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## How has HIV Pre-Exposure Prophylaxis (PrEP) changed sex? A review of research in a new era of bio-behavioral HIV prevention

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### Abstract

In 2012, the U.S. FDA approved the first drug for use as HIV Pre-Exposure Prophylaxis (PrEP), which is nearly 99% effective when taken as a prescribed. Although the manifest function of PrEP is to prevent HIV infection in the event of exposure, the drug has also had a significant impact on various facets of sexuality. In this review, we focus on research that emerged in the near decade since PrEP’s approval, with a specific focus on the ways in which different elements of sex and sexuality have been impacted for gay, bisexual, and other men who have sex with men (GBMSM), cisgender women, and transgender individuals. We highlight evidence showing how PrEP has enhanced sexual self-esteem, improved sexual pleasure, reduced sexual anxiety, and has increased sexual agency for those taking it. For many, PrEP also serves as a gateway to improve routine health and increase sexual healthcare utilization. Additionally, we review the question of whether PrEP is associated with increased sexual risk taking (i.e., risk compensation), and note that, although some data are mixed, PrEP is not intended as an intervention to reduce condomless anal sex or STIs: it aims to prevent HIV. Finally, our review highlights that, although the volume of research on PrEP among GBMSM is robust, it is underdeveloped for cisgender women and transgender populations and insufficient for inclusion in such a review for cisgender heterosexual men was. PrEP research with these populations is an important direction for future research. Finally, from 2012 to 2019, a single PrEP formulation and delivery method was FDA approved (oral emtricitabine/tenofovir disoproxil fumarate). As additional drug formulations (e.g., emtricitabine/tenofovir alafenamide) and delivery methods (e.g., microbicides, vaginal ring, injectable) come to market, it will be important to examine how these, too, impact the spectrum of sexuality.

### Keywords

Pre-Exposure Prophylaxis; sexual behavior; sexual satisfaction; sexual anxiety; gay and bisexual men; transgender; women

## Introduction

After a many-year plateau in HIV incidence, in 2012, the U.S. Food and Drug Administration (FDA) approved the use of a once-daily pill containing emtricitabine/tenofovir disoproxil fumarate (brand name Truvada) for use as HIV pre-exposure prophylaxis (PrEP). When taken as prescribed, PrEP has upwards of 99% efficacy at preventing HIV (Anderson et al., 2012; Donnell et al., 2014; Spinner et al., 2016). Although PrEP has been available for nearly a decade, the *anticipation* of PrEP's approval (i.e., during clinical trials) dates back more than 15 years. As a result, there has been an accumulation of research into how we *thought* PrEP would impact individuals' sexual behavior (if effective and approved for use), as well as how it has *actually* impacted sex since its approval.

We recognize that the definition of “sex” includes a wide range of behaviors (e.g., kissing, oral sex, anal sex, vaginal sex) and sexual responses (e.g., orgasm). “Sexuality” can include a wide range of topics ranging from sexual satisfaction, sexual relationships, partner selection practices, sexual anxiety and sexual functioning, sexual self-esteem, sexual communication, and community mores about sexual behavior. In this review, we examine the impact of PrEP on sexual behavior. We note that much of the extant research has taken public health perspectives and, thus, focused on topics such as whether barrier protection (e.g., condoms) was used or changes in behaviors that convey STI risk. Additionally, we focus on other aspects of sexuality given that PrEP has changed the way we think about HIV in relation to sex. PrEP *removes* the act of HIV prevention from the immediacy of the act of sex itself—in contrast to condom use, which intrinsically *ties* that act of HIV prevention to the act of sex. Because of the scope of this journal, the focus of our review will not be to discuss the impact of PrEP on the HIV epidemic (i.e., PrEP's manifest function), but instead we will focus on PrEP's impact on sex and sexuality more broadly (i.e., PrEP's latent functions). Further, given the huge volume of research that now exists on PrEP's *actual* impact since approval, we focus on research published since 2012, and especially on 2018–20, a period during which there has been especially significant research activity regarding PrEP.

Further, we focus primarily on oral Truvada, the formulation of PrEP that was approved by the FDA in 2012. Truvada was the formulation described in nearly all of the PrEP studies over the past decade. A second once-daily pill formulation of PrEP, Descovy, was FDA approved in 2019, expanding the options for consumers, particularly those for whom the earlier version might have resulted in rare and reversible hepatic side effects (FDA, 2019; Gilead, 2019b; Pilkington, Hill, Hughes, Nwokolo, & Pozniak, 2018; Solomon et al., 2014). We also wish to highlight that other formulations of PrEP, as well as different drug delivery methods—including long-acting injectables, vaginal rings, and topical microbicides—are actively being studied in clinical trials (PrEPwatch, 2020c). In fact, one clinical trial of injectable PrEP (HPTN 083) concluded in mid-2020, years earlier than planned, because of the strongly promising initial results (Landovitz et al., 2020). It is possible long-acting injectable PrEP could be available to consumers as early as 2021. Certainly, although none of these other formulations and delivery methods for PrEP have been approved by the FDA for use at the time of writing this review, researchers are already gathering data on hypothetical willingness to use these alternative formulations and methods, as well as

hypothetical impacts on sexual behavior (John, Whitfield, Rendina, Parsons, & Groves, 2018; Parsons, Rendina, Whitfield, & Groves, 2016; Peitzmeier et al., 2017; van der Straten et al., 2016). However, we judged that the collective body of literature on other formulations of PrEP was not yet mature enough for inclusion in this review.

Next, we note that much of the research described in this review was conducted in North America, particularly in the U.S., as well as other high-income, Westernized countries (e.g., Europe, the UK, and Australia). These locations represent the places where PrEP was first approved for use and subsequently supported by government health and insurance systems—thus, increasing access. For example, the European Medicines Agency did not approve Truvada for use as PrEP in European Union (EU) member states until 2016 (Groves & Kumar, 2018). As PrEP access is expanded globally, we believe that research will follow about how it has impacted sexuality in those new regions and cultures.

For this manuscript, we have reviewed literature published predominantly in academic peer-reviewed journals. However, as a means understanding perspectives in context, we also examined published conference abstracts from professional meetings, the so-called ‘grey literature,’ and official policy statements/issue briefs put forward by leading non-governmental organizations. We extracted literature from a wide range of databases, including PubMed, Google Scholar, EBSCO, ProQuest, National Library of Medicine, JSTOR, Medley, and PsycINFO. Search terms included but were not limited to “pre-exposure prophylaxis,” “PrEP,” “Truvada,” “emtricitabine/tenofovir disoproxil fumarate,” and “FTC/TDF.” Our goal in this review is to provide coverage of key themes observed in the literature and to synthesize them to describe the state of this research and its evolution over the past decade. Non-peer reviewed, non-scientific publications were excluded from our review, e.g., blog postings, trending topics on social media, or grassroots conversations about PrEP and sexuality in, for example, private Facebook groups. That said, we wish to direct readers’ attention to the Facebook group, *PrEP Facts*, which had over 21,000 members at the time of this review and which frequently includes rich and candid first-person accounts about the ways in which PrEP has changed sexuality ([www.facebook.com/groups/PrEPFacts](http://www.facebook.com/groups/PrEPFacts)). For the most part, we do not discuss studies on the pharmacogenetics of PrEP in the human body, animal studies, or otherwise clinical (bench) science. We do briefly describe properties of PrEP as they relate to adherence, insofar as adherence is associated with PrEP effectiveness.

Finally, we note that our review includes literature that extends across three key populations—cisgender gay, bisexual, and other men who have sex with men (GBMSM), cisgender women, and transgender populations. Research on PrEP’s impact on sex and sexuality is most expansive for GBMSM and decidedly less so for cisgender women and transgender populations. Nevertheless, we believe that the collective body of work for cisgender women and transgender populations was sufficient for inclusion in this review, and we are committed to focusing on those groups precisely because the field has not done so. A population excluded from our review was heterosexual cisgender men as, unfortunately, there is very little published research. In our conclusion section, we offer recommendations for future research that include a greater understanding of the impact of PrEP on heterosexual cisgender men.

## What is PrEP?

The first formulation of PrEP was approved in 2012, and a second once-daily pill in 2019 in the form of emtricitabine and tenofovir alafenamide (brand name Descovy). Unlike Truvada, which was approved for all adult populations—in 2018, approval was expanded to include adolescents who weighed 77+ pounds (Gilead, 2019b; Hosek et al., 2017)—Descovy was *not* approved for use in persons assigned female at birth who are at risk of acquiring HIV from vaginal sex, because research on its effectiveness had yet to be studied. After significant pushback from researchers and community activists, the manufacturer of Descovy, Gilead Sciences, indicated that it would begin studying the drug in women (Gilead, 2019a).

Both oral formulations of PrEP were FDA approved for once-daily use. Researchers have noted that the Truvada formulation of PrEP has a relatively long half-life and, thus, protective concentrations of the drug can accumulate in the bloodstream with regular adherence. At a concentration of approximately 700 f/mol, individuals are thought to be protected from HIV (Haaland et al., 2017). This corresponds to about four out of seven pills per week (Glidden, Anderson, & Grant, 2016). Although the full pharmacokinetics of both drugs are still under investigation, given the research to date, there is consensus that individuals taking Truvada maintain high levels of protection even with occasional missed doses. There is some evidence that Descovy provides similar protective capabilities although data remain forthcoming.

### 2-1-1 Dosing

Initial recommendations for PrEP noted that it took approximately seven days of daily dosing for blood concentrations of the drug to build up to protective levels in rectal tissue, and about 20 days in vaginal tissue (CDC, 2017; Mascolini, 2014). Thus, individuals beginning PrEP were told to wait for those time windows to elapse before engaging in HIV transmission risk behaviors like condomless anal or vaginal sex. However, further study of the drug has shown that protective levels can be achieved with other dosing strategies. Although not FDA-approved, one dosing strategy with broad consensus as a reasonably safe alternate to daily dosing is “2-1-1” dosing (also known as “on demand,” “intermittent,” “episodic,” or “sex-driven” dosing; Beymer, Holloway, Pulsipher, & Landovitz, 2019; Blackstock & Daskalakis, 2019; Glidden et al., 2016; Molina et al., 2015; Straube, 2019), which involves taking PrEP *around the time* of the potential exposure (i.e., having sex) instead of every day. A 2-1-1 dosing strategy involves taking two pills between 2 and 24 hours *prior* to sex, and then taking one pill the day after sex (24 hours later), and one pill the following day (48 hours later). 2-1-1 dosing has been widely recommended for GBMSM (Blackstock & Daskalakis, 2019; Straube, 2019; WHO, 2019). Because the pharmacologic components of Truvada appear to take longer to protect vaginal tissue than rectal tissue, 2-1-1 dosing has not yet been endorsed for vaginal sex.

Because two doses of PrEP need to be taken between 2–24 hours prior to sex occurring to reach protective levels, the effectiveness of 2-1-1 dosing relies heavily on an individual’s ability to accurately predict ahead of time when sex might occur. There has been limited research on whether individuals can accurately make such a prediction. However, in one

daily diary study of gay and bisexual men, participants were asked every day whether they thought they would have sex the *following* day (Parsons, Rendina, Groves, Ventuneac, & Mustanski, 2015). Subsequently, participants were asked if they had engaged in sex *that* day. Thus, the researchers were able to capture the extent to which participant's predictions (guesses from the day before) were ultimately accurate (on the following day's diary). The study found that participants tended to overestimate their likelihood of having sex (i.e., predict they will have sex the following day, but sex ultimately did not occur). If these participants had been following 2-1-1 dosing, it would mean that they would have taken PrEP in instances when it was not needed. However, that outcome (being protected when protection was not necessary) is better than the reverse—false negative guesses would mean that they were not protected by PrEP. In fact, in this study, although participants tended to overestimate their likelihood of having sex on the following day, they were very accurate in predicting when they would *not* have sex. That is, if a participant estimated a zero percent chance of having sex on the following day, chances were that they were ultimately correct about that (e.g., “I will be spending the weekend visiting my parents, so I know I will not be having sex tomorrow”). It is worth noting that, in this study, the window of prediction was 24 hours into the future, whereas the window for 2-1-1 dosing is as few as *two* hours in the future. It may be that individuals would be significantly better able to forecast future sexual behavior given a shorter time window. However, to our knowledge, there have been no recent empirical studies that test this hypothesis.

### Who Should Take PrEP and Who is Actually Taking it?

Public health officials, activists, and community groups have varied both in which populations they think PrEP is best indicated for, as well as how to develop messages to reach those individuals. The World Health Organization (WHO) has indicated that *all* men who have sex with men should consider PrEP as part of their proverbial HIV prevention toolkit (WHO, 2014). However, the U.S. Centers for Disease Control and Prevention (CDC) has suggested that many fewer men should be taking PrEP, i.e., only about one-in-four GBMSM, who would need to meet a behavioral risk criteria (CDC, 2015; Lopez, 2015). Messaging and recommended criteria for PrEP rollout for other populations has also varied. However, there is consensus that greater risk of potential exposure to HIV would equate to greater benefit from PrEP's protection. Relatedly, access to PrEP has been tied to policies about who is believed to be able to benefit most from PrEP's protection. Since 2012, governments have grappled with decisions regarding which populations to fund prescriptions for PrEP and PrEP-related care. We point readers to [www.PrEPwatch.org](http://www.PrEPwatch.org), which maintains a comprehensive cataloging of how PrEP coverage has expanded across the globe (PrEPWatch, 2020b).

The patent for Truvada expired in 2020. Thus, for the first eight years after its FDA approval, Truvada was only available in the brand name formulation in the U.S. Without insurance, a 30-day supply of the drug could cost more than \$1,500 in the U.S. Although there were some programs to help make PrEP affordable/free—in terms of assistance with co-payments for those with insurance, or drug coverage for those without—gaining affordable access to the drug required navigating complex systems of state and local programs, private and public. This effectively served as administrative barriers to access

to PrEP (Huang, Tao, Smith, & Hoover, 2020; Whitfield, John, Rendina, Groves, & Parsons, 2018). And because younger people and people of color are less likely to have insurance or more likely to be under-insured, they were more likely to face these barriers. Thus, the roll-out of PrEP had the potential to further exacerbate racial disparities in HIV incidence (Calabrese, Krakower, & Mayer, 2017; Goedel et al., 2018; Jenness et al., 2019).

As of April 2020, an estimated 580,000 individuals were taking PrEP worldwide, with the U.S. accounting for approximately 225,000 of that number (PrEPWatch, 2020a). That is a marked increase over the 380,000 estimated to be on PrEP worldwide in October 2018 (Pebody, 2018), the 77,000 estimated to be on PrEP in the U.S. in 2016, and the 8,768 estimated to have been on PrEP in the U.S. in 2012 (AIDS Vu, 2016). PrEP uptake has been highest among GBMSM, although need still outpaces prescriptions (John, Rendina, Groves, & Parsons, 2017; Parsons, Rendina, Lassiter, et al., 2018).

In the following sections, we describe PrEP's impact on three distinct populations: GBMSM, cisgender women, and transgender individuals.

### **How has PrEP changed sex... *for cisgender gay, bisexual, and other men who have sex with men (GBMSM)?***

In conceptualizing the question—"How has PrEP changed sex for GBMSM?"—we must examine potential changes to the behavior of the HIV-negative GBMSM who seek and take PrEP, the HIV-negative GBMSM who do not, and HIV-positive GBMSM. Answering the question solely focused on the experiences of HIV-negative men who seek and take PrEP would be overly focused on the individual experience, and would fail to take into account the changes to the broader sexual context in which partner seeking and sexual behavior occur.

In this section, we review the empirical literature that aims to answer our target question. To do so thoroughly, we first highlight early research about PrEP, describe the demographic and behavioral correlates of GBMSM who are and are not taking PrEP, and then summarize the data on the correlates of PrEP use across a broad range of variables: health knowledge (HIV, STIs, PrEP), patient-provider communication about sex and sexuality, sexual behavior, sexual risk for HIV acquisition, sexual risk for STI acquisition, partner selection, partner dynamics, sexual communication with partners (sexual desires, sexual risk limits), sexual satisfaction, sexual anxiety, and HIV stigma.

#### **PrEP and Healthcare Knowledge**

As discussed previously, taking PrEP is not a singular behavior. PrEP-taking is a proxy for a host of experiences: persistent engagement with the healthcare system, interactions with health insurance providers, daily (or periodic) pill taking, and more. Thus, in hypothesizing about the potential influence of PrEP on sex for GBMSM, one must assume that the totality of their PrEP experiences plays a role. One potential pathway to changes in sex for GBMSM on PrEP is through increased health knowledge. Knowledge about how to use PrEP as prescribed, and the bounds of its effectiveness even when used properly—accurate or inaccurate—is likely to influence behavior. In one web-based study of 573 sexually active

GBMSM in 2015 (of whom only 2% were taking PrEP), researchers found high levels of accurate functional PrEP knowledge among their participants about PrEP adherence (85%), the need for condom use (93%), and the ongoing risk of STI acquisition even on PrEP (84%), although a much smaller proportion accurately identified PrEP's efficacy (44%) (Kahle, Sullivan, & Stephenson, 2018).

Similar findings have been reported in qualitative studies of PrEP-using GBMSM as well. In one study of 22 GBMSM of various PrEP- and HIV-statuses, participants shared their perspective that knowledge about HIV prevention had increased *because of PrEP*—through regular contact with healthcare providers and diffused through ever-more-common conversations about PrEP and HIV treatment-as-prevention (TasP) in social and sexual contexts (Tester & Hoxmeier, 2020). For many men on PrEP who are accustomed to seeing a healthcare provider once (or less) annually, having at least four healthcare encounters per year is a significant increase. Participants described the near-ubiquitous knowledge among their peers that having anti-HIV medications in their bloodstream, be it for PrEP or HIV treatment, put them “at a very low chance of contracting HIV.” These points are consistent with some of our own qualitative work with 103 PrEP-taking GBM in New York City (Pantalone et al., 2020). Although there was no explicit question about HIV knowledge, our inductive coding process produced a theme, *The men are generally knowledgeable about the science of HIV and behavioral risk reduction*, reflecting the advanced HIV knowledge that the men showcased in answering other questions. They were aware of both recent news stories about PrEP, including research successes (like intermittent dosing) and failures (seroconversions of men prescribed PrEP), as well as generally nuanced knowledge about sexual risk behaviors for HIV. Many participants spoke with confidence about highly nuanced health education content, and provided examples of how they used this knowledge to inform their sexual decision-making. There remains an open question about how much or how accurate knowledge is held by GBMSM on PrEP versus those who have never been on PrEP—that is, what is the additive effect of PrEP on HIV knowledge? In the future, researchers should include this question in study planning.

### PrEP and Sexual Behavior

One of the primary questions raised about PrEP use among GBMSM is whether it increases sexual behavior (i.e., do GBMSM taking PrEP have *more* sex?), changes sexual behavior (i.e., do GBMSM taking PrEP engage in *different* sexual behaviors, or have sex with *different* partners?) and, especially, whether taking PrEP results in risk compensation (i.e., do GBMSM taking PrEP have “riskier” sex (*behaviorally*) because they are protected by PrEP (*biologically*?). Indeed, there has been a range of data from longitudinal cohort studies of PrEP-taking GBMSM that attempt to answer the latter question. Risk compensation in this context is the notion that individuals taking PrEP, emboldened by the knowledge of the medication's protective power, would eschew protective behaviors and that the resulting “behavioral disinhibition” would negate any benefits of PrEP (Hogben & Liddon, 2008). Ostensibly, an individual engaging in PrEP-associated risk compensation would experience no net protection from PrEP or, worse, they would experience increased risk. However, an “increased risk... of what?” is the central question.

In short, the answer to the question about how PrEP has changed sexual behavior is that it depends on which aspects of sexual behavior are being measured. Given that PrEP prescriptions are not indicated for GBMSM who are not sexually active, it would be unlikely that studies would be able to demonstrate increases in sexual activity generally. We will address, below, the few studies that provide data on the part of the question that deals with changes in behavior or partner selection. Indeed, most studies focus on the potential for PrEP-taking to be associated with “risky sex.” Some findings in this area point to PrEP as being an especially helpful HIV prevention strategy for GBMSM who were not using condoms 100% of the time anyway (Golub, Kowalczyk, Weinberger, & Parsons, 2010; Groves, Rendina, Whitfield, Ventuneac, & Parsons, 2016; Groves, Whitfield, Rendina, Ventuneac, & Parsons, 2015). Indeed, from a meta-analysis of 16 PrEP studies that enrolled approximately 5,000 GBMSM, Traeger et al. (2018) found most studies showed evidence of an increase in condomless sex among PrEP users. However, the authors concluded that “[although] changes in self-reported sexual risk behavior varied across study populations, most instances reflected an increased number of different condomless partners or a decrease in overall condom use, rather than a change in [the] proportion of men engaging in any condomless sex... These findings suggest that risk compensation is most prominent among GBMSM already engaging in behaviors that place them at risk of HIV” (p. 684).

A 2019 narrative review published in *The Lancet HIV* (Powell, Gibas, DuBow, & Krakower, 2019) concluded that “[s]tudies of risk compensation during PrEP use have produced mixed results, with some finding no evidence of risk compensation and others finding increases in condomless anal sex and STIs among PrEP users” (p. 28). For example, data from the follow-up period of the IPERGAY trial of on-demand PrEP revealed that, on average, 83% of participants protected themselves by PrEP intake, condom use, or both during the trial—and the investigators observed no increases in risk behavior (Sagaon-Teyssier et al., 2016). There appears to have been a temporality to the pattern of findings observed by Powell and colleagues, such that earlier investigations did not show increases in condomless sex but later studies did. Powell and colleagues (2019) wrote: “... more recent data from open-label and observational studies of PrEP after its efficacy had been demonstrated suggest that GBMSM are more likely to engage in condomless anal sex while using PrEP... There is also evidence that GBMSM have a higher incidence of bacterial STIs after initiating PrEP, even when controlling for increased screening and diagnoses that accompany comprehensive PrEP care... This effect appears to be stronger in later studies, which suggests that PrEP may be having a greater impact on STI diagnoses as awareness of its effectiveness is disseminated” (p. 28).

An increasing number of recent studies echo that there is no straightforward change in reports of GBMSM’s condom use after starting PrEP (e.g., Gafos et al., 2019). Some men note no changes to condom use because they always have used them and plan to continue to do so. Some men report no changes in condom use because they never used them anyway. Some men describe using condoms less because of the increased protection of PrEP. In some relevant qualitative work, participants described their experiences of taking PrEP as leading them to re-consider their decision-making about condom use and clarify their risk limits, whether they changed them post-PrEP (Pantalone et al., 2020). Participants, all of whom were taking PrEP, noted a number of factors that they consider in making decisions



about condom use for themselves or insistence on condom use by their sexual partners. One common sentiment was the insight that taking PrEP allows them to be in control of their own HIV risk independent from any specific behavior on the part of their partner.

In the Powell and colleagues (2019) review paper and many others, the authors construe condomless anal sex and incident STIs as evidence of risk compensation. Risk compensation is often operationalized from the perspective of behavioral disinhibition, which is only one component of risk compensation: GBMSM start taking PrEP and stop using condoms. However, the purest operationalization of risk compensation would be to measure whether, despite PrEP use, *HIV incidence* actually increased. The intent of PrEP is to reduce HIV infections and not to increase condom use or even to decrease STI acquisition. Most studies on risk compensation tend to frame their questions through the latter lenses, though.

In a commentary, Rojas Castro, Delabre, and Molina (2019) share their perspective that the field has mis-applied the concept of risk compensation in that way. They imply that, perhaps, relying on condom use instead of incident infections as a primary outcome reflect pathologizing attitudes about condomless sex akin to debates about contraception in the 1960s (Calabrese & Underhill, 2015)—and may have contributed to the public’s narrative of PrEP being for “sluts” (Pawson & Groves, 2018). Rojas Castro and colleagues wrote, “to accurately claim that a bio-behavioral intervention leads to an increased risk for HIV, a randomized control trial would have to compare a group believing that the intervention would reduce risk with another group believing that the intervention would not reduce risk [but,] because of ethical issues, this design is not a viable option” (p. 51). Although the study did not test that question specifically, in an early PrEP efficacy study of PrEP for GBMSM and transgender women, authors found no association between participants’ beliefs that they were receiving the active drug and increased condomless receptive anal sex (Marcus et al., 2013).

Rojas Castro and colleagues argued that, even if studies were to identify changes in behavior, such as increases in condomless anal sex, those behaviors are unlikely to override the demonstrated high levels of effectiveness of PrEP and, thus, that would not provide genuine evidence of risk compensation (Rojas Castro et al., 2019). Another point made by these authors and others is that there is ample evidence to suggest that condom use has been decreasing among GBMSM since long before the widespread use of PrEP and, thus, it cannot be attributed solely to risk compensation for PrEP-taking (Paz-Bailey, Mendoza, et al., 2016). Various metrics of decreasing condom use have been observed, including longer-term increases in the number of partners with whom GBMSM were engaging in condomless anal sex (e.g., Traeger et al., 2018), and decreases in the proportion of participants reporting no condomless anal sex (e.g., Chen, Snowden, McFarland, & Raymond, 2016)—all predating PrEP. The latter finding comes from the National Health Behavior Survey: the proportion of GBMSM reporting no condomless anal sex partners gradually dropped from a high of 61% in 2004 to a low of 40% in 2014, and consistent condom use decreased gradually from a high of 37% in 2004 to a low of 18% in 2014. Given the push for PrEP to be prescribed to GBMSM who were already engaging in condomless anal sex, cross-sectional investigations are especially poorly suited to risk compensation-type research questions. Indeed, some authors argue that, to understand the

true impact of risk compensation, it would take a community-level approach (e.g., Holt & Murphy, 2017). Holt and Murphy (2017) wrote that “changes in risk perceptions and behavior (could occur) as a result of increased optimism about avoiding HIV among people not directly protected by PrEP” (p. 1568). However, at the community level, given increased PrEP uptake, protection actually appears to have increased, in terms of reductions in HIV incidence in recent years (Sullivan et al., 2018).

In contrast, there are other data that describe the limits to PrEP’s efficacy. Many of the preceding points about risk compensation are predicated on the assumption of adequate adherence and persistence to PrEP for GBMSM taking it. Thus, in the context of suboptimal PrEP adherence, non-use of other risk reduction strategies (like condoms) alongside high-risk behaviors like condomless anal sex increases the possibility of HIV transmission. Taking adherence into consideration, in one longitudinal study of young GBMSM followed for 18 months (Newcomb, Moran, Feinstein, Forscher, & Mustanski, 2018)—some on PrEP and others not on PrEP—the researchers found higher rates of condomless anal sex for partnerships occurring in the context of PrEP use compared to partnerships in which neither man was taking PrEP. Even more concerning, from a public health standpoint, the team found that participants taking PrEP who reported the highest rates of receptive condomless anal sex were *the same men* who reported suboptimal adherence, leaving those men at increased risk of HIV acquisition (compared to the men with greater adherence). Another important element is the demonstrated high rates of PrEP discontinuation. Therefore, it is important to acknowledge that most PrEP users are unlikely to be *lifetime* PrEP users and, thus, PrEP’s protective abilities may be more ephemeral than expected (Koester et al., 2017).

More research is needed that investigates the HIV protective behaviors of former PrEP users, or even current PrEP users who have missed PrEP doses and, thus, risk decreased protection for a limited time. We conducted a qualitative study with PrEP-taking GBMSM to assess their behavioral responses to having missed PrEP doses (Groves et al., 2018). Participants provided potentially contradictory narratives, with some decidedly unscientific rationales for their decisions. About half of the participants described making no changes in their sexual behavior after a missed dose, and about 10% said the decision to adjust their behavior would be contingent upon how many doses they missed. Although most participants endorsed an understanding that the protection from PrEP decreased with multiple missed doses, there was considerable variation in their beliefs about how much protection was retained or lost, as well as the inherent HIV acquisition risk for various sex acts. More research is needed in this area.

Other researchers have made recommendations: “Because risk compensation is exhibited differently among PrEP users, future research should ensure the collection of data on a wider range of sexual behaviors and report within-participant changes, as opposed to proportional changes across the whole cohort... More descriptive reporting of other sexual risk behaviors, such as participation in group sex and the viral load of HIV-positive partners, may further enhance our understanding of individuals’ behavioral responses to PrEP use and how trends in STIs will be affected” (Traeger et al., 2018, p. 684). Further, some providers have expressed a fear that some men who may have become accustomed to not using condoms because of being protected by PrEP will continue to not use condoms even with lapsed

PrEP use (because the pill taking and sexual behavior are not close in time so not as classically linked). It will be essential for researchers to attend to adherence and persistence in accurately elucidating net changes in HIV risk for PrEP-taking GBMSM.

In sum, as Marcus and colleagues (2019) wrote: “Even if risk compensation occurs among PrEP users, we believe clinicians should offer PrEP to patients at risk for HIV infection. Making PrEP more widely available, regardless of patients’ intended condom use, won’t lead to sexual anarchy. Rather, it will promote patients’ sexual health; clinicians’ ability to offer patient-centered, evidence-based care; and public health efforts to combat the ongoing HIV epidemic” (p. 512).

### **PrEP and Sexual Health Outcomes (STIs)**

A significant corollary of questions about PrEP-related risk compensation for GBMSM is whether PrEP increases bacterial, viral, or both types of STIs. Marcus and colleagues (2019) have argued that “STIs are an important public health problem, given their clinical sequelae and the growing threat of multidrug-resistant gonorrhea, and new biomedical and behavioral approaches are needed for addressing this problem” (p. 511). Several questions emerge: do GBMSM have more STIs after vs. before taking PrEP? Or, do PrEP-taking GBMSM have more STIs than non-PrEP-taking GBMSM? As well, this question can be understood in its more nuanced forms, for example, if it does appear that PrEP is associated with incident STIs, is that higher risk genuinely attributable to “risk compensation” (operationalized as more condomless anal sex or a greater number of sex partners) or is it an expectable artifact of the increased STI testing that occurs within required quarterly PrEP visits?

Concerns about PrEP leading to increases in STI diagnoses are not unfounded (Marcus, Katz, Krakower, & Calabrese, 2019, p. 511) and the answer to this latter question is “it depends.” Although some studies have demonstrated increased STI acquisition among PrEP users (Kojima, Davey, & Klausner, 2016), some have not (Parsons, Rendina, Whitfield, & Groves, 2018), and this topic continues to be debated (Harawa et al., 2017). In attempting to examine questions about the potential for PrEP being associated with increased STIs, it is important to acknowledge that PrEP plays a complicated role in the ongoing STI epidemic among GBMSM (Powell et al., 2019). PrEP does not protect against non-HIV STIs and, thus, all sexually active persons taking PrEP remain at the same risk of STI acquisition. STIs are commonly spread by some behaviors that are high risk for HIV transmission, such as condomless anal sex, and some behaviors that are low risk for HIV transmission, such as receiving oral sex. This makes incident STIs a solid reflection of sexual activity overall but a poor proxy for any specific behaviors, like condomless anal sex.

With that said, it is certainly the case that many PrEP studies have shown a high prevalence of STIs. In one study of nearly 1,000 patients in a Northern California health system who began PrEP, during their first year of follow-up, 42% were diagnosed with gonorrhea, chlamydia, or syphilis (Marcus et al., 2016). In a large Australian cohort (comprising 98.5% GBMSM), almost 3,000 PrEP-taking men were followed for one year (Traeger et al., 2019). During that time, 48% of participants were diagnosed with an STI (1,434 chlamydia, 1,242 gonorrhea, 252 syphilis)—and after adjusting for testing frequency, the increase in STI incidence was significant for any STI (adjusted IRR, 1.12 [95% CI, 1.02–1.23]). These are

concerning findings, especially the high rates of gonorrhea—modern strains of which are increasingly medication-resistant and present their own challenge to public health (Unemo & Nicholas, 2012).

These findings also must be understood in context. PrEP is indicated for sexually active individuals who report HIV risk, including multiple partners and condomless anal sex. Thus, seeing high rates of STIs in any cross-sectional sample should be no surprise. This is especially true given that STI incidence has been increasing, and had been increasing for several years before PrEP rollout began, both in the U.S. (e.g., Mayer et al., 2017) and globally (Unemo et al., 2017). We could identify relatively few examples of longitudinal studies that investigated changes in STI incidence from pre- to post-PrEP, or rigorous comparison studies that followed PrEP-taking GBMSM and non-PrEP-taking GBMSM—studies employing the research designs that best answer the core question about STIs. Some evidence against increases in STIs from pre- to post-PrEP comes from a systematic review of 10 trials (Freeborn & Portillo, 2018), in which the authors found high rates of STIs across all groups, and no conclusive evidence that PrEP users increased sexual risk behaviors or experienced a change in STI incidence between baseline and follow-up. An earlier meta-analysis on the association between PrEP use and STIs found that GBMSM enrolled in PrEP studies were between 11 and 45 times more likely to be diagnosed with an STI compared to GBMSM enrolled in non-PrEP-based cohort studies, a finding that perhaps says more about the risk level of research participants in early PrEP studies than it does about PrEP initiation per se (Kojima et al., 2016). Returning to the concerning findings from Traeger et al. (2019), there is some hopeful news in there as well: it was 736 participants (25%) who accounted for 2237 (76%) of all STIs. That is, in their large cohort of PrEP-using GBMSM, the incident STIs were highly concentrated among a subset of men.

In one mathematical modeling study, results indicated that higher levels of PrEP coverage among GBMSM could lead to significant decline in STI incidence, with concomitant quarterly healthcare visits facilitating early detection and treatment of asymptomatic STIs (Jenness et al., 2017). In another, investigators assessed the impact of PrEP on gonorrhea and HIV incidence for high-HIV-risk GBMSM in the Netherlands (Reitsema et al., 2020), adjusting their models for the presence or absence of risk compensation in the form of condom use. Results were highly promising. Without risk compensation, the authors estimated that PrEP could lead to a reduction of 49–61% of new gonorrhea infections between 2018–2027. With risk compensation, this reduction could be 46–63%. As the authors wrote, “In all scenarios, gonorrhea prevalence decreased after introducing PrEP” (Reitsema et al., 2020, p. 621).

Much has been written about the potential for high rates of STI diagnoses among PrEP-taking GBMSM to be attributable, at least in part, to increased STI screening in multiple anatomic sites that accompanies PrEP care (e.g., Marcus et al., 2019). Some studies have examined post-PrEP STI incidence by controlling for testing frequency (e.g., Traeger et al., 2019) and many of those studies have uncovered what appear to be a greater burden of STIs. Concerns about STIs can be mitigated, at least in part, by hypotheses put forward by researchers who take a developmental view of GBMSM’s adjustment to the protective power of PrEP and its effect on their sexual behavior. “Decreases in condom use may be

counteracted by the benefits accrued from the early diagnosis and treatment of STIs in the context of PrEP use” (Traeger et al., 2018, p. 684), and repeat STI testing may result in behavior change, especially among those who see the limits of PrEP (e.g., repeat STIs) and therefore adopt or return to other prevention methods (Rojas Castro, Delabre, & Molina, 2019). Future research should evaluate empirically these and other hypotheses.

Findings related to STIs from our qualitative work with PrEP-taking GBMSM echo several of these points, and raise some novel points as well (Pantalone et al., 2020). Despite the relatively large number of studies reporting on the associations between PrEP use and STI incidence for GBMSM, we could identify almost no published work that presented a first-person account of those experiences and the decision-making process that undergirds it. The relevant emergent theme from our study was *GBM acknowledged that engagement in PrEP-protected condomless sex carries a significant STI risk, and expressed gratitude for the routine STI screening accompanying PrEP care*. Participants understood the increased STI risk that accompanied reductions in condom use and that PrEP did not protect them from those. We found that, in contrast to the men’s nuanced knowledge of HIV, participants appeared much less knowledgeable about STIs. Some recognized the permanence of viral STIs (e.g., genital herpes) but others implied that all STIs were bacterial (i.e., curable) and minimized the impact of STIs on their health as merely a nuisance. No participants explicitly highlighted the connection between active STIs and increased HIV risk. Nearly every participant spontaneously extolled the benefits of routine PrEP-related healthcare visits that include STI testing.

Participants’ praise for the increased contact with the healthcare system, and especially a higher frequency of STI screening, has been acknowledged in multiple studies (e.g., Marcus et al., 2019). That is, having a structured opportunity to diagnose and treat STIs in various anatomical sites, especially asymptomatic STIs, is critical to preventing subsequent transmission and has downstream influences on HIV incidence (Freeborn & Portillo, 2018). In response to concerns that providers may be reluctant to prescribe PrEP out of fear of STI increases, Powell and colleagues (2019) noted that, “While drug resistance and risk compensation can occur with PrEP use, these are not valid reasons to withhold PrEP from patients given its substantial protective benefits” for HIV prevention (p. 1).

### Psychological Effects of PrEP

**Sexual Satisfaction.**—Some recent studies, primarily qualitative but a few quantitative, have begun to pose research questions concerning the psychological impacts of PrEP-taking. Most of the PrEP-consequences literature has taken a disease prevention perspective with a focus on objective measures of sexual behavior or STIs, with many fewer articles focused on the potential for PrEP to increase sexual agency and sexual satisfaction and decrease mental health symptoms. This may be a result of the field’s relative unwillingness to grapple with sexuality and sexual pleasure as worthy variables within the scope of HIV research. Kane Race (2016) argued that, “In its carefully cultivated posture of disinterest toward the intensities of sex, HIV science compounds this aversion, producing the sexual as a domain to recoil from rather than actively confront or otherwise embrace in a spirit of engagement.”

Investigators from multiple PrEP research groups have published similar sentiments in the past several years, noting the limitations of an approach to PrEP rollout that neglects the behavioral and social elements and only prioritizes negative or problematic aspects of sexuality such as STIs. The theme of sexual pleasure has been the focus of some campaigns promoting HIV risk reduction and PrEP use (e.g., Calabrese & Underhill, 2015), however, it is still the exception and not the norm. In their commentary in the *New England Journal of Medicine*, Marcus and colleagues (2019) wrote that, although many clinicians may be narrowly focused on HIV prevention or may value sex for reproduction more than sex for other purposes, “patient-centered care requires recognizing that disease prevention may not be the most important health outcome to patients... By enabling condomless sex with less fear of HIV transmission, PrEP has the potential to facilitate the intimacy and pleasure that can enhance sexual well-being for many people” (p. 511). In their commentary in the *American Journal of Public Health*, Boone and Bowleg (2020) made complementary points, highlighting that “sexual pleasure is inextricably linked to sexual health and sexual rights” and that “[r]esearch on sexual pleasure... was virtually nonexistent for Black men regardless of sexual identity. With few exceptions... risk, danger, and deficit, not sexual pleasure, were the primary frame for Black GBMSM’s sexualities and sexual health” (p. 157). A review of the literature on PrEP and sexual pleasure makes it clear that there is much more research needed, especially for PrEP-using GBMSM of color.

Several recent qualitative studies have found that for some, sexual pleasure, intimacy and empowerment can result from using PrEP (Bil, van der Veldt, Prins, Stolte, & Davidovich, 2016; Mabire et al., 2019; Newman, Guta, Lacombe-Duncan, & Tepjan, 2018; Philpot et al., 2020; van Dijk et al., 2020). Likewise, one study reported that participants’ experienced increased sexual “confidence” (Lea et al., 2018), and another found that PrEP use facilitated more “adventurous” sexual experiences (Prestage et al., 2019). Investigators interviewed 45 participants who had been enrolled in the ANRS-IPERGAY trial of on-demand PrEP in France and Canada. Results of their thematic analysis yielded three main categories, all strongly interconnected: participants’ relationship with condoms; intimacy and pleasure; and achieving a better sexual quality of life (Mabire et al., 2019). Many participants reported that taking PrEP allowed them to improve their sexual satisfaction by reducing or discontinuing (with some partners) the use of condoms for anal sex, which they viewed as a material and symbolic barrier to intimacy—both in terms of physical intimacy (which they defined as ‘physical closeness’) and psychological intimacy (which they defined as ‘coziness, familiarity’). These findings accord with previous work in non-PrEP-taking samples in which GBMSM identify condoms as a barrier to trust, intimacy, and spontaneity, resulting in a decisional balance between sexual satisfaction and the risk of HIV infection (Starks, Payton, Golub, Weinberger, & Parsons, 2014; Whitfield et al., 2019). Mabire and colleagues’ (2019) participants described having a real or anticipated reduction in sexual pleasure when using condoms and, thus, they viewed taking PrEP as a facilitator of increased sexual satisfaction. Overall, GBMSM reported that condom use, including the physical act of putting on the condom as well as engagement in condom-protected penetrative sex, were major obstacles to sexual satisfaction. Some men reported that using the condom dulled the physical sensations of intercourse so much that it actually prevented erection, a finding that replicates pre-PrEP research showing that some GBMSM resorted

to the use of erectile-enhancing medications primarily to maintain an erection while using a condom (Pantalone, Bimbi, & Parsons, 2008).

Additionally, relevant to PrEP being considered as a condom replacement, men in the study drew connections between PrEP as a condom replacement and their sexual satisfaction through their choice of, and comfort with, different sexual positions:

“The position taken during the sexual act (top/insertive or bottom/receptive) played a role in sexual fulfillment, and this sometimes depended on condom or PrEP use for some participants. Those desiring sexual intercourse, but who were unable to use condoms because they inhibited erection, were more likely to take the bottom/receptive position. The top/insertive position was perceived by participants to be less risky in terms of infection and adopted as a risk-reduction strategy, the bottom/receptive position was perceived to be more pleasurable. For some participants, receiving sperm was associated with more pleasure while taking the receptive position... The possibility, thanks to PrEP, to freely choose one’s position, and to choose to receive sperm or not, was associated with increased sexual pleasure and sexual satisfaction.” (p. 5)

Mabire and colleagues (2019) hypothesized that pleasure-seeking was a strong motivation to participate in the ANRS-IPERGAY trial, a hypothesis that appears to be borne out by the data. Their participants identified a variety of ways that PrEP-taking allows them to increase their sexual satisfaction, including eschewing condoms, flexibly taking an insertive or receptive position in anal sex, and sperm-taking. These authors suggested that pleasure-seeking, sexual satisfaction, and other positive elements of sexuality should be considered in research and public health practice as a primary and not a secondary (e.g., Underhill, 2015) influence on GBMSM’s decision-making about PrEP initiation and persistence.

Few other studies conducted have addressed questions about PrEP and sexual satisfaction and, thus, more research in this area is needed. In one quantitative study, authors analyzed longitudinal data from 137 PrEP-taking GBMSM before and after starting PrEP (Whitfield et al., 2019). Although they found some mental health benefits (discussed below), there were null findings related to increases in sexual satisfaction. In other studies, participants extolled the benefits of PrEP-protected condomless sex (e.g., Pantalone et al., 2020).

Such findings hearken back to the sentiments expressed by participants in the study by Mabire and colleagues (2019), and also some innovative work by Gamarel and Golub (2019, 2020). In one paper, the authors presented the results of two studies which show that, among GBMSM, desiring more closeness with a primary partner and believing that condoms interfere with intimacy were independent predictors of PrEP adoption attitudes and behaviors (2019). In a second paper (2020), these same authors collected mixed-methods data from 145 HIV-negative GBMSM in primary relationships. They asked participants to report on their sexual health goals and three main goal content categories emerged: HIV/STI prevention, sexual satisfaction, and intimacy. The authors concluded that “[u]nderstanding the relational needs for closeness and intimacy in motivating prevention behavior is critical” (Gamarel & Golub, 2019, p. 270).

**Anxiety reduction.**—A seemingly robust finding is reported reductions in anxiety and fear for GBMSM taking PrEP. Data in support of this hypothesis appear across multiple qualitative studies (and a few quantitative studies) and from different research groups across the U.S. and internationally (Bil et al., 2016; Gaspar et al., 2019; Girard, Patten, LeBlanc, Adam, & Jackson, 2019; Keen et al., 2020; Newman et al., 2018; van Dijk et al., 2020). Decreased anxiety about sex and HIV emerged from the qualitative study on sexual satisfaction discussed in detail earlier (Mabire et al., 2019), as well as others. Participants across studies described PrEP as providing a positive feeling of serenity through decreased anxiety and fear about acquiring HIV during sex. Their participants reported improved psychological functioning via reductions in anxiety, fear, and guilt and improvements in confidence, reflexivity, and agency. In another qualitative study, researchers conducted one-on-one interviews with 20 past or present PrEP-taking GBMSM in Atlanta, Georgia (Devarajan, Sales, Hunt, & Comeau, 2020), with participants reporting decreased anxiety surrounding sex after starting PrEP. Similar comments were shared by young, Black GBMSM focus group participants from the U.S. Midwest (Quinn et al., 2020), with the themes of ‘reduced sexual and HIV anxiety’ and ‘increased sexual comfort and freedom’ emerging. Other studies reported the same theme with slight variations, including ‘greater peace of mind’ (Yang et al., 2020) and ‘decreasing HIV fear’ (Tester & Hoxmeier, 2020). Participants in the latter study described greater sexual confidence and less timidity. Finally, a national cross-sectional study in Australia found that 22.8% of non-PrEP users also experienced reductions in HIV-related concerns as a result of increased community PrEP use (Holt et al., 2019).

Participants in yet another study, a qualitative sub-study of one of the seminal PrEP studies (IPREX OLE), described the experience of PrEP as one of helping them to articulate a longstanding and pervasive anxiety about HIV, ranging from discomfort to outright terror. Analogous views arose in several other qualitative studies, with several sets of authors noting that one of the psychological sequelae of the HIV epidemic for many GBMSM was an intense fear of HIV and any behaviors that increased their risk for HIV—such as condomless sex, even in the context of PrEP—irrespective of whether they engaged it in themselves or not.

Results from a few recent quantitative studies support the qualitative findings. Although most of the findings from the qualitative studies were focused on decreased anxiety specifically in relation to sex and HIV, some of the participants seemed to be describing PrEP-related reductions in global anxiety. A finding like that, if replicated quantitatively, could have important implications given the high and disproportionate rates of anxiety disorders for GBMSM relative to heterosexual men (e.g., 41.2% vs. 18.6%, respectively, from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)) (Bostwick, Boyd, Hughes, & McCabe, 2010).

In a cross-sectional sample of GBMSM recruited from a geosocial networking application in 2016 (Moeller, Seehuus, Wahl, & Gratch, 2020), the authors investigated correlates of mental health and sexual behaviors of HIV-negative PrEP-taking men ( $n = 273$ ), HIV-negative non-PrEP-taking men ( $n = 1,581$ ), HIV-positive men ( $n = 262$ ), and men unaware of their HIV status ( $n = 289$ ). The authors discovered that the use of PrEP was associated



with lower levels of anxiety (measured as generalized anxiety disorder symptoms) compared to the other groups and was associated with lower levels of anxiety despite a higher number of condomless anal sex (CAS) partners. The authors noted that, although having a higher number of CAS partners was associated with increased anxiety among participants who were not on PrEP, whether HIV-positive or HIV-negative, the PrEP use seems to moderate this association. Among PrEP users, the relations between number of CAS partners and anxiety was not statistically significant. In another study, this one following a longitudinal cohort of 1,071 GBMSM, researchers sought to investigate the impact of PrEP on the sexual anxiety of GBM (Whitfield et al., 2019). Participants' responses before taking PrEP ( $n = 137$ ) were compared to their later responses. Within adjusted multilevel models, the investigators observed a significant decrease in sexual anxiety. Taken together, these findings reflect a small but growing literature detailing the potential positive psychological elements association with PrEP use.

### **PrEP's Effects on Sexual Communication and Gay Community Norms**

Scant few studies have focused on other aspects of the psychosocial experience of GBMSM taking PrEP other than sexual satisfaction and anxiety reduction. Across these primarily qualitative inquiries, there appears to be some convergence of topics that, we hope, will guide future research in this area. Collectively, these studies address several overlapping areas: sexual communication, especially HIV status disclosure; comfort with sexual and romantic engagements with HIV-positive partners; and HIV stigma and community perceptions about HIV.

**Sexual communication and HIV disclosure.**—Earlier in the HIV epidemic, there was a persistent belief that HIV status disclosure within a serodiscordant partnership would lead to the use of barrier protection. However, that assumption was not borne out consistently by the data then (e.g., Simoni & Pandalone, 2004) although there are certainly published examples which do indeed provide support to it (e.g., Okafor, Li, Hucks-Ortiz, Mayer, & Shoptaw, 2020; Spieldenner, 2016). HIV status disclosure is multiply determined and best conceptualized as a process rather than a discrete event (Chaudoir, Fisher, & Simoni, 2011). In qualitative studies on the topic, participants reported that being on PrEP helped to increase their comfort discussing HIV status with sex partners. Some participants suggest this increased comfort was the result of reduced fears about HIV acquisition, knowing that they were well-protected no matter how their partner responded. In response to their disclosures, men reported overall a sense of relief when a partner disclosed also being HIV-negative and taking PrEP—as well as indication of self-respect and responsibility.

In the study by Tester and Hoxmeier (2020), participants mentioned that being on PrEP gave them “the license” (p. 7) to bring up HIV. Their participants noted that it is more common in the era of PrEP for GBMSM to proactively disclose their HIV status in application profiles and even in-person. Some men suggested that they were more comfortable having such discussions because having them with providers was practice for having them in other settings. In contrast to these findings, two qualitative studies reported that, once participants began taking PrEP, they felt less compelled to disclose their own HIV status or to inquire about their partner's status (Grace, Jollimore, MacPherson, Strang, & Tan, 2018), especially

in settings in which it was not possible or desirable to talk about HIV status (Mabire et al., 2019). Before PrEP's introduction, the topic of "seroadaptation" received significant attention—the use of behavioral HIV risk reduction strategies other than condom use, including, strategic positioning, withdrawal without ejaculation, and serosorting (e.g., Grov, Rendina, Moody, Ventuneac, & Parsons, 2015; Parsons et al., 2005). Participants in these qualitative studies noted that those strategies were not needed in the context of PrEP. Being on PrEP facilitated risk-reduction in a partnership, without negatively impacting intimacy. Findings that PrEP use facilitate HIV disclosure appear relatively novel and are worthy of further empirical attention in the future.

**Engaging with HIV-positive partners.**—One consistent finding that emerged across four qualitative studies was that when taking PrEP, GBMSM reported greater comfort arranging for sex with or dating HIV-positive men. Although by no means characterizing all GBMSM, some men—even when potentially engaging in barrier protected anal sex or low-risk activities such as oral sex—were reluctant or unwilling to partner with HIV-positive men (Courtenay–Quirk, Wolitski, Parsons, Gomez, & Seropositive Urban Men's Study Team, 2006). As some authors cleverly noted, PrEP may finally be a bridge across the "serodivide" that has interfered in the relationships of GBMSM throughout the HIV epidemic (Koester et al., 2018). In a study by Yang and colleagues (2020), GBMSM in serodiscordant relationships noted that they felt a kind of relationship solidarity with their HIV-positive partners. Authors noted that taking their respective medications was a mutual support activity that also promoted adherence. Decreased fear and anxiety about HIV, especially related to (or during) sex with an HIV-positive partner, was an experience referenced also by participants in other studies (Mabire et al., 2019; Devarajan et al., 2020). Moreover, one quantitative study found that more PrEP-users (29%) were comfortable with the idea of having sex with HIV-positive partners than non-PrEP users (3%), and an even greater number of PrEP-using participants reported confidence with hypothetical partners who were virally suppressed (Holt, Draper, Pedrana, Wilkinson, & Stoové, 2018).

Across the qualitative studies, participants shared similar insights. GBMSM in the Tester and Hoxmeier (2020) study explicitly discussed what felt like a longstanding division between HIV-negative and HIV-positive GBMSM—that was now, with PrEP, improving. One 40-year old male participant said that, before he started taking PrEP, "It was just like, immediately, 'Oh, you are HIV-positive? No!'" (p. 7). Another male participant, age 45, said that, pre-PrEP, he "had not knowingly had sex with someone living with HIV" and was "very hesitant" to do so—although he was decidedly more open now (p. 6). In this study, the authors also spoke with HIV-positive GBMSM about their perceptions of how PrEP had changed their interactions with HIV-negative men, especially potential sex or dating partners. HIV-positive participants noted that, prior to PrEP being commonplace, the conversations they had with HIV-negative men in which they disclosed their HIV-positive status were, at best, "a series of negotiations" and, at worst, "horrifying" (p. 8). HIV-positive participants attributed the improvements in their experience of those conversations to decreased fear of infection on the part of the PrEP-taking men.

Positive sexual relationships with people living with HIV was a theme that emerged in Quinn and colleagues' (2020) focus group study of current and former PrEP-using Black

GBMSM. Participants raised the topic of PrEP increasing sexual fulfillment and decreasing anxiety in serodiscordant relationships. Although it was not true for all participants, many expressed that, since beginning to take PrEP, their willingness and comfort increased in terms of sexual and dating partners who were HIV-positive. Participants echoed the points mentioned by those in other studies and discussed having an increased risk tolerance, both because of the protection afforded to them by PrEP but also because of having greater knowledge about the biology of HIV transmission risk through conversations with healthcare providers. Future research should continue to assess PrEP-taking GBMSM's decision-making related to HIV-positive partners.

**HIV stigma in GBMSM communities.**—Participants in several of the recent qualitative studies also noted that a consequence of PrEP as “bridger-of-the-serodivide” is a decrease in HIV stigma within GBMSM communities overall. This was reported by HIV-negative and HIV-positive participants in the recent qualitative studies, both as they reflected on their own experiences and as they empathized with the experience of men ‘on the other side’ (Skinta, Brandrett, & Margolis, 2020). Early adopters of PrEP have spoken with pride about their role as de facto health educators, with many making notes on their sex and dating profiles encouraging others to ask them questions about PrEP.

HIV-positive participants were surprised and relieved to note that, over and above an increased openness for sex and dating, HIV-negative men on PrEP appeared more willing to pursue friendships with them. Some participants reflected the notion that PrEP is engaging GBMSM in conversations about HIV prevention (Tester & Hoxmeier, 2020, p. 8), a topic about which GBMSM had previously felt fatigued. Themes about relationship solidarity with serodiscordant partners emerged (Yang et al., 2020). Participants described seeing changes in the language used to describe people living with HIV, for example, with colloquial and stigmatizing language (e.g., “Are you clean?”) being replaced by more specific and neutral terminology (e.g., asking about the date of his last HIV test).

Across the qualitative work in this area, the impact of PrEP on GBMSM communities was frequently discussed as a positive. Paradoxically, two qualitative studies reported that while PrEP had the potential to allay HIV-related stigmas, participants also reported experiencing stigmatizing reactions as a result of their PrEP use (Grace et al., 2018; Pawson & Groves, 2018). Likewise, participants expressed frustration in seeing decreases in condom use and increases in frequent multi-partner sex among GBMSM, and attributed that decrease primarily to increases in PrEP-taking (Hammack, Toolis, Wilson, Clark, & Frost, 2019; Pantalone et al., 2020). Moving forward, it will be necessary to continue to assess HIV-negative and HIV-positive men alike, and those taking medications (PrEP or HIV treatment) and not, about their perceptions of the GBMSM communities they inhabit. Seeing some comments that reflect a strong internalized stigma against condomless sex should not be surprising, considering that the predominant message for the first 30 years of the epidemic was, essentially, to ‘use condoms or die of AIDS.’ Although, with treatment, an HIV diagnosis is no longer a death sentence, we are left with a more complex morass of community messages to sort through.

## How has PrEP changed sex... *for cisgender women?*

In contrast to the literature on PrEP among cisgender GBMSM, the literature with other key populations is far less mature. Although the Truvada formulation of PrEP is FDA approved for adult women of all ages, it has been highlighted as a particularly useful prevention strategy for members of several key populations, including Black women in the U.S., young women in sub-Saharan Africa, and female sex workers residing anywhere—all of whom are particularly vulnerable to HIV acquisition (CDC, 2017; UNAIDS, 2019). Globally, women comprise 52% of all people living with HIV, with most cases concentrated in high-incidence African countries, including 27 nations in which women make up more than 60% of people living with HIV (AMFAR, 2019; Rosner & Ritchie, 2019). In the U.S., in 2018, Black women represented 57% of new HIV diagnoses among women, despite constituting only 14% of the population of U.S. women (CDC, 2018a; U.S. Census Bureau, 2019). Additionally, approximately 80% of sex workers are women globally. Female sex workers are an important population who stand to benefit from PrEP's protection, with one meta-analysis estimating a 17% pooled prevalence of HIV among U.S. female sex workers (Paz-Bailey, Noble, Salo, & Tregear, 2016). Globally, HIV prevalence among female sex workers ranges from 8–46% (Kerrigan et al., 2012).

Despite demonstrated need for PrEP among women, early roll-out of PrEP for women was stymied (The Well Project, 2019; U.S. Women and PrEP Working Group, 2013). The first major barrier was that early clinical trials with women failed to demonstrate sufficient protection, with findings leading to concerns about the ability of PrEP to adequately prevent HIV acquisition in women (Corneli et al., 2014; Marrazzo et al., 2015; Sheth, Rolle, & Gandhi, 2016; Van Damme et al., 2012). However, underperforming early clinical trials were discovered to result from low medication adherence rather than a pharmacokinetic failure (Van Damme et al., 2012). Additionally, the lack of inclusion of cisgender women in early U.S. clinical trials and demonstration projects led to key gaps in our understanding of the social and behavioral characteristics of women's PrEP use, hindering the rollout of PrEP for at-risk U.S. women (Diallo, Aaron, & Marshall, 2013; National Women's Health Network, 2013; Sheth et al., 2016; U.S. Women and PrEP Working Group, 2013). These elements have had long-term implications for PrEP rollout among U.S.-based women, as uptake of PrEP among women continues to lag other key populations (Ya-lin, Zhu, Smith, Harris, & Hoover, 2018). Delayed uptake of PrEP among women was not unique to the U.S. context, however, with many high-incidence African nations facing uptake challenges as well (O'Malley, Barnabee, & Mugwanya, 2019).

In recent years, behavioral studies have sought to fill important gaps in the literature about women's experiences and beliefs about PrEP. However, additional research is needed to answer questions more fully about how PrEP has changed sex for women in the U.S and abroad. Currently, the extant literature is limited largely to assessments of knowledge and attitudes about PrEP, as well as implementation barriers that hinder uptake (Bradley et al., 2019; Celum et al., 2015; Goparaju et al., 2017; Pinto, Lacombe-Duncan, Kay, & Berringer, 2019). Data on how PrEP has changed women's sexual satisfaction, relationships, partner selection, sexual anxiety, sexual self-esteem, sexual communication, and community norms are limited.

However, some findings have begun to emerge from mixed methods and qualitative studies that explore how PrEP has or could impact women's lived experiences, including those related to sex and relationships (Auerbach, Kinsky, Brown, & Charles, 2015; Bazzi et al., 2019; Flash et al., 2014; Van der Elst et al., 2013; van der Straten et al., 2014). Thus, the size and scope of the canon of published literature on the subject are much more limited than that of GBMSM. This knowledge disparity reflects a long history of women's underrepresentation in HIV clinical trials and behavioral research more generally (Blackstock, 2019; Liu & Mager, 2016; Mandavilli, 2019; Marill, 2020). Further, within the context of sexual and reproductive health research, the study of women's sexual pleasure has routinely been understudied compared to gendered relationship dynamics, sexual scripts, and condom negotiation—a pattern that is replicated in the extant literature on women and PrEP (Higgins & Hirsch, 2008; Pascoe, 2020).

We largely lack data on how PrEP has *actually* changed sex, but there are a number of published studies focused on how we *think* (thought) it will (would) change sex. Several studies have suggested that women believe PrEP is a useful HIV prevention strategy in the context of monogamous relationships, for those with multiple sex partners, for women in violent relationships, as well as for those engaged in commercial sex (Bond & Gunn, 2016; Braksmajer, Senn, & McMahan, 2016; Tomko et al., 2019; Wingood et al., 2013). One important way in which PrEP may change sex for women is by providing the first truly user-controlled HIV prevention tool (Auerbach & Hoppe, 2015). For example, a mixed-methods study of 119 Black U.S. women illustrated that participants value PrEP as an empowering strategy that allows women to control autonomously their own sexual health (Bond & Gunn, 2016). Beyond autonomy and user-control, daily oral PrEP regimens do not revolve around episodes of sex. Oral PrEP's coital independency removes HIV prevention both physically and temporally from sexual encounters themselves, which can significantly reduce concerns about acquiring HIV from sex even when partners refuse barrier protection (Grant & Koester, 2016). For example, findings from a qualitative study of women from Malawi, South Africa, Uganda, and Zimbabwe highlighted that women preferred both oral or injectable PrEP compared to other strategies like condoms and microbicides, which can interrupt foreplay and disrupt sex (van der Straten et al., 2017). For these reasons, some women have reported preferring oral PrEP to other HIV prevention strategies, a preference with the potential to substantially alter the experience of sex for PrEP-using women.

Upon its release, many HIV experts hypothesized that PrEP could be a particularly useful HIV prevention strategy especially for women who did not wish to disclose their PrEP use to sexual partners. However, early microbicide PrEP trials showed that some women *did* wish to communicate their trial participation and subsequent PrEP use with primary partners (Mngadi et al., 2014; Montgomery et al., 2012; Montgomery et al., 2011). Moreover, some of these trials showed that partner notification and support was important for PrEP adherence, as some of the women's partners encouraged and aided pill-taking behaviors (Mngadi et al., 2014; Montgomery et al., 2011; Montgomery et al., 2015). Results from several more recent studies corroborate earlier findings that some women wish to communicate with male partners about their oral PrEP use, although this literature remains underdeveloped (Felsher et al., 2020; Scorgie et al., 2020). For example, results from a qualitative study of women from Johannesburg and Mwanza revealed that, although

many were eager to disclose their PrEP use to partners, some were more reluctant and others eschewed disclosure (Scorgie et al., 2020). Similarly, a study of women who inject drugs explored the motivating factors behind decisions to communicate with partners about PrEP use. Themes included communicating a benefit to their partners, increasing social connectedness, and meeting a perceived obligation to partners (Felsher et al., 2020).

Researchers studying women's HIV risk have primarily addressed sexual scripts, relationship power dynamics, and condom use negotiation, with a good deal of the literature targeting Black/African American heterosexual couples who are vulnerable to HIV (Bowleg et al., 2015; Bowleg, Lucas, & Tschann, 2004; Dworkin, Beckford, & Ehrhardt, 2007; Hill, Granado, & Stotts, 2017; Hill, Granado, Villarreal, et al., 2017). Further, HIV prevention interventions aimed at Black women have routinely focused on improving condom negotiation skills and navigating relationship power dynamics with the intent of improving condom use (Downs et al., 2018; Robinson et al., 2017; Yarber et al., 2018). With that said, there is a need for future research to explore women's decision-making processes and skills in navigating PrEP-related partner communications, which may be able to build on insights gleaned from past research focused on condom use negotiation, to inform future interventions.

Nevertheless, the near-invisibility of PrEP use allows women to protect themselves effectively without consultation, permission, or participation from male partners, making PrEP a unique HIV prevention strategy compared to the typical male-controlled strategies (e.g., condoms) that require cooperation (Flash et al., 2014; Montgomery et al., 2019). A qualitative study of 92 South African youth, including 62 young women, reported that the *invisibility* of PrEP emerged as an important user preference, with participants highlighting they did not always wish to disclose their PrEP use to partners (Montgomery et al., 2019). Similarly, several qualitative studies of women both in the U.S. and in sub-Saharan Africa have emphasized the importance of oral PrEP's *discreetness*, allowing women to forgo conversations about protection and trust while protecting themselves from HIV (Bond & Gunn, 2016; Flash et al., 2014; Van der Elst et al., 2013; van der Straten et al., 2014). PrEP's invisibility and discreetness are characteristics that can help avoid conflict with partners who may interpret condom use within the context of monogamous relationships as indicative of infidelity on the woman's part or lack of trust towards him (Montgomery et al., 2015). PrEP provides an unparalleled strategy for women facing condom coercion, reproductive coercion, and lopsided or abusive relationship power dynamics (or even IPV) by removing the need for partner cooperation. Despite this flexibility, some women have expressed that further invisibility, in the form of longer-acting forms of PrEP could make PrEP that much more useful to them (Montgomery et al., 2019; van der Straten et al., 2017; Willie et al., 2020).

A growing body of literature has focused on PrEP's ability to protect women from HIV in the context of IPV and other forms of sexual violence (Bazzi et al., 2019; Braksmajer et al., 2016; Hartmann et al., 2016; O'Malley, Hawk, Egan, Krier, & Burke, 2020; Roberts et al., 2016; Willie, Kershaw, Campbell, & Alexander, 2017; Willie, Stockman, Overstreet, & Kershaw, 2018). The pre-biomedical era of HIV prevention required condom use negotiation between partners—regardless of whether a male or female condom was used—a challenge in the face of unequal power dynamics, reproductive coercion, and potential violence. Thus,

with PrEP's approval, experts quickly identified how PrEP could shift HIV prevention from an interpersonal negotiation to a strategy enacted autonomously and covertly, and increasing women's control over their sexual health (Braksmajer et al., 2016). However, studies of PrEP's hypothetical and actual impact on women facing violence have yielded mixed results (O'Malley et al., 2020). For example, although studies report moderate to high interest in PrEP among women with IPV histories, several unique barriers to use have been identified (O'Malley et al., 2020). A few studies have reported that partner resistance to daily oral PrEP acts as a barrier to use and adherence for women who have experienced IPV, with partners assuming infidelity, undisclosed seropositivity, or lack of trust as a result of women's PrEP use (Braksmajer, Leblanc, El-Bassel, Urban, & McMahon, 2019; Roberts et al., 2016; Willie et al., 2017). For example, a qualitative study of women in Uganda revealed that adherence challenges were sometimes a result of partners throwing away or threatening to dispose of women's PrEP pills (Roberts et al., 2016). Additionally, among a sample of mostly Black U.S.-based women, participants reporting IPV expressed that they were unlikely to use PrEP covertly for fear of partner discovery and subsequent increased violence (Braksmajer et al., 2019). These potential conflicts appear to act as real-world barriers for women using PrEP in the context of violent relationships.

### **Cisgender Female Sex Workers**

Female sex workers are also highly vulnerable to HIV due to violence, occupational exposure, and barriers to HIV prevention and testing (Blanchard et al., 2018; Shannon et al., 2018; Sherman et al., 2019). PrEP offers an important strategy for female sex workers to protect themselves from HIV in the event they are exposed through commercial sex or sexual violence. Although PrEP has the potential to act as an empowering and autonomous HIV prevention strategy for sex workers, it has typically been explored within frameworks of HIV prevention, as well as within the context of violence. Further, the available literature on the subject is often focused on the various implementation and uptake barriers to PrEP use among female sex workers, rather than exploring how PrEP has changed transactional and non-transactional sex for female sex workers globally.

Data on PrEP use among female sex workers are limited. However, several studies have reported strong interest in PrEP among female sex workers, who are quick to recognize the benefits for themselves and other female sex workers (Abou Ghayda et al., 2020; Van der Elst et al., 2013; Ye et al., 2014). However, knowledge of PrEP among female sex workers remains low in many countries, with several studies reporting low awareness among samples of female sex workers in Malawi, Kenya, Mexico, South Africa, China, and the U.S. (Abou Ghayda et al., 2020; Eakle et al., 2019; Lancaster et al., 2019; Tomko et al., 2019; Wang et al., 2017). In addition to low awareness, studies suggest that barriers to PrEP use among this population include criminalization of sex work, inadequate healthcare access, and stigmatizing clinical environments (Lancaster et al., 2019; Tomko et al., 2019). A recent meta-analysis found that anticipated stigma from partners and family, concerns about side effects, and low perceived risk were also salient barriers to PrEP use in this population (Abou Ghayda et al., 2020). Further, several studies have shown that greater knowledge of PrEP is integral to improved uptake among female sex workers (Abou Ghayda et al., 2020). In a qualitative study conducted in Kenya, authors reported that

female sex workers expressed an interest in learning about PrEP from other sex workers, illuminating that a peer-model of engagement could be particularly useful for disseminating key information about PrEP and overcoming barriers to clinic-led education (Bazzi et al., 2019). Additionally, in another study, a discrete choice experiment for female sex workers in Malawi revealed that the location dispensing PrEP was the most valued attribute in the care continuum, with participants preferring to receive PrEP from family planning clinics or NGO-run drop-in clinics rather than STI clinics or those specializing in the distribution of anti-retrovirals (Lancaster et al., 2019). Such findings suggest that stigma about STIs and HIV act as additional barriers to PrEP care, along with the stigmatization and criminalization of sex work.

Although most research on PrEP use among female sex workers has explored HIV risk, violence, and implementation challenges, several studies offer partner-level and intrapersonal-level findings that suggest how PrEP may change sex and intimate relationships for this population. Prior research highlights that female sex workers report inconsistent condom use with non-paying primary partners (Bowring et al., 2020). Thus, PrEP may provide an important HIV prevention strategy that affords protection both to sex workers and their primary partners, who may choose not to use condoms with one another. For example, a qualitative study of female sex workers in South Africa reported that women felt “peace of mind” from PrEP’s protection, particularly in the context of primary partnerships, which were often “defined” by a lack of condom use (Eagle et al., 2019). Although the researchers attempted to generate discussion about PrEP’s impact on women’s sex lives, both with transactional partners and romantic partners, emergent themes remained focused more on the utility of PrEP for sex workers rather than the women’s personal experiences of sex.

## **How has PrEP changed sex ... *for transgender individuals?***

### **Limited Data on the Health of Transgender Populations**

We next describe research on PrEP for transgender populations. Our definition of transgender individuals includes transgender men as well as transgender women as these binaries are the focus of much of the research we identified. We note, however, that many gender diverse and non-binary individuals do not identify within the gender binary, may not use these labels for their own identities, and that their experiences may absent from the academic research that serves as the basis of this review. Further, compared to other populations, there is an overall paucity of data about transgender individuals’ sexuality and sexual health. Although some of the major PrEP studies, such as the iPrEx PrEP efficacy study, did permit enrollment of transgender individuals—these studies were not designed specifically to address the experiences of transgender populations and, thus, were underpowered and unable to conduct subgroup analyses that would have allowed meaningful conclusions to be drawn (Grant et al., 2016). There have been several calls for additional PrEP-related research that is culturally sensitive and specific to the needs and concerns of transgender individuals (Mayer, Grinsztejn, & El-Sadr, 2016; Sevelius, Deutsch, & Grant, 2016; Williamson, 2010).



Over the past two decades, and especially since 2010, there has been an increasing focus on the health of transgender individuals—enough even to populate several review papers—with attention to sexual health generally (Reisner et al., 2016) and HIV prevalence and HIV prevention specifically (Poteat, Reisner, & Radix, 2014; Poteat, Scheim, Xavier, Reisner, & Baral, 2016; Poteat et al., 2015; Reisner et al., 2016; Wansom, Guadamuz, & Vasan, 2016). In fact, according to a review conducted by Reisner and colleagues (2016), sexual and reproductive health was the second most common line of research focused on transgender individuals, only following mental health (Reisner et al., 2016). Unfortunately, many of these sexual and reproductive health studies focused on transgender individuals who were assigned male sex at birth, reflecting the disproportionate focus on HIV/STI prevention rather than attending to psychosocial experiences of sex or sexual pleasure (Reisner et al., 2016). In this section, we briefly describe the necessity of PrEP for transgender persons through the current status of transgender-focused HIV epidemics, HIV risk factors associated with PrEP eligibility among transgender populations, current transgender PrEP use and common barriers to use, as well as unique PrEP considerations within the fluid landscape of transgender sexuality.

### Impacts of the HIV Epidemic

The emphasis on HIV prevention among transgender persons is warranted. In 2013, Baral et al. published a systematic review and meta-analysis of data published in 2000–2011 from several countries with on-going HIV epidemics—including the U.S., six Asia-Pacific countries, five in Latin America, and three in Europe (Baral et al., 2013). They estimated a pooled HIV prevalence of 19% among (95% CI: 17.4 – 20.7) among all 11,066 transgender women and a slightly higher prevalence for the transgender women recruited from higher income countries 22% (95% CI: 18.8 – 24.3; low- and middle-income countries 17.7%, 95% CI: 15.6 – 19.8; (Baral et al., 2013). In the U.S., previous estimates of HIV prevalence among transgender populations have ranged from 2–40% among trans feminine populations and 0.5–4% for trans masculine populations (Herbst et al., 2008; Poteat et al., 2016).

### PrEP use Among Transgender Populations

PrEP eligibility and awareness varies across study populations in the literature. Golub and colleagues found that only 23% of 1,808 transgender men participating in their study met one or more indications of PrEP eligibility (Golub, Fikslin, Starbuck, & Klein, 2019). Another study found that 62% of a sample of 180 young transgender women met one or more indications for PrEP. However, only 31% of their participants reported ever having heard of PrEP, and a mere 5% reported ever having taken PrEP (Kuhns et al., 2016). Similarly low PrEP use estimates have been found in other studies of transgender individuals (Eaton et al., 2017; Reisner et al., 2017; Rowniak, Ong-Flaherty, Selix, & Kowell, 2017). Further, among those who appeared to be PrEP-eligible, only 34% had received PrEP information from a medical provider and 11% had actually received a prescription (Golub et al., 2019). The differences in findings across studies reflect a broader issue: not all transgender individuals have the same vulnerability for HIV acquisition and tailored approaches for transgender individuals are necessary to address the diverse sexual orientations and behavioral histories that characterize transgender populations.

## How Sexual Behavior may Influence PrEP Use

The impact of PrEP on sex for transgender populations is difficult to discern, given the limited data and the typical framing of sexual behavior studies of transgender individuals through the lens of HIV risk. The few studies of transgender individuals that have focused on sexual pleasure and sexual functioning have primarily been focused on the context of hormone therapies and gender affirming medical procedures, rather than PrEP use per se (Stephenson et al., 2017; Wierckx et al., 2014). However, a review of the extant literature suggests the question is not “How PrEP will modify sexual behavior?”—at least not at the current stage of limited PrEP use among sexually active transgender individuals—but rather “How will sexual behavior determine PrEP use?”

**Dynamic sexual identities among transgender populations.**—One of the challenges of PrEP as HIV prevention among transgender populations is the lack of specific research on PrEP among transgender study participants and a dearth of specific PrEP information tailored for transgender communities. Often, transgender women have been lumped into a “high HIV risk” category with cisgender GBMSM (Grant et al., 2016; Sevelius, Deutsch, et al., 2016). Further, transgender women and transgender men have different sexual health needs and desires. In one study of 452 transgender and gender diverse participants, 43% identified as queer, 19% as other non-binary, 16% as bisexual, 12% as heterosexual, and 10% as gay (Katz-Wise, Reisner, Hughto, & Keo-Meier, 2016). In general, it appears that heteronormative definitions of sexual orientation do not work very well for transgender individuals, given that they are typically based on a binary conceptualization of the gender of the individuals’ objects of sexual attraction (Galupo, Henise, & Mercer, 2016). Transgender individuals’ sexuality appears to be more fluid than static (Rowniak, Chesla, Rose, & Holzemer, 2011). In fact, partner gender-orientations are only one element of how many transgender individuals define their sexuality. Galupo and colleagues (2016) found that transgender adults often used multiple labels (queer being preferable and more inclusive because it does not imply any specific gender identity); focused on the person (and not their gender) to whom or specific body parts to which they were attracted; based their sexual orientation on the person who they were currently dating; or based their sexual orientation on their sexual positioning preferences (e.g., submissive; Galupo et al., 2016).

Further complicating researcher’s attempts to lump transgender populations into “high HIV risk” categories are sexual attraction changes that can occur throughout transgender individuals’ lifetimes and through the experiences of gender transitions or gender affirming medical interventions (Dadasovich et al., 2017; Rowniak & Chesla, 2013). Some qualitative research has described how the gender affirmation process provides important context for the development of and changes in sexual orientation (Fox Tree-McGrath, Puckett, Reisner, & Pantalone, 2018). Katz-Wise and colleagues reported that 58% of their sample of transgender and gender diverse participants reported having experienced lifetime changes in their sexual attractions, and 65% experienced changes in sexual attraction after engaging in the gender affirmation process (Katz-Wise et al., 2016). This fluidity appears to vary by transgender population, with transmasculine individuals being 1.69 times the odds (95% CI: 1.34–2.12) to report sexual fluidity in their lifetime compared to trans feminine individuals (Katz-Wise et al., 2016). Often, transgender persons may be ill-prepared to be immersed

in a new community and unaware of different sexual “risks” posed by joining a new sexual network (Rowniak et al., 2011; White Hughto, Reisner, & Mimiaga, 2015). Many existing public health interventions center on HIV prevention for cisgender GBMSM. As the research indicates, attempts to treat transgender individuals and cisgender GBMSM as a monolithic group fails to acknowledge the unique elements of gender and sexual orientation diversity that characterize transgender individuals. Trans-competent healthcare providers who are knowledgeable about PrEP, who can aid their patients in determining and re-evaluating their PrEP eligibility and need, are critical to effects to increase PrEP uptake among transgender populations.

#### **Competing motives between HIV prevention versus gender-affirming care.—**

An important barrier to PrEP use among transgender populations are their concerns about potential drug interactions among PrEP, hormones, and (for some) birth control. For transgender individuals with female reproductive organs, the literature shows widespread concern about interactions between PrEP and hormonal contraception, and a prioritization of contraception over HIV prevention (Rowniak et al., 2017; Sevelius, Keatley, Calma, & Arnold, 2016). Although there is currently no evidence to suggest such PrEP-associated drug-drug interactions (CDC, 2018b; Sevelius, Deutsch, et al., 2016), the limited data collected in clinical trials involving transgender persons means less information is available to dissuade these concerns—which could drive reduced interest in PrEP despite its significant potential to reduce HIV incidence (Sevelius, Deutsch, et al., 2016; Wood, Lee, Barg, Castillo, & Dowshen, 2017). Considerations of how hormone use and gender-affirming medical procedures among transgender individuals impact sexual behavior are important for assessing PrEP eligibility and need.

For transgender women, hormone therapies and gender-affirming medical procedures have been reported in some studies to decrease sex drive (Kosenko, 2011; Wierckx et al., 2014). However, among transgender men, taking testosterone has been associated with increased sex drive and sexual activity (Dadasovich et al., 2017; Kosenko, 2011; Rowniak et al., 2011). Indeed, research has indicated that, among transgender men in particular, gender affirmation can precipitate a “second adolescence” (Kosenko, 2010) and sexual experimentation (Rowniak & Chesla, 2013). Sex can be used by some transgender individuals as validation of their affirmed gender (Fox Tree-McGrath et al., 2018; Kosenko, 2010; Nuttbrock et al., 2009; Rowniak et al., 2011; Sausa, Keatley, & Operario, 2007; Sevelius, 2013). However, although some transgender individuals have reported an increase in the number of sexual partners and increased sexual engagement overall, they expressed concerns about their ability to negotiate condom use or, more generally, conversations with partners about behavioral HIV risk reduction (Kosenko, 2010, 2011). Often, broader concerns about disclosure of one’s transgender identity to a new partner—and the concomitant emotional and physical risks—outweigh concerns about HIV risk (Kosenko, 2010, 2011; Rowniak et al., 2011). Findings from Kosenko and colleagues’ (2010) qualitative study with transgender men expand on the concept of “safe sex.” Participants variously defined “safe sex” to include condom use as well as other risk reduction “rules”: sex only with people who do not use drugs, sex only with people who they believed were STI-free, and sex only with people

who they already knew and trusted (Kosenko, 2010). Some definitions of sexual safety also included attention to physical and emotional safety (Kosenko, 2010).

Other research has revealed that, for some transgender individuals, pregnancy concerns outweigh HIV acquisition concerns (Rowniak et al., 2017). In one study of trans-masculine individuals, participants described major concerns about drug-drug interactions between hormonal contraception and PrEP. Many instead opted to use condoms because, they reported, the condoms protected against both pregnancy and HIV (Rowniak et al., 2017). Based on the presented research, hormone therapies and gender-affirming medical procedures, especially for transgender men, appear to increase potential HIV vulnerability through changes in sexual activity in addition to potential increases in sexual activity. The same hormones that allow transgender individuals to live in their affirmed gender also appear to pose challenges to their PrEP uptake and use.

The current state of the literature on the health of transgender populations is perhaps overly focused on negative health outcomes such as STI/HIV acquisition. Although they are important, of course, the narrow emphasis on health risks neglects other important areas of inquiry. There is an urgent need for a broader portfolio of PrEP-related research with transgender individuals, including but not limited to sexual behavior, health disparities (especially as they relate to intersectional identities of transgender individuals), inclusion of transgender participants in clinical trials, and research to evaluate biomedical HIV prevention interventions—especially as they relate to hormonal contraception and gender affirmation interventions like hormone therapy—as well as studies focused on the psychosocial experiences of PrEP-taking and its impact on sexual behavior, functioning, and satisfaction. Until then, our task is to provide transgender populations with more research and better resources so they can make informed decisions about their sexual health care.

## Conclusion

In this paper, we reviewed the published literature on PrEP's impact on a variety of facets of sexuality, including behavior, satisfaction, sexual anxiety, esteem, IPV, sexual agency, and more—and did so across of a range of key populations at the highest risk for HIV acquisition: GBMSM, cisgender women, and transgender individuals. As we noted throughout, the manifest function of PrEP is to *prevent HIV transmission*. However, this biomedical intervention serves myriad latent functions across the spectrum of sexual health, with many common themes emerging across populations.

As is also evident from our review, there has been a substantial growth in literature in the near decade since PrEP was FDA-approved in the U.S., with much of that research emerging in the last several years. With options for PrEP expanding, including both drug formulations (Descovy vs. Truvada) as well as novel delivery methods, we anticipate a growing need for and expansion of such research. Although PrEP clinical trials have included participants from across the globe (answering the question of “how well does PrEP work pharmacologically?”), much of the research on PrEP's *implementation* has been based on samples from the Global North. There are certainly some notable studies on PrEP from the Global South (Edeza et al., 2019; Hoagland et al., 2017; To & Lee, 2018; Wheelock

et al., 2013), though, and we expect this body of research to become more robust in the coming years, especially as PrEP rollout continues in the Caribbean and Latin America (Galea, Baruch, & Brown, 2018). And, as more individuals adopt PrEP, the pool of potential research participants for PrEP research will expand. That is, we can broaden the scope of PrEP studies away from primarily in urban areas or from clinical settings.

There are clear disparities in the amount and type of research across the populations we investigated, with the greatest focus on GBMSM compared to cisgender women and transgender individuals. Because the primary outcome of PrEP-taking is preventing new HIV infections, much of the published PrEP research has been conducted through a more negative lens of disease prevention as opposed to other more positive lenses like sexual agency, sexual satisfaction, or sexual esteem. It is clear that, at least for GBMSM individuals, the literature has begun to expand to include constructs consistent with those lenses, and we sincerely hope a similar pattern will evince itself for the others in the ensuing years. We also note that, for this review, we were not able to include literature on PrEP for cisgender heterosexual men. Although there is some research on that population, it is was so small as to be insufficiently robust at the time of this review. PrEP can be helpful for *anyone* at risk for HIV, including heterosexual men. Heterosexual men of color in the U.S., as well as heterosexual men in many developing nations, have relatively high lifetime odds of contracting HIV. More research is needed with heterosexual cisgender men, and we urge PrEP researchers to engage with a perspective that allows an expansive view of multiple facets of sexuality.

Despite the disparities in the scope and volume of research on PrEP's effects across gender and sexual orientation spectrums, several common themes emerged. First, it is clear that PrEP has many unintended effects that serve to improve the sexual lives of many diverse individuals and populations. These effects include greater sexual agency, reduced anxiety about having sex, improved sexual pleasure, as well as an enhanced sense of intimacy with partners. To the question of whether PrEP "causes" risk compensation, it is clear from the literature that posing the question in the traditional way, with the traditional measures (condomless sex, STIs), could be detrimental to the rollout of PrEP among populations who would benefit most from it.

Finally, we conclude this review at a time of great uncertainty in the world. Since late 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19, began spreading across all across the world and was declared a global pandemic. With many countries instituting travel restrictions, stay-at-home orders, the closure of businesses deemed non-essential, and guidelines about mask-wearing, physical distancing, and otherwise limiting exposure to other people out of fear of infection—we have begun to see impacts on sexual behavior overall, including patterns of PrEP use (Döring, 2020; Hammoud et al., 2020; Lehmler, Garcia, Gesselman, & Mark, 2020; Sanchez, Zlotorzynska, Rai, & Baral, 2020; Stephenson et al., 2020). Reported changes have included self-imposed reductions in the number of partners, reductions in access to available partners through the closure of physical spaces where they could meet, as well as reductions in access to sexual health services including PrEP care, and transitions to telehealth. Even with vaccine dissemination beginning at the end of 2020, it may take years (if ever) before

the virus is eradicated, with (at least at present) clear disparities in vaccine access between wealthy and developing countries and across sociodemographic groups within countries. It is beyond the scope of this review to speculate how exactly the pandemic will affect HIV prevention or PrEP use. For our readers, we highlight that this, too, will likely become a pivotal moment that significantly shapes human behavior—and research findings—in the decade(s) to come.

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