STD TREATMENT GUIDELINES TABLES: NATURAL HISTORY/EPIDEMIOLOGY

Author/Citation	Study Design	Population, Sample Size, Methods	Outcome measures	Summary Points
Alberto STD 2012	Systematic review and meta analysis	Medline search from February 1971-Until August 2010	Odds of prevalent HPV infection, incident infection, HPV clearance, or EGW	14 studies MC associated with lower odds of genital HPV prevalence OR 0.57 (0.42-0.77) For hrHPV prevalence, similar association observed 0.67 (0.54-0.82) MC not significantly associated with incident infection, clearance of infection, or genital warts For HPV incidence, combined results of 4 studies that used both RR and OR? (summary statistic 1.01, 0.66-1.53) High heterogeneity among studies for each outcome except between RCTs
Larke JID 2011	Systematic review and meta analysis	Until Pubmed and EMBASE until Sept 2010	Odds of prevalent HPV infection, acquisition of new infection, clearance	14 studies (predominantly HIV-neg men) MC associated with lower odds of genital HPV prevalence OR 0.57 (0.45-0.71) MC not significantly associated with clearance of infection, or genital warts HPV incidence: only used 3 of 4 studies summarized in Alberto et al 2012 that reported RR, summary RR for 3 studies was 0.75 (0.57-0.99)
Backes Int J Cancer 2012	Nested cross sectional study within MC RCT	HIV-negative men N=151 MC N=124 control VIA at 24 mos, penile scraping	Flat AW penile lesions on VIA HPV 16/18/31 VL (High >=250 copies/scraping) HPV genotype (PCR)	Prevalent flat lesions 0.7%-circumcised arm 26%-control arm (AOR 0.2, 0.003-0.1) Odds of flat lesions higher if +HPV DNA or high HPV VL HPV56 (29%) and 16 (25.8%) were most common among men with penile lesions
Poyten STD 2012	Prospective cohorts (Health in Men, Positive Health	MSM N=1427 HIV-negative N=245 HIV-positive	HPV 16 Seroprevalence, seroincidence, and risk factors	HIV-25.4% HPV16+ @ baseline HIV+-44.3% HPV16+ @ baseline HIV-HPV16 seroincidence 3/100py (seroincidence >3 until age 45)

	study)	Annual in person, q6 mos by phone, self report warts and circumcision status (validated by clinician)		HIV+HPV16 seroincidence 1.3/100py (very limited number of incidents and small #s) In MSM who practiced IAI, circumcision assoc w/ lower seroincident HPV16 (HR 0.43, 0.21-0.88, p=0.021) Serology not sensitive (60%), seroconversion may happen up to 18 months after DNA detection High seroincidence until age 45-implications for HPV vax of older MSM
Templeton JID 2009	Prospective cohort (Health in Men)	MSM N=1427 HIV-negative Annual in person, q6 mos by phone, self report warts and circumcision status (validated by clinician)	Effect MC on Prevalent and incident STDs and self-reported warts	No effect of MC for prevalent or incident EGW or anal warts Prevalent EGW, OR 0.84 (0.57-1.24 NS), anal warts OR 1.29 (0.96-1.73, NS) Incident EGW, HR 0.74 (0.39-1.41), anal warts HR 1.05 (0.62-1.78)
VanBuskirk STD 2011	Prospective cohort	Male univ students N=477 Q 4 month visit, exfoliated cells from scrotum, shaft, glans	Incident HPV acquisition by circumcision status (HR types + HPV6, 11)	ND for incident HPV infection (HR 0.9, 0.7-1.21) or # of types acquired Uncircumcised men more likely to have same HPV type detected at 3 sites

MC and HPV in Women				
Wawer et al *Lancet,* 2011	RCT, follow-up 2 years	HIV negative men and HIV neg female partners N=648 MC, 597 control, SCVS at 0, 12, 24 mo	Female HPV infection • Prevalent HR infection • Incident HR infection • Genotype specific clearance in women with prevalent infection	Yr 2 prevalent HR HPV 27.8%-MC arm 38.7%-control arm (PRR 0.72, 0.6-0.85, p<0.001) Incident HR-HPV 20.7/100py vs 26.9/100py (IRR 0.77, 0.63-0.93) Genotype specific clearance was higher in wives of MC arm (RR 1.12, 1.02-1.22) MC reduces prevalent and incident HR HPV in female partner and increases HR hpv clearance
Tobian Lancet Infect Dis 2011	RCT follow-up 2 years	HIV-positive men and and female partners N=211 MC and 171 control (delayed MC) SCVS at 0, 12, 24 mo	Female HPV infection • Prevalent HR infection • Incident HR infection • Genotype specific clearance	Yr 2 prevalent HR HPV 55.4%-MC arm 51.9%-control arm (PRR 1.07 NS) Incident HR-HPV 32/100py vs 30.6/100py (IRR 1.05 NS) No difference in genotype specific clearance between arms (RR 0.96 NS) MC of HIV+ men does not affect HPV transmission to female partners

Wart natural history

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Anic JID 2011	Prospective cohort	2487 men (HPV in Men) 10 visits every 6 mos over 4 years	Incident EGW per 1000 person/y 24 mo cumulative incidence of EGW following incident HPV	Incident EGW Overall: 2.35/1000 py, men 18-30=3.43/1000 py 24 mo CI of warts HPV 6 and/or HPV11+=14.6% (7.5-21.1)

				Median time to EGW 17.1 mos (12.4-19.3) overall and 6.2 mos if HPV 6/11+ (5.6-24.2)
Arima JID 2010	Prospective cohort	418 sexually active male university students Q 4 month visits, mean f/up was 24.6 months At least 2 study visits needed for inclusion Mean # visits 6.7 Warts not tested for HPV DNA	24 mo cumulative incidence of EGW following incident HPV Time between incident HPV and genital wart development	Incident HPV infections: HPV6=40 men,HPV11=4 men HPV6 + HPV11=2 men, Other HPV type=161 men 22 incident EGW: HPV6/11-18 cases, other HPV-2 cases, negative for HPV-2 cases 24 mo CI of warts: Overall=4.2% (2.4-7.2) If HPV6 and/or HPV11+=57.9% (38.1-79.1) If other HPV+=2.0% (0.5-7.9) HPV negative=0.7% (0.2-2.8) Median time to EGW was 10.6 mos if HPV 6/11+
Blomberg JID 2012	Prospective cohort	N=16155 men and 32,933 women with EGW dx at Danish hospitals (1978-2008) CAs and EGW identified via ICD-8 or ICD-10 (depending on yr) Multiple episodes counted once, at time of incident EGW	Standardized incidence ratios of HPV related cancers in pts with EGW compared to expected incidence in Danish population	Anal CA SIRs 21.5 men, 7.8 women Vulvar CA SIR 14.8, Vaginal CA SIR 5.9 Cervical CA SIR 1.5, Penile CA SIR 8.2 Head and neck CA subsites likely to be HPV related SIR 3.5 men, 4.8 women Increased SIR for NHL, HL, non-melanoma skin CA, smoking related CAs Hospital-dx EGW (may be more severe/persistent), other outpt providers may not report No info on MSM status, HIV status, SES, smoking

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Dolev AIDS 2008 Updated data in MASSAD 2011	Prospective cohort	Womens Interagency HIV Study 1790 HIV infected women 772 HIV neg women (subset w 8y f/up) Subgroups recruited 1994-1995 and 2001-2002	CI of warts over 8 year f/up (Prevalent HPV infection was allowed)	HIV-negative CI EGW 9.3% (6.3-12.2) HIV+ HAART CI EGW 28.4% (21.7-34.5) HIV+ no ART CI EGW 25.1% (18.4-31.2) 45% of all participants were HPV positive (types not specified, data not shown by HIV status) 67% of participants with EGW had prevalent HPV

		Q 6 month visits with gyn exam EGW dx made based on clinical appearance		infection at baseline visit
Garland JID 2009	RCT (placebo arm)	N=8800 Post hoc analysis of placebo arm of FUTURE II/III Exam at month 1, 3 (future1 only) 7, 12, 24, 36, 48 Mean f/up 3.9 years	GW incidence	N=351 women had 520 warts diagnosed, incidence of GW 0.87 cases/100 py, 86% attributable to HPV 6 or 11 Median time to detection of GW (pts + for HPV6/11 at 0, 3 mos or 7 mos) for HPV6 was 6 mos and HPV11 was 4.9 mos For pts neg for HPV 6/11 at 0, 3, 7 mos who later developed warts due to HPV 6/11: median time to detection of EGW for HPV 6: 25 mos and HPV 11: 23.8 mos
Low BMC Infectious diseases 2011	Prospective cohort	Yerelon Cohort (Burkina Faso) N=765 women, 273 (35%) HIV+ and high risk HIV-neg women (CSWs) Q 4 mos study visits, maximum 6 visits Median f/up time 1.7 years	Incidence of EGW by HIV status, stratified by nadir CD4≤200 or >200 (incidence over entire duration of f/up?) Prevalence of EGW	40 women developed incident warts Incidence: HIV-neg 1.1/100 py HIV+ nadir CD4 ≤200=14.6/100 py HIV+ nadir CD4 >200=7.4/100 py Prevalence 3.5%
Massad Obstet Gynecol 2011	Prospective cohort	WIHS Cohort 2317 HIV infected women 830 HIV negative women Update of 2008 paper by Doley et al See methods above	Annual incidence EGW per 100/py CI of EGW (up to 13 years) Spontaneous regression of warts	479 women dx with incident warts 3.1/100 py in HIV+, 0.6/100 py in HIV neg (1994-95) 2.5/100 py HIV+, 0.6/100py in HIV neg (2001-02) After up to 13 y f/up, CI of EGW 33% (30-36) HIV+ 9% HIV- (6-12) Regression among N=554 women w/ prevalent and incident warts who were not treated, adequate f/up 451 (83%) regressed in up to 5 yrs of follow-up regression more likely among HIV negative (41/43 95% regressed

				Most regression in year 1 (60% HIV+, 80% HIV-neg)

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Winer Cancer Epi biomarkers 2012	Prospective cohort	Female university students N=303 Q4 month visits for HPV and Pap testing	Incident HPV acquisition, clearance, repeat detection after clearance	303 incident type specific infections detected Median time to 1st neg test 9.4 mos (7.8-11.2) 90.6% undetectable after 2 years 19.4% of 173 incident infections became undetectable and then redetectable within 1 year
Giuliano Lancet 2011	Prospective Cohort	1159 men f/ Brazil, US, Mexico (HIM cohort study) Q6 mo visits, median f/up 27.5 mo	Incident genital HPV acquisition, time to clearance	38.4/1000 person-months (34.3-43.0) Median duration of HPV infection7.52 mo (6.8-8.6)
HPV AMONG COUPLES				
Burchell JID 2011	Prospective cohort	N=179 heterosexual couples discordant for >+1 HPV type, q 4 month visit x 2 Women: SCVS Men: penile/scrotum exfoliation	Transmission events	73 transmission events, 83.6% 1 HPV type M-to-F, 3.5/100 pm (2.7-4.5) F to M, 4/100 pm (3.0-5.5) No difference with lifetime # of partners, suggesting no decline in susceptibility even with high partner #s
Mbulawa J of Infect (UK) 2013	Prospective cohort	N=486 Heterosexual couples 162, both partners negative, 115 both partners HIV+ 163 female+ , male -negative, 46 male + / female –negative Visits at 0, 6, 12, 18, 24	Transmission events	F to M HPV transmission rate = 2.80/100 pm (95% CI: 2.03-3.86) M to F HPV transmission rate was 1.17/100 person-months (95% CI: 0.82-1.67). HIV-positive women at higher risk of HPV infection transmitted from their male partners compared to HIV-negative women (RR (relative risk): 2.31, 95% CI: 1.08e4.92 High loss to f/up almost 50% by visit 1
Nyitray JID 2012	Cross sectional	N=88 heterosexual couples No history of HPV-associated disease	Type specific positive concordance (≥1 HPV type in common), negative concordance (neither partner had HPV), factors associated with concordance	75% in monogamous relationship for past 6 mos 23.9% had positive concordance (≥1 HPV type in common 62.5% had discordance for ≥1 HPV type 35% had negative concordance
Reiter Cancer Epi Biomarkers	Meta analysis	Search of Pubmed and EMBASE until Dec 2008	Concordance of ≥1 HPV types between couples	33 studies, 2972 couples (mostly cross sectional) 25.5% concordant ≥1 HPV types (95% CI 17.2-36.1)

2010				Among couples where both were HPV+, 63.2% (49.1-75.3) had positive concordance
Widdice JID 2013	Prospective cohort	N=25 heteorsexual couples where female had incident HPV and willing male partner 5 visits, of varying lengths over 6 weeks including 1 period with abstinence for 48 hours, and 1 visit 24 hours after intercourse After visit 3 couples were to resume normal sex frequency	Transmission events between different orifices + hand (oral, genital, anal, hand)	Genital to genital transmission over visits: F to M transmission 26.8 - 187.5 per 100 person-months M to F 14.5 to 100 per 100 person-months Highest at visit immediately after intercourse. After 48 hours abstinence, concordance back to baseline

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