U.S. patient preferences for long-acting HIV treatment: a discrete choice experiment

Vincent Marconi, Emory University
SM Graham, University of Washington School of Medicine
D Barthold, University of Washington
B Hauber, University of Washington
AT Brah, University of Washington School of Medicine
E Saldarriaga, University of Washington
AC Collier, University of Washington School of Medicine
RJY Ho, University of Washington
JM Simoni, University of Washington

Journal Title: Journal of the International AIDS Society
Volume: Volume 26, Number S2
Publisher: (publisher) | 2023-07-01, Pages e26099-e26099
Type of Work: Article
Publisher DOI: 10.1002/jia2.26099
Permanent URL: https://pid.emory.edu/ark:/25593/w7tv9

Final published version: http://dx.doi.org/10.1002/jia2.26099
Accessed November 18, 2023 12:16 PM EST
U.S. patient preferences for long-acting HIV treatment: a discrete choice experiment

Susan M. Graham1,2,3,§, Douglas Barthold4, Brett Hauber4,5, Aaron T. Brah1, Enrique Saldarriaga4, Ann C. Collier1, Rodney J. Y. Ho6, the Emory PREFER Team*, Vincent C. Marconi7,8 and Jane M. Simoni2,9

§Corresponding author: Susan M. Graham, Box 359909, 325 Ninth Avenue, Seattle, WA 98104, USA. Tel: 206-351-0414. (grahamsm@uw.edu)

Abstract

Introduction: Recent advances in long-acting antiretroviral therapy (LA-ART) could provide new options for HIV treatment and reduce adherence barriers, if regimens are acceptable to patients. We elicited preferences for key attributes of potential LA-ART regimens among people with HIV (PWH) in the United States, focusing on four treatment modes (oral tablets, subcutaneous injections, intramuscular injections, and implants), product characteristics and location of administration.

Methods: A discrete choice experiment was conducted among PWH aged ≥18 years recruited from HIV clinics in Washington State and Atlanta, Georgia from March 2021 to June 2022. Participants responded to 17 choice scenarios, each with three options: two systematically generated hypothetical LA-ART regimens and a constant opt-out (their current daily oral treatment). LA-ART regimen descriptions included treatment mode, pain, dosing frequency, location, pre-treatment time with undetectable viral load, pre-treatment negative reaction testing and “late-dose leeway” (i.e. flexibility or forgiveness in timing the next dose). We used conditional logistic regression, with an interaction between treatment mode and pain, to estimate preference weights for all attribute levels.

Results: Seven hundred participants (350 at each site) enrolled, with median age 51 years (range 18–73); 70% identified as cisgender male, 24% as cisgender female and 6% as non-binary or transgender. LA oral tablets were the only mode preferred over current daily oral treatment, with annual implants and injections the next most preferred LA-ART option. Longer time between doses was preferred, and administration at home was preferred to clinics, which were preferred to pharmacies. Attributes with less impact on preferences included oral lead-in treatment to achieve viral suppression or test for negative reactions and late-dose leeway around the prescribed dosing interval. Participants in Atlanta were more likely to prefer their current daily oral ART than participants from Seattle.

Conclusions: PWH in the United States may soon have several options for LA-ART. Our results suggest that LA oral tablets will be preferred by many patients over their current daily oral treatment, while implants and injections with longer duration may be acceptable to some. Future research should investigate sources of preference heterogeneity and actual uptake of and adherence to LA-ART products, when available.

Keywords: antiretroviral agents; antiretroviral therapy; choice behaviour; delayed-action preparations; HIV; patient preference

1 INTRODUCTION

In 2020, the Centers for Disease Control and Prevention estimated that for every 100 people who were diagnosed with HIV, only 74 had received HIV care and 65 were virally suppressed, based on their most recent viral load result [1]. Disparities in U.S. HIV care cascade outcomes (i.e. HIV diagnosis, engagement in care and viral suppression) have been reported among adolescents and young adults [2, 3], Blacks [2–5], Hispanic persons [6], injection drug users [3], women [3], heterosexual men [3, 4], foreign-born persons [4] and those of low socio-economic status [3]. New approaches to optimizing antiretroviral therapy (ART) uptake, adherence and retention are clearly needed, in order to overcome challenges that undermine treatment success, such as HIV stigma, treatment fatigue, missed visits or refills, forgetfulness and side effects [7–9].

Recent advances in long-acting antiretroviral therapy (LA-ART) could provide new options for HIV treatment and reduce adherence barriers, if regimens are acceptable to
patients. Initial results from the first LA-ART regimen to reach the market have been promising. In the LATTE-2 randomized, open-label phase 2b trial, participants were randomly assigned (2:2:1) to receive two intramuscular injections of long-acting cabotegravir plus rilpivirine at 4- or 8-week intervals or a comparable daily pill-based regimen [10]. The regimen at either frequency was as effective as daily oral combination therapy at maintaining HIV viral suppression through 96 weeks [10]. This regimen was well accepted and tolerated, with 97% of 254 participants reporting 5 or 6 on a 6-point scale of treatment satisfaction and 99% stating they would be "highly satisfied to continue" their long-acting injectable (LAI) ART [10]. In a qualitative study associated with this trial, 39 in-depth interviews were conducted with participants and providers from the United States and Spain [11]. Despite commonly experienced injection site reactions [10], participants were generally tolerant of the regimen, finding injections convenient, with reduced potential for HIV disclosure and elimination of the "daily reminder of living with HIV" [11].

Due to the early success of the cabotegravir/rilpivirine regimen, research on patient acceptance and preferences has focused on injectable regimens. For example, Williams and colleagues surveyed 400 adults taking daily ART at two clinical sites, reporting that 61%-85% would "definitely or probably" try LAI ART, depending on the dosing interval, with over one quarter saying they would try an injectable regimen even if it cost "much more" than their current regimen [12]. In a survey conducted by an Italian patient advocacy group [13], Russo et al., reported that 55% of the 488 respondents knew about LAI ART and 83% would appreciate not taking pills on a daily basis. Furthermore, 30% said they would benefit even if hospital-based injections were required every month and an additional 39% would benefit if hospital-based injections were required every 2 months [13]. While the injectable cabotegravir/rilpivirine regimen was first on the market, a number of promising LA-ART products are in development that could result in effective combination regimens with less frequent administration, fewer injections or other potential advantages [14]. Our recent interviews with key informants involved in HIV drug development and clinical trials revealed that experts thought implants, subcutaneous injections and long-acting oral tablets could also become available for HIV treatment in the near future [15]. Data on patient preferences for this wider range of LA-ART modalities are currently sparse.

Discrete choice experiments (DCEs) are used to measure and quantify preferences in the absence of revealed preference data from field studies [16, 17]. In a DCE, individuals are asked to choose between different hypothetical alternatives, each defined by a set of attributes with varying levels. Responses can be used to determine whether participants' preferences are significantly influenced by the attributes, the relative importance of each attribute and the trade-offs (i.e. marginal rates of substitution) patients are willing to make among attributes [18]. DCEs may be particularly helpful when interventions are still in development or when a comparison of multiple different options in observational studies or trials would be too costly or impractical. Therefore, the results of a DCE conducted at an early stage of product development can generate important insights for product developers and help inform features that will increase acceptability.

To obtain patient preferences on a range of potential long-acting treatment modalities without over-emphasizing the first LA-ART regimens on the market, we conducted key informant interviews to identify treatment modalities most likely to become available in the next 5–10 years [15]. Based on this qualitative work and our prior research on LAI ART acceptability with both patients and providers [19, 20], we developed and pilot-tested a DCE to capture the preferences of patients engaged in HIV care with respect to key attributes of these long-acting regimens [21]. The results of the pilot testing informed the experimental design of a fully deployed DCE at research sites in Seattle, Washington and Atlanta, Georgia. Our objective in this analysis is to present the results of this fully deployed DCE, which investigated preferences related to four different treatment modalities (oral tablets, subcutaneous injections, intramuscular injections and implants) and their characteristics, compared to patients' current daily oral HIV regimen.

2 | METHODS

2.1 | Population and setting

We recruited DCE participants from the University of Washington HIV clinics in Bremerton, Everett, Federal Way, Olympia, and Seattle, Washington and from Emory University’s Infectious Diseases Program in Atlanta, Georgia. Recruitment was conducted between March 2021 and June 2022 through outreach to patients by e-mail or telephone using contact information from the HIV patient registries at each site, or in person at their regular clinic appointments. Our target enrolment was 350 at each site, for 700 participants overall. Eligibility criteria included living with HIV, age ≥18 years, established care at one of the research sites, fluency in English and ability to provide informed consent. Exclusion criteria included currently taking an LAI regimen and being an "elite controller" who has a very low viral load without requiring ART (approximately 0.1%-2.5% of all HIV infections worldwide [22]). In addition, individuals judged to be cognitively impaired or under the influence of drugs or alcohol during in-person screening were excluded.

2.2 | Ethical oversight

The University of Washington (UW) and Emory University reviewed and approved the study protocol and informed consent documents, with the UW serving as the single institutional review board of record (STUDY00007390). All participants provided electronic informed consent.

2.3 | DCE design

We developed our DCE based on feedback from key informants about potential treatment modes and their likely frequency of administration [15]. This feedback led to the selection of four LA-ART treatment modes (long-acting oral tablets, subcutaneous injections, intramuscular injections and implants) and six additional attributes: dosing frequency, location of treatment administration, pain with administration/insertion, pre-treatment time undetectable (should viral
suppression be required before initiating LA-ART), pre-
treatment “negative reaction” testing (implementing an oral
lead-in to assess tolerability or to exclude reactions such as
“an allergic rash or abnormal liver test results” should this
be required before starting LA-ART) and “late-dose leeway”
(i.e. flexibility or forgiveness in dosing timing before break-
through viremia). These concepts were carefully explained to
DCE participants in the survey introduction (details in Sup-
porting Information 1).

Attribute levels were restricted based on what key infor-
mants considered feasible. For long-acting oral medications,
attributes were restricted to: no pain, administration at home
and frequency 1 or 4 weeks. For subcutaneous injections,
attributes were restricted to: no or mild pain; administra-
tion at home, clinic or pharmacy; and frequency 1, 4, 8
or 12 weeks. For intramuscular injections, attributes were
restricted to: mild or moderate pain; administration at clinic
or pharmacy; and frequency 4, 8 or 12 weeks. For implants,
attributes were restricted to: mild or moderate pain, inser-
tion at clinic and frequency 26 or 52 weeks. If the location
was clinic or pharmacy, the dosing frequency was restricted
to ≥4 weeks. The other attributes had no restrictions. Choices
for pre-treatment time undetectable were 0, 3 and 6 months.
Negative reaction testing was needed or not needed. Late-
dose leeway was a duration of time set at 50% or 100% of
the dosing interval for that specific LA-ART option, with 50%
referred to as a “short” late-dose leeway and 100% referred
to as a “long” late-dose leeway.

2.4 Survey components

The DCE survey (Supporting Information 1) was pilot tested
with 50 participants over a series of waves with iterative
improvements [21]. The survey started with an overall intro-
duction, then introduced each treatment mode or “option,”
along with visual images. The ability to remove an implant
if a negative reaction occurred was included in the descrip-
tion of that treatment mode. Because effective HIV treat-
ment requires two or more antiretroviral medications and to
avoid mixing treatment modes, we advised participants that
each hypothetical LA-ART regimen would require two pro-
ducts, both administered by the same mode [15]. This introd-
uction was followed by three comprehension questions about
these treatment options to ensure understanding. Next, the
first three attributes or “features,” including location of treat-
ment, frequency of dosing and pain experienced, were intro-
duced. Participants were also asked to make the following
assumptions as they considered their choices: (1) all options
would work equally well (i.e. could suppress viral load but not
cure HIV); (2) there would be no difference in costs com-
pared to participants’ current regimen; and (3) the safety
of treatment administration locations would not be impacted
by COVID-19. An instructional video with narrative descrip-
tions explaining how the choice sets were to be read pre-
vented the practice choice set with only the treatment modes
and the first three attributes. After this practice choice set,
preset-treatment time undetectable and pre-treatment negative
reaction testing were introduced, followed by a comprehen-
sion question, then finally late-dose leeway was introduced,
followed by its own comprehension question. Another instruc-
tional video introduced the more complicated choice sets with
all these attributes, followed by another practice choice set.

DCE participants responded to 17 choice scenarios, each
with three options: two systematically generated hypothetical
LA-ART regimens and a constant opt-out (i.e. the participant’s
current daily oral treatment). Figure 1 presents an example
of the choice sets used. Participants were randomized to 1 of
4 blocks of 16 choice scenarios (out of 64 possible), which
were presented in a random order. The 17th question pre-
mitted two different types of long-acting oral regimens that
were compared to the same constant opt-out. The DCE was
designed using Ngene software (ChoiceMetrics, Sydney, Aus-
tralia). The experimental design was unlabelled, and was con-
structed using a modified Federov algorithm and D-optimal
main effects [21].

2.5 Data collection

Individuals could access the survey at home through an e-
mailed invitation link or in a private area within the clinic
(after COVID-19 restrictions on in-person research were
lifted). Research staff were available for assistance if needed,
either by telephone or in-person (for clinic participation). Par-
ticipants were screened for eligibility and consented, if eli-
gible, using a questionnaire available in REDCap, an elec-
tronic data capture tool hosted by the UW. After consent-
ating, participants were linked from REDCap directly to the
DCE survey, which was administered in SurveyEngine (Sur-
veyEngine GmbH, Berlin, Germany), an online data collection
platform specifically designed for preference research. After
the introduction described above and before being presented
with the 17 choice scenarios, participants were asked ques-
tions about their HIV history, their current and past ART reg-
imens, and their experience with injections, pill storage and
clinic visits. At the end of the choice sets, additional data
were collected on quality of life, provider support, social sup-
port, socio-demographic characteristics and preferences for
reminders about clinic visits or treatment administration. In
addition, six questions on internalized stigma were included,
based on a validated scale [23]. If the participant consented
to chart linkage, clinical data, including the participant’s cur-
rent HIV regimen, most recent CD4 count, most recent viral
load and number of HIV and non-HIV medications taken daily,
were also abstracted from the medical record.

2.6 Data analysis

Descriptive statistics were used to summarize participant
characteristics, overall and by site, with comparisons across
sites using independent-sample t tests for continuous vari-
ables and Chi-square or Fisher exact tests for categorical
variables. Each HIV stigma question was scored from 1 (no
stigma) to 4 (high-level stigma), and an average score for all
stigma questions answered was calculated. Conditional logis-
tic regression was used to analyse the participants’ choices
across all tasks using attribute levels as the covariates. Data
were clustered by participant, to account for intra-individual
correlation. All attribute levels were categorical effects-coded,
with the omitted level estimated from the negative sum of
all other levels in the model. The primary endpoints were all
Figure 1. Example choice set presenting two different long-acting antiretroviral therapy (LA-ART) regimens (Option A and Option B) and the constant Option C opt-out (current daily oral regimen). For each LA-ART option, attributes presented included treatment type, location, frequency, pain, pre-treatment time undetectable, pre-treatment negative reaction testing and late-dose leeway. "Long" late-dose leeway was defined as 100% of the dosing interval and "short" late-dose leeway was defined as 50% of the dosing interval for that specific treatment option.

<table>
<thead>
<tr>
<th>Treatment type - How do I take this treatment?</th>
<th>Option A</th>
<th>Option B</th>
<th>Option C - your current HIV regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-acting oral pills</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injections under the skin</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Location - Where would I get this treatment?</th>
<th>Home</th>
<th>Local pharmacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency - How often would I get this treatment?</td>
<td>Once a week</td>
<td>Once a month</td>
</tr>
<tr>
<td>Pain - How much pain would I feel?</td>
<td>None</td>
<td>Mild</td>
</tr>
<tr>
<td>Pre-treatment time undetectable - How long would I need to be undetectable on daily pills before starting this treatment?</td>
<td>3 months</td>
<td>None</td>
</tr>
<tr>
<td>Pre-treatment negative reaction testing - Would I need to take daily pills to check for negative reactions before starting the treatment?</td>
<td>Needed</td>
<td>Not needed</td>
</tr>
<tr>
<td>Late dose leeway - How late can I be for a dose of this treatment and still remain undetectable?</td>
<td>1 week</td>
<td>1 week</td>
</tr>
<tr>
<td>Which do you prefer?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Table 1. Characteristics of 700 participants by study site

<table>
<thead>
<tr>
<th></th>
<th>Total (N = 700)</th>
<th>Atlanta (n = 350)</th>
<th>Seattle (n = 350)</th>
<th>p Value for comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>48.6 (12.1)</td>
<td>49.3 (12.2)</td>
<td>48.0 (12.0)</td>
<td>0.15</td>
</tr>
<tr>
<td>Median [min, max]</td>
<td>51 [18, 73]</td>
<td>51 [18, 72]</td>
<td>50 [22, 73]</td>
<td></td>
</tr>
<tr>
<td><strong>Hispanic ethnicity, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>623 (89.0%)</td>
<td>325 (92.9%)</td>
<td>298 (85.1%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Yes</td>
<td>61 (8.7%)</td>
<td>17 (4.9%)</td>
<td>44 (12.6%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>16 (2.3%)</td>
<td>8 (2.3%)</td>
<td>8 (2.3%)</td>
<td></td>
</tr>
<tr>
<td><strong>Race, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>259 (37.0%)</td>
<td>23 (6.6%)</td>
<td>236 (67.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Black</td>
<td>331 (47.3%)</td>
<td>295 (84.3%)</td>
<td>36 (10.3%)</td>
<td></td>
</tr>
<tr>
<td>Other/Mixed</td>
<td>94 (13.4%)</td>
<td>24 (6.9%)</td>
<td>70 (20.0%)</td>
<td></td>
</tr>
<tr>
<td>Prefer not to say</td>
<td>16 (2.3%)</td>
<td>8 (2.3%)</td>
<td>8 (2.3%)</td>
<td></td>
</tr>
<tr>
<td><strong>Gender, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Woman</td>
<td>168 (24.0%)</td>
<td>135 (38.6%)</td>
<td>33 (9.4%)</td>
<td></td>
</tr>
<tr>
<td>Man</td>
<td>493 (70.4%)</td>
<td>197 (56.3%)</td>
<td>296 (84.6%)</td>
<td></td>
</tr>
<tr>
<td>Transgender woman</td>
<td>15 (2.1%)</td>
<td>8 (2.3%)</td>
<td>7 (2.0%)</td>
<td></td>
</tr>
<tr>
<td>Transgender man</td>
<td>6 (0.9%)</td>
<td>4 (1.1%)</td>
<td>2 (0.6%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>10 (1.4%)</td>
<td>3 (0.9%)</td>
<td>7 (2.0%)</td>
<td></td>
</tr>
<tr>
<td>Prefer not to say</td>
<td>8 (1.1%)</td>
<td>3 (0.9%)</td>
<td>5 (1.4%)</td>
<td></td>
</tr>
<tr>
<td><strong>Sexual orientation, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heterosexual</td>
<td>227 (32.4%)</td>
<td>173 (49.4%)</td>
<td>54 (15.4%)</td>
<td></td>
</tr>
<tr>
<td>Lesbian, gay or bisexual</td>
<td>419 (59.9%)</td>
<td>143 (40.9%)</td>
<td>276 (78.9%)</td>
<td></td>
</tr>
<tr>
<td>Prefer not to say</td>
<td>30 (4.3%)</td>
<td>24 (6.9%)</td>
<td>6 (1.7%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>24 (3.4%)</td>
<td>10 (2.9%)</td>
<td>14 (4.0%)</td>
<td></td>
</tr>
<tr>
<td><strong>Employment, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Full time</td>
<td>192 (27.4%)</td>
<td>55 (15.7%)</td>
<td>137 (39.1%)</td>
<td></td>
</tr>
<tr>
<td>Part time</td>
<td>79 (11.3%)</td>
<td>33 (9.4%)</td>
<td>46 (13.1%)</td>
<td></td>
</tr>
<tr>
<td>Not working</td>
<td>407 (58.1%)</td>
<td>248 (71.0%)</td>
<td>159 (45.4%)</td>
<td></td>
</tr>
<tr>
<td>Prefer not to say</td>
<td>22 (3.1%)</td>
<td>14 (4.0%)</td>
<td>8 (2.3%)</td>
<td></td>
</tr>
<tr>
<td>Any health insurance, N (%)</td>
<td>577 (82.4%)</td>
<td>237 (67.7%)</td>
<td>340 (97.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HIV stigma score</td>
<td>2.17 (0.79)</td>
<td>2.14 (0.80)</td>
<td>2.20 (0.77)</td>
<td>0.33</td>
</tr>
<tr>
<td><strong>Time on ART (years)</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.035</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>15.6 (8.7)</td>
<td>16.3 (8.9)</td>
<td>14.9 (8.5)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>10 (1.4%)</td>
<td>3 (0.9%)</td>
<td>7 (2.0%)</td>
<td></td>
</tr>
<tr>
<td><strong>Time with HIV (years)</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.026</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>17.9 (9.8)</td>
<td>18.7 (9.9)</td>
<td>17.0 (9.6)</td>
<td></td>
</tr>
<tr>
<td><strong>Most recent CD4 count (cells/mm³)</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.0006</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>601 (316)</td>
<td>558 (338)</td>
<td>641 (289)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>30 (4.3%)</td>
<td>25 (7.1%)</td>
<td>5 (1.4%)</td>
<td></td>
</tr>
<tr>
<td><strong>Self-reported AIDS diagnosis, N (%)a</strong></td>
<td>292 (41.7%)</td>
<td>164 (46.9%)</td>
<td>128 (36.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Viral load undetectable, N (%)</strong></td>
<td>500 (71.4%)</td>
<td>224 (64.0%)</td>
<td>276 (78.9%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>HIV pills per day, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>One tablet</td>
<td>390 (55.7%)</td>
<td>230 (65.7%)</td>
<td>160 (45.7%)</td>
<td></td>
</tr>
<tr>
<td>Two tablets</td>
<td>200 (28.6%)</td>
<td>72 (20.6%)</td>
<td>128 (36.6%)</td>
<td></td>
</tr>
<tr>
<td>Three or more tablets</td>
<td>92 (13.1%)</td>
<td>39 (11.1%)</td>
<td>53 (15.1%)</td>
<td></td>
</tr>
<tr>
<td>Prefer not to say/missing</td>
<td>9 (2.6%)</td>
<td>9 (2.6%)</td>
<td>18 (9.2%)</td>
<td></td>
</tr>
<tr>
<td><strong>Number of scenarios in which Option C (the constant opt-out) was chosen, Mean (SD)</strong></td>
<td>5.4 (6.4)</td>
<td>6.3 (7.0)</td>
<td>4.6 (5.7)</td>
<td>0.0004</td>
</tr>
</tbody>
</table>

(Continued)
Table 1. (Continued)

<table>
<thead>
<tr>
<th>Respondents selecting Option C (the constant opt-out) at least once, N (%)</th>
<th>Total (N = 700)</th>
<th>Atlanta (n = 350)</th>
<th>Seattle (n = 350)</th>
<th>p Value for comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCE participation site, N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>299 (42.7%)</td>
<td>34 (9.7)</td>
<td>265 (75.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Clinic</td>
<td>376 (53.7%)</td>
<td>312 (89.1)</td>
<td>64 (18.3)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>25 (3.6%)</td>
<td>4 (1.1)</td>
<td>21 (6.0)</td>
<td></td>
</tr>
</tbody>
</table>

Note: Comparisons were made across sites using independent-sample t tests for continuous variables and Chi-square or Fisher exact tests for categorical variables. SD: standard deviation; DCE: discrete choice experiment.*Data were missing for 14 participants, 9 from Atlanta and 5 from Seattle.

Table 2. Point estimates and 95% confidence intervals (CI) from conditional logistic regression for preference weights, entire study population

<table>
<thead>
<tr>
<th>Preference weight</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current therapy (alternative-specific constant)</td>
<td>0.03</td>
</tr>
<tr>
<td>Long-acting oral—no pain*</td>
<td>0.89</td>
</tr>
<tr>
<td>1-year implant—mild pain</td>
<td>−0.08</td>
</tr>
<tr>
<td>1-year implant—moderate pain</td>
<td>−0.03</td>
</tr>
<tr>
<td>6-month implant—mild pain</td>
<td>−0.15</td>
</tr>
<tr>
<td>6-month implant—moderate pain</td>
<td>−0.34</td>
</tr>
<tr>
<td>Injectable—no pain</td>
<td>−0.06</td>
</tr>
<tr>
<td>Injectable—mild pain</td>
<td>−0.09</td>
</tr>
<tr>
<td>Injectable—moderate pain</td>
<td>−0.13</td>
</tr>
<tr>
<td>Frequency—3 months</td>
<td>0.41</td>
</tr>
<tr>
<td>Frequency—2 months</td>
<td>0.22</td>
</tr>
<tr>
<td>Frequency—1 month</td>
<td>−0.14</td>
</tr>
<tr>
<td>Frequency—1 week*</td>
<td>−0.49</td>
</tr>
<tr>
<td>Location—clinic</td>
<td>−0.01</td>
</tr>
<tr>
<td>Location—pharmacy</td>
<td>−0.14</td>
</tr>
<tr>
<td>Location—home*</td>
<td>0.16</td>
</tr>
<tr>
<td>Time undetectable—6 months</td>
<td>−0.05</td>
</tr>
<tr>
<td>Time undetectable—3 months</td>
<td>−0.04</td>
</tr>
<tr>
<td>Time undetectable—none*</td>
<td>0.09</td>
</tr>
<tr>
<td>Negative reaction testing—needed</td>
<td>−0.06</td>
</tr>
<tr>
<td>Negative reaction testing—not needed*</td>
<td>0.06</td>
</tr>
<tr>
<td>Late-dose leeway—long*</td>
<td>0.07</td>
</tr>
<tr>
<td>Late-dose leeway—short*</td>
<td>−0.07</td>
</tr>
</tbody>
</table>

Notes: Thin lines separate the different attributes assessed. Preference weights are relative to the mean effect. Non-overlapping 95% confidence intervals for preference weights of different levels of the same attribute indicate significantly different utilities between the two levels compared. *Late-dose leeway was defined as the flexibility or "forgiveness" in dosing timing before breakthrough viremia, with long leeway defined as 100% of the dosing interval and "short" leeway defined as 50% of the dosing interval for that specific treatment option. For each attribute, the omitted level, which was estimated from the negative sum of all other levels in the model, is indicated by an asterisk.
DISCUSSION

In this diverse population of 700 people with HIV (PWH) engaged in care at our study sites, we found that participants strongly preferred long-acting preparations with longer intervals between dosing, less pain with administration, and greater privacy and convenience in terms of administration. In addition, participants preferred minimal barriers to LA-ART initiation (i.e. no lead-in testing for reactions or a requirement for viral load suppression) and greater tolerance for delays in product administration. There were differences in preferences across sites, with participants in Seattle more open to switching from their current daily oral regimen than in Atlanta. However, preferences for the different treatment modes when presented with the restrictions used in this DCE were fairly consistent, with more participants preferring long-acting oral tablets than injections, and more participants preferring injections than implants.

To our knowledge, this is the first DCE investigating the preferences of PWH in the United States with respect to a broad range of potential LA-ART regimens, including long-acting oral tablets, subcutaneous and intramuscular injections, and implants. One published study evaluated the acceptability of LA-ART in general, and asked participants to choose the one mode they would most prefer, “if all options cost the same and worked equally well” [25]. The options provided were oral pills, injections given every 1–2 months, implants inserted every 6–12 months or an intravenous infusion administered every 2–4 weeks. Among 374 participants, 61% reported that they were likely or very likely to use LA-ART; 41% preferred pills, 40% preferred injections and 18% preferred an implant, with only 1% preferring an infusion [25]. While these results are interesting, the method used did not include trade-offs between different products with varying attributes, such as frequency and site of administration, so results should be interpreted with caution. Our study extends that work and adds to the literature by using a rigorous DCE methodology to elicit patient preferences.

While long-acting oral tablets were most preferred overall in our study, it is unclear when a long-acting oral HIV treatment regimen will become available. Gilead Sciences and Merck have developed an LA-ART regimen composed of weekly oral lenacapavir combined with weekly oral islatravir: a randomized trial (NCT05052996) of this regimen among PWH with viral suppression at baseline is ongoing, with a lower dose of islatravir than initially planned (due to toxicity).
and an estimated completion date of December 2027 [26]. Currently, there is only one complete LA-ART regimen on the market: the cabotegravir/rilpivirine regimen (Cabenuva, Viiv Healthcare, Brentford, United Kingdom). This regimen was approved by the U.S. Food and Drug Administration in 2021 with a once-monthly dosing schedule [27], based on the ATLAS and FLAIR randomized controlled trials demonstrating the equivalence of this regimen to standard daily oral ART [28, 29]. The FDA approved every 2-month administration of injectable cabotegravir/rilpivirine in 2022 [30], based on results of the ATLAS-2 M study [31], which demonstrated the non-inferiority of this dosing schedule. Viiv Healthcare is working on drug delivery technology to enable the delivery of larger doses with less pain, leading to an “ultra-long-acting” product dosed every 3 months or longer [32]. Evidence suggests that these regimens are tolerable in practice: in the week 124 FLAIR study, while injection site reactions were the most common adverse event (occurring after 21.3% of injections across all participant visits), they were generally mild (grade 1 or 2), short-lived (median duration 3 days) and less frequent over time, and only 2.1% (11 of all 515 participants) discontinued LA cabotegravir/rilpivirine due to injection site pain or reactions [33]. While less frequent dosing and only mild pain could overcome concerns about injections, LA oral regimens have other advantages, such as greater convenience and privacy with home administration, that will likely influence preferences.

Participants in our DCE preferred LA-ART regimens without a requirement for viral suppression before initiation, although this attribute had a relatively weak influence on choices. While each potential LA-ART regimen we examined could lead to increased patient satisfaction if available, the extent to which LA-ART regimens will address gaps in ART adherence and help attain viral suppression targets remains unclear [34]. Of note, in the study by Dandachi et al. asking participants to select their most preferred LA-ART type, the likelihood of LA-ART use did not correlate with adherence or viral suppression [25]. An ongoing AIDS Clinical Trial Group study called “LATITUDE” (NCT03635788) is investigating the use of injectable cabotegravir/rilpivirine compared to daily oral therapy among patients with a history of poor adherence, who were specifically excluded from prior trials [35]. While LATITUDE was originally designed with an oral lead-in period of 6 months during which conditional economic incentives would promote viral suppression [35], new evidence suggests that viral suppression may not always be needed prior to starting cabotegravir/rilpivirine [36]. Results of the LATITUDE trial and other studies could provide important evidence on the extent to which LA injectable treatment may address current gaps in viral suppression. Further research on preferences for LA-ART that includes populations who have struggled with adherence and viral suppression, such as adolescents and those with substance use or mental health problems, will be important as new regimens become available.

Our DCE participants also preferred LA-ART regimens without a requirement for allergic reaction or other side effect testing before initiation and those with some “leeway” or forgiveness in dosing. Of note, the requirement for oral lead-in for “negative reaction” testing has been waived for injectable cabotegravir/rilpivirine, based on the week 124 FLAIR results [33]. While an oral lead-in period to identify and manage potential adverse drug reactions is no longer an issue for cabotegravir/rilpivirine, it may still be needed for other regimens. In addition, missed or late administration could lead to antiretroviral resistance mutations, regardless of treatment mode [34]. Resistance to injectable cabotegravir/rilpivirine has been reported for a small number of participants in recent clinical trials [37]. While they may be less influential for patients, concerns about managing adverse reactions and ensuring adequate leeway in the event of a missed dose will be key attributes influencing the preferences of providers.

Switching to LA-ART may not be of interest to patients who are doing well on their current daily regimen. Indeed, in a separate analysis exploring associations with selecting the “Option C” constant opt-out in this DCE, we found that PWH who were older, more adherent, more averse to injections and had lower educational attainment more frequently chose their current daily regimen in this DCE [38]. A striking finding of the current study is the difference in preferences by geographic site, which were evaluated nominally in stratified analysis for this manuscript, with no direct statistical comparison. Atlanta participants were more positive about their current daily oral regimen than were Seattle participants, and their preferences for treatment mode were less strong, with the 95% CI for current regimen overlapping those of long-acting oral treatment and injections. While they clearly did not prefer implants, they also did not have a preference for home over the clinic. Atlanta participants were more likely to be unemployed and uninsured, and gaps in insurance coverage have led to challenges implementing injectable cabotegravir/rilpivirine at the Atlanta site [39]. These structural problems may underlie patients’ stronger preference for their current daily oral therapy, despite our request that patients assume there would be no difference in cost for the LA-ART options presented relative to their current daily oral regimen. Site differences may also have been influenced by the greater proportion of cisgender women in Atlanta and their experiences with injections and implants for contraception; in addition, women had higher stigma scores than men (2.27 vs. 2.13, p = 0.04), which may also have impacted preferences. Another possibility is that medical mistrust is more prevalent in the Atlanta participant sub-population, which was more likely to be Black. Of note, in an extension of the ATLAS study that investigated the safety of “direct-to-injection” cabotegravir/rilpivirine initiation as an option alongside the standard pre-treatment negative reaction testing, Black participants were less likely than White participants to opt for “direct to injection” [40]. Future studies of patient preferences for LA-ART options should consider including measurement of medical mistrust and evaluating structural barriers to treatment access that may alter preferences.

This study has a number of limitations. First, we only targeted patients who were engaged in HIV care at our clinical sites, and so missed PWH in the study areas who were not diagnosed or engaged in care. In addition, patients who volunteered for the study, especially those who participated online, may differ from those who did not. Second, our work was conducted in only two U.S. regions and our study population is, therefore, not representative of PWH in other geographic
areas or settings. While an online study could potentially reach a larger group of PWH, there is a trade-off between the challenges of online recruitment and recruitment from clinical settings in which HIV status can be confirmed and other clinical data are available. Third, we may have excluded potential LA-ART products (e.g., infusions of broadly neutralizing antibodies) that may come on the market eventually or included product modalities that may turn out not to be feasible. That said, we developed our DCE based on feedback from 12 experts in the field in the year immediately prior to study launch, using the best information available at the time. Fourth, we were unable to fully examine differences between subcutaneous and intramuscular injections due to the complexities of the restrictions used and did not compare regimens that included mixed modalities due to concerns about cognitive overload. In addition, because the home location was restricted to those modes that could be self-administered with ease, we could not distinguish preference for home location from preference for self-administration. Fifth, DCEs ask individuals to make hypothetical choices, which may differ from choices patients would actually make when opportunities arise in the real world, especially if recommended by their physician. Finally, our focus was to provide a comprehensive assessment of preferences within the study sample, and additional exploration is needed in order to assess preference heterogeneity across participant subgroups; this work will be forthcoming. Despite these limitations, the present analysis builds on prior patient preference research on LA-ART by expanding the options participants considered beyond the injectable products first on the market, and is, therefore, a unique and valuable contribution.

5 | CONCLUSIONS

In conclusion, PWH in the United States may soon have several options for LA-ART. Our results suggest that LA oral tablets will be preferred by many patients over their current treatment, while implants and injections with longer duration may be acceptable to some patients. Future research should investigate sources of preference heterogeneity and actual uptake of and retention on products, when available.

AUTHORS’ AFFILIATIONS

1Division of Allergy & Infectious Diseases, Department of Medicine, University of Washington, Seattle, Washington, USA; 2Department of Global Health, University of Washington, Seattle, Washington, USA; 3Department of Epidemiology, University of Washington, Seattle, Washington, USA; 4The Comparative Health Outcomes, Policy, and Economics (CHOICE) Institute, University of Washington, Seattle, Washington, USA; 5Pfizer, Inc, New York, New York, USA; 6Department of Pharmaceutics and Bioengineering, University of Washington, Seattle, Washington, USA; 7Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia, USA; 8Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, Georgia, USA; 9Department of Psychology, University of Washington, Seattle, Washington, USA

COMPETING INTERESTS

BH is an employee of Pfizer. SMG has received support from Gilead and Cepheid for her research. VCM has received investigator-initiated research grants (to the institution) and consultation fees (both unrelated to the current work) from Eli Lilly, Bayer, Gilead Sciences and VIIV. The other authors declare that they have no competing interests directly relevant to the content of this article.

AUTHORS’ CONTRIBUTIONS

SMG, JMS, BH and DB designed the study; SMG and JMS acquired funding; VCM oversaw the Atlanta site; ATB and the Emory PREFER Team collected data; DB and ES analysed the data; ACC and RJYH contributed expertise in long-acting treatment development and testing; and SMG wrote the initial manuscript. All authors contributed to and approved the final manuscript.

ACKNOWLEDGEMENTS

We again thank the key informants who were interviewed in our pilot work, as well as participants in our DCE pilot testing work. Special thanks in this article go to our patient participants in Atlanta and western Washington State for their contributions.

FUNDING

Financial support for this study was provided by National Institutes of Health (NIH) grant R01 MH121142, the University of Washington/Fred Hutch Center for AIDS Research (P30 AI027757) and the Emory University Center for AIDS Research (P30AI050409). SMG and JMS were also supported by the University of Washington Behavioral Research Center for HIV (BIRCH), an NIMH-funded program (P30 MH123248). RJYH and ACC are funded in part by NIH grants UM1 AI120176; AI 148055; AI149665; and UNITAID 2020-39-GLAD. The funding agreements ensured the authors’ independence in designing the study, interpreting the data, and writing and publishing the report. This project also utilized REDCap electronic data capture, which is supported at the University of Washington by grants UL1 TR002131, KL2 TR002131 and TL1 TR002318 from NCATS/NIA. De-identified data will be made available in the Harvard Dataverse upon publication.

REFERENCES


SUPPORTING INFORMATION

Additional information may be found under the Supporting Information tab for this article:

Supporting Information 1. Project PREFER SurveyEngine Questionnaire & DCE

Figure S1A. Long-acting antiretroviral treatment (LA-ART) preference weights from conditional logistic regression for Seattle participants.

Figure S1B. Long-acting antiretroviral treatment (LA-ART) preference weights from conditional logistic regression for Atlanta participants.

Table S1. Point estimates and 95% confidence intervals from logistic regression for preference weights, Seattle participants.

Table S2. Point estimates and 95% confidence intervals (CI) from conditional logistic regression for preference weights, Atlanta participants.