

**His Health PrEP 2.0 CME/CNE**

**Supplemental Reading**

**Research Articles**

1. Tepper, V., Zaner, S., & Ryscavage, P. (2017). HIV healthcare transition outcomes among youth in North America and Europe: a review. *Journal of the International AIDS Society*, *20*(Suppl 3), 21490. DOI: http://doi.org/10.7448/IAS.20.4.21490

The transition from paediatric to adult care poses risks to the health of young adults living with HIV if unsuccessful, including interruptions in care and poor health outcomes. Evolving best practices in HIV healthcare transition should ideally be informed by real-world qualitative and quantitative clinical healthcare transition outcomes. There has been a recent proliferation of HIV healthcare transition outcome research, largely from Europe and North America. In this paper, study investigators review data on HIV healthcare transition outcomes in North America and Europe. Internal and external factors which may impact the success of HIV healthcare transition are examined. They describe ongoing research efforts to capture transition outcomes in the North America and Europe. Clinical, operational, and implementation science research gaps that exist to date are highlighted. Efforts to improve HIV healthcare transition research through country-level surveillance networks and large multicentre cohorts, including data integration and linkage between paediatric and adult cohorts are discussed.

1. Millett, G.A., Peterson, J.L., Flores, S.A., Hart, T.A., et al. (2012). Comparisons of disparities and risks of HIV infection in Black and other men who have sex with men in Canada, UK, and USA: a meta-analysis. *Lancet Infectious Diseases*. *380*(9839), 341-348. DOI: 10.1016/S0140-6736(12)60899-X

Study investigators conducted a meta-analysis to assess factors associated with disparities in HIV infection in black men who have sex with men (MSM) in Canada, the UK, and the USA. They searched Embase, Medline, Google Scholar, and online conference proceedings from Jan 1, 1981, to Dec 31, 2011, for racial comparative studies with quantitative outcomes associated with HIV risk or HIV infection. Key words and Medical Subject Headings (US National Library of Medicine) relevant to race were cross-referenced with citations pertinent to homosexuality in Canada, the UK, and the USA. Data were aggregated across studies for every outcome of interest to estimate overall effect sizes, which were converted into summary ORs for 106,148 black MSM relative to 581,577 other MSM.

1. Grant, R.M., Lama J.R., Anderson, P.L., McMahan, V., et al. (2010). Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex With Men. *New England Journal of Medicine*. *363*(27), 2587–2599. DOI: 10.1056/NEJMoa1011205

Study investigators randomly assigned 2499 HIV-seronegative men or transgender women who have sex with men to receive a combination of two oral antiretroviral drugs, emtricitabine and tenofovir disoproxil fumarate (FTC-TDF), or placebo once daily. All subjects received HIV testing, risk-reduction counseling, condoms, and management of sexually transmitted infections.

1. Buchbinder, S.P., Glidden, D.V., Liu, A.Y., McMahan, V., et al. (2014). HIV Pre-exposure Prophylaxis in Men Who Have Sex With Men and Transgender Women: A Secondary Analysis of a Phase 3 Randomised Controlled Efficacy Trial. *Lancet Infectious Diseases*. *14*(6), 468–475. DOI: 10.1016/S1473-3099(14)70025-8

For maximum effect pre-exposure prophylaxis should be targeted to the subpopulations that account for the largest proportion

of infections (population-attributable fraction [PAF]) and for whom the number needed to treat (NNT) to prevent infection is

lowest. Study investigators aimed to estimate the PAF and NNT of participants in the iPrEx (Pre-Exposure Prophylaxis Initiative) trial. The iPrEx study was a randomised controlled efficacy trial of pre-exposure prophylaxis with coformulated tenofovir disoproxil fumarate and emtricitabine in 2499 men who have sex with men (MSM) and transgender women. Participants aged 18 years or older who were male at birth were enrolled from 11 trial sites in Brazil, Ecuador, Peru, South Africa, Thailand, and the USA. Participants were randomly assigned (1:1) to receive either a pill with active pre-exposure prophylaxis or placebo, taken daily. Study investigators calculated the association between demographic and risk behaviour during screening and subsequent seroconversion among placebo recipients using a Poisson model, and we calculated the PAF and NNT for risk behaviour subgroups.

5. Mujugira A., Baeten J.M., Donnell D., Ndase P., et al. (2011) Characteristics of HIV-1 Serodiscordant Couples Enrolled in a Clinical Trial of Antiretroviral Pre-Exposure Prophylaxis for HIV-1 Prevention. *PLoS ONE.* 6(10): e25828. <https://doi.org/10.1371/journal.pone.0025828>

Stable heterosexual HIV-1 serodiscordant couples in Africa have high HIV-1 transmission rates and are a critical population for evaluation of new HIV-1 prevention strategies. The Partners PrEP Study is a randomized, double-blind, placebo-controlled trial of tenofovir and emtricitabine-tenofovir pre-exposure prophylaxis to decrease HIV-1 acquisition within heterosexual HIV-1 serodiscordant couples. We describe the trial design and characteristics of the study cohort.

6. Thigpen M.C., Kebaabetswe P.M., Smith D.K., et al. Daily oral antiretroviral use for the prevention of HIV infection in heterosexually active young adults in Botswana: results from the TDF2 study. 6th IAS Conference on HIV Pathogenesis, Treatment and Prevention; Rome, Italy. 17–20 July 2011; p. Abstract WELBC01.

navigation.

7. Martin, M., Vanichseni, S., Suntharasamai, P., Sangkum, U., Chuachoowong, R., et al. (2011). Enrollment Characteristics and Risk

Behaviors of Injection Drug Users Participating in the Bangkok Tenofovir Study, Thailand. *PLoS One*. *6*(9):e25127. DOI: [10.1371/journal.pone.0025127](https://dx.doi.org/10.1371%2Fjournal.pone.0025127)

The Bangkok Tenofovir Study was launched in 2005 to determine if pre-exposure prophylaxis with tenofovir will reduce the risk of HIV infection among injecting drug users (IDUs). Study investigators describe recruitment, screening, enrollment, and baseline characteristics of study participants and contrast risk behavior of Tenofovir Study participants with participants in the 1999–2003 AIDSVAX B/E Vaccine Trial. The Bangkok Tenofovir Study is an ongoing, phase-3, randomized, double-blind, placebo-controlled, HIV pre-exposure prophylaxis trial of daily oral tenofovir. The Tenofovir Study and the Vaccine Trial were conducted among IDUs at 17 drug-treatment clinics in Bangkok. Tenofovir Study sample size was based on HIV incidence in the Vaccine Trial. Standardized questionnaires were used to collect demographic, risk behavior, and incarceration data.

8. Molina, J.M., Capitant, C., Spire, B., Pialoux, G., et al. (2015). On-Demand Preexposure Prophylaxis in men at High Risk for HIV-1 Infection. *New England Journal of Medicine*. *373*(23), 2237-2246. DOI: 10.1056/NEJMoa1506273

Antiretroviral preexposure prophylaxis has been shown to reduce the risk of human immunodeficiency virus type 1 (HIV-1) infection in some studies, but conflicting results have been reported among studies, probably due to challenges of adherence to a daily regimen. Study investigators conducted a double-blind, randomized trial of antiretroviral therapy for preexposure HIV-1 prophylaxis among men who have unprotected anal sex with men. Participants were randomly assigned to take a combination of tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) or placebo before and after sexual activity. All participants received risk-reduction counseling and condoms and were regularly tested for HIV-1 and HIV-2 and other sexually transmitted infections.

9. McCormack, S., Dunn, D., Desai, M., Dolling, D.I., et al. (2016). Pre-exposure Prophylaxis to Prevent the Acquisition of HIV-1 Infection (PROUD): Effectiveness Results from the Pilot Phase of a Pragmatic Open-Lbel Randomised Trial. *Lancet Infectious Diseases*. *387*(10013), 53-60. DOI: 10.1016/S0140-6736(15)00056-2

PROUD is an open-label randomised trial done at 13 sexual health clinics in England. We enrolled HIV-negative gay and other men who have sex with men who had had anal intercourse without a condom in the previous 90 days. Participants were randomly assigned (1:1) to receive daily combined tenofovir disoproxil fumarate (245 mg) and emtricitabine (200 mg) either immediately or after a deferral period of 1 year. Randomisation was done via web-based access to a central computer-generated list with variable block sizes (stratified by clinical site). Follow-up was quarterly. The primary outcomes for the pilot phase were time to accrue 500 participants and retention; secondary outcomes included incident HIV infection during the deferral period, safety, adherence, and risk compensation.

10. Jenness, S.M., Goodreau, S.M., Rosenberg, E., Beylerian, E.N., et al. (2016). Impact of the Centers for Disease Control’s HIV Preexposure Prophylaxis Guidelines for Men Who Have Sex With Men in the United States. *The Journal of Infectious Diseases*. *214*(12), 1800-1807. DOI: [10.1093/infdis/jiw223](https://dx.doi.org/10.1093%2Finfdis%2Fjiw223)

Preexposure prophylaxis (PrEP) is effective for preventing human immunodeficiency virus (HIV) infection among men who have sex with men (MSM) within trial settings. Population impact will depend on clinical indications for PrEP initiation, coverage levels, and drug adherence. No modeling studies have estimated the impact of clinical practice guidelines for PrEP issued by the Centers for Disease Control and Prevention (CDC). Mathematical models of HIV transmission among MSM were used to estimate the percentage of infections averted (PIA) and the number needed to treat (NNT) under behavioral indications of the CDC's PrEP guidelines. We modeled the contribution of these indications while varying treatment coverage and adherence.

11. Mera, R., McCallister, S., Palmer, B., Mayer, G., Magnuson, D., & Rawlings, K. (2016). Truvada (TVD) for HIV Pre-exposure Prophylaxis (PrEP) Utilization in the United States (2013-2015). *Journal of Acquired Immune Deficiency* Syndromes. *19*(Suppl 5):30

In 2012 Truvada (TVD) was licensed for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 for adults at high risk in the USA. Study investigators describe the TVD for PrEP utilization in the US, including user and prescriber characteristics.

12. Hosek, S.G., Rudy, B., Landovitz, R., Kapogiannis, B., et al. (2017). An HIV Preexposure Prophylaxis Demonstration Project and Safety Study for Young MSM. *Journal of Acquired Immune Deficiency Syndromes*. *74*(1), 21-29. DOI: 10.1097/QAI.0000000000001179

Young men who have sex with men (YMSM) are a key population for implementation of preexposure prophylaxis (PrEP) interventions. This open-label study examined adherence to PrEP and assessed sexual behavior among a diverse sample of YMSM in 12 US cities.  Eligible participants were 18- to 22-year-old HIV-uninfected MSM who reported HIV transmission risk behavior in the previous 6 months. Participants were provided daily tenofovir disoproxil fumarate/emtricitabine (Truvada). Study visits occurred at baseline, monthly through week 12, and then quarterly through week 48. Dried blood spots were serially collected for the quantification of tenofovir diphosphate (TFV-DP).

13. Smith, D.K., Van Handel, M., Wolitski, R., Stryker, J.E., et al. (2015). Vital Signs: Estimated Percentages and Numbers of Adults with Indications for Preexposure Prophylaxis to Prevent HIV Acquisition. *Morbidity and Mortality Weekly Report.* *64*(46), 1291-1295.

The Centers for Disease Control and Prevention analyzed nationally representative data to estimate the percentages and numbers of persons in the United States, by transmission risk group, with indications for PrEP consistent with the 2014 U.S. Public Health Service's PrEP clinical practice guideline.

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15. Smith, D.K., Van Handel, M., Wolitski, R., Stryker, J.E., et al. (2015). Vital Signs: Estimated Percentages and Numbers of Adults with Indications for Preexposure Prophylaxis to Prevent HIV Acquisition. *Morbidity and Mortality Weekly Report.* *64*(46), 1291-1295.

The Centers for Disease Control and Prevention analyzed nationally representative data to estimate the percentages and numbers of persons in the United States, by transmission risk group, with indications for PrEP consistent with the 2014 U.S. Public Health Service's PrEP clinical practice guideline.

16. Bush, R.S., Magnuson, K., et al. (2016). Utilization of Emtricitabine/Tenofovir (FTC/TDF) for HIV Pre-exposure Prophylaxis in the United States by Gender (2013-1Q2016). *Journal of the International AIDS Society.* *19*(Suppl 7), 14-15.

**Reports and Factsheets**

1. US department of Health and Human Services Centers for Disease Control and Prevention. HIV Incidence: Estimated Annual Infections in the U.S., 2008-2014 Overall and by Transmission Route. (2017). Retrieved from: https://www.cdc.gov/nchhstp/newsroom/docs/factsheets/hiv-incidence-fact-sheet\_508.pdf

The fact sheet offers information on the estimated annual infections of HIV in the U.S. from the period of 2008-2014, with a focus on gay and bisexual men.

2. US department of Health and Human Services Centers for Disease Control and Prevention. HIV Surveillance Report 2014. Vol 26. Retrieved from: https://www.cdc.gov/nchhstp/newsroom/docs/factsheets/hiv-incidence-fact-sheet\_508.pdf

This report includes case report data from 50 states, the District of Columbia, and 6 U.S. dependent areas (American Samoa, Guam, the Northern Mariana Islands, Puerto Rico, the Republic of Palau, and the U.S. Virgin Islands) in which laws or regulations require confidential reporting to the jurisdiction (not to CDC), by name, for adults, adolescents, and children with confirmed diagnoses of HIV infection.

3. US department of Health and Human Services Centers for Disease Control and Prevention. (2014). Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014, A Clinical Practice Guide.” Retrieved from: https://www.cdc.gov/hiv/pdf/prepguidelines2014.pdf

This publication provides a comprehensive clinical practice guideline for the use of PrEP for the prevention of HIV infection in the United States. It incorporates and extends information provided in interim guidance for PrEP use with MSM, with heterosexually active adults, and with IDU (also called persons who injection drugs [PWID]).

**Presentations**

1. Wheeler, D.P., Fields, S., Nelson, L.E., Wilton, L., et al. (2016). HPTN 073: PrEP Uptake and Use by Black Men Who Have Sex With Men in 3 US Cities. 23rd Conference on Retroviruses and Opportunistic Infections. February 22-25, 2016. Boston, MA. Abstract 883LB.

HIV-uninfected BMSM were enrolled in three U.S. cities (Washington, DC., Los Angeles CA, & Chapel Hill, NC) All participants were offered once daily oral FTC/TDF combined with client-centered care coordination (C4)–a theory-based counseling approach to promote and support PrEP use, which combined service referral, linkage and follow-up strategies to assist participants in addressing unmet psychosocial needs. Each participant was offered PrEP and followed for a total of 12 months. 226 BMSM men were recruited; 209 (92%) completed 12 month of follow-up. 40% were <25 years, 27% were unemployed, 31% did not have health insurance. The median number of male partners in the prior 3 months was 3 (IQR 1-4), 33% reported a primary partner and 73% casual male partners. PrEP was accepted by 178 (79%) of study participants (see Figure); 68% remained on PrEP at 26 weeks. Self-reported adherence above 50% was 85% at 4 weeks and 78% at 26 weeks. 23/24 (96%) men reporting an HIV+ primary partner and 104/120 (86%) of men reporting casual partners with unknown or HIV+ status accepted PrEP. Those agreeing to take PrEP utilized a median of 6 C4 sessions (range 3–8) compared to men not accepting PrEP (median 4 range 2-6]). Among the 178 men who ever accepted PrEP, 5 HIV infections occurred in 172 person years (PY) (incidence=2.9 95%CI(0.9-6.8)) compared to 3 in 39 PY (incidence=7.7 95%CI1.6-22.5) in men who never accepted PrEP. Of the 5 seroconverters who ever took PrEP, 2 had discontinued PrEP at 50 and 272 days prior to seroconversion.

2. Hoornenborg, Elske & Godelieve de Bree (2011). Acute Infection with a Wild-type HIV-1 Virus in a PrEP User with High TDF Levels. 24th Conference on Retroviruses and Opportunistic Infections. February 14-16, 2017. Seattle, WA. Abstract 953.

Study investigators report a case with potentially very high HIV-1 exposure who was infected with wild-type HIV-1 while adhering well to a daily PrEP regimen. A 50-year-old men who has sex with men (MSM) started daily PrEP via the Amsterdam PrEP (AMPrEP) study. At enrollment, he tested HIV negative (4th generation HIV Ag/Ab test and HIV RNA test). Pill counts and daily diary information indicated adequate adherence of 7 pills per week. This was confirmed by a TDF-DP level in DBS of 2234 and 2258 fmol/punch at respectively 6 and 8 months after start of PrEP. HIV Ag/Ab tests during follow-up were repeatedly negative at 1, 3 and 6 months after starting PrEP. The number of episodes of condomless anal sex (CAS) was remarkably high.

3. Grant, R.M., Liu, A., Hecht, J., Buchbinder, S.P., et al. (2015). Scale-Up of Preexposure Prophylaxis in San Francisco to Impact HIV Incidence. 22nd Conference on Retroviruses and Opportunistic Infections. February 23-26, 2015. Seattle, WA. Abstract 25.

A simple model was developed to forecast HIV transmission with expanded PrEP use. The model considers infectiousness and partnering practices of diagnosed and undiagnosed persons with HIV infection, viral suppression rates, and transmission to uninfected people having low, moderate, or high numbers of partners. Model parameters for SF were derived from surveillance, local research on seroadaptive behaviors, and SF-specific data from cohort studies, including the iPrEx Open Label Extension (OLE). Adherence in OLE was monitored by drug concentrations in dried blood spots and mapped to efficacy using global iPrEx data. The optimistic scenario assumes PrEP uptake will attract and retain people with higher exposure to HIV, as was observed at SF's OLE site. The realistic scenario assumes incidence rates that are typically observed in SF cohorts that did not include access to PrEP.

4. Scanlin, K.K., Salcuni, P.M., Edestein, Z.R., Daskalasis, D.C., et al. Increasing PrEP Use Among Men Who Have Sex With Men. 23rd Conference on Retroviruses and Opportunistic Infections. February 22-25, 2016. Boston, MA. Abstract 888.

Since 2012, the New York City (NYC) Department of Health and its partners have launched programs to support PrEP uptake. Using data from routine behavioral surveillance among men who have sex with men (MSM), study investigators examined recent trends and associations with PrEP use. Data were derived from annual surveys conducted in-person and online, 2013-2015. Eligible respondents were NYC residents, who were born male, aged 18-40, and reported anal sex with a man (past 6 months). This analysis excluded those who reported being diagnosed with HIV. PrEP use was defined as use in the past 6 months. Demographic factors examined included age (18-29/30-40 years), race/ethnicity (black/Hispanic/white/other), education (college degree) and insurance status. Behavioral factors were condomless sex or known HIV-positive partner at last sexual encounter and number of condomless partners (3 or more) and/or post-exposure prophylaxis (PEP) use in the past 6 months. Using logistic regression, study investigators assessed associations between PrEP use and year, factors, and year-factor interaction terms. Those associated bivariately (p<0.05) were added to a multivariate model with age, race/ethnicity, insurance, survey type (in-person/online) and year.