

Pre-exposure prophylaxis for men who have sex with men: *A systematic review*

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Systematic review write up

Background

An estimated 35.3 million people globally are living with HIV (UNAIDS, 2013). A number of prevention methods are available, from condoms to male circumcision, prevention of mother-to-child transmission to clean needles, but to date these have not been sufficient to stop the epidemic. In 2012 alone, an estimated 2.3 million people became newly infected (UNAIDS, 2013). Additional safe and effective approaches to HIV prevention are urgently needed.

Men who have sex with men (MSM) have a disproportionate burden of HIV in most countries in the world, even in many countries with generalized HIV epidemics. Worldwide, for MSM, the odds of being infected with HIV are 19.3 times higher than for men in the general population (Baral et al., 2007). Although there are a variety of existing efficacious HIV prevention interventions for MSM, they face political and structural barriers to accessing services in many settings due to their stigmatized and marginalized status. The disproportionate burden of HIV faced by MSM suggests that existing methods of HIV prevention are not sufficient and additional prevention modalities would be helpful.

Pre-exposure prophylaxis (PrEP) is the use of an antiretroviral drug to block the acquisition of HIV infection by uninfected people. Proof of concept has long been established in the laboratory by animal studies and in real world application by the prevention of mother-to-child transmission and post-exposure prophylaxis. The safety of the drugs being considered for PrEP, tenofovir and emtricitabine, has been established through their use for treatment and in safety trials in uninfected people (Peterson et al., 2007). Five trials of effectiveness (Phase IIb and Phase III) have been conducted in the last decade. These focus on effectiveness of PrEP among people who inject drugs, serodiscordant couples, heterosexual women and high risk MSM.

The first trial to produce results was the iPrEx trial (Grant et al., 2010). This Phase III clinical trial tested whether a daily combination of tenofovir and emtricitabine could safely and effectively prevent HIV infection among MSM. Of the five effectiveness trials, this trial conducted in six countries on four continents was the only one to examine efficacy in MSM.

The iPrEx study demonstrated a 44% reduction in HIV transmission on the modified intention-to-treat analysis. Adherence to the recommended regimen was lower than expected, though it varied by country. For those men who reported taking the pills on 90% or more days, however, the efficacy of PrEP was 73%. Resistance was only found in two participants who had an existing acute HIV infection undetected at baseline and who were randomized to active drug. Few concerns about safety were detected. A marked trend toward risk reduction, specifically increased condom use and decreased number of partners, was reported in both arms and all sites.

In 2012, WHO developed guidelines for PrEP for serodiscordant couples, MSM, and transgender people (TG) at high risk of HIV (WHO, 2012). This systematic review updates the review of PrEP for MSM that was completed for those guidelines. This systematic review examined the following PICO question: Should oral PrEP (containing tenofovir (TDF)) be used for HIV prevention among men who have sex

with men? A few minor changes were made to the PICO question from the earlier guidelines. First, the new PICO question includes only MSM, not transgender people. Second, the new PICO question covers all oral PrEP containing tenofovir, as opposed to the previous PICO question which focused specifically on the combination of emtricitabine (FTC 200mg) and tenofovir (TDF 300 mg) used in the iPrEx study.

In addition, in 2011, a review of values and preferences of MSM about PrEP was conducted through a review of published literature. However, most of the studies available at that time were based on data collected before the iPrEx trial results were available. Values and preferences may have changed now that MSM are aware of the partial effectiveness of PrEP. This values and preferences literature review was also updated to capture literature through the end of 2013, with a focus on studies that collected data after iPrEx study results were released.

Methods

PICO question

PICO 1: Should oral PrEP (containing tenofovir (TDF)) be used for HIV prevention among men who have sex with men?

P: Men who have sex with men

I: Oral PrEP (containing tenofovir (TDF))

C: Placebo

O: (1) HIV infection, (2) any adverse event, (3) any stage 3 or 4 adverse event, (4) condom use, and (5) number of sexual partners

Inclusion criteria

To be included in the review, an article had to meet the following criteria:

- 1) Randomized controlled trial evaluating the use of oral PrEP (containing tenofovir (TDF)) to prevent HIV infection among MSM participants.
- 2) Measured one or more of the following key outcomes: (1) HIV infection, (2) any adverse event, (3) any stage 3 or 4 adverse event, (4) condom use, and (5) number of sexual partners.
- 3) Published in a peer-reviewed journal, or presented as an abstract at a scientific conference, between January 1, 1990 and January 1, 2014.

No restrictions were placed based on location of the intervention. No language restrictions were used on the search. Articles in languages other than English were translated where necessary.

Following the GRADE approach, if direct evidence from MSM populations was limited for one or more of the key outcomes, indirect evidence from other populations (e.g., heterosexual men) would have been instead, but downgraded for indirectness. If evidence from other populations was limited, evidence from non-randomized but controlled studies would have been used instead, but also downgraded for directness.

Search strategy

The following electronic databases were searched using the date ranges January 1, 1990 to January 1, 2014: PubMed, CINAHL (Cumulative Index to Nursing and Allied Health Literature), and EMBASE. Secondary reference searching was conducted on all studies included in the review. Further, selected experts in the field were contacted to identify additional articles not identified through other search methods.

Abstracts from the following conferences were searched from January 1, 1990 to January 1, 2014: International AIDS Conference (IAC) and IAS Conference on HIV Pathogenesis, Treatment, and Prevention (IAS). We had planned to search the Conference on Retroviruses and Opportunistic Infections (CROI) as well, but abstracts from this conference were no longer available online to the public at the time the search was conducted.

Search terms

The following terms were entered into all computer databases:

("men who have sex with men" or MSM or transgender or TG or "gay men") AND ("pre-exposure prophylaxis" or PrEP or emtricitabine or tenofovir or Truvada or FTC or TDF) AND (HIV OR AIDS)

The search for abstracts was more difficult given the search engines available on conference websites. For each conference, a search was first conducted for all abstracts including the word "PrEP". These search results were then further searched for keywords regarding MSM.

Screening abstracts

Titles, abstracts, citation information, and descriptor terms of citations identified through the search strategy were screened by two reviewers. Full text articles were obtained for all selected abstracts and both reviewers independently assessed all full-text articles for eligibility to determine final study selection. Differences were resolved through consensus.

Articles not meeting the inclusion criteria for the review, but presenting potentially interesting background information relevant to PrEP among MSM, including review articles, qualitative studies, cost or cost-effectiveness analyses, or descriptions of interventions without an evaluation component, were included in an annotated bibliography of additional articles.

Data extraction and management

Data were extracted independently by two reviewers using standardized data extraction forms. Differences in data extraction were resolved through consensus and referral to a senior team member from WHO when necessary. Study authors were contacted when additional information or data were needed.

The following information was gathered from each included study:

- Study identification: Author(s); type of citation; year of publication

- Study description: Study objectives; location; population characteristics; description of the intervention; study design; sample size; follow-up periods and loss to follow-up
- Outcomes: Analytic approach; outcome measures; comparison groups; effect sizes; confidence intervals; significance levels; conclusions; limitations

Risk of bias was assessed using the Cochrane Collaboration's tool for assessing risk of bias (Cochrane Handbook, chapter 8.5 – Higgins & Green, 2011). This tool assesses random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias) incomplete outcome data (attrition bias), and selective reporting (reporting bias). Methodological components of the studies were assessed and classified as high, low, or uncertain risk of bias.

Data analysis

Data were analyzed according to coding categories and outcomes. If multiple studies reported the same outcome, meta-analysis would have been conducted using random-effects models to combine effect sizes with the program Comprehensive Meta-Analysis (CMA). Data were summarized in GRADE tables, summary of finding tables, and risk/benefit tables.

Results

Combining search results from both the 2011 and 2014 searches, initial database searching yielded 764 citations and 139 conference abstracts; one additional study was identified through other means, such as searching through the reference lists of relevant articles (Figure 1). Once all duplicates were removed, 609 records were reviewed and 348 article citations and 119 abstracts were excluded for being unrelated to the study topic. After thoroughly reviewing the remaining 142 articles and abstracts, 3 were excluded for being unrelated to the study topic, 4 did not meet the study design criteria, and 128 were coded as background or values and preferences; an additional 3 conference abstracts presented preliminary data and were used in the 2011 review, although all 3 were later published as peer-reviewed articles and thus were duplicative of other included articles. Ultimately, 4 studies reported in 5 articles were deemed eligible for inclusion in our review. Of these, one was a Phase III efficacy trial, while three were smaller pilot feasibility/acceptability or extended safety studies. Given the discrepancies in the study purposes, drug regimens/dosing schedule, and size/statistical power (and thus imprecision and quality according to the GRADE framework), we generally present results from the primary Phase III efficacy trial below and in GRADE tables, and present additional findings from the smaller studies in the results below along with the efficacy trial. However, for the HIV infection outcome, we were able to merge the results from two studies with the same drug regimen.

The primary Phase III efficacy trial meeting all inclusion criteria was the iPrEx trial (Grant et al., 2010). This study was a randomized controlled trial to evaluate the safety and efficacy of once-daily oral FTC-TDF as compared with placebo for the prevention of HIV acquisition among MSM. The trial was conducted among 2499 participants in 6 countries: Peru, Ecuador, South Africa, Brazil, Thailand, and the United States. All study participants were born male, although 29 (1%) reported their current gender identity as female. Participants' ages ranged from 18 to 67 years. Using the Cochrane Risk of Bias tool, the study was judged to have low risk of bias across all of the following categories: random sequence

generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), and selective reporting (reporting bias). The study measured all five key outcomes for this review: 1) HIV infection, 2) Any adverse event, 3) Any stage 3 or 4 adverse event, 4) Condom use, and 5) Number of sexual partners.

The smaller safety study was the US CDC Safety Study, a phase II, randomized, double-blind, placebo-controlled, extended safety trial of TDF in MSM in the United States (Grohskopf et al., 2013; Liu et al., 2013). The trial was conducted among 400 MSM aged 18-60 in 3 US cities: Atlanta, Boston, and San Francisco. Participants were randomized in equal numbers to one of 4 study arms: (1) daily TDF beginning at enrollment, (2) daily placebo beginning at enrollment, (3) daily TDF beginning 9 months after enrollment, and (4) daily placebo beginning 9 months after enrollment.

The smaller pilot feasibility and acceptability study was Project PrEPare, a study to examine the feasibility of a combination prevention intervention, including PrEP, for young MSM in the United States (Hosek et al., 2013). The study was conducted among 58 young MSM aged 18-22 in Chicago. Participants were randomized to one of 3 study arms: (1) a behavioral HIV prevention intervention called Many Men, Many Voices (3 MV) alone, (2) 3 MV combined with PrEP (FTC-TDF), and (3) 3 MV combined with placebo.

Finally, one small study examined safety and adherence to intermittent or daily oral FTC-TDF among Kenyan MSM and female sex workers (Mutua et al., 2012). This study randomized 67 MSM and 5 female sex workers to daily FTC-TDF or placebo, or intermittent FTC-TDF or placebo in a 2:1:2:1 ratio.

HIV infection

In the iPrEx study, incident HIV infection was significantly reduced among participants in the FTC-TDF study arm as compared to the control arm using both an intention-to-treat analysis and a modified intention-to-treat excluding participants who had HIV RNA detected at baseline (Grant et al., 2010). In the intention-to-treat analysis, there were 38 incident cases of HIV infection out of 1251 participants in the FTC-TDF study arm and 72 incident HIV infections out of 1248 participants in the control group, resulting in a hazard ratio of 0.53 (95% CI 0.36-0.78, $p=0.001$). In the modified intention-to-treat analysis, there were 36 incident cases of HIV in the FTC-TDF group (N=1251) and 64 incident cases of HIV in the control group (N=1248). For this analysis, the hazard ratio of HIV infection comparing those in the FTC-TDF group to the control was 0.56 (95% CI 0.37-0.85, $p=0.005$), thus showing a 44% reduction in the relative risk of HIV infection.

The CDC safety study had 7 seroconversions among 400 participants (Grohskopf et al., 2013). None occurred among participants taking TDF (n=201), 3 occurred among participants taking placebo (n=99), and 3 occurred among delayed arm participants who had not yet started drug (n=100). One occurred in a participant assigned to placebo who was HIV-1 antibody negative at screening and enrollment and then was seropositive at the 1-month visit.

Project PrEPare had zero seroconversions among 58 study participants (Hosek et al., 2013). The Kenya intermittent PrEP study had one incident infection in the placebo arm (Mutua et al., 2012).

Any adverse event

In the iPrEx study, there was no statistically significant difference in reported adverse events between the two study arms (Grant et al., 2010). In the FTC-TDF arm, 867 out of 1251 patients (69%) reported having any adverse event compared to 877 out of 1248 patients (70%) in the control group. The relative risk of having any adverse event comparing the intervention to control group was 0.99 (95% CI 0.94-1.04), which was not statistically significant.

The CDC safety study also found that there was no statistically significant difference in reported adverse events between the two study arms; overall, 2428 adverse events occurred among 334 (90%) participants, with most of mild or moderate severity (Grohskopf et al., 2013).

Project PrEPare reported 6 adverse events total, 5 of which were possibly or probably related to the study drug, all in the FTC-TDF arm.

The study on intermittent PrEP in Kenya found that both dose regimens had similar rates of adverse events (Mutua et al., 2012).

Any stage 3 or 4 adverse event

In the iPrEx study, both study arms also reported similar rates of grade 3 and 4 adverse events (Grant et al., 2010). In the FTC-TDF study arm, 151 out of 1251 patients (12%) reported having a grade 3 or 4 adverse event compared to 164 out of 1248 patients (13%) in the control arm. The relative risk of having any grade 3 or 4 adverse event was 0.92 (95% CI 0.75-1.13) comparing the intervention to control arm, thus showing no statistical difference between the two groups.

The CDC safety study also found that there was no statistically significant difference in grade 3 and 4 adverse events between the two study arms (TDF: 36 events, 13.2 per 100 person-years (py); Placebo: 26 events, 9.9 per 100 py, rate ratio: 1.13 (95% CI: 0.61, 2.11, p=0.703) (Grohskopf et al., 2013). This finding remained consistent in multivariable analyses dichotomized by adherence levels.

Project PrEPare reported three grade 3 adverse events which were possibly or probably related to the study drug, all in the FTC-TDF arm (Hosek et al., 2013).

The study on intermittent PrEP in Kenya found no study-related serious adverse events (Mutua et al., 2012).

Condom use

The iPrEx study found that both groups reported increased condom use (defined as the percent of partners using condoms during receptive intercourse) over the course of the intervention, but that differences in condom use rates between the FTC-TDF arm (N=1251 at baseline) and control arm (N=1248) did not differ significantly (p=0.36) (Grant et al., 2010). To examine this relationship, a linear mixed regression model was fitted with a random intercept and fixed effects for treatment visit and treatment by visit interaction. The p-value is from a Wald test of the treatment by visit interaction which corresponds to whether or not there is a difference during the study period between the FTC-TDF and control groups. The description of the analysis conducted was received as correspondence from the study authors and was not included in the original publication.

The CDC safety study found that overall, the proportion of MSM reporting unprotected anal sex (UAS) in the past 3 months decreased significantly, from 57% at baseline to 48% during months 3-9 and 52% during months 12-24 ($p < 0.001$) (Liu et al., 2013). The change in proportion of men reporting UAS from baseline to months 3-9 was similar between the immediate vs. delayed arms ($p = 0.15$). The proportion of men reporting UAS did not change significantly after initiation of study drug in the delayed arm ($p = 0.41$) or with continuation of drug in the immediate arm (incident rate ratio (IRR)=1.17, 95% CI: 0.98 to 1.39, $p = 0.09$).

Project PrEPare found no statistically significant differences in the distribution of male-to-male UAS acts among the 3 treatment groups across study visits (Hosek et al., 2013). Percentages of participants reporting UAS in the past month at baseline and week 24 were 42% and 42% for the PrEP arm, 40% and 10% for the placebo arm, and 31% and 23% for the no pill arm. There was a non-significant trend of decreasing UAS across all treatment arms from baseline to week 24.

Number of sexual partners

In the iPrEx study, in both study arms, the number of receptive sexual intercourse partners declined from baseline to follow-up over the course of the study; however, there was no significant difference between the number of partners reported in each study group at each time point ($p = 0.97$) (Grant et al., 2010). Results were calculated by fitting a linear mixed regression model with a random intercept and fixed effects for treatment visit and treatment by visit interaction. The p-value is from a Wald test of the treatment by visit interaction which corresponds to whether or not there is a difference during the study period between the arms in the number of sexual partners (total male partners at over a 12 week recall period with whom the participant had oral or anal sex). These results and a description of the analysis conducted were received as correspondence from the study authors and were not included in the original publication.

The CDC safety study found that overall, mean number of sex partners in the past 3 months decreased significantly from 7.25 at baseline to 6.02 during months 3-9 and 5.71 during months 12-24 ($p < 0.001$) (Liu et al., 2013). These declines were similar between the immediate and delayed study arms during months 3-9 ($p = 0.67$), and the mean number of partners did not differ in months 12-24 vs. months 3-9 with initiation of study drug in the delayed arm (IRR=0.93, $p = 0.22$) or continuation of drug in the immediate arm (IRR=0.96, $p = 0.56$).

The Kenya intermittent PrEP study reported slight changes in number of sexual partners over time but did not assess statistical significance.

Figure 1: Disposition of citations during the search and screening process

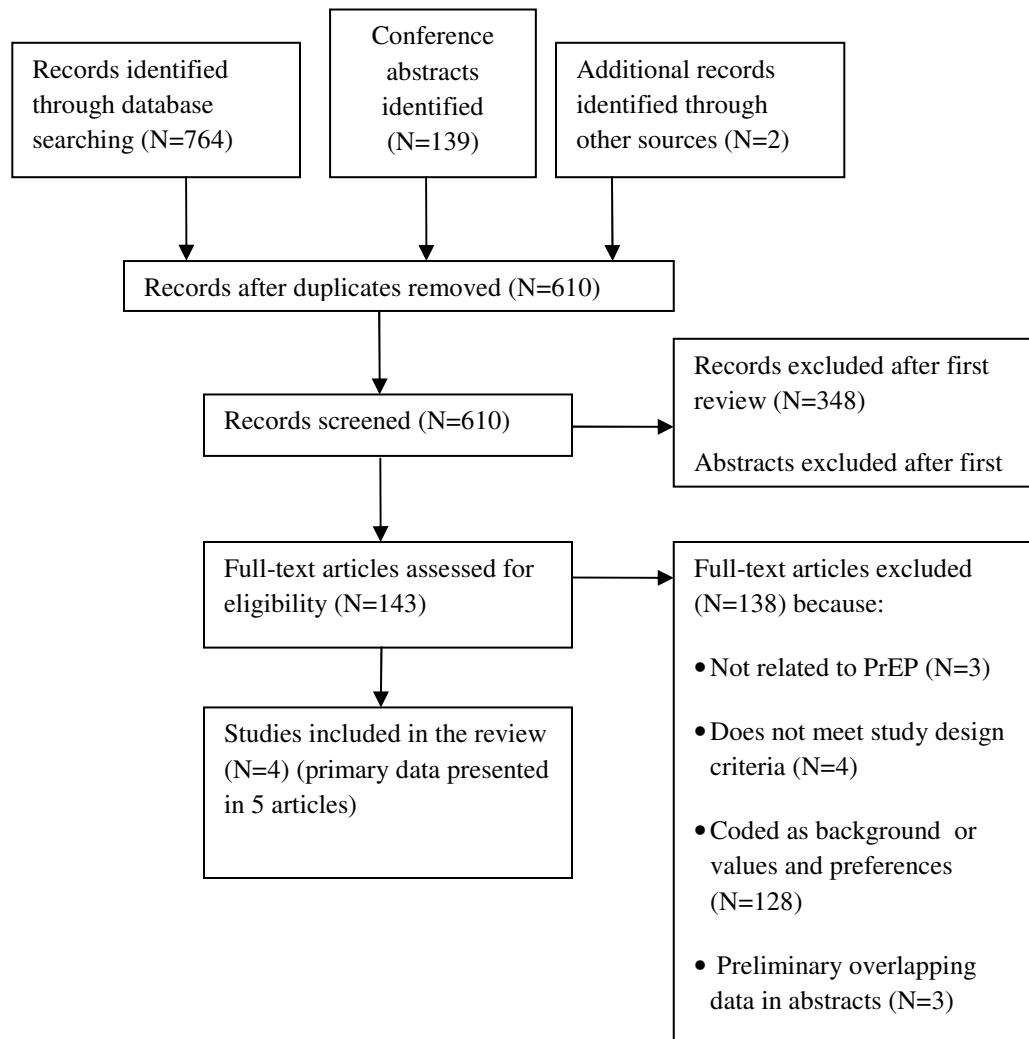


Table 1: Risk-benefit table

Factor	Explanation / Evidence
Quality of Evidence	One multi-country RCT without serious limitations. All study outcomes rated as “high quality” in GRADE. Additional data from 3 smaller studies.
Balance of Benefits vs. Harms	<p><i>HIV infection</i> In iPrEx, oral PrEP was associated with reduced risk of HIV in both intention-to-treat analysis (HR: 0.53, 95% CI 0.36-0.78, p=0.001) and modified intention-to-treat analysis (HR: 0.56, 95% CI 0.37-0.85, p=0.005). Other studies were not powered for this outcome, but the CDC safety study found 7 incident infections (0 PrEP, 3 placebo, 3 delayed, 1 placebo who was HIV+ at 1-month visit). Project PrEPare had 0 incident infections, and the Kenya intermittent PrEP study had 1 incident infection in the placebo group.</p> <p><i>Adverse events</i> In iPrEx, there was no significant difference in reported adverse events between the FTC-TDF and control arms for either any adverse event (RR: 0.99, 95% CI 0.94-1.04) or grade 3 and 4 adverse events (RR: 0.92, 95% CI 0.75-1.13). Analyses from additional studies show no major differences in adverse events or grade 3 or 4 adverse events across treatment and control groups.</p> <p><i>Condom use</i> In iPrEx, both the FTC-TDF and control study arms reported increased condom use from baseline to follow-up over the course of the study; there was no significant difference in condom use rates between study arms over time (p=0.36). Both the CDC safety study and Project PrEPare found decreased unprotected sex over time, and no significant differences across study arms.</p> <p><i>Number of sexual partners</i> In iPrEx, both the FTC-TDF and control study arms reported reduced number of receptive sexual intercourse partners from baseline to follow-up over the course of the study; there was no significant difference in the reported number of sexual partners between study arms over time (p=0.97). The CDC safety study found decreased numbers of sexual partners over time, and no significant differences across study arms.</p>
Values and Preferences	Despite a proliferation of relevant literature, reported values and preferences of PrEP use among MSM have remained relatively consistent when compared with results from a previous systematic review conducted in 2011 (see page 13). Awareness of PrEP among MSM continues to be limited globally, although several studies suggest awareness has increased since the release of the iPrEx results. Willingness to use PrEP varies widely across studies, with some reporting high interest, others reporting low acceptance, and the majority of studies reporting willingness to use PrEP between 40-70%. Main barriers and facilitators to PrEP use include effectiveness, side-effects, and cost. Concerns about accessibility, mistrust of healthcare providers, stigma, and risk compensation were also mentioned. Few studies reported on preferred PrEP dosing, administration, and dispensing sites. All studies measuring potential risk compensation found evidence that at least some participants anticipated changing their sexual behavior as a result of PrEP.

	<p>Providers generally expressed awareness and support of PrEP, although fewer had prescribed it. Providers' concerns included drug resistance, risk compensation, availability of ART (in Peru), poor adherence, lack of local guidelines, and concern that PrEP doesn't fit well in current (US) models of care that do not include frequent, regular clinic visits.</p>
Resource Use	<p>Cost-effectiveness studies of PrEP among MSM were located mostly in the US, but also Australia and Peru. Cost-effectiveness estimates varied widely depending on model parameter estimates, including efficacy of PrEP, cost of PrEP, HIV incidence and age of the target population, the impact of PrEP on risk compensation and community-level outcomes, and program prioritization and roll-out.</p> <p>In the US and Australia, results range from multiple estimates of PrEP being cost-saving to multiple estimates of PrEP costing over US\$300,000 per QALY saved. In Peru, PrEP could be a cost-effective addition to current MSM prevention programs at US\$1,702-\$2755 per DALY saved, below the WHO recommended threshold for cost-effective interventions for the region.</p> <p>In concentrated epidemics in the US, authors of post-iPrEX studies agreed that PrEP use among MSM could have a significant impact on the domestic HIV epidemic.</p>
Feasibility	<p>Oral PrEP for MSM has proven feasible in various trial settings and acceptability studies (including among young MSM). Issues of criminalization, stigma and discrimination, and violence should be considered during implementation, especially where MSM behavior is illegal.</p>

Values and preferences review of the literature

Description of studies

Since 2011 the number of studies describing values and preferences of PrEP use among men who have sex with men (MSM) has increased dramatically. Our systematic review identified 36 peer-reviewed articles and 17 conference abstracts/presentations that reported on values and preferences of PrEP use among MSM, plus an additional 6 articles and 1 conference abstract that reported on perceptions of health care providers.

For values and preferences among MSM, study locations included the United States,¹⁻²⁶ China,²⁷⁻³¹ Thailand,³²⁻³⁵ Peru,³⁶⁻³⁸ France,^{39,40} United Kingdom,^{41,42} Australia,^{43,44} Kenya,^{45,46} Canada,⁴⁷ and Germany.⁴⁸ Two studies were conducted regionally, one in North America⁴⁹ and the other in Latin America (including Spain and Portugal),⁵⁰ and three studies were conducted across multiple settings globally.⁵¹⁻⁵³

Across studies the majority of participants were MSM with HIV-negative or unknown serostatus. Several studies also included HIV-positive MSM,^{25,40,43} MSM in serodiscordant relationships,^{3,14,16,30,51} and a minority of non-MSM groups.^{20,47} Nine studies specified the inclusion of transgender individuals in addition to MSM.^{6,8,9,23,33,35-37} Other studies included key populations in addition to MSM, including female sex workers,^{30,45,46,51} injection drug users, and serodiscordant couples.⁵¹ In most studies, participants were PrEP naïve, but some included participants from the iPrEx trial,^{7,15,33} other PrEP trials based in Kenya⁴⁵ and the US,¹⁵ and an HIV vaccine trial.⁵ One study focused on young MSM aged 16-20 years.¹²

PrEP awareness

Knowledge of PrEP has increased since the release of the iPrEx study results but remains limited. Studies from the US that surveyed MSM both pre- and post-release of iPrEx results found increases in PrEP knowledge from 21% to 28% in Denver,¹ 11% to 19% in Boston,¹⁹ and 12.7% to 18.6% in a nationally-based survey.²²

In one global survey of over 5,000 MSM, 60% reported no knowledge of PrEP.⁵³ An Internet-based survey conducted in Latin America, Spain, and Portugal found 11% awareness of PrEP among 36,477 MSM surveyed.⁵⁰ A global study of 2197 MSM found less awareness but more PrEP acceptability in the Global South as compared to the Global North.⁵² PrEP awareness was higher among certain populations. For example, in a sample of 593 HIV-positive MSM in France, 41.8% reported awareness of PrEP and 29.5% had had discussions about PrEP.⁴⁰ Among a sample of serodiscordant couples in the United States, 62% reported having heard of PrEP, but a quarter of participants confused PrEP with PEP.¹⁴

Willingness to use PrEP

Reported willingness to use PrEP was generally high but measurement of PrEP acceptance and/or willingness varied greatly across studies, thus making comparison difficult. The highest rate of willingness to use PrEP was found in a US-based study of MSM in serodiscordant relationships with 94% reporting willingness to use PrEP if available.¹⁶ However, qualitative results from another study among serodiscordant couples found ambivalence and low support for PrEP.¹⁴ A study among 650 MSM in China reported 91.9% of participants would accept PrEP if it was safe, effective, and free.²⁸ More commonly, studies reported a range of willingness to use, acceptance of, or interest in PrEP among 40-70% of those surveyed across a variety of settings.^{1, 2, 10, 21, 29, 30, 38, 41, 47, 50, 51} Willingness to use PrEP was low in several studies. One study from Australia found the majority of participants were unwilling to use PrEP,⁴⁴ and another study from Thailand found only a third of MSM surveyed were interested in PrEP after being read a statement explaining results from the iPrEx study.³²

Among studies comparing acceptability of PrEP before and after the release of the iPrEx results, willingness to use PrEP did not change significantly following the release of results. For example, one study from the US found 66% willingness to use PrEP, assuming no side effects, before the release of iPrEx results and 62% after the release.¹ Another study found high interest in PrEP both before (75%) and after (79%) the release of iPrEx results.¹⁹ A nationally-based survey from the US found that 78.4% and 76.9% of MSM reported being likely to use PrEP before and after the release of iPrEx results, respectively.²²

Barriers and facilitators to PrEP

Commonly mentioned factors affecting willingness to use PrEP included effectiveness, side-effects, and cost. One study found that PrEP acceptability declined as hypothetical effectiveness decreased and potential side-effects increased.¹ Another study found that willingness to use daily PrEP fell once monthly HIV testing and a \$60 co-pay per visit to receive PrEP were added as stipulations.²³ Among young MSM surveyed in Chicago, interest in PrEP was higher if dosing and side-effects were not inconvenient and perceived benefits were high.¹² A qualitative study among a sample of female sex workers, MSM, and transgender individuals in Peru found that cost and side-effects were the largest factors in PrEP acceptability.³⁶ Among a sample of 40 MSM who reported using club drugs in the US, 80% reported that their willingness to use and adhere to PrEP would decrease if the cost of PrEP limited their ability to afford their current lifestyle, including substance use and going out to meet men.²¹ Among MSM in Thailand, factors of PrEP acceptability included having private insurance, a lifetime history of sexually transmitted infections, previous HIV testing, regularly planned sex, and infrequent sex.³⁵

Other barriers to PrEP use included long-term effects on health, limited accessibility, stigma associated with taking HIV-related medicine, medical monitoring, burden of daily regimen, site of PrEP dispensing, risk compensation, and response of peers.^{3, 20} Among a study of MSM and

transgender individuals in California, lack of community awareness and confusion about PrEP were also mentioned as barriers.⁶ PrEP associated stigma, discrimination, and mistrust of healthcare providers were cited as barriers to PrEP in a study including MSM, transgender individuals, and female sex workers in Peru.³⁶ One study among high-risk substance-using MSM in Boston found that concerns about using PrEP differed with type of sexual partner. Primary partners were seen as sources of support for PrEP whereas discussing PrEP with casual partners was seen as unnecessary, in part due to HIV-related stigma and substance use.¹¹ One US-based study found that reasons for interest in PrEP differed between white and black participants, suggesting a need for targeted PrEP messaging.²⁴

Regarding adherence, participants reported client-centered counseling, receiving daily reminders, and individualized routines as important factors.^{7, 15, 17} Among studies with iPrEx trial participants in the US and Thailand, participants reported factors facilitating adherence were receiving quality health care as part of the trial, including non-judgmental medical staff and counseling.^{7, 33} Barriers to adherence included changes in routine, side-effects, and stress among US participants,⁷ and for Thai participants contextual factors surrounding PrEP, such as social life, conflicts with partners, being mistakenly identified as HIV-positive, and unintentional disclosure of sexual identity negatively affected adherence.³³ Among a US-based sample of PrEP naïve and PrEP experienced MSM, barriers to adherence included mental health issues, stigma, and relationships with healthcare providers.¹⁵

PrEP dosing, route of administration, and dispensing site

Several studies reported on participants' preference for the dosing and administration of PrEP. In one study among MSM in Boston, 90% of participants preferred daily PrEP over intermittent options.²¹ In the UK, 80.2% of respondents reported they would prefer daily PrEP while 19.8% preferred coital dosing.⁴² In Thailand, daily oral PrEP or a long-lasting injection were the preferred routes.³⁴ However, female sex workers and MSM involved in a PrEP trial in Kenya favored intermittent dosing, but noted challenges with intermittent use, particularly with post-coital dosing.⁴⁵ A study from Germany found that 55.6% of participants would use PrEP only as-needed while 19.5% would use it daily.⁴⁸

Three studies based in Peru, Kenya, and the US reporting on PrEP dispensing sites found that participants preferred obtaining PrEP from health care providers.^{22, 36, 46} In the US-based study, 40.9% of participants preferred obtaining PrEP from primary healthcare providers, followed by other healthcare settings and the internet.²² In Peru participants preferred health centers as opposed to pharmacies,³⁶ and in Kenya participants preferred obtaining PrEP from existing health centers followed by HIV/family planning centers.⁴⁶ A multi-site study found that the PrEP dispensing site was an important attribute of PrEP for MSM in South Africa.⁵¹

Risk compensation

All studies measuring potential risk compensation found varying degrees of hypothetical behavior changes related to PrEP use. A US-based Internet survey of 1155 MSM found that 75% anticipated no change to their condom use while on PrEP, even though 21% perceived themselves at less risk of HIV infection from unprotected insertive anal sex and 39% from receptive anal sex while on PrEP.²⁶ Another US-based study found that over 80% of respondents said their condom use would not decline during anal sex while taking PrEP both before and after the release of the iPrEx results.²² A study involving 121 MSM in the UK found that 67.2% would not change condom use while on PrEP and 87.3% would not have more sexual partners.⁴² Other studies reported participants would significantly reduce condom use as a result of using PrEP. For example, a US-based study among 180 MSM in New York City found that 35% would decrease condom use while on PrEP.⁹ A study from China also found that 35% of respondents were less likely to use condoms while taking PrEP.³¹ In a study among MSM in serodiscordant relationships, 26% said they were more likely to have unprotected sex with an HIV-infected partner while taking PrEP, and 27% said it would be difficult to take daily PrEP and consistently use condoms.¹⁶ A study of 329 MSM from Germany found that 44.7% would neglect condom use while on PrEP but that quality of life on PrEP was expected to increase among 83.6% of participants.⁴⁸

Health care provider perspectives

Six additional peer-reviewed articles and one conference abstract examined health care provider perspectives on PrEP for MSM. Most studies were conducted in the US and Canada, though one was conducted in Peru and one was conducted in Kenya.

In the US and Canada, several surveys have shown that most providers have heard of PrEP (69%-90%) and support PrEP, but fewer (9-19%) had actually prescribed it.⁵⁴⁻⁵⁶ PrEP prescribing practices were variable and clinicians reported many barriers to its real-world provision.⁵⁵ Greatest concerns about prescribing PrEP included antiretroviral resistance (32%), risk compensation (22%) and poor adherence (21%).⁵⁴ In qualitative interviews conducted in 2011, US providers believed that current models of care (which do not involve routine, frequent office visits) were not well suited for prescribing PrEP, highlighted the need to build capacity, and were concerned about monitoring side effects and adherence.⁵⁷ Finally, one study found that US medical students' racial stereotypes about sexual risk compensation impacted willingness to prescribe PrEP to Black vs. White MSM.⁵⁸

In Peru, a survey of 186 health care providers found that 57.5% were aware of PrEP while 44.6% said they would be likely to prescribe it now.⁵⁹ Lack of local guidelines, concern about risk compensation, antiretroviral drug resistance, and limited availability of antiretroviral treatment (ART) for HIV-infected individuals were the most common barriers to prescribing PrEP. Likelihood of prescribing was higher if PrEP were supported by local guidelines (70.3%), if

more trials supported its effectiveness (68.5%), and if intermittent use were effective (62.2%).⁵⁹ In Kenya, a qualitative study of 16 providers identified training needs for dealing with MSM clients around topics like PrEP.⁶⁰

Conclusion

Despite a proliferation of relevant literature, reported values and preferences of PrEP use among MSM have remained relatively consistent when compared with results from a previous systematic review conducted in 2011. Awareness of PrEP among MSM populations continues to be limited globally, although several studies suggest awareness has increased since the release of the iPrEx results. Willingness to use PrEP varies widely across studies, with some reporting high interest, others reporting low acceptance, and the majority of studies reporting willingness to use PrEP between 40-70%. Main barriers and facilitators to PrEP use include effectiveness, side-effects, and cost. Concerns about accessibility, mistrust of healthcare providers, stigma, and risk compensation were also mentioned. Few studies reported on preferred PrEP dosing, administration, and dispensing sites. All studies measuring potential risk compensation found evidence that at least some participants anticipated changing their sexual behavior as a result of PrEP. Providers generally expressed awareness and support of PrEP, although fewer had prescribed it. Providers' concerns included drug resistance, risk compensation, availability of ART (in Peru), poor adherence, lack of local guidelines, and concern that PrEP doesn't fit well in current (US) models of care that do not include frequent, regular clinic visits.

Annexes

Annex 1: GRADE table

Author(s): Caitlin Kennedy, Virginia Tedrow

Date: 2014-04-06

Question: Should oral PrEP (containing tenofovir (TDF)) be used in men who have sex with men (MSM)?

Settings: Lima and Iquitos, Peru; Guayaquil, Ecuador; Cape Town, South Africa; Rio de Janeiro and Sao Paulo, Brazil; Chiang Mai, Thailand; Boston and San Francisco, USA

Bibliography: Grant, R. M., Lama, J. R., Anderson, P. L., McMahan, V., Liu, A. Y., Vargas, L., et al. (2010). Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *NEJM*, 363, (27), 2587-99. Hosek, S., Siberry, G., Bell, M., Lally, M., Kapogiannis, B., Green, K., Fernandez, M.I., Rutledge, B., Martinez, J., Garofalo, R., Wilson, C.M.; Adolescent Trials Network for HIV/AIDS Interventions (ATN). (2012). The acceptability and feasibility of an HIV Pre-Exposure prophylaxis (PrEP) trial with young men who have sex with men (YMSM). *JAIDS*, 64, (4), 447-56.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral PrEP (containing tenofovir (TDF))	Control	Relative (95% CI)	Absolute		
HIV infection (follow-up median 1.2 years; assessed with: intention to treat analysis)												
2 ^{1,2}	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	38/1280 (3%)	72/1277 (5.6%)	HR 0.53 (0.36 to 0.78) ³	27 fewer per 1000 (from 12 fewer to 37 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
HIV infection (follow-up median 1.2 years; assessed with: modified intention to treat analysis)												
1 ¹	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	36/1251 (2.9%)	64/1248 (5.1%)	HR 0.56 (0.37 to 0.85)	22 fewer per 1000 (from 8 fewer to 32 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Any adverse events (follow-up median 1.2 years)												
1 ¹	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	867/1251 (69.3%)	877/1248 (70.3%)	RR 0.99 (0.94 to 1.04)	7 fewer per 1000 (from 42 fewer to 28 more)	⊕⊕⊕⊕ HIGH	IMPORTANT
Any grade 3 or 4 adverse events (follow-up median 1.2 years)												
1 ¹	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	151/1251 (12.1%)	164/1248 (13.1%)	RR 0.92 (0.75 to 1.13)	11 fewer per 1000 (from 33 fewer to 17 more)	⊕⊕⊕⊕ HIGH	IMPORTANT

PrEP for MSM - systematic review – to inform the WHO Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations

										more)		
Condom use (percent of receptive anal partners with which condoms were used) (follow-up median 1.2 years)												
1 ¹	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	1251 ⁴	1248 ⁴	p=0.36 ⁵	-	⊕⊕⊕⊕ HIGH	IMPORTANT
Number of sexual partners (mean number of anal receptive partners) (follow-up median 1.2 years)												
1 ¹	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	1251 ⁴	1248 ⁴	P=0.97 ⁶	-	⊕⊕⊕⊕ HIGH	IMPORTANT

¹ Grant et al. 2010 – iPrEx study

² Hosek et al., 2012 – Project PrEPare

³ Hazard Ratio from Grant et al. 2010

⁴ Total baseline sample size

⁵ This was a comparison between the two study arms of the percent of partners using condoms during receptive anal intercourse. The results were calculated by fitting a linear mixed regression model with a random intercept and fixed effects for treatment visit and treatment by visit interaction. The p-value is from a Wald test of the treatment by visit interaction which corresponds to whether or not there is a difference during the study period between the arms in the percent of partners using condoms during receptive anal intercourse.

⁶ This was a comparison between the two study arms of the total number of sexual partners reported. Results were calculated by fitting a linear mixed regression model with a random intercept and fixed effects for treatment visit and treatment by visit interaction. The p-value is from a Wald test of the treatment by visit interaction which corresponds to whether or not there is a difference during the study period between the arms in the number of sexual partners (total male partners at over a 12 week recall period with whom the participant had oral or anal sex).

Annex 2. Annotated bibliography

New Primary Studies - Efficacy (n= 2 studies, 3 articles)

1. **Grohskopf, L. A., et al. (2013). "Randomized trial of clinical safety of daily oral tenofovir disoproxil fumarate among HIV-uninfected men who have sex with men in the United States." J Acquir Immune Defic Syndr 64(1): 79-86.**

OBJECTIVES: To evaluate the clinical safety of daily tenofovir disoproxil fumarate (TDF) among HIV-negative men who have sex with men. **DESIGN:** Randomized, double-blind, placebo-controlled trial. Participants were randomized 1:1:1:1 to immediate or delayed study drug (TDF, 300 mg orally per day, or placebo). **METHODS:** Four hundred healthy HIV-uninfected men who have sex with men reporting anal sex with another man within the previous 12 months enrolled in Atlanta, Boston, and San Francisco. HIV serostatus, clinical and laboratory adverse events (AEs), adherence (pill count, Medication Event Monitoring System, and self-report), and sexual and other sociobehavioral data were assessed at 3-month intervals for 24 months. Primary outcomes were clinical safety, assessed by incidence of AEs and laboratory abnormalities. **RESULTS:** Study drug was initiated by 373 (93%) participants (186 TDF and 187 placebo), of whom 325 (87%) completed the final study visit. Of 2428 AEs reported among 334 (90%) participants, 2366 (97%) were mild or moderate in severity. Frequencies of commonly reported AEs did not differ significantly between TDF and placebo arms. In multivariable analyses, back pain was more likely among TDF recipients ($P = 0.04$); these reports were not associated with documented fractures or other objective findings. There were no grade ≥ 3 creatinine elevations; grades 1 and 2 creatinine increases were not associated with TDF receipt. Estimated percentage of study drug doses taken was 92% by pill count and 77% by Medication Event Monitoring System. Seven seroconversions occurred: 4 on placebo and 3 among delayed arm participants not yet on study drug. **CONCLUSIONS:** Daily oral TDF was well tolerated, with reasonable adherence. No significant renal concerns were identified.

2. **Liu, A. Y., et al. (2013). "Sexual risk behavior among HIV-uninfected men who have sex with men participating in a tenofovir preexposure prophylaxis randomized trial in the United States." J Acquir Immune Defic Syndr 64(1): 87-94.**

OBJECTIVE: To evaluate for changes in sexual behaviors associated with daily pill use among men who have sex with men (MSM) participating in a preexposure prophylaxis trial. **DESIGN:** Randomized, double-blind, placebo-controlled trial. Participants were randomized 1:1:1:1 to receive tenofovir disoproxil fumarate or placebo at enrollment or after a 9-month delay and followed for 24 months. **METHODS:** Four hundred HIV-negative MSM reporting anal sex with a man in the past 12 months and meeting other eligibility criteria enrolled in San Francisco, Atlanta, and Boston. Sexual risk was assessed at baseline and quarterly visits using Audio Computer-Assisted Self-Interview. The association of pill taking with sexual behavior was evaluated using logistic and negative-binomial regressions for repeated measures. **RESULTS:** Overall indices of behavioral risk declined or remained stable during follow-up. Mean number of partners

and proportion reporting unprotected anal sex declined during follow-up ($P < 0.05$), and mean unprotected anal sex episodes remained stable. During the initial 9 months, changes in risk practices were similar in the group that began pills immediately vs. those in the delayed arm. These indices of risk did not differ significantly after initiation of pill use in the delayed arm or continuation of study medication in the immediate arm. Use of poppers, amphetamines, and sexual performance-enhancing drugs were independently associated with one or more indices of sexual risk. **CONCLUSIONS:** There was no evidence of risk compensation among HIV-uninfected MSM in this clinical trial. Monitoring for risk compensation should continue now that preexposure prophylaxis has been shown to be efficacious in MSM and other populations and will be provided in open-label trials and other contexts.

3. Hosek, S., et al. (2012). "The acceptability and feasibility of an HIV Pre-Exposure prophylaxis (PrEP) trial with young men who have sex with men (YMSM)." Journal of Acquired Immune Deficiency Syndromes.

BACKGROUND: This study examined the feasibility of a combination prevention intervention for young men who have sex with men (YMSM), an anticipated target population for HIV pre-exposure prophylaxis (PrEP). **METHODS:** Project PrEPare, a pilot study using a randomized 3-arm design, compared an efficacious behavioral HIV-prevention intervention (3MV) alone, 3MV combined with PrEP (tenofovir/emtricitabine), and 3MV combined with placebo. Eligible participants were 18-22 year old HIV-uninfected men who reported unprotected anal intercourse (UAI) in the past year. Participants were screened for preliminary eligibility at youth venues and community organizations, and were also referred through social networks. Laboratory screening determined final eligibility. Behavioral and biomedical data were collected at baseline and every 4 weeks thereafter for 24 weeks. **RESULTS:** Sixty-eight youth (mean age = 19.97 years; 53% African-American, 40% Latino) were enrolled; 58 were randomized. Self-reported medication adherence averaged 62% (range 43-83%) while rates of detectable tenofovir in plasma of participants in the FTC/TDF arm ranged from 63.2% (week 4) to 20% (week 24). There were 5 (greater-than or equal to) Grade 2 adverse events possibly/probably related to the study medication. Sexual risk behavior declined from baseline to week 24 in all study arms. **CONCLUSIONS:** The feasibility of enrolling at risk youth, particularly YMSM of color, into Project PrEPare has been demonstrated. The acceptability of the group intervention along with counseling and testing was high. Self-reported medication adherence and corresponding plasma drug concentrations were low indicating the need for enhanced adherence counseling. Exploration of PrEP use among youth in non-randomized, open label trials is warranted.

New Primary Studies - Values and Preferences (n=36 articles and 17 conference abstracts/presentations)

1. Aghaizu, A., et al. (2013). "Who would use PrEP? Factors associated with intention to use among MSM in London: a community survey." **Sex Transm Infect** 89(3): 207-211.

OBJECTIVE: To assess current and intended future use of pre-exposure prophylaxis (PrEP) among men who have sex with men (MSM) and characterise those attending sexual health clinics, the anticipated PrEP delivery setting. DESIGN: Cross-sectional study. METHODS: Self-administered survey of 842 HIV negative MSM recruited from social venues in London in 2011. RESULTS: One in 10 (10.2%, 83/814, 95% CI 8.2% to 12.5%) and one in 50 (2.1%, 17/809, 95% CI 1.2% to 3.3%) reported having ever used post-exposure prophylaxis (PEP) and PrEP respectively. Half reported they would be likely to use PrEP if it became available as a daily pill (50.3%, 386/786, 95% CI 46.7% to 53.9%). MSM were more likely to consider future PrEP use if they were <35 years (adjusted OR (AOR) 1.57, 95% CI 1.16 to 2.14), had unprotected anal intercourse with casual partners (AOR 1.70, 95% CI 1.13 to 2.56), and had previously used PEP (AOR 1.94, 95% CI 1.17 to 3.24). Over half of MSM (54.8% 457/834 95% CI 51.3 to 58.2) attended a sexual health clinic the previous year. Independent factors associated with attendance were age <35 (AOR 2.29, 95% CI 1.68 to 3.13), and ≥ 10 anal sex partners in the last year (AOR 2.49, 95% CI 1.77 to 3.52). CONCLUSIONS: The concept of PrEP for HIV prevention in the form of a daily pill is acceptable to half of sexually active MSM in London. MSM reporting higher risk behaviours attend sexual health clinics suggesting this is a suitable setting for PrEP delivery.

2. Al-Tayyib, A. A., et al. (2013). "Knowledge of Pre-exposure Prophylaxis (PrEP) for HIV Prevention Among Men Who Have Sex with Men in Denver, Colorado." **AIDS Behav.**

As part of the National HIV Behavioral Surveillance System among men who have sex with men (MSM) in Denver, Colorado, we assessed knowledge of pre-exposure prophylaxis (PrEP); willingness to use PrEP; and potential changes in risk behaviors among HIV-negative participants reporting sexual activity with a male partner in the preceding 12 months. We examined knowledge of PrEP before (2008) and after (2011) results of the iPrEx trial were available. Of the 425 participants in the 2008 sample, 91 (21 %) were aware of PrEP compared to 131 (28 %) of the 461 participants in the 2011 sample (adjusted prevalence ratio: 1.43, 95 % confidence interval: 1.18, 1.72). Despite the increase in 2011, few MSM in Denver were aware of PrEP. Educating high-risk MSM about the potential utility of PrEP as an adjunct to other effective prevention methods is needed when considering the addition of PrEP to the HIV prevention arsenal.

- 3. Barash, E. A., et al. (2010). "Awareness and use of HIV pre-exposure prophylaxis among attendees of a Seattle gay pride event and sexually transmitted disease clinic." AIDS Patient Care STDs. 24(11):689-91**

We surveyed a convenience sample of 215 HIV-negative men who have sex with men (MSM) recruited at a Gay Pride event and in an STD clinic about their willingness to use pre-exposure prophylaxis (PrEP). Overall, 44% reported that they would take PrEP every day if it helped prevent HIV. There was no association between sexual risk behavior and interest in taking PrEP.

- 4. Brooks, R. A., et al. (2012). "Sexual risk behaviors and acceptability of HIV pre-exposure prophylaxis among HIV-negative gay and bisexual men in serodiscordant relationships: a mixed methods study." AIDS Patient Care STDs. 26(2):87-94**

The objective of this mixed methods study was to examine current sexual risk behaviors, acceptability and potential adoption of pre-exposure prophylaxis (PrEP) for HIV prevention, and sexual behavior intentions with PrEP adoption among HIV-negative gay and bisexual men (GBM) in HIV serodiscordant relationships. A multiracial/ethnic sample of 25 HIV-negative GBM in serodiscordant relationships completed a qualitative interview and a brief interviewer-administered survey. A modified grounded theory approach was used to identify key themes relating to acceptability and future adoption of PrEP. Participants reported engaging in sexual risk behaviors that place them at risk for HIV infection. Participants also reported a high level of acceptability for PrEP and willingness to adopt PrEP for HIV prevention. Qualitative themes explaining future PrEP adoption included: (1) the opportunity to engage in sex using a noncondom HIV prevention method, (2) protection from HIV infection, and (3) less anxiety when engaging in sex with an HIV-positive partner. Associated with the future adoption of PrEP, a majority (64%) of participants indicated the likelihood for an increase in sexual risk behaviors and a majority (60%) of participants also indicated the likelihood for a decrease or abandonment of condom use, both of which are in contrast to the findings from the large iPrEx study. These findings suggest that the use of PrEP by HIV-negative GBM in serodiscordant relationships carries with it the potential for risk compensation. The findings suggest that PrEP only be offered as part of a comprehensive HIV prevention strategy that includes ongoing risk reduction counseling in the delivery of PrEP to help moderate risk compensation.

- 5. Brooks, R. A., et al. (2011). "Motivators, concerns, and barriers to adoption of preexposure prophylaxis for HIV prevention among gay and bisexual men in HIV-serodiscordant male relationships." AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV 23(9): 1136-1145.**

The purpose of this study was to identify factors that may facilitate or impede future adoption of preexposure prophylaxis (PrEP) for HIV prevention among gay and bisexual

men in HIV-serodiscordant relationships. This qualitative study utilized semistructured interviews conducted with a multiracial/-ethnic sample of 25 gay and bisexual HIV-serodiscordant male couples (n=50 individuals) recruited from community settings in Los Angeles, CA. A modified grounded theory approach was employed to identify major themes relating to future adoption of PrEP for HIV prevention. Motivators for adoption included protection against HIV infection, less concern and fear regarding HIV transmission, the opportunity to engage in unprotected sex, and endorsements of PrEP's effectiveness. Concerns and barriers to adoption included the cost of PrEP, short- and long-term side effects, adverse effects of intermittent use or discontinuing PrEP, and accessibility of PrEP. The findings suggest the need for a carefully planned implementation program along with educational and counseling interventions in the dissemination of an effective PrEP agent. (copyright) 2011 Taylor & Francis.

6. Eisingerich, A. B., et al. (2012). "Attitudes and acceptance of oral and parenteral HIV preexposure prophylaxis among potential user groups: a multinational study." PLoS One 7(1): e28238.

BACKGROUND: The use of antiviral medications by HIV negative people to prevent acquisition of HIV or pre-exposure prophylaxis (PrEP) has shown promising results in recent trials. To understand the potential impact of PrEP for HIV prevention, in addition to efficacy data, we need to understand both the acceptability of PrEP among members of potential user groups and the factors likely to determine uptake. **METHODS AND FINDINGS:** Surveys of willingness to use PrEP products were conducted with 1,790 members of potential user groups (FSWs, MSM, IDUs, SDCs and young women) in seven countries: Peru, Ukraine, India, Kenya, Botswana, Uganda and South Africa. Analyses of variance were used to assess levels of acceptance across different user groups and countries. Conjoint analysis was used to examine the attitudes and preferences towards hypothetical and known attributes of PrEP programs and medications. Overall, members of potential user groups were willing to consider taking PrEP (61% reported that they would definitely use PrEP). Current results demonstrate that key user groups in different countries perceived PrEP as giving them new possibilities in their lives and would consider using it as soon as it becomes available. These results were maintained when subjects were reminded of potential side effects, the need to combine condom use with PrEP, and for regular HIV testing. Across populations, route of administration was considered the most important attribute of the presented alternatives. **CONCLUSIONS:** Despite multiple conceivable barriers, there was a general willingness to adopt PrEP in key populations, which suggests that if efficacious and affordable, it could be a useful tool in HIV prevention. There would be a willingness to experience inconvenience and expense at the levels included in the survey. The results suggest that delivery in a long lasting injection would be a good target in drug development.

7. **Fuchs, J. D., et al. (2013). "Intentions to use preexposure prophylaxis among current phase 2B preventive HIV-1 vaccine efficacy trial participants." J Acquir Immune Defic Syndr 63(3): 259-262.**

In November 2010, the iPrEx study reported that preexposure prophylaxis (PrEP) with daily tenofovir disoproxil fumarate/emtricitabine reduced HIV infections by 44% among men who have sex with men and subsequent trials corroborated efficacy among heterosexual men and women. During regularly scheduled follow-up visits from January to March 2011, participants in an ongoing phase 2b vaccine efficacy trial completed an anonymous Web survey about PrEP. Among 376 respondents, 17% reported they were very likely to use PrEP in the next year. Nonwhite participants were more likely to use PrEP. Among those with some level of interest, intent to use PrEP was greatest if the drug were available through the clinical trial or health insurance. Most (91%) believed taking PrEP would not change their willingness to stay in the vaccine trial and few thought it would affect recruitment. As key stakeholders, currently enrolled trial participants can offer vital input about emerging prevention technologies that may affect the design of future HIV vaccine and nonvaccine prevention trials.

8. **Galea, J. T., et al. (2011). "Acceptability of pre-exposure prophylaxis as an HIV prevention strategy: barriers and facilitators to pre-exposure prophylaxis uptake among at-risk Peruvian populations." Int J STD AIDS 22(5): 256-262.**

This study examined pre-exposure prophylaxis (PrEP) acceptability among female sex workers, male-to-female transgendered persons and men who have sex with men in Lima, Peru. Focus groups explored social issues associated with PrEP acceptability and conjoint analysis assessed preferences among eight hypothetical PrEP scenarios with varying attribute profiles and their relative impact on acceptability. Conjoint analysis revealed that PrEP acceptability ranged from 19.8 to 82.5 out of a possible score of 100 across the eight hypothetical PrEP scenarios. Out-of-pocket cost had the greatest impact on PrEP acceptability (25.2, $P < 0.001$), followed by efficacy (21.4, $P < 0.001$) and potential side-effects (14.7, $P < 0.001$). Focus group data supported these findings, and also revealed that potential sexual risk disinhibition, stigma and discrimination associated with PrEP use, and mistrust of health-care professionals were also concerns. These issues will require careful attention when planning for PrEP roll-out.

9. **Galindo, G. R., et al. (2012). "Community member perspectives from transgender women and men who have sex with men on pre-exposure prophylaxis as an HIV prevention strategy: implications for implementation." Implement Sci 7: 116.**

BACKGROUND: An international randomized clinical trial (RCT) on pre-exposure prophylaxis (PrEP) as an human immunodeficiency virus (HIV)-prevention intervention found that taken on a daily basis, PrEP was safe and effective among men who have sex with men (MSM) and male-to-female transgender women. Within the context of the HIV epidemic in the United States (US), MSM and transgender women are the most

appropriate groups to target for PrEP implementation at the population level; however, their perspectives on evidenced-based biomedical research and the results of this large trial remain virtually unknown. In this study, we examined the acceptability of individual daily use of PrEP and assessed potential barriers to community uptake. **METHODS:** We conducted semi-structured interviews with an ethnographically diverse sample of thirty HIV-negative and unknown status MSM (n = 24) and transgender women (n = 6) in three California metropolitan areas. Given the burden of disease among ethnographic minorities in the US, we purposefully oversampled for these groups. Thematic coding and analysis of data was conducted utilizing an approach rooted in grounded theory. **RESULTS:** While participants expressed general interest in PrEP availability, results demonstrate: a lack of community awareness and confusion about PrEP; reservations about PrEP utilization, even when informed of efficacious RCT results; and concerns regarding equity and the manner in which a PrEP intervention could be packaged and marketed in their communities. **CONCLUSIONS:** In order to effectively reduce HIV health disparities at the population level, PrEP implementation must take into account the uptake concerns of those groups who would actually access and use this biomedical intervention as a prevention strategy. Recommendations addressing these concerns are provided.

10. Gilmore, H. J., et al. (2013). "Participant experiences and facilitators and barriers to pill use among men who have sex with men in the iPrEx pre-exposure prophylaxis trial in San Francisco." AIDS Patient Care STDS 27(10): 560-566.

In 2010, the iPrEx study demonstrated efficacy of daily emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) pre-exposure prophylaxis (PrEP) in reducing HIV acquisition among men who have sex with men. Adherence to study product was critical for PrEP efficacy, and varied considerably, with FTC/TDF detection rates highest in the United States. We conducted a qualitative study to gain insights into the experiences of iPrEx participants in San Francisco (SF) where there was high confirmed adherence, to understand individual and contextual factors influencing study product use in this community. In 2009 and 2011, we conducted focus groups and in-depth interviews in 36 and 16 SF iPrEx participants, respectively. Qualitative analyses indicate that participants joined the study out of altruism. They had a clear understanding of study product use, and pill taking was facilitated by establishing or building on an existing routine. Participants valued healthcare provided by the study and relationships with staff, whom they perceived as nonjudgmental, and found client-centered counseling to be an important part of the PrEP package. This facilitated pill taking and accurate reporting of missed doses. Adherence barriers included changes in routine, side effects/intercurrent illnesses, and stress. Future PrEP adherence interventions should leverage existing routines and establish client-centered relationships/ environments to support pill taking and promote accurate reporting.

11. Golub, S., et al. (2012). "Psychosocial predictors of acceptability and risk compensation for pre-exposure prophylaxis (PrEP): Results from 3 studies of critical populations." Journal of the International Association of Physicians in AIDS Care 11(6): 394.

Background: Pre-exposure prophylaxis (PrEP) has the potential to become a powerful HIV prevention tool; however, many questions remain about its acceptability and impact on behavior among men who have sex with men (MSM). Brief surveys have been conducted to assess willingness to take PrEP, but almost no studies have examined psychosocial predictors of both PrEP acceptability and its potential influence on sexual risk-taking. Methods: Data were collected from 3 populations critical to the success of PrEP as a prevention strategy: a) lesbian, gay, bisexual, and transgender (LGBT) youth (aged 16-24 years) in the Ballroom scene in New York City (n = 85); b) blackidentified MSM never tested for HIV (n = 45); and c) highly sexually active MSM (median of 20 partners in the past 90 days; n = 80). Participants completed self-report surveys about PrEP knowledge, acceptability, and risk compensation. All data were collected between March and December 2011 (ie, after the release of the iPrEx results.) Results: Among youth, the most important predictor of PrEP acceptability was a desire to escape constant worry about HIV infection. On the other hand, youth expressed concern about the association of daily antiretroviral (ARV) medication use with nullbeing sick.null Among Black MSM, HIV conspiracy beliefs- especially negative beliefs about HIV medications- were the strongest predictor of resistance to PrEP. Among highly sexually active MSM, 34% reported that taking PrEP would increase their risk behavior. Risk compensation was strongest among MSM who a) make decisions about condom use based on situational risk perception (p < .001) and b) prefer unprotected sex because they consider it transgressive (p < .001). Conclusions: Findings from all 3 studies underscore the importance of social-behavioral data in the development of PrEP polices and interventions. The creation of effective PrEP messaging must acknowledge an existing sociopolitical context around HIV prevention formany MSM, which may influence the way messages are interpreted and internalized. Behavioral interventions to support PrEP use are critical, and must recognize the role of risk perception and affect in sexual decision making.

12. Golub, S. A., et al. (2013). "From efficacy to effectiveness: facilitators and barriers to PrEP acceptability and motivations for adherence among MSM and transgender women in New York City." AIDS Patient Care STDS 27(4): 248-254.

This study examined potential facilitators and barriers to pre-exposure prophylaxis (PrEP) use and their association with PrEP acceptability and motivations for adherence among 184 MSM and transgender women living in New York City. Participants were presented with educational information about PrEP and completed a computerized survey. Overall, 55.4% of participants reported willingness to take PrEP. The most highly endorsed barriers to PrEP use were health concerns, including both long-term impacts and short-term side effects, questions about PrEP's impact on future drug resistance, and concerns

that PrEP does not provide complete protection against HIV. The most highly endorsed facilitator was free access to PrEP, followed by access to support services such as regular HIV testing, sexual health care/monitoring, and access to one-on-one counseling. Participants of color rated both barriers and facilitators as more important than their White counterparts. In multivariate models, barrier and facilitator scores significantly predicted not only PrEP acceptability, but also motivation for PrEP adherence among those who were likely to use PrEP. PrEP implementation programs should consider addressing these barriers and facilitators in protocol and policy development. Findings underscore the importance of support services, such as sexual health counseling, to the success of PrEP as a prevention strategy.

13. Holt, M., et al. (2013). "HIV-negative and HIV-positive gay men's attitudes to medicines, HIV treatments and antiretroviral-based prevention." AIDS Behav 17(6): 2156-2161.

We assessed attitudes to medicines, HIV treatments and antiretroviral-based prevention in a national, online survey of 1,041 Australian gay men (88.3% HIV-negative and 11.7% HIV-positive). Multivariate analysis of variance was used to identify the effect of HIV status on attitudes. HIV-negative men disagreed with the idea that HIV drugs should be restricted to HIV-positive people. HIV-positive men agreed and HIV-negative men disagreed that taking HIV treatments was straightforward and HIV-negative men were more sceptical about whether HIV treatment or an undetectable viral load prevented HIV transmission. HIV-negative and HIV-positive men had similar attitudes to pre-exposure prophylaxis but divergent views about 'treatment as prevention'.

14. Holt, M., et al. (2012). "Willingness to use HIV pre-exposure prophylaxis and the likelihood of decreased condom use are both associated with unprotected anal intercourse and the perceived likelihood of becoming HIV positive among Australian gay and bisexual men." Sex Transm Infect. 88(4):258-63.

Objectives: To investigate willingness to use HIV preexposure prophylaxis (PrEP) and the likelihood of decreased condom use among Australian gay and bisexual men. Methods: A national, online cross-sectional survey was conducted in April to May 2011. Bivariate relationships were assessed with χ^2 or Fisher's exact test. Multivariate logistic regression analysis was performed to assess independent relationships with primary outcome variables. Results: Responses from 1161 HIV-negative and untested men were analysed. Prior use of antiretroviral drugs as PrEP was rare (n=6). Just over a quarter of the sample (n=327; 28.2%) was classified as willing to use PrEP. Willingness to use PrEP was independently associated with younger age, having anal intercourse with casual partners (protected or unprotected), having fewer concerns about PrEP and perceiving oneself to be at risk of HIV. Among men who were willing to use PrEP (n=327), only 26 men (8.0%) indicated that they would be less likely to use condoms if using PrEP. The likelihood of decreased condom use was independently associated with older age, unprotected anal intercourse with casual partners (UAIC) and perceiving oneself to be at

increased risk of HIV. Conclusions: The Australian gay and bisexual men the authors surveyed were cautiously optimistic about PrEP. The minority of men who expressed willingness to use PrEP appear to be appropriate candidates, given that they are likely to report UAIC and to perceive themselves to be at risk of HIV.

15. Jackson, T., et al. (2012). "Cognitive, psychosocial, and sociodemographic predictors of willingness to use HIV pre-exposure prophylaxis among Chinese men who have sex with men." *AIDS Behav* 16(7): 1853-1861.

This study was designed to identify predictors of lower versus higher willingness to use pre-exposure prophylaxis (PrEP) to reduce HIV among men who have sex with men (MSM) in China. Participants were 570 MSM who completed self-report measures of willingness to use HIV PrEP, beliefs about HIV, psychosocial factors, sexual experiences and sociodemographic characteristics. Results of a hierarchical binary logistic regression analysis indicated that membership in a higher willingness group was predicted by previous consultation about HIV, more reported barriers to using condoms, and elevations in depressive symptoms. Independent of these factors, higher willingness to use HIV PrEP was predicted by beliefs that the intervention was low in stigma and high in potential benefits. In sum, the study highlighted the utility of broad-based assessment of demographic, behavioral, personality, and cognitive factors in identifying Chinese MSM who express willingness to use a promising biologically-based intervention to lower HIV risk.

16. Krakower, D. S., et al. (2012). "Limited Awareness and Low Immediate Uptake of Pre-Exposure Prophylaxis among Men Who Have Sex with Men Using an Internet Social Networking Site." *PLoS One* 7(3): e33119.

BACKGROUND: In 2010, the iPrEx trial demonstrated that oral antiretroviral pre-exposure prophylaxis (PrEP) reduced the risk of HIV acquisition among high-risk men who have sex with men (MSM). The impact of iPrEx on PrEP knowledge and actual use among at-risk MSM is unknown. Online surveys were conducted to assess PrEP awareness, interest and experience among at-risk MSM before and after iPrEx, and to determine demographic and behavioral factors associated with these measures.

METHODS AND FINDINGS: Cross-sectional, national, internet-based surveys were administered to U.S. based members of the most popular American MSM social networking site 2 months before (n = 398) and 1 month after (n = 4 558) publication of iPrEx results. Comparisons were made between these samples with regards to PrEP knowledge, interest, and experience. Data were collected on demographics, sexual risk, and experience with post-exposure prophylaxis (PEP). Regression analyses were performed to identify factors associated with PrEP awareness, interest, and experience post-iPrEx. Most participants were white, educated, and indicated high-risk sexual behaviors. Awareness of PrEP was limited pre- and post-iPrEx (13% vs. 19%), whereas interest levels after being provided with a description of PrEP remained high (76% vs. 79%). PrEP use remained uncommon (0.7% vs. 0.9%). PrEP use was associated with

PEP awareness (OR 7.46; CI 1.52-36.6) and PEP experience (OR 34.2; CI 13.3-88.4). PrEP interest was associated with older age (OR 1.01; CI 1.00-1.02), unprotected anal intercourse with ≥ 1 male partner in the prior 3 months (OR 1.40; CI 1.10-1.77), and perceiving oneself at increased risk for HIV acquisition (OR 1.20; CI 1.13-1.27).

CONCLUSIONS: Among MSM engaged in online networking, awareness of PrEP was limited 1 month after the iPrEx data were released. Utilization was low, although some MSM who reported high-risk behaviors were interested in using PrEP. Studies are needed to understand barriers to PrEP utilization by at-risk MSM.

17. Leonardi, M., et al. (2011). "Awareness of, usage of and willingness to use HIV pre-exposure prophylaxis among men in downtown Toronto, Canada." Int J STD AIDS 22(12): 738-741.

Pre-exposure prophylaxis (PrEP) is a promising strategy whereby HIV-uninfected people could take antiretroviral (ARV) medications to reduce their risk of HIV acquisition. Reports suggest that unsupervised PrEP use has been occurring in gay communities of USA cities before human safety and efficacy data became available. We administered a 20-item questionnaire to men undergoing HIV testing at Hassle Free Clinic, a sexual health clinic in the gay village of Toronto. Questionnaire items enquired about demographics, sexual partners, substance use and awareness of, usage of and willingness to use PrEP. Logistic regression was used to identify characteristics associated with PrEP-related outcomes. Of 256 participants, 11.7% were aware of PrEP, with more men who have sex with men (MSM) aware (14.1%) than non-MSM (4.9%). No participants reported PrEP usage. Willingness to consider PrEP use was high and associated with high-risk activities, suggesting opportunities for PrEP use in the future.

18. Lorente, N., et al. (2012). "Acceptability of an "on-demand" pre-exposure HIV prophylaxis trial among men who have sex with men living in France." AIDS Care 24(4): 468-477.

Although predictors of willingness to take daily, self-administered pre-exposure HIV prophylaxis (PrEP) for men who have sex with men (MSM) have been studied in the context of several PrEP trials internationally, little is known about MSM interested in participating in a trial on the use of PrEP on an "on-demand" basis, i.e., taking a first dose of combined tenofovir/emtricitabine a few hours before possible HIV sexual exposure and a second dose a few hours afterwards. A double-blind placebo randomized PrEP trial will soon begin in France to evaluate the effectiveness of PrEP in terms of reducing HIV infection rates, among MSM self-administering "on-demand" PrEP. To assess potential participants' characteristics associated with willingness to participate in the trial and identify barriers and facilitators to implementation, MSM completed a self-administered questionnaire, distributed via gay venues and community websites. Among the 443 respondents who reported being HIV-negative, 40% reported being interested in participating. Factors independently associated with interest included: reporting lower educational level, more than 20 male sexual partners in the previous year, reporting

unprotected anal sex with casual partners and preferring PrEP follow-up visits in a devoted area within a hospital. There is great interest in participating in a future "on-demand" PrEP trial among HIV-negative MSM and particularly in those at potentially high risk of HIV exposure. Providing confidentiality and tailored counseling during PrEP follow-up are important issues.

19. Metsch, L., et al. (2012). "Willingness to take daily pre-exposure prophylaxis (PrEP) among MSM in two HIV epicenters in the United States." Journal of the International AIDS Society 15: 97.

Background: We examined knowledge, attitudes, and practices toward use of daily PrEP among MSM and factors associated with their willingness to take PrEP if available and offered for free or covered by health insurance. Methods: Between August-December 2011, MSM in two U.S. metropolitan areas heavily impacted by HIV (Miami, Florida and Washington, D.C.) were recruited and interviewed through venue based sampling for the CDC National HIV Behavioral Surveillance study. Multivariable logistic regression analysis assessed demographic, socioeconomic, drug use and sexual risk correlates of being very willing to take PrEP for each city. Results: The samples included 321 in Miami (median age=29;18% black, 10% white, 71% Hispanic, 1% Other) and 323 in Washington D.C. (median age=32, 28% black, 49% white, 13% Hispanic, 10% Other). Fifteen percent of men in Miami and 30% in Washington D.C. had heard information about PrEP, few knew anyone who had taken PrEP (3% in both cities), and none reported having taken it themselves. Almost half (49%) of MSM in Miami and almost two-thirds (61%) in Washington D.C. reported they would be willing to take PrEP. In Miami, only non-injection drug use in the past year was associated with decreased willingness to use PrEP (OR=.59, 95% CI (.36, .96). In Washington, D.C., >33 years of age (OR=.45, 95% CI (.28, .74) and having fewer sexual partners (OR=.57, 95% CI (.33, .98) were associated with decreased willingness to use PrEP; non-injection drug use (OR=1.67, 95% CI (1.02, 2.73) was associated with increased willingness to use PrEP. Conclusion: Awareness and use of PrEP in these two US HIV epicenters is low; innovative strategies are needed to inform and educate MSM about this new prevention strategy. Willingness to use PrEP may be impacted by drug use and sexual risk behaviors. Future studies are needed to understand how non-injection drug use may impact PrEP use.

20. Mimiaga, M. J., et al. (2014). "Sexual Partnerships and Considerations for HIV Antiretroviral Pre-Exposure Prophylaxis Utilization Among High-Risk Substance Using Men Who Have Sex with Men." Arch Sex Behav 43(1): 99-106.

Men who have sex with men (MSM) remain at great risk of HIV in the United States, representing 65 % of incident HIV infections. One factor contributing to the high rate of HIV infection among MSM is use of "recreational" drugs that are highly associated with unprotected anal sex. Pre-exposure chemoprophylaxis (PrEP) is a novel biomedical HIV prevention strategy that has the potential to reduce HIV transmission in MSM. Main and casual sex partners play a role in HIV prevention efforts for MSM. The study aimed to

qualitatively explore the perceived influences of sexual relationships on promoting and inhibiting PrEP use among high-risk MSM who report regular drug use. Semi-structured qualitative interviews were conducted with 40 participants recruited in Boston, Massachusetts. Data were analyzed using descriptive qualitative analysis. Casual partners presented a distinct set of concerns from primary partnerships. MSM generally viewed main partners as a potential source of support for taking PrEP. Given their informal and often temporary nature, PrEP disclosure to casual partners was considered unnecessary. HIV-related stigma and substance use were also perceived as barriers to discussing PrEP use with casual partners. MSM articulated a high degree of personal agency regarding their ability to take PrEP. Findings suggest that behavioral interventions to improve PrEP utilization and adherence for high-risk MSM should be tailored to sex partner type and the parameters established between sex partners. Approaches to PrEP disclosure and partner engagement should be informed by the relative benefits and limitations characterized by these different types of relationships.

21. Mitty, J., et al. (2012). "Preference for daily versus intermittent prep dosing among substance-dependent high-risk MSM." Journal of the International Association of Physicians in AIDS Care 11(6): 395.

Background: Pre-exposure prophylaxis (PrEP) has been shown to decrease HIV transmission in high-risk men who have sex with men (MSM), but to be effective, adherence must be optimized. MSM who use drugs (eg, crystal meth/GHB/cocaine/ecstasy/poppers) to enhance sexual activity are at increased risk for HIV acquisition and may be a particularly important group to consider when designing PrEP intervention and uptake protocols. Methods: We are collecting 40 semistructured qualitative interviews with HIV-uninfected MSM who meet DSM-IV criteria for substance abuse/dependence and report unprotected anal sex with a casual or serodiscordant male partner while using drugs in the past 3 months. The interview guide addresses: substance use, sexual-risk, social-support, healthcare, employment/housing, knowledge of PrEP, and logistical considerations for PrEP utilization. Interviews were recorded, transcribed, and examined using thematic-analysis. Results: Twenty participants have completed the interviews thus far. The mean age was 36 years (SD = 12.0), 33% were black and Latino, and their mean number of partners in the last 3 months was 7 (SD = 5.8). Seventy-two percent had heard of PrEP, and 86% were nullikelynull to use it. The most salient theme regarding perceived PrEP adherence was the preference for daily PrEP rather than PrEP before sex. Although benefits of intermittent use (eg, mitigating side effects, cost) were discussed, subthemes to contextualize preferences for daily use included 1) ease of integrating PrEP with other medications/ into daily routines; 2) concerns about missing doses of intermittent PrEP due to drug/alcohol use; 3) ambivalence of using PrEP around casual partners due to privacy concerns; 4) reluctance to carry pills away from their residence; and 5) inability to plan ahead about sex. Conclusions: Among substance using, high-risk MSM, daily dosing of PrEP may enhance acceptability/adherence to this HIV prevention strategy. Further data elucidating

facilitators and barriers to PrEP will inform intervention development to improve access and utilization of biomedical prevention among this population.

22. Mustanski, B., et al. (2013). "Perceived Likelihood of Using HIV Pre-exposure Prophylaxis Medications Among Young Men Who Have Sex with Men." AIDS & Behavior 17(6): 2173-2179.

23. Peinado, J., et al. (2013). "Acceptability of oral versus rectal HIV preexposure prophylaxis among men who have sex with men and transgender women in Peru." J Int Assoc Provid AIDS Care 12(4): 278-283.

OBJECTIVE: Oral preexposure prophylaxis (PrEP) with antiretrovirals (ARVs) is at the forefront of biomedical HIV prevention research, and ARVs are also being tested for rectal administration to target people practicing unprotected receptive anal intercourse (URAI) and at risk of HIV infection. This study assessed the acceptability of daily oral PrEP and rectal PrEP during URAI among men who have sex with men (MSM) and transgender women (TGW) in Peru. **METHODS:** During the 2008 HIV sentinel surveillance survey conducted in 3 Peruvian cities (Lima, Iquitos, and Pucallpa), MSM and TGW reported being "versatile," "most of the time receptive," and "exclusively receptive" during anal sex behavior where surveyed on their acceptability of oral and rectal PrEP. **RESULTS:** Among 532 individuals, high acceptance of either oral (96.2%) or rectal (91.7%) PrEP products was reported. If both products were efficacious/available, 28.6% would prefer a pill, 57.3% a rectal lubricant, and 14.1% either. A trend toward higher acceptance was observed as receptive anal sex behavior exclusivity rose ($P = .013$). Being receptive most of the time (adjusted odds ratio [aOR]: 9.1, $P = .01$) and exclusively receptive (aOR: 7.5, $P = .01$), compared to being versatile, were independently associated with oral PrEP acceptability. A similar association was found with the acceptability of rectal formulations (aOR: 2.3, $P = .07$; and aOR: 2.5, $P = .02$; respectively). **CONCLUSIONS:** Oral and rectal PrEP were highly acceptable among Peruvian MSM and TGW, particularly among those at the highest HIV infection risk. These data can guide the implementation of PrEP programs in Peru and similar settings and populations.

24. Rosenthal, E., et al. (2013). "Preexposure prophylaxis (PrEP) of HIV infection in France: A nationwide cross-sectional study (PREVIC study)." AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV.

Although preliminary studies showed that preexposure prophylaxis (PrEP) lowers the HIV transmission in individuals with HIV, confirmative trials are ongoing and PrEP is not routinely recommended. The aim of this study was to assess whether individuals with HIV share antiretroviral (ARV) drugs for PrEP and to describe awareness and discussion on PrEP in this population. A cross-sectional survey was conducted in France in 23 representative departments of infectious diseases and internal medicine. Physicians administered an anonymous standardized questionnaire to all individuals with HIV

receiving ARVs and followed between 24 and 31 October 2011. The questionnaire included items regarding PrEP (awareness; discussion with their close circle, physician or patients' association; experience), personal sociodemographic characteristics, risk behaviors and HIV status of the participants. Five hundred and ninety three participants were recruited: male 74.2% (men who have sex with men 52.4%, heterosexuals 21.6%), member of patient's association 9.8%. Half of them (50.6%) lived with a stable partner and 35.2% with an HIV-negative partner. Almost half (41.8%) were aware and 29.5% had had discussion about PrEP. In logistic regression, awareness and discussion on PrEP were more frequent: (1) among males, in patients' association members ($p < 0.001$ for both) and in nonheterosexuals ($p = 0.023$ and 0.057 , respectively); (2) among women, in those not living with a stable partner ($p = 0.035$ and $p = 0.03$, respectively) or living with an HIV-negative partner ($p = 0.049$ and $p = 0.083$, respectively). One percent of the participants declared having shared ARVs with someone and 8.3% reported PrEP in their close circle. Men reporting PrEP in their close circle shared ARVs more frequently than those who did not (10.3% vs. 0.2%, $p < 0.001$). Today, individuals with HIV do not seem to widely share personal ARVs for PrEP with seronegative people. A significant number of individuals with HIV are aware of and commonly discuss PrEP. (copyright) 2013 Taylor & Francis.

25. Rucinski, K. B., et al. (2013). "Knowledge and use of pre-exposure prophylaxis among an online sample of young men who have sex with men in New York City." AIDS Behav 17(6): 2180-2184.

Understanding prior knowledge and experience with pre-exposure prophylaxis (PrEP) among men who have sex with men (MSM) is critical to its implementation. In fall 2011, NYC MSM were recruited via banner advertisements on six popular dating websites and asked questions about their knowledge and use of PrEP ($n = 329$). Overall, 123 (38%) respondents reported knowledge of PrEP, of whom two (1.5%) reported PrEP use in the past 6 months. Knowledge of PrEP was associated with high educational attainment, gay identity and recent HIV testing, suggesting an uneven dissemination of information about PrEP and missed opportunities for education. To avoid disparities in use during scale-up, MSM should be provided with additional information about PrEP.

26. Saberi, P., et al. (2012). "Ambiguity, ambivalence, and apprehensions of taking HIV-1 pre-exposure prophylaxis among male couples in San Francisco: a mixed methods study." PLoS One 7(11): e50061.

OBJECTIVE: We conducted a mixed-methods study to examine serodiscordant and seroconcordant (HIV-positive/HIV-positive) male couples' PrEP awareness, concerns regarding health care providers offering PrEP to the community, and correlates of PrEP uptake by the HIV-negative member of the couple. **DESIGN:** Qualitative sub-study included one-on-one interviews to gain a deeper understanding of participants' awareness of and experiences with PrEP and concerns regarding health care providers offering PrEP to men who have sex with men (MSM). Quantitative analyses consisted of a cross-

sectional study in which participants were asked about the likelihood of PrEP uptake by the HIV-negative member of the couple and level of agreement with health care providers offering PrEP to anyone requesting it. **METHODS:** We used multivariable regression to examine associations between PrEP questions and covariates of interest and employed an inductive approach to identify key qualitative themes. **RESULTS:** Among 328 men (164 couples), 62% had heard about PrEP, but approximately one-quarter were mistaking it with post-exposure prophylaxis. The majority of participants had low endorsement of PrEP uptake and 40% were uncertain if health care providers should offer PrEP to anyone requesting it. Qualitative interviews with 32 men suggest that this uncertainty likely stems from concerns regarding increased risk compensation. Likelihood of future PrEP uptake by the HIV-negative member of the couple was positively associated with unprotected insertive anal intercourse but negatively correlated with unprotected receptive anal intercourse. **CONCLUSIONS:** Findings suggest that those at greatest risk may not be receptive of PrEP. Those who engage in moderate risk express more interest in PrEP; however, many voice concerns of increased risk behavior in tandem with PrEP use. Results indicate a need for further education of MSM communities and the need to determine appropriate populations in which PrEP can have the highest impact.

27. Sineath, R. C., et al. (2013). "Knowledge of and interest in using preexposure prophylaxis for HIV prevention among men who have sex with men in Thailand." *J Int Assoc Provid AIDS Care* 12(4): 227-231.

Little is known about HIV preexposure prophylaxis (PrEP) acceptability among men who have sex with men (MSM) in Thailand. The authors recruited an online convenience sample of Thai MSM (n = 404) to assess the knowledge of and interest in PrEP. Less than 7% had heard of PrEP; however, 35% indicated interest in PrEP after an explanation of its possible efficacy. Regression modeling demonstrated that HIV knowledge and risk behavior, but not demographics, are significant predictors of PrEP interest. More information and education about PrEP is necessary and more research is needed to examine PrEP acceptability and to inform the message for PrEP uptake.

28. Smith, D. K., et al. (2012). "Attitudes and program preferences of African-American urban young adults about pre-exposure prophylaxis (PrEP)." *AIDS Educ Prev* 24(5): 408-421.

We elicited attitudes about, and service access preferences for, daily oral antiretroviral pre-exposure prophylaxis (PrEP) from urban, African-American young men and women, ages 18-24 years, at risk for HIV transmission through their sexual and drug-related behaviors participating in eight mixed-gender and two MSM-only focus groups in Atlanta, Georgia. Participants reported substantial interest in PrEP associated with its perceived cost, effectiveness, and ease of accessing services and medication near to their homes or by public transportation. Frequent HIV testing was a perceived benefit. Participants differed about whether risk-reduction behaviors would change, and in which

direction; and whether PrEP use would be associated with HIV stigma or would enhance the reputation for PrEP users. This provides the first information about the interests, concerns, and preferences of young adult African Americans that can be used to inform the introduction of PrEP services into HIV prevention efforts for this critical population group.

29. Tangmunkongvorakul, A., et al. (2013). "Facilitators and barriers to medication adherence in an HIV prevention study among men who have sex with men in the iPrEx study in Chiang Mai, Thailand." AIDS Care 25(8): 961-967.

In 2008, the Pre-exposure Prophylaxis Initiative (iPrEx) study expanded to include men who have sex with men (MSM) in Chiang Mai, Thailand. In total, 114 participants from Chiang Mai joined this international double-blinded trial of daily FTC-TDF (Truvada(R)) or placebo as a pre-exposure prophylaxis (PrEP) HIV prevention strategy. To better understand the characteristics of iPrEx participants specifically from this underserved population in Thailand, and gain insights into their experiences of trying to take a daily tablet as part of this blinded PrEP trial, we conducted a qualitative study. In 2010, 32 MSM iPrEx participants provided in-depth interviews and an additional 14 joined focus group discussions. Results of the qualitative analyses suggested that participants held generally positive attitudes toward the iPrEx study and study medication and related this to high rates of adherence to the daily regimen. Participants also reflected on the provision of quality health care as part of participation in the trial, as well as support from clinical research staff, family and friends as helpful in supporting high rates of study medication adherence. Discourse concerning challenges to adherence included medication taking behavior, which was contextualized by lifestyle, living arrangement, social life, social stigma in terms of being mistakenly identified as HIV positive or unintentional disclosure of sexual identity to family and friends, and relationship conflicts with partners. The results provide broader perspectives of participant experiences of the study medication and daily adherence in the larger contexts of the MSM community, close relationships, and the study climate, and can be leveraged in constructing PrEP adherence support approaches within these communities.

30. Taylor, W., et al. (2012). "Enhancing pre-exposure prophylaxis adherence in men who have sex with men: Determining optimal content for a prep adherence package." Journal of the International Association of Physicians in AIDS Care 11(6): 392.

Background: Pre-exposure prophylaxis (PrEP) is a promising biomedical approach to primary HIV prevention for men who have sex with men (MSM). Recent clinical trials showed that effectiveness was closely tied to medication adherence. The purpose of the current study was to determine the optimal content for a comprehensive PrEP package that can maximize adherence and minimize risk compensation. Methods: In order to understand barriers and facilitators of PrEP adherence, we conducted 2 focus groups (N = 18) with HIV-uninfected MSM who participated in the iPrEx or CDC PrEP studies at

Fenway Health Institute, Boston, Massachusetts, and who were currently taking PrEP. Participants were asked questions about their experiences taking PrEP, perceived barriers and facilitators affecting PrEP adherence, and their suggestions for interventions that could improve PrEP adherence. Focus groups were recorded, transcribed, and examined using thematic analysis. Results: Participants' mean age was 44 (SD = 7.4). Fourteen MSM identified as white, 4 as African American/black, and one as Hispanic/Latino. Participants expressed a high level of motivation to participate in PrEP adherence interventions that could enhance PrEP efficacy. Several descriptive themes to enhance PrEP adherence emerged: 1) providing a better understanding of PrEP effectiveness; 2) addressing substance use and mental health barriers; 3) using novel facilitators (text message reminders, alarm clock/phone); 4) educating about the problems of inconsistent use (drug resistance if acutely infected) and/or long-term use (bone-density loss); 5) addressing potential HIV stigma from friends and partners; and 6) training providers of PrEP in rapport building. Conclusions: These themes were used to inform the development of a PrEP curriculum adherence package, which consists of PrEP psycho-education, solving adherence barriers, promoting individualized facilitators, and managing possible stigma associated with taking PrEP. The next step is to conduct a pilot of this intervention to assess feasibility and enhance participant acceptability.

31. Thng, C., et al. (2012). "Acceptability of HIV pre-exposure prophylaxis (PrEP) and associated risk compensation in men who have sex with men (MSM) accessing GU services." HIV Medicine 13: 84.

Background: HIV prevention strategies amongst men who have sex with men (MSM) remain an important area of research. A large multinational, randomised, double blind, placebo controlled, clinical trial (iPrEx) of daily oral antiretrovirals (tenofovir [TDF] and emtricitabine[FTC]) has demonstrated the safety and efficacy of daily TDF/FTC in reducing HIV acquisition in a men who have sex with men (MSM) population exposed to HIV through sexual transmission. We gathered data regarding the acceptability of the treatment and frequency of monitoring, the likelihood of adherence and any possible risk compensation behaviours which may emerge from taking PrEP. Methods: All MSM, aged 18 years or more, who attended the Manchester Centre for Sexual Health between 02/11/2011 and 18/01/2012 and who reported practicing unprotected receptive anal intercourse were eligible to participate in this study. These were identified by the doctor or nurse during the consultation and given a patient information leaflet (PIL) and a questionnaire to complete. Results: There were 3127 new GU attendees during this time of which 12.6% were MSM. 95/112 questionnaires were completed and returned. The mean age of the participants was 28.2 years. 80% were White Caucasian. The most common number of sexual partners in 12 months was 4. 84.2% said that they used condoms at least 50% of the time. Having casual sex with another man of unknown HIV status was the main risk of HIV in 80% of responders. Staying HIV negative was important to 87.4%. 64.2% of MSM practicing receptive anal sex were willing to take PrEP. 20% would only take coital PrEP and 50.5% would take daily PrEP for more than 6 months. 90.5% of MSM taking PrEP would adhere to monitoring and 85.3% would

accept the side effects described in the PIL. 66.3% claimed that taking PrEP would not change the frequency of condom use and none said that they would stop condom use altogether. 86.3% would have the same number of partners and 80% would still seek post-exposure prophylaxis after sexual exposure (PEPSE) despite taking PrEP.

Conclusion: PrEP has been proven to be an effective prevention strategy for at-risk MSM in a number of clinical trials. Our survey shows that the majority of MSM attending GU services in Manchester would accept an offer of PrEP, and that daily PrEP was the preferred regimen. Individuals on PrEP would not be expected to change their current sexual practice, although this would need to be assessed in larger prospective studies.

32. Tripathi, A., et al. (2013). "Perceptions and attitudes about preexposure prophylaxis among seronegative partners and the potential of sexual disinhibition." South Med J 106(10): 558-564.

OBJECTIVES: Preexposure prophylaxis (PrEP) is a promising strategy to prevent human immunodeficiency virus (HIV) infection, especially among high-risk individuals such as seronegative partners; however, many caveats such as the potential risk of sexual disinhibition and noncompliance need to be considered. We explored the sociodemographic and behavioral factors associated with the adoption of PrEP among HIV seronegative men who have sex with men and heterosexual partners. **METHODS:** A prepiloted self-administered survey was conducted among seronegative partners in a Ryan White HIV/AIDS Clinic in South Carolina from 2010 to 2011. Bivariate and multivariable analyses were used to explore the data. **RESULTS:** The survey was completed by 89 seronegative partners. The median age was 42 years (interquartile range 32-50) and a majority was men (56%), black (70%), and heterosexual (74%). A majority (94%) was willing to use PrEP if available; however, 26% of subjects suggested that they would be more likely to have unprotected sex with an HIV-positive partner while using PrEP, and 27% suggested that it would be difficult to take a daily dose of PrEP and consistently use condoms. The multivariable results suggest that the belief that a condom is no longer needed while taking PrEP was more likely among those who did not use a condom during their last sexual intercourse (adjusted odds ratio 7.45; 95% confidence interval 1.57-35.45) and among those with a higher HIV knowledge score (adjusted odds ratio 0.43; 95% confidence interval 0.23-0.78). **CONCLUSIONS:** Overall, these results suggest high acceptability of PrEP among seronegative partners to lower the risk of HIV transmission; however, there is a substantial risk of sexual disinhibition and noncompliance while using PrEP that may be reduced by ongoing education.

33. Underhill, K., et al. (2013). "Could FDA Approval of Pre-exposure Prophylaxis Make a Difference? A Qualitative Study of PrEP Acceptability and FDA Perceptions Among Men Who Have Sex with Men." AIDS Behav.

The FDA has approved tenofovir-emtricitabine for use as HIV pre-exposure prophylaxis, but it is unknown how approval may affect PrEP acceptability among US men who have sex with men. We conducted 8 focus groups among 38 Rhode Island MSM, including 3

groups among 16 male sex workers and 5 groups among 22 men in the general MSM community. Participants reported wide-ranging beliefs regarding consequences and meanings of FDA approval. Some participants would not use PrEP without approval, while others perceived approval as irrelevant or less significant than other sources of information. Our results suggest that FDA approval sends a signal that directly shapes PrEP acceptability among some MSM, while indirect influences of approval may affect uptake by others. Efforts to educate MSM about PrEP can increase acceptability by incorporating information about FDA approval, and outreach strategies should consider how this information may factor into personal decisions about PrEP use.

34. Van der Elst, E. M., et al. (2013). "High acceptability of HIV pre-exposure prophylaxis but challenges in adherence and use: qualitative insights from a phase I trial of intermittent and daily PrEP in at-risk populations in Kenya." AIDS Behav 17(6): 2162-2172.

This paper used qualitative methods to explore experiences of men who have sex with men and female sex workers in Nairobi and Mtwapa, Kenya, who used oral pre-exposure prophylaxis (PrEP) for HIV prevention as part of a four-month trial of safety, acceptability and adherence. Fifty-one of 72 volunteers who took part in a randomized, placebo-controlled, blinded trial that compared daily and intermittent dosage of PrEP underwent qualitative assessments after completing the trial. Analyses identified three themes: (i) acceptability of PrEP was high, i.e. side effects were experienced early in the study but diminished over time, however characteristics of pills could improve comfort and use; (ii) social impacts such as stigma, rumors, and relationship difficulties due to being perceived as HIV positive were prevalent; (iii) adherence was challenged by complexities of daily life, in particular post-coital dosing adherence suffered from alcohol use around time of sex, mobile populations, and transactional sex work. These themes resonated across dosing regimens and gender, and while most participants favored the intermittent dosing schedule, those in the intermittent group noted particular challenges in adhering to the post-coital dose. Culturally appropriate and consistent counseling addressing these issues may be critical for PrEP effectiveness.

35. Wade Taylor, S., et al. (2013). "Optimizing Content for Pre-exposure Prophylaxis (PrEP) Counseling for Men Who Have Sex with Men: Perspectives of PrEP Users and High-Risk PrEP Naive Men." AIDS Behav.

Existing trials of antiretroviral (ARV) medication as chemoprophylaxis against HIV reveal that the degree of protection is primarily dependent on product adherence. However, there is a lack of data on targets for behavioral interventions to improve adherence to ARV as prevention. Information from individuals who have used ARV as pre-exposure prophylaxis (PrEP) can inform behavioral intervention development. Thirty-nine HIV-uninfected MSM at high risk for HIV acquisition participated in one of four semi-structured focus groups. Two of the focus groups consisted of MSM who had been prescribed and used PrEP in the context of a clinical trial; the other two consisted of

high-risk MSM who had not previously used PrEP. An in-depth, within-case/across-case content analysis resulted in six descriptive themes potentially salient for a PrEP adherence behavioral intervention: (1) motivations to use PrEP, (2) barriers to PrEP use, (3) facilitators to PrEP use, (4) sexual decision-making in the context of PrEP, (5) prospective PrEP education content, and, (6) perceived effective characteristics of PrEP delivery personnel. Addressing these themes in behavioral interventions in the context of prescribing PrEP may result in the optimal "packaging" public health programs that implement PrEP for high-risk MSM.

36. **Wei, S. S., et al. (2011). "[Acceptability and influencing factors of pre-exposure prophylaxis among men who have sex with men in Guangxi]." Zhonghua Liu Xing Bing Xue Za Zhi 32(8): 786-788.**

OBJECTIVE: To study the acceptability of pre-exposure prophylaxis (PrEP) to prevent the transmission of HIV among men who have sex with men (MSM) in Guangxi, China. **METHODS:** Snow-balling methods were used to recruit 650 MSM in Guangxi. Questionnaires and interview were administrated to these 650 men, using a self-designed questionnaire and face to face interviews to collect information on HIV-related risk behaviors, knowledge and acceptability of PrEP. **RESULTS:** After an introduction on PrEP by interviewers, followed by as the statement-'If PrEP was effective, safe and free of charge', 597 (91.9%) of the 650 MSM claimed that they would accept it, with the main reason as the recognition of 'PrEP can decrease the risk of HIV infection'. For those who refused to use it, most of them said that were afraid of the side-effect and doubted on the effectiveness of PrEP. Data from logistic regression analysis showed that those who had found partners through friends (OR = 6.21, P = 0.020) and those who would advise his friend to use PrEP (OR = 39.32, P = 0.000) were more likely to accept PrEP. Those who thought they could protect themselves from HIV infection (OR = 0.32, P = 0.010) or not having sex with the ones who refused to use a condom (OR = 0.34, P = 0.010) were less likely to accept PrEP. **CONCLUSION:** Effectiveness, safety and cost seemed to be the main influential factors related to the acceptability of PrEP. Peer education might improve the acceptability of PrEP.

37. **Wheelock, A., et al. (2013). "Are Thai MSM willing to take PrEP for HIV prevention? An analysis of attitudes, preferences and acceptance." PLoS One 8(1): e54288.**

OBJECTIVE: We aimed to understand the attitudes, preferences and acceptance of oral and parenteral PrEP among men who have sex with men (MSM) in Thailand. **BACKGROUND:** Pre-exposure prophylaxis (PrEP), the use of antiretrovirals to prevent HIV acquisition, has shown promising results in recent trials. To assess the potential impact of this new HIV prevention method, in addition to efficacy data, we need to understand which psychosocial factors are likely to determine its uptake among members of potential user groups. **METHODS AND FINDINGS:** Surveys of willingness to use PrEP products were administered to MSM. Spearman's rank tests were used to uncover

associations between questionnaire items. Mann-Whitney tests were performed to ascertain differences between groups. Conjoint analysis was used to examine the attitudes and preferences of MSM towards PrEP attributes. Most participants were willing to consider taking PrEP (39.2% "yes, definitely" and 49.2% "yes, probably") and perceived PrEP as giving them new possibilities in their lives (38.5% "a lot of hope" and 55.8% "some hope"), even after being instructed of potential side effects and costs. HIV testing was considered the most important attribute and a daily pill and longer lasting injection in the arm were the preferred routes of administration. CONCLUSIONS: Despite its multiple challenges, MSM in Thailand would be willing to take PrEP, even if they had to experience inconvenience and expense. If PrEP were to be implemented in Thailand, our findings show that its uptake could be considerable.

38. Yang, D., et al. (2013). "Acceptability of pre-exposure prophylaxis among men who have sex with men and transgender women in Northern Thailand." PLoS One 8(10): e76650.

BACKGROUND: Northern Thailand has a high burden HIV epidemic among MSM and TG. Oral pre-exposure prophylaxis (PrEP) with tenofovir-emtricitabine has demonstrated efficacy in preventing HIV among MSM and TG in Chiang Mai, Thailand. Determinants of PrEP acceptability are needed to gauge the potential uptake of this prevention strategy. METHODS: From January to February 2012, 238 MSM and TG participants, who self-reported as HIV-uninfected or of unknown status, completed a self-administered survey on hand-held computers. Participants were recruited by venue-day-time sampling and asked to rate their likelihood of using oral PrEP for HIV prevention with an efficacy of 50%. PrEP acceptability was defined as being "very likely" to use PrEP. Odds ratios and 95% CIs were calculated to identify correlates of acceptability. RESULTS: 131 MSM and 107 TG responded, with mean ages of 23.7 and 21.8, respectively. 24% of MSM engaged primarily in receptive anal sex vs. 74% of TG. 21% of MSM and 44% of TG reported regular medication use. Prior awareness of PrEP was high at 66% among both MSM and TG respondents. 41% of MSM and 37% of TG were "very likely" to use PrEP. Among MSM, factors associated with PrEP acceptability included a prior history of STIs (AOR 4.6; 95% CIs 1.7-12.6), previous HIV testing (AOR 2.4 95% CIs 1.1-5.3), regularly planned sex (AOR 2.8 95% CIs 1.1-7.2), and infrequent sex (AOR 2.9 95% CIs 1.3-6.3). Among TG, factors associated with acceptability included prior awareness of PrEP (AOR 3.3; 95% CIs 1.2-9.0) and having private insurance (AOR 5.0; 95% CIs 1.3-19.0). CONCLUSION: MSM and TG in Northern Thailand are distinct groups in terms of sexual behaviors, patterns of medication use, and correlates of PrEP acceptability. Efforts to maximize PrEP uptake should include expanded HIV testing services and the provision of financial subsidies to reduce the cost of PrEP.

39. Zhang, Y., et al. (2013). "Attitudes toward HIV pre-exposure prophylaxis among men who have sex with men in western China." AIDS Patient Care STDS 27(3): 137-141.

Pre-exposure prophylaxis (PrEP), as demonstrated in recently published clinical trials, is one promising approach for controlling the emerging epidemic among men who have sex with men (MSM). We evaluated the attitudes towards use of PrEP among MSM in western China. A total of 1402 participants completed a self-administered questionnaire. Overall, 22% of the participants reported that they had heard of PrEP, <1% had ever used medicine to prevent HIV, and 64% reported that they were absolutely willing to use PrEP if it were proven to be safe and effective. The predictors of willingness to use PrEP included lower education, moderate income compared with the lowest income, never or rarely finding sexual partners through the Internet in the past 6 months, sexually transmitted infection (STI) history, more knowledge of AIDS, worrying about HIV as a threat to themselves and their family, having previously heard of PrEP, and believing that PrEP was effective in preventing HIV. This study demonstrates that Chinese MSM have moderate awareness of PrEP and a high interest in using it.

40. Zhong, X., et al. (2012). "Attitude on pre-exposure prophylaxis (PrEP) among drug users from high-risk population of aids in western China." Academic Journal of Second Military Medical University 33(4): 374-379.

Objective To investigate the attitude on pre-exposure prophylaxis (PrEP) among drug users from high-risk population of AIDS in western China and its influencing factors. **Methods** A total of 190 drug users were recruited by snowball sampling from high-risk population of AIDS including those involved in men having sex with men (MSM), female sex workers (FSW) and the spouse or sex partner (PAR) of HIV carrier in Chongqing, Sichuan, Guangxi and Xinjiang. Self-administered questionnaire survey was conducted with the assistance of investigators. Univariate and multivariate logistic regression was employed for statistical analysis. **Results** MSM, FSW and PAR accounted for 34.74% (66/190), 48.42% (92/190) and 16.84% (32/190) among the 190 drug users, respectively. The positive attitude rate for PrEP among drug users reached 70% in the premise of drug safety and effectiveness, which increased with favorable condition provided. The results of multivariate logistic regression analysis indicated that the factors significantly associated with the positive attitude for PrEP included awareness of AIDS seriousness (OR- 2.66, 95% CI: 1.14-6.25, P = 0.024 2), attitudes towards HIV patients (OR. 4.41, 95% CI: 1.68-11.58, P = 0.002 6, OR-. 2.99, 95% CI: 1.05-8.54, P = 0.040 3) and virus detection of AIDS (OR-. 1.94, 95% CI: 0.98-3.87, P = 0.058 1). **Conclusion** The attitude for PrEP among drug users from AIDS high-risk population is mainly related to the attitude for AIDS, AIDS-related knowledge and behavior, and preventive measures for AIDS, indicating that PrEP should be implemented and promoted with a sound social background, and education on HIV/AIDS prevention should be reinforced. Positive attitude towards AIDS prevention need to be developed among drug users by various behavioral therapies, so as to improve the attitude for PrEP among drug users with high HIV risks.

41. Zhou, F., et al. (2012). "Willingness to accept HIV pre-exposure prophylaxis among Chinese men who have sex with men." PLoS One 7(3): e32329.

OBJECTIVE: We investigated the awareness and acceptability of pre-exposure prophylaxis (PrEP) among men who have sex with men (MSM) and potential predicting factors. **METHODS:** This study was conducted among MSM in Beijing, China. Study participants, randomly selected from an MSM cohort, completed a structured questionnaire, and provided their blood samples to test for HIV infection and syphilis. Univariate logistic regression analyses were performed to evaluate the factors associated with willingness to accept (WTA) PrEP. Factors independently associated with willingness to accept were identified by entering variables into stepwise logistic regression analysis. **RESULTS:** A total of 152 MSM completed the survey; 11.2% had ever heard of PrEP and 67.8% were willing to accept it. Univariate analysis showed that age, years of education, consistent condom use in the past 6 months, heterosexual behavior in the past 6 months, having ever heard of PrEP and the side effects of antiretroviral drugs, and worry about antiretroviral drugs cost were significantly associated with willingness to accept PrEP. In the multivariate logistic regression model, only consistent condom use in the past 6 months (odds ratio [OR]: 0.31; 95% confidence interval [CI]: 0.13-0.70) and having ever heard of the side effects of antiretroviral drugs (OR: 0.30; 95% CI: 0.14-0.67) were independently associated with willingness to accept PrEP. **CONCLUSIONS:** The awareness of PrEP in the MSM population was low. Sexual behavioral characteristics and knowledge about ART drugs may have effects on willingness to accept PrEP. Comprehensive prevention strategies should be recommended in the MSM community.

42. Mayer, K., Krakower, D. Rosenberger, J., Novak, D., Mitty, J., Mimiaga, M. What do at risk American men who have sex with men (MSM) know about pre-exposure prophylaxis (PrEP)?: results of a national on-line survey. IAS 2011.

- 43. Background:** MSM increasingly meet sex partners, and get health information, on line. To better understand their response to the first PrEP efficacy data, online surveys of HIV-uninfected American MSM were conducted before and after the iPrEx publication
- Methods:** MSM members of a large sexual/social networking site were invited to complete a survey about PrEP knowledge, interest and experience in September-October, 2010 and January, 2011. Chi squares were use to compare attitudes before and after iPrEx release.
- Results:** Pre-iPrEx, 458 MSM responded to the survey, and afterwards, 4,325 did. Their median age was 40. Most participants were Caucasian (83.6%). Most of the MSM had completed high school (93.6%). Most (73%) reported at least one unprotected anal sex

episode in the prior 3 months. MSM surveyed after iPrEx data release were much more likely to have heard about PrEP than those surveyed before (18.6% vs. 12.7%, $p < .05$). The majority reported they were likely to use PrEP if it were available either time (78.4% vs. 76.9%, NS). Only 0.8% of post-iPrEx men reported having already used PrEP, and only 1.8% had used PEP. More than 80% of the men in either wave indicated they did not think they would decrease condom use during anal sex while taking PrEP. Although most men (82.0%) had a primary care provider, the majority (66.5%) had not discussed having anal sex without condoms with providers. The men's preference's for obtaining PrEP included their primary care providers (40.9%), other healthcare settings (22.7%) or via the internet (28.3%).

Conclusion: The majority of these high risk MSM were not familiar with PrEP. Programs designed to educate providers in risk assessment are needed if chemoprophylaxis is to have an impact in arresting the spread of HIV among MSM. The use of sexual/social networking sites to educate at risk MSM about PrEP could facilitate appropriate use.

44. R. Irvin, A. Liu, L. Kroboth, E. Vittinghoff, R. Tarver, P. Sullivan, S. Golub, B. Koblin, S. Buchbinder. Risk compensation and pre-exposure prophylaxis (PrEP): a post-iPrEx survey of US men who have sex with men (MSM). IAS 2011.

Background: In November 2010, iPrEx results were published demonstrating a 44% reduction in HIV infections in MSM given daily tenofovir/emtricitabine (TDF/FTC). In the trial, behavioral risk declined as participants were given a comprehensive prevention package. However, with known efficacy, risk compensation could undermine benefits.

Methods: We administered an online survey to US MSM recruited from Facebook and Black Gay Chat from 11/30/10-12/14/10. Participants were told about PrEP efficacy and answered questions about risk practices with/out TDF/FTC. We used logistic regression to identify correlates of risk perception and pressure to have unprotected anal sex with/out TDF/FTC.

Results: Overall, 1,155 HIV-negative MSM responded: 73% white, 7% African-American, 12% Hispanic. Mean age was 33 and 38% completed college. Seven percent anticipated less frequent condom use with PrEP, 75% anticipated no change in condom use, 8% anticipated more condom use, and 10% wouldn't use PrEP. However, 21% perceived less risk of HIV infection from unprotected anal insertive sex (UAI) and 39% perceived less risk from unprotected anal receptive sex (UAR) with PrEP versus no PrEP. Likelihood of PrEP use was positively associated with perceptions that PrEP decreases HIV risk of both UAI (AOR=1.63; 95%CI 1.20-2.21) and UAR (AOR=1.88; 95%CI 1.46-2.42). One-third believed they would feel increased pressure from others to have unprotected anal sex were they on PrEP; these individuals were more likely to have completed college (AOR=1.55; 95%CI 1.14-2.10), used a condom during last anal sex (AOR=1.48; 95%CI 1.11-1.98), and not have been HIV-tested in the last 12 months

(AOR=1.44; 95%CI 1.08-1.93), controlling for age and race.

Conclusion: PrEP offers promise. Most respondents did not anticipate changing their risk practices on PrEP but there was a substantial minority that might adjust their risk practices, potentially offsetting benefit. It will be important to educate MSM populations on PrEP's partial efficacy and offer ongoing risk reduction counseling.

45. J.R.Lama, et al. Willingness to use pre-exposure prophylaxis (PrEP) among men who have sex with men (MSM) at high-risk for HIV acquisition in Lima, Peru. : 19th International AIDS Conference: Abstract no. WEPE279.

Background: The use of PrEP to prevent HIV acquisition among people at high-risk is one of the prevention tools that would be operationally implemented in public-health funded settings. Barriers for implementing PrEP include willingness to use, associated costs, periodic

health monitoring among others factors. This study investigates the perception and willingness of using PrEP among MSM with high-risk sexual behaviors in Lima, Peru.

Methods: A counselor-driven structured interview sub-study was included into a HIV Sentinel Surveillance conducted in Lima, Peru in June-October 2011. In this survey, MSM with high-risk sexual behavior who were unaware of their HIV serostatus, participated in this survey for the assessment of HIV and syphilis status, and demographics and sexual behavior patterns. Topics assessed for this sub-study included perceptions and willingness to use daily oral PrEP. Logistic regression was used to study factors associated with willingness to use PrEP as a HIV prevention strategy.

Results: Among the 495 participants enrolled, 323 (65.3%) considered at least probable that they will use PrEP aimed to prevent HIV infection. In a multivariate analysis, having pressure to have unprotected anal sex was associated with 50% reduction in the odds of willingness to use PrEP (OR=0.51,95%CI: 0.26-1.13). Similarly, men, who consider that unprotective receptive anal sex increase their levels of pleasure, were 47% less likely to consider using PrEP (OR=0.54, 95%CI: 0.28-0.91). Other factors such as age, and education were not independently associated with willingness to use PrEP.

Conclusions: Before considering PrEP as an HIV prevention intervention, it is important to study and understand concerns and fears in the target population.

46. D.Krakower, et al. Anticipated risk compensation with pre-exposure prophylaxis use among North American men who have sex with men using an internet social network. : 19th International AIDS Conference: Abstract no. TUAC0302.

Background: The iPrEx study demonstrated that pre-exposure prophylaxis (PrEP) can reduce HIV incidence among at-risk men who have sex with men (MSM). However, risk

compensation (RC) could negate the benefits of PrEP.

Methods: After the release of iPrEx results, North American members (n=5035) of an Internet social network for MSM completed an online survey regarding PrEP.

Demographics, sexual risk behaviors, PrEP interest, and anticipated RC with PrEP use were assessed through self-report. Multivariable logistic regression procedures adjusted for age, race/ethnicity, and education examined the association between sociodemographic variables, sexual risk behaviors and anticipated RC.

Results: The mean age was 39 (SD=12.8), 90% were from the US, 84% were homosexual/gay and 84% were white. Ninety-three percent completed some college, 68% earned \geq \$30,000/year, 25% had a history of depression, and 5% had received substance abuse treatment. Sixty-one percent indicated unprotected anal intercourse with \geq 1 male partner in the prior 3 months (UAI-3), and 24% reported UAI after \geq 5 drinks. On a scale of 1 (no risk) to 10 (high risk), the average self-perceived risk of HIV acquisition was 3.3 (SD=2.3). Seventy-five percent reported interest in using PrEP. While using PrEP, 20% anticipated they would decrease condom use for insertive anal sex, whereas 14% indicated they would for receptive anal sex. Factors associated with increased odds of anticipated RC for insertive anal sex were UAI-3 (aOR=1.58; 95% CI: 1.22-2.04; p=0.0005) and prior substance abuse treatment (aOR=2.04; 95% CI: 1.32-3.16; p=0.002). Factors associated with increased odds of anticipated RC for receptive anal sex were UAI-3 (aOR=1.57; 95% CI: 1.16-2.13; p=0.004), UAI after \geq 5 drinks (aOR=1.43; 95% CI: 1.09-1.88; p=0.01) and increased self-perceived risk of HIV acquisition (aOR=1.10; 95% CI: 1.05-1.17; p=0.0003).

Conclusions: A substantial minority of MSM using an Internet social network anticipate increased unprotected anal sex with PrEP use. Interventions to minimize risk compensation are warranted.

47. **S.Arreola, et al. PrEP, HIV testing and treatment access among gay and other men who have sex with men: social and structural barriers and facilitators in the Global South and Global North. : 19th International AIDS Conference: Abstract no. LBPE45.**

Background: Gay men and other men who have sex with men (Gay/MSM) have disproportionately higher risk for HIV infection globally. Although PrEP and HIV treatment hold significant HIV prevention potential for gay/MSM, little is known about barriers and facilitators of access to these interventions.

Methods: In April 2012, a convenience sample of 2,197 self-identified gay/MSM (Global South (GS)=67%; Global North (GN)=33%) was recruited to complete a 30-minute global online survey. Survey announcements were circulated online among community-based organizations and regional networks serving gay/MSM worldwide, and

web banners posted on regionally popular gay/MSM websites. We used multivariable linear and logistic regression to examine social/structural predictors of PrEP acceptability and access to HIV-related services.

Results: Compared to GN, GS respondents reported 1) lower PrEP knowledge ($p < .005$) but higher PrEP acceptability ($p < .005$); and 2) less access to HIV-testing ($p < .005$), HIV treatment ($p < .025$), condoms ($p < .005$), and lubricants ($p < .005$). Among HIV-negative respondents, PrEP acceptability was associated with the following scales (each ranging from 1 to 5): PrEP knowledge ($\beta = -0.137$ 95%CI: [-0.2;-0.07]), perceived stigma related to PrEP ($\beta = -0.516$ [-0.57;-0.46]); and being "out" as a gay man/MSM ($\beta = -0.201$ [-0.27;-0.14]). HIV testing access was associated with: connection to gay community (AOR=1.3 [1.1;1.6]), and comfort with provider (AOR=1.8 [1.5;2.1]). Among HIV-positive men, homophobia was associated with decreased odds of HIV treatment access (AOR=0.5 [0.3;0.8]). Adjusting for facilitators and barriers, compared to high-income countries, respondents in middle-income countries had lower odds of HIV testing access (AOR=0.4 [0.3;0.6]); and respondents in low and middle-income countries had lower odds of access to condoms (AOR=0.6 [0.5;0.9]); and lubricants (AOR=0.4 [0.3;0.6]).

Conclusions: Implementation planning for new prevention strategies like PrEP should account for social/structural factors impacting access to HIV prevention and treatment services among gay/MSM, with particular attention to needs of gay/MSM living in the global south, especially low and middle-income countries.

48. **W.Engeran-Cordova, et al. Community survey indicates low viability of PrEP for HIV prevention. : 19th International AIDS Conference: Abstract no. WEPE265.**

Background: Results from a Pre-Exposure Prophylaxis (PrEP) clinical trial revealed that a daily dose of Truvada, a medication typically used to treat HIV infections, was 42% effective in preventing infections among sexually active Men who have Sex with Men (MSM) and transgender people. AIDS Healthcare Foundation (AHF) implemented a study to better understand the acceptability of PrEP among the aforementioned populations.

Methods: AHF developed an online questionnaire to assess the acceptability of PrEP. A third-party marketing research firm was hired to conduct this survey. Participants were screened for eligibility; inclusion criteria required that respondents were over 18 years old, and identified as gay, bisexual, MSM and/or transgender. Participation was voluntary.

Results: The survey was completed by 822 male and transgender respondents representing racially diverse backgrounds: 32% White, 30% Hispanic/Latino, 15% Black/African American, and 23% Asian/Pacific Islander or Native American. The majority of respondents, 51%, were between 30 and 54 years old. A total of 665 respondents (81%) reported being sexually active, of these, 24% reported never or rarely

using a condom. Overall, 79% of participants said they would be willing to take a pill daily that was > 90% effective at preventing HIV infections. The acceptability reduced to 69% when participants were asked about taking the pill every day *and* getting monthly HIV/ STD tests. Participants were asked about acceptability of paying a \$60 co-pay to cover the cost of the medication and labs each month; under this stipulation, only 41% stated that they would be willing to take a pill to prevent HIV.

Conclusions: Attitudes towards a pill under 'real life' conditions including co-pays, doctor's visits and labs, decreased acceptability substantially. More in-depth research is necessary to understand the acceptability of PrEP, given that clinical trials have only shown to be 42% effective in preventing HIV infections.

49. **T.Sandfort, et al. Knowledge of and attitudes toward PrEP in a New York City sample of sexually active MSM. : 19th International AIDS Conference: Abstract no. WEPE277**

Background: Following the publication of the iPrEx study showing partial efficacy of Pre-Exposure Prophylaxis (PrEP), we assessed whether men who have sex with men had heard about PrEP, and what they knew and thought about it.

Methods: An ethnically diverse group of 480 men who reported having had sex with other men in the preceding six months participated in a street-intercept survey during New York City's 2011 Gay Pride events.

Results: Over a third of all men (38.8%) had heard of PrEP; men who were Black and HIV-positive were most likely to have heard of PrEP. Substantial proportions of men, ranging from 25.0% to 40.9%, answered "Don't know" to attitude and knowledge questions. More than half of the men (58.4%) thought PrEP use should be encouraged, while 32.5% did not know; Latino men were most likely and White men least likely to support encouraging use. Men who did not endorse encouraging PrEP were more likely than those who supported encouragement or did not know to think that if PrEP became available, gay men would stop using condoms. A substantial proportion of men (50.9%) said it was (very) likely that they would use PrEP if it became easily available while 14.1% did not know. Compared to other ethnic/racial groups, White men were the least likely to say they would use PrEP (38.1%). Men who considered themselves at high risk for HIV infection would be more likely to use it (81.4%) compared to men at low or no risk (46.7% and 46.5%, respectively). Men who thought that PrEP has a lot of side effects were the least likely to say they would use it.

Conclusions: While there is interest in PrEP as an HIV prevention strategy, findings indicate a strong need for informational campaigns targeting potential PrEP users

50. **G.-M.Santos, et al. Predictors of knowledge and interest for PEP and PrEP use to prevent HIV: results from a global, multilingual survey of men who have sex with men (MSM). : 19th International AIDS Conference: Abstract no. WEPE275**

Background: Post-exposure prophylaxis (PEP) and Pre-exposure prophylaxis (PrEP) of antiretroviral medications have decreased the risk of HIV-infection in observational studies and randomized controlled trials. As PEP and PrEP are rolled out, it is imperative to assess awareness and interest for PEP and PrEP among populations disproportionately impacted by HIV, including MSM.

Methods: In 2010, we conducted a global online survey (in Chinese, Russian, Spanish, French, and English) among 5,046 MSM and collected data on PrEP and PEP knowledge and interest; access to basic HIV prevention services; perceived levels of external homophobia and self-esteem. We used multivariable logistic regression to evaluate predictors of knowledge and interest for PrEP and PEP, controlling for age and HIV-status, and excluding health providers.

Results: “No knowledge” of PEP and PrEP was reported by 53% and 60% of MSM, respectively. “Strong interest” in the use of PEP and PrEP to prevent HIV was reported by 70% and 74% of MSM, respectively. Knowledge of PEP was associated with older age(AOR=1.2[95% CI=1.1-1.3]), region(Asia: AOR=0.3[0.3-0.4]; Central/South America/Caribbean: AOR=0.64[0.4-0.9]), and basic HIV prevention access(AOR=1.5[1.4-1.7]). Knowledge of PrEP was associated with older age(AOR=1.3 [1.1-1.4]), region(Asia: AOR=0.7[0.5-0.9]), and basic HIV prevention access(AOR=1.4 [1.3-1.6]). Strong interest in PEP was associated with younger age(AOR=0.7[0.7-0.8]), region(Asia=AOR 5.0[3.0-8.2]; Central/South America/Caribbean: AOR=3.0[2.2-4.0]), and basic HIV prevention access(AOR=0.7[0.6-0.8]), having sex with men only(AOR=1.6[1.1-2.5]), perceived external homophobia(AOR=1.4[1.2-1.7]), and self-esteem(AOR=1.6[1.2-2.1]). Strong interest in PrEP was associated with younger age(AOR=0.8[0.7-0.9]), region(Asia: AOR=1.9[1.4-2.5]; Central/South America/Caribbean: AOR=3.8[2.2-6.4]) lower access to basic HIV prevention interventions(AOR=0.8[0.6-0.9]), external homophobia(AOR=1.3[1.1-1.5]), and self-esteem(AOR=1.8[1.4-2.4]).

Conclusions: In this sample, there was consistency in the predictors for knowledge and interest across PEP and PrEP. Although knowledge of PEP and PrEP were limited, there is considerable interest in the use of PEP and PrEP to prevent HIV. Efforts to disseminate information about PEP and PrEP are strongly desired and needed by MSM.

51. **M. Mimiaga, K. Biello, D. Novak, J. Rosenberger, K. Mayer. MSM in Latin America, Spain and Portugal using an internet social networking site have limited awareness but high interest in pre-exposure prophylaxis to prevent sexual acquisition of HIV. IAS 2013**

Background: Antiretroviral pre-exposure prophylaxis (PrEP) has the promise to reduce HIV acquisition for uninfected individuals. Internationally, use, awareness and interest in PrEP are largely unknown. We assessed awareness, prior use, and interest in PrEP among men who have sex with men (MSM) using an online survey across Latin America, Spain and Portugal.

Methods: Active members of a popular MSM internet social networking site in Latin America, Spain and Portugal were invited to participate in a cross-sectional, internet-based survey focused on sexual health. Logistic regression analyses were performed to identify factors associated with PrEP awareness, reported use and interest among 36,477 participants.

Results: Most participants were educated, middle-class and lived in urban areas. Sixty-seven percent had a physical examination with a healthcare provider in the past year and 75% had ever had an HIV test. Fifty-five percent of men reported condom use during most recent intercourse. Awareness of PrEP was limited (11%) and reported prior use was low (< 1%). Interest in participating in a PrEP trial was high (69%). In multivariate models, significant ($p < 0.05$) predictors of PrEP awareness were: older age, having had a physical exam, ever having HIV test, recent condom use, prior PrEP use, higher perceived PrEP effectiveness and preference for participating in a PrEP trial (vs. HIV vaccine study). Significant multivariate predictors of PrEP use were: awareness of PrEP, higher perceived PrEP effectiveness and preference for participating in a PrEP trial. Significant multivariate predictors of interest in participating in a PrEP trial were: younger age, living in Latin America, higher perceived PrEP effectiveness, preference for participating in a PrEP trial, and willingness to use an HIV home test.

Conclusions: Similar to research in the United States, PrEP use was low and awareness was limited among MSM members of an online networking site. Importantly, interest in PrEP was substantial with MSM who were younger, lived in Latin America and believed that PrEP was very effective being more interested in participating in a PrEP trial. Increasing knowledge of PrEP effectiveness may promote interest in, assist in future delivery of, and increase subsequent utilization of PrEP among high-risk MSM.

52. **T. Sanchez, C. Sineath, C. Kelley, B. O'Hara, P. Frew, J. Peterson, C. del Rio, P. Sullivan¹ Perceptions of HIV pre-exposure prophylaxis use vary among white and black men who have sex with men. IAS 2013.**

Background: HIV pre-exposure prophylaxis (PrEP) is efficacious at preventing HIV infection among men who have sex with men (MSM), but to realize maximum impact, we must understand patient perceptions of PrEP. Because HIV disproportionately impacts black MSM in the United States, we must also understand whether perceptions vary by race.

Methods: InvolveMENT is a prospective cohort study to explain HIV infection disparities between black and white MSM in Atlanta. Current PrEP use is assessed at each follow-up visit. Knowledge and perceptions were assessed at either baseline or a single follow-up visit.

Results: Of 422 MSM enrolled, 1 is using PrEP, 23% (97/422) had heard of PrEP, and 44% (185/422) were interested in using PrEP. Knowledge and interest did not significantly differ by race, but reasons for PrEP interest/disinterest significantly differed (Table 1). White MSM were more likely to report that a provider or counselor recommendation would increase their interest. White MSM were more likely to be disinterested because they thought their partner was HIV negative or they did not want to see a doctor every 3 months. Black MSM were more likely to be disinterested because they were not sexually active. Many MSM who were initially disinterested in PrEP said that more research showing PrEP was more effective and insurance coverage of PrEP would potentially change their interest. White MSM were more likely to report changes in sexual partners as a reason to change their interest. Most participants (58%, 146/422) were willing to pay ≤\$25/month for PrEP.

Conclusions: Many MSM were interested in using PrEP, but the reasons for interest and disinterest varied between black and white MSM and may require targeted messaging. Many common patient perceptions regarding PrEP are related to personal risk assessment or structural barriers that may be assuaged with improved information and support tools.

53. **I. Krznicaric, N. Hanhoff, P. Ingiliz, A. Bodtlaender, G. Knecht. Attitudes towards pre-exposure prophylaxis (PrEP) among MSM in Germany. IAS 2013.**

Background: Use of PrEP is being widely discussed with different approaches being taken in various guidelines. We wanted to examine risk behavior, PrEP awareness and use, as well as attitudes towards PrEP among MSM in Germany.

Methods: Data were collected from July-Dec. 2012 via an on-line questionnaire. Pamphlets, distributed on Christopher Street Day, through HIV medical centers and NGOs, as well as an interview in a gay magazine were used to inform potential participants of the survey.

Results: 329 MSM (median age 41 yrs.; 22% HIV+, 37% HIV-, 41% unknown HIV-status) participated in the survey. 60.1% reported no risk behavior, while 31.7% reported having 1-5 risk contacts/month, 4.3% 6-10 contacts and 4% >10 contacts. 58.1% had heard of PrEP, 5.5% (n=18) had used it. PrEP awareness was associated with HIV status (53.7% of HIV- vs. 83.1% of HIV+ persons, $p < 0.001$). PrEP use was associated with number of monthly risk contacts ($p < 0.001$). Of the 18 persons with a history of PrEP use, 13 indicated medication use as follows: TDF and FTC (n=13) either alone or with DRV/r (n=1), EVF (n=3), NVP (n=1) or RPV (n=2). The extent of PrEP use was evenly

distributed between 1-5 times, 6-10 times and >10times. Investigating attitudes towards PrEP in all participants (n=329), one-quarter (24.9%) reported not wanting to use it (37.5% of the HIV+, 42.2% of the HIV-, 2.9% of HIV-unknown population, $p < 0.001$), 55.6% would use it on an as-needed basis, 19.5% would use it daily. This differed significantly for those persons with a PrEP use history, 61.1% of who would prefer daily use ($p < 0.001$). With PrEP, 44.7% stated they would omit condom use (55.6% of HIV+ vs. 27.4% of HIV- individuals, $p < 0.001$) with a subsequent increase in quality of life expected by 83.6%. When asked about PrEP costs, most participants expect them to be either $< €200$ (35.6%) or $> €500$ (31.5%).

Conclusions: We found that $>50\%$ of MSM were aware of PrEP and $>75\%$ would be willing to use it. These findings indicate an urgent need for more information on PrEP.

54. B.P. Ngongo, J. Mbogua, B. Bender, F. Manguyu, J. Ndegwa. A survey of community opinions and preferences on PrEP, microbicides and vaccines in 5 regions and with key populations in Kenya. IAS 2013.

Background: Recent results of PrEP, Microbicides and vaccine trials have received mixed reactions at community level. Studies have shown successful introduction of health products is often affected by community perceptions and delivery preferences. We documented community preferences for New Prevention Technologies (NPT) in Kenya.

Methods: Respondents across 4 regions, 3 groups of key populations, government health officials and trainers were invited to participate in a workshop on NPT throughout 2012. A questionnaire was administered after each workshop and followed by FGDs. Quantitative data was analyzed using Ms Access 2007 and stata version 11. FGD tapes and notes were transcribed and analyzed by two independent researchers who identified key emerging concepts and themes.

Results: 42% of respondents (N=158) were involved in HIV/AIDS for more than 5 years and 20% were involved in NPT research and advocacy for more than 5 years. 62% reported having a fairly good knowledge of the HIV vaccine field and discourse of the recent results against 51% for microbicides and 50% for PrEP. The minimal efficacy level that most respondents would be comfortable to advocate for introduction and use in their community was 74% for vaccines, 71% for microbicides and 76% for PrEP. The majority of respondents preferred microbicide gels (78%), injectable vaccines (69%) and injectable PrEP (67%). However, higher preference for microbicides ring was noted with SW and oral vaccine and oral PrEP with MSM. The highest preference for product regimen was every 5 years for a vaccine (64%), before and after sex for microbicides (61%), and twice a week for PrEP (59%) with varied preferences between key populations. Most preferred service delivery modes for all NPTs were existing health centers followed by family planning /HIV centers. Vaccine was selected as preferred NPT

across key populations but was equally ranked with microbicides for heterosexual women. Microbicides were ranked second across most key populations. PrEP was ranked highest for discordant couples, MSM and MSW. Choices were guided by product characteristics, expected cost, accessibility, inclusivity, side-effect, efficacy and associated stigma.

Conclusion: Understanding evolving community preferences should be proactive and conducted in sync with socio-behavioral data conducted at trial and demonstration projects.

Background- Related to Values and Preferences of Providers (n=6 articles and 1 conference abstract)

- 1. Arnold, E. A., et al. (2012). "A qualitative study of provider thoughts on implementing pre-exposure prophylaxis (PrEP) in clinical settings to prevent HIV infection." PLoS One 7(7): e40603.**

BACKGROUND: A recent clinical trial demonstrated that a daily dose tenofovir disoproxil fumarate and emtricitabine (TDF-FTC) can reduce HIV acquisition among men who have sex with men (MSM) and transgender (TG) women by 44%, and up to 90% if taken daily. We explored how medical and service providers understand research results and plan to develop clinical protocols to prescribe, support and monitor adherence for patients on PrEP in the United States. **METHODS:** Using referrals from our community collaborators and snowball sampling, we recruited 22 healthcare providers in San Francisco, Oakland, and Los Angeles for in-depth interviews from May-December 2011. The providers included primary care physicians seeing high numbers of MSM and TG women, HIV specialists, community health clinic providers, and public health officials. We analyzed interviews thematically to produce recommendations for setting policy around implementing PrEP. Interview topics included: assessing clinician impressions of PrEP and CDC guidance, considerations of cost, office capacity, dosing schedules, and following patients over time. **RESULTS:** Little or no demand for PrEP from patients was reported at the time of the interviews. Providers did not agree on the most appropriate patients for PrEP and believed that current models of care, which do not involve routine frequent office visits, were not well suited for prescribing PrEP. Providers detailed the need to build capacity and were concerned about monitoring side effects and adherence. PrEP was seen as potentially having impact on the epidemic but providers also noted that community education campaigns needed to be tailored to effectively reach specific vulnerable populations. **CONCLUSIONS:** While PrEP may be a novel and clinically compelling prevention intervention for MSM and TG women, it raises a number of important implementation challenges that would need to be addressed. Nonetheless, most providers expressed optimism that they eventually could prescribe and monitor PrEP in their practice.

2. **Calabrese, S. K., et al. (2013). "The Impact of Patient Race on Clinical Decisions Related to Prescribing HIV Pre-Exposure Prophylaxis (PrEP): Assumptions About Sexual Risk Compensation and Implications for Access." AIDS Behav.**

Antiretroviral pre-exposure prophylaxis (PrEP) has received increasing recognition as a viable prescription-based intervention for people at risk for HIV acquisition. However, little is known about racial biases affecting healthcare providers' willingness to prescribe PrEP. This investigation sought to explore medical students' stereotypes about sexual risk compensation among Black versus White men who have sex with men seeking PrEP, and the impact of such stereotypes on willingness to prescribe PrEP. An online survey presented participants (n = 102) with a clinical vignette of a PrEP-seeking, HIV-negative man with an HIV-positive male partner. Patient race was systematically manipulated. Participants reported predictions about patient sexual risk compensation, willingness to prescribe PrEP, and other clinical judgments. Bootstrapping analyses revealed that the Black patient was rated as more likely than the White patient to engage in increased unprotected sex if prescribed PrEP, which, in turn, was associated with reduced willingness to prescribe PrEP to the patient.

3. **Karris, M. Y., et al. (2013). "Are We Prepped for Preexposure Prophylaxis (PrEP)? Provider Opinions on the Real-World Use of PrEP in the United States and Canada." Clin Infect Dis.**

Background. Preexposure prophylaxis (PrEP) with tenofovir disoproxil fumarate and emtricitabine (Truvada) has demonstrated efficacy in placebo-controlled clinical trials involving men who have sex with men, high-risk heterosexuals, serodiscordant couples, and intravenous drug users. To assist in the real-world provision of PrEP, the Centers for Disease Control and Prevention (CDC) has released guidance documents for PrEP use. **Methods.** Adult infectious disease physicians were surveyed about their opinions and current practices of PrEP through the Emerging Infections Network (EIN). Geographic information systems analysis was used to map out provider responses across the United States. **Results.** Of 1175 EIN members across the country, 573 (48.8%) responded to the survey. A majority of clinicians supported PrEP but only 9% had actually provided it. Despite CDC guidance, PrEP practices were variable and clinicians reported many barriers to its real-world provision. **Conclusions.** The majority of adult infectious disease physicians across the United States and Canada support PrEP but have vast differences of opinion and practice, despite the existence of CDC guidance documents. The success of real-world PrEP will likely require multifaceted programs addressing barriers to its provision and will be assisted with the development of comprehensive guidelines for real-world PrEP.

4. **Taegtmeier, M., et al. (2013). "Challenges in providing counselling to MSM in highly stigmatized contexts: results of a qualitative study from Kenya." PLoS One 8(6): e64527.**

The role of men who have sex with men (MSM) in the African HIV epidemic is gaining recognition yet capacity to address the HIV prevention needs of this group is limited. HIV testing and counselling is not only a critical entry point for biomedical HIV prevention interventions, such as pre-exposure prophylaxis, rectal microbicides and early treatment initiation, but is also an opportunity for focused risk reduction counselling that can support individuals living in difficult circumstances. For prevention efforts to succeed, however, MSM need to access services and they will only do so if these are non-judgmental, informative, focused on their needs, and of clear benefit. This study aimed to understand Kenyan providers' attitudes towards and experiences with counselling MSM in a research clinic targeting this group for HIV prevention. We used in-depth interviews to explore values, attitudes and cognitive and social constructs of 13 counsellors and 3 clinicians providing services to MSM at this clinic. Service providers felt that despite their growing experience, more targeted training would have been helpful to improve their effectiveness in MSM-specific risk reduction counselling. They wanted greater familiarity with MSM in Kenya to better understand the root causes of MSM risk-taking (e.g., poverty, sex work, substance abuse, misconceptions about transmission, stigma, and sexual desire) and felt frustrated at the perceived intractability of some of their clients' issues. In addition, they identified training needs on how to question men about specific risk behaviours, improved strategies for negotiating risk reduction with counselling clients, and improved support supervision from senior counsellors. This paper describes the themes arising from these interviews and makes practical recommendations on training and support supervision systems for nascent MSM HIV prevention programmes in Africa.

5. Tang, E. C., et al. (2013). "Provider Attitudes toward Oral Pre-Exposure Prophylaxis for HIV Prevention among High-Risk MSM in Lima, Peru." AIDS Res Hum Retroviruses.

Oral pre-exposure prophylaxis (PrEP) was the first biomedical intervention to demonstrate efficacy in preventing HIV infection among men who have sex with men (MSM). Healthcare providers attitudes toward PrEP will be critical in translating this finding into effective public health rollout programs. In a convenience sample of 186 healthcare providers in Peru, we assessed knowledge, barriers, and attitudes to prescribe and monitor HIV PrEP for high-risk MSM and transgender women (TGW), the populations with the highest HIV incidence in this setting. 57.5% reported awareness of PrEP, and awareness was independently associated with caring for more than 50 MSM (OR: 3.67, $p < .002$). Lack of local guidelines, concern about increased high-risk behavior, antiretroviral drug resistance, and limited availability of antiretrovirals for HIV-infected individuals were the most common barriers to prescribing PrEP. 44.6% of all physicians indicated that they would be likely to prescribe oral PrEP now; likelihood to prescribe was higher if PrEP were supported by local guidelines (70.3%, $p < .001$), if more trials supported its effectiveness (68.5%, $p < .001$), and if intermittent use were shown to be effective (62.2%, $p = .019$). Physicians were more likely to prescribe PrEP now if they care for more than 50 MSM (OR: 6.62, $p = .010$). Infectious Disease (ID) specialists were

less likely to prescribe PrEP (OR: .10, $p=.003$) than non-specialists. Successful large-scale implementation of PrEP in Peru will require focused educational campaigns to increase awareness and address concerns among healthcare providers.

6. Tellalian, D., et al. (2013). "Pre-exposure prophylaxis (PrEP) for HIV infection: results of a survey of HIV healthcare providers evaluating their knowledge, attitudes, and prescribing practices." *AIDS Patient Care STDS* 27(10): 553-559.

Antiretroviral medications can be taken by HIV-negative persons to prevent HIV infection, also known as pre-exposure prophylaxis (PrEP). PrEP was first shown to be effective during the iPrEX study. We conducted a survey involving HIV healthcare providers to document their attitudes and prescribing practices about PrEP in response to this study. An online survey was completed by 189 members and credentialed of the American Academy of HIV Medicine between April 2011 and September 2011. Ninety percent of respondents were familiar with the results of the iPrEX study, and most (78%) were familiar with CDC's interim guidance regarding the use of PrEP in MSM. Only 19% of respondents had prescribed PrEP. The majority of PrEP prescribers were compliant with CDC interim guidance; however, only 61% screened for hepatitis B. Of PrEP prescribers, 78% prescribed to MSM, 31% to MSW, and 28% to WSM. Greatest concerns about prescribing PrEP included development of antiretroviral resistance (32%), potential increase in high-risk behavior, (22%) and poor medication adherence (21%). Fifty-eight percent stated that HIV serodiscordance within a relationship most influenced their decision to prescribe PrEP to the HIV-seronegative partner. This study demonstrates that, despite awareness of the efficacy of PrEP, its use is limited. Survey participants used PrEP most commonly in MSM; however, a significant percentage also prescribed PrEP to women. The best candidate for PrEP is felt to be individuals in an HIV-serodiscordant relationship. Limitations to our study included a low response rate, changes in the evidence base, and the novelty of PrEP.

7. A.Kapur, et al. Knowledge, attitudes and willingness of New York City providers to prescribe oral pre-exposure prophylaxis (PrEP) for HIV prevention. : 19th International AIDS Conference: Abstract no. WEPE273

Background: Recent studies in men who have sex with men (MSM), heterosexual men and women, and serodiscordant couples at high-risk for HIV infection demonstrated efficacy of PrEP in reducing HIV acquisition. PrEP initiation requires monitoring for side effects, regular risk reduction counseling, and HIV testing. Effective and safe use will be limited in clinical practice if healthcare providers are not knowledgeable about risks and benefits of this strategy. Data on providers' attitudes and experience in prescribing antiretrovirals for prevention are limited.

Methods: An anonymous web-based survey was administered to HIV and non-HIV providers in NYC to assess knowledge about, and willingness to prescribe, PrEP to high-risk populations. HIV and non-HIV providers' responses were compared using Chi square and Fisher's exact tests; variables associated with willingness to prescribe PrEP were

assessed using multivariable logistic regression.

Results: 47.7% (83/174) were Internal Medicine practitioners; 15% Infectious Disease specialists; 54% identified as both HIV and non-HIV providers; 29.4% practice in non-academic community-based clinics. A high degree of knowledge of post-exposure prophylaxis (PEP) but lower awareness of PrEP was found. 69% of respondents had heard of PrEP; only 9.8% had prescribed it. Of those who had prescribed PrEP, majority (15/17, 88.2%) were physicians who care for over 100 HIV-positive patients and MSM. HIV providers were more likely to be knowledgeable about PrEP (OR=6.04, 95% CI 1.37-26.7) compared to non-HIV providers. The most common concerns about prescribing PrEP were limited clinical trials demonstrating its efficacy, lack of formal Center for Disease Control and Prevention or Department of Health guidelines, and development of antiretroviral resistance.

Conclusions: These results highlight the importance of increasing awareness and knowledge of PrEP among providers. Further clinical trial data demonstrating PrEP efficacy as well as formal CDC guidelines may alleviate concerns regarding PrEP use.

Background- Predictors of PrEP Use (n=3 articles and 2 conference abstracts)

1. **Mehta, S. A., et al. (2011). "Awareness of post-exposure HIV prophylaxis in high-risk men who have sex with men in New York City." Sex Transm Infect 87(4): 344-348.**

OBJECTIVES: To understand the factors associated with knowledge of non-occupational post-exposure prophylaxis (nPEP) and pre-exposure prophylaxis (PrEP), bathhouse patrons in New York City (NYC) were surveyed. **METHODS:** 554 men who have sex with men (MSM) at two NYC bathhouses were given a standardised survey focused on nPEP and PrEP at the time of HIV testing. **RESULTS:** In the previous 90 days, 63% of respondents reported unprotected sex with a male partner and 7% reported any sex with a known HIV-positive male partner. Less than half reported having a primary provider (primary care practitioner) who was aware of their MSM behaviour. 201 men (36%) were aware of nPEP or PrEP. In univariate analyses, race/ethnicity, previous HIV testing, gay self-identification, higher education level, having a primary provider aware of MSM behaviour, reported interaction with the healthcare system, use of the internet for meeting sex partners, reporting unprotected sex in the previous 90 days, reporting any sex with an HIV-positive male partner in the previous 90 days and having a higher number of sex partners were each significantly associated with being aware of nPEP or PrEP. In multivariate analysis, having a higher number of sex partners was significantly associated (OR 5.10, p=0.02) with post-exposure prophylaxis (PEP)/PrEP knowledge and disclosure to a primary care provider was also associated, although less robustly (OR 2.10, p=0.06). **CONCLUSIONS:** Knowledge of nPEP or PrEP among sexually active MSM in NYC is low and is associated with having a primary provider aware of their patient's same-sex behaviours. These findings show the need for improving education about nPEP among high-risk MSM in NYC and the role of providers in these efforts.

2. Zablotska, I. B., et al. (2012). "The informal use of antiretroviral medications for pre-exposure prophylaxis (PrEP) of HIV among gay men in Australia." Journal of Acquired Immune Deficiency Syndromes.

BACKGROUND: We aimed to describe the current use of antiretroviral medications (ARVs) before unprotected anal intercourse (UAI) among Australian gay men, which may represent informal HIV pre-exposure prophylaxis (PrEP). **METHODS:** Using data from Australian Gay Community Periodic Surveys conducted in 2011, we assessed the preventive use of ARVs before UAI and its association with socio-demographic characteristics, and sexual practices and drug use in the preceding six months. Associations were assessed using multivariate logistic regression analysis. **RESULTS:** Of 3,677 sexually active, non-HIV positive men, 2.5% reported taking ARVs before UAI. The likelihood of ARV use before UAI was significantly higher if any of the following behaviours were also reported: more than one sex partner; UAI with casual partners, irrespective of reporting UAI with regular partners (Adjusted Odds Ratio (AOR)=2.36; 95%CI: 1.24-4.48) or not (AOR=2.71; 95%CI: 1.44-5.07); injecting drugs at least monthly (AOR=2.56; 95%CI: 1.03-6.36); using 'party' drugs, occasionally (AOR=2.23; 95%CI: 1.33-3.73) or regularly (AOR=5.34; 95%CI: 2.99-9.56); and group sex while using party drugs, occasionally (AOR=2.42; 95%CI: 1.29-4.53) or regularly (AOR=5.31; 95%CI: 2.62-10.76). Among non-HIV positive men in regular relationships with HIV positive partners or partners of unknown HIV status, 1.7% and 4.7%, respectively, reported preventive ARV use before UAI. **CONCLUSION:** Our findings illustrate sporadic use of ARVs before UAI among gay men in Australia, which was associated with high risk casual sex and 'party' drug use. These initial data contribute to a much needed understanding of the informal use of ARVs for HIV prevention.

3. Zablotska, I. B., et al. (2013). "The informal use of antiretrovirals for preexposure prophylaxis of HIV infection among gay men in Australia." Journal of Acquired Immune Deficiency Syndromes 62(3): 334-338.

Background: We aimed to describe the current use of antiretrovirals (ARVs) before unprotected anal intercourse (UAI) among Australian gay men, which may represent informal HIV preexposure prophylaxis (PrEP). **Methods:** Using data from Australian Gay Community Periodic Surveys conducted in 2011, we assessed the preventive use of ARVs before UAI and its association with sociodemographic characteristics, sexual practices, and drug use in the preceding 6 months. Associations were assessed using multivariate logistic regression analysis. **Results:** Of 3677 sexually active non-HIV-positive men, 2.5% reported taking ARVs before UAI. The likelihood of ARV use before UAI was significantly higher if any of the following behaviors were also reported: > 1 sex partner; UAI with casual partners, irrespective of reporting UAI with regular partners [adjusted odds ratio (AOR) = 2.36; 95% confidence interval (CI): 1.24 to 4.48] or not (AOR = 2.71; 95% CI: 1.44 to 5.07); injecting drugs at least monthly (AOR = 2.56; 95% CI: 1.03 to 6.36); using "party" drugs, occasionally (AOR = 2.23; 95% CI: 1.33 to 3.73)

or regularly (AOR = 5.34; 95% CI: 2.99 to 9.56); and group sex while using party drugs, occasionally (AOR = 2.42; 95% CI: 1.29 to 4.53) or regularly (AOR = 5.31; 95% CI: 2.62 to 10.76). Among non-HIVpositive men in regular relationships with HIV-positive partners or partners of unknown HIV status, 1.7% and 4.7%, respectively, reported preventive ARV use before UAI. Conclusions: Our findings illustrate sporadic use of ARVs before UAI among gay men in Australia, which was associated with high-risk casual sex and party drug use. These initial data contribute to a much needed understanding of the informal use of ARVs for HIV prevention. Copyright (copyright) 2012 by Lippincott Williams and Wilkins.

4. **J.Zhang, et al. Factors associated with willingness to use oral PrEP among men who have sex with men in Shenyang, China. : 19th International AIDS Conference: Abstract no. MOPE261**

Background: This cross sectional study examined pre-exposure prophylaxis (PrEP) acceptability among MSM in Shenyang, China. Understanding the demographic and behavioral predictors of intent to use PrEP may prove useful to identify clinical trial participants.

Methods: During 2011, 274 MSM were enrolled at VCT through snowball sampling in gay community in Shenyang, China. After a brief introduction about the results of Truvada clinical trial by trained staffs, interviewer -assisted questionnaire were used to collect demographic, behavioral information and attitude to use Truvada as a daily prevention method. All participants were tested for HIV and syphilis. Data were analyzed by univariate and multivariate logistic regression by SPSS 13.0.

Results: The prevalence of HIV and syphilis was 5.5% and 27.4%. The majority of participants had never heard of PrEP (83.0%). 49.6% of the participants were willing to use PrEP, and 6.6% were very willing to use. Mean age of all participants was 29.0 (SD=8.8), 70.6% were younger than 30. In the past-three-month, 17.5% had female sex partners; 8.2% have sold sex to male clients; 13.8% have used drug. The prevalence of group sex in the past-three-month was 11.3%. Independent associated predictors of willing to use PrEP (each $P < 0.05$) included family support of the use of PrEP (aOR=4.97); expectation of more sex partners after use of PrEP (aOR=2.01); have heard of PrEP before (aOR=2.09); have sold sex in the past-three-month (aOR=2.47).

Conclusions: PrEP acceptance of Chinese MSM was correlated with awareness and family support. Future PrEP trial participants' enrollment also oral PrEP promotion should focus on medicine orientation propaganda and raising family support of the participants.

5. **R.Landovitz, et al. Factors associated with use of PrEP and PEP in young MSM who use GRINDR in Los Angeles, California. : 19th International AIDS Conference: Abstract no. TUPE235.**

Background: Young MSM disproportionately contribute to incident and prevalent HIV infections in the United States. Combination HIV Prevention strategies which include biomedical interventions may reduce HIV infections in these groups. Accessing YMSM for epidemiologic study, study recruitment, and HIV prevention interventions has been challenging in the U.S.

Methods: GRINDR, a GPS-based social networking application used on smart-phone platforms, was used to recruit a sample of 375 YMSM. Random venue-date-time sampling was used to recruit YMSM local to venues via GRINDR. Participants were administered a CASI-based survey.

Results: The sample was 42.4% white, 6.4% African-American, and 33.6% Latino. 359 (95.7%) self-reported HIV-uninfected status and a mean of 3.8 (SD 7.2) anal sex partners in the past month, with approximately 41% reporting inconsistent condom use; 20% of partners were HIV-infected or of unknown serostatus. 274 (76.3%) believed that they were unlikely or very unlikely to become HIV-infected in their lifetime. 42 (11.2%) had previously participated in a research study, and only 54 (14.4%) expressed no interest in an HIV prevention trial; 194 (51.7%) stated they definitely would participate. 13 (3.6%) reported previous use of PEP, and 6 (1.7%) reported previous use of PrEP. In multivariable analysis, prior PEP or PrEP use was associated with meeting a sex partner at work (OR 3.6 [95%CI 1.1-12.2]), an increase in number of sex partners since beginning to use GRINDR (OR 4.7 [1.6-14.3]), methamphetamine use in the past month (OR 5.8 [1.5-21.9]), and non-Latino race (OR 9.3 [1.1-76.9]).

Conclusions: Although PrEP has been shown to be efficacious in MSM, demonstration projects for PrEP face challenges in accessing highest-risk populations. YMSM may be targeted by using novel technology-based methods. Uptake of PEP and PrEP is currently limited among YMSM, particularly Latino MSM. Social networking applications such as GRINDR may be useful for recruiting for prevention interventions as well as educational messaging.

Background- Previous reviews related to PrEP (n=5 articles)

1. **Holt, M. (2013). "HIV pre-exposure prophylaxis and treatment as prevention: a review of awareness and acceptability among men who have sex with men in the Asia-Pacific region and the Americas." Sex Health.**

2. Krakower, D. and K. H. Mayer (2012). "Engaging healthcare providers to implement HIV pre-exposure prophylaxis." Curr Opin HIV AIDS 7(6): 593-599.

PURPOSE OF REVIEW: Recent randomized controlled trials have demonstrated that HIV pre-exposure prophylaxis (PrEP) can decrease HIV incidence among several at-risk populations, including men who have sex with men, serodiscordant couples, and heterosexual men and women. As PrEP is a biomedical intervention that requires clinical monitoring and a high level of medication adherence, maximizing the public health effectiveness of PrEP in real-world settings will require the training of a cadre of healthcare providers to prescribe PrEP. Therefore it is critical to understand provider knowledge, practices, and attitudes towards PrEP prescribing, and to develop strategies for engaging and training providers to provide PrEP. **RECENT FINDINGS:** Limited numbers of studies have focused on PrEP implementation by healthcare providers. These studies suggest that some providers are knowledgeable about PrEP, but many are not, or express misgivings. Although many clinicians report willingness to provide PrEP, few have prescribed PrEP in clinical practice. Provider comfort and skills in HIV risk assessment are suboptimal, which could limit identification of individuals who are most likely to benefit from PrEP use. **SUMMARY:** Further studies to understand facilitators and barriers to HIV-risk assessment and PrEP prescribing by practicing clinicians are needed. Innovative training strategies and decision-support interventions for providers could optimize PrEP implementation and therefore merit additional research.

3. Okwundu, C. I., et al. (2012). "Antiretroviral pre-exposure prophylaxis (PrEP) for preventing HIV in high-risk individuals." Cochrane Database Syst Rev 7: CD007189.

BACKGROUND: More than 30 years into the global HIV/AIDS epidemic, infection rates remain alarmingly high, with over 2.7 million people becoming infected every year. There is a need for HIV prevention strategies that are more effective. Oral antiretroviral pre-exposure prophylaxis (PrEP) in high-risk individuals may be a reliable tool in preventing the transmission of HIV. **OBJECTIVES:** To evaluate the effects of oral antiretroviral chemoprophylaxis in preventing HIV infection in HIV-uninfected high-risk individuals. **SEARCH METHODS:** We revised the search strategy from the previous version of the review and conducted an updated search of MEDLINE, the Cochrane Central Register of Controlled Trials and EMBASE in April 2012. We also searched the WHO International Clinical Trials Registry Platform and ClinicalTrials.gov for ongoing trials. **SELECTION CRITERIA:** Randomised controlled trials that evaluated the effects of any antiretroviral agent or combination of antiretroviral agents in preventing HIV infection in high-risk individuals **DATA COLLECTION AND ANALYSIS:** Data concerning outcomes, details of the interventions, and other study characteristics were extracted by two independent authors using a standardized data extraction form. Relative risk with a 95% confidence interval (CI) was used as the measure of effect. **MAIN RESULTS:** We identified 12 randomised controlled trials that meet the criteria for the review. Six were ongoing trials, four had been completed and two had been terminated

early. Six studies with a total of 9849 participants provided data for this review. The trials evaluated the following: daily oral tenofovir disoproxil fumarate (TDF) plus emtricitabine (FTC) versus placebo; TDF versus placebo and daily TDF-FTC versus intermittent TDF-FTC. One of the trials had three study arms: TDF, TDF-FTC and placebo arm. The studies were carried out amongst different risk groups, including HIV-uninfected men who have sex with men, serodiscordant couples and other high risk men and women. Overall results from the four trials that compared TDF-FTC versus placebo showed a reduction in the risk of acquiring HIV infection (RR 0.51; 95% CI 0.30 to 0.86; 8918 participants). Similarly, the overall results of the studies that compared TDF only versus placebo showed a significant reduction in the risk of acquiring HIV infection (RR 0.38; 95% CI 0.23 to 0.63, 4027 participants). There were no significant differences in the risk of adverse events across all the studies that reported on adverse events. Also, adherence and sexual behaviours were similar in both the intervention and control groups. **AUTHORS' CONCLUSIONS:** Finding from this review suggests that pre-exposure prophylaxis with TDF alone or TDF-FTC reduces the risk of acquiring HIV in high-risk individuals including people in serodiscordant relationships, men who have sex with men and other high risk men and women.

4. Schackman, B. R. and A. A. Eggman (2012). "Cost-effectiveness of pre-exposure prophylaxis for HIV: a review." Curr Opin HIV AIDS 7(6): 587-592.

PURPOSE OF REVIEW: The US Food and Drug Administration (FDA) recently approved the use of tenofovir-emtricitabine for pre-exposure prophylaxis (PrEP) for HIV prevention. PrEP is also being investigated in clinical trials as a component of HIV prevention in resource-limited settings. Cost-effectiveness models are useful in identifying health programs with the greatest societal value and projecting long-term program impacts. This review examines six recent studies of the cost-effectiveness of PrEP for preventing HIV transmission in the USA and South Africa. **RECENT FINDINGS:** Studies used both individual-level and population-level transmission models. PrEP was found to be a cost-effective HIV-prevention intervention in high-risk MSM with HIV incidence at least 2% in the USA (<US\$100 000 per quality-adjusted life year) and in young women in South Africa (cost per life year <GDP per capita). Results were sensitive to the cost and efficacy of PrEP and to assumptions about HIV testing and access to treatment in the absence of PrEP. **SUMMARY:** Future cost effectiveness studies should consider PrEP implementation issues (uptake in high-risk versus low-risk groups, duration on PrEP, adherence), budget impact, and the role of PrEP as part of combination HIV-prevention strategies including expanded testing and treatment access.

5. Young, I. and L. McDaid (2013). "How Acceptable are Antiretrovirals for the Prevention of Sexually Transmitted HIV?: A Review of Research on the Acceptability of Oral Pre-exposure Prophylaxis and Treatment as Prevention." AIDS Behav.

Recent research has demonstrated how antiretrovirals (ARVs) could be effective in the prevention of sexually transmitted HIV. We review research on the acceptability of oral pre-exposure prophylaxis (PrEP) and treatment as prevention (TasP) for HIV prevention amongst potential users. We consider with whom, where and in what context this research has been conducted, how acceptability has been approached, and what research gaps remain. Findings from 33 studies show a lack of TasP research, PrEP studies which have focused largely on men who have sex with men (MSM) in a US context, and varied measures of acceptability. In order to identify when, where and for whom PrEP and TasP would be most appropriate and effective, research is needed in five areas: acceptability of TasP to people living with HIV; motivation for PrEP use and adherence; current perceptions and management of risk; the impact of broader social and structural factors; and consistent definition and operationalisation of acceptability which moves beyond adherence.

Background- Modeling and cost-effectiveness (n=8 articles)

- 1. Borquez, A., et al. (2011). "The potential impact of pre-exposure prophylaxis for HIV prevention among men who have sex with men (MSM) in Lima, Peru." Sexually Transmitted Infections 87: A350.**

Background: HIV Pre-exposure prophylaxis (PrEP), the use of antiretroviral drugs by those HIV uninfected individuals to prevent HIV infection, recently demonstrated effectiveness in preventing acquisition in a high risk population of men who have sex with men (MSM). There is a need to understand if and how PrEP can be used cost-effectively. This study examines the programmatic implications of the iPrEX study: the only randomised controlled trial of PrEP among men who have sex with men (MSM) published last December in the New England Journal of Medicine. Methods: We developed a mathematical model representing the HIV epidemic among Men who Have Sex with Men (MSM) and transgender people in Lima, Peru as a test-case. It considers differential infectiousness by stage, including the impact of antiretroviral treatment and different sexual practices, such as partnerships type and sexual positioning. The model was used to investigate the population-level impact, cost, and cost-effectiveness of PrEP under a range of implementation scenarios, and to develop possible strategies by which PrEP could be implemented. Results: The epidemiological impact of PrEP is largely driven by Programme characteristics-coverage, prioritisation strategy and time to scale up-as well as individual's adherence behaviour. If PrEP is prioritised to key groups, it could be a cost-effective way to avert infection and save lives (up to 8% less new infections with 5% coverage). Across all our scenarios the estimated highest cost perDALY gained (US\$2755) is below the WHO recommended threshold for cost effective interventions for the region (<US\$4608/DALY gained) see Abstract LBO-1.2 Figure 1. The impact of PrEP is reduced if those on PrEP decrease condom use, especially if the program has low coverage; but only extreme behaviour changes and a low PrEP efficacy

would adversely impact the epidemic overall. However, PrEP will not arrest HIV transmission in isolation, due to its incomplete effectiveness, dependence on adherence, and the high total cost of programmes limiting attainable coverage levels. Conclusions: This study quantifies the epidemic and financial implications of different programmatic scenarios. While the implementation of a strategic PrEP intervention has potentially important financial implications (a substantial expenditure would likely be required to generate significant reductions in incidence), PrEP among vulnerable populations could be a cost-effective option comparable to currently available interventions for Men who Have Sex with Men (MSM) populations. (Figure presented) .

2. **Gomez, G. B., et al. (2011). "The Potential Impact of Pre-Exposure Prophylaxis for HIV Prevention among Men Who Have Sex with Men and Transwomen in Lima, Peru: A Mathematical Modelling Study." PLoS Medicine 9(10): e1001323-e1001323.**
3. **Gomez, G. B., et al. (2013). "The cost and impact of scaling up pre-exposure prophylaxis for HIV prevention: a systematic review of cost-effectiveness modelling studies." PLoS Med 10(3): e1001401.**

BACKGROUND: Cost-effectiveness studies inform resource allocation, strategy, and policy development. However, due to their complexity, dependence on assumptions made, and inherent uncertainty, synthesising, and generalising the results can be difficult. We assess cost-effectiveness models evaluating expected health gains and costs of HIV pre-exposure prophylaxis (PrEP) interventions. **METHODS AND FINDINGS:** We conducted a systematic review comparing epidemiological and economic assumptions of cost-effectiveness studies using various modelling approaches. The following databases were searched (until January 2013): PubMed/Medline, ISI Web of Knowledge, Centre for Reviews and Dissemination databases, EconLIT, and region-specific databases. We included modelling studies reporting both cost and expected impact of a PrEP roll-out. We explored five issues: prioritisation strategies, adherence, behaviour change, toxicity, and resistance. Of 961 studies retrieved, 13 were included. Studies modelled populations (heterosexual couples, men who have sex with men, people who inject drugs) in generalised and concentrated epidemics from Southern Africa (including South Africa), Ukraine, USA, and Peru. PrEP was found to have the potential to be a cost-effective addition to HIV prevention programmes in specific settings. The extent of the impact of PrEP depended upon assumptions made concerning cost, epidemic context, programme coverage, prioritisation strategies, and individual-level adherence. Delivery of PrEP to key populations at highest risk of HIV exposure appears the most cost-effective strategy. Limitations of this review include the partial geographical coverage, our inability to perform a meta-analysis, and the paucity of information available exploring trade-offs between early treatment and PrEP. **CONCLUSIONS:** Our review identifies the main considerations to address in assessing cost-effectiveness analyses of a PrEP intervention--cost, epidemic context, individual adherence level, PrEP programme coverage, and prioritisation strategy. Cost-effectiveness studies indicating where resources can be

applied for greatest impact are essential to guide resource allocation decisions; however, the results of such analyses must be considered within the context of the underlying assumptions made.

4. Hellinger, F. J. (2013). "Assessing the cost effectiveness of pre-exposure prophylaxis for HIV prevention in the US." PharmacoEconomics 31(12): 1091-1104.

About 50,000 people are infected with HIV in the US each year and this number has remained virtually the same for the past decade. Yet, in the last few years, evidence from several multinational randomized clinical trials has shown that the provision of antiretroviral drug to uninfected persons (i.e. pre-exposure prophylaxis) reduces the incidence of HIV by about 50 %. However, evidence from cost-effectiveness studies conducted in the US yield widely varying estimates of the cost per quality-adjusted life-year (QALY) gained, and this variation reflects the substantial uncertainty surrounding the determinants of HIV transmission (e.g. adherence rates to prophylactic medications, the average number of sexual partners, the number and types of sexual acts, the viral load of infected partners, and the proportion of contacts where condoms are used), as well as different approaches to translating a reduction in HIV cases into an estimate of the increase in the number of QALYs. (copyright) 2013 Springer International Publishing Switzerland (outside the USA).

5. Juusola, J. L., et al. (2012). "The cost-effectiveness of preexposure prophylaxis for HIV prevention in the United States in men who have sex with men." Ann Intern Med 156(8): 541-550.

BACKGROUND: A recent randomized, controlled trial showed that daily oral preexposure chemoprophylaxis (PrEP) was effective for HIV prevention in men who have sex with men (MSM). The Centers for Disease Control and Prevention recently provided interim guidance for PrEP in MSM at high risk for HIV. Previous studies did not reach a consistent estimate of its cost-effectiveness. **OBJECTIVE:** To estimate the effectiveness and cost-effectiveness of PrEP in MSM in the United States. **DESIGN:** Dynamic model of HIV transmission and progression combined with a detailed economic analysis. **DATA SOURCES:** Published literature. **TARGET POPULATION:** MSM aged 13 to 64 years in the United States. **TIME HORIZON:** Lifetime. **PERSPECTIVE:** Societal. **INTERVENTION:** PrEP was evaluated in both the general MSM population and in high-risk MSM and was assumed to reduce infection risk by 44% on the basis of clinical trial results. **OUTCOME MEASURES:** New HIV infections, discounted quality-adjusted life-years (QALYs) and costs, and incremental cost-effectiveness ratios. **RESULTS OF BASE-CASE ANALYSIS:** Initiating PrEP in 20% of MSM in the United States would reduce new HIV infections by an estimated 13% and result in a gain of 550,166 QALYs over 20 years at a cost of \$172,091 per QALY gained. Initiating PrEP in a larger proportion of MSM would prevent more infections but at an increasing cost per QALY gained (up to \$216,480 if all MSM receive PrEP). Preexposure chemoprophylaxis in only high-risk MSM can improve cost-effectiveness. For MSM with an average of 5

partners per year, PrEP costs approximately \$50,000 per QALY gained. Providing PrEP to all high-risk MSM for 20 years would cost \$75 billion more in health care-related costs than the status quo and \$600,000 per HIV infection prevented, compared with incremental costs of \$95 billion and \$2 million per infection prevented for 20% coverage of all MSM. RESULTS OF SENSITIVITY ANALYSIS: PrEP in the general MSM population would cost less than \$100,000 per QALY gained if the daily cost of antiretroviral drugs for PrEP was less than \$15 or if PrEP efficacy was greater than 75%. LIMITATION: When examining PrEP in high-risk MSM, the investigators did not model a mix of low- and high-risk MSM because of lack of data on mixing patterns. CONCLUSION: PrEP in the general MSM population could prevent a substantial number of HIV infections, but it is expensive. Use in high-risk MSM compares favorably with other interventions that are considered cost-effective but could result in annual PrEP expenditures of more than \$4 billion.

6. **Koppenhaver, R. T., et al. (2011). "The cost-effectiveness of pre-exposure prophylaxis in men who have sex with men in the United States: an epidemic model." J Acquir Immune Defic Syndr 58(2): e51-52.**
7. **Mitchell, K. M., et al. (2012). "Sexual mixing patterns between men who have sex with men in southern India: Implications for modelling the HIV epidemic and predicting the impact of targeted oral preexposure prophylaxis." Journal of the International AIDS Society 15: 106-107.**

Background: In southern India, the identity of men who have sex with men (MSM) is closely related to role taken in anal sex, but little is known about sexual mixing between identity groups. Both role segregation and assortative (within-group) mixing are known to affect HIV epidemic size in other settings. This study aimed to explore how different mixing patterns affect estimated HIV trends and intervention impact for MSM in Bangalore. Methods: Deterministic models describing HIV transmission between three MSM identity groups (mostly insertive panthis/bisexuals (PB), mostly receptive kothis/hijras (KH) and versatile double deckers (DD)), were parameterised with data collected in Bangalore for the evaluation of the Avahan intervention. These models were used to explore four different mixing patterns (table). 300,000 randomly (Table presented) sampled parameter sets were obtained from data ranges and used to find multiple fits to group-specific HIV prevalence data in 2006 and 2009. Model fits were used to compare predicted HIV time trends. To compare the impact of a new intervention scenario, condom use was assumed to decline from high levels in 2010 due to condomintervention fatigue. Oral pre-exposure prophylaxis (PrEP) was introduced in 2015, assuming 42% effectiveness (efficacy x adherence) and 60% coverage, targeted at KH and DD (the groups easiest to reach). Results: Large differences in levels of assortative mixing were seen for fits identified using different mixing patterns (Table 1), but little difference was projected in HIV prevalence trends (A). Different mixing patterns gave somewhat different estimates for group-specific impact of the PrEP intervention (B), but overall

impact in the whole MSM population was very similar (< 10% difference in % infections averted). Conclusion: A variety of different mixing patterns are consistent with the data. However, model predictions of future HIV epidemic trends and overall impact of a targeted intervention are robust to the different mixing patterns and intervention scenario explored here.

8. Schneider, K., et al. (2014). "A cost-effectiveness analysis of HIV pre-exposure prophylaxis for men who have sex with men in Australia." Clin Infect Dis.

Background. Antiretroviral therapy (ART) used as pre-exposure prophylaxis (PrEP) by human immunodeficiency virus (HIV)-seronegative individuals reduces the risk of acquiring HIV. However, the population-level impact and cost-effectiveness of using PrEP as a public health intervention remains debated. Methods. We used a stochastic agent-based model of HIV transmission and progression to simulate the clinical and cost outcomes of different strategies of providing PrEP to men who have sex with men (MSM) in New South Wales (NSW), Australia. Model outcomes were reported as incremental cost effectiveness ratios (ICERs) in 2013 Australian dollars per quality-adjusted life year gained (\$/QALYG). Results. The use of PrEP in 10-30% of the entire NSW MSM population was projected to cost an additional \$316-952 million dollars over the course of 10 years, and cost more than \$400,000 per QALYG compared with the status quo. Targeting MSM with sexual partners ranging between more than 10 to more than 50 partners within six months cost an additional \$31-331 million dollars, and cost more than \$110,000 per QALYG compared with the status quo. We found pre-exposure prophylaxis is most cost-effective when targeted for HIV-negative MSM in a discordant regular partnership. The ICERs ranged between \$8,399 and \$11,575, for coverage ranging between 15% and 30%, respectively. Conclusion. Targeting HIV-negative MSM in a discordant regular partnership is a cost-effective intervention. However, this highly targeted strategy would not have large population-level impact. Other scenarios are unlikely to be cost-effective.

Background- Other (n=17)

1. (2012). Guidance on Pre-Exposure Oral Prophylaxis (PrEP) for Serodiscordant Couples, Men and Transgender Women Who Have Sex with Men at High Risk of HIV: Recommendations for Use in the Context of Demonstration Projects. Geneva, World Health Organization.

These recommendations have been developed specifically to address the daily use of antiretrovirals in HIV-uninfected people to block the acquisition of HIV infection. This prevention approach is known as pre-exposure prophylaxis. At this stage evidence is available from studies with two groups: men and transgender women who have sex with men; and serodiscordant heterosexual couples. In parallel, WHO also is preparing new

recommendations on the use of antiretroviral drugs in people living with HIV to prevent transmission of infection.

2. (2012). "Interim guidance for clinicians considering the use of preexposure prophylaxis for the prevention of HIV infection in heterosexually active adults." MMWR Morb Mortal Wkly Rep 61(31): 586-589.

In the United States, an estimated 48,100 new human immunodeficiency virus (HIV) infections occurred in 2009. Of these, 27% were in heterosexual men and women who did not inject drugs, and 64% were in men who have sex with men (MSM), including 3% in MSM who inject drugs. In January 2011, following publication of evidence of safety and efficacy of daily oral tenofovir disoproxil fumarate 300 mg (TDF)/emtricitabine 200 mg (FTC) (Truvada, Gilead Sciences) as antiretroviral preexposure prophylaxis (PrEP) to reduce the risk for HIV acquisition among MSM in the iPrEx trial, CDC issued interim guidance to make available information and important initial cautions on the use of PrEP in this population. Those recommendations remain valid for MSM, including MSM who also have sex with women. Since January 2011, data from studies of PrEP among heterosexual men and women have become available, and on July 16, 2012, the Food and Drug Administration (FDA) approved a label indication for reduction of risk for sexual acquisition of HIV infection among adults, including both heterosexuals and MSM. This interim guidance includes consideration of the new information and addresses pregnancy and safety issues for heterosexually active adults at very high risk for sexual HIV acquisition that were not discussed in the previous interim guidance for the use of PrEP in MSM.

3. Anderson, P. L., et al. (2012). "Emtricitabine-tenofovir concentrations and pre-exposure prophylaxis efficacy in men who have sex with men." Sci Transl Med 4(151): 151ra125.

Drug concentrations associated with protection from HIV-1 acquisition have not been determined. We evaluated drug concentrations among men who have sex with men in a substudy of the iPrEx trial (1). In this randomized placebo-controlled trial, daily oral doses of emtricitabine/tenofovir disoproxil fumarate were used as pre-exposure prophylaxis (PrEP) in men who have sex with men. Drug was detected less frequently in blood plasma and in viable cryopreserved peripheral blood mononuclear cells (PBMCs) in HIV-infected cases at the visit when HIV was first discovered compared with controls at the matched time point of the study (8% versus 44%; $P < 0.001$) and in the 90 days before that visit (11% versus 51%; $P < 0.001$). An intracellular concentration of the active form of tenofovir, tenofovir-diphosphate (TFV-DP), of 16 fmol per million PBMCs was associated with a 90% reduction in HIV acquisition relative to the placebo arm. Directly observed dosing in a separate study, the STRAND trial, yielded TFV-DP concentrations that, when analyzed according to the iPrEx model, corresponded to an HIV-1 risk reduction of 76% for two doses per week, 96% for four doses per week, and 99% for

seven doses per week. Prophylactic benefits were observed over a range of doses and drug concentrations, suggesting ways to optimize PrEP regimens for this population.

4. Bekker, L. G., et al. (2012). "Southern African guidelines for the safe use of pre-exposure prophylaxis in men who have sex with men who are at risk for HIV infection: Guidelines." Southern African Journal of HIV Medicine 13(2): 40-55.

Background. The use of oral antiretrovirals to prevent HIV infection among HIV-negative men who have sex with men (MSM) has been shown to be safe and efficacious. A large, randomised, placebo-controlled trial showed a 44% reduction in the incidence of HIV infection among MSM receiving a daily oral fixed-dose combination of tenofovir disoproxil fumarate and emtricitabine (Truvada) in combination with an HIV prevention package. Improved protection was seen with higher levels of adherence. **Aim.** The purpose of this guideline is to: (i) explain what pre-exposure prophylaxis (PrEP) is; (ii) outline current indications for its use; (iii) outline steps for appropriate client selection; and (iv) provide guidance for monitoring and maintaining clients on PrEP. **Method.** PrEP is indicated for HIV-negative MSM who are assessed to be at high risk for HIV acquisition and who are willing and motivated to use PrEP as part of a package of HIV prevention services (including condoms, lubrication, sexually transmitted infection (STI) management and risk reduction counselling). **Recommendations.** HIV testing, estimation of creatinine clearance and STI and hepatitis B screening are recommended as baseline investigations. Daily oral Truvada, along with adherence support, can then be prescribed for eligible MSM. PrEP should not be given to MSM with abnormal renal function, nor to clients who are unmotivated to use PrEP as part of an HIV prevention package; nor should it be commenced during an acute viral illness. Three-monthly follow-up visits to assess tolerance, renal function, adherence and ongoing eligibility is recommended. Six-monthly STI screens and annual creatinine levels to estimate creatinine clearance are recommended. Hepatitis B vaccination should be provided to susceptible clients. Gastro-intestinal symptoms and weight loss are common side-effects, mostly experienced for the first 4 - 8 weeks after initiating PrEP. There is a risk of the development of antiretroviral resistance among those with undiagnosed acute HIV infection during PrEP initiation and among those with sub-optimal adherence who become HIV infected while on PrEP. Risk compensation (increasing sexual behaviours that can result in exposure to HIV) while on PrEP may become a concern, and clinicians should continue to support MSM clients to continue to use condoms, condom-compatible lubrication and practice safer sex. Research is ongoing to assess optimum dosing regimens, potential long-term effects and alternative PrEP medications. Recommendations for the use of PrEP among other at-risk individuals, and the components of these recommendations, will be informed by future evidence.

5. Beyrer, C. (2014). "Strategies to manage the HIV epidemic in gay, bisexual, and other men who have sex with men." Curr Opin Infect Dis 27(1): 1-8.

PURPOSE OF REVIEW: HIV epidemic spread continues among gay, bisexual, and other MSM globally in 2013. These epidemics are occurring in rapidly shifting contexts among

these men, which have important impacts on HIV spread, HIV programs, access to services and human rights. Current HIV prevention strategies are inadequate and are taken to insufficient scale to control HIV spread. RECENT FINDINGS: We reviewed recent reports on epidemiology, HIV prevention advances, human rights, and epidemic disease control among MSM to understand why HIV epidemics among these men remain poorly controlled. Network level factors appear to be critically important for HIV epidemic spread among MSM. The only new prevention technology with evidence for efficacy in this population, daily oral chemoprophylaxis (PrEP), has been little used, particularly in low and middle-income countries. SUMMARY: Much more vigorous prevention efforts are required, including the adaptation and expanded use of PrEP, if we are to reduce new infections among gay, bisexual and other MSM.

6. Chandhiok, N., et al. (2013). "Acceptability of oral and topical HIV chemoprophylaxis in India: implications for at-risk women and men who have sex with men." Sex Health.

With reducing HIV prevalence, India has made gains in containing the epidemic. Yet, unprotected sex and commercial sex work, unprotected anal sex between men and needle sharing among intravenous drug users continue to drive the epidemic. Development of effective, safe and acceptable topical (microbicides) and oral (pre-exposure prophylaxis (PrEP)) chemoprophylaxis could augment the already available tools for HIV prevention. This paper reviews the acceptability of topical microbicides and oral PrEP, in the context of the nature of the HIV epidemic, the sociocultural norms and the acceptability data obtained from studies carried out in India. Overall, men and women have a positive attitude towards the concept and use of microbicide products. Self-perceptions of HIV risk, product attributes, ease and convenience of use during sex, gender norms, the sociocultural context and the potential for undisclosed use were important factors influencing acceptability. A multipurpose product that would simultaneously address women's contraceptive and disease prevention needs would be devoid of the stigma attached to an anti-HIV product and may be more acceptable. Limited information on the acceptability of oral PrEP amongst high-risk groups merits further research, including carrying out demonstration projects for program introduction.

7. Duncan, S. and C. Duncan (2012). "Are we Prepared? Quality of information available to patients in the UK about PREP on the internet." Journal of the International AIDS Society 15: 133.

Professional bodies in the UK (BASHH/BHIVA) do not currently recommend pre-exposure prophylaxis (PREP) to prevent HIV acquisition for men who have sex with men (MSM) [1]. Conversely, although Federal Drug Administration approval is awaited, the Centers for Disease Control (CDC) have issued clinicians in the USA with interim guidance to facilitate PREP prescriptions [2]. Increasingly patients search the internet for information on HIV treatment, but disparate international policy can lead to confusing patient messages. This study was conducted to systematically assess the quality of internet information available to patients in the UK about PREP. More than 90% of

internet searches in the UK are performed using 'Google.co.uk' and 'Bing' [3]. Using pre-specified criteria, we reviewed the first 100 hits retrieved from each search engine when the following searches were performed: [nullHIV pre-exposure prophylaxisnull]; [nullHIV PREPnull]; [nullHIV PREP guidelinesnull]; [nullHIV PREP guidelines UKnull]; [nulltruvada prophylaxis HIVnull]. Of 172 unique websites identified, 124 websites were active at the time of the review (July 2012). 33 websites were links to academic journals including commentaries and clinical trials, not intended to specifically provide patient information; 5 were internet portals directing users to alternative sites and 10 websites contained no information about PREP. Of the remaining 76 websites, 28 were written by medical professionals and 48 were written by journalists, where 7/48 (15%) were individual blogs. 64/76 (84%) contained a definition of PREP; 63/76 (83%) discussed the rationale and 58/76 (76%) reported efficacy data. Advantages and disadvantages of PREP were presented in 56/76 (74%) and 41/76 (54%) of websites respectively. Only 21/76 (28%) of sites referenced existing national guidelines (CDC/BASHH). A minority of sites described the current clinical practice in the UK (7/76, 9%) with an even smaller number presenting the contrast in clinical stance between the CDC and BASHH/BHIVA (3/76, 4%). The use of PREP is evolving, and the internet is an important patient resource. However, current clinical practice in the UK is seldom described in accessible websites. Avoiding ad hoc and unsupervised use of PREP is crucial to prevent future drug resistance and risky sexual behaviour. More should be done to engage at-risk groups and ensure patients in the UK have access to comprehensive information including the current UK PREP professional guidance.

8. Fioreck, K. (2013). "Cultural Conundrums: The Ethics of Epidemiology and the Problems of Population in Implementing Pre-Exposure Prophylaxis." Dev World Bioeth.

The impending implementation of pre-exposure prophylaxis (PrEP) has prompted complicated bioethical and public health ethics concerns regarding the moral distribution of antiretroviral medications (ARVs) to ostensibly healthy populations as a form of HIV prevention when millions of HIV-positive people still lack access to ARVs globally. This manuscript argues that these questions are, in part, concerns over the ethics of the knowledge production practices of epidemiology. Questions of distribution, and their attendant cost-benefit calculations, will rely on a number of presupposed, and therefore, normatively cultural assumptions within the science of epidemiology specifically regarding the ability of epidemiologic surveillance to produce accurate maps of HIV throughout national populations. Specifically, ethical questions around PrEP will focus on who should receive ARVs given the fact that global demand will far exceed supply. Given that sexual transmission is one of the main modes of HIV transmission, these questions of 'who' are inextricably linked to knowledge about sexual personhood. As a result, the ethics of epidemiology, and how the epidemiology of HIV in particular conceives, classifies and constructs sexual populations will become a critical point of reflection and contestation for bioethicists, health activists, physicians, nurses, and researchers in the multi-disciplinary field of global health. This paper examines how

cultural conundrums within the fields of bioethics and public health ethics are directly implicated within the ethics of PrEP, by analyzing the problems of population inaugurated by the construction of the men who have sex with men (MSM) epidemiologic category in the specific national context of South Africa.

9. Hosek, S. G., et al. (2013). "Integrating Behavioral HIV Interventions into Biomedical Prevention Trials with Youth: Lessons from Chicago's Project PrEPare." J HIV AIDS Soc Serv 12(3-4).

On the heels of several trials demonstrating the efficacy of pre-exposure prophylaxis (PrEP) and the recent approval by the FDA of the supplemental indication for Truvada as PrEP, researchers, advocates, and community providers are calling for the investigation of implementation strategies that combine behavioral interventions with biomedical prevention. This paper describes the modification and integration of an evidence-based group-level intervention into a small PrEP pilot trial with young men who have sex with men (YMSM). The behavioral intervention as well as ongoing risk reduction counseling sessions were found to be highly acceptable among a sample of racially diverse YMSM.

10. Liu, A., et al. (2012). "The spectrum of engagement in HIV prevention: Proposal for a pre-exposure prophylaxis (PREP) cascade." Journal of the International Association of Physicians in AIDS Care 11(6): 393.

Introduction: Pre-exposure prophylaxis (PrEP) is a rapidly emerging HIV prevention strategy. Following release of iPrEx results, several demonstration projects are being planned to evaluate PrEP delivery in real-world settings. While steps in the spectrum of engagement in HIV care have been defined and used to identify gaps and build interventions to improve health on the individual and population level, a similar framework has not been developed for daily PrEP in HIV-uninfected populations. We propose a cascade of PrEP delivery as a model to define metrics of success in PrEP implementation programs. Description: Adapting models of engagement in HIV care, we define 6 key steps in the cascade of PrEP delivery: 1) identification of potential PrEP candidates (including confirmed HIV-negative individuals who meet behavioral eligibility criteria); 2) individual decision to adopt PrEP as a prevention strategy; 3) successful referral and linkage of individuals from the testing site to the PrEP program; 4) initiation of PrEP among those assessed to be medically and behaviorally eligible; 5) retention in the PrEP program over time; and 6) maintaining adherence and persistence to PrEP medication to achieve a detectable drug level associated with protection. Clinic-based metrics (steps 4-6) can be obtained through data collected at the PrEP delivery site, while measures on identification, interest, and referrals (steps 1-3) may require use of existing and novel outreach and surveillance strategies (eg, use of electronic health records). Lessons Learned: The PrEP cascade provides a framework for understanding individual and structural factors which may determine the overall public health impact of PrEP programs. These metrics can evaluate the relative magnitude of gaps at each stage of PrEP delivery and whether gaps vary by key populations (eg, men of color, young men

who have sex with men); findings may signify the need for targeted interventions to achieve equity in PrEP outcomes across diverse populations. Recommendations: We suggest use of a cascade of PrEP delivery to plan data collection in upcoming PrEP demonstration projects and to evaluate their success. Use of common metrics will also allow for meaningful comparisons across different PrEP programs. Once populated with actual data from these projects, modeling can be conducted to evaluate the impact of potential interventions targeting various stages of the PrEP cascade with the goal of maximizing public health impact.

11. Marcus, J. L., et al. (2013). "No Evidence of Sexual Risk Compensation in the iPrEx Trial of Daily Oral HIV Preexposure Prophylaxis." PLoS One 8(12): e81997.

OBJECTIVE: Preexposure prophylaxis (PrEP) with emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) reduced HIV acquisition in the iPrEx trial among men who have sex with men and transgender women. Self-reported sexual risk behavior decreased overall, but may be affected by reporting bias. We evaluated potential risk compensation using biomarkers of sexual risk behavior. **DESIGN AND METHODS:** Sexual practices were assessed at baseline and quarterly thereafter; perceived treatment assignment and PrEP efficacy beliefs were assessed at 12 weeks. Among participants with ≥ 1 follow-up behavioral assessment, sexual behavior, syphilis, and HIV infection were compared by perceived treatment assignment, actual treatment assignment, and perceived PrEP efficacy. **RESULTS:** Overall, acute HIV infection and syphilis decreased during follow-up. Compared with participants believing they were receiving placebo, participants believing they were receiving FTC/TDF reported more receptive anal intercourse partners prior to initiating drug (12.8 vs. 7.7, $P = 0.04$). Belief in receiving FTC/TDF was not associated with an increase in receptive anal intercourse with no condom (ncRAI) from baseline through follow-up (risk ratio [RR] 0.9, 95% confidence interval [CI]: 0.6-1.4; $P = 0.75$), nor with a decrease after stopping study drug (RR 0.8, 95% CI: 0.5-1.3; $P = 0.46$). In the placebo arm, there were trends toward lower HIV incidence among participants believing they were receiving FTC/TDF (incidence rate ratio [IRR] 0.8, 95% CI: 0.4-1.8; $P = 0.26$) and also believing it was highly effective (IRR 0.5, 95% CI: 0.1-1.7; $P = 0.12$). **CONCLUSIONS:** There was no evidence of sexual risk compensation in iPrEx. Participants believing they were receiving FTC/TDF had more partners prior to initiating drug, suggesting that risk behavior was not a consequence of PrEP use.

12. Mulligan, K., et al. (2013). "Decreases in cholesterol in HIV-seronegative men using emtricitabine/tenofovir pre-exposure prophylaxis: Lipid results of iPrEx." Antiviral Therapy 18: A6-A7.

Objectives: Daily use of oral emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) for pre-exposure prophylaxis (PrEP) decreases HIV acquisition. In HIV treatment, substitution of TDF or FTC/TDF for other antiretrovirals (ARV) or addition of TDF to an ARV regimen generally improves lipids, although decreases in HDL cholesterol have been seen. In a small study in seronegative subjects, 2 weeks' use of TDF decreased total

and LDL cholesterol. We report the effects of prolonged treatment with FTC/TDF on lipids in the absence of HIV infection and other ARV use. **Methods:** In a metabolic substudy of iPrEx, an international randomized trial of PrEP in seronegative men who have sex with men, fasting serum samples for lipid measurements were collected at baseline and 24-week intervals and analysed centrally. Plasma tenofovir (TFV) and FTC levels were measured at weeks 24, 48 and 72, and intracellular TFV and FTC diphosphate were measured at week 24. Net changes in lipids are reported in those randomized to FTC/TDF who had detectable drug levels, compared with those randomized to placebo, as change in FTC/TDF minus change in placebo (95% CI). P-values are based on a linear mixed model. **Results:** 474 participants (237 FTC/TDF, 237 placebo) had baseline lipid measurements, with variable periods of follow-up. At baseline there were no significant differences between randomized groups in mean (plus or minus)sd levels (mg/dl) of triglycerides (103 (plus or minus)59) or total (163 (plus or minus)35), LDL (95 (plus or minus)28), HDL (47 (plus or minus)13), or non-HDL (116 (plus or minus)35) cholesterol. In those randomized to FTC/TDF, drug was detected in 109/185 participants at week 24, 78/153 at week 48, and 42/82 at week 72. At week 24, the FTC/ TDF group with detectable drug had modest but significant decreases in total (-9.2 [-14.5 to -3.8] mg/dl, P=0.001), LDL (-5.8 [-10.4 to -1.2] mg/dl, P=0.01), HDL (-3.6 [-5.5 to -1.8] mg/dl, P<0.001) and non-HDL (-5.4 [-10.5 to -0.4] mg/dl, P=0.03) cholesterol. At week 48, the significant decrease in HDL cholesterol persisted (-4.0 [-6.1 to -1.9] mg/dl, P<0.001), while other values tended to rebound. Triglycerides did not change significantly in any analyses. By week 72 there were no significant treatment differences in any lipid measured. Results were similar by intent-to-treat analysis or when data in those randomized to FTC/TDF with detectable drug were compared to those with no detectable drug instead of placebo. **Conclusions:** In HIV-negative men taking FTC/TDF for PrEP, there were small but statistically significant across-the-board decreases in cholesterol that were most pronounced at week 24 and tended to rebound by week 72. These results demonstrate an effect of FTC/TDF on cholesterol that is independent of HIV suppression.

13. Mutua, G., et al. (2012). "Safety and adherence to intermittent pre-exposure prophylaxis (PrEP) for HIV-1 in African men who have sex with men and female sex workers." PLoS One 7(4): e33103.

BACKGROUND: Little is known about safety of and adherence to intermittent HIV PrEP regimens, which may be more feasible than daily dosing in some settings. We present safety and adherence data from the first trial of an intermittent PrEP regimen among Kenyan men who have sex with men (MSM) and female sex workers (FSW). **METHODS/PRINCIPAL FINDINGS:** MSM and FSW were randomized to daily oral FTC/TDF or placebo, or intermittent (Monday, Friday and within 2 hours after sex, not to exceed one dose per day) oral FTC/TDF or placebo in a 2:1:2:1 ratio; volunteers were followed monthly for 4 months. Adherence was assessed with the medication event monitoring system (MEMS). Sexual activity data were collected via daily text message (SMS) queries and timeline followback interviews with a one-month recall period. Sixty-

seven men and 5 women were randomized into the study. Safety was similar among all groups. Median MEMS adherence rates were 83% [IQR: 63-92] for daily dosing and 55% [IQR:28-78] for fixed intermittent dosing ($p = 0.003$), while adherence to any post-coital doses was 26% [IQR:14-50]. SMS response rates were low, which may have impaired measurement of post-coital dosing adherence. Acceptability of PrEP was high, regardless of dosing regimen. CONCLUSIONS/SIGNIFICANCE: Adherence to intermittent dosing regimens, fixed doses, and in particular coitally-dependent doses, may be more difficult than adherence to daily dosing. However, intermittent dosing may still be appropriate for PrEP if intracellular drug levels, which correlate with prevention of HIV acquisition, can be attained with less than daily dosing and if barriers to adherence can be addressed. Additional drug level data, qualitative data on adherence barriers, and better methods to measure sexual activity are necessary to determine whether adherence to post-coital PrEP could be comparable to more standard regimens. TRIAL REGISTRATION: ClinicalTrials.gov NCT00971230.

14. Pines, H. A., et al. (2013). "Sexual risk trajectories among MSM in the United States: implications for pre-exposure prophylaxis delivery." J Acquir Immune Defic Syndr.

BACKGROUND:: Despite evidence supporting pre-exposure prophylaxis (PrEP) efficacy, there are concerns regarding the feasibility of widespread PrEP implementation among men who have sex with men (MSM). To inform the development of targeted PrEP delivery guidelines, we characterized sexual risk trajectories among HIV-negative MSM. METHODS:: At semiannual visits from 2003-2011, HIV-negative MSM (N=419) participating in the Multicenter AIDS Cohort Study provided data on sexual risk behaviors since their last visit. Based on reported behaviors, participants were assigned a sexual risk behavior (SRB) score at each visit as follows: (0) no insertive or receptive anal intercourse (IAI/RAI), (1) no unprotected IAI/RAI (UIAI/URAI), (2) only UIAI, (3) URAI with 1 HIV-negative partner, (4) condom-serosorting, (5) condom-seropositioning, and (6) no seroadaptive behaviors. Group-based trajectory modeling was used to examine SRB scores (<4 vs. ≥ 4) and identify groups with distinct sexual risk trajectories. RESULTS:: Three sexual risk trajectory groups were identified: low risk (N=264; 63.0%), moderate risk (N=96; 22.9%; mean duration of consecutive high risk intervals approximately 1 year), and high risk (N=59; 14.1%; mean duration of consecutive high risk intervals approximately 2 years). Compared to low risk group membership, high risk group membership was associated with younger age (in years) (adjusted odds ratio [AOR]=0.92, 95% confidence interval [CI]: 0.88-0.96), being White (AOR=3.67, 95% CI: 1.48-9.11), earning an income \geq \$20,000 (AOR=4.98, 95% CI: 2.13-11.64), distress/depression symptoms (CESD \geq 16) (AOR=2.36, 95% CI: 1.14-4.92), and substance use (AOR=2.00, 95% CI: 1.01-3.97). CONCLUSION:: Screening for the socio-demographic and behavioral factors described above may facilitate targeted PrEP delivery during high risk periods among MSM.

15. Smith, D. K., et al. (2011). "Interim guidance: Preexposure prophylaxis for the prevention of HIV infection in men who have sex with men." Morbidity and Mortality Weekly Report 60(3): 65-68.
16. Sugarman, J. and K. H. Mayer (2013). "Ethics and pre-exposure prophylaxis for HIV infection." Journal of Acquired Immune Deficiency Syndromes 63(SUPPL. 2): S135-S139.

There is increasing evidence that the use of antiretroviral agents (ARVs) can be a safe and effective means of preventing HIV infection. In fact, a combination of ARVs, tenofovir-emtricitabine, was recently approved by the US Food and Drug Administration (FDA) for use as "pre-exposure prophylaxis"(PrEP), and the US Centers for Disease Control and other regulatory authorities have issued guidance concerning PrEP use. Clinicians and policy makers are now faced with questions about the appropriateness of prescribing ARVs to healthy persons who are at risk of becoming infected with HIV, and those at risk of being infected must decide whether to use PrEP. In addition, researcher stakeholders must grapple with determining whether and how PrEP should be included in future HIV prevention research. In addressing such issues, it is important that their ethical dimensions are identified. When using PrEP, 2 broad ethical domains are of special relevance: well-being and justice. Ethical issues related to well-being include safety, parameters of use, risk behaviors, resistance, stigma, and diversion. Those related to justice include access and competing priorities. In research involving PrEP, ethical issues include determining the appropriate control arm and whether PrEP should be included as a part of the prevention package provided to all at risk participants. Although PrEP could play an important role in HIV prevention, understanding and addressing the related ethical issues is critical to its safe, effective, and appropriate use in practice and future research. Copyright (copyright) 2013 by Lippincott Williams & Wilkins.

17. Volk, J. E., et al. (2012). "Sexual frequency and planning among at-risk men who have sex with men in the United States: implications for event-based intermittent pre-exposure prophylaxis." J Acquir Immune Defic Syndr 61(1): 112-115.

Intermittent dosing of pre-exposure prophylaxis (iPrEP) has potential to decrease costs, improve adherence, and minimize toxicity. Practical event-based dosing of iPrEP requires men who have sex with men (MSM) to be sexually active on fewer than 3 days each week and plan for sexual activity. MSM who may be most suitable for event-based dosing were older, more educated, more frequently used sexual networking websites, and more often reported that their last sexual encounter was not with a committed partner. A substantial proportion of these MSM endorse high-risk sexual activity, and event-based iPrEP may best target this population.

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