Preferences for pre-exposure prophylaxis (PrEP) among sexual and gender minorities: a discrete choice experiment in Brazil

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Summary

Background Men who have sex with men (MSM) and transgender women (TGW) are disproportionally affected by HIV infection in Latin America. This study aims to assess pre-exposure prophylaxis (PrEP) preferences among sexual and gender minorities (SGM) and identify attributes and levels that are related to PrEP uptake and adherence, both crucial for PrEP success.

Methods We conducted a discrete choice experiment (DCE) among SGM from all Brazilian regions (September–December/2020). The survey was administered face-to-face (five Brazilian capitals) and online (entire country). We used a D-efficient zero-prior blocked experimental design to select 60 paired-profile DCE choice tasks.

Findings The total sample size was 3924 (90.5% MSM; 7.2% TGW and 2.3% non-binary or gender diverse persons). In random-effects logit models, highest levels of protection and "no side effects" were the most important attribute levels. For "presentation", injectable and implant were preferred over oral. Participants were willing to accept a 4.1% protection reduction to receive injectable PrEP or a 4.2% reduction if PrEP were taken monthly. The largest class in the latent class models was defined predominantly by the preference for the highest HIV protection level (p < 0.005). Respondents in this class also preferred no side effects, injectable and implant presentations.

Interpretation Higher HIV protection, no side effects, and presentation, whether injectable or implant, were the most important attributes in PrEP preferences. Protection against HIV was the most important attribute. PrEP programs should make available technologies such as long-acting presentations that could reunite the most desired attributes, thus maximizing acceptability and user-appropriateness.

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Keywords: Human immunodeficiency virus; Pre-exposure prophylaxis; Men who have sex with men; Sexual and gender minorities; LGBTQIA+; Transgender women; Latin America; PrEP preferences; Injectable PrEP

Introduction

Brazil is the country in Latin America with the largest population living with HIV/AIDS. Gay, bisexual, and other men who have sex with men (MSM) are disproportionally affected.[1] Approximately 50% of reported HIV infections among men are attributed to male-to-male sexual contact, and new infections are on the rise in this population, especially among younger MSM.[1–3] Across all key populations, transgender women (TGW) bear the highest epidemic burden in the country.[4,5] Daily

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oral pre-exposure prophylaxis (PrEP) with emtricitabine and tenofovir disoproxil fumarate (FTC/TDF) has been offered within the Brazilian Public Health System (SUS) since 2017 without any direct costs to the users. The PrEP program includes testing, counselling, consultations, and other services covered in the official guidelines for those at risk of HIV acquisition, including MSM and TGW.[6]

Optimal adherence is paramount to the effectiveness of PrEP.[7–12] Data from different PrEP programs show a decline in use after the initial months, as daily pill-taking may be challenging.[11] Conversely, event-driven PrEP demands users take FTC/TDF at least 2 h before sex and then after sex, if it indeed occurs.[7] However, planning sexual intercourse may also constitute a challenge to many. Therefore, the needs of specific populations must be taken into account to improve PrEP uptake and adherence. Hence, it is necessary to investigate the factors that influence the decisions to initiate PrEP and to continue its use with adequate adherence and persistence in the long run. Alternative PrEP agents are under development or undergoing clinical trials to provide a broader portfolio. The options under consideration include long-acting injectables, which could potentially overcome the adherence difficulties inherent to a daily oral regimen. Likewise, implants, vaginal rings and films, and transdermal compounds are being studied to increase the pool of biomedical possibilities to meet the needs and preferences of the greatest possible number of users.[8,13]

There is still a need to understand the surrounding aspects of the decision-making process for PrEP among MSM and TGW. For instance, a Brazilian trans-specific PrEP demonstration study called *PrEParadas* showed a high uptake and adherence among TGW, despite being a hard-to-engage population.[9] A systematic review identified and grouped the reasons for suboptimal adherence to oral PrEP: side effects, low-risk perception,

stigma, logistics of the daily life medication regimen, and socioeconomic status.[12] Another systematic review investigating PrEP use among transgender populations showed low awareness and described many barriers to adherence, including distrust in health services and concerns regarding interactions with hormone treatment.[14] Despite challenges encountered worldwide regarding PrEP uptake and use, Brazil's first PrEP demonstration project (PrEP Brasil) showed a high interest in PrEP, with approximately 61% uptake.[15] To increase the demand for PrEP and sustain compliance, it is essential to better understand the PrEP preferences among MSM and TGW. This knowledge is necessary to tailor strategies and offer the best alternatives for long-term positive outcomes.

Preferences for PrEP can be assessed by presenting hypothetical scenarios to individuals and asking them to choose the best options. These strategies are classified as stated preference techniques, and discrete choice experiments are one of those techniques that use an attribute-based approach to collect this type of data.[16,17] DCE consists of presenting respondents with choice sets comprised of two or more competing alternatives that vary along with several attributes, which are the factors that affect choice. An attribute is a qualitative characteristic of PrEP, while a level is one of several values one attribute might take. DCEs allow identifying the most relevant attributes and their respective levels. For example, an attribute could be the frequency of PrEP use and the attribute levels, daily, event-driven, or yearly.

Discrete choice experiments for PrEP

DCEs have been used in health for a few decades,[18–20] including in HIV research,[21–23] and a few studies have solely investigated PrEP preferences.[24–31] A study conducted in the U.S. investigated PrEP delivery programs for MSM.[24] Another study in Uganda explored factors

associated with the acceptability and potential uptake of PrEP among fishing communities.[25] A study in South Africa considered youths' preferences for PrEP, focusing on relevant product delivery characteristics and modifiable attributes.[26] Another study among South African young males focused on long-acting injection and implant preferences.[27] In Malawi, a DCE study explored the preferences for PrEP delivery modes among HIV-uninfected female sex workers.[28] In Ukraine, a study investigated the best strategies to implement PrEP for MSM.[29] In Mumbai and Chennai, India, research was done to understand the willingness to use PrEP among MSM.[30] The most important attributes in these studies were PrEP presentation, affordability (or cost), HIV prevention effectiveness, dosing strategy, and dispensing location. Additionally, a DCE study among MSM in Canada found that an on-demand pill was the most preferred formulation, followed by monthly injection, a daily pill, and an on-demand rectal gel.[31] Although some of the attributes in these studies (i.e., direct costs and or affordability) do not apply to health systems with universal healthcare such as Brazil, they emphasize the importance of specific attributes such as presentation and dosing frequency. One crucial point about the current DCE literature is that it does not address PrEP preferences for TGW. In addition, to the best of our knowledge, no PrEP DCEs have been published in Latin America.

Given the lack of information on the preferences of sexual and gender minorities (SGM) in Latin America, especially in Brazil, regarding PrEP, this study aims to assess it using a discrete choice experiment (DCE) and to identify attributes and levels that may be related to PrEP uptake and adherence, which are crucial for PrEP's strategic success.

Methods
A DCE based on Random Utility Theory[32] was developed to measure preferences for PrEP. It is assumed that individuals make choices that maximize their utility. Nevertheless, it is important to keep in mind that the individual choice for an alternative is not only a function of the attractiveness of the alternative but of the socio-economic and other individual characteristics. Furthermore, individuals will, most of the times, choose a specific alternative, but when they do not, it may be due to random factors. The experiment aimed to estimate preferences according to a particular set of attributes. The first step was to identify and select a set of attributes that would reflect all the relevant characteristics for the choice of PrEP. The attributes (for example, presentation of PrEP, whether a pill or an injection) were broken down by their different levels (e.g. pill, injection, or implant). The levels of the attributes were varied systematically and shown in a series of different choice sets, each with the same number of alternatives. The

preference weights for attributes and their levels made up for the overall utility of each alternative. The observed choices can inform about the relative weights of preferences for attributes and levels and the overall utility of each alternative.

We followed current guidelines from ISPOR[33–35] and the mainstream DCE literature on how to identify and select attributes and levels by following these steps: conducted a review of the literature around PrEP presentation and products; compiled and systematized the evidence obtained; did a consultation with experts on PrEP; conducted 20 in-depth qualitative interviews with current and non-users of PrEP as relevant actors; carried out pilot tests, and, lastly, conducted the DCE both face-to-face with the aid of tablets and online. The detailed methodological steps are presented in the protocol.[36]

Literature review, evidence synthesis, and qualitative phase
The literature review was conducted following a pre-specified search strategy (see Supplementary file S1) and identified essential characteristics related to PrEP uptake and adherence, both in terms of existing technologies and new technologies in the pipeline. PrEP with oral FTC/TDF and long-acting injectable cabotegravir are recommended by the World Health Organization (WHO). Although highly efficacious in preventing HIV, oral FTC/TDF may not be optimal for some vulnerable populations that would like to receive PrEP. Novel oral agents, long-acting injectables, vaginal rings, topical products (tablets, gels, films, enemas), and neutralizing monoclonal antibodies, among other multipurpose technologies, were found in the literature, whether undergoing clinical trials or with potential for test and use in the near future.[8,12,37–39]

Consultation of healthcare professionals, TGW and MSM users, and non-user of PrEP
We carried out in-depth interviews with healthcare professionals working in HIV care and PrEP delivery to MSM and TGW groups. In these interviews, we validated the list of a priori PrEP attributes and levels from the literature review, and these professionals emphasized the most important ones based on their experiences and assessments of patients' realities.

After that, we conducted qualitative in-depth interviews with current PrEP and non-PrEP users (MSM or TGW) during the first semester of 2020. Participants were recruited at Instituto Nacional de Infectologia Evandro Chagas (INI-FIOCRUZ), HIV prevention services, including testing and PrEP provision. In the interviews, participants provided their general views about PrEP regarding attributes and levels, challenges, and what made PrEP desirable or not. In addition, interviews with current PrEP users investigated how they felt about the current PrEP presentations, adherence levels, and difficulties experienced. When interviewing

non-PrEP users, the goal was to understand their perceptions about PrEP and eventual barriers to access. The overarching goal was to assure all-important attributes and levels were correctly covered by the DCE and that none of the chosen attributes would be dominant. Furthermore, we also conducted in-depth interviews with three LGBTQIA+ community engagement workers, which were able to voice the most important PrEP characteristics and challenges in using the technology. All individuals participated voluntarily and gave informed consent before being included in the study.

Design of DCE

After the literature review and qualitative studies, we had a list of five attributes with three or five levels (Table 1). It is important to mention that these five attributes used in the study reflect PrEP characteristics that were brought up by study participants and considered the most important ones to be elicited. We used the Ngene software (version 1.2.1, 2018, build 18121) to develop the DCE.[40] We took the number of attributes (5) and levels (3 or 5) into consideration to obtain the optimal number of choice sets. The goal was to ensure the number of choice sets would be a reasonable cognitive task. We used a D-efficient zero-prior blocked experimental design[40,41] consisting of 4 blocks of 15 unique choice tasks (D-error = 0.03). Implausible and dominant combinations of attribute levels were not included. However, as additional questions, we added two questions we considered dominant at the end of the experiment (contrasting the least and most desired attribute levels identified in the qualitative phase of the study).[33] In these two questions, one of the alternatives had attribute levels that were all better than the attributes of the other alternative. In this

study, we did not exclude any participants from the analyses based on those answers since there were no systematic differences between the 3.4% of respondents who did not choose the better option and the rest of the sample. The experiment did not include an opt-out option provided that the main goal was to focus on attributes and not on the likelihood of PrEP adoption.[42] The survey was programmed at Alchemer®.

Study procedures

We recruited twelve professionals with previous experience and engagement with SGM communities to administer the tablet-assisted face-to-face DCE. Specific training regarding DCEs was provided to them. Individual pilot interviews using tablets were conducted with a dozen individuals to ensure the wording was appropriate and that questions were understandable, feasible, and appropriate. Data collection occurred between September and November 2020.

User preferences for different PrEP presentations were elicited through the administration of a DCE. The same inclusion criteria were used for face-to-face or online recruitment: 18 years of age or older; TGW, non-binary persons or MSM; negative HIV serology (self-reported in the online component and based upon testing in the recruitment sites). Recruitment for the face-to-face step took place at HIV testing sites, which also provided free PrEP according to the Brazilian guidelines located in five Brazilian capitals located in all geographic regions of the country: Rio de Janeiro (Southeast), Brasília (Midwest), Salvador (Northeast), Porto Alegre (South) and Manaus (North). All participating sites were clinic-based settings within the Brazilian Public Health System (SUS) who provided HIV prevention services, such as HIV testing, PrEP and PEP. Some of the recruited participants could have also been enrolled in other studies within the ImPrEP Project, a transnational project in Latin America to generate evidence on PrEP among MSM and TGW.[39,43,44] The DCE used the infrastructure of other studies under the umbrella of the ImPrEP study for data collection but had its own training of interviewers and protocols. Participation in the DCE did not influence the other studies. We performed online recruitment at dating apps used by SGM populations (Hornet and Grindr) through paid advertisements that led to the study link.

During the presentation of the DCE, survey respondents were introduced to some PrEP-related options. We then explained they would face hypothetical situations in which they would have to choose between two products (Product A or Product B) considering the characteristics described for each one (Fig. 1). We clarified that some of the products might still be under research and development and that the characteristics presented were hypothetical, that is, they may not reflect the reality of products already available for PrEP. Subsequently, we provided extensive written and pictorial

Attributes	Levels
Presentation	Oral pill
	Injectable
	Implant
Frequency of use	Daily
	On-demand
	Monthly
	Once per bimester
	Once per year
Frequency of visits to health services	Once per bimester
	Once per trimester
	Annually
Side effects	None
	Mild
	Moderate
Protection against HIV	9 in 10 remain HIV negative
	8 in 10 remain HIV negative
	7 in 10 remain HIV negative

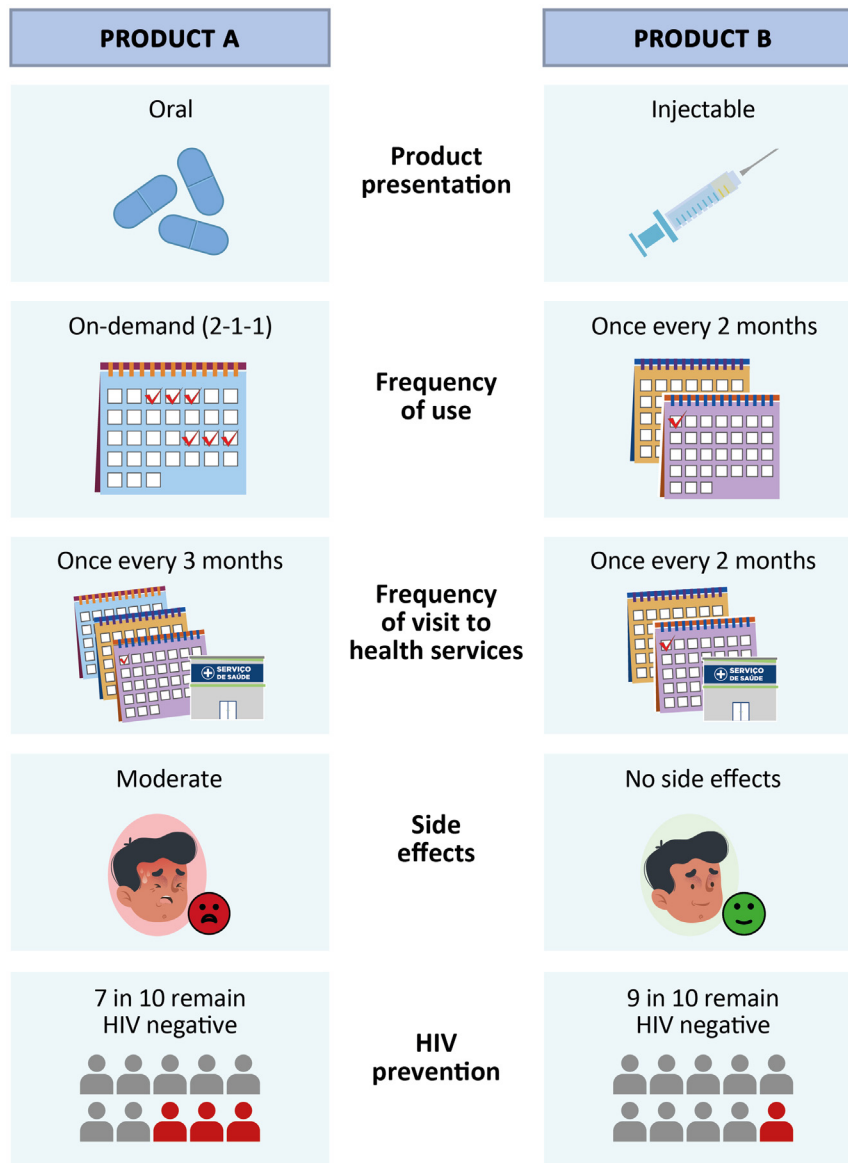*Table 1:* List of attributes and levels for PrEP.

Fig. 1: Example of a choice set in the Discrete Choice Experiment (DCE).

explanations of all attributes and levels. Respondents were told to choose only one of two options, which would be their preferred option, with no right or wrong answer. The survey contained additional questions that include a checkbox for inclusion criteria, sociodemographic variables, sexual behaviour, and PrEP use (full survey available in Supplementary files S2 and S3).

Sample size

We followed the recommendations given by Orne,[45] who suggested that if the purpose were to compare groups and detect significant differences, the target sample size should be large enough to accommodate a minimum of 200 individuals per group, so our initial target sample was 1000 participants in total.[36] Given our interest in four sub-groups (MSM currently using PrEP, MSM not using PrEP, TGW/non-binary persons currently using PrEP, and TGW/non-binary persons not using PrEP), our actual sample size was 3924 participants (3553 MSM and 371 TGW/non-binary persons). The distribution was 1050 in-person and 2874 online.

Variables

We collected socioeconomic variables such as age, categorized as 18–24; 24–35 and older than 25 years old; race (White/Asian; Pardo; Black); level of education

(elementary; high school; college degree or higher); income (2 Brazilian minimum wages or less; 2–6 minimum wages; more than 6 minimum wages); region of the country where participant resided (North; Northeast; Midwest; Southeast and South); reporting not having enough food and behavioural variables such as number of sexual, which was measured by asking participants how many persons they had any sexual relationship in the past 6 months regardless of gender and type of sex (oral, vaginal and anal). The rationale for this question was to access the total number of sexual partners. We also collected information on not having a steady partner. We also assessed if participants engaged in condomless anal sex or condomless receptive anal sex (past 6 months); if they had transactional sex (past 6 months) and PrEP-related factors, such as previous PrEP use and willingness to use it.

Statistical analyses

We provide descriptive statistics on the study sample and used random-effects logit models to obtain the preferences of SGM regarding PrEP. In terms of the relative preference weights for chosen attributes and levels, data was analyzed using a random-parameter logit and latent class models[46] in Stata, Release 16.1.[47] The preference weights allowed the description of the relative strength of each attribute and level in comparison, respectively, with all other attributes and levels. For calculating ratios describing the trade-offs respondents were willing to make among the attributes, we used risk equivalence (maximum acceptable risk) or time equivalence for changes in attributes or attribute levels.[33] Latent class analyses were estimated using the Stata modules lclogit2 and lclogitml2.[48] Models with different number of latent classes were compared, and the choice was based upon the log-likelihood, information criteria, and in terms of appropriate interpretation of classes.[48] Analyses were performed according to best practices and recommendations published by the International Society for Pharmacoeconomics and Outcome Research (ISPOR).[33–35]

Ethics

This DCE was approved by the local internal review board (*Comitê de Ética em Pesquisa do Instituto Nacional de Infectologia Evandro Chagas da Fundação Oswaldo Cruz*, approval number 3.979.759, CAAE: 28416220.2.1001.5262, issued on April 18, 2020). Additionally, we obtained IRB approval in each local study site as follows: Brasília, FIOCRUZ Brasilia, approval number 4.218.010, CAAE 28416220.2.2002.8027 (17 August, 2020); Manaus, *Fundação de Medicina Tropical Dr Heitor Vieira Dourado*, approval number 4.172.506, CAAE 28416220.2.2001.0005 (24 July, 2020); Salvador, *Secretaria da Saúde do Estado da Bahia - SESAB*, approval number 4.291.299, CAAE 28416220.2.2003.0052 (22 September, 2020); Porto Alegre, Secretaria Municipal de Saúde de Porto Alegre/SMSPA,

approval number 4.188.326, CAAE 28416220.2.2004.5338.

Results

Participants' characteristics are presented in Table 2. In total, 3924 participants completed the survey (90.5% MSM; 7.2%% TGW and 2.3% non-binary or gender diverse persons). As shown in Table 2, respondents had a mean age of 32.8 years (SD 9.1). Most of the participants were recruited online (73.2%). 64.4% of respondents had never used PrEP, whereas 29% were current users and 6.5% were past users. Among those who never used PrEP, 62.1% reported willingness to use it. 94% of PrEP users declared to be under a daily oral regimen. TGW and non-binary persons had a higher percentage of Blacks and *Pardos* than MSM (74.1% versus 41.6%). MSM who answered the online questionnaire had a higher percentage of respondents with a college degree (75.2%), higher income (30%), and who were White (63.9%) than other sub-groups. A higher percentage of MSM declared to have engaged in condomless anal sex (68.4%) than TGW (59.3%) or non-binary persons (57.1%).

The respondents were randomly distributed across the four versions of the questionnaire, which only differed regarding the choice sets (four blocks), with n = 1.005 (25.6%) respondents completing block 1, n = 955 (24.3%) block 2, n = 989 (25.2%) block 3 and n = 975 (24.8%) block 4 (Table 2). We conducted sub-group analyses by geographic region, and they all reflected the same preferences depicted in the overall analyses, mainly the importance of the level of protection in choosing PrEP.

We found no statistically significant differences in preferences between online and on-site recruitments, so these sub-group analyses were omitted. Random-effects logit model results are presented in Table 3. Except for the coefficient for frequency of use "on demand" and level of protection "8 in 10 will remain HIV-", all attributes or levels respectively were significant at the 0.05 level, indicating that they were relevant in choosing PrEP in the model for all participants. The attribute levels for "level of protection 9 in 10 remain HIV-" and "not having side effects" were the two most important ones, meaning participants placed a higher value on them in the selection of PrEP (Table 3). For "presentation," injectable and implant were preferred compared to oral.

For the attribute "level of protection," the attribute level "7 in 10 will remain HIV negative" was determined as the reference category. Three hypothetical levels of

Variables	TGW N (%)	Non-binary persons N (%)	MSM in loco N (%)	MSM online N (%)	Overall N (%)
Total	280	91	679	2874	3924
Socio-demographic factors					
Age, years—mean (SD)	29.8 (9.1)	29.0 (7.9)	30.9 (8.2)	33.7 (9.2)	32.8 (9.1)
18–24	91 (32.5)	29 (31.9)	158 (23.3)	392 (13.6)	670 (17.1)
24–35	126 (45.0)	45 (49.5)	358 (52.7)	1465 (51)	1994 (50.8)
>35	63 (22.5)	17 (18.7)	163 (24.0)	1017 (35.4)	1260 (32.1)
Race/Ethnicity					
White/Asian	72 (26.0)	44 (48.4)	237 (35.4)	1810 (63.9)	2163 (55.9)
Pardo	114 (41.2)	19 (20.9)	248 (37.1)	699 (24.7)	1080 (27.9)
Black	91 (32.9)	28 (30.9)	184 (27.5)	325 (11.5)	628 (16.2)
Level of Education					
Elementary	107 (38.5)	6 (6.7)	48 (7.1)	68 (2.4)	229 (5.9)
High School	142 (51.1)	41 (45.6)	298 (44.0)	642 (22.4)	1123 (28.7)
College Degree	29 (10.4)	43 (47.8)	332 (49.0)	2152 (75.2)	2556 (65.4)
Income					
≤2 minimum wages	214 (83.9)	47 (54.0)	281 (43.3)	725 (26.1)	1267 (33.7)
2–6 minimum wages	31 (12.2)	29 (33.3)	263 (40.5)	1215 (43.8)	1538 (40.9)
≥6 minimum wages	10 (3.9)	11 (12.6)	105 (16.2)	833 (30.0)	959 (25.5)
Region of the country					
North	25 (8.9)	4 (4.4)	98 (14.4)	36 (1.3)	163 (4.2)
Northeast	41 (14.6)	17 (18.7)	88 (13.0)	253 (8.8)	399 (10.2)
Midwest	41 (14.6)	7 (7.7)	91 (13.4)	186 (6.5)	325 (8.3)
Southeast	162 (57.9)	50 (54.9)	333 (49.0)	2055 (71.5)	2600 (66.3)
South	11 (3.9)	13 (14.3)	69 (10.2)	344 (12)	437 (11.1)
Person/room in the house	0.6 (1.2)	0.5 (0.3)	0.4 (0.3)	0.4 (0.6)	0.9 (1.6)
Crowdedness ratio					
Worrying not having enough food (last 30 days)					
Never	68 (24.3)	42 (46.2)	402 (59.2)	1834 (63.8)	2346 (59.8)
Sometimes	60 (21.4)	24 (26.4)	164 (24.2)	752 (26.2)	1000 (25.5)
Most of the time/Always	152 (54.3)	25 (27.5)	113 (16.6)	288 (10.0)	578 (14.7)
Behavioral factors					
Number of sexual partners (mean, SD)[a]	28.3 (107.1)	7 (12.1)	10.1 (16.7)	9.7 (17.8)	11 (33.5)
Number of sexual partners[a]					
<5	175 (62.5)	61 (67.0)	411 (60.5)	1716 (59.7)	2363 (60.2)
≥5	105 (37.5)	30 (33.0)	268 (39.5)	1158 (40.3)	1561 (39.8)
No steady partner	153 (54.6)	55 (60.4)	311 (45.8)	1954 (68.0)	2473 (63.0)
Engaged in condomless anal sex[a]	166 (59.3)	52 (57.1)	506 (74.5)	1964 (68.3)	2688 (68.5)
Engaged in condomless receptive anal sex[a]	150 (53.6)	41 (45.1)	366 (53.9)	1391 (48.4)	1948 (49.6)
Transactional sex[a]	142 (50.7)	9 (9.9)	59 (8.7)	205 (7.1)	415 (10.6)
PrEP-related factors					
PrEP use					
Never	165 (58.9)	60 (65.9)	252 (37.1)	2051 (71.4)	2528 (64.4)
Current	83 (29.6)	24 (26.4)	391 (57.6)	641 (22.3)	1139 (29.0)
Past	32 (11.4)	7 (7.7)	36 (5.3)	182 (6.3)	257 (6.5)
Willingness to use PrEP	59 (35.8)	27 (45.0)	120 (47.6)	1365 (66.6)	1571 (62.1)
Recruited online					2868 (73.1)
Randomization					
Block 1					1005 (25.6)
Block 2					955 (24.3)
Block 3					989 (25.2)
Block 4					975 (24.8)

TGW: transgender women; MSM: gay, bisexual, and other cisgender men who have sex with men. [a]Past 6 months.

Table 2: Socio-demographic, behavioural characteristics, and recruitment of participants in the study, Brazil, 2020.

Attributes	Levels	All participants [n = 3924]	
		Coefficients	95% CI
Presentation	Injectable	**0.39**	(0.28–0.49)
	Implant	**0.22**	(0.14–0.29)
	Oral (Reference)	–	–
Frequency of use	On demand	0.03	(–0.04 to 0.11)
	Monthly	**0.44**	(0.36–0.52)
	Every two months	**0.42**	(0.34–0.50)
	Yearly	**0.40**	(0.32–0.47)
	Daily (Reference)	–	–
Frequency of visit to health services	Every two months	**0.13**	(0.07–0.18)
	Annually	**0.16**	(0.07–0.26)
	Quarterly (Reference)	–	–
Side Effects	None	**0.85**	(0.79–0.91)
	Mild	**0.40**	(0.33–0.46)
	Moderate (Reference)	–	–
Level of protection	9 in 10 will remain HIV-	**2.08**	(2.02–2.15)
	8 in 10 will remain HIV-	1.05	(0.98–1.10)
	7 in 10 will remain HIV- (Reference)	–	–
Constant		**–1.73**	(–1.81 to –1.65)
lnsig2u		–18.5 (23.17)	(–63.9 to 26.9)

Coefficients represent the log odds change from the reference category to the attribute level. Bold coefficients are significant at 0.05 level.

Table 3: Random effects logistic regression model of PrEP attribute preference for all survey participants in Brazil, 2020.

protection were included from lowest to highest: 7 in 10 will remain HIV-; 8 in 10 will remain HIV- and 9 in 10 will remain HIV- (Table 1). DCEs allow for the inclusion of hypothetical scenarios such as these. Our goal was to make users reflect on how important it would be to have different levels of higher protection above a baseline of 7 in 10 remaining HIV-. The highest level of protection, "9 in 10 will remain HIV negative," was the most important attribute level for the respondents in all models, with a coefficient of 2.08 (95% CI: 2.02–2.15) in the model for all participants, followed by "no side effects." The highest level of side effects, "moderate," was the reference category (0.85, 95% CI: 0.79–0.91).

Marginal rates of substitutions or trade-offs between the attributes were calculated using the command WTP in Stata for level of HIV protection (most important attribute in the DCE). Table 4 shows how respondents were willing to trade a reduction in HIV protection modelled as a continuous variable for the other attribute levels in the experiment. For example, participants were willing to accept a 4.1% protection reduction to receive injectable PrEP or accept a 4.2% reduction in protection if PrEP were to be used monthly.

The latent class estimates are presented in Tables 4 and 5. Three latent classes, numbered from one to three, were identified based on log-likelihood and information criteria.[48] The respective class shares or memberships and coefficients, as well as the standard errors and 95% confidence intervals, are presented in Table 4. The class shares were 0.58 for class 1 and 0.191 for class 2, and 0.231 for class 3. The first and largest class, with an average membership of 58%, was defined predominantly by the preference for HIV highest protection level (p < 0.005). Respondents in this class also preferred the lowest level of side effects (none) and injectable presentation, followed closely by implants. At this point, it is important to emphasize the importance of the statistical significance of differences between levels of the same attribute. For example, in class 1 of the latent class analysis, both injection and implant are statistically significant, but they are not statistically significantly different from one another. This indicates that while both are preferred to oral, neither injection nor implant is preferred to the other. The "intermittent PrEP frequency" had a significant negative effect on this class. The second-largest class (class 3) had an average membership of 23.1% and showed stronger preferences for injectable and implant presentation, followed by "monthly frequency of PrEP use" (p < 0.005). The third-largest class (class 2) showed the highest preferences for HIV protection "9 in 10 are HIV protected", and no side effects, however, with smaller coefficients than class 1. Compared to TGW and non-binary individuals, MSM were more likely to belong to class 1 than class 3 (reference class). Those with previous use of PrEP were less likely to belong to class 2 than 3. Respondents 24 years of

Attribute/level	Coefficients WTA[b]	% Reduction in protection level participants are willing to accept to receive the attribute/level	Confidence intervals
Injectable Presentation	−0.041	4.1	(−0.045 to −0.037)
Implant Presentation	−0.285	2.9	(−0.315 to −0.254)
On demand frequency	−0.008	0.1	(−0.012 to −0.005)
Once per month frequency	−0.399	4.0	(−0.412 to −0.371)
Every two months frequency	−0.422	4.2	(−0.452 to −0.391)
Yearly frequency	−0.322	3.2	(−0.352 to −0.291)
Visit health services every 3 months	−0.121	1.2	(−0.143 to −0.010)
Visit health services yearly	−0.014	0.1	(−0.018 to −0.010)
Mild side-effects	−0.100	1.0	(−0.103 to −0.098)
Moderate side-effects	−0.048	0.5	(−0.050 to −0.045)

WTA, willingness to accept. [a]Level of protection was modelled as a continuous variable. [b]Negative coefficients means the percentage reduction in protection level participants are willing to receive the other attribute level.

Table 4: Marginal rates of substitutions for changes in protection level[a].

age or older were more likely to belong to class 3 and those younger than 24 years old were more likely to belong to classes 1 and 2.

Discussion

This study has investigated preferences for PrEP among SGM in Brazil using a DCE in two modes of administration (online and face-to-face). It is the first to focus on TGW populations and the first in Latin America to focus on MSM, TGW, and non-binary or gender diverse persons. The results highlighted higher HIV protection, no side effects, and PrEP presentation, whether injectable or implant, as the most important attributes in the preferences. Protection against HIV was the most important attribute overall, and it was slightly more important to MSM than TGW/non-binary persons. This result was evidenced in all modelling strategies used in the study. The same pattern was observed for side effects, as MSM had stronger preferences for no side effects. In third place, frequency of use was slightly more important than the presentation itself, and monthly, and yearly frequency of use had similar strengths of preference.

The importance of PrEP presentation is noteworthy as there was a willingness to trade some efficacy to use injectables, for example. Moreover, this finding is in line with the new developments in the field, such as clinical trials for injectable presentations or subdermal implants,[49] and the recent recommendation of long-acting injectable cabotegravir by WHO.[50]

The literature corroborates the importance of PrEP product efficacy as it translates into the level of protection against HIV.[24,25,29,51] It was an important attribute brought up in the qualitative exploratory phase of the study, and its importance was confirmed in the DCE. However, the qualitative phase also stressed daily pill-taking difficulties, leading to poor adherence.

Our study and results contribute to minimizing the scarceness of studies on TGW in general[14] and, more importantly, considering their preferences.[52] The differences between TGW and MSM emphasize the specific needs of this population in Brazil, where they predominantly live in a context of structural social exclusion and marginalization, violence, and transphobia, thus increasing their vulnerability to HIV infection. They are also more likely to engage in HIV risk behavior and face more barriers to accessing healthcare.[53,54] A study suggested that transwomen bore the highest HIV burden among any population at risk in Brazil, and the high proportion of diagnoses among young participants pointed to the need for tailored long-term healthcare and prevention services to curb the epidemic and improve their quality of life.[55]

In general, TGW/non-binary persons expressed higher preference for injectables and implants than MSM, likely reflecting more difficulties with daily oral presentations. Overall, injectables were more preferred than implants, possibly indicating some perception of inconvenience regarding implants. The ImPrEP demonstration study[11] has shown that younger persons, TGW, people with lower educational levels and Blacks have lower adherence to PrEP. That study has also found higher preferences for long-acting PrEP, so future programs could offer this modality to such groups that have lower adherence to daily oral PrEP. Given the long-acting technologies currently available or under development are injectable or implant, for example, the study corroborates the importance of providing technologies with such attributes to fulfill the need among these groups, that include young MSM and TGW.

On-demand frequency of use was the least important level, and it was not significant for TGW/non-binary persons. Spaced-out frequencies of use (monthly, bimonthly, annually) were preferred over on-demand

Class	Choice	Coefficient	SE	p-value	95% Confidence Interval	
Class 1 Share = 0.578	Injectable	0.530***	0.058	0.000	0.417	0.644
	Implant	0.523***	0.048	0.000	0.428	0.618
	On-demand	−0.156**	0.050	0.002	−0.255	−0.058
	Monthly freq	0.433***	0.041	0.000	0.351	0.515
	Service trimester	0.162***	0.027	0.000	0.108	0.217
	Service yearly	0.170**	0.053	0.001	0.067	0.273
	No side effects	1.470***	0.028	0.000	1.415	1.525
	9 in 10 HIV-	3.520***	0.058	0.000	3.405	3.634
Class 2 Share = 0.191	Injectable	−0.971***	0.068	0.000	−1.104	−0.839
	Implant	−1.665***	0.070	0.000	−1.803	−1.528
	On-demand	0.080	0.074	0.282	−0.065	0.224
	Monthly freq	0.100**	0.045	0.024	0.013	0.187
	Service trimester	0.066*	0.034	0.057	−0.002	0.133
	Service yearly	−0.046	0.080	0.562	−0.202	0.110
	No side effects	0.632***	0.036	0.000	0.563	0.702
	9 in 10 HIV-	0.477***	0.036	0.000	0.406	0.547
Class 3 Share = 0.231	Injectable	1.266***	0.066	0.000	1.138	1.395
	Implant	1.830***	0.069	0.000	1.694	1.964
	On-demand	−0.026	0.060	0.669	−0.143	0.092
	Monthly freq	0.888***	0.048	0.000	0.796	0.981
	Service trimester	0.100**	0.031	0.001	0.039	0.161
	Service yearly	−0.162*	0.067	0.015	−0.294	−0.031
	No side effects	0.771***	0.037	0.000	0.698	0.844
	9 in 10 HIV-	0.401***	0.034	0.000	0.333	0.468
No observations	117,720					
No persons	3924					
Log-likelihood	−25,802.8					
BIC	51,845.5					

Monthly freq = monthly frequency of PrEP use; Service trimester = visit health services every three months; Service yearly = annual visit to health services. SE: standard error; BIC Bayesian Information Criterion; Significance: *p < 0.05, **p < 0.01, ***p < 0.001.

Table 5: Estimation of the latent class model with 3 classes.

compared to daily frequency. These results may reflect the difficulties with planning for on-demand pill taking and highlighting preferences for modalities of PrEP with less frequent use. These findings are in accordance with PrEP studies carried out in other countries.[24–27,29,30,56] For example, the study conducted by Minnis and colleagues to investigate PrEP preferences among South African youth showed that duration of effectiveness or different frequency of use was the most important attribute, with a strong preference for less frequent dosing.[26] Our study did not show the strength of preference for the less frequent dosing option (annually). For example, participants did not have a stronger preference for annually compared to monthly or bimonthly. Differently, a study conducted in Toronto identified an on-demand pill as the most preferred formulation.[31] Lower levels of side effects were preferred in our study. Accordingly, in a systematic review of adherence to oral PrEP for HIV, side effects were identified as one of the main reasons for non-adherence.[12]

The mean age of respondents was 32.8 years. Those younger than 24 years of age belonged to classes with stronger preferences for the highest levels of protection of HIV, lowest levels of side effects, injectable and implant presentations. A study carried out in different Brazilian cities to analyze willingness to use PrEP has identified that combination HIV prevention is most needed among young men who identify as gay/homosexual due to higher levels of engagement in high-risk behavior for HIV acquisition but also identified increases in willingness to use PrEP over time.[57]

This preference study has some limitations that need to be mentioned. Only a limited number of attributes and corresponding levels can be included in any DCE; otherwise, the tasks become highly complex, and the decision-making process demands a high cognitive burden, thus compromising efficiency and data quality.[17] Therefore, selecting attributes and attribute levels is at the core of the DCE design. Although multiple efforts were made to select attributes and levels through

systematic literature search and qualitative research, as current guidelines recommend,[33–35] there is always the possibility that other relevant attributes may have been left out from the study. A further limitation could be the lack of an opt-out option which forced all respondents to make an explicit choice between the two alternatives in the experiment.

The mixed-mode nature of our study could also be pointed as a limitation and a strength. On the one hand, part of the survey participants counted with the help of an interviewer to assist them in answering the DCE. On the other hand, respondents who answered the online experiment did not have that help. Nevertheless, we made the best effort to keep the choice sets as simple as possible by using coloured pictorial designs for the attributes and levels. A strength of the mixed-mode nature was recruiting a large number of participants, and In our internal analysis, the results did not differ by mode. The online version may leave people at ease to respond more freely to the questions, so as long as we reach as many sub-groups, considering all relevant age groups, SES levels, and minorities, this should be a cost-effective way of conducting DCEs, especially during specific limitations, such as the COVID-19 pandemic in the case of the current study. Although the study faces these limitations, it provides valuable insights into important aspects regarding PrEP preferences in key populations.

Conclusions

This study demonstrates the relative importance of attribute levels in choosing PrEP in Brazil, with participants placing a higher value on the high level of protection, absence of side effects, and alternative presentations to daily pill taking. The lower value on the frequency of visits to health services and "on-demand" PrEP presentations should be noted. Taken together, these findings highlight the importance of measuring preferences in specific settings and populations as these may differ, possibly due to cultural differences. Brazil was the first country in Latin America to make PrEP a public policy, making it available at no cost to users since its implementation, so as the country continues to provide PrEP and develop its policies, these finds will be useful to guide in the adoption of new technologies as they become available in the market, for example, those that require less frequency of use while maintaining maximum levels of protection.

Furthermore, future PrEP programs and research should emphasize the most important attribute levels identified, focusing on the PrEP technologies that may fill these existing gaps, such as long-acting presentations that could unite the most desired attributes, thus maximizing acceptability and user-appropriateness.

Contributors

CCAP, TST, BG, and VGV conceived and designed the DCE Study and also conceived and supervised the current analysis and manuscript preparation.

CCAP, TST, PML, BG, and VGV interpreted the findings and drafted the manuscript. CCAP, TST, and PML accessed, verified the data and did the statistical analyses. BH, AF, JDUB, MVGL, DARS, MB, and MCP helped with data acquisition, interpretation of the findings, and drafting the manuscript. CCAP, TST, BG, and VGV were involved in revising the manuscript for important intellectual content. All authors read and approved the final manuscript. CCAP, TST, PML, BH, AF, JDUB, MVGL, DARS, MB, MCP, BG, and VGV had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Appendix A. Supplementary data
Supplementary data related to this article can be found at https://doi.org/10.1016/j.lana.2023.100432.

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