Modeling Strategies to Maximize PrEP Impact in the United States With Twice-Yearly Lenacapavir

TUPEC162

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Conclusions

- Projected reductions in HIV-1 incidence and progress toward Ending the HIV Epidemic (EHE) goals in the US by 2030 were greater when lenacapavir (LEN) for pre-exposure prophylaxis (PrEP) was prioritized for certain populations (i.e., uninsured and Black, Indigenous, and People of Color [BIPOC]) than when LEN was unavailable or distributed according to 2025 population proportions
- Prioritizing LEN uptake in these same populations also reduced disparities and improved health equity in PrEP uptake

Plain Language Summary

- PrEP is a type of medicine that helps prevent HIV. People can take PrEP as a daily pill or as a long-acting injection. One long-acting injectable option is lenacapavir, which is given every 6 months
- Many people who could benefit from PrEP do not use it. Access is not equal for everyone, and some people find it hard to take a pill every day
- We used a computer simulation to estimate how many new HIV infections may happen in the United States by 2030. We looked at different situations, including how many people use daily PrEP pills or lenacapavir, and how lenacapavir is used in different groups of people
- The results showed that adding lenacapavir could prevent more HIV infections than using daily PrEP pills alone. Even more infections could be prevented if lenacapavir reached the people who need it most
- However, some people who could benefit from PrEP would still not be using it and could still get HIV. This shows that more work is needed to help prevent HIV infections

Background

- HIV-1 remains a major public health concern in the United States (US): Roughly 38,400 individuals were newly diagnosed with HIV-1 in 2024, with reductions in HIV-1 incidence continuing to fall well short of the "90% by 2030" goal (relative to 2017) set by the EHE initiative[1,2]
- HIV PrEP is a key tool in achieving EHE goals; highly effective options for PrEP include daily oral pills and long-acting injectables, including twice-yearly LEN[3]
- PrEP uptake, however, is disproportionate to prevention needs in some populations[4]
  - Non-White men who have sex with men (MSM) and heterosexual women are using PrEP at lower rates relative to their need compared to the national average[4]
- In addition, adherence to daily pills is lower in some populations (e.g., younger and heterosexual individuals) indicating that these populations may benefit from long-acting PrEP options[5]

Objective

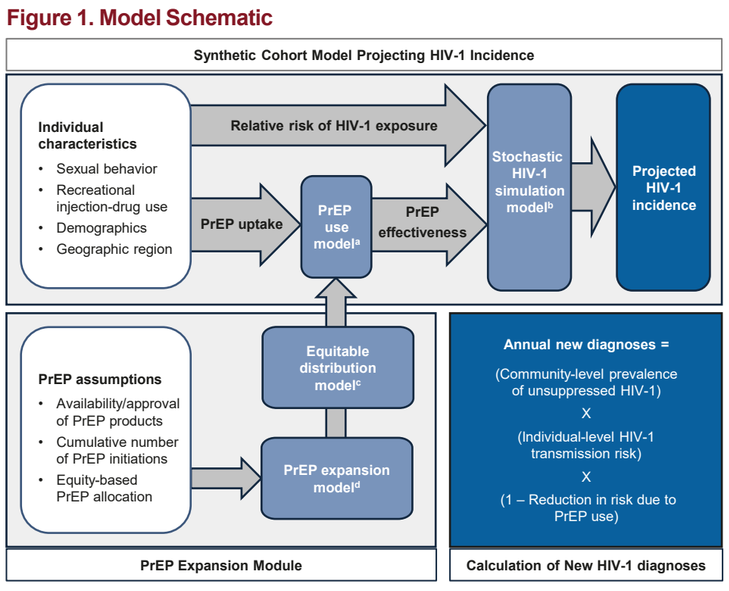
- To investigate how the impact of PrEP on HIV-1 incidence and health equity can be improved by expanding PrEP uptake and prioritizing LEN use in minority populations and uninsured individuals

Methods

Algorithm for Projecting HIV-1 Incidence in 2030

- A static cohort model was developed to project PrEP uptake and new HIV-1 diagnoses in the US population in 2030, stratified by county, race, age, gender, sexual behavior, injection-drug use, and insurance status (**Figure 1**)[6–14]
  - PrEP indication rates were based on previously published data[12,13]
  - The model was calibrated to HIV-1 prevalence and incidence in 2022 and trends in annual PrEP prescriptions from 2012–2023[8]

Figure 1. Model Schematic



[a]PrEP-use model was parameterized with real-world data on persistence, product choice, and adherence stratified by demographics, from 2021 to 2024, and product effectiveness from clinical studies. [b]Stochastic simulation model was calibrated with PrEP uptake and HIV-1 incidence within the US in 2022, stratified by demographics, type of HIV-1 vulnerability, and geography. [c]The equitable distribution model reallocates new PrEP uptake and lenacapavir for PrEP use by geographic and demographic variables. [d]PrEP expansion model was parameterized with data on PrEP uptake, stratified by demographics, type of HIV-1 vulnerability, and geography from 2012 to 2023.
PrEP, pre-exposure prophylaxis.

Scenarios

- HIV-1 incidence was projected under two overall scenarios:
  - Baseline scenario (S_{base}): PrEP use maintained at 2025 levels (652,000 PrEP users, 0% LEN)
  - Expanded uptake: Number of PrEP users increased to 1.1 million, with varying proportions of LEN users
- Four main expanded uptake scenarios were explored:
  - 0% LEN uptake ($S_{0\%}$): No PrEP users take LEN (100% daily oral pill use)
  - Projected LEN uptake ($S_{37\%proj}$): LEN taken by 37% of all PrEP users (matching the proportion of PrEP users in 2025 using PrEP options other than emtricitabine/tenofovir disoproxil fumarate)
  - Optimized LEN uptake ($S_{37\%opt}$): LEN taken by 37% of all PrEP users, with new oral PrEP uptake and LEN redistributed by geography, demographics, and insurance status to minimize HIV-1 infections
  - 100% LEN uptake ($S_{100\%}$): All PrEP users take LEN (0% daily oral pill use)
- A fifth expanded uptake scenario (S_{pbr}) explored the impact of a population-based rollout of 100% LEN
  - Populations received 0% or 100% LEN, with 100% LEN assigned sequentially based on priority status
  - Priority was assigned in descending order of marginal infections averted per PrEP user switching from oral PrEP to LEN

Metrics Used to Assess Scenario Outcomes

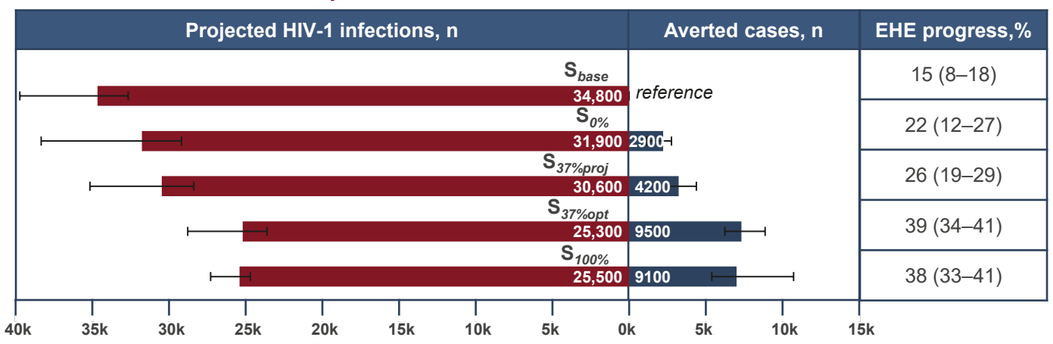
- Projected number of new HIV-1 diagnoses
- Number of infections averted, relative to S_{base}
- Percent reduction in new HIV-1 diagnoses, relative to 2017 (EHE goal: 90% reduction)
- Percent of individuals with a PrEP indication taking PrEP, weighted by HIV-1 exposure (effective coverage)
- Ratio of PrEP users to new HIV-1 diagnoses (PrEP-to-need ratio [PNR])
  - High PNR values indicate better PrEP coverage relative to the HIV-1 incidence in a population
  - A population's **PrEP shortfall** is the number of new PrEP users required to raise the PNR to the national average
- Health equity across populations was assessed with the Weighted Index of Disparity (WID)[15]
  - WID was calculated for HIV-1 incidence, effective coverage, and PNR
  - Higher index numbers indicate greater disparity (lower equity) between population groups; 0% indicates no disparity

Results

HIV-1 Cases in 2030

- Compared with baseline, projected reductions in HIV-1 incidence in 2030 were greatest with optimized 37% LEN uptake ($S_{37\%opt}$) and maximized LEN uptake ($S_{100\%}$), with each averting over 9000 HIV-1 cases (**Figure 2**)
  - With projected LEN use ($S_{37\%proj}$), 4200 HIV-1 cases were averted
  - Without LEN ($S_{0\%}$), only 2900 HIV-1 cases were averted
- Similarly, projected progress toward EHE goals was greatest under $S_{37\%opt}$ and $S_{100\%}$, with similar results for both (**Figure 2**)
  - However, reductions in new HIV-1 diagnoses still fell short of the 90% by 2030 goal

Figure 2. Projected HIV-1 Infections, Cases Averted, and Progress Toward EHE Goals for the US in 2030 Under Four Scenarios of LEN Uptake



Error bars indicate and percentage range indicate 95% CIs.
CI, confidence interval; EHE, Ending the HIV Epidemic Initiative; k, 1000 individuals; LEN, lenacapavir.

Health Equity

- Compared with baseline PrEP use (S_{base}), optimizing LEN uptake ($S_{37\%opt}$) reduced disparity and improved health equity (**Table 1**)
  - Little change from baseline was observed under the remaining scenarios
- Across populations, lower HIV-1 incidence and higher effective coverage and PNR were observed with $S_{37\%opt}$ versus $S_{37\%proj}$ (**Figure 3**)
  - The largest improvements were seen in the uninsured population and in those who were Black, Hispanic, or American Indian and Alaska Native
  - Although PNR was lower in $S_{37\%opt}$ than $S_{37\%proj}$ in those aged >65 years, non-Hispanic White, and Asian, PNR values remained above the overall median value

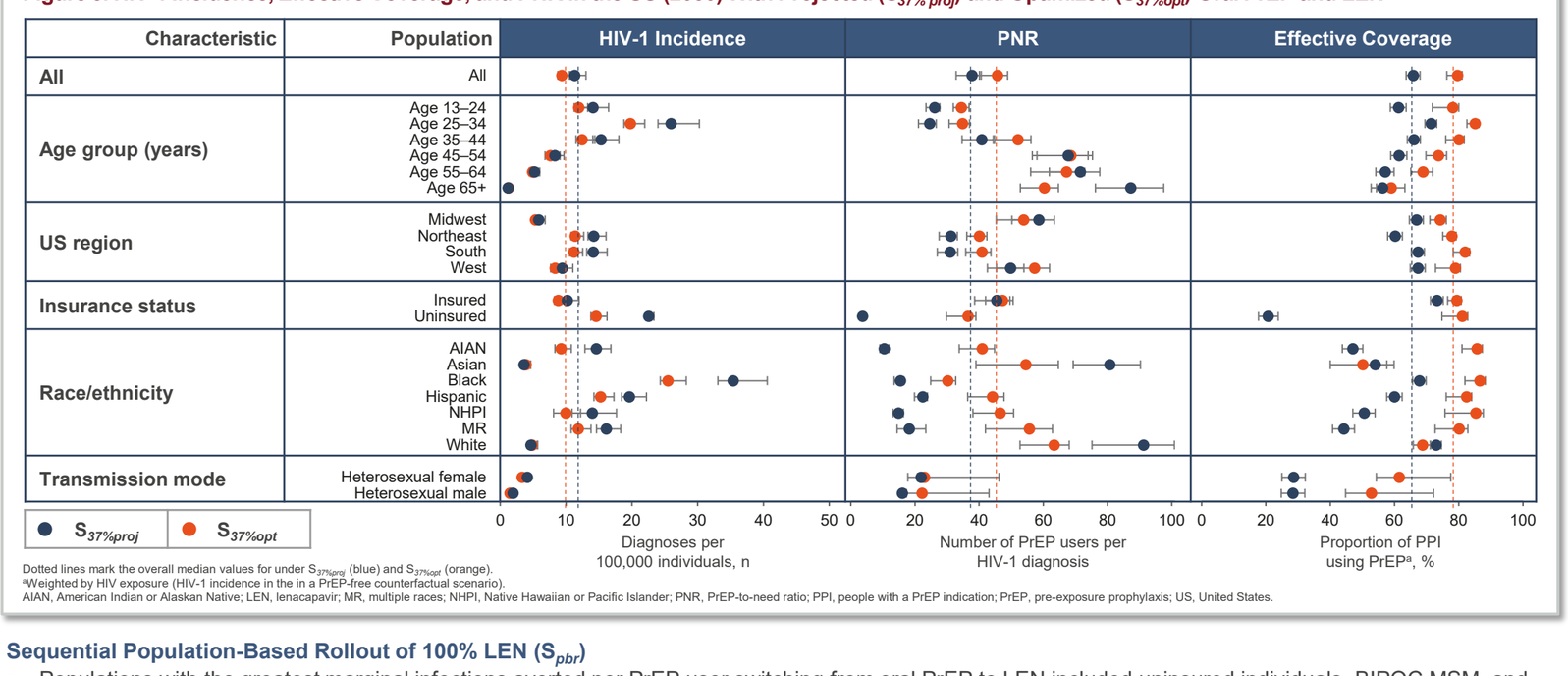
Table 1. Weighted Index of Disparity Values for Projected Outcome Measures for 2030 Under Five Scenarios of PrEP Uptake in the US

Scenario	HIV-1 incidence	PNR	Effective coverage
S_{base}	92	92.1	74
$S_{0\%}$	92.3	95.7	62
$S_{37\%proj}$	92.1	97.4	63.4
$S_{37\%opt}$	78.5	65.1	49.2
$S_{100\%}$	92.3	105.8	69.2

Lower disparity among populations (higher equity) — Higher disparity among populations (lower equity)

WID was calculated by taking the weighted average of the absolute differences between each subgroup and the overall population, expressed as a percentage. HIV-1 incidence was weighted by the number or PrEP indications and PNR and effective coverage were weighted the number of HIV-1 infections. WID values can be greater than 100% when disparity is very high.
PNR, PrEP-to-need ratio; PrEP, pre-exposure prophylaxis; WID, weighted index of disparity.

Figure 3. HIV-1 Incidence, Effective Coverage, and PNR in the US (2030) With Projected ($S_{37\%proj}$) and Optimized ($S_{37\%opt}$) Oral PrEP and LEN

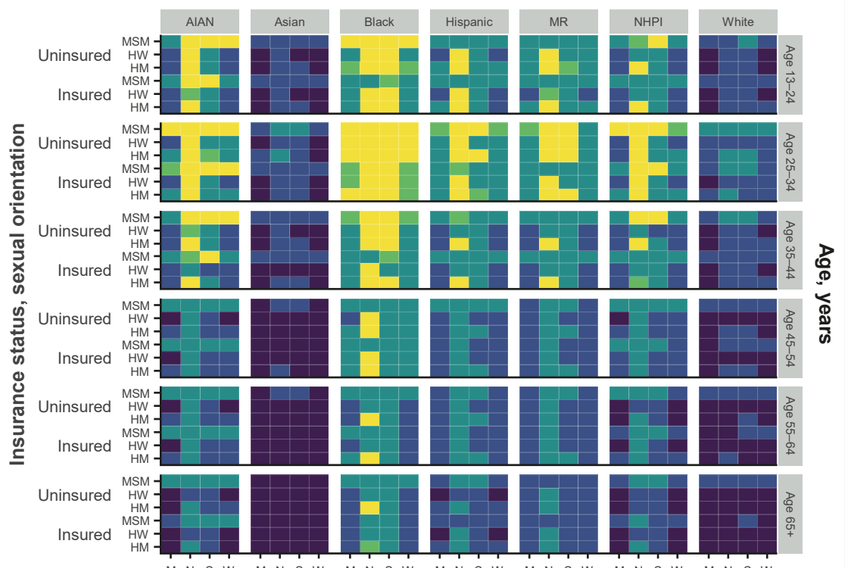


Dotted lines mark the overall median values for under $S_{37\%proj}$ (blue) and $S_{37\%opt}$ (orange).
[a]Weighted by HIV exposure (HIV-1 incidence in the in a PrEP-free counterfactual scenario).
AIAN, American Indian or Alaskan Native; LEN, lenacapavir; MR, multiple races; NHPI, Native Hawaiian or Pacific Islander; PNR, PrEP-to-need ratio; PPI, people with a PrEP indication; PrEP, pre-exposure prophylaxis; US, United States.

Sequential Population-Based Rollout of 100% LEN (S_{pbr})

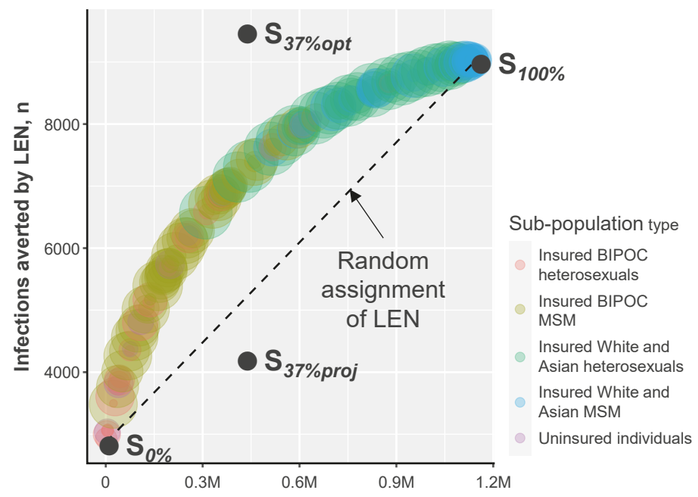
- Populations with the greatest marginal infections averted per PrEP user switching from oral PrEP to LEN included uninsured individuals, BIPOC MSM, and BIPOC heterosexual individuals (**Figure 4**)
- In S_{pbr}, the projected numbers of averted HIV-1 infections per new LEN user initially increased steeply (**Figure 5**)
  - However, more infections were averted with $S_{37\%opt}$ at similar numbers of LEN users
  - Of note, $S_{37\%proj}$ underperformed random assignment of LEN

Figure 4. Heatmap Showing Population Prioritization in the US for Optimal PrEP Expansion With LEN, by LEN Dose Availability



AIAN, American Indian and Alaska Native; HM, heterosexual men; HW, heterosexual women; k, thousand; LEN, lenacapavir; M, million; MSM, men who have sex with men; M, midwest; MR, multiple races; N, northeast; NHPI, Native Hawaiian or Pacific Islander; PrEP, pre-exposure prophylaxis; S, south; W, west.

Figure 5. Averted HIV-1 Infections in the US in 2030 With Sequential Population-Based Rollout of 100% LEN (S_{pbr}) Compared With Other Expanded PrEP Use Scenarios



Each circle indicates the sequential addition of a specific subpopulation, in descending order of impact on averted HIV-1 infections. Circle size indicates subpopulation size; circle color indicates population category. Dotted line represents the number of HIV-1 cases averted given randomly assigned LEN uptake with the overall population (dotted line). Black circles indicate projected outcomes of other assessed expanded PrEP use scenarios.
BIPOC, Black, Indigenous, and People of Color, excluding Asian; LEN, lenacapavir; M, million; MSM, men who have sex with men; PrEP, pre-exposure prophylaxis.

Limitations

- Modeling results should be interpreted as estimates, as they rely on assumptions about future PrEP use scenarios informed by current trends, which may shift over time. The projected LEN uptake scenarios were chosen to reflect current trends and to show the range of potential outcomes
- The "optimal" scenario is intended to illustrate the potential impact of eliminating barriers to PrEP uptake among populations with unmet need and should not be interpreted as a prescriptive implementation strategy
- This model did not account for real-world barriers to PrEP uptake, such as stigma, affordability, access, and awareness, which may affect the real-world impact of PrEP interventions

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