Expected Impact of Twice-yearly Lenacapavir on PrEP Coverage Disparities and HIV Incidence in the US

Poster 1087

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Conclusions

- The introduction of twice-yearly lenacapavir for pre-exposure prophylaxis (PrEP) may substantially affect the US HIV-1 epidemic due to its high effectiveness and longer dosing interval, which may improve adherence
- Results of this modelling study showed improved progress toward Ending the HIV Epidemic (EHE) in the US goals with expanded PrEP uptake and moderate (37%) lenacapavir use versus stable PrEP uptake levels
  - — However, the reduction in new HIV-1 diagnoses under this expanded PrEP scenario was 25%, falling short of the EHE goal of a 90% (relative to 2017) reduction by 2030
- In 2030, shortfalls in PrEP coverage were projected among those who were heterosexual, uninsured, younger than age 35 years, Black or Hispanic, and those who lived in the Northeast or South
- Unmet need for PrEP was greatest among younger Black and Hispanic individuals living in the Northeast or South, younger White individuals who were uninsured, and among men who have sex with men (MSM) overall
- Prioritizing PrEP and lenacapavir toward populations with the greatest unmet need could further improve progress toward EHE goals and reduce disparities in HIV-1 burden across different populations

Plain Language Summary

We used a computer simulation to predict how many new HIV infections would occur in the US in 2030 when different numbers of people were using HIV prevention medications (PrEP), including daily pills and lenacapavir, a new PrEP product taken every 6 months.

The simulation showed that adding lenacapavir as an option for PrEP could prevent more HIV infections than relying only on daily pills, but that many people who could benefit from PrEP would still not be using it.

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Background

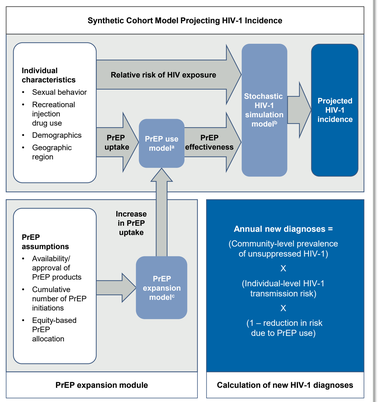
- The EHE set a goal to reduce HIV-1 incidence by 90% from 2017 to 2030 using a combination of improved testing, treatment, and use of PrEP[1,2]
- Despite its effectiveness, the impact of PrEP on the US HIV-1 epidemic has been modest, potentially due to challenges in PrEP uptake and adherence in some populations[3–5]
  - — Younger and Black/Hispanic populations have much lower projected PrEP-to-need ratios (PNR) than the national average, indicating higher unmet needs for PrEP in these populations[3,5]
- Lenacapavir is a twice-yearly injectable PrEP medication approved for use in the US in 2025[6]
  - — In clinical studies, lenacapavir was significantly more effective at preventing HIV-1 acquisition than daily oral PrEP[7,8]
  - — In addition, the longer dosing interval of lenacapavir may improve adherence and reduce discontinuation[6,9]
- To inform future policy decisions related to PrEP, epidemiology projections are needed to understand the potential impact of lenacapavir on HIV-1 incidence
- Here, we project the impact of introducing lenacapavir over the next 5 years (2026–2030) on progress toward EHE goals across different populations in the US

Methods

Algorithm

- A cohort model was developed to project PrEP uptake and new HIV-1 diagnoses in the US population stratified by county, race, age, gender, sexual behavior, injection drug use, and insurance status between 2026–2030 (**Figure 1**)[10–18]
  - — PrEP indication rates were based on previously published data[16,17]
  - — The model was calibrated to HIV-1 prevalence and incidence in 2022 and trends in annual PrEP prescriptions from 2012–2023[12]

Figure 1. Model Schematic



[a]PrEP use model was parameterized with real-world data on persistence, product choice, and adherence stratified by demographics, from 2021–2024, 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]PrEP expansion model was parameterized with data on PrEP uptake, stratified by demographics, type of HIV-1 vulnerability, and geography from 2012–2023. PrEP, pre-exposure prophylaxis.

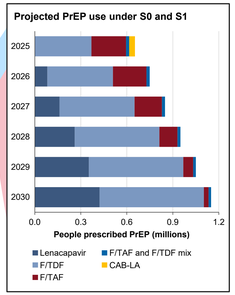
Methods

Scenarios

- HIV-1 incidence was projected under a main scenario reflecting overall PrEP expansion as well as 37% lenacapavir uptake by 2030 (S1) versus *status quo* 2025 PrEP use (S0, baseline) (**Figure 2**)
  - — Lenacapavir uptake in S1 was limited to the share of PrEP users prescribed cabotegravir or emtricitabine/tenofovir alafenamide (F/TAF) in 2025
- Four additional scenarios were explored with baseline (S3) or expanding PrEP uptake (S2, S4, S5) and varying proportions of lenacapavir users
- In all expanded-uptake scenarios, the number of PrEP users increased 12% annually
  - — Expansion was calibrated to National HIV surveillance survey data (2012–2023)

Figure 2. Description of PrEP Use Scenarios with Details for Baseline (S0) and Main (S1) Scenarios[a]

Uptake scenario	Scenario description[a]	Proportion of LEN in 2030	Averted infections[b] in 2030, n (95% CI)
Primary scenarios considered			
S0	Baseline: PrEP use in 2026–2030 is identical to 2025	0%	*ref*
S1	Main scenario: Moderate lenacapavir uptake[c] with expanding PrEP use	37%	13,700 (10,800–18,300)
Alternative scenarios			
S2	Rapid lenacapavir uptake with expanding PrEP use	85%	23,800 (19,100–33,700)
S3	All PrEP users switch to lenacapavir at 2025 PrEP use levels	100%	22,400 (12,200–47,200)
S4	All PrEP users switch to lenacapavir with expanding PrEP use	100%	37,400 (26,800–61,200)
S5	No PrEP users use lenacapavir, but overall PrEP use expands	0%	9400 (4600–11,500)



[a]Baseline 2025 values were 652,000 PrEP users in the US with 0% using lenacapavir; in expanding scenarios, the number of PrEP users increased to 1.15 million by 2030. [b]Additional infections averted relative to the baseline scenario. [c]Lenacapavir expansion limited to the proportion of PrEP users prescribed cabotegravir or F/TAF in 2025. CAB-LA, cabotegravir long-acting; CI, credible interval; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; LEN, lenacapavir; PrEP, pre-exposure prophylaxis; ref, reference population; S, scenario.

Assessment of Progress Toward EHE Goals

- The following three metrics were used to evaluate progress toward the 2030 EHE goals, overall and stratified by population:
  1. Percent reduction of new annual HIV-1 diagnoses relative to 2017
  2. 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
  3. Number of annual PrEP prescriptions necessary to prevent one infection (number-needed-to-prevent, NNP)
     - — NNP values increase with decreasing overall HIV-1 incidence
     - — Low NNP values indicate a higher number of infections prevented per each new PrEP user
- Underserved populations were identified as those with both below-average PNR and below-average NNP

Results

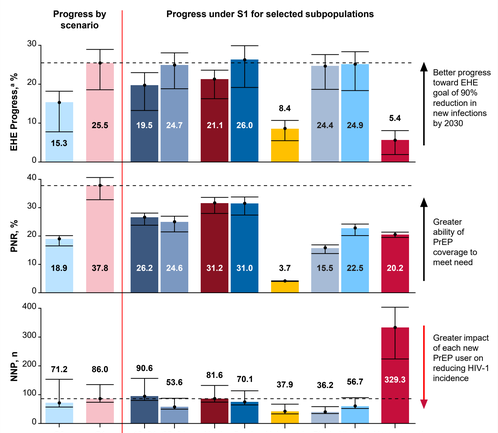
Scenario Outcomes

Baseline and main scenario outcomes for the overall population

- Between 2026 and 2030, an additional 13,700 cases of HIV-1 were averted in S1 relative to S0 (**Figure 2**)
- Progress toward the 2030 EHE goals improved in S1 compared with S0 (**Figure 3**)
  - — New HIV-1 diagnoses were reduced by 15% in S0 and by 25% in S1, relative to 2017
  - — However, reductions were still short of the 90% by 2030 EHE goal
- PNR increased from 19.0 in S0 to 37.8 in S1
- NNP increased from 71.2 in S0 to 86.0 in S1 due to decreasing overall HIV-1 incidence

Results

Figure 3. Progress Toward EHE[a], PNR, and NNP Projected for the US in 2030 Under Baseline 2025 PrEP Uptake (S0) and Expanding PrEP Uptake with Moderate (37%) Lenacapavir Use by 2030 (S1)



Dashed line indicates the mean value for the overall population. Colors used to indicate different populations. Error bars indicate the 95% credible interval. [a]Defined as percentage reduction in new HIV-1 cases relative to 2017.
EHE, Ending the HIV Epidemic; MSM, men who have sex with men; NNP, number of annual PrEP prescriptions necessary to prevent one infection; PNR, PrEP-to-need ratio; PrEP, pre-exposure prophylaxis.

*Disparities in EHE, PNR, and NNP values in 2030 projected under the main scenario (**Figure 3**)*

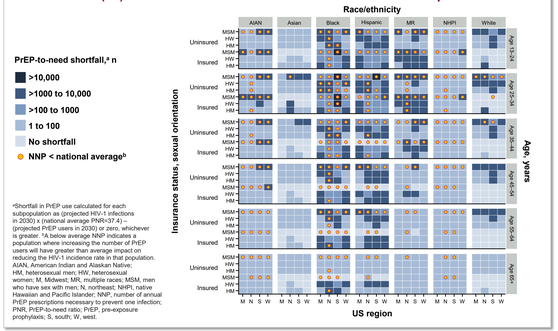
- Progress toward EHE goals was lowest among those who were heterosexual, uninsured, aged 13–24 years, and those who lived in the northeast or south
  - — The smallest reductions in new HIV-1 diagnoses were observed among heterosexuals (5.4% and uninsured individuals (8.4%)
- PNRs below the overall average (37.8) were observed among those who were heterosexual, uninsured, aged <35 years, Black or Hispanic, and those who lived in the northeast or south, indicating a deficit in PrEP use in these populations
  - — The lowest PNRs were observed among uninsured individuals (3.7) and Black individuals (15.5)
- NNPs below the overall average (86.0) were observed among those who were uninsured (37.9) and among Black individuals (36.2)
  - — These low NNPs indicate that adding PrEP users in these populations would produce greater-than-average reductions in HIV-1 acquisition

Identifying Priority Populations

*Intersectionality of underserved populations under the main scenario (**Figure 4**)*

- Populations projected to have the greatest shortfalls in PrEP coverage in 2030 included those who were Black or Hispanic overall, particularly among those who were younger and who lived in the Northeast or South
  - — Among White individuals, projected PrEP shortfalls were more often observed among those who were uninsured
- NNPs were most often below the national average for MSM and for those who were Black or Hispanic, particularly Black or Hispanic individuals who were younger and who lived in the Northeast or South
  - — Below average NNPs were also observed among younger American Indian and Alaskan Natives (AIAN) and individuals of multiple races living in the Northeast, regardless of sexual orientation

Figure 4. Populations With Projected PrEP Shortfalls and Low NNPs in 2030 Under the Main Scenario (S1) Where Added Resources Could Have the Greatest Impact



[a]Shortfall in PrEP use calculated for each subpopulation as (projected HIV-1 infections in 2030) x (national average PNR-37.4) – (projected PrEP users in 2030) or zero, whichever is greater. [b]A below average NNP indicates a population where increasing the number of PrEP users will have greater than average impact on reducing the HIV-1 incidence rate in that population. AIAN, American Indian and Alaskan Native; HM, heterosexual men; HW, heterosexual women; M, Midwest; MR, multiple races; MSM, men who have sex with men; N, northeast; NHPI, native Hawaiian and Pacific Islander; NNP, number of annual PrEP prescriptions necessary to prevent one infection; PNR, PrEP-to-need ratio; PrEP, pre-exposure prophylaxis; S, south; W, west.

Outcomes for Alternative Scenarios

Alternative scenario outcomes for the overall population

- Relative to the baseline scenario (S0), the number of averted HIV-1 cases increased to 22,400–37,400 with ≥85% lenacapavir uptake (S2–S4), even with no expansion of PrEP uptake (S3), compared with 13,700 cases in S1 (**Figure 2**)
  - — Expanding PrEP coverage alone with no introduction of lenacapavir (S5) averted 9400 HIV-1 cases
- Progress toward EHE goals was greatest with expanding PrEP coverage and ≥85% lenacapavir use (**Table 1**)
  - — In S2 and S4 compared with S1, reductions in new HIV-1 diagnoses were greater (36–38% versus 25%), PNRs were higher (44–45% versus 38%), and NNPs were lower (63–66 versus 86)

Outcomes for the Overall Population

Table 1. Progress Toward EHE Goals[a], PNR, and NNP in 2030 Under Different PrEP Uptake Scenarios

PrEP scenario	Reduction in cases since 2017[a] % (95% CI)	PNR, % (95% CI)	NNP, n (95% CI)
Primary scenarios considered			
S0	15.3 (7.8–18.2)	18.9 (16.5–20.1)	71.2 (57.0–153.3)
S1	25.5 (18.6–28.9)	37.8 (32.8–40.7)	86.0 (73.7–135.0)
Alternative scenarios			
S2	35.7 (31.8–37.7)	43.8 (40.8–45.2)	65.6 (61.3–74.4)
S3	26.4 (23.0–30.2)	21.9 (20.8–22.4)	47.6 (43.5–54.5)
S4	37.7 (33.3–40.9)	45.4 (42.2–46.7)	62.5 (58.7–70.4)
S5	22.5 (12.0–26.9)	36.3 (30.1–39.6)	95.0 (77.6–199.9)

[a]Progress toward EHE goals was assessed as the reduction in new HIV-1 cases in 2030 relative to 2017.
CI, credible interval; EHE, Ending the HIV Epidemic; PrEP, pre-exposure prophylaxis; S, scenario.

Limitations

- A static cohort model was used rather than a dynamic model; therefore, the model did not account for potential future demographic or behavioral shifts
- Because of the timing of the COVID-19 pandemic, which reduced rates of HIV-1 testing and diagnoses, HIV-1 prevalence and incidence in 2022 were used to calibrate the model
- Modeling results should be interpreted as estimates, as they rely on assumptions about future PrEP use scenarios informed by current trends — trends which may shift over time. The projected lenacapavir uptake scenarios were chosen to reflect current trends and to show the range of potential outcomes
  - — Emerging real-world evidence will help clarify and validate the impact of lenacapavir on progress toward EHE goals
  - — Public health decision makers may wish to consider alternative scenarios with differing numbers of PrEP users by regimen and subpopulation