PrEP IN EUROPE

A research briefing

Sex, PrEP and HIV in trans and non-binary people: What does the research tell us?

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This research briefing aims to answer the following questions:

1. How many trans people are there?
2. What are their HIV prevention needs?
3. How many have HIV?
4. How many know about and have used PrEP (pre-exposure prophylaxis)?
5. Does it work for them?
6. Does PrEP work differently for trans people, e.g. due to interactions with hormones?
7. What do trans people think of it?
8. How can we develop trans-friendly PrEP services?

Executive summary

1 How many trans people are there?

This question is important to answer because we cannot gauge trans people's health or other social needs otherwise. Estimates vary widely, depending on local cultural acceptability of trans identity, how the question is asked and whether it is based on external indicators such as use of gender-affirming hormone therapy, or on people's expressed gender identity. Extremes range from one in 10,000 people to one person in 20. A couple of US studies have both found that about one in 250 people may identify as transgender. Jump to read full research.

2 What are the HIV prevention needs of trans people?

It had been assumed that HIV risk and incidence in trans women were high because they essentially had the same risks as gay and bisexual men, i.e. receptive condomless anal intercourse. But there has been increasing recognition in the last few years that trans women are not 'men who have sex with men', not only because they do not identify as such but because their sexual networks and partners are different. This has led to a re-evaluation of exactly how trans women are acquiring HIV, but so far, without more research into the risks of their partners, the answers are unclear. Similar research has not even been done into the sexual networks of trans men. Jump to read full research.

3 How many trans people have HIV?

Early studies suggested that trans women were more vulnerable to HIV than almost any other group with localised prevalences in the region of 65%. However, these figures may have been so high because they concentrated on more disadvantaged and/or visible groups such as street sex workers. More recent studies tend to find prevalences somewhat higher than those in gay and bisexual men but not as high as earlier estimates – a global synthesis of studies found a pooled estimate of 19%. A later US synthesis found a prevalence of 14%, but this was strongly skewed by race and underlying inequalities, with Black trans women having an HIV prevalence of 44%. As for trans men, this varies by whether they are gay-identified or not, but prevalence tends to be in the region of 1-3%, higher than in the general population but not as high as in cis gay and bisexual men. Jump to read full research.

4 How many trans people know about and have used PrEP?

As in estimates of population size and HIV prevalence, this depends on the cultural position and visibility of trans people. But early PrEP studies found either very low participation of trans people or, if there was participation, low adherence. In a country with fairly high visibility, Brazil, the proportion of participants in PrEP studies targeted at 'men who have sex with men' who were in fact trans women has fairly consistently been around 5%. Studies of individual clinic programmes have tended to find very low knowledge and PrEP use until trans-specific and trans-friendly services have been set up. Even in San Francisco in 2018, possibly the city with the highest knowledge of and use of PrEP in the world, although 80% of trans women had heard of PrEP, only 12% had used it (a much lower rate than among cis gay men). Knowledge of PrEP in trans men tends to be slightly higher than in trans women. Use in some studies is lower, possibly because of perception of lower risk, but the most recent US study found the same level of use as in a separate survey of trans women. Jump to read full research.

5 Does PrEP work for trans people?

This is a surprisingly difficult question to ask, largely because recent PrEP studies have not included enough trans people to establish an answer. There is no evidence that daily PrEP should work any less well for trans women or men (also see the next section). Early studies such as iPrEx featured very low adherence in trans participants so efficacy results were not statistically significant, though there were no infections in trans participants with evidence of more than four-days-a-week dosing. Studies either recently completed (e.g. HPTN083, IMPACT) or underway (e.g. LITE, STAY) may provide more data. Jump to read full research.

6 Does PrEP work differently for trans people, e.g. due to interactions with hormones?

Interaction between gender-affirming hormone therapy and antiretroviral medications has often been expressed by trans people as a concern and a reason to avoid antiretroviral therapy or PrEP. Several well-designed studies have been conducted to explore this issue. In summary, there is no evidence that the drugs in oral PrEP either raise or lower levels of gender-affirming hormones. When it comes to the effect of gender-affirming hormone therapy on PrEP, there is consistent evidence that it may reduce the levels of tenofovir by 10-30% in the blood and possibly more in the tissues in trans women. There does not appear to be the same interaction in trans men. This means that the levels of drug achieved in daily PrEP are still well above the levels needed for efficacy. However, more research is needed before event-based dosing can be recommended for either trans women or men. Jump to read full research.

7 What do trans people think of PrEP?

Earlier concerns about interactions with hormones seem, in recent studies, to have become less important and to be replaced by the kind of concerns expressed about PrEP by other groups – cost, side effects, and stigma. Qualitative studies suggest that the factors most likely to deter trans people from seeking PrEP are issues such as misgendering and ignorance of trans-specific sexual behaviour and health issues by medical staff. Factors that encourage use include actual or perceived risk (such as participation in sex work or the likelihood of non-consensual sex) and the encouragement of peers and peer advocates from the trans community. Encouragingly, one recent study from Philadelphia found that it was exactly the members of the trans female community one would most wish to target for PrEP who were beginning to express the most trusting attitude in PrEP and in healthcare providers of it, in a reversal from previous findings. Jump to read full research.

8 How can we develop trans-friendly PrEP services?

Experience from the US, UK, Thailand and Vietnam show that services that attract strong interest in and usage of PrEP by trans people have certain factors in common: a service designed by or in close consultation with trans people themselves; visibly trans members of staff; materials specifically developed, often by the clinic itself, with the risks and interests of trans people in mind; medical protocols designed to preserve the privacy and dignity of trans people; and training of cisgender members of staff in trans issues. Experience has shown that if services with these characteristics are put in place, participation of trans people can suddenly increase. Equally, if only tokenistic efforts are made and the space provided is not conspicuously welcoming and empowering, efforts to engage trans people may fail. Jump to read full research.

What does the research tell us?

1 How many trans people are there?

It might seem inappropriate to start with a discussion of definitions. On the one hand, some would simply say that trans people are those assigned the incorrect gender at birth. But this would be to neglect how individuals, including trans people themselves, think of gender in different cultures: whether it is primarily biological, social or spiritual, for instance. It also excludes people who reject the idea of being a gendered person altogether.

It also neglects the internal, developmental experience of self-definition: of processing a feeling or experience that may be inborn, but then assigning it a name or cognitive category. Even if some children are born with an innate difference between their biological and experienced gender, they have to come to a conclusion about what it means for them, and may do this at an early age, or much later. The same applies to other invisible or concealable differences, such as sexual orientation.

This is important, because research that has concentrated on reporting behaviours (e.g. seeking gender-affirming therapy), as opposed to identity, appears to have drastically underestimated – and concealed – the size of the trans and differently gendered population.

One other aspect of transgender and other differently gendered identities is that as social space, however limited, opens up for people to declare gender identities other than cisgender ones, so the identities that people adopt have proliferated – non-binary, genderqueer, non-gendered and so on. The research has not yet caught up with this and the majority of studies cited below tend only to deal with transgender women, transgender men and sometimes non-binary people or those described as 'other'. When data on non-binary identities are included they are mentioned in this briefing, but many studies still only report data on transgender women and men.

In 2016 Lindsay Collin, Sari Reisner and colleagues conducted a systematic review of 27 international studies estimating the size of the trans population[1]. They found that averaged through these papers, only 6.8 out of 100,000 people in the adult population had received an official diagnosis by a healthcare professional as transgender or transgender-related (e.g. of gender dysphoria). Somewhat more (9.2 out of 100,000) had surgical or hormonal gender-affirming therapy in their records.

Only six of the 27 studies (three in the US, two in Europe (Netherlands and Belgium) and one in Taiwan) reported trans/non-binary *identity* – how people defined themselves. This found population prevalence 50 to 100 times higher. In these studies, 335 people out of 100,000 identified as trans or non-binary – if the Taiwanese study was excluded. It was excluded because it was an outlier, finding that 2200 people out of 100,000 identified as trans or non-binary – 4.5%, or similar to the prevalence of LGBT people reported in some studies. Prevalence for trans men or transmasculine people was even higher, at 7.3%.

Although the authors do not comment on this, the Taiwanese result may indicate that some Asian cultures are more open than others to the existence of people with trans or non-gender-conforming identity. It was also conducted in 5010 first-year university students, who might have been more open to identifying as non-gender conforming.

In the US, one study by Sari Reisner and colleagues found a population prevalence of 330 per 100,000. A later meta-analysis by Esther Meerwijk and Jae Sevelius of the University of California San Francisco, [2] which tried to correct for the heterogeneity of different studies, found a similar estimate of 390 adults per 100,000 – one in 250. This implies there might be one million transgender people in the US alone.

" ... the issue of self-definition affects the questions needed to elucidate the true prevalence of the trans and non-binary population."

As researchers have found out, the issue of self-definition affects the questions needed to elucidate the true prevalence of the trans and non-binary population. Studies in Africa, for instance, have found that many people who might be described in other cultures as trans women or men do not identify as trans, but simply as women or men. For instance a study of men who have sex with men in Senegal[3] found a high proportion – 20% – who identified either as trans women or simply as women.

As a result it is now regarded as good practice in surveys [4] to elucidate trans identity by asking two questions: one, the sex assigned at birth (or whether they are the same sex as that assigned at birth, both with a 'prefer not to say' option), and the other offering choices about their current identity (such as male, female, transgender and 'do not identify as one of the above').

1 Collin L et al. *Prevalence of Transgender Depends on the "Case" Definition: A Systematic Review.* The Journal of Sexual Medicine, 13: 613-626, April 2016. doi: 10.1016/j.jsxm.2016.02.001

2 Meerwijk EL, Sevelius JM. *Transgender Population Size in the United States: a Meta-Regression of Population-Based Probability Samples*. American Journal of Public Health, 107: e1-e8, January 2017. doi: 10.2105/AJPH.2016.303578

3 Mukandavire C et al. *Estimating the contribution of key populations towards the spread of HIV in Dakar, Senegal.* Journal of the International AIDS Society, 21: e25126, July 2018. doi: 10.1002/jia2.25126

4 Lee Badgett MV et al. *Best practices for asking questions to identify transgender and other gender minority respondents on population-based surveys* (GenIUSS). UCLA School of Law Williams Institute, September 2014.

2 What are the HIV prevention needs of trans people?

How much has the size of the trans population to do with HIV risk? The reason it is important is that it could both overestimate or underestimate HIV risk in the trans population and also, by failing to identify them, deprive them of the opportunity to have their HIV prevention and other sexual health and safety needs met.

One particular issue in HIV science has been that trans women have tended to be lumped in with gay and bisexual men, as 'men who have sex with men' (MSM). This category (and analogous ones such as MSW, WSM, etc.) was adopted in the early 1990s as a way of trying to avoid stigmatising particular populations as more likely to have HIV. It was also advocated for by some researchers and activists from countries in the global South who regarded categories such as 'gay' as products of White Western culture.

Primarily, though, MSM was regarded as useful because it was a behavioural category rather than a social identity. HIV didn't care who you were, it proclaimed; all that influenced your risk of getting it was what you did sexually.

Behaviour would also at first sight seem to be a more reliable guide to HIV risk than identity. It was assumed that individuals who have allied social identities, such as trans or gay, might have similar behaviours, and HIV risk as a function of sexual behaviour works for a population whose networks are homogeneous. But the self-concept, potential partners, sexual networks and therefore the HIV risks of trans people are, in the main, quite different from those of gay and bisexual men, even if their risk behaviours (such as being the receptive partner in anal intercourse) are similar. So categorising them alongside gay and bisexual men made them invisible or 'hard to reach' and may have over- or underestimated their HIV risk. To put it simply: trans women aren't men.

This problem was recognised in 2005 study of 'men who have sex with men' in Thailand[5] who were current or former opiate users, by Chris Beyrer of Johns Hopkins and colleagues. We put the term 'men who have sex in men' in quotes because one of the problems the researchers encountered in establishing the HIV risk faced by these men was that most of them actually were *not* MSM.

Thailand has long had a culture that recognises transgender women or Kathoey as a third gender. The authors comment: "Men who have sex with men (MSM) in Thailand, who often do so with transgendered men (sic) known as Kathoey, do not perceive themselves to be engaging in sex between men, and are consequently requiring culturally appropriate targeted prevention."

In fact, in this study, 85% of the cisgender 'MSM' participants had sex exclusively with transgender women. A further 11% had sex exclusively with other cisgender men, and might better be described as gay men. There was very little overlap.

5 Beyrer C et al. *High HIV, hepatitis C and sexual risks among drug-using men who have sex with men in northern Thailand.* AIDS, 19: 1535-40, September 2005. doi: 10.1097/01.aids.0000183122.01583.c7

Although this is about the partners of trans women rather than the women themselves, it is still part of the same problem. Both trans women and their sexual partners require different prevention messages, relevant materials, and friendly and supportive approaches as well as a proper understanding of their sexual and friendship networks if they are to receive effective HIV prevention.

" In 2012, Stefan Baral from Johns Hopkins and colleagues reported the first and so far only systematic review and meta-analysis of HIV prevalence in transgender women."

In this study, as the authors note themselves, "We do not have data on how many men (or women) self-identified as Kathoey. Studies of HIV and other health concerns among Kathoey are urgently needed to assess [their] prevention needs."

This was not due to invisibility. The authors point out that a Google search for Kathoey resulted in more than 25,000 results detailing bars, clubs, dating services and chat rooms, whereas a Medline search "yielded no scientific publications. Although HIV and sexual health research may have overlooked Kathoey, the sex and tourism industries have not." (See aidsmap report here [6].)

A 2019 study from Lima in Peru[7] also found very little overlap between the partners of transgender women and those of gay men. This study found that 97% of the 203 most recent sexual partners of transgender women were cisgender men. These partners reported that their own recent sexual partners were trans women (100%), cis women (55%) and cis men (7%).

Similar research has not been done into the sexual networks of trans men, though there is some evidence that their sexual orientation and choice of partners is quite varied across the gay-to-heterosexual spectrum.

6 Bernard EJ *Drug-using MSM and transgendered Katoey in Thailand require culturally appropriate HIV and Hepatitis C targeted prevention.* aidsmap report, 8 September 2005.

7 Long JE et al. *Little to no overlap of sexual networks of transgender women and MSM in Lima, Peru*. Conference on Retroviruses and Opportunistic Infections, Seattle, poster presentation, abstract no 841, 2019. See also aidsmap report: www.aidsmap.com/news/mar-2019/partners-transgender-women-form-separate-hiv-risk-group-peruvian-study-finds

3 How many trans people have HIV?

It is often assumed that trans people, especially trans women, have extremely high levels of HIV and HIV risk. Surveys early in the HIV epidemic certainly found this: a not untypical example from 1993[8] found that 68% of a group of 53 trans women in Atlanta in the US had HIV. A similar survey from Rome, Italy in 1998[9] found the same proportion, with 68% of trans female sex workers of Brazilian origin having HIV – though it was only 5% in ones of north African origin. This was probably a reflection of HIV prevalence in their home countries, though the study also found an annual incidence (rate of new infections) of 10% in its Latin American participants.

These studies, however, probably sampled specific sub-sections of the trans community, with multiple HIV risks. Most of the Atlanta participants were Black and nearly all of those sex workers, with many of them having histories of crack cocaine and injecting drug use. They also clearly had very poor health care or healthcare engagement, reflected in the fact that 79% of them had syphilis (an easily cured condition). The subjects of the Italian study were all migrants and sex workers, and in addition were already attending an HIV help and prevention centre.

Even the language of the studies reflects that the researchers may have been sampling participants who embodied a certain image of what a transsexual woman was. The Atlanta researchers even referred to its participants as "male transvestite prostitutes", a common way of describing trans women sex workers at the time.

A 2001 survey in San Francisco[10] of 415 trans people was one of the first among trans people to involve respondent-driven sampling, a way of using social networks to find participants rather than simply asking people who were already presenting as clients for HIV prevention needs. It was also one of the first to recruit trans men, who represented 30% of participants. It found an HIV prevalence of 35% in trans women – still very high, and at least 50% higher than that in local gay and bisexual men, but lower than the localised prevalences seen in previous studies. HIV prevalence was only 2% in trans men, despite their reporting high levels of condomless anal sex with both cis men and trans women.

In 2012, Stefan Baral from Johns Hopkins and colleagues reported the first and so far only[11] systematic review and meta-analysis of HIV prevalence in transgender women. (See aidsmap report here [12].)

8 Elifson KW et al. *Male Transvestite Prostitutes and HIV Risk.* American Journal of Public Health, 83: 260-662, February 1993. doi: 10.2105/ajph.83.2.260

9 Spizzichino L et al. *HIV infection among foreign people involved in HIV-related risk activities and attending an HIV reference centre in Rome: the possible role of counselling in reducing risk behaviour.* AIDS Care, 10: 473-80, 1998. doi: 10.1080/09540129850124000

10 Clements-Knolle K et al. *HIV prevalence, risk behaviors, health care use, and mental health status of transgender persons: implications for public health intervention.* American Journal of Public Health, 91: 915-21, June 2001. doi: 10.2105/ajph.91.6.915

11 Baral SD et a. *Worldwide burden of HIV in transgender women: a systematic review and meta-analysis.* The Lancet Infectious Diseases, 13: 214-222, March 2013. doi: 10.1016/S1473-3099(12)70315-8

12 Carter M. *Meta-analysis shows the massive global burden of HIV among transgender women.* aidsmap report, 27 March 2013.

Data were only available for 39 studies from countries with male-predominant HIV epidemics; this included the US, six Asia-Pacific countries, five in Latin America, and three in Europe.

The pooled HIV prevalence was 19.1% in 11,066 transgender women worldwide, with little difference between low- and middle-income countries (17.7%) and high-income countries (21.6%). This indicated that trans women were 49 times more likely to be infected with HIV than the general population in those countries. Estimates for individual countries ranged from ten times more likely in Thailand, to around 200 times more likely in India and Indonesia.

Global prevalence in gay and bisexual men in a similar systematic review published by the same team[13], was only a quarter to a third of this in some regions (Europe, east Asia, Australasia), but roughly the same in others (sub-Saharan Africa, south and south-east Asia, the Americas and the Caribbean). However, the second review included many countries where there had been no large studies of HIV prevalence in trans women, so direct comparisons are difficult.

" Data were only available for 39 studies from countries with male-predominant HIV epidemics;"

In 2018, Jeffrey Becasen and colleagues from the US Centers for Disease Control and Prevention (CDC) conducted a systematic review and meta-analysis[14] of HIV among both trans women and men in the United States, covering 88 studies conducted between 2006 and 2017.

Self-reported HIV infection was 21% in trans women and 1.2% in trans men. Laboratory-confirmed infection was higher than this in trans men – 3.2% – but actually considerably lower in trans women, at 14%. It is unusual to find a population of people where more people believe they have HIV than actually do. The studies appear to have included both trans women who correctly suspected they had HIV infection despite not having tested for HIV and also women who had a fatalistic but incorrect belief that they were at inevitable risk of infection.

One other statistic that stood out, however, was that the overall HIV infection rate among Black trans women was 44%, and in Latina women was 26%, but was less than 7% in White women. This partly reflects the higher prevalence of HIV infection in the US Black population, including in the gay Black population, but the difference between races is more extreme: for instance, in 2018 about 29.5% of US cisgender Black gay men and 10.5% of cisgender White gay men[15] This extreme difference seems, on the face of it, not to have changed since the early 1990s and may reflect the overall health care and social disadvantages of this group.

13 Beyrer C et al. *Global epidemiology of HIV infection in men who have sex with men.* The Lancet, 380: 367-377, July 2012. doi: 10.1016/S0140-6736(12)60821-6

14 Becasen J et al. *Estimating the prevalence of HIV and sexual behaviors among the US transgender population: a systematic review and meta-analysis,* 2006–2017. American Journal of Public Health, 109: e1-e8, January 2019. doi: 10.2105/AJPH.2018.304727

15 Centers for Disease Control and Prevention. *Estimated HIV incidence and prevalence in the United States, 2014–2018.* HIV Surveillance Supplemental Report, 25 (No. 1), 2020.

Trans men – a population less researched, less described and therefore even more poorly served by HIV information than trans women – may have in the past, and as a result, been less aware of their HIV risk. A 2020 study[16] by Nadav Antebi-Gruszka of Hunter College, New York and colleagues of 192 US trans men who defined as gay or bisexual found that 71% of the trans men had ever tested for HIV compared with 88% of cis men. On the other hand, 62% of both cis and trans men had tested in the most recent year, so this awareness gap may have been closed. (See aidsmap report here[17])

" Trans men ..more poorly served by HIV information than trans women – may have in the past, and as a result, been less aware of their HIV risk."

A 2017 CDC review[18] found that of 2351 transgender people diagnosed with HIV between 2009 and 2014, 379 (16%) were trans men. (This figure included 16 men who were non-binary or who identified themselves in other ways, such as genderqueer.)

As for Europe, there has not been a similar regional systematic review of HIV prevalence among trans people. There is data on trans men, though. The huge second EMIS study of gay and bisexual men in 2017 found 1049 men who described themselves either as trans or assigned female at birth among its 125,000 respondents[19]. Some had been assigned male at birth but still considered themselves to be trans men.

HIV prevalence in the majority group of cis men was 10.5%. It was lower in assigned-male-at-birth trans men (7.1%) and very much lower in assigned-female-at-birth men (2%). After adjustment for the confounding effects of age, country and employment status, trans men and assigned-female-at birth men, depending on self-definition, were between 36 and 88% less likely than cisgender, assigned-male-at-birth gay men to have HIV.

16 Antebi-Gruszka N et al. *Sociodemographic and behavioural factors associated with testing for HIV and STIs in a US nationwide sample of transgender men who have sex with men.* Sexually Transmitted Infections, 96: 422-427, June 2020. doi: 10.1136/sextrans-2020-054474

17 Carter M. *Large numbers of transgender MSM have never tested for HIV or STIs*. aidsmap report, 20 August 2020.

18 Clarke H et al. *Diagnosed HIV Infection in Transgender Adults and Adolescents: Results from the National HIV Surveillance System,* 2009-2014. AIDS Behaviour, 21: 2774-2783, September 2017. doi: 10.1007/s10461-016-1656-7

19 Hickson F et al. *Sexual and Mental Health Inequalities across Gender Identity and Sex-Assigned-at-Birth among Men-Who-Have-Sex-with-Men in Europe: Findings from EMIS-2017*. International Journal of Environmental Research and Public Health, 17: 7379, October 2020. doi: 10.3390/ijerph17207379

4 How many trans people know about and have used PrEP?

Participation by trans people in PrEP studies is clearly very dependent on the population sampled, whether there have been positive efforts to find them, and the culture in which they are embedded.

For instance, in one of the earlier PrEP trials in the US for men who have sex with men and transgender women, the PrEP DEMO Project[20], only 14 out of 1075 participants who were assessed for PrEP by the researchers were trans women and only seven out of the 557 who ended up taking it were (1.3%).

In contrast, a post-study review by the researchers of the iPrEx trial[21] the first to demonstrate PrEP efficacy in gay and bisexual men – found (after some re-defining of participants' gender categories), that 339 out of the 2499 participants (14%), in the words of the researchers, "reported one or more characteristics and are classified as transgender women for the purpose of this study".

The majority of participants in the iPrEX trial came from Peru and Ecuador, including from the remote Amazon port of Iquitos. Anthropological studies were undertaken before it even started[22], in order to understand the makeup of the gay and bisexual male and trans female populations in this part of Latin America, with the aim of being as inclusive as possible. As a result, iPrEx recruitment was directed at people with varied genders and preferred sex roles, and at people with different levels of integration with the gay community, from men who identified as gay to men who paid cis male and trans female sex workers but were not gay.

This inclusivity probably made this pioneering study more complex in terms of its logistics and in understanding its result; but it emphasised that the first thing researchers should do when running a prevention or sexual health study in any area is to ensure they understand the population.

Although iPrEx recruited relatively large numbers of trans women, it did not find efficacy for PrEP in them, because adherence in the trans participants was very much lower – for more details see section 5.

In Brazil, another Latin American country with relatively high levels of visibility of the trans population (though also of violence and discrimination against them), the proportion of trans women recruited for trials predominantly of gay and bisexual men has stayed fairly constant at around 5% since the first PrEP Brasil trial in 2015[23].

20 Cohen SE et al. *High Interest in Pre-exposure Prophylaxis Among Men Who Have Sex with Men at Risk for HIV-Infection: Baseline Data from the US PrEP Demonstration Project.* Journal of Acquired Immune Deficiency Syndromes, 68: 439-448, April 2015. doi: 10.1097/QAI.0000000000000479

21 Deutsch MB et al. *HIV pre-exposure prophylaxis in transgender women: a subgroup analysis of the iPrEx trial.* The Lancet HIV, 2: e512-9, December 2015. doi: 10.1016/S2352-3018(15)00206-4

22 Goicochea P et al. *Finding the community in 'community consultation' to prepare for biomedical HIV prevention trials.* Conference on Retroviruses and Opportunistic Infections, Denver, abstract 898, 2006. See aidsmap report: www.aidsmap.com/news/mar-2006/new-directions-hiv-prevention-circumcision-and-prep

23 Hoagland B (presenter Grinsztejn B) *Pre-exposure prophylaxis (PrEP) uptake and associated factors among MSM and TGW in the PrEP Brasil demonstration project.* Eighth IAS Conference on HIV Pathogenesis, Treatment and Prevention, Vancouver, abstract TUAC0205LB, 2015. See aidsmap report: www.aidsmap.com/news/aug-2015/first-brazilian-prep-data-reinforce-evidence-prep-most-used-those-greatest-risk

For example, a study of trans women's knowledge of PrEP in Brazil[24] published in 2018 found that 38% had heard of PrEP, and 78% were willing to try it once informed, but only 6% had taken it.

In the US, there have been signs that, from a very low base, the proportion of both trans men and women who have been included in PrEP studies in the US and who have heard of it in general has been creeping up. The Callen-Lorde sexual health clinic in New York reported that they went from only one to two trans people a month seeking PrEP in 2014 to 15 a month in 2016, with 81% of trans people starting PrEP being women and 19% men (see more from this study in section 8 below).[25]

"Limited engagement with PrEP could not be explained by limited engagement with health care"

Findings from the San Francisco Bay area were presented by Albert Liu[26] at the 2018 HIV Research for Prevention (HIVR4P) conference, which outlined the continuing need for more trans-specific healthcare resources. Despite living in one of the most PrEP-aware cities in the world, only a third of trans women in the study had talked to a healthcare provider about PrEP in the last six months and just 12% were taking it.

Data from 368 HIV-negative trans women were compared with 399 local cisgender gay and bisexual men. Socio-economic disadvantages were far more commonly reported by those in the trans cohort – less education (26% with a college degree versus 69% in the MSM cohort), unemployment (50% vs 26%), income below the poverty limit (71% vs 16%) and homelessness (8% vs 4%).

Nearly all the gay and bisexual men (97%) had heard of PrEP, compared with 79% of the trans women; and 40% of gay and bisexual men had used it, compared with only 12% of the trans women

Limited engagement with PrEP could not be explained by limited engagement with health care – 94% of trans women had seen a healthcare provider in the past year, 93% had health insurance and 74% were currently using hormones. Of note, San Francisco offers universal health care, eliminating barriers to engagement in health care that exist in other parts of the United States.

The other social disparities between the two cohorts might have contributed to trans women's limited engagement with PrEP, but in addition, Liu noted that earlier PrEP marketing activities in the city were directed towards gay men, many trans people express mistrust of the healthcare system, and the intersection of racial and gender-related stigma created multiple other needs that may take precedence over HIV prevention.

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24 Jalil EM et al. *Awareness, Willingness, and PrEP Eligibility Among Transgender Women in Rio de Janeiro, Brazil.* Journal of Acquired Immune Deficiency Syndromes, 79: 445-452, December 2018. doi: 10.1097/QAI.0000000000001839 See aidsmap report: www.aidsmap.com/news/aug-2015/first-brazilian-prep-data-reinforce-evidence-prep-most-used-those-greatest-risk

25 Radix A et al. T*ransgender patients at risk: ensuring access to PrEP in a NYC community health centre.* 21st International AIDS Conference, Durban, abstract WEAC0202, 2016. See programme.aids2016.org/Abstract/Abstract/8512 and aidsmap report: www.aidsmap.com/news/sep-2016/new-york-clinic-outlines-how-improve-uptake-prep-transgender-people

26 Liu A et al. *Substantial Gaps in the PrEP Continuum Among Transwomen Compared With MSM in San Francisco.* HIV Research for Prevention (HIVR4P), Madrid, abstract OA04.06, 2018. See www.professionalabstracts.com/hivr4p2018/iPlanner/#/presentation/231 and aidsmap report: www.aidsmap.com/news/oct-2018/substantial-gaps-prep-care-continuum-trans-women-san-francisco

This is a pattern we have seen throughout the US and indeed worldwide. Trans and non-binary people express knowledge of and interest in PrEP, but uptake and adherence have been low. A 2019 study from Baltimore and Washington DC, for instance, found that although as many as 87% of Black and Latina trans women had heard of PrEP, only 17% had taken it.[27]

" Women engaged in sex work, aged over 24 or who used drugs were more likely to have used PrEP."

As for trans men, a 2019 nationwide survey by Sarit Golub[28] found that of 1808 transgender men, two-thirds of them under 30, 25% of them were at risk of HIV and eligible for PrEP according to CDC criteria. Of these 439 men, 285 had been tested for HIV, 145 knew of PrEP but only 48 (11%) had ever taken it. Another interesting aspect of this study was that this group of trans men were diverse in terms of their declared sexual orientation: the most popular self-designation was queer (38%), but 14% defined as gay, 13% as bisexual and 10% as heterosexual.

A second survey by Harvard's Sari Reisner[29] found that of 857 largely gay-identified trans men who were recruited through Grindr and other gay dating apps, 84% had heard of PrEP and 67% were interested in it. This was actually rather more than the 55% of survey participants whose data indicated that they were at sufficient risk of HIV to need PrEP. Twenty-eight per cent had ever taken PrEP and 18% described themselves as currently taking it, though the survey did not establish adherence levels.

The 55% whose HIV risk indicated a need for PrEP were more likely to identify as gay men; were more likely to use drugs and/or alcohol; scored higher for levels of mental distress; and, in one interesting finding, were more likely to report that they had been stigmatised for being trans by cis male partners.

Lately, the needs of trans women in the US do seem to be being taken more seriously. One signal of this is the ongoing LITE (Leading Innovation for Transgender Women's Health and Empowerment) study [30], which aims to recruit a prospective cohort of 1100 HIV-negative trans women in six urban areas. Participants are offered HIV testing every three months and will be followed for two years.

A 2019 survey [31] of trans women participating in LITE found that of 882 participants, 82% had heard of PrEP but only 27% had ever taken it. Women engaged in sex work, aged over 24 or who used drugs were more likely to have used PrEP.

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27 Poteat T et al. *A gap between willingness and uptake: findings from mixed methods research on HIV prevention among Black and Latina transgender women.* Journal of Acquired Immune Deficiency Syndromes, 82: 131-140, October 2019. doi: 10.1097/QAI.0000000000002112 See aidsmap report: www.aidsmap.com/news/jun-2019/high-awareness-low-uptake-prep-among-black-and-hispanic-transgender-women-us-study

28 Golub SA et al. *High Rates of PrEP Eligibility but Low Rates of PrEP Access Among a National Sample of Transmasculine Individuals.* Journal of Acquired Immune Deficiency Syndromes, 82: e1-e7, September 2019. doi: 10.1097/QAI.0000000000002116 See aidsmap report: www.aidsmap.com/news/sep-2019/first-data-prep-uptake-trans-men

29 Reisner SL et al. *The Pre-Exposure Prophylaxis Cascade in At-Risk Transgender Men Who Have Sex with Men in the United States*.LGBT Health, online ahead of print, February 2021. doi: 10.1089/lgbt.2020.0232

30 Radix *A Lost in Translation: PrEP Implementation and Transgender People.* Tenth International AIDS Society Conference on HIV Science (IAS 2019), Mexico City, session MOPL01, 2019. See aidsmap report: www.aidsmap.com/news/aug-2019/barriers-prep-implementation-transgender-people-worldwide

31 Wirtz A et al. *Pre-exposure prophylaxis (PrEP) indication, use, and adherence among transgender women in eastern and southern US: Interim findings from the LITE cohort, 2018-19.* Tenth International AIDS Society Conference on HIV Science (IAS 2019), Mexico City, abstract TUPEC482, 2019.

Sixteen per cent had used PrEP in the last 30 days, and 11% (90 women) said they had been taking it seven days a week over that time.

It is striking that the figures in the last two US surveys are almost identical for trans men and women: awareness (84% in men, 82% in women), ever taken PrEP (28%, 27%) and recent use (18%, 16%).

Another study for trans people based in San Francisco, the Stay Study[32], ended in December 2020[33]. It was a PrEP demonstration project and recruited 158 individuals. The PrEP was provided as part of comprehensive and affirmative health care for trans and gender non-conforming people. Each of the four study sites specialised in providing trans-specific health care.

One interesting US study published by Paul A. D'Avanzo, Jae Sevelius and colleagues in 2019 may offer indirect evidence that knowledge of PrEP and interest in it is, thanks to community-centred programmes like these, spreading through the trans population – and encouragingly, among those most in need of it. This study recruited 78 trans women, from Philadelphia, to ask them about their opinions of PrEP and interactions with medical carers.

The main analysis[34] looked at contrasts in two distinct clusters among the 43 participants who provided enough demographic information to split them into those two groups. One group (N=26) was predominantly Black (69%), only 23% had received any tertiary education, and high proportions had been homeless and/or had had transactional sex. The other group (N=17) was predominantly White (88%), employed and had had tertiary education (53%).

What was unexpected and encouraging is that the first group reported higher levels of knowledge and interest in PrEP, and more trust in their healthcare providers, than the second group. For instance, on a scale of zero to ten where zero means 'strongly disagree' and ten means 'strongly agree', group one averaged a score of 9/10 in reply to the statement "PrEP is safe and effective for trans women to use" compared with 7/10 in group 2.

One of the biggest differences was in the response to the statement "Doctors don't want to treat people like me", which scored 4/10 in group two but 0/10, i.e. unanimous disagreement, in group one.

"This study is significant…in diverging from what is expected", say the authors. They go on to say that, although it is only a study of a small group in one location, "This study seems to indicate that participating trans women of colour were actually more likely to have heard PrEP messages that had been delivered in gender- affirming, trans-competent health care settings, of which there are notable instances in Philadelphia. This is an important finding."

32 STAY study: see staystudy.org/en/home-2/

33 STAY study: See clinicaltrials.gov/ct2/show/NCT03120936

34 D'Avanzo PA et al. *Medical Mistrust and PrEP Perceptions Among Transgender Women: A Cluster Analysis.* Behavioral Medicine, 45: 143-152, February 2019.

5 Does PrEP work for trans people? Efficacy studies

There is no evidence that *daily* PrEP should work any less well for trans women or men – whether they have front-receptive, rear-receptive or insertive sex – than it does for cis women. (Studies of interactions with gender-affirming hormone therapy, discussed in the next section, suggest that event-driven PrEP – '2-1-1 dosing' or 'on-demand' [35] PrEP – might not be sufficiently effective.)

Nonetheless, we still do not yet have trial data that confirms conclusively that daily PrEP does work. We have to analogise from cisgender people. This is because the few studies that have enough trans participants to demonstrate efficacy are either rather old and their trans participants had low adherence, or are ongoing, or are so recent that efficacy in trans participants has not been analysed.

The 2015 post-study analysis of the 339 trans and non-binary people in the iPrEx study[36] has already been mentioned. This did not find efficacy in its trans female population overall, in contrast to the overall 42% efficacy reported in 2012 that led to PrEP being licensed by the US Food and Drug Administration.

In the study, eleven trans women in the PrEP arm caught HIV and ten in the placebo group – a non-significant difference. However, none of the eleven who acquired HIV in the PrEP arm had detectable levels of PrEP drug in their blood.

None of the minority of trans women with drug levels indicating they took at least four doses a week became infected, as was also the case for gay and bisexual men. Annual HIV incidence among trans women was zero if drug was detected and 4.9% a year if drug was not detected, compared with 0.4% and 2.8%, respectively, among gay and bisexual men. The higher incidence in non-adherent trans women on PrEP was probably due to the fact that their HIV risk was higher: 88% of trans participants told researchers they had had condomless receptive anal sex in the last three months compared with 55% of gay and bisexual men.

However, it was only a minority who were adherent. Drug level monitoring in the later open-label study iPrEx OLE[37], which measured drug levels in all its participants, found that only 18% of the 70 transgender women in that study had drug levels indicating they took four or more doses of *Truvada* a week, compared with 36% of gay and bisexual men.)

35 Gonzalez L *Men, the HIV prevention pill just got easier.* Get the '2-1-1' on what to know. Bhekisisa, 25 February 2019.

36 See Deutsch MB 2015 above and aidsmap report: www.aidsmap.com/news/nov-2015/truvada-prep-appears-work-transgender-women-only-if-used-consistently

37 Grant RM et al. *Results of the iPrEx open-label extension (iPrEx OLE) in men and transgender women who have sex with men: PrEP uptake, sexual practices, and HIV incidence.* 20th International AIDS Conference, Melbourne, abstract TUAC0105LB, 2014. See aidsmap report: www.aidsmap.com/news/nov-2015/truvada-prep-appears-work-transgender-women-only-if-used-consistently

Other studies that could give us an answer in future include the Leading Innovation for Transgender Women's Health and Empowerment (LITE) study,[38] which has already been mentioned. There may also be data from England's IMPACT demonstration study of PrEP, which eventually recruited 1038 participants (4% of the total) who were not gay and bisexual cis men. Just over half of these were trans: 359 trans women, 152 trans men and 35 non-binary people. This may be enough to establish whether PrEP efficacy in those groups differed from efficacy in gay and bisexual men.

Another recently completed study might provide an answer quite soon. This is HPTN 083[39], the study that looked at the efficacy of two-monthly injections of the antiretroviral drug cabotegravir and compared its performance with daily oral PrEP using tenofovir and emtricitabine. This study mainly enrolled gay and bisexual men but 550 of its 4500 participants (12%) were transgender women.

"We still do not yet have trial data that confirms conclusively that daily PrEP does work. We have to analogise from cisgender people."

Overall, the study found that annual HIV incidence in study participants allocated to oral PrEP was 1.21%, but only 0.38% in those receiving cabotegravir – a nearly 70% lower rate of infection.

Given that very few participants missed the clinic appointments at which they received injections, this study has a real chance of establishing the contrasting efficacy of oral versus injectable PrEP in trans women – and in relating that to levels of adherence in those taking oral PrEP.

What it will not be able to do is establish the absolute efficacy of PrEP (injectable and oral) in stopping HIV in trans women, compared to women who did not take PrEP, because there was no placebo arm. However, it will be feasible to estimate what the incidence of HIV would have been on placebo by using so-called 'counterfactuals'. These can be HIV incidence in historical controls before PrEP (from several years ago, adjusted for demographic differences), in geographic controls (from areas not covered by the study), or in a representative selection of trans women from the same community who did not join the trial, paired with similar participants who did.

38 LITE study: see https://www.litestudy.org/

39 Landovitz RJ et al. *HPTN083 interim results: Pre-exposure prophylaxis (PrEP) containing long-acting injectable cabotegravir (CAB-LA) is safe and highly effective for cisgender men and transgender women who have sex with men (MSM,TGW).* 23rd International HIV Conference (AIDS 2020: Virtual), abstract OAXLB0101, 2020. See aidsmap report: www.aidsmap.com/news/jul-2020/injectable-prep-offers-superior-efficacy-oral-prep-clinical-trial

6 Does PrEP work differently for trans people? Drug/hormone interaction studies

One theme that has emerged in talking to trans people about PrEP is their concerns about side effects and drug interactions, and in particular that PrEP drugs might interfere with gender-affirming hormone therapy (GAHT).

In 2016, the Positively Trans survey[40] had already found that HIV-positive trans people prioritised GAHT, care for its side effects, non-discriminatory health care and mental health care all above HIV treatment. In particular, many respondents were reluctant to take antiretroviral therapy (ART) because they were concerned about how hormone therapy might interact with antiretroviral drugs.

A 2017 study[41] also found that transgender women living with HIV were hesitant to use ART because of concerns about drug interactions with feminising hormones. The researchers recruited 87 self-identified trans women from a community-based AIDS service organisation in Los Angeles. Just over half were HIV positive. Sixty-four per cent were currently using GAHT.

Although 57% of HIV-positive women reported concerns about antiretroviral drug and hormone interactions, only 49% had discussed this with a healthcare provider. Forty per cent said this was a reason for not taking ART, hormone therapy or both as directed.

Do HIV-negative trans women have the same concerns regarding PrEP? A 2019 study of trans women's attitudes to PrEP[42] in Los Angeles found that they had similar reservations, though these were less to do with specific concerns about interactions with hormones, and more about PrEP simply adding to the burden of medications they were already taking and making it more likely they got side effects.

One 48-year-old participant put it this way:

"I'm on hormones...and I'm not the tender age of 20 or 30 anymore. I'm just sceptical about all the stuff that I'm putting into my body. I want to live a vibrant, vivacious, stunning life and I don't want anything I don't have. Not today."

A 24-year old Latina participant echoed this:

"I drink sometimes and I just don't want to mix. I take hormone pills, and shots every two weeks. I just didn't want too much drugs."

Because of these concerns, there have been several studies of the interactions between the PrEP drugs tenofovir and emtricitabine and GAHT.

40 Highleyman L *Positively Trans Survey Looks at Lives of Transgender People Living with HIV.* HIVandHepatitis.com, 27 April 2016. See also Positively Trans: transgenderlawcenter.org/programs/positively-trans/research

41 Braun HM et al. (Lake JE presenting) *High levels of treatment non-adherence due to concerns for interactions between antiretroviral therapy and feminizing hormones among transgender women in Los Angeles, CA*. Ninth International AIDS Society Conference on HIV Science, Paris, abstract WEPEB0586, 2017. See aidsmap report: www.aidsmap.com/news/aug-2017/trans-women-wary-antiretroviral-drug-and-hormone-interactions

42 Nieto O et al. *PrEP discontinuation among Latino/a and Black MSM and transgender women: A need for PrEP support services.* PLOS ONE, 15: e0241340, November 2020. doi: 10.1371/journal.pone.0241340

In summary, the evidence we have indicates that PrEP does not seem currently to significantly affect the blood levels of the hormones studied. However, some feminising hormones do seem to produce slightly lower levels of the PrEP drug tenofovir. While these reductions in drug levels are probably not large enough to affect efficacy with reasonable adherence, it is probably wise not to recommend event-based dosing or 'on-demand' PrEP usage for trans women until we have better evidence.

The sparser evidence on trans men has not so far found significant drug interaction effects.

" The sparser evidence on trans men has not so far found significant drug interaction effects."

The evidence is inconclusive partly because GAHTs vary widely and dosing is attuned to the individual. Also, PrEP levels are generally measured in the blood whereas is it the mucosal and intracellular levels of PrEP that are assumed to matter when it comes to efficacy.

(Of note, trans people may also have specific anatomical vulnerabilities that are little studied, including the degree of neovaginal susceptibility to HIV infection in trans women and whether vaginal atrophy in trans men adds to susceptibility.)

One of the first studies done regarding PrEP/hormonal interactions[43] was the iFACT 1 study by the Thai Red Cross HIV clinic, reported in 2018. In this study, tenofovir levels in the blood were reduced by 13% in trans women taking GAHT, but remained above the level shown to confer protection, while tenofovir did not reduce the GAHT levels. (A description of this study can be viewed in PrEP in Europe's webinar on PrEP and the trans community here.[44])

The researchers recruited 20 transgender women who were all using the feminising hormone estradiol plus the testosterone blocker cytoproterone. After three weeks on this, they also started tenofovir/emtricitabine PrEP. Two weeks later, they stopped their GAHT so they were only on PrEP. Three weeks after this, they resumed GAHT and stayed on both GAHT and PrEP until the end of the study seven weeks later.

Drug level measurements were taken at week three (when they had only been taking GAHT), week five (when they had been taking both regimens) and week seven (after two weeks solely taking PrEP) were taken. There was no difference in either estradiol or testosterone concentrations at any time point, but 13% lower tenofovir levels at week five than at week eight. Emtricitabine levels were not measured.

(This study was later supplemented by the iFACT 2 study[45,] which looked at GAHT and ART levels in 20 HIV-positive transgender women. The only difference in regimens from the previous study was that the participants were taking efavirenz as well as tenofovir and emtricitabine.

43 Hiransuthikul A et al. *Drug-drug interactions between the use of feminizing hormone therapy and pre-exposure prophylaxis among transgender women: the iFACT study.* 22nd International AIDS Conference (AIDS 2018), Amsterdam, abstract TUPDX0107LB, 2018. See programme.aids2018.org/Abstract/Abstract/13177 and aidsmap report: www.aidsmap.com/news/jul-2018/prep-does-not-lower-feminising-hormone-level-transgender-women

44 See www.youtube.com/watch?v=NfpH7lfh9ek

45 Hiransuthikul A et al. *Drug-drug Interactions Among Thai Transgender Women Living with Human Immunodeficiency Undergoing Feminizing Hormone Therapy and Antiretroviral Therapy: The iFACT Study.* Clinical Infectious Diseases, 72: 396-402, February 2021. doi:10.1093/cid/ciaa038 See aidsmap report: www.aidsmap.com/news/feb-2020/hiv-drugs-reduce-feminising-hormone-levels-36-hiv-positive-trans-women-thai-study

In this case the reduction in tenofovir was similar, at 17%: but there was also a 36% reduction in levels of estradiol. However, since there were no differences in testosterone levels, it is not clear whether, at least in the short term, this would have any clinical significance.)

" ... blood levels of estradiol, the one hormone all of the transgender women took in one form or another, did not appear to be affected by PrEP"

A small study by Eugenie Shieh and Craig Hendrix of Johns Hopkins University[46] later that year did raise some concerns about the impact of GAHT on PrEP. It found that trans women who are taking both GAHT and PrEP had levels of tenofovir and emtricitabine in their blood that were about 25% lower than those in cisgender men, and levels in rectal tissue cells about 40% lower. Again, blood levels of estradiol, the one hormone all of the transgender women took in one form or another, did not appear to be affected by PrEP.

This study was very small, comparing drug levels in eight trans women versus four cis men. All participants were observed taking PrEP each day for eight days (directly observed therapy). There were as many different hormone regimens as there were transgender subjects. All were taking estradiol or estradiol analogues but in different combinations; as oral pills, and/or intramuscular injections, and/or as the estradiol analogue pill Premarin. In addition, six out of eight were taking the androgen inhibitor spironolactone, and one was also taking progesterone.

The researchers compared PrEP levels between the trans women and cis men in blood, in T-cells and in rectal tissue cells. The difference in tenofovir and emtricitabine levels were roughly equivalent to the difference between someone taking four doses of PrEP a week and someone taking all seven.

In 2020, a study by iPrEX lead investigator Bob Grant and colleagues, the iBREATHe study[47], allayed some of these concerns, and is also the only one to look at interactions in trans men. In this study, 24 trans women and 24 trans men on GAHT were directly observed to take a daily dose of tenofovir/emtricitabine. It was found that the levels of the two PrEP drugs, as measured in dried spots, were similar to the levels seen in similar cis men and women, and were all above efficacious levels.

Again, taking PrEP resulted in no significant changes in GAHT levels in either trans women or men.

All 24 trans women were taking estradiol, oral or injected. Four were also taking progesterone and nine were also taking the testosterone-blocking drug spironolactone. All but one of the 24 trans men were taking testosterone, and all but two of those as injections or implants. Three were also on the androgen moderator finasteride, which moderates undesired side effects of testosterone.

46 Shieh E et al (presenter Hendrix C). *Transgender women on estrogen have significantly lower tenofovir/emtricitabine concentrations during directly observed dosing when compared to cis men.* HIV Research for Prevention conference (HIVR4P), Madrid, abstract OA23.03, 2018. See www.professionalabstracts.com/hivr4p2018/iPlanner/#/presentation/205 and aidsmap report: www.aidsmap.com/news/nov-2018/transgender-women-taking-prep-have-lower-levels-prep-drugs-especially-rectal-tissues

47.Grant RM et al. *Sex Hormone Therapy and Tenofovir Diphosphate Concentration in Dried Blood Spots: Primary Results of the Interactions Between Antiretrovirals And Transgender Hormones Study.* Clinical Infectious Diseases, ciaa1160, August 2020.. doi: 10.1093/cid/ciaa1160 See aidsmap report: See aidsmap report: www.aidsmap.com/news/sep-2020/trans-and-cis-women-and-men-all-have-similar-levels-prep-drugs-blood-directly

Levels of tenofovir were, unexpectedly, highest in cisgender women, and were lowest in transgender women – about 30% lower. The blood levels seen in trans men and cis men were comparable with each other, at around 23% lower than the levels seen in cis women.

The median level of tenofovir seen in trans women at 900 fmol/punch was higher than the average level one would expect from taking at least four days a week of 700mg/punch, but not as high as the level expected from taking six doses a week (1050 fmol/punch). Levels in all other groups were over the six-doses-a-week level.

“ … suggests that PrEP levels in trans men on GAHT do not differ significantly from levels in cis men. ”

The main limitation to the study is that drug concentrations were measured in red blood cells. These can stand being dried out so are convenient to transport and store, but are not the cells infected by HIV. So researchers would need to repeat the same measurements in vaginal and rectal mucosal cells to confirm the findings.

Taken together, these studies show that in HIV-negative trans people at least, there is no evidence that tenofovir/emtricitabine oral PrEP reduces or otherwise impacts on GAHT levels. On the other hand, they also show fairly consistently that PrEP levels observed in trans women are slightly lower than they are in comparable cis men. While this is nowhere near enough to affect the efficacy of daily PrEP, it may be sufficient to suggest that event-driven PrEP (‘2-1-1 dosing’) should not yet be recommended for trans women.

We have less evidence for trans men but what we do have suggests that PrEP levels in trans men on GAHT do not differ significantly from levels in cis men. Although levels do differ from those in cis women, there is no evidence that this could result in any difference in efficacy. However, this question is not completely settled, and it will take further studies, particularly of PrEP levels in mucosal tissue, to answer it.

7 What do trans people think of PrEP?

In baseline data gathered from trans women in six US cities taking part in the LITE study, they described their reasons for not taking PrEP or for discontinuing it. The three most common reasons, at just below 40%, were: dislike of having to take a daily pill; concern about or experience of side effects; and the fear that PrEP might stigmatise them as promiscuous. Thirty per cent thought they were at low risk of HIV; another 30% were concerned that if partners found out they were on PrEP, they would refuse to use condoms. Perhaps reassuringly, few LITE participants said they had specific concerns about interactions with gender-affirming hormones.

In the trans men's survey by Sari Reisner cited in section 4 above[48] about a third of participants were not interested in PrEP. Among these men, by far the most common reason for not being interested was the perception of being at low risk of HIV (cited by 77% of those not interested). Other reasons given were cost (35%), concern about side effects (27%) and concern about reactions with hormones (25%).

" ...One of the issues most often mentioned by interviewees was how they resented being lumped together with cisgender gay and bisexual men, with whom they felt little in common.

In qualitative studies, trans people have emphasised that they are interested in PrEP as long as it is offered as part of a package of health services designed with the needs of trans people in mind, and offered in a trans-friendly environment.

In 2019 Augustus Klein and Sarit Golub of the City University of New York worked with trans researchers to seek the views of 28 trans women and two non-binary interviewees[49]. Half of the participants were on PrEP already, though all were eligible for it under CDC guidelines.

Over half the interviewees were under 30, three-quarters identified as a person of colour, almost all were not in the workforce, most had an annual income below $12,000 and almost all were publicly insured.

One of the issues most often mentioned by interviewees was how they resented being lumped together with cisgender gay and bisexual men, with whom they felt little in common. This forced them to get health care in a system that did not affirm their gender identity. One interviewee explained:

"I went to a city sexual clinic and they gave me a piece of paper that said, are you a man who has sex with men/trans woman. And I literally looked at them and was like: 'Are you comparing a man and a trans woman on this piece of paper? This is completely ridiculous.' When you put man and trans woman together, you're already saying that these two [are] comparable...a lot people are not going to want to answer these kinds of questions because, if you answer it, you may be validating this transphobic thing. But if you don't answer it, you might not get the care that you need."

48 See Reisner SL 2021 above.

49 Klein A & Golub S. *Increasing Access to Pre-Exposure Prophylaxis Among Transgender Women and Transfeminine Nonbinary Individuals*. AIDS Patient Care and STDs, 33: 262-269, June 2019. doi: 10.1089/apc.2019.0049 See aidsmap report: www.aidsmap.com/news/jun-2019/transgender-women-tell-researchers-how-increase-uptake-prep-their-community

Questions people were asked about sexual risks did not accurately reflect their sexual activities or the context in which they are having sex:

"Like no doctor has ever really asked me if my dick still worked or if I could top with it, unless I brought something up about it."

HIV prevention interventions must acknowledge and address the structural factors associated with HIV risk in this community. A lack of housing and employment opportunities, for instance, forced people into situations (such as sex work) where survival was intrinsically linked to HIV risk. Being vulnerable to sexual assault was also described as a fact of life:

" Messaging needs to be transgender inclusive and gender affirming, "

"Not every time I have had sex have I been a willing participant. I've been sexually assaulted a few times. I mean, definitely when it happened, one of the first things I worried about was HIV. Now, at least I'm taking PrEP, if, god forbid, it [being sexually assaulted] were to happen again, at least it's one less thing for me to really worry about. You know, because the chance is so miniscule [of getting HIV], if you're taking your PrEP."

Messaging needs to be transgender inclusive and gender affirming, with imagery reflecting diversity within the transgender community:

"A lot of the trans people that they've been using in a lot of these campaigns and stuff have been. Quote, unquote, for lack of a better term, more passable. And that's not always the reality with our community, and that's not always what our community looks like."

Healthcare providers need to be actively engaged with patients, having ongoing (rather than one-off) discussions about PrEP. These should occur within a person's ongoing gender-affirming health care, rather than requiring people to seek out PrEP-related care specifically.

"When I was asked – I mean I knew what PrEP was, I'd heard of it, but I was just asked if I was interested in PrEP. And so, if I didn't know what it was, I would've just said no, not really knowing what I was being asked."

Participants said that learning about PrEP from someone they trusted, with whom they had established relationship, and who they felt was 'like' them, opened the door to seek out more information and ultimately get on PrEP.

"While I was considering if I wanted to take it or not – I was seeing people who were on it talk about it. Like friends of mine who were on it. So, encouraging people to talk about being on it [PrEP] is important."

This is typical of social science studies. But when it comes to exploring the complexity of decisions trans people have to make to achieve a stable and serene sense of self, and a life that minimises personal risk, including but not restricted to sexual health risk, and maximises self-realisation, there is no substitute for their personal stories.

Just a couple of accounts from the UK include this short film about the experience of transgender people considering and taking PrEP [50], and this celebration of the sense of freedom PrEP brought to a non-binary member of the UK's PrEP advocacy group PrEPster [51].

50 See www.youtube.com/watch?v=J-sceHHpzPo

51 Singer D. *Why PrEP Matters For Trans People Like Me.* Huffington Post, 2 May 2019

8 How can we develop trans-friendly PrEP services?

How can we design trans-friendly sexual health and PrEP services that will meet the needs of one of the populations most vulnerable to HIV?

At AIDS 2016, Asa Radix of the Callen-Lorde Community Health Centre in New York[52] outlined the dedicated efforts centres like his needed to make to engage transgender women and men. Callen-Lorde is the largest specialist provider of health services for the LGBT+ communities in New York. It has over 15,000 clients, including 3095 trans men and women. Over half of its trans clients are Black or Latinx, one third do not have health insurance and 15% are homeless or unstably housed.

Demand for PrEP has been high overall, Radix said, but uptake by transgender clients took some time to develop. By the time he spoke, 195 of the 2324 individuals who had ever received PrEP from the centre were transgender. Radix outlined the steps necessary for a clinic to achieve this.

As well as there being a dearth of trans-inclusive PrEP information materials and concerns about potential interactions between PrEP and GAHT, many trans people had a general mistrust of medicine, due to their experiences of hostile or uninformed providers.

It was vital to create a safe and supportive environment. The registration forms and electronic patient records at the clinic were redesigned to be trans-inclusive. They can accommodate differences between the sex an individual was assigned at birth, the sex listed on their health insurance documents and the gender the person currently identifies with. Patients are asked to specify the name and pronoun they would like to be used.

"Many people underestimate how very difficult it is when you come into a health centre and you are being misgendered," said Asa Radix. "Calling people by a gender they don't identify with, or using *Ma'am or Sir i*ncorrectly, can be incredibly uncomfortable for people."

An emphasis is put on respecting privacy and confidentiality. Staff at the in-house pharmacy are familiar with trans issues. At commercial pharmacies, staff may be disconcerted by apparent discrepancies between a person's official documents and their current gender identity.

Trans-identified staff have been recruited, are visible to clients, and are involved in developing clinic policies. A community advisory board allows trans advocates and service users to provide input. Resources including positive and inclusive images of trans people were developed specifically by Callen-Lorde.

As some clients found physical examinations traumatic or exposing, self-swabbing kits for STIs are offered and have had a dramatic impact on the uptake of STI screening. Self-swabbing has also reduced the burden on clinical staff.

Dedicated staff help clients with health insurance and coverage issues. This kind of support has been important for a wide range of clients seeking PrEP, including trans people. Uninsured patients are linked to medication assistance programmes or low/no cost health insurance plans. Medical staff had to be trained on these issues.

52 See Radix A 2016 above.

The services at Callen-Lorde are just one example of trans-friendly clinics being set up in a number of countries to meet the needs of the trans community. In the UK, consideration of a trans-specific HIV and sexual health resource started as far back as 2012, resulting in CliniQ, the UK's first sexual health clinic for trans people[53]. This is now located at King's College Hospital in south London and has been followed by other resources such as the 56T clinic[54] at London's 56 Dean Street sexual health clinic and ClinicT at the Lawson Unit in Brighton[55].

Trans resources developed outside the high-income world include the Tangerine Clinic in Bangkok, Thailand, set up by the Thai Red Cross Society AIDS Research Centre in 2015. It was the first clinic in Asia to target services exclusively to the transgender community. Within two years, Tangerine had provided services to 972 trans women and 212 trans men.

In an interview with *Spotlight*, Tangerine clinic staff said that its planning involved meaningful participation of the transgender communities from the start. The clinic's transgender staff have proven essential to ensuring that the clinic continues to offer accessible, transgender-friendly services and remains in close contact with the needs of the community it serves.

" Tangerine increased the visibility of transgender people in the Thai National AIDS Program "

There was an active programme of knowledge exchange between the trans community and health professionals who were not themselves trans. From the start, Tangerine integrated gender-affirmative hormone services and sexual health services and not kept them separate. This had been effective in increasing access to and retention in HIV testing and PrEP services.

Data from Tangerine increased the visibility of transgender people in the Thai National AIDS Program and was used to develop and refine health services and policy for transgender people in Thailand.

Tangerine's model was influential in setting up a successful PrEP programme for trans people in another south-east Asian country, Vietnam[56]. HIV prevalence in transgender women is 18% in Vietnam. Modelling in 2013-14 showed that targeting HIV prevention at certain key groups[57] including trans women could drastically cut HIV transmission generally. Partly due to this, the Vietnamese government and international funders supported the establishment of key population-led clinics for key affected populations. The model is that leaders from the key affected populations are given national and international funding and managerial guidance to set up 'one-stop-shop clinics' providing a range of services. In line with the country's 'socialist-oriented market economy'[58] philosophy, they largely own and run their own initiatives.

53 cliniQ: see cliniq.org.uk/

54 56T: see dean.st/trans-non-binary/

55 ClinicT: see brightonsexualhealth.com/service/clinic-t/

56 Green K et al. *Trans-forming PrEP in Vietnam: rethinking service delivery to enhance access among transgender women.* 23rd International AIDS Conference, abstract OAD0603, 2020. See aidsmap report: www.aidsmap.com/news/jul-2020/community-run-prep-programme-vietnamese-trans-women-sees-hundredfold-rise-users-three

57 Kato M et al. *The potential impact of expanding antiretroviral therapy and combination prevention in Vietnam: towards elimination of HIV transmission.* Journal of Acquired Immune Deficiency Syndromes, 63: e142-9, August 2013. doi: 10.1097/QAI.0b013e31829b535b See aidsmap report: www.aidsmap.com/news/jun-2013/combination-prevention-could-eliminate-hiv-transmissions-vietnam-model-projects

58 See en.wikipedia.org/wiki/Socialist-oriented_market_economy

There are currently 12 one-stop shop clinics in Vietnam, including five – four community-owned ones in Ho Chi Minh City and Hanoi, and one trans-friendly private clinic in Hanoi – which offer community-run services for transgender women.

Although PrEP has been available through these clinics since March 2017, it was realised early on that PrEP needed better promotion among the transgender population. Despite high awareness of HIV risk among trans women, enrolment was much lower than among gay and bisexual men, and had plateaued.

At this point transgender women leaders, key population-clinic staff and the PATH Healthy Markets Team formulated a new approach to PrEP provision for transgender women.

Community services had found that fear both of side effects in general, but also specifically of PrEP interfering with levels of gender-affirming hormones, were deterring many trans women from starting PrEP. The approach therefore was to directly address these concerns in written information, peer PrEP counselling given online and in-person by transgender peer PrEP experts, and small networking and engagement events. The Tangerine Clinic[59] was also invited to provide training for PrEP clinic staff and community providers in transgender-competent care.

" ...promising results are being used to inform the development of national guidelines in Vietnam "

Additional services were added: routine hormone-level testing and advice on safe and effective use; referral to gender-affirming surgery; and substance use and mental health assessment and support. Transgender women are employed by the clinics as lay health workers and provide dedicated counselling and support, in collaboration with four existing NGOs for trans people.

This resulted in an immediate increase in PrEP initiations to around 20 enrolments per month in the first quarter of 2019, and a near-doubling of cumulative enrolments every six months, from 132 in the second quarter of 2019, to 266 in the fourth quarter, to 409 up to March 2020.

Retention in the programme, which was lagging behind a similar programme for gay and bisexual men until last year, had by 2020 exceeded that in the gay men's programme, with 98% of clients returning for their quarterly PrEP refills.

These improvements show that transgender-competent care and addressing underlying concerns about PrEP are essential for accessible services. Transgender people needed to be engaged as service providers, preferably in clinics that were transgender-owned and led.

These promising results are being used to inform the development of national guidelines in Vietnam on HIV service delivery and expansion among transgender populations.

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59 Mahavongtrakul M. Transitioning healthcare. Bangkok Post, 5 January 2016.