**Background**: The Ending the HIV Epidemic (EHE) initiative seeks to reduce HIV incidence in the US by 90% over a decade. Pre-exposure prophylaxis (PrEP) is a key component in this effort. Long-acting injectable (LAI) PrEP reduces the risk of HIV acquisition more than oral PrEP, in part due to increased adherence, but it’s potential to impact local HIV epidemics remains unclear.

**Methods**: The Johns Hopkins HIV Economic Epidemiological model (JHEEM) is a dynamic, compartmental model of HIV transmission in 32 high priority urban areas in the United States. We leveraged JHEEM to project the incidence of HIV among men who have sex with men (MSM) from 2020-2030 under a range of interventions aimed at increasing PrEP use.

In each of the 32 cities, we ran 1,000 simulations testing an uptake of PrEP of 10% and 25% for both LAI and Oral-PrEP, an uptake of 5% Oral-PrEP and 5% LAI-PrEP, and an uptake of 12.5% Oral-PrEP and 12.5% LAI-PrEP, scaling up from 2023 to 2027. We varied the persistence of Oral PrEP according to published estimates and the persistence of LAI-PrEP to be from the reported Oral-PrEP persistence to twice Oral-PrEP persistence.

Our primary outcome was the reduction in incidence among MSM from 2020 to 2030 under each intervention. We report mean reduction and 95% credible interval (CrI) across 1,000 simulations.

**Results**: Baseline PrEP coverage was X% averaged across 32 cities with a range of Y% to Z%. In the absence of any intervention, simulations projected a reduction in HIV incidence of X% (95% CrI YY% to ZZ%) among MSM from 2020-2030 across all 32 cities. With 10% PrEP uptake, LAI-PrEP demonstrated a higher reduction in incidence of X% (95% CrI YY% to ZZ%) compared to Oral PrEP of X% (95% CrI YY% to ZZ%) and Oral and LAI PrEP combined of X% (95% CrI YY% to ZZ%). Similarly, with 25% uptake, LAI-PrEP reduced incidence by X% (95% CrI YY% to ZZ%) while Oral PrEP reduced incidence by X% (95% CrI YY% to ZZ%) and Oral PrEP and LAI-PrEP combined reduced incidence by X% (95% CrI YY% to ZZ%).

There was variation between cities; at 10% uptake we observed the highest reduction in incidence in city X, and least in city Y. Similarly at 25% uptake, the highest reduction was observed in city X, and least in city Y.

**Conclusion:** Oral-PrEP alone is unlikely to help achieve reductions in line with EHE goals. However, LAI-PrEP can play an important role in expanding PrEP coverage.

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|  | No Int | 10% PrEP Uptake | | | 25% PrEP Uptake | | |
| 10% Oral PrEP | 5% Oral PrEP  5% LAI PrEP | 10% LAI PrEP | 25% Oral PrEP | 12.5% Oral PrEP 12.5% LAI PrEP | 25% LAI PrEP |
| Total |  |  |  |  |  |  |  |
| City 1 |  |  |  |  |  |  |  |
| City 2 |  |  |  |  |  |  |  |
| City 3 |  |  |  |  |  |  |  |
| City 4 |  |  |  |  |  |  |  |
| City 5 |  |  |  |  |  |  |  |
| City 6 |  |  |  |  |  |  |  |