

Predictors of HIV Pre-Exposure Prophylaxis Preferences Using the Health Belief Model: Twice-Yearly Subcutaneous Lenacapavir Versus Daily Pills in the PURPOSE 1 Trial

TUPEC057

PURPOSE 1

Leila E Mansoor¹, Limakatso Lebina², Philisiwe Makhoba³, Logashvari Naidoo⁴, Gonasagrie Nair⁵, Dylan Mezzio⁶, Gary Leung⁶, Xin Li⁶, Alexander Kintu⁶, Moupali Das⁶, Quarraisha Abdool Karim¹

¹Centre for the AIDS Programme of Research in South Africa, University of KwaZulu-Natal, Durban, South Africa; ²Africa Health Research Institute, Somkhale Research Campus, Durban, South Africa; ³Qhakaza Mbokodo Research Clinic, Ladysmith, Durban, South Africa; ⁴HIV and Other Infectious Diseases Research Unit, South African Medical Research Council, Durban, South Africa; ⁵Desmond Tutu Health Foundation, University of Cape Town, Cape Town, South Africa; ⁶Gilead Sciences, Inc., Foster City, CA, USA

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Conclusions

- Feelings of increased confidence in maintaining adherence on pre-exposure prophylaxis (PrEP) and of increased protection from HIV with twice-yearly injections were significantly associated with twice-yearly PrEP injection preference
 - Anticipated level of injection-site pain (mild, moderate, or severe) did not significantly impact participants' preference for twice-yearly injections versus daily oral pills
- As PrEP modality options expand beyond daily oral pills, identifying factors that may predict PrEP preference will help PrEP users and their providers choose the optimal PrEP option for them

Summary

- PrEP is a medicine that helps prevent HIV
- Most PrEP is taken as a daily oral (by mouth) pill, which many people find difficult to do
- Lenacapavir (LEN) is a new kind of PrEP that is given as a shot just twice a year (every 6 months)
- A large study called PURPOSE 1 showed that LEN can help protect cisgender women from getting HIV
- The study also found that most people preferred getting a shot twice a year instead of taking an oral pill every day
- The goal of this study was to look at why people might choose one PrEP option over the other
- People are more likely to change their health habits if they believe they are at risk for a serious illness, they believe a medicine will help, and they see clear benefits from taking that medicine
- The study found that people who thought they would be better at sticking to the injection schedule than taking an oral pill daily, and felt more protected with the shot than the oral pills, were more likely to choose the injection
- As more types of PrEP become available, it is important to provide information to people who can benefit from PrEP and their prescribers, to ensure they are able to make an informed choice. Participant experience data, as collected in this trial, may help to inform people about the use of LEN for PrEP

Introduction

- In the Phase 3 PURPOSE 1 trial, twice-yearly subcutaneous (SC) LEN demonstrated 100% efficacy in preventing HIV and was superior to daily oral emtricitabine/tenofovir disoproxil fumarate (F/TDF), with no safety concerns, in cisgender women in South Africa and Uganda¹
- Understanding the experience of people who use PrEP, including their administration preferences, could help to inform people who want or need PrEP about real-life experiences, thus facilitating people-centered discussions with healthcare providers about PrEP options
- In the randomized blinded phase of PURPOSE 1, the majority of participants reported a preference for twice-yearly injections over daily oral pills, and this preference was maintained through 52 weeks in most participants²
 - Many participants reported greater confidence in their ability to remain adherent to PrEP and that they would feel more protected from HIV if PrEP was administered as twice-yearly injections versus as daily oral pills²

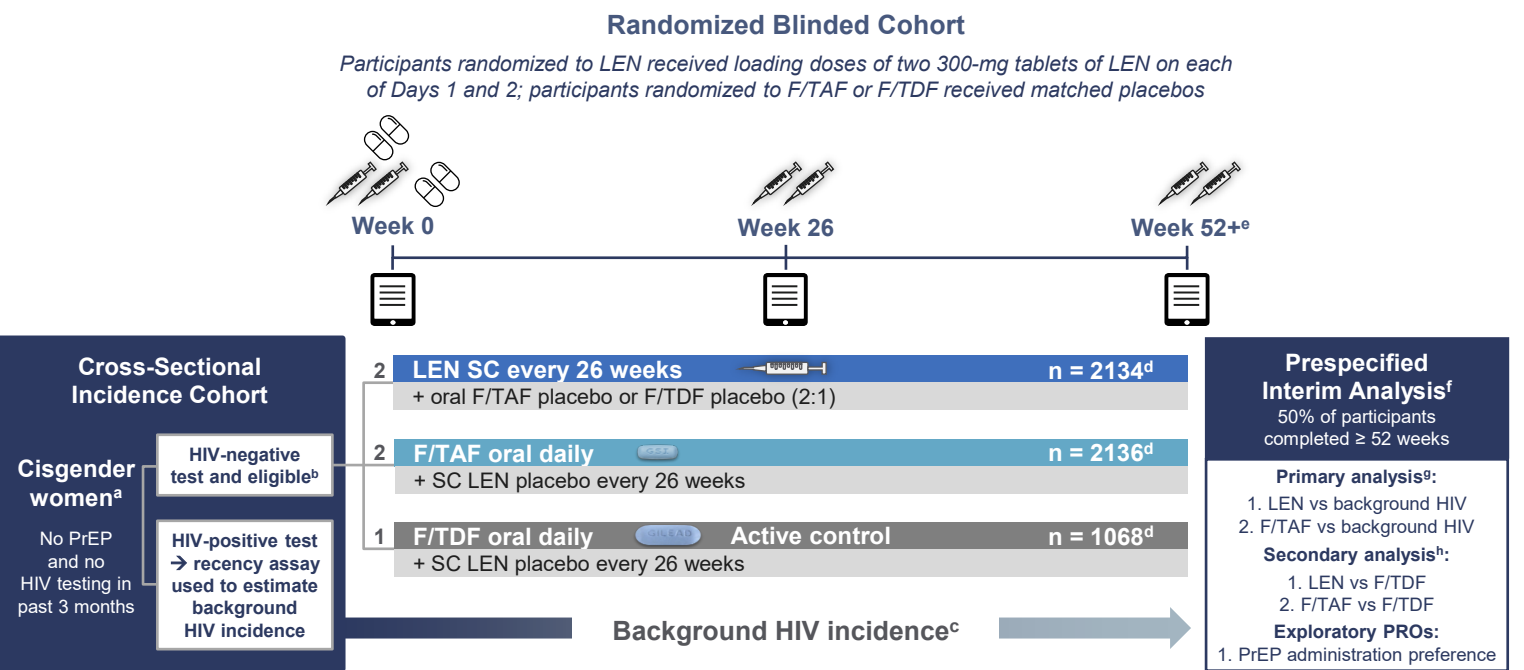
Objective

- To analyze factors that may predict preference for twice-yearly SC LEN for PrEP

Methods

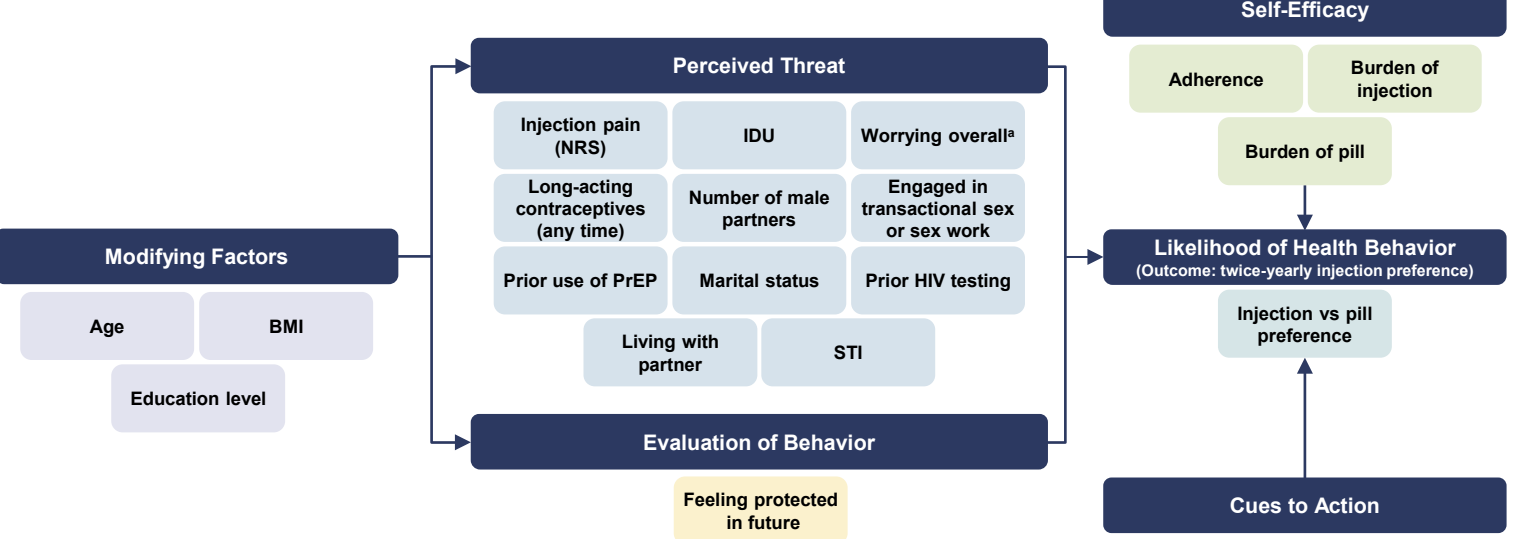
- PURPOSE 1 (NCT04994509) was a Phase 3, double-blind, randomized controlled trial (**Figure 1**)
 - Cisgender women aged 16-25 years were randomized 2:2:1 to receive SC LEN every 26 weeks, oral emtricitabine/tenofovir alafenamide (F/TAF) daily, or oral F/TDF daily, along with the alternate SC or oral placebo
- The Health Belief Model (HBM) was used to identify predictors of twice-yearly injection preference
 - The HBM is based on the idea that beliefs about health conditions, such as perception of disease severity, susceptibility to the disease, and perceived barriers, influence health behaviors³
- Participants who received PrEP injections at baseline, Week 26, and Week 52 visits, and daily oral pills, were included
- During baseline, Week 26, and Week 52 visits, participants completed electronic surveys, which included Likert scale and multiple-choice questions about preference for twice-yearly injections or daily oral pills and factors that might affect preference
- A logistic regression model was pre-specified using the HBM framework and fitted to explore covariates predicting twice-yearly injection preference at Week 52 (**Figure 2**)
 - Selected variables included baseline demographics, sexually transmitted infections, prior HIV testing and PrEP use, sexual behaviors, self-reported injection pain at Week 52, stigma-related concerns, and other reported feelings about PrEP by type
 - Only Week 52 electronic survey responses were included in the HBM, as these provided the most robust and final preference data following multiple injections
- Standard-fit statistics were used; a two-tailed *P* value < 0.05 was considered statistically significant

Figure 1. PURPOSE 1 Study Design¹



PURPOSE 1, ClinicalTrials.gov: NCT04994509. ^aThe first participant was screened in August 2021, the 50th-percentile participant was randomized in May 2023, and the last participant was randomized in September 2023. ^bEligibility criteria included: weight ≥ 35 kg, eGFR ≥ 60 mL/min, not pregnant. ^cBackground HIV incidence is the incidence expected without PrEP that would have been expected in a placebo group (the counterfactual HIV incidence). ^dn numbers represent the full analysis set for efficacy analyses. ^eOnly Week 52 responses were included in the HBM. ^fBecause the randomized blinded phase was stopped early owing to an efficacy outcome, the interim analysis served as the primary analysis. ^gIRR was assessed using a Wald test or likelihood ratio test if there were zero infections. ^hIRR was assessed using Poisson regression or an exact conditional Poisson regression model in case of zero infections. eGFR, estimated glomerular filtration rate; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; HBM, Health Belief Model; IRR, incidence rate ratio; LEN, lenacapavir; PrEP, pre-exposure prophylaxis; PRO, participant-reported outcome; SC, subcutaneous.

Figure 2. Variables Selected for the HBM



^aParticipants were asked whether they worried about other people finding out and judging them for taking PrEP medication during the past week. BMI, body mass index; HBM, Health Belief Model; IDU, injectable drug use; NRS, Numerical Rating Scale; PrEP, pre-exposure prophylaxis; STI, sexually transmitted infection.

Results

Participants

- A total of 1997 participants met the preference study criteria; median age was 21 years (**Table 1**)
- Most participants (n = 1638; 82.1%) had undergone previous HIV testing; a minority (n = 102; 5.1%) reported any previous use of PrEP

Table 1. Baseline Demographics

Characteristic	Participants (N = 1997)
Age, years, median (range)	21.0 (16.0-25.0)
BMI, kg/m ² , median (range)	25.1 (15.0-62.7)
Any prior use of PrEP, n (%)	102 (5.1)
Any prior HIV testing, n/N (%)	1638/1995 (82.1)
Highest education level, n/N (%)	
Primary school or lower	1179/1994 (59.1)
Completed secondary school	635/1994 (31.8)
Some college or university	180/1994 (9.0)
Number of male partners, n/N (%)	
0	132/1885 (7.0)
1-2	1106/1885 (58.7)
≥ 3	647/1885 (34.3)
Married, n/N (%)	42/1994 (2.1)
Living with partner, n/N (%)	153/1993 (7.7)
Engage in transactional sex or sex work, n/N (%)	534/1967 (27.1)
Injectable drug use, n/N (%)	22/1972 (1.1)
≥ 1 STI, n/N (%)	451/1992 (22.6)
Long-acting contraceptive use (any time), n/N (%)	1440 (72.1)
Feelings of worry in past week about people finding out about and judging PrEP use, n (%)	
Strongly agree/agree	317 (15.9)
Neither agree nor disagree	108 (5.4)
Strongly disagree/disagree	1572 (78.7)

^aPain was rated using the NRS; scores of 0-3 were associated with mild pain; scores of 4-7 were associated with moderate pain; scores of 8-10 were associated with severe pain. BMI, body mass index; NRS, Numerical Rating Scale; PrEP, pre-exposure prophylaxis; STI, sexually transmitted infection.

Overall Preference

- At Week 52, 71.2% (n = 1422) of participants preferred twice-yearly injections over daily oral pills
 - 64.2% (n = 1282) of participants reported that they would expect to be more adherent to PrEP medication with twice-yearly injections versus daily oral pills; 27.5% (n = 550) reported that they would expect to be more adherent with daily oral pills versus twice-yearly injections
 - 63.7% (n = 1272) of participants reported that they would expect to feel more protected from HIV infection with twice-yearly injections versus daily pills; 26.9% (n = 538) reported that they would feel more protected with daily oral pills versus twice-yearly injections

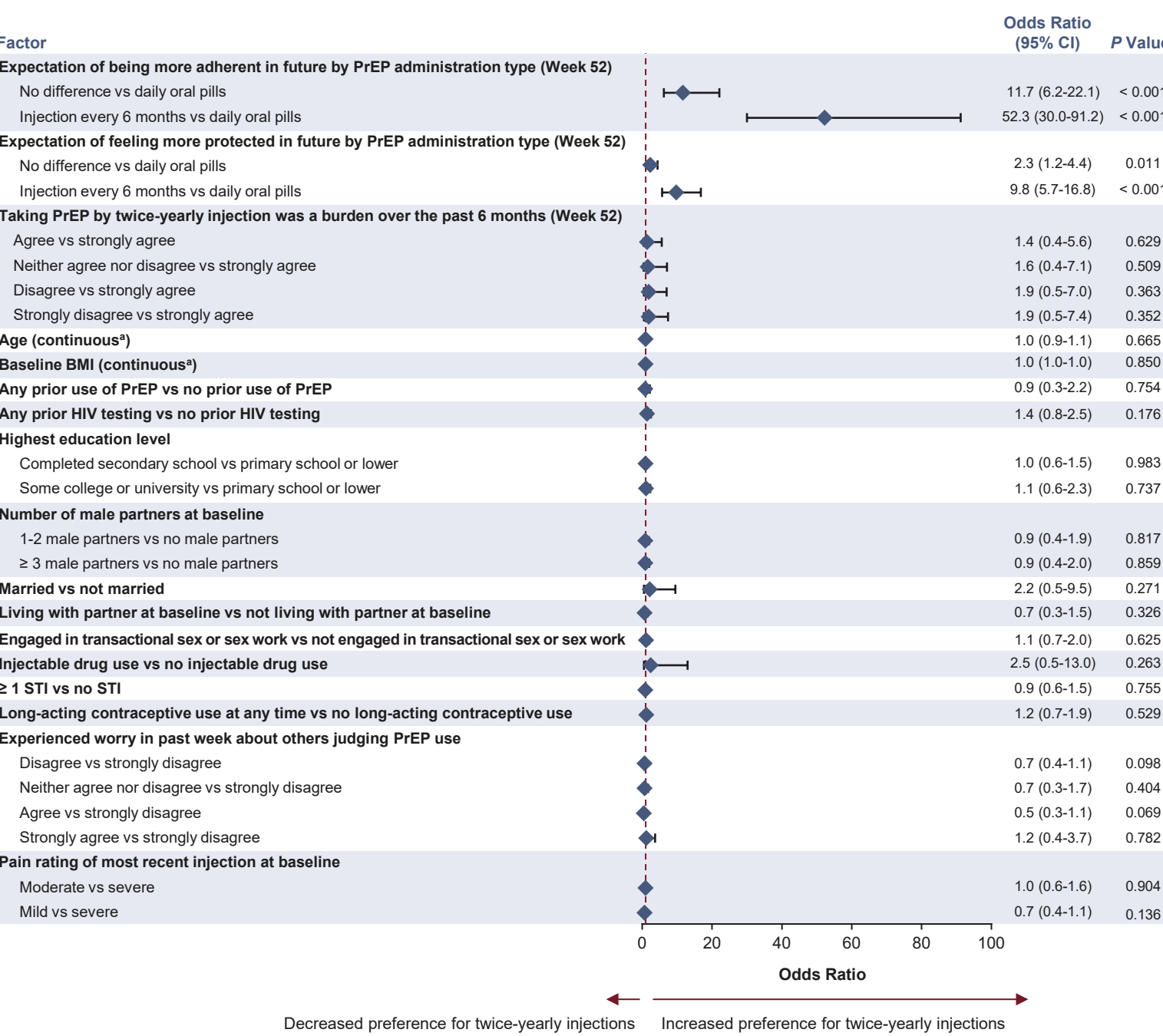
Model Goodness-of-Fit

- The logistic regression model demonstrated a substantial improvement in fit and ability to explain data when covariates were included, as demonstrated by strong improvements in standard measures of logistic regression model quality (see poster footnotes^{*)}
- Overall, these results support the adequacy and statistical strength of the covariate-adjusted logistic regression model, demonstrating that the model fits the data well and that the results are dependable

HBM: Predictors of PrEP Preference

- Participants who expected greater adherence with twice-yearly injections or who felt more protected from HIV with twice-yearly injections were 52.3 (95% CI: 30.0-91.2) and 9.8 (95% CI: 5.7-16.8) times more likely to prefer injections over daily pills, respectively (both *P* < 0.0001) (**Figure 3**)
- No other variables were statistically significantly associated with reported preferences
 - Notably, anticipation of injection-site pain level (mild, moderate, or severe) did not statistically significantly impact participants' preference for twice-yearly injections versus daily oral pills
 - Additionally, perceived risk, as demonstrated by number of male sexual partners, did not affect preference for twice-yearly injections versus daily oral pills

Figure 3. Forest Plot of Factors Affecting PrEP Preference



^aThe direction of continuous variable is a one-unit increase in age/BMI. BMI, body mass index; PrEP, pre-exposure prophylaxis; STI, sexually transmitted infection.

Limitations

- This ad hoc analysis of the PURPOSE 1 clinical trial used a cross-sectional design, which does not capture how participant behavior may change over time. To better understand those changes, a follow-up real-world study using a longitudinal model may be helpful to follow participants for a longer period of time and use additional measures to better understand preference
- While we used individual items from several questionnaires based on the HBM, future studies could explore models that use concept-level scores, when such scores are available for the relevant questionnaires. This approach would allow for interpretation at the concept level (groups of related items) and reduce the number of variables needed in the model

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Correspondence: Dylan Mezzio, Dylan.Mezzio@gilead.com.

^{*}The -2 log-likelihood decreased from 2176.5 in the intercept-only model to 783.2 in the full model, whereas the Akaike Information Criterion dropped from 2176.5 to 841.2, and the Schwarz Criterion dropped from 2184.0 to 1000.9. A global test of the null hypothesis that all regression coefficients are zero was highly significant across the likelihood ratio, score, and Wald tests (all *P* < 0.0001, with 28 degrees of freedom), indicating that the inclusion of covariates significantly improved the model's explanatory power. The Hosmer-Lemeshow goodness-of-fit test yielded a chi-square of 13.3 (*P* = 0.10), suggesting no evidence of poor fit and indicating good calibration of the model to the observed data.

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