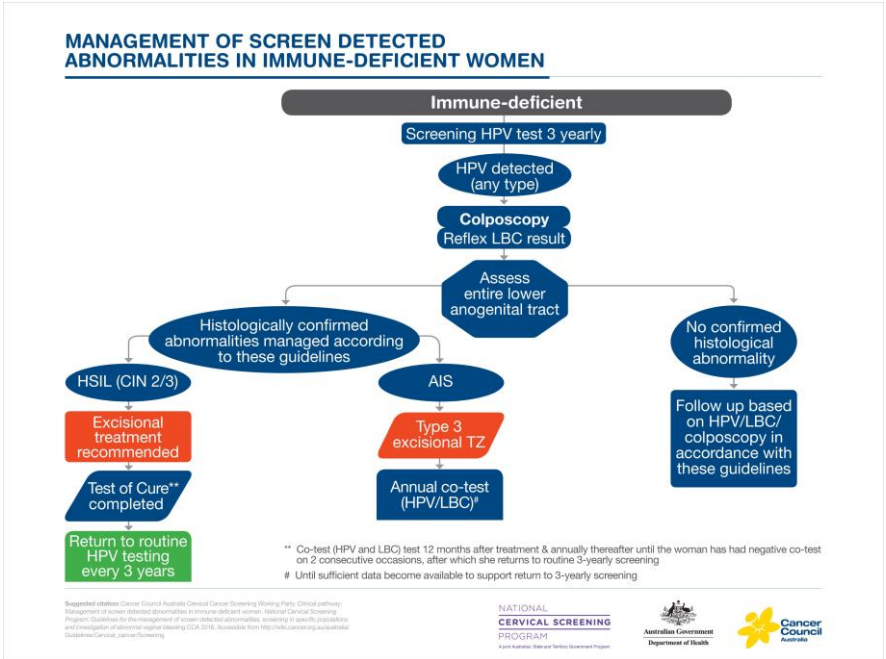
Association of antiretroviral therapy with high-risk human papillomavirus, cervical intraepithelial neoplasia, and invasive cervical cancer in women living with HIV: a systematic review and meta-analysis

Kelly H, Weiss HA, Benavente Y et al. The Lancet HIV
Volume 5, Issue 1, Pages e45-e58 (January 2018)

Meta-analysis of the prevalence of high-risk HPV and HSIL-CIN2+ among ART users compared with ART-naive



VCS FOUNDATION



Screening interval recommendations

REC16.1: Immune-deficient women in whom oncogenic HPV is not detected

Immune-deficient women who have a HPV test in which oncogenic HPV types are **not** detected should be screened every 3 years with a HPV test.

Management of abnormalities

REC16.2: Colposcopy referral: positive oncogenic HPV test result (any type) in immune-deficient women

Women who are immune-deficient and have a positive oncogenic HPV (any type) test result should be referred for colposcopic assessment informed by the reflex LBC.

REC16.3: Colposcopy assessment and treatment in immune-deficient women

Assessment and treatment of immune-deficient women with screen-detected abnormalities should be by an experienced colposcopist or in a tertiary centre.

Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding.
https://wiki.cancer.org.au/australia/Guidelines:Cervical_cancer/Screening.

VCS FOUNDATION

Screening pathway recommendations

REC16.4: Colposcopy of whole lower genital tract in immune-deficient women

The entire lower anogenital tract should be assessed, as the same risk factors apply for cervical, vaginal, vulval, perianal and anal lesions.

REC16.5: Treatment in immune-deficient women

When treatment of the cervix is considered necessary in immune-deficient women, it should be by excisional methods.

REC16.6: Histological abnormalities of the cervix in immune-deficient women

Women with histologically confirmed abnormalities should be managed according to the same guidelines as women who are not immune-deficient.

REC16.7: Test of Cure for treated immune-deficient women

Women who are immune-deficient and treated for HSIL (CIN2/3) should have follow-up with Test of Cure as recommended in the **Test of Cure after treatment for HSIL** guidelines. Women who complete Test of Cure should return to routine 3-yearly screening with a HPV test.

Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding.
https://wiki.cancer.org.au/australia/Guidelines:Cervical_cancer/Screening.

VCS FOUNDATION

Screening recommendations

REC16.9: Screening women with a new diagnosis of HIV

Women aged between 25 and 74 years who have a new diagnosis of HIV should have a review of their cervical screening history to ensure they are up to date with screening in line with the recommended 3-yearly interval for this group.

REC16.11: Regular screening for immune-deficient women

Women who are immune deficient should be educated regarding the increased risk from HPV infection and encouraged to attend for regular screening.

REC16.12: Young women with long term immune deficiency

For young women who are sexually active and who have been immune deficient for more than 5 years, a single HPV test between 20 and 24 years of age could be considered on an individual basis (regardless of HPV vaccination status).

Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding. https://wiki.cancer.org.au/australia/Guidelines:Cervical_cancer/Screening.

VCS FOUNDATION

Unresolved issues

There is insufficient evidence available to determine the optimal cervical screening strategy in immune-deficient women. Current recommendations reflect a cautious approach until further data become available. The effect of ART on progression of cervical disease is still unclear.

Future research priorities

Long-term randomised controlled trials, comparing screening strategies in immune-deficient women, are needed to inform future guidelines. It is anticipated that the renewed NCSP and the National Cancer Screening Register will facilitate the collection of data on immune-deficient women to support future recommendations. Modelled analysis may help in determining whether routine 5-yearly screening could be suitable for this group of women.

Guidelines for the management of screen-detected abnormalities, screening in specific populations and investigation of abnormal vaginal bleeding. https://wiki.cancer.org.au/australia/Guidelines:Cervical_cancer/Screening.

VCS FOUNDATION

Nine valent HPV vaccine

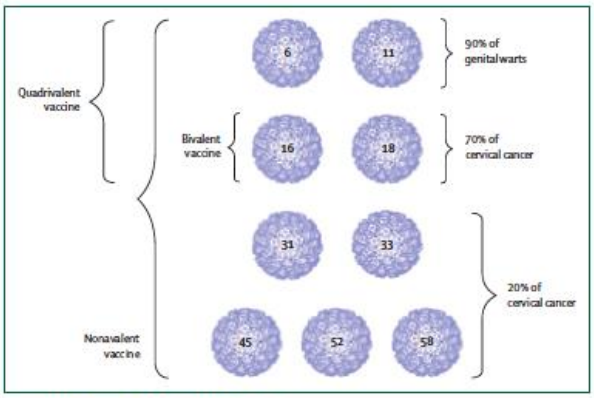


Figure 2: HPV VLP types in the nonavalent VLP vaccine
VLPs in the bivalent, quadravalent, and the nonavalent vaccines are shown with the proportion of neoplasistic disease attributed to each group. HPV=human papillomavirus. VLP=virus-like particle.

- **Recommended in 3 doses regardless of age for immune-deficient**
- **Funded to age 19**
- **9vHPV not routinely recommended for those previously vax with 4vHPV but consider for immune-deficient**
- **Immunogenic and safe in HIV+**
- **Limited efficacy data in HIV+ (McClymont et al, CID, in press)**

Schiller & Muller. *Next generation prophylactic human papillomavirus vaccines*. Lancet Oncol. 2015 May;16(5):e217 - e225

National HPV Vaccination Program Register

Thank you

jbrother@vcs.org.au

- VCSR is funded by the Victorian Government and operated by VCS
- Thank you to all investigators of the Victorian data linkage study especially Michael Malloy, Anneke van der Walt, Emma Foster, and Vilija Jokubaitis for permission to share unpublished findings

State Government Victoria
VCS acknowledges the support of the Victorian Government
C4 Centre of Research Excellence in Cervical Cancer Control
VCS FOUNDATION