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Transgender Women's Concerns and Preferences on Potential Future Long-Acting Biomedical HIV Prevention Strategies: The Case of Injections and Implanted Medication Delivery Devices (IMDDs)

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Abstract

There are several long-acting biomedical HIV prevention products in the development pipeline, including injections and implanted medication delivery devices (IMDDs). It is critical to understand concerns and preferences on the use of these products in populations that shoulder a disproportionate burden of the HIV epidemic, such as transgender women. This will allow researchers and public health professionals to construct interventions tailored to the needs of these women to promote optimal use of these tools. In studies of other biomedical HIV prevention products (e.g., oral PrEP) it is clear that transgender women have unique concerns related to the use of these strategies. This may have an impact on this group's uptake and sustained use of longacting HIV prevention products. This study conducted four focus groups with N = 18 transgender women in New York City to understand their concerns and preferences on long-acting PrEP injections and IMDDs. Findings showed that participants were overwhelmingly positive about long-acting HIV prevention strategies, though they had some apprehensions. Overall, participants felt that injections and IMDDs could help address adherence challenges, and that transgender-specific needs should be addressed during clinical trials. Also, there were concerns related to injection or IMDD logistics, concerns about injections' or IMDDs' presence in the body, and familiarity with these products affected participants' opinions on them. Findings from this work can be used to inform protocols, measures, materials, and adherence interventions in future initiatives for transgender women using PrEP injections or IMDDs.

Keywords Biomedical HIV prevention · Transgender women · Transwomen · Cabotegravir · Cabotegravir · Longacting PrEP · Pre-exposure prophylaxis · Systemic PrEP · PrEP injections · PrEP implants

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Introduction

Long-acting biomedical HIV-prevention strategies, such as injections and implanted medication delivery devices (IMDDs), show promise in clinical trials [1–9]. Understanding the social and behavioral components of how people use these strategies is critical to product effectiveness [10–12]. Specifically, researchers must routinely re-conceptualize how tools should be designed, tested, delivered, and introduced to key populations to make them feasible, acceptable, sustainable, and cost-effective for end-users [13]. This may be especially important for transgender women. These women shoulder a disproportionate burden of the HIV epidemic [14, 15], yet are critically underrepresented in biomedical HIV prevention research [16, 17]. Thus, we know little about how long-acting pre-exposure prophylaxis (PrEP) might fit into their lives. The present work builds our understanding of transgender women's barriers and facilitators to long-acting HIV-prevention injections and IMDDs. Findings may help to design protocols and procedures related to these HIV prevention strategies that more directly address the needs of this group. In turn, this work has the potential to improve uptake and adherence to these products.

Designing biomedical HIV prevention products and PrEP delivery protocols tailored to the needs of transgender women is critical, since HIV prevalence in transgender women in the United States is estimated to be 21.7% [18]. These women experience unique barrers to the uptake and sustained use of HIV prevention tools. Other work shows that these barriers include concerns about cross-interactions with gender-affirming hormones, and that biomedical HIV prevention products are designed for men who have sex with men (MSM)) [16, 19, 20]. To our knowledge, with the exception of one study [21], there are no trials of biomedical HIV prevention products that aim to understand how these medications work for transgender women. The iPrEx study attempted to address this issue by enrolling a cohort of 339 transgender women. However, the trial did not yield definitive results with respect to PrEP efficacy in this group [22]; this may have been due to issues with medication adherence. iPrEx's problems with adherence in the transgender cohort highlights the need to understand this group's concerns and preferences related to long-acting biomedical HIV prevention products. This will allow clinicians and public health professionals to more effectively construct policies, protcols, and procedures to address transgender issues, which may improve uptake and adherence in this group [20].

Promising long-acting products for PrEP are progressing through the prevention pipeline including injections and IMDDs. In Phase II clinical trials, cabotegravir injections for PrEP were safe, well tolerated [3, 5, 23–25], and the HIV prevention effects of these injections could last up to eight weeks [26, 27]. Cabotegravir injections for PrEP are currently being evaluated in Phase III studies to examine their safety and efficacy as a single injection administered every 8 weeks (HPTN-083, -084) [28–30]. Long-acting PrEP IMDDs are currently being explored in pre-clinical phases (Sustained Long-Acting Protection from HIV; SLAP-HIV), and Phase I/II studies (CAPRISA-018) [31, 32].

The present work was situated within the SLAP-HIV trial, which aims to test and clinically develop a long-acting drug delivery system (e.g., injections, IMDDs) through a competitive elimination process (e.g., during the trials process, the most promising drug and drug delivery method will be identified and further developed; inferior drugs/delivery modalities will be discontinued). The delivery modality selected, based on clinical factors and input by potential users, will contain one of the following antiretroviral medications: TAF, rilpivirine, cabotegravir, or the tenofovir analog CMX-157 [33, 34]. This study used focus groups to understand transgender women's concerns and preferences on long-acting PrEP products, including injections and IMDDs. Findings from this work can be used to inform transgender-focused policies and procedures for the use of PrEP injections or IMDDs

Methods

Participants

Eligible participants for this study were at least 18 years old, lived in the New York City area, self-identified as a transgender women, had been sexually active within the last 3 months (defined as anal or vaginal sex with a cisgender man), were not currently taking oral PrEP, HIV-negative (self-report), and were willing to take a rapid HIV test after completing a brief survey described elsewhere [20].

Procedures

Recruitment took place from September 2016 through February 2017 from a convenience sample that was a part of a large longitudinal cohort study to learn about transgender identity development (Project AFFIRM). After completing a quantitative survey to characterize our sample [20], transgender women were invited to participate in one of the four focus groups, which occurred at a later date. Focus group discussion topics included participants' perceptions and knowledge of oral PrEP, and their opinions, preferences, and concerns about the methods in development (PrEP injections and IMDDs). Specifically, focus group discussion topics first covered oral

PrEP pills, which are currently available on the market. Then, the discussion focused on potential future long-acting HIV-prevention strategies, including injections and implants for PrEP. The new PrEP methods were introduced sequentially, after description of the current use of each delivery method (including descriptions of any necessary oral lead-in procedures to detect drug allergy). After presenting this information (e.g., injections to deliver antiobiotics, IMDDs for contraception), participants were asked about their likes and dislikes concerning each delivery method, their considerations as transgender women, and foreseen barriers and facilitators to uptake and adherence to the potential new methods. In-depth details of the methods and analyses used can be found in Rael et al. [20].

Results

There were N = 18 transgender women who participated in our focus groups. Participants had a median age of 29.9, were mostly of a race other than white (82.4%), and almost two-thirds had completed high school/GED (64.7%). Discussions of each HIV prevention method yielded major common themes, which are discussed below. Specifically, major themes included: [1] injections and IMDDs could help to overcome challenges with adherence to daily pills, [2] transgender-specific needs must be addressed during the clinical trials process, [3] concerns related to injection or IMDD logistics, [4] concerns related to injections or IMDDs presence in the body, and [5] familiarity with injections or IMDDs for other health conditions affects opinions about these products for PrEP.

Injections and IMDDs Could Help to Overcome Challenges with Adherence to Daily Pills

Overall, participants liked that they would not have to adhere to a daily product intake in order to have reliable protection against HIV. This was especially important because all participants, regardless of whether or not they had ever used oral PrEP, felt that it would be fairly easy to miss a pill.

> *"I really like injections a lot because an injection is liquid. It's just a quick pain and you don't have to worry if you've taken your pill everyday. This is a very important point."* (Focus Group 4)

Transgender-Specific Needs Must be Addressed as a Part of the Clinical Trials Process

Participants worried that the medications contained in long-acting HIV prevention strategies could interact with gender-affirming hormones. Though the research team explained that this was unlikely, participants remained skeptical. They felt that in order to have wide appeal in the transgender community, biomedical HIV prevention studies must demonstrate that strategies in development do not impede the effectiveness of gender-affirming hormones.

> *"… it's much safer to assume that you're going to have the potential to interact with hormones than not… It has to not interact negatively with hormones in order for it to gain any traction in the trans community."* (Focus Group 2)

Additionally, participants felt that clinical studies should examine the effects that biomedical HIV prevention strategies have on transgender women as a distinct group with distinct needs. Overwhelmingly, they endorsed the idea that transgender women's bodies are different from cisgender women's and men's bodies. Therefore, participants felt that medications contained in long-acting HIV prevention products would impact them differently, and therefore it would be important to understand specifically what this would mean for them.

> *"I mean, it's no disrespect, but a cis woman's body is different from a transgender woman's body. So, I mean, there's going to be different side-effects, different effects. Our bodies are going to take these medicines differently, so I want to know what did it do to this trans person."* (Focus Group 3)

Concerns Related to Injection or IMDD Logistics

Concern About Administering Injections in the Gluteal Muscle

Some participants expressed concern over injection in the gluteal muscle. Specifically, participants acknowledged that some transgender women have silicone (or other synthetic materials) injected or implanted in their buttocks, hips, or thighs to feminize their shape. These women would be unable to receive injections in in the area used by existing clinical trials protocols.

"But the people in the community who have silicone – well overall they are going to say, 'I'm not able to use this. This injection method is not something I'm able to use.' If this is on the upper hip, they're not going to be able to inject them…" (Focus Group 4)

Some participants expressed anxiety that receiving repeated injections in their gluteal muscle could cause scarring or other marking on the skin. One person explained that scarring near her gluteal area was something she would be unable to tolerate.

"Well if there's scarring, I don't want it near my butt. That's just it." (Focus Group 3) Others in our groups reminded these participants that noticeable scarring did not typically happen with hormone injections. Therefore, it would be unlikely that PrEP injections would cause scarring.

"…My ass looks great and I take needles in my ass… So I don't think this would be any different as far as the scarring." (Focus Group 3)

Dislike Meeting with a Healthcare Provider to Inject PrEP

Overwhelmingly, participants felt that visits with their healthcare provider to administer injectable PrEP were cumbersome and inconvenient. They explained that transgender women are often already juggling multiple doctor's appointments, and adding additional visits was undesirable.

"You have to keep your clientele and patients in mind. Specifically, we don't particularly enjoy a lot of doctor's visits, but that is different for every person." (Focus Group 1)

Other participants felt that intramuscular injections were something they could do at home. This is because transgender women often already self-administer intramuscular injections for hormone medications. Thus, participants felt that this is a skill that is translatable to other injectable medications.

"It's better for the trans woman to get an injection of that…because we have to inject our hormones anyways, so that's what I'm saying. I mean, some of us use needles anyway. They show us how to do it anyway. But I think it's better for us to use needles like this also." (Focus Group 1)

Dislike the Oral Lead-In Required for Injections

Among most participants, the 30-day oral lead in required for the injection was unpopular. When we explained that the purpose of the month-long course of pills was to detect potential drug allergies, participants were understanding, but unwaivering in their dislike for this approach.

"Yeah, I'm down for the injections. I'm just not down for taking the pills first and then take the injections. I'm not cool with that" (Focus Group 2)

Concerns Related to Injections' or IMDDs' Presence in the Body

Visibility and Perceptibility of IMDDs

Most participants did not want the IMDD to be perceptible. This was primarily because they were concerned that potential sex partners would make assumptions about it, or might ask unwanted questions.

"I think this is unpopular, because if you can still see and feel it, people are going to be weird…" (Focus Group 2)

Alternatively, some participants preferred the IMDD to be visible, since this made them feel confident that the device was in place and working properly. Specifically, for some participants, being able to physically tell where the IMDD was located meant that it was secure and doing its job.

"…Once it's not visible, it's hard to be like, 'Am I still protected? I know it's in my body somewhere, but…'" (Focus Group 2)

Concerns About Potential Clinical Issues Associated with IMDD Use

Some participants expressed concerns about issues they felt could occur with IMDD use. These included: concerns about what could happen if the IMDD were bumped, potential for migration of the IMDD, scarring associated with the insertion/removal processes, skin reactions (including IMDD "rejection" or "infection") that could occur with IMDD use, and general unpredicatible reactions (e.g., allergy) that might result from the IMDD. One participant detailed how she worries about accidentally knocking the IMDD against something.

"*You might make a wrong move or something or other, you know? It might start acting up… If I get up in the nighttime or you're doing something kinky and something or other and hit it or something and… It's like, 'Oh no! Wait a minute!'"* (Focus Group 1)

Other participants felt nervous that the IMDD could move from its initial insertion location.

"…so if they could, you know, make it more secure somehow. I think that's another thing that kind of bothers me is that it doesn't look very secure…it just looks like I could go like that and it would move." (Focus Group 1)

Some transgender women disliked the potential for scarring, and identified scarring as a reason that some prospective IMDD users may ultimately decide not to use this HIV prevention strategy.

"…A lot of people feel weird about scarring, so they might not…they might not like this…I don't think the potential of scarring or of an infection in that areas is like…that's just no…" (Focus Group 1)

Alternatively, other participants acknowledged that surgical procedures that are comparatively more complex (e.g., gender-affirming procedures) often leave only a small scar, indicating that the scarring left from IMDD insertion and removal would likely be minimal.

"Yeah, for example, the scar from my breast implants is very small, but they put in a large implant. So, I would imagine that the scar from that small straw would be almost nothing." (Focus Group 4)

Some participants worried that the IMDD could cause a reaction on the surface of their skin once it was inserted.

"…Pain, bleeding, blood blisters, scarring, or infection. Is that worth this to me? No." (Focus Group 1)

Other transgender women worried that the IMDD could become infected under their skin or that their bodies might "reject" the device.

"…what if it got infected inside of your skin?…that's a big concern…What can happen? You won't know unless your skin – if your skin turns purple." (Focus Group 3)

Another participant compared having the IMDD inserted to getting a piercing that
became infected.

"…it's basically the same thing as getting a piercing…getting a piercing, right? The body can reject it." (Focus Group 2)

Other participants feared that users could have an unpredictable reaction to IMDDs. Specifically, they felt that it would be impossible to know how their bodies might react to PrEP implants until they actually had the device inserted. Participants worried that they could have an allergic reaction, or dislike how the IMDD made them feel physically.

"A lot of stuff that you implant, a lot of them – they do come with extra side-effects… I don't know why that's the case, but my best friend, she has…she was on birth control and she decided to get the ring, the IUD, and she started getting sick. She lost a ton of weight she… she was a mess. Honestly, she looked way worse and then when she finally got it removed and she got back on the pill, she's better now. And that's the thing that's my biggest concern because I know for a fact that these things, the way it's applied, it will affect you very differently." (Focus Group 3)

IMDD Size

Overwhelmingly, participants indicated that a smaller IMDD was better.

"Bigger is better, but not this time…isn't there smaller? I'm just guessing." (Focus Group 1)

Participants elaborated that they would like IMDDs to be approximately the size of a matchstick, or ideally, smaller.

"[I'd like it to be] smaller than a matchstick. Half the size of a matchstick" (Focus Group 4).

Concerns About the Side-Effects of PrEP medications

Some participants were concerned about potential side-effects of the medication contained in PrEP injections. Several transgender women feared that injectable medications would have side-effects similar or worse than those associate
d with the tenofovir dipivoxil and emtricitabine's (Truvada) "start-up syndrome" (e.g., nausea, loss of appetite). This was true for both participants who had and had not previously used oral PrEP.

"But what if the injection has side-effects worser than the pills? The injectables have never been treated, has never been tested on animals nor on humans so…" (Focus Group 1)

Injections and IMDDs Should Last for a Prolonged Period of Time

Overall, participants were excited about the concept of long-acting HIV prevention strategies. Although theys differed over exactly how long they would want the HIV prevention effects to last, all participants agreed that injection/IMDD effects should last for a prolonged period. Specifically, some transgender women wanted these methods to last for 6 months.

"…for every six months a lot of transwomen would find that more manageable and, like, easier to deal with." (Focus Group 1).

Though some participants felt that 6 months was reasonable, this was the least amount of time anybody found acceptable. Many participants felt that 6 months was too short, and explained that they wanted the IMDD to last for a year or more.

"*The benefit to this - it would mean that I wouldn't have to think about it for a year. I would have 12 months of not having to worry about taking a pill or any other…"* (Focus Group 3).

Familiarity With Injections or IMDDs for Other Health Conditions Affects Opinions About These Products for PrEP

Familiarity with Injections Made use of this HIV Prevention Strategy More Acceptable

Participants were familiar with injections, since many of these individuals already administer gender-affirming hormones in this way. Subsequently, they were open to the idea of receiving injected PrEP for long-acting HIV prevention.

"I don't mind injectables because… my hormone shots are injectables, so it's not something that I am dreading or I dread. So, I'm an open mind. It's like a one-minute shot. Boom, bang, and I'm out the door for three months" (Focus Group 3).

Other individuals explained that injectable PrEP felt like it was directed to transgender women in a more meaningful way, because taking injectable hormones is often a large part of the transition process. Thus, this PrEP delivery method appeared to be more congruent with transgender women's existing preferences and behaviors.

"I feel like this is directly marketed to transwomen in some way. Like, injections are fairly common with transwomen, but not so much with gay, lesbian, and bi. Because there's just…they usually have no need for it. Like, if they're trying to prevent HIV they use condoms or they'll use PrEP. But we have our hormones and that's one specific thing…" (Focus Group 1)

Perceived High Cost of Long-Acting PrEP IMDDs

Overwhelmingly, participants believed that PrEP IMDDs would be prohibitively expensive. This was typically informed by their cisgender peers' cost experiences with IMDDs for contraception.

"…If the current state of medical care in this country is anything to judge, implants like this are extremely expensive now. They have this exact same method for use as a method of birth control, right? It's hugely expensive, and most insurances don't cover it." (Focus Group 2)

Discussion

This study identified transgender women's concerns and perceptions on potential future long-acting biomedical HIV prevention products, including PrEP injections and IMDDs. Some findings related to the clinical trials process, while others were relevant to device design and use preferences. Findings from both domains have the potential to affect transgender women's "real world" use of these products.

Clinical Trials Preferences

Participants were adamant that it was necessary for researchers to do a better job addressing transgender-specific needs during the clinical trials process (e.g., identifying cross-interactions with hormones, documenting how clinical effects of PrEP differ in transgender women). This is a theme observed in other work about biomedical HIV prevention with this population [16, 19, 20, 22]. By doing so, product developers could address transgender-specific needs during the design phase, therefore making end-products more feasible and acceptable for "real world" use by this population. One reason that previous work has failed to address transgender concerns is because clinical trials have not recruited transgender women in significant numbers. Those that have, (e.g., iPrEX) experienced severe adherence issues that undermined statistical analyses [22]. Though we can only speculate, one explanation for this issue could be that biomedical HIV prevention trials are typically designed for MSM or cisgender women—not transgender women. Therefore, transgender participants may feel uncomfortable in the study setting, or with study products, which could affect overall HIV prevention method use. Future research should explore how biomedical HIV prevention trials could more effectively recruit, retain, and support transgender participants, so that topics relevant to this population can be explored, measured, and addressed. Doing so could improve transgender uptake and adherence to these products in non-clinical trials settings.

To be explicit, addressing transgender-specific concerns in clinical trials could have implications for product use in the "real world." Specifically, future work should generate data on the themes that transgender women find important and/or have identified as barriers to product use in the past. Subsequently, transgender women who are considering PrEP will be able to take these findings into account to make more informed decisions on product use. Secondly, data on how transgender women use HIV prevention products could be

used to develop and refine interventions to facilitate uptake and adherence by CBOs and public health providers once these tools are on the market.

Device Design and Use Preferences

Participants reported that injections and IMDDs should last for a prolonged period of time. These time periods varied from as few as 6 months to as long as a year or more. The desire for extended periods of effectiveness was not unanticipated, since users would be required to undergo processes that are somewhat uncomfortable (e.g., needlestick for injections; trochar implantation for IMDDs) to have these PrEP products administered. Additionally, many transgender women already take gender-affirming hormone injections (e.g., weekly, bi-weekly) [35]; desire to avoid frequently injecting an additional medication may increase transgender women's favorability towards long-acting injection or IMDD products.

Currently, PrEP IMDDs are still in pre-clinical or Phase I/II trials, so there is no clear estimate as to how long they could last. However, these findings indicate that the length of protection of a single product application is an important motivational factor for product use; the longer the protection lasts, the more appealing the product is to transgender women. Cabotegravir injections for PrEP are in Phase III of the clinical trials process (HPTN-083/084), and at this moment, last for 8 weeks [36], though this could change as drug development advances.

Participants disliked the oral lead-in necessary for PrEP injections. Since this product is not removable once it is administered, this is an unsurmountable limitation; the oral lead-in facilitates the identification of drug allergies. This highlights the importance of messaging, and the care with which we must construct educational materials around this theme. Future studies should consider how to communicate the reasons for the oral lead in more effectively. Alternatively, individuals who persist in their dislike for the oral lead-in may comprise a market for removable long-acting products (e.g., IMDDs). Specifically, since IMDDs could be removed at any time if a user were to have an adverse reaction to the medication contained in the device, the oral lead-in is unnecessary. Similar devices have been used in cisgender women to deliver contraceptive medications (e.g., Nexplanon®). Users of these contraceptive products can to elect to have the device removed by a healthcare provider at any time if they observe undesirable side-effects [37] or simply wish to discontinue use. Following a similar protocol for PrEP implants could be beneficial transgender women and other users.

Despite issues with the oral lead-in, participants viewed injections favorably. They especially liked that this long-acting mechanism could help overcome issues with adherence to daily products. It is unknown why they noted this strength for injections, but not for IMDDs. One reason could be transgender women's familiarity with injections, compared to IMDDs; transgender women frequently use injections to deliver gender-affirming hormones [38]. Therefore, participants in our groups may have perceived this method to be more convenient. Also for this reason, transgender women reported that PrEP injections felt more congruent with their existing health behaviors. Focusing on these strengths could be important tools for recruiting and retaining transgender women in PrEP injection programs once this product is on the market. Specifically, if researchers highlight this strategy's similarities to transgender women's existing health routines, prospective transgender users may feel this tool is suited to their needs, rather than adapted from men's health directives. This is important, since previous studies have shown that transgender women view existing biomedical HIV prevention strategies (e.g., oral PrEP) as primarily for MSM, which is off-putting [19, 20]. By focusing on the ways that injections are tailored to the strengths of transgender women, this strategy could gain support in this community.

Another way to build upon the strengths of transgender women would be to allow these users to self-administer injections. Transgender women felt that visits to healthcare providers to deliver injections were a barrier to product use and identified self-injection as a way to overcome this. Specifically, participants reported that some transgender women already self-administer gender-affirming hormone injections to the gluteal muscles and other sites; self-administering PrEP injections could be an appropriate way to build upon this skill. In addition to transgender women, other groups have long self-administered intramuscular gluteal injections for other purposes, including treatment for female infertility, and multiple sclerosis [39, 40], indicating that this is neither novel nor impossible. Work is needed to determine the feasibility and acceptability of self-administering injectable PrEP among transgender women, since this could potentially boost interest in and adherence to this HIV prevention strategy.

On the other hand, participants acknowledged that administering injections in the gluteal muscle would exclude a subset of transgender women. Individuals with gluteal implants or fillers are unable to use this HIV prevention strategy, since implants prevent the intramuscular delivery of the clinical product. Currently, studies examining the use of injectable PrEP in MSM and transgender women (e.g., HPTN-083) use this as exclusion criteria [41]. Specifically, cabotegravir injections in Stage III PrEP studies are 3 mL in volume, thusly requiring injection in a large muscle; injection sites apart from the gluteal muscle are not currently under investigation. This highlights two things: 1) the need for continued development of PrEP injections, with a particular emphasis on reducing injection volume (which could, a) improve

self-injection experiences for users, and b) allow for delivery in a smaller muscle, which would allow transgender women with fillers or implants in their hips, buttocks, or thighs to use this strategy), and 2) the continued development of other biomedical HIV prevention products; in particular, a diverse suite of tools that act for varying lenghs of time and are administered in different ways to different parts of the body. In the contraceptive literature, the use of birth control methods other than oral pills has increased with the advent of new options. This is especially true for long-acting forms of contraception [42]. Having a diverse set of options has allowed women to use the contraceptive type that fits their current need [43]. The same is possible for PrEP. To ensure that PrEP, particularly long-acting PrEP, is accessible and usable by all, it is imperative to explore multiple forms and modes of administration of these emerging methods.

In addition to having choices about HIV prevention strategies, it is equally important that these methods are low-cost. Participants in our groups anticipated that HIV prevention IMDDs would be more costly than other long-acting HIV prevention strategies, which would act as a barrier to uptake. This was true even though almost everyone in our groups was covered by public or private health insurance [20]. This belief is not unfounded. The American Sexual Health Association identifies, "large initial cost" as a "con" to all types of contraceptive IMDD, including those that are similar to the one explored in this study [44]. Additionally, Planned Parenthood estimates the up-front cost of the contraceptive implant (e.g., Nexplanon®) to be between $0 and $1300. This has the potential to be far more expensive than other birth control methods, including contraceptive injections ($0–$100), and oral contraceptive pills ($0–$50) [45].

Participants differed in their opinion on whether PrEP IMDDs should be visible or perceptible. On one hand, participants felt that visibility could be dangerous, since sexual partners might ask unwanted questions or make assumptions about users' willingness to have condomless sex. On the other hand, participants felt that being able to see or feel the implant was reassuring, since to them, this meant that the device was in the correct place and working properly. Implantation of the PrEP IMDD will likely be similar to contraceptive IMDDs. Currently, contraceptive IMDDs are implanted at a depth so that it is not visible to others, yet users should be able to feel the rod when they press on the area where it is located. That is, when properly inserted, users are able to feel the implant only if they press on the inside of their upper arm; it is not otherwise detectable [46]. It is important tha we devise communication strategies so that transgender women who are considering PrEP IMDDs understand this, to assuage fears around device perceptibility.

Participants expressed concern over potential clinical issues associated with IMDDs. For example, some transgender women in our groups worried that bumping the implant through daily activities could cause it to break or migrate to a different area of the body. Breakage of contraceptive IMDDs is extremely rare, though not unheard of [47, 48]. Given this, it is imperative that device manufacturers not only test implants to ensure that breakage will not occur, but devise communication strategies to relay these results to potential users. Additionally, migration of the PrEP IMDD was a concern to participants in our groups. Migration of contraceptive IMDDs is also uncommon, but has happened in rare cases. This was serious in some instances; for example, there are reports of contraceptive IMDDs that migrated into the pulmonary artery [49]. The newest iteration of contraceptive IMDDs (e.g., Nexplanon®) can be detected via radiograph [50], which could be a useful innovation to address device migration, should it occur in PrEP IMDDs. Furthermore, the contraceptive literature shows that IMDD migration and breakage can largely be mitigated through correct device placement [51, 52]. Unequivocally, all providers administering PrEP implants should be appropriately trained on how to place this product.

A minority of participants were concerned about scarring from the insertion and removal processes, as well as skin reactions (e.g., infections) that might occur as a result of exposure to IMDD medications or the device itself. These types of reactions with existing contraceptive IMDDs are rare. A review of clinical implant study data found that adverse skin reactions, including pain, redness, bruising, scarring, and swelling of the insertion site was observed in only 4% of women [55]. Additionally, though the scar left at the IMDD site should be very small, clinicians can further reduce the appearance of marks left by implant removal by using paper sutures (left in for 1 week), applying a sterile dressing, encouraging the patient to keep the wound dry for the 48 h following the procedure, and applying a pressure bandage [56]. Furthermore, correct placement of the device can minimize the odds of adverse skin reactions [52], which further illustrates the need for proper physician training on IMDD application.

Given the concern about the risks above, it is imperative to consider how to appropriately communicate the risks of IMDDs to potential users. Icon arrays could be a useful place to start. Icon arrays are graphical representations consisting of a number of icons (e.g., circles) symbolizing individuals who are affected by a risk [53]. Icon arrays have been shown to more effectively communicate risk in treatments that carry low medical risk by drawing readers' attention to unaffected patients. This strategy is especially effective for populations that have a wide range of numeracy skills [54].

Lastly, participants reported that they wanted the study device to be small. Though a device the size of a matchstick was acceptable, an IMDD that was even smaller was viewed as favorable. Though a PrEP IMDD that is smaller

than a matchstick does not appear to be on the horizon, contraceptive implants have continuously grown smaller over time. For instance, the original Norplant® birth control IMDD was made up of six flexible rods. Relatively soon after it came on the market, it was replaced by the Norplant-II®, which had only two rods [57]. Today, the Nexplanon® contraception IMDD is made up of only one rod [58], indicating that over time, it may be possible to reduce the size of the device.

Conclusions

We believe that our findings are important, given the limited research on this topic. Results of this work can be used to inform future HIV prevention programs targeting or including transgender participants. Additionally, future studies of these products should include measures to assess trans-specific concerns, such as cross-interactions with hormones and/or exploring alternative sites to administer medications. With relationship to the injection, future studies could highlight how this product is congruent with the existing health behaviors (e.g., hormone injection) of many transgender women. Moreover, this work could build off of this familiarity by exploring alternative clinical protocols (e.g., self-injection) that could better meet the needs of women in this group. In terms of the IMDD, future studies should continue to monitor devices for safety (e.g., potential for migration, breakage, insertion/removal-site reactions) and assess potential ways that transgender women's responses to these products could differ from non-transgender individuals. It is important that there is a widespread effort to thoroughly train all providers who will administer this IMDDs on proper insertion/removal techniques, since this appears to have a large impact on user outcomes.

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