Preferences for pre-exposure prophylaxis for HIV: A systematic review of discrete choice experiments

Luh Putu Lila Wulandari,a,b,1 Shi Yi He,c,1 Christopher K. Fairley,d,e Benjamin R. Bavinton,a Heather-Marie Schmidt,f,g Virginia Wiseman,a,h Rebecca Guy,a Weiming Tang,i Lei Zhang,c,d,e,1** and Jason J. Ongc,d,e,j,2*

aThe Kirby Institute, University of New South Wales, Sydney, Australia
bFaculty of Medicine, Udayana University, Bali Indonesia
cChina-Australia Joint Research Center for Infectious Diseases, School of Public Health, Xi’an Jiaotong University Health Science Center, Xi’an, China
dMelbourne Sexual Health Centre, Alfred Health, Melbourne, Australia
eCentral Clinical School, Monash University, Melbourne, Australia
fUNAIDS Regional Office for Asia and the Pacific, Bangkok, Thailand
gGlobal HIV, Hepatitis and STIs Programme, World Health Organization, Geneva, Switzerland
hDepartment of Global Health and Development, London School of Hygiene & Tropical Medicine, London, United Kingdom
iDepartment of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, United States
jDepartment of Clinical Research, London School of Hygiene & Tropical Medicine, Keppel Street London, London, United Kingdom

Summary

Background
We aimed to systematically review the health preference literature using discrete choice experiments (DCEs), an attribute-based stated preference method, to investigate patient preferences for HIV pre-exposure prophylaxis (PrEP).

Methods
A search in PubMed, Scopus, CINAHL, and Embase was conducted on July 1, 2021, and updated on November 3, 2021. We used two concepts to create our search strategy: (1) discrete choice experiments/conjoint analysis/best-worst scaling, and (2) HIV PrEP. The study is registered in PROSPERO (CRD42021267026).

Findings
In total, 1060 studies were identified, and 18 were included in the analysis. Various attributes were examined, including dosing regimen, type of PrEP products, side effects, other side benefits, cost, effectiveness, dispensing venue, and additional support services. Dosing frequency, cost, the effectiveness of PrEP, dispensing venue, and side effects were the most common attributes examined in DCEs. Despite significant heterogeneity in preferences across subpopulations, overall, the most important attributes were cost (28%, 5/18), effectiveness (28%, 5/18) followed by dosing frequency (17%, 3/18).

Interpretation
Notably, in studies where all of these three attributes were examined, some individuals would trade effectiveness for cost or vice versa. Ensuring PrEP is low cost or free, widely disseminating information of its effectiveness and advancements in reducing dosing frequency could accelerate the uptake of PrEP for those who would benefit from PrEP the most.

Funding
None.

Copyright © 2022 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

Keywords: Systematic review; Discrete choice experiment; Preferences; HIV; Pre-exposure prophylaxis
Introduction
HIV pre-exposure prophylaxis (PrEP) is the use of antiretroviral medications by people without HIV and offers up to 99% protection against HIV infection when taken as prescribed.1 HIV PrEP is of benefit at an individual level and, by reducing HIV transmission, potentially at the population level as well.2,3 Due to its proven benefits, PrEP was recommended by the World Health Organization (WHO) in 2015 as an additional prevention option for people at substantial risk of HIV as part of combination HIV prevention approaches.4,5 This was updated in 2019 to include the recommendation on event-driven or on-demand PrEP,10 and in 2021 on vaginal ring PrEP.11

Current levels of PrEP access are not sufficient to significantly affect the course of the HIV pandemic.12 Despite strong evidence on the benefits of PrEP, and a commitment by the United Nations to have 3 million people at high risk of HIV infection accessing PrEP by 2020,13 it is estimated that 927,277 were using PrEP at the end of 2020.14 In Q3 of 2021, the figure had increased to 1,544,777,14 with the majority of users located in the Americas (42%) and Africa (34%).12,15,16 Further, while the intention is for PrEP to be used dynamically in accordance with risk (i.e., particularly to be used during periods of risk), a systematic review reported that at least one-third of PrEP users had discontinued PrEP within six months.17 Several barriers were noted at the individual and structural levels, such as internalized stigma about risk behaviours (including stigma towards key populations and personal feelings of shame about having condomless sex), inaccurate perception of risk, financial or language barriers, and segmented health systems.1,18

The design of a successful PrEP program, including the type of products being used and how products are delivered through the program, should involve affected communities from inception to implementation. This includes eliciting individuals’ preferences so that programs can be tailored to meet their needs and preferences, consequently improving the appeal and uptake of PrEP. One method increasingly used to quantitatively measure preferences is discrete choice experiments (DCEs).19 Government bodies increasingly utilize DCE surveys in their decision-making.20,21 In a DCE survey, participants are asked to choose their preferred option among two or more alternatives describing a product or service as a combination of attribute levels. These choice data provide information about the strength of preferences for attributes and how individuals trade off one attribute against another. In HIV research, DCEs have been used to elicit preferences towards several aspects of HIV care, including HIV testing and self-testing22-24 and HIV treatment services.25

As PrEP programs continue to be scaled up globally, using different service delivery approaches and a range of new PrEP products (including injections16 or vaginal rings27), it is critical to understand and account for the values and preferences of people who would benefit from PrEP. In recent years, studies have been conducted to evaluate the preferences for PrEP using DCEs, however, there has not been a systematic review to synthesize the overall health preference evidence on this topic. These data could help inform guideline development, program planning, and implementation.28 Thus, we aimed to review the existing health preference data for PrEP as elicited from DCEs.

Methods
We conducted a systematic review following guidance from the Cochrane Handbook 5.1.29 The study was registered in the international prospective register of systematic reviews (PROSPERO, CRD42021267026).

Inclusion criteria
We included studies if they met the following criteria: (i) reported participant preferences for PrEP; and (ii) presented primary data using a DCE. No restrictions were placed on the publication date. We excluded qualitative studies, studies without primary data, duplicates, studies not in English, studies with no full text, conference papers, study protocols, and commentaries.

Search strategy
A literature search was conducted on July 1, 2021, and updated on November 3, 2021. We searched PubMed, Scopus, CINAHL, and Embase using two concepts to create our search strategy, combining the Mesh terms and free text words and synonyms of: (1) discrete choice experiments/conjoint analysis/best-worst scaling, and (2) HIV pre-exposure prophylaxis. Further details are provided in Supp.1.

Data screening and extraction
Two reviewers (LW, SH) independently screened the titles and abstracts for inclusion and identified eligible studies using the software, Covidence (Veritas Health Innovation, Australia). Subsequently, full texts were read independently by two reviewers (LW, SH) to determine their inclusion. All discrepancies were resolved by a third reviewer (JO). Full texts of the eligible studies were then independently extracted by two authors (LW, SH), and again checked by the third reviewer (JO) who resolved any discrepancies. We extracted the following data: author, country, year of publication, study year, the aim of the study, sampling strategy, inclusion criteria, recruitment site, number of participants, participants’ risk group, experience with the PrEP product, and type of PrEP. We also extracted data related to the conduct of the DCE (survey administration,
attribute selection strategies, whether the DCE was piloted, experimental design, attributes and attribute levels used in the DCE, number of choice tasks per person, statistical models, and results). The quality of the study was evaluated using the PREFS checklist, a published tool used to assess the quality of studies examining preferences.30

Data synthesis
Descriptive statistics were used to summarize the study characteristics (i.e. frequencies and percentages). We used narrative synthesis to provide an overview of included studies, focusing on how DCEs were conducted and their main results. We report our findings following The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.31

Role of the funding source
No specific funding was received for this study. All authors took the decision to submit for publication. LPLW and HSY had access to the data.

Results
Study characteristics
In total, 1060 studies were found, and 18 studies were included in the analyses (Figure 1). Table 1 summarizes the major characteristics of the studies. Briefly, most studies (85%, 15/18) were published in or after 2018. Most focused on preferences of men who have sex with men (MSM) (ten studies), followed by female sex workers (FSW) (five studies), four among youth or adolescents, and two included injecting drug users (IDUs).

Figure 1. Schematic flowchart demonstrating the identification, screening and inclusion of studies, based on the inclusion and exclusion criteria.
| Authors            | Year of study | Country                  | Population          | Inclusion Criteria                                                                                                                                 |
|--------------------|---------------|--------------------------|---------------------|---------------------------------------------------------------------------------------------------------------------------------------------------|
| Browne et al\(^{11}\) | 2016-2017     | Zimbabwe and South Africa | Women               | Aged 18-31 years, Female, HIV-negative, Sexually active, Microbicide and PrEP naïve, Not pregnant.                                                   |
| Chakrapani et al\(^{18}\) | 2016-2017     | India                    | MSM                 | Aged 18 years or more, Self-identified as kothi, gay, bisexual, versatile, panthi or MSM, Sexually active with another man in the previous month, Willing to provide consent for participation, Willing to invite peers. |
| Dubov et al\(^{16}\)  | 2016          | Ukraine                  | MSM                 | Aged 18 years or more, Self-reported HIV-negative, Any sexual contact with another man in the past six months, No previous history of using Truvada for PrEP. |
| Dubov et al\(^{14}\)  | 2015          | U.S.                     | MSM                 | Aged 18 years or more, Self-identifying as MSM, Self-reported HIV-negative, No previous PrEP experience.                                               |
| Eisingerich et al\(^{22}\) | 2010-2011     | Peru, Ukraine, India, Kenya, Botswana, Uganda and South Africa | FSW, MSM, IDU, SDC and young women | Aged 18 (16 for young women in Botswana) years or more, Self-reporting a negative or unknown HIV serostatus, Sexually active, Not participating in a market research study in the past 12 months. |
| Galea et al\(^{13}\)   | -             | Peru                     | FSW, male-to-female TG, MSM | Self-reported HIV-negative                                                                                                                         |
| Gutierrez et al\(^{10}\) | 2020          | U.S.                     | U.S. military MSM and trans-individuals | Self-reported HIV-negative                                                                                                                         |
| Kuteesa et al\(^{13}\)  | 2016-2017     | Uganda                   | Residents of the fishing community | Aged 18 years or more, Residence in the fishing community for over three months.                                                                   |
| Lancaster et al\(^{27}\) | 2016-2017     | Malawi                   | FSW                 | Aged 18 years or more, Be able to speak English or Chichewa, the predominant local language, HIV-negative.                                            |
| Minnis et al\(^{31}\)   | 2017-2019     | South Africa             | Youth               | Aged 18 to 24 years, Female and male youth, Had not participated in a biomedical HIV prevention trial of a PrEP product.                            |
| Minnis et al\(^{16}\)   | 2015-2017     | South Africa and Kenya   | Young women          | Aged 18 to 30 years, Young women, Had participated in a biomedical prevention trial of PrEP product (TRIO Study), Women from the same communities who had not used the three PrEP products in the same study. |
| Montgomery et al\(^{12}\) | 2017-2019     | South Africa             | Youth including MSM | Aged 18–24 years, Residing in the sampled residential plot, Had not participated in a biomedical HIV prevention trial of a PrEP product.            |
| Authors                     | Year of study | Country     | Population | Inclusion Criteria                                                                                                                                 |
|-----------------------------|---------------|-------------|------------|---------------------------------------------------------------------------------------------------------------------------------------------------|
| Pines et al<sup>64</sup>    | 2016-2017     | Mexico      | FSW        | Aged 18 years or more, Cisgender female, HIV-negative, Reported exchanging sex for money, drugs, or goods (past month),                           |
|                             |               |             |            | Reported condom-protected vaginal/anal sex with a client (past month), Agreed to accept free treatment if they tested STI-positive, Owned a cell phone.|
| Quaife et al<sup>65</sup>   | 2015          | South Africa| Adult males and females, adolescent girls, FSW | Adult men and women, and adolescent girls, Adolescent girls did not require to be sexually active, Had tested negative for HIV at least once in the past six months, |
|                             |               |             |            | self-reported sexual penetration or oral sex in the last six months with at least eight men, having exchanged money, drugs, alcohol or gifts for sex a minimum of 8 times in the last month, |
| Salinas-Rodriguez et al<sup>66</sup> | 2018-2019 | Mexico     | MSW        | Aged 18 years or more, Assigned male sex at birth, Be able to read and speak Spanish fluently, Had tested negative for HIV at least once in the past six months, |
|                             |               |             |            | self-reported sexual penetration or oral sex in the last six months with at least eight men, having exchanged money, drugs, alcohol or gifts for sex a minimum of 8 times in the last month, |
| Shrestha et al<sup>67</sup> | 2016          | U.S.        | IDUs       | Aged 18 years or more, HIV-negative, Drug- or sex-related HIV risk behaviours in the past six months.                                               |
|                             |               |             |            |                                                                                                                                                |
| Tan et al<sup>68</sup>      | 2019          | Singapore   | MSM        | Aged 18 years or more, Identify as a cisgender or transgender male, Identify as non-heterosexual,                                                |
|                             |               |             |            | Being a Singapore citizen, resident, or a foreign national residing in Singapore for more than a year at the point of the survey, HIV-negative.    |
| Wheelock et al<sup>67</sup> | 2011          | Thailand    | MSM, TGW   | Aged 18 years or more, Self-identifying as MSM, Self-reporting a negative or unknown HIV serostatus, Being sexually active, Not participating in a market research study in the past 12 months. |

Table 1: Characteristics of 18 included discrete choice experiment studies on pre-exposure prophylaxis for HIV.

PrEP = HIV Pre-exposure prophylaxis; MSM = Men who have sex with men; kothi = feminine gender expression, mostly receptive sexual role; versatile = insertive and receptive sexual roles, self-identified as “double-decker” in Chennai; panthi = masculine gender expression, primarily insertive sexual role; FSW = female sex workers; IDU = injecting drug users; SDC = serodiscordant couples; male-to-female TG = male-to-female transgender; PrEP product = i.e. vaginal gel, vaginal ring, oral tablet or injection; TRIO study = the Tablet, Ring, Injection as Options Study; Adult = aged 18 to 49 years; adolescent = age 16 to 17 years; STI = Sexually transmitted infections; MSW = male sex workers; IDUs = injecting drug users; TGW= transgender women.
The studies were conducted in 13 countries. Three studies (17%) were conducted in multiple countries, four (22%) were from high-income countries, ten (56%) were from middle-income countries, and two (11%) were from low-income countries (Figure 2).

The implementation of the DCE
Among these 18 studies, 13 (72.2%) were conducted face-to-face. Fifteen (83%) explicitly mentioned the use of formative research before the conduct of the DCE, including through focus group discussions or interviews with target groups or communities, academics, or policymakers. Twelve (67%) studies reported conducting a pilot DCE survey before the main study. The number of choice tasks per person ranged from 4 to 14, with a median of 8. Among those studies that provided the information, two recruited product naïve participants, and three involved both product naïve and experienced participants. (Table 2).

Attributes included in DCE studies
Various attributes were examined, including dosing regimen, type of PrEP products, side effects, other side benefits, cost, effectiveness, dispensing venue, and additional support services. Dosing frequency, cost, the effectiveness of PrEP, dispensing venue, and side effects were the most common attributes examined in DCEs. Despite variations in preferences across subpopulations, overall, important attributes most frequently preferred by the participants were cost (28%, 5/18), effectiveness (28%, 5/18) followed by dosing frequency (17%, 3/18). Notably, in studies where all these three attributes were examined, some individuals would trade effectiveness for cost or vice versa (Table 3).

Assessment of the study quality
The overall reporting quality was acceptable but left some room for improvement. Fifteen studies met four of the five PREFS criteria and three met only three. The mean score was 3.83 (standard deviation [SD] 0.38), and the scores ranged from 3 to 4 (Supp. 2). None of the studies reported on differences between responders and non-responders, which might lead to non-response bias. Also, three studies excluded some responders from the analysis but did not investigate the impact of these exclusions on study results. The most commonly noted reasons for exclusion were that responders failed the comprehension test or did not answer enough choice tasks.

Discussion
This systematic review synthesizes the existing health preference data for PrEP as elicited from published DCEs. Our study adds to the literature by highlighting the values and preferences of populations that would benefit from PrEP. We found 18 studies that were conducted in 13 countries. These studies revealed that dosing frequency, cost, the effectiveness of PrEP, dispensing venue, and side effects were the most common attributes included in DCEs. Notwithstanding
| Authors          | Type of participants (experience with the product) | Survey administration | Attributes Selection | Pilot tested DCE | Experimental study design | Number of choice tasks per person | Statistical models               |
|------------------|---------------------------------------------------|-----------------------|----------------------|------------------|--------------------------|----------------------------------|----------------------------------|
| Browne et al     | Product-experienced and product-naïve             | Face-to-face, using a tablet device | Literature review    | Yes              | D-efficient design       | 8                                | Random-parameters logit (RPL) model |
| Chakrapani et al | Not clear                                         | Face-to-face, using a tablet device | Literature review and qualitative research with MSM | Yes              | D-efficient design       | 8                                | RPL                              |
| Dubov et al      | Product-naïve                                     | Online survey         | Literature review, in-depth discussions with multiple stakeholders, including public health researchers, PrEP community activists, and MSM | Yes              | Sawtooth Software’s experimental design module | 14                               | Latent class analysis (LCA)       |
| Dubov et al      | Product-naïve                                     | Online survey         | Literature review, and in-depth discussions with multiple stakeholders | Yes              | Sawtooth Software’s experimental design module | 14                               | LCA                              |
| Eisingenich et al| Not clear                                         | Face-to-face           | Literature review, discussions with academic, policy, and industry experts | Yes              | ‘Efficient’ design using SAS 9.3 software | 10                               | Hierarchical Bayes (HB) model     |
| Galea et al      | Not clear                                         | Face to face           | Literature review, focus group discussions | Yes              | Fractional factorial orthogonal design | 8                                | One-way analysis of variance (ANOVA) model |
| Gutierrez et al  | Product-experienced and product-naïve             | Online survey         | Literature review, in-depth qualitative interviews among PrEP experts and military MSM | Yes              | Sawtooth Software’s experimental design module | 8                                | HB                              |
| Kuteesa et al    | Not clear                                         | Face to face           | Scoping review, focus group discussions and individual interviews | Yes              | D-efficient design       | 10                               | Multinomial logit (MNL) + LCA     |
| Lancaster et al  | Not clear                                         | Face to face, interviewer-administered | Literature review, focus group discussions and individual interviews | Not clear       | Sawtooth Software’s experimental design module | 8                                | RPL                              |
| Minnis et al     | Not clear                                         | Face-to-face, interviewer assisted | In-depth interviews, focus group discussions, expert consultations, feedback, and pretesting | Yes              | D-efficient design       | 9                                | RPL                              |
| Minnis et al     | Product-experienced and product-naïve             | Face-to-face           | In-depth interviews | Yes              | D-efficient design       | 8                                | RPL                              |
| Montgomery et al | Not clear                                         | Face to face, tablet-device Interviewer-administered, face to face survey | Formative research | Yes              | Not clear | 9                                | LCA                              |
| Pines et al      | Not clear                                         | Interviewer-administered, face to face tablet-device | Literature review | Not clear | D-efficient design       | 12                               | MNL                              |
| Quafe et al      | Not clear                                         | Interviewer-administered, face to face tablet-device | Literature review and focus-group discussions | Yes              | D-efficient design       | 10                               | MNL + LCA                        |
| Shrestha et al   | Not clear                                         | Audio computer-assisted self-interview | Literature review, discussions with experts | Not clear | Fractional factorial orthogonal design | 8                                | ‘Conjoint analysis’               |
| Tan et al        | Not clear                                         | Online                | Literature review | Yes              | Sawtooth Software’s experimental design module | 4                                | MNL, generalized multinomial logit model (GMLNL), LCA |
| Wheelock et al   | Not clear                                         | Interviewer-administered, face to face survey | Literature review, and discussions with experts | Not clear | Orthogonal fractional factorial design | 10                               | HB                              |
| Salinas-Rodriguez et al | Not clear                       | Face to face, via computer tablets. | Literature review | Yes              | Not clear | 8                                | MNL, RPL and rank-ordered logit   |

**Table 2: Conduct of the discrete choice experiments.**
| Authors                  | Dosing regimen | Type of PrEP | Benefits                                             | Extra services | Additional benefits               | Barriers         | Access               | Most Important                  |
|-------------------------|----------------|--------------|------------------------------------------------------|----------------|-----------------------------------|------------------|----------------------|-------------------------------|
| Browne et al⁴⁵          | Timing         | Mode of insertion | Effectiveness of HIV prevention                      | Pregnancy prevention, Use in secret | Side effects | Effectiveness of HIV prevention |
| Chakrapani et al⁵⁸      | Timing         | Mode of insertion | Effectiveness of HIV prevention                      | Cost, Side effects | Dispensing location | Cost |
| Dubov et al³⁹           | Timing         | Product form  | Monitoring, Adherence support                        | Cost            | Dispensing location | Cost, Side effects, Cost |
| Dubov et al⁶¹           | Timing         | Monitoring    | Cost                                                  | Cost            | Dispensing location | Cost |
| Eisengirich et al⁵²      | Timing         | Product form  | Monitoring, Adherence support                        | Time spent obtaining PrEP | Dispensing location, Frequency of pick up | Timing |
| Galea et al⁴²           | Timing         | Effectiveness of HIV prevention                      | Cost, Side effects | Dispensing location, Provider type | Cost |
| Gutierrez⁵⁰             | Product form   | Monitoring    | Pregnancy/STI prevention                              | Waiting time    | Dispensing location, Provider type | Effectiveness of HIV prevention |
| Kuteeza⁵⁴              | Product form   | Effectiveness of HIV prevention                      | Waiting time    | Dispensing location, Provider type | Dispensing location |
| Lancaster⁵⁷            | Product form   | Additional preventive services                        | Waiting time    | Dispensing location, Provider type | Dispensing location |
| Minnis et al⁵¹          | Timing         | Product form, Delivery location on the body          | Side effects    | Dispensing location, Provider type | Dispensing location |
| Montgomery et al⁵⁵      | Timing         | Product form, Delivery location on the body          | Side effects, Impact on menstruation                 | Dispensing location | Timing |
| Pines et al⁶⁴          | Timing         | Product form  | Effectiveness of HIV prevention                      | STI prevention  | Cost, Side effects | Dispensing location, Product form |
| Quaife et al⁶⁵          | Timing         | Product form  | Effectiveness of HIV prevention                      | Pregnancy/STI prevention | Side effects | Effectiveness of HIV prevention |
| Salinas-Rodriguez et al⁶⁶ | Timing        | Product form  | Incentives (amount, format, type), Adherence test    | Incentives type | Incentives type |
| Shrestha et al⁴⁷        | Timing         | Effectiveness of HIV prevention                      | Monitoring     | Cost, side effects | Dispensing location | Cost |
| Tan et al⁵⁶             | Timing         | Effectiveness of HIV prevention                      | Monitoring     | STI prevention | Cost |
| Wheelock et al⁶⁷        | Timing         | Monitoring    | Waiting time                                          | Dispensing location, Frequency of dispensing medication | Monitoring |

Table 3: Attributes included in the discrete choice experiment studies.
variations in preferences across subpopulations, cost, PrEP effectiveness and dosing frequency were the main drivers for PrEP use across the studies.

Despite there being at least 84 countries with PrEP programs and 120 countries adopting PrEP recommendations in their national guidelines, our systematic review found only 18 studies from 13 countries with data on PrEP preferences elicited from DCEs. These were mostly conducted in countries such as the U.S., South Africa, and Thailand, with relatively larger numbers of PrEP initiations. In contrast, we did not find choice data from countries with lower rates of PrEP initiatives but with higher rates of HIV incidence among key populations, such as the Philippines. This highlights gaps in the current literature and the importance of focusing efforts on deriving preference data to improve program acceptability and efficiency. As has been seen in the case of contraceptives, methods involving different attributes whereby individuals could choose and trade one characteristic for another, have the potential to play a significant role in promoting uptake and coverage.

The methods used to elicit preferences under the DCE approach are important when involving respondents from marginalized populations. We found that the majority of DCE surveys were conducted using face-to-face interviews. This method may enable respondents to ask questions or receive assistance with the DCE survey if required but could lead to social desirability bias (i.e., the tendency to provide a socially desirable response). This must be balanced against the convenience and confidentiality of an online DCE survey, which may overrepresent those with better education and higher income. Some studies did not conduct a pilot test before the DCE survey. This may impact the comprehensibility of the survey, particularly when participants have lower education levels, or are from a different cultural background. It is also worth noting that some studies included experienced PrEP users while others only recruited PrEP-naïve participants. Although we did not find significant differences in preferences across these two groups, it should be acknowledged that preferences may change depending on experience and contact with the products. This might also be important for countries newly introducing PrEP or those with limited availability and low awareness of PrEP versus countries with well-established programs with good community awareness. Therefore, we recommend that future DCEs include both PrEP-experienced and PrEP-naïve respondents where possible, to assess whether preferences differ between the two groups.

The cost was a significant driver in the choice to use PrEP across a range of settings and populations. For example, in Ukraine, the high cost of PrEP played a prominent role in the choice of MSM to use PrEP and making PrEP on demand more attractive. Similarly, in a study from Singapore, cost-related issues were the main barriers to accessing PrEP, as PrEP remains unsubsidized by the government. In the United States, IDUs reported higher acceptability of PrEP if the cost was covered by insurance. Furthermore, a study from Peru found that people were significantly more likely to use PrEP with a low out-of-pocket cost or when it was supplied free of charge. Key populations and their sexual partners accounted for 65% of new HIV infections globally in 2020; they are also underserved by HIV prevention programs, highlighting major gaps in access to effective biomedical prevention methods like PrEP. Together, this reinforces the importance of the need for free or subsidized PrEP to reach populations who would benefit most from PrEP. Increasing efforts by countries to integrate WHO PrEP recommendations into national guidelines should also be supported through technical assistance to design financial subsidies for national PrEP programs, including the integration of PrEP into the national health insurance coverage schemes.

The perceived effectiveness of PrEP was another important driver of the choice to use PrEP. Evidence of the effectiveness of oral PrEP is well-established and closely linked with adherence. For example, in a study of young women in South Africa and Kenya, HIV prevention effectiveness was the most important factor influencing the choice to use PrEP. Interestingly, although women continue to have high rates of HIV acquisition in Sub-Saharan Africa, the majority were willing to exchange higher effectiveness for other desired attributes (such as the impact on vaginal wetness, pregnancy prevention and dosing regimen), according to a study of women in South Africa and Zimbabwe. Research has shown that the perceptions of effectiveness among target populations influence the acceptance and in turn, the uptake of biomedical interventions. Therefore, wider promotion of PrEP’s high effectiveness may attract people to consider PrEP. The potential use of dating apps to promote PrEP information may be considered, as it has been shown elsewhere to positively affect beliefs about PrEP effectiveness. For example, Grindr (one of the most popular dating apps) users are more likely to be interested in taking and initiating PrEP.

Dosing frequency was another important driver of choices around the use of PrEP. This is particularly important as new PrEP products come onto the market. Notably, we found this attribute differed significantly across populations, emphasizing the need to obtain context-specific values and preferences data, particularly in regards to the dosing frequency of PrEP. For example, one US study reported that daily oral PrEP was the most desired option for US military MSM and trans-individuals, whereas bi-monthly PrEP injection was most preferred by those who had never used PrEP before. Another study showed that youth in South Africa favoured long-acting options: females and MSM...
preferred an injection, which could indicate a strong concern for discreteness in HIV product selection, whereas MSW preferred an implant. Confidentiality was a prominent issue that influenced dosing frequency, particularly among key populations. The stigma associated with PrEP also remains a barrier to its uptake, use, and maintenance. In addition, dosing frequency is related to adherence to medication. A meta-analysis reported that reducing the dosage frequency from multiple dosing to one daily dose increases the likelihood of better adherence to therapies across acute and chronic diseases. This could also apply to PrEP use, where evidence shows a preference among users for injectable or implantable PrEP with long-acting characteristics compared with oral PrEP; and better adherence to less frequently dosed injectable PrEP than daily oral PrEP. This may also support the WHO’s recommendation on event-driven (as an alternative to daily PrEP), to allow users to have PrEP interruptions during periods of low risk, as a way to improve sustainable PrEP uptake. Therefore, programs should effectively support users to adjust their dosing frequency according to fluctuations in their risk level.

Finally, as different service delivery models are considered for scaling up PrEP, it is important to understand the preferences of those who would benefit from PrEP. In general, we found that most participants were willing to receive PrEP in a healthcare setting, but there was some variation in preferences for services. For example, a study in Malawi reported that dispensing location was most important for female sex workers, who preferred accessing PrEP from a family planning clinic or non-government organization (NGO)-run drop-in centre, compared with HIV clinics, STI clinics or NGO-run mobile outreach facilities. A DCE of MSM in India found that participants preferred to acquire PrEP from a government hospital rather than a private one. This may be because participants believe that government-funded PrEP programs are only available through public hospitals. A study from Peru among MSM, transgender individuals and sex workers reported that even though participants shared concerns about stigma and discrimination among health care professionals, they suggested that these professionals were more qualified to distribute PrEP than pharmacists.

A key strength of this systematic review is that it provides an overview of PrEP preferences from a range of geographical settings, population target groups, product attributes, and survey approaches. We specifically focused on studies that used a DCE methodology, as this is one of the recommended methods to elicit preferences for new medical products or services that do not currently exist. Our study should also be read in light of some limitations. First, due to the differences in study attributes, performing a meta-analysis was unlikely to be meaningful. Instead, we qualitatively synthesized and summarized the range of attributes that may be helpful in the formative stage of attribute selection in future DCE surveys examining PrEP preferences. Similarly, due to unknown differences in the scale of the part-worth utilities from each study, we were not able to perform a statistical assessment of this variation. Second, this review was limited only to studies published in English, which may lead to language bias. While we intentionally focused on studies in peer-reviewed journals - excluding the grey literature to ensure the quality of studies selected - we may have missed other relevant literature. Finally, most DCE studies have focused on product attributes and used simplistic attributes related to service delivery (such as dispensing venue or additional support services). It would be beneficial for future research to provide greater detail regarding how PrEP services should be designed to optimize uptake.

In conclusion, this systematic review synthesized the global evidence on preferences for PrEP elicited using the DCE approach. Cost, PrEP effectiveness and dosing frequency were the main drivers of choice for PrEP use across the studies. We also found significant variation in preferences across subpopulations. This underscores the importance of conducting context-specific health preference research to optimize PrEP use among people who would benefit from PrEP the most.

Contributors
LPLW and HSY: identification of papers and data extraction, formal analysis, validation, visualisation, writing — original draft, and writing — review & editing, contributed equally. JJO: conceptualisation, identification of papers and data extraction, formal analysis, investigation, resources, software, supervision, validation, writing — original draft, and writing — review & editing. LZ: contribute to the supervision of the study. All other authors: conceptualisation, writing — review & editing. All authors took the decision to submit for publication.

Data sharing statement
Datasets of this study are available upon reasonable request to the corresponding author (JJO).

Declaration of interests
Dr. Bavinton reports grants from ViiV Healthcare, grants from Gilead Sciences, personal fees from Gilead Sciences, personal fees from Gilead Sciences, outside the submitted work. All other authors have nothing to declare.

Funding
There was no funding source for this study.
48 Bineau L, Lambert D, Truszczynski N, Hansen N, Lauckner C. Dating app use among rural men who have sex with men and its relationship to HIV prevention and risk behaviors: a mixed-methods analysis. Rural Remote Health. 2021;21(2):1445–6354.

49 Hoenigl M, Little SJ, Grelotti D, et al. Grindr users take more risks, but are more open to Human Immunodeficiency Virus (HIV) pre-exposure prophylaxis: could this dating app provide a platform for HIV prevention outreach? Clin Infect Dis. 2020;71(7):E135–E140.

50 Gutierrez J, Dubov A, Altice F, Vlahov D. Preferences for pre-exposure prophylaxis among U.S. military men who have sex with men: results of an adaptive choice based conjoint analysis study. Military Med Res. 2021;8.

51 Minnis AM, Atujuna M, Browne EN, et al. Preferences for long-acting pre-exposure prophylaxis (PrEP) for HIV prevention among South African youth: results of a discrete choice experiment. J Int AIDS Soc. 2020;23(6):e25328.

52 Montgomery ET, Browne EN, Atujuna M, et al. Long-acting injection and implant preferences and trade-offs for HIV prevention among South African male youth. J Acquir Immune Defic Syndr. 2021;87(3):928–936.

53 Calabrese SK. Understanding, contextualizing, and addressing PrEP stigma to enhance PrEP implementation. Curr HIV/AIDS Rep. 2020;17(6):579–588.

54 Srivastava K, Arora A, Kataria A, Cappelleri JC, Sadosky A, Peterson AM. Impact of reducing dosing frequency on adherence to oral therapies: a literature review and meta-analysis. Patient Prefer Adherence. 2013;7:419–434.

55 Montgomery ET, Atujuna M, Krogstad E, et al. The invisible product: preferences for sustained-release, long-acting pre-exposure prophylaxis to HIV among South African youth. J Acquir Immune Defic Syndr. 2019;80(5).

56 Bavinton BR, Grulich AE. HIV pre-exposure prophylaxis: scaling up for impact now and in the future. Lancet Public Health. 2021;6(7):e528–e535.

57 Lancaster KE, Lungu T, Bula A, et al. Preferences for pre-exposure prophylaxis service delivery among female sex workers in Malawi: a discrete choice experiment. AIDS Behav. 2020;24(1):1294–1303.

58 Chakrapani V, Newman PA, Cameron M, et al. Willingness to use pre-exposure prophylaxis (PrEP) and preferences among men who have sex with men in Mumbai and Chennai, India: a discrete choice experiment. AIDS Behav. 2021;25(10):3074–3084.

59 Egger M, Juni P, Bartlett C, Holenstein F, J S. How important are comprehensive literature searches and the assessment of trial quality in systematic reviews? Empirical study. Health Technol Assess. 2003;7(1).

60 Ayorinde AA, Williams J, Mannion R, et al. Publication and related biases in health services research: a systematic review of empirical evidence. BMC Med Res Methodol. 2020;20(1):117.

61 Dubov A, Oguntbajo A, Altice FL, Frenkel L. Optimizing access to PrEP based on MSM preferences: results of a discrete choice experiment. AIDS Care. 2019;31(6):543–553.

62 Eisingerich AB, Wheelock A, Gomez GB, Garnett GP, Dybul MR, Piet PK. Attitudes and acceptance of oral and parenteral HIV pre-exposure prophylaxis among potential user groups: a multinational study. PLoS One. 2012;7(1):e28238.

63 Kutesa MO, Quaife M, Biziro S, et al. Acceptability and predictors of uptake of anti-retroviral pre-exposure prophylaxis (PrEP) among fishing communities in Uganda: a cross-sectional discrete choice experiment survey. AIDS Behav. 2019;23(6):2674–2686.

64 Pines HA, Strathdee SA, Hendrix CW, et al. Oral and vaginal HIV pre-exposure prophylaxis product attribute preferences among female sex workers in the Mexico-US border region. Int J STD AIDS. 2019;30(1):44–55.

65 Quaife M, Eakle R, Cabrera Escobar MA, et al. Divergent preferences for HIV prevention: a discrete choice experiment for multipurpose HIV prevention products in South Africa. Med Decis Making. 2018;38(1):120–133.

66 Salinas-Rodríguez A, Sosa-Rubí SG, Chivardi C, et al. Preferences for conditional economic incentives to improve pre-exposure prophylaxis adherence: a discrete choice experiment among male sex workers in Mexico. AIDS Behav. 2021.

67 Wheelock A, Eisingerich AB, Ananworanich J, et al. Are Thai MSM willing to take PrEP for HIV prevention? An analysis of attitudes, preferences and acceptance. PLoS One. 2015;10(1):e0124488.