

STD TREATMENT GUIDELINES TABLES: HIVRISK CIN/Genital warts/AIN

Author/Citation	Study Design	Population, Sample Size	Outcome	Summary Points
Huchko MJ, et al.2013	Case-control evaluation of paired plasma/cervical wick specimens	44 HIV-infected women with CIN2/3 and 44 age matched HIV infected women with normal cervical findings	Evaluate the relationship between CIN 2/3 and HIV genital shedding	➤ No relationship between CIN2/3 and HIV genital shedding (mean of HIV-1 in cases was 2.93, controls 2.72 log ₁₀ copies)
Tobian AAR, et al. 2013	Case control study	Uncircumcised HIV—negative men 15-49 years from Uganda 44 cases (HIV seroconverters), 787 controls	Evaluation of HR/LR HPV and HIV acquisition and clearance and acquisition Recruitment of macrophages, dendritic cells and T cells in genital tract is thought to occur during HPV clearance, potentially providing target cells for HIV acquisition.	➤ Cases and controls significantly different across different behavioral and demographic variables including sex behavior, STI symptoms, HSV, condom use, sex partners, marital status ➤ HR-HPV and LR-HPV were not associated with HIV acquisition, after adjusting for sexual behaviors ➤ Clearance was associated with seroconversion. ➤ The median CD1a+ dendritic cell density in the foreskin epidermis was higher among males who cleared HPV
Mhatre M, et al. 2012.	Cross-sectional analysis	106 HIV-negative women, ages 19-66 (57 negative, remaining with cervical abnormalities)	Evaluation of inflammatory mediators to describe differences in women with CIN which may account for increased risk for HIV acquisition.	➤ Women with CIN3 had higher levels of proinflammatory cytokines including IL-1 alpha, IL-1 beta, and IL-8, and lower levels of antiinflammatory mediators and antimicrobial peptides, including IL-1 receptor antagonist, secretory leukocyte protease inhibitor and human B defensins 2 and 3. <<proinflammatory cytokines increased with CIN3—translation? >>

Diouf K, et al. 2011.	Nested evaluation within an RCT of male condoms +/- diaphragm/gel.	2027 HIV-negative women in Zimbabwe, cumulative HIV incidence 4.3%	HIV incidence among 199 women who underwent cervical procedures, compared to women who did not	<ul style="list-style-type: none"> ➤ No statistically significant increase in HIV acquisition in women with procedures, similar results when adjusted for baseline variables associated with HIV acquisition. ➤ Small study but suggests HIV acquisition not associated with cervical procedures <p><<Previous study by T Wright suggested increased shedding with cervical procedures, this study, albeit small, suggest no increased risk of HIV transmission>></p>
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Jin F, et al. 2010	Cohort (open) from 2000-2004 (HIM)	1427 MSM (median age 35 years) in Australia, twice yearly evaluation by phone, annual face to face	Evaluation of anal condyloma and STIS (self report) and incident HIV	<ul style="list-style-type: none"> ➤ 53 HIV seroconversions during study (0.78 per 100 person years) ➤ The associations of HIV infection with study visit diagnosis of anal gonorrhea (HR = 7.12, 95% CI: 2.05 to 24.75) and interval diagnosis of anal warts (HR = 3.63, 95% CI: 1.62 to 8.14) remained significant (control for number of episodes on non-sero discordant UAI). ➤ Limitations of study include self report of STIs and unclear exact interval preceding HIV acquisition.
Smith-McCune KK, et al. 2010.	Cohort study	2049 18-49 year old females from Zimbabwe, followed median 21 months	HIV acquisition and HPV infection Substudy within RCT of	<ul style="list-style-type: none"> ➤ HIV acquisition associated with baseline prevalent HPV, HSV-2, incident STI, new sex partner, condom use, concurrent infection with non-oncogenic types.

			diaphragm nd lubricant gel	<ul style="list-style-type: none"> ➤ Oncogenic HPV types within previous 6 months independently associated with HIV acquisition. ➤ Prevalent HPV infection was 24.5% (MY09/MY11 method)
Averbach SH, et al. 2010	Case-Control study	18-35 year old females from Zimbabwe 145 cases with incident HIV and 446 controls	Evaluation of T-1 (visit before HIV acquisition) for HPV infection: no infection, persistent or loss of infection	<ul style="list-style-type: none"> ➤ Odds of acquire HIV 2.4 times higher in women with prior cervical HPV infection after adjustment for behavioral and biologic risk factors. ➤ Clearance of at least 1 HPV type was associated with HIV acquisition ➤ Cases and controls incompletely matched on numerous variables including primary partner risk, marital status, living with partner, hormonal contraceptive (residual confounding cannot be r/o).
Smith JS, et al. 2010.	Nested evaluation of RCT of male circumcision	2168 uncircumcised 18-24 year old men from Kenya	Comparison of HIV acquisition by baseline HPV and circumcision status, HRs for different baseline characteristics	<ul style="list-style-type: none"> ➤ Cumulative HIV incidence at 42 months was 5.8% ➤ Adjusted hazard of HIV infection was 1.6 times higher among men with HPV detected ➤ Did not differ by multiple/single types, or HR/LR types, or combination of types (all were associated with HIV acquisition) ➤ Effect estimates similar before and after adjustment for HSV-2, GC, CT and other aconfounders
Chin Hong PV, et al 2009	Cohort evaluation of MSM and risk for HIV seroconversion	1409 HIV-negative men who have sex with men from Boston, Denver, NY, SF (EXPLORE trial)	Evaluation of anal HPV and HIV seroconversion 1409 men with 4375 person-years of follow-up, 51 HIV-seroconverted.	<ul style="list-style-type: none"> ➤ 1409 men: 57% had anal HPV, and 32% had abnormal anal cytology ➤ In univariate analysis LSIL and ASCUS had an elevated odds (not sufficient HSIL cases), but in multivariable analysis –there was no independent effect of anal cytology abnormalities. ➤ Infection with at least 2 HPV types, controlling for sex activity, substance use, occurrence of other sti and demographic variables (ARR 3.5, 95% CI 1.2-10.6)

				<ul style="list-style-type: none"> ➤ Other risk factors for seroconversion were UAI with unknown status partner, and drug use
Auvert B, et al. 2011	Nested evaluation of RCT of low-dose N 9 microbicide to evaluate HPV and HIV incidence	187 HIV-uninfected FSW ages 19-45 years from South Africa	Evaluation of incident HIV-1 infection by CV rinses for HPV at baseline (Roche reverse line blot assay)	<ul style="list-style-type: none"> ➤ Small study but high HIV seroconversion (28.4% seroconverted) ➤ HR HPV was associated with HIV acquisition when controlling for LR HPV ➤ Total number of genotypes increased the risk
Veldhuijzen NJ, et al. 2010	Nested evaluation of prospective cohort to evaluate HIV incidence in high-risk women	397 HIV-negative high-risk women from Rwanda	Evaluation of HPV and risk of HIV acquisition—HR HPV prevalence at month 6 (10 HIV-seroconverters, 314 controls)	<ul style="list-style-type: none"> ➤ HR HPV prevalence higher among HIV seroconverters (no controlling for confounding factors)—HPV 52 the most common HR type found ➤ Residual confounding likely
Houlihan CF, et al. 2012	Systematic review and Meta-analysis	8 studies included	Evaluation of risk of HIV acquisition with prevalent HPV	<ul style="list-style-type: none"> ➤ 7 studies found an association between prevalent HPV and HIV acquisition, risk of HIV acquisition doubled (adjustment for confounders was often inadequate). ➤ Effect similar for high-risk and low risk types ➤ Two studies in men found an association between HPV and HIV acquisition. ➤ Residual confounding a concern for most studies
Brown B, et al. 2012	Review of studies on HPV and HIV in MSM from 1998-2012	11 studies—3 cohort studies, 8 cross-sectional	Evaluation of HPV and HIV	<ul style="list-style-type: none"> ➤ Only one study highlighted the association between HPV and HIV acquisition in MSM—another study ongoing in Peru

References

1. Huchko MJ, et al. Is there an association between HIV-1 genital shedding and CIN2/3 among women on antiretroviral therapy? *J Low Gen Tract Dis*;2013:17
2. Diouf K, et al. Investigating Potential Associations between cervical procedures and HIV acquisition. *Ob Gyn* 2011;1-5.
3. Mhatre M, et al. Cervical Intraepithelial Neoplasia is associated with genital tract mucosal inflammation. *STD* 2012;39:591-597.
4. Tobian AAR, et al. Human Papillomavirus Clearance Among Males is Associated with HIV Acquisition and Increased Dendritic Cell Density in the Foreskin. *JID* 2013; e pub
5. Chin Hong PV, et al. Anal human papillomavirus infection is associated with HIV acquisition in men who have sex with men. *AIDS* 2009;23:1135-1142.
6. Jin F, et al. Anal sexually transmitted infections and risk of HIV infection in homosexual men? *JAIDS* 2010;53:144-149.
7. Smith-McCune KK, et al. Type-Specific Cervico-Vaginal Human Papillomavirus Infection Increases Risk of HIV Acquisition Independent of Other Sexually Transmitted Infections. *PLoS ONE* 2010;5:e10094
8. Averbach SH, et al. The association between cervical human papillomavirus infection and HIV acquisition among women in Zimbabwe; *AIDS* 2010;24:1035-1042.
9. Smith JS, et al. Increased Risk of HIV Acquisition among Kenyan Men with Human Papillomavirus Infection; *JID* 2010;201(11):1677-1685.
10. Auvert B, et al. High-risk Human Papillomavirus is associated with HIV acquisition among South African Female Sex Workers. *ID in Ob Gyn* 2011;
11. Veldhuijzen NJ, et al. HIV acquisition is associated with prior high-risk HPV among high-risk women in Rwanda; *AIDS 2010 Research Letters* page 2289-2294.
12. Houlihan CF, et al. Human papillomavirus infection and increased risk of HIV acquisition. A systematic review and meta-analysis; *AIDS* 2012;26:2211-2222.
13. Brown B, et al. The Role of Human Papillomavirus in Human Immunodeficiency Virus Acquisition in Men who Have Sex with Men: A Review of the Literature. *Viruses* 2012;4:3851-3858.