



What people want from sex and preexposure prophylaxis

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Purpose of review

As demand for preexposure prophylaxis (PrEP) increases, we are learning more about what people want from sex and PrEP.

Recent findings

PrEP demand has reached a tipping point in the USA and is increasing rapidly. Although the primary benefit of PrEP use is biological, to reduce risk of HIV infection, PrEP users often express an alternative set of social and emotional benefits that are provided by PrEP. These collateral benefits of PrEP have salience, affect, and are experienced in the present, which are compelling drivers of human behavior. PrEP use has been associated with feeling safe during sex, usually in contrast to ruminations related to fear of HIV or intimate partner violence or control. PrEP can create empowerment, or agency, defined as the capacity and autonomy to act on one's own behalf, because it provides control over one's vulnerability to HIV and relief to women and men who may otherwise worry about whether their partners will use a condom, take antiretroviral therapy, or disclose their HIV status accurately. Planning for sexual and social goals in calm moments is also empowering. These highly desired collateral benefits of PrEP could be undermined, or eliminated, if PrEP is implemented in ways that are coercive or that foment fear of sexual risk compensation, drug resistance, toxicity, or moral judgment.

Summary

Current PrEP implementation provides direct and indirect benefits that are highly desired.

Keywords

agency, HIV, preexposure prophylaxis, sexual practices

INTRODUCTION

The experience of preexposure prophylaxis (PrEP) users provides important insights into sexual practices and motivations to use PrEP, which go beyond wanting to stay free of HIV. We review emerging literature on the everyday experiences of PrEP users, which emphasizes the importance of benefits that are salient, experienced in the present, and have strong a effect.

DEMAND FOR PREEXPOSURE PROPHYLAXIS REACHED A TIPPING POINT IN THE USA

Knowledge and use of PrEP remained low for several years after the publication of research findings demonstrating safety and efficacy [1–4]. More recent information indicates that PrEP demand in the USA hit a tipping point in late 2013, and has increased 332% during 2014 [5]. The database used for this analysis reflects only 39% of prescriptions dispensed and does not account for dispensations

supported by patient access programs, demonstration projects, nor prescriptions filled by public insurance. According to this limited database, 8512 persons had been dispensed PrEP. Thus, one low estimate of the total numbers having received PrEP in the USA would be 21 825 (8512/0.39). Large increases in demand for PrEP during 2014 were reported in San Francisco [6,7,8[■]] and New York [9].

The growing demand for PrEP in the USA is consistent with the high proportion of participants in open-label demonstration projects who elect to start PrEP when it is offered. Uptake of PrEP was 76% in the Iniciativa Profilaxis Pre-Exposición (iPrEx) open-label extension (OLE) [10], 60% in the US

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KEY POINTS

- Demand for PrEP reached a tipping point in the USA in 2013, with rapidly expanding use during 2014.
- PrEP users report fringe benefits including feeling safer during sex, less anxiety, less HIV stigma, and stronger relationships.
- Insights from the field of behavioral economics suggest that PrEP's fringe benefits are compelling because they have salience, affect, and are experienced in the present.
- PrEP empowers users by allowing greater control over their HIV risk, rather than relying on partners to use condoms, take antiretroviral therapy, or accurately disclose their serostatus.
- PrEP inspires people to plan for sexual and social goals during calm moments, when multiple options can be considered with longer-term benefits.

demonstration project in sexual health clinics [11], >95% in the Partners Demonstration Project [12], and 86% in the Botswana TDF/FTC Oral HIV Prophylaxis Trial (TDF2) OLE [13]. Uptake was high regardless of whether or not the person had prior experience in a PrEP trial, whether the person was in the USA or Africa, or whether the person was a man or a woman. Prior knowledge of PrEP was associated with about 1.5-fold higher uptake [11].

Even as demand grows, it is clear that not everyone vulnerable to HIV wants PrEP. The most common reasons for refusing PrEP when offered include fear of side-effects and toxicity [10]. Other reasons are fear of stigma arising from perceptions of promiscuity, sexual orientation, or HIV status. Some refuse PrEP because of inexperience with taking oral tablets, and perception of low HIV risk.

INSIGHTS FROM BEHAVIORAL ECONOMICS REGARDING PREEXPOSURE PROPHYLAXIS DEMAND

Behavioral economics is a field that arose from psychology and economics to understand what drives human behavior [14,15]. Linnemayr [16] identifies three common themes from behavioral economics that are likely drive the use, or nonuse, of biomedical prevention strategies: 'salience', 'present bias', and 'affect'.

'Salience' is the tendency for people to act on information that first comes to mind rather than making use of all available knowledge. Salient information that can bias perceptions of risk and influence sexual behavior includes a prospective

partner's healthy appearance [17,18], although such perceptions about a partner's serostatus are often incorrect [19,20]. Effective PrEP use mitigates the consequences of HIV serostatus misperceptions.

'Present bias' is the tendency of people to respond to short-term temptations at the expense of long-term benefits. Present concerns about social connections, staying in school, avoiding violence, finding housing, and employment often eclipse concerns about HIV, which becomes a threat over the long term [21]. As noted below, PrEP's collateral benefits are typically experienced in the present, which makes them compelling drivers of PrEP demand.

'Affect' is when the decisions people make are impacted by their emotional state. Loewenstein [22] characterizes hot and cold affective states that differ in how decisions are made. Sexual intercourse, and the period leading to it, are affectively hot states during which plans for condom use, serodisclosure, or nonpenetrative sex may be forgotten. PrEP does not require action during hot states; rather PrEP is sought and taken during 'cold' states during which longer-term goals can be contemplated and pursued. PrEP provides an opportunity to plan for staying safe during sex, while acknowledging that sexual hot states may disrupt expectations and plans. [23**].

Importantly, the processes elucidated in behavioral economics commonly influence all decision making, including decisions made by political leaders, organizations, scientists, healthcare providers, community advocates, and patients. Examples relevant to the provision of PrEP are the low level of knowledge of PrEP among general practitioners ('salience'), hesitancy to invest now to avoid paying more for the HIV epidemic later ('present bias'), and fear of sex ('affect').

PREEXPOSURE PROPHYLAXIS WORKS WHEN TAKEN

Belief in PrEP efficacy is an important motivator of adherence [24]. Indeed, the tipping point in demand for PrEP in the USA came soon after publication that PrEP works well when taken [25–27] and this information circulated in social media [see post from Damon Jacobs on 1 July 2013 at (website: <https://www.facebook.com/groups/PrEPFacts/>)]. Perhaps more importantly, PrEP demonstration projects were well underway providing salient, present, and affective anecdotes from PrEP users who were having sex and avoiding HIV infection [10,11].

A comparative study of efficacy messaging compared 'gist' messages like 'Prep works when taken'

with quantitative messages like ‘PrEP is more than 90% effective when taken daily’ [28]. The gist messages were preferred and motivating for adherence. In contrast, there was confusion and misunderstanding about how to interpret the quantitative messages. Aversion to ambiguity, another concept from behavioral economics, is known to undermine action [29]. This bias is strong when choices that appear to have certain benefits are compared with choices having possibly greater but less certain benefits. If choices are made one at a time, ambiguity aversion is less important [29]. If so, the science practice of quantitatively comparing efficacy between prevention interventions creates a quagmire that undermines the will to adopt any intervention at any level. These comparisons are less helpful when diverse interventions are compatible with each other, such as condoms, treatment, and PrEP. Simplifying the question to ‘should I take (or provide) PrEP?’ and providing information that ‘PrEP works when taken’ was pivotal for fostering demand and adherence. More effective management of ambiguity aversion could also increase uptake of HIV treatment.

PLEASURE

PrEP users have reported that PrEP enhances sexual pleasure, and that this is sufficient motivation for their using PrEP [30]. Sexual pleasure may have multiple dimensions including bonding [31], intimacy [32–34], spontaneity [24], and adventure [23¹¹], all of which are potentially enhanced by PrEP. Perhaps more importantly, PrEP is shaping users relationship to sex in meaningful ways [35], thus, creating an opportunity to expand our depth of understanding of sexual practices. Kane Race, cultural studies scholar, observed that PrEP has created opportunities to consider pleasures of sexual practices more fully...

‘...one of the tacit commitments of HIV prevention science is to manage the affective intensities and complications of sex. These days it is possible to sit through entire conferences apparently devoted to HIV prevention in which the issue of sexual practice is barely mentioned... One of the new prevention strategies that, despite its biomedical lineage, has thus far been unable to shake its contaminating associations with the apparent excesses of sexual pleasure is PrEP’ [23¹¹].

Race pushes us to recognize that HIV prevention research has become arguably divorced from sex, or worse, is antagonistic toward sex. The antagonism

associated with sex and HIV prevention may be considered a form of stigma in which sexual practices that are so full of meaning for people are reduced to HIV risk, a negatively valued characteristic. Stigma of this nature is too often reinforced by medical providers who serve as gatekeepers to biomedical interventions and may subtly convey stigmatizing messages about sexual behavior rather than adopting a sexual wellness approach.

PREEXPOSURE PROPHYLAXIS AND INTERCOURSE WITHOUT A CONDOM

PrEP is attractive to some people because it allows for sexual intercourse without a condom with less risk of HIV. Qualitative research has consistently shown that serodiscordant couples prioritize relationship factors, that is, intimacy over and above the use of condoms [36–40]. When condoms are perceived to interfere with intimacy, they are less likely to be used [33]. PrEP has created opportunities to recognize previously unarticulated concerns about condoms including decreased sensation, interference with erectile function, and disruption of spontaneity. PrEP is preferentially being taken up by people who are not using condoms consistently [10,11].

LESS FEAR DURING SEX

PrEP use reduces fear of HIV [35,41]. PrEP has created a space for users to voice their deeply felt fears associated with becoming infected with HIV [42]. For many PrEP has been an antidote to those fears. Feeling safe during sex is a present-oriented benefit that has strong affective value, and is salient (readily perceived). As such, this benefit of PrEP may be valued more highly than PrEP’s actual capacity to prevent HIV infection, although the two are related. The benefit is best expressed by PrEP users themselves in the following quotes:

‘At the beginning of the interview I said HIV scared me. Even when I was being safe it scared me. I don’t want to say it doesn’t scare me, but I think it scares me less now, if that makes any sense? ... So, in general, the anxiety, the HIV anxiety, is gone. I won’t say it’s gone-gone. But it’s not in the front of my head as it used to be, where I was obsessively worried about it while sex was happening’ iPrEP OLE participant. [35]

‘PrEP would allow me to have sex without fear for the first time in my life. It would remove that month long hangover of psychological anguish after sex, worrying about whether or not I might have put myself at risk of HIV and looking for the

slightest sign. If I get a cold or a rash my mind will instantly jump to conclusions because of the anxiety I have around HIV' HIV-seronegative gay man. [43]

As indicated by the previous quotes, fear of acquiring HIV infection has been a preoccupation for many gay men. In a survey conducted in New York, 49% of MSM reported thinking about HIV most of the time or all of the time during sex [44]. Once PrEP became available, a set of 'fringe' benefits (a phrase invented by Gilmore [41]) quickly surfaced including decreased anxiety, decreased depression, and decreased sexual compulsivity [45].

Notwithstanding predictions from theories of risk compensation, diminished fear of HIV has not been associated with increases in risky behavior [1–4,46,47,48]. In general, sexual practices remain unchanged or tend to become safer during PrEP use, both in the context of clinical trials and demonstration projects. Reasons for safer behavior may arise from testing and counseling services that are provided as part of PrEP services, although such testing and counseling of HIV-negative people was not highly effective when offered as stand-alone services [49]. In addition, PrEP may lead to safer sexual practices by fostering relationships [31], increasing interactions with HIV-positive people, and through daily contemplation of HIV during calm (affectively 'cold' moments).

LESS HIV STIGMA

HIV stigma negatively impacts both HIV-positive and HIV-negative people [42]. PrEP diminishes HIV stigma, as revealed in the following quote from a gay man in the United States.

'I'm a HIV positive man, I'm on treatment and I'm undetectable; so it's really unlikely I'm going to pass HIV on to my partner. But relationships can be a challenge as HIV can be a big barrier between me and guys I date. Sometimes sex lacks intimacy and you don't always get close to each other. There's always that fear in the back of your mind that HIV could be passed on. If we had PrEP it would take that fear away.' HIV-positive gay man [43].

PrEP facilitates greater interaction between HIV-negative and positive people, including the possibility of safer sexual interactions. Such interactions lead to increased sensitivity to HIV issues, and greater inclusion of HIV-positive people in social networks that were previously exclusionary [50,51]. Among HIV-seronegative people, such

preference for sexual partners who are also seronegative, or serosorting, is not known to be effective [52]. Acute HIV infection, delays in HIV testing, and miscommunication are some ways that seronegative serosorting can fail to prevent HIV transmission. The social harms of serosorting have included its fostering HIV stigma, and by excluding HIV-positive people from social networks. Seronegative men on PrEP find that they have more opportunities for dating and partnerships, learn more about HIV, and in general are less inclined to be suspicious of a partner's purported negative HIV status.

PRESERVATION OF VALUED RELATIONSHIPS

PrEP provides a way to further stabilize couples in serodiscordant relationships. Qualitative research identified that love in the relationship was a major driver of adherence and PrEP uptake [31]. Serodiscordant status threatens these relationships creating a dilemma about whether to stay in the relationship despite the threat of HIV transmission. PrEP was perceived as a solution to this serodiscordant dilemma. These quotes come from participants in a research study of PrEP for serodiscordant couples before PrEP was proven [31].

'I feel stuck. I love my wife. I want to have sex. I don't like condoms. I don't want to get infected, either. It's not easy. It's difficult. It's a dilemma.'

'I wanted to stay married to my partner because we fell in love. What happened, happened. I found myself negative when she is positive. I still want to be with my wife. So when the doctor told us about this study, I saw it as an opportunity. You never know, it might work!'

SAFER CONCEPTION

PrEP has a role to play in safer conception. Couples had the highest level of adherence to PrEP during the periconception period [53]. Safer conception options for serodiscordant couples in which the man is HIV-positive include sperm washing with in-vitro fertilization or intrauterine insemination, suppressive antiretroviral therapy in the HIV positive partner, PEP and/or PrEP for the HIV negative partner, and/or timed condomless intercourse. Such safer conception options are often used in combination [54]. Assisted reproductive services are not available in all places, and can be expensive [55]. PrEP provides an extra layer of protection for couples desiring pregnancy, allows use of the

partner's semen for fertilization, and reinforces intimacy and strengthening relationships.

AGENCY

Some PrEP users report feeling empowered [56]. The empowerment comes from having control over one's own protection, rather than relying on partners to use condoms, take antiretroviral therapy, or accurately disclose their HIV serostatus. Empowerment also comes from planning for sex and safety in calm (or cold) moments, which allows more proactive consideration of sexual and partnership goals. PrEP can be used anytime during the day and without the knowledge of sexual partners. As such, PrEP is one of the only prevention interventions that is controlled by the receptive partners.

ADAPTABILITY

People want prevention strategies that can be adapted to situations when HIV risk is most present and salient. PrEP is adaptable in that the tablet can be taken any time during the day, with or without food, and started and stopped as needed. The preferential use of PrEP during periods of highest risk is the basis for a novel concept of 'prevention effective adherence' [57].

People move in and out of seasons of risk [58¹¹]. Seasons of risk can begin with the breakup of a long-term relationship, with substance use, migration to a new city, starting sex work, or coming out as a gay man. People want to stop PrEP if they find other ways to protect themselves. As such, PrEP may serve as a bridge to a variety of protective, health-promoting conversations, to relationship agreements with new or existing partner(s), to suppressive therapy with an HIV-positive partner [59], to managing use of stimulants, to access to clean injection materials, or to becoming empowered to insist on condoms among sex work clients.

People seeking to adapt PrEP to their seasons of risk want some guidance on how to start and stop PrEP. Pharmacological modeling and observed relationships between effectiveness and drug concentrations suggest that 5–7 doses of PrEP (using emtricitabine and tenofovir disoproxil fumarate) are required for full protection for rectal exposure to HIV [60¹²]. Fewer tablets appear to provide some protection [10]. Full protection from vaginal exposure is less well known but likely requires a longer loading period; the Centers for Disease Control estimates a 20-day period is required before full protection from vaginal sex is achieved [61], which is consistent with pharmacological modeling of vaginal drug concentrations [62]. Less information

is available about how to stop PrEP, although it is reasonable to suggest using PrEP for 28 days after the last possible exposure to HIV [63]; this emulates postexposure prophylaxis recommendations and provides time for people to consider whether the most recent exposure to HIV will be the last.

One way to adapt PrEP dosing to people's sexual practices would be through nondaily dosing before and after sex. Dosing tenofovir/emtricitabine PrEP before and after sex was shown to be effective in the Intervention Préventive de l'Exposition aux Risques avec pour les Gays, or French for Prevention intervention for risk exposure among gay men (IPERGAY) trial of MSM [64]. The IPERGAY participants reported frequent sexual activity (several times per week), leading to average use of 16 PrEP tablets/month; this level of PrEP use was associated with nearly 100% protection in the iPrEx OLE, which recommended daily use of PrEP, although adherence varied [10]. More evidence is needed on nondaily dosing and for now, daily PrEP dosing is recommended by the Food and Drug Administration and the Centers for Disease Control in the USA [61]. In an open-label PrEP study that included a randomized comparison of daily versus sex event-driven dosing, daily dosing was associated with higher coverage of sex events with pre- and post-sex dosing, higher adherence, and higher concentrations of drug [65–67]. Higher concentrations of drug provide more forgiveness for occasional missed doses.

UNCERTAINTIES ABOUT IMPLEMENTATION

These highly desired collateral benefits of PrEP could be undermined, or eliminated, if PrEP is implemented in ways that overly focus on 'getting pills into bodies' [68¹³]. PrEP programs that are overly focused on the strictly biological aspects, for example, medical appointments and adherence, rather than on how PrEP may fit with people's sexual and social goals, could become tacitly or overtly coercive. Fomenting shame of sexual practices under the rubric of 'risk compensation' is another hazard that could undermine implementation, agency, and adherence. Fear of drug resistance and toxicity is not warranted based on recent evidence, and inciting these fears undermines the credibility of antiretroviral medications used for both treatment and prevention.

CONCLUSION

Much will be learned from PrEP use. Further study to understand to the extent to which concepts such as

agency, preservation of relationships, and pleasure resonate for young persons (particularly women) in high prevalence settings is an important next step in PrEP research. Although the intended purpose of PrEP was to lower the incidence of HIV infection, PrEP users report being attracted to benefits that are salient, affective, and occur in the present. Such PrEP benefits include more pleasure, more intimacy, stronger relationships, feeling safer, less stigma, feeling empowered by planning for sexual and partnership goals, and ability to plan families. Creating a compelling narrative around sexual and social goals was an important lesson learned from successes in perinatal transmission prevention [69^{***}]. Focus on these benefits will provide insights and a compelling narrative that may bolster our struggle to end HIV transmission.

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Conflicts of interest

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