Background HIV acquisition is fueled by infection with HSV-2 and HPV. Microbicides that target all three STIs may more effectively limit HIV incidence. We previously showed that a gel containing the NNRTI MIV-150, zinc acetate (Z) and carrageenan (C, MZC) significantly protected macaques from vaginal SHIV-RT challenge, while ZC also protected mice against HSV-2 vaginally and rectally. Here we evaluate a new formulation of MZC optimised for clinical use against SHIV-RT, HSV-2, and HPV.
Methods Toxicity was measured using the HSV-2 increased susceptibility model in mice. Macaques received gels vaginally every day for 14d followed by SHIV-RT (10^3 $TCID_{50}$) 8 or 24h post-last gel or SHIV-RT plus HSV-2 (2×10^8 pfu) 8h post-last gel. Rectally, gels were applied 1h before SHIV-RT. Anti-HSV-2 and anti-HPV16 PsV activities were assessed by vaginally or rectally challenging mice with different viral doses 24h before to 8h after single gel application. Significance was determined by Fisher's exact or Mann Whitney U tests ($P < 0.05$).
Results MZC pretreatment did not enhance HSV-2 infection of mice. MZC protected macaques against vaginal SHIV-RT infection (in the presence or absence of HSV-2) for up to 8h ($p < 0.0001$ vs. C) and rectal SHIV-RT infection (0/5 MZC infected vs. 1/4 C; C barrier effect). While MZC only reduced vaginal HSV-2 infection of macaques by 27% after challenge with 2×10^8 pfu, MZC significantly reduced vaginal ($p < 0.0001$) and rectal ($p = 0.0187$) HSV-2 infection of mice when 10^6 pfu were applied immediately and also when 5×10^3 pfu were applied between 8h before and 2h after vaginal challenge ($p < 0.0021$). Protection of mice against HPV16 PsV was significant ($p < 0.0001$ vs. HEC) for MZC applied up to 24h before and 2h after challenge.
Conclusion MZC provides a durable window of protection against SHIV-RT, HSV-2, and HPV *in vivo*, making MZC an excellent candidate microbicide for clinical use.

0.11 - HIV prevention and lessons learned from trials of HIV pre-exposure prophylaxis

011.1 HERPES SIMPLEX VIRUS (HSV) INFECTION IN THE VOICE (MTN 003) STUDY: PRE-EXPOSURE PROPHYLAXIS (PREP) FOR HIV WITH DAILY USE OF ORAL TENOFOVIR, ORAL TENOFOVIR-EMTRICITABINE, OR VAGINAL TENOFOVIR GEL

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Background In subSaharan Africa, HSV-2 infection is common, and increases risk of HIV transmission and acquisition. Tenofovir gel applied before and after vaginal intercourse provided partial protection from HSV-2 acquisition in the CAPRISA 004 study. We enrolled women in a 5-arm, randomised, double-blind, placebo-controlled trial assessing the safety and efficacy of daily use of oral tenofovir, oral tenofovir-emtricitabine, and 1% vaginal tenofovir gel as HIV PrEP, and assessed characteristics of women with baseline HSV and risk of HSV seroincidence during the study.
Methods From September 2009-June 2011, 12,379 women were screened at 15 sites in South Africa, Uganda, and Zimbabwe. Eligibility criteria included normal renal, hematologic and hepatic function, report of vaginal intercourse in prior 3 months, negative pregnancy test, and willingness to use effective contraception throughout. Testing for HSV-2 type-specific antibody (Focus HerpeSelect EIA) was performed on plasma from enrollment and study exit.
Results Of 5,029 participants, baseline HSV serology was available for 4996 (99.3%). Most were from Durban (62%), followed by Johannesburg (14%), Zimbabwe (13%), Uganda (6%), and Klerksdorp (5.2%). Mean age was 25.3 years; 79% were unmarried. Over follow-up of 5,511 person years, end-of-study retention was 91%. Using a cutoff index value of > 3.5, 46% of participants were HSV-2 and 95% HSV-1 seropositive at enrollment. Country- and age-specific HSV-2 seroprevalence ranged from 32% (Zimbabwe) to 63% (Uganda). Seroincidence of HSV-2 by arm will be presented.
Conclusions In this population of women at risk for HIV-1, seroprevalence of HSV-2 was high, with potentially important differences by age and site of enrollment.

011.2 SEXUAL BEHAVIOUR OF HETEROSEXUAL MEN AND WOMEN RECEIVING ANTIRETROVIRAL PRE-EXPOSURE PROPHYLAXIS FOR HIV PREVENTION: POST-UNBLINDING ANALYSIS OF THE PARTNERS PREP STUDY

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Background Limited data are available to assess the potential for increased sexual risk-taking by persons using antiretroviral pre-exposure prophylaxis (PrEP) for HIV prevention. In July 2011, the Partners PrEP Study, a randomised trial of daily oral tenofovir and emtricitabine/tenofovir PrEP among HIV-uninfected members of African heterosexual HIV serodiscordant couples, demonstrated efficacy of PrEP for HIV prevention and use of placebo was discontinued in the trial. Follow-up of study participants on active PrEP through December 2012 provided an opportunity to evaluate risk behaviour on PrEP after efficacy was announced.
Methods Among participants assigned to active PrEP pre-unblinding who continued follow-up after the placebo arm was stopped, we used zero-inflated negative binomial regression with robust standard errors and adjusted for baseline sexual behaviour, age, gender, and secular changes to compare the frequency of unprotected sex up to 12 months before versus after knowledge of PrEP efficacy.
Results We analysed 54,876 person-months (33,254 pre- versus 21,622 post-unblinding) from 3024 HIV-uninfected subjects (64% male). On average, the observed frequency of unprotected sex with the HIV-infected study partner was 58 per 100 person-months pre-unblinding versus 53 per 100 person-months post-unblinding, reflecting no immediate change or change in trend over time following unblinding ($p = 0.734$ and 0.264, respectively). The annual average total number of unprotected sex post-unblinding was 6 acts versus 5 that would have been expected in the counterfactual situation had unblinding not occurred. There was no significant increase in diagnoses of incident sexually transmitted infections or pregnancy post- versus pre-unblinding ($p > 0.05$).
Conclusion The transition from a blinded, placebo-controlled trial to all participants aware they were receiving active PrEP in the Partners PrEP Study provided a "natural experiment" to evaluate behavioural risk compensation. PrEP, provided as part of a comprehensive prevention package, may not result in substantial changes in risk-taking sexual behaviour in HIV serodiscordant couples.

011.3 USING HCV INCIDENCE TRENDS TO DISENTANGLE THE LIKELY IMPACT OF HIV ANTI-RETROVIRAL TREATMENT ON DECREASING HIV INCIDENCE AMONGST INJECTING DRUG USERS: A MODELLING ANALYSIS

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Background Two epidemiological studies (Vancouver/Baltimore) have used ecological correlations between community measures of HIV viral load (CVL) and HIV incidence to postulate that scaled-up HIV anti-retroviral treatment (ART) has decreased HIV transmission amongst injecting drug users (IDUs). However, for both studies HCV incidence decreased concurrently with observed decreases in HIV incidence suggesting that reductions in injecting risks may also have played a role. We use modelling to estimate the likely importance of ART in producing the observed reductions in HIV incidence in Vancouver from 1997 to 2007.

Methods A joint HIV and HCV transmission model, calibrated to the Vancouver IDU HIV epidemic (60% chronic HCV prevalence and 20% HIV prevalence) explored what combinations of ART recruitment and decreases in injecting risk could produce the observed relative reductions in HIV (> 66%) and HCV (> 50%) incidence for Vancouver. For each, the relative importance of ART was assessed. Sensitivity analyses considered the implications of behavioural uncertainty.

Results Model projections suggest modest reductions in injecting risk (~30%) result in large reductions in HIV (~70%) and HCV (~45%) incidence over 10 years, whereas ART scale-up (10% per year) only reduces HIV incidence (~40%). If we assume that HIV and HCV incidence decreased by 83% and 50% in Vancouver, respectively, then projections suggest 31–45% of the HIV impact was possibly due to ART. However, the combined intervention's impact is less than the sum of its parts, with the estimated HIV incidence decrease only reducing by < 15% with no ART. For smaller assumed reductions in HIV incidence and/or larger decreases in HCV incidence then projections suggest a smaller contribution due to ART.

Conclusions Our analysis suggests ART may not have been too important for producing observed HIV incidence declines in Vancouver, and highlights the importance of considering HCV incidence trends in similar analyses.

011.4 POPULATION-BASED HIV INCIDENCE AMONG MEN DIAGNOSED WITH INFECTIOUS SYPHILIS, 2000–2011

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Abstract 011.4 Table

	HIV-negative P&S syphilis cases	Newly diagnosed HIV	Person-years at risk	Annual HIV incidence (%)	95% CI (HIV incidence)
Total in NYC	3034	426	12850.10	3.32	3.01–3.64
Male	2805	423	11714.18	3.61	3.27–3.97
Age					
13–19	178	35	646.12	5.42	3.83–7.45
20–24	449	73	1654.75	4.41	3.48–5.51
25–29	484	83	1897.18	4.37	3.51–5.40
30–34	472	80	2107.84	3.80	3.03–4.70
35–39	489	76	2284.96	3.33	2.64–4.14
40–44	345	43	1511.29	2.85	2.08–3.80
45–49	186	23	742.20	3.10	2.01–4.58
50+	202	10	869.84	1.15	0.58–2.05
Race/ethnicity					
White	751	126	3064.03	4.11	3.44–4.88
Black	898	169	3597.64	4.70	4.03–5.45
Hispanic	94	94	2480.61	3.79	3.08–4.62
Other	34	34	960.85	3.54	2.49–4.89
Sexual behaviour/risk					
MSM	1884	389	7000.55	5.56	5.02–6.13
MSW	373	20	1661.05	1.20	0.76–1.83
Other, IDU, & unknown	548	14	3052.57	0.46	2.61–7.51
Syphilis stage					
Primary	859	103	3905.50	2.64	2.16–3.18
Secondary	1946	320	7808.68	4.10	3.67–4.57
Bacterial infections					
Syphilis only	2310	281	9718.04	2.89	2.57–3.24
Syphilis with concurrent CT/GC/LGV	103	12	348.96	3.44	1.86–5.85
Syphilis and subsequent CT/GC/LGV	392	130	1647.18	7.89	6.62–9.24
Year of syphilis					
2000	47	9	430.40	2.09	1.02–3.84
2001	133	31	1085.93	2.85	1.97–4.00
2002	186	52	1333.22	3.90	2.94–5.07
2003	231	58	1503.69	3.86	2.96–4.95
2004	274	44	1665.15	2.64	1.94–3.51
2005	255	53	1283.46	4.13	3.12–5.36
2006	272	40	1164.34	3.44	2.49–4.63
2007	360	45	1236.88	3.64	2.69–4.82
2008	443	61	1121.37	5.44	4.20–6.94
2009	406	24	691.97	3.47	2.27–5.08
January-June 2010	198	6	197.78	3.03	1.23–6.31