

Research News in Clinical Context

Danielle Solomon¹, Rayner Kay Jin Tan², Francesca Ceccherini-Silberstein³, Weiming Tang⁴, Monica Desai⁵

¹ Institute for Global Health, University College London

² University of North Carolina Project-China, Guangzhou, China

³ Department of Experimental Medicine, University of Rome Tor Vergata, Rome, Italy

⁴ Division of Infectious Diseases, Department of Medicine, UNC School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

⁵ MRC Clinical Trials Unit at UCL, London, UK

Correspondence to Dr Danielle Solomon, Mortimer Market Centre, Capper Street, London, WC1E 6JB; danielle.solomon@ucl.ac.uk

A call for improved syphilis testing and prevention efforts in vulnerable populations

Syphilis testing and incidence were reviewed among 8455 people living with HIV (PLHIV) who were seen at four US clinical sites in 2014-2018. Over 29,568 person-years (py) of follow-up, testing rates were 118/100 py; 57% were tested at least every 12 months, increasing to 68% among men who have sex with men. Syphilis incidence (based on rapid plasma reagin [RPR] patterns) was 4.7 cases/100 py overall. Rates were highest among younger men who have sex with men, transgender women, those who injected drugs, Hispanic people, and those with detectable HIV RNA, rectal STIs, or hepatitis C. The findings identify multiple sub-populations among PLHIV who should be prioritised for syphilis testing and interventions for syphilis prevention.

Menza TW, Berry SA, Dombrowski J, Cachay E, Dionne-Odom J, Christopoulos K, Crane HM, Kitahata MM, Mayer KH. Syphilis testing and diagnosis among people with HIV engaged in care at four United States clinical sites, 2014-2018. *Clin Infect Dis*. 2021 Nov 12;ciab944. doi: 10.1093/cid/ciab944. Epub ahead of print. PMID: 34788808

Assisted partner notification helps increase HIV testing among sexual contacts

Assisted partner notification – when providers help people living with HIV to inform sexual partners of the HIV diagnosis – offers the potential to increase early HIV detection among those at risk. A clinical trial in China randomised 187 newly HIV diagnosed men who have sex with men (MSM) to either assisted (n=97) or passive (n=90) partner notification. The assisted notification group was offered a choice between HIV self-testing kits to give to contacts or anonymous outreach to contacts. Rates of partner notification within three months were similar in the two groups (58% vs. 57% for assisted vs. passive notification). However, HIV testing among sexual partners of index cases increased significantly in the assisted notification group (35% vs. 17%). Assisted partner notification is a promising strategy for increasing HIV testing among contacts of newly diagnosed MSM.

Hu QH, Qian HZ, Li JM, Leuba SI, Chu ZX, Turner D, Ding HB, Jiang YJ, Vermund SH, Xu JJ, Shang H. Assisted Partner Notification and Uptake of HIV Testing among Men Who Have Sex with Men: A Randomized Controlled Trial in China. *Lancet Reg Health West Pac*. 2021 Jun 10;12:100171. doi: 10.1016/j.lanwpc.2021.100171. PMID: 34527967; PMCID: PMC8356101.

A comprehensive picture of anal HPV infection before HPV vaccination to guide anal cancer prevention in men

A systematic review and meta-analysis evaluated the age-specific prevalence of anal HPV and high-grade squamous intraepithelial lesions (HSIL) in men, stratified by HIV status and sexuality. Among 29,900 men from 64 studies, prevalence of HPV16 and other high-risk HPV types was lowest in HIV-negative heterosexual men, followed by HIV-positive heterosexual men and HIV-negative MSM, and was highest in HIV-positive MSM. Prevalence of anal HPV16 increased rapidly with age among MSM aged 15-24 years and was consistently high in MSM aged ≥ 25 years. Despite substantial heterogeneity in HSIL detection, HIV infection and HIV-related immunosuppression were significant predictors of anal HSIL. The findings highlight the importance of both primary prevention of HPV and HIV infection and secondary prevention of HPV-related anal cancer[1], particularly for high-risk populations.

Wei F, Gaisa MM, D'Souza G, Xia N, Giuliano AR, Hawes SE, Gao L, Cheng SH, Donà MG, Goldstone SE, Schim van der Loeff MF, Neukam K, Meites E, Poynten IM, Dai J, Combes JD, Wieland U, Burgos J, Wilkin TJ, Hernandez AL, Iribarren Díaz M, Hidalgo-Tenorio C, Valencia Arredondo M, Nyitray AG, Wentzensen N, Chow EP, Smelov V, Nowak RG, Phanuphak N, Woo YL, Choi Y, Hu Y, Schofield AM, Woestenber PJ, Chikandiwa AT, Hickey AC, de Pokomandy A, Murenzi G, Péré H, Del Pino M, Ortiz AP, Charnot-Katsikas A, Liu X, Chariyalertsak S, Strong C, Ong JJ, Yunihastuti E, Etienney I, Ferré VM, Zou H, Segondy M, Chinyowa S, Alberts CJ, Clifford GM. Epidemiology of anal human papillomavirus infection and high-grade squamous intraepithelial lesions in 29 900 men according to HIV status, sexuality, and age: a collaborative pooled analysis of 64 studies. *Lancet HIV*. 2021 Sep;8(9):e531-e543

Remdesivir modestly reduces Ebola virus RNA in semen

Among survivors, Ebola virus RNA may persist in semen for months or even years following acute infection and potentially result in sexual transmission[2]. Remdesivir is a nucleotide analogue prodrug that distributes efficiently into the testes. A trial in Liberia and Guinea randomised 38 men to receive intravenous remdesivir (n=20) or matching placebo (n=18) for five days. The mean assay negative rate (i.e., lack of viral RNA detection in semen) in the two arms was higher in the treatment arm: 85% vs. 76% over day 1-28 ($p=0.27$) and 96% vs. 81% over month 2-6 ($p=0.04$). Whilst a more extensive study is needed to validate these findings, potential applications of remdesivir in outbreak management are currently limited by the need for intravenous infusion.

Elizabeth S Higgs, Dehkontee Gayedyu-Dennis, William A Fischer II, Martha Nason, Cavan Reilly, Abdoul Habib Beavogui, Jamila Aboulhab, Jacqueline Nordwall, Princess Lobbo, Ian Wachekwa, Huyen Cao, Tomas Cihlar, Lisa Hensley, H Clifford Lane, PREVAIL IV: A Randomized, Double-Blind, 2-Phase, Phase 2 Trial of Remdesivir vs Placebo for Reduction of Ebola Virus RNA in the Semen of Male Survivors, *Clinical Infectious Diseases*, Volume 73, Issue 10, 15 November 2021, Pages 1849–1856

Published in STI - The Editor's Choice: Long-acting injectable regimens for HIV treatment are acceptable to both patients and clinicians

Long-acting injectable regimens are a recent addition to antiretroviral treatment (ART) options. In a survey of 688 people living with HIV and 120 HIV physicians in Germany, Italy, the UK, and France during 2019, 69% of people living with HIV expressed interest in trying the new regimens. Main perceived benefits included convenience when travelling (56%) and minimising transmission risk (50%); the predominant perceived disadvantage was the need to schedule frequent appointments to receive treatment (37%). Physicians were willing to offer long-acting ART if required, particularly for patients experiencing significant side effects (88-93%), privacy concerns (87%), suboptimal adherence (84%), and for improved convenience (84%), although there was some concern about resource implications (58%).

Overall, both groups viewed the new regimens as having the potential to address multiple unmet needs.

Akinwunmi B, Buchenberger D, Scherzer J, Bode M, Rizzini P, Vecchio F, Roustand L, Nachbaur G, Finkielstejn L, Chounta V, Van de Velde N. Factors associated with interest in a long-acting HIV regimen: perspectives of people living with HIV and healthcare providers in four European countries. *Sex Transm Infect.* 2021 Dec;97(8):566-573. doi: 10.1136/sextrans-2020-054648. Epub 2021 Feb 25. PMID: 33632889.

Characteristics of incident HIV infections among men using cabotegravir for PrEP

In the HPTN083 trial of cabotegravir (CAB) vs. TDF/FTC for HIV PrEP, there have been 12 and 39 incident HIV infections documented, respectively. In the CAB arm, 5 infections occurred in the absence of CAB exposure, 3 during the oral lead-in phase (potentially before target drug concentrations were attained), and 4 during the injection phase (despite mostly on-time CAB injections and expected plasma concentrations). Diagnosis of HIV infection was delayed in 7/12 cases due to prolonged viral suppression and delayed antibody expression. The delay was more frequent and longer with CAB than TDF/FTC, leading to ongoing PrEP use among some participants with undetected infection and increasing risk of potential drug resistance.

Marzinke MA, Grinsztejn B, Fogel JM, Piwowar-Manning E, Li M, Weng L, McCauley M, Cummings V, Ahmed S, Haines CD, Bushman LR, Petropoulos C, Persaud D, Adeyeye A, Kofron R, Rinehart A, St Clair M, Rooney JF, Pryluka D, Coelho L, Gaur A, Middelkoop K, Phanuphak N, Cohen MS, Hendrix CW, Anderson P, Hanscom B, Donnell D, Landovitz RJ, Eshleman SH. Characterization of Human Immunodeficiency Virus (HIV) Infection in Cisgender Men and Transgender Women Who Have Sex With Men Receiving Injectable Cabotegravir for HIV Prevention: HPTN 083. *J Infect Dis.* 2021 Nov 16;224(9):1581-1592. doi: 10.1093/infdis/jiab152. PMID: 33740057; PMCID: PMC8599849.

Funding statement:

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing Interests Statement:

The authors report no competing interests.

Contributorship Statement:

DS, RKJT, FC-S, WT and MD each drafted a section of the manuscript, and the final draft was approved by all authors.

References:

- 1 de Martel C, Plummer M, Vignat J, *et al.* Worldwide burden of cancer attributable to HPV by site, country and HPV type. *Int J Cancer* 2017;**141**:664–70.
doi:10.1002/ijc.30716
- 2 Deen GF, Broutet N, Xu W, *et al.* Ebola RNA Persistence in Semen of Ebola Virus Disease Survivors — Final Report. *N Engl J Med* 2017;**377**:1428–37.
doi:10.1056/nejmoa1511410