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PROJECTED IMPACT OF EXPANDED LONG-ACTING INJECTABLE PREP USE AMONG MEN WHO HAVE SEX WITH MEN ON LOCAL HIV EPIDEMICS

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Abstract

Background: Pre-exposure prophylaxis (PrEP) is a key component in helping to reduce HIV incidence in the United States. Long-acting injectable (LAI) PrEP is a new alternative to oral PrEP; its potential to impact local HIV epidemics remains unclear.

Methods: The Johns Hopkins HIV Economic Epidemiological model (JHEEM) is a dynamic model of HIV transmission in 32 US urban areas. We used JHEEM to project the HIV incidence among men who have sex with men (MSM) from 2020–2030 under a range of interventions aimed at increasing PrEP use.

Results: In the absence of any intervention (i.e. current levels of oral PrEP and HIV care engagement), we projected a 19% reduction (95% credible interval, CrI 1–36%) in HIV incidence among MSM from 2020–2030 across all 32 cities. Adding 10% LAI PrEP uptake (above a base

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case of all oral PrEP) reduced incidence by 36% (95% CrI 23–50%) by year 2030. This effect varied between cities, ranging from 22% in Atlanta to 51% in San Francisco. At 25% additional LAI PrEP uptake, this incidence reduction increased to 54% (95% CrI 45–64%) Reductions in incidence after introducing LAI PrEP were driven primarily by increased uptake and sustained usage rather than increased efficacy.

Conclusion: LAI PrEP has the potential to substantially reduce HIV incidence among MSM, particularly if it increases PrEP uptake and continued use beyond existing levels. Since potential effects vary by city, the effectiveness of expanding PrEP use is dependent on local dynamics.

Keywords

HIV; Ending the HIV Epidemic; Dynamic Transmission Model; Pre-exposure Prophylaxis (PrEP); Injectable PrEP; MSM

BACKGROUND:

In the United States, HIV imposes a substantial health burden, with an estimated 36,000 new infections and 1.2 million prevalent cases in 2019; two-thirds of new infections were among men who have sex with men (MSM)[1]. Pre-exposure prophylaxis (PrEP) is a key tool in ongoing efforts to reduce HIV incidence in the United States[2], and has been shown to be effective among men who have sex with men (MSM)[1,3,4].

In 2017, the CDC estimated that 1.1 million adults have indications for PrEP use, but only 100,000 accessed PrEP[5,6]. To date, only oral formulations of PrEP are approved for use, and at-risk groups have demonstrated mixed adherence to a daily oral regimen[7]. Furthermore, approximately 44% of MSM discontinue PrEP use during their first year [8]. Long-acting injectable (LAI) formulations of PrEP may help to address these challenges of uptake and continuation[8–10] and be preferable for some individuals who are less likely to take a pill on a daily basis[11–15]. Injectable cabotegravir, given every 8 weeks, was recently shown to have superior efficacy compared to oral PrEP in cis- and trans-gender men who have sex with men[10].

The potential population-level benefit of implementing LAI PrEP in the context of local HIV epidemics remains unclear. The Johns Hopkins HIV Economic Epidemiological model (JHEEM) is a dynamic, compartmental model of HIV transmission in 32 high-burden US cities[16]. We applied JHEEM to project the effects of PrEP expansion and LAI PrEP availability on future HIV transmissions among MSM in these 32 cities.

METHODS:

JHEEM is a dynamic, compartmental transmission model stratified by age, race/ethnicity, sex/sexual behavior, and intravenous drug use (never use, active use, and prior use), at the local level[16]. The entire adult population in each modeled location is represented according to HIV infection status, awareness of infection and PrEP status (Figure S1). HIV acquisition in each population subgroup reflects the modeled frequency of sexual or needle-sharing pairings both within and across subgroups (for example, MSM may partner with

heterosexual women), as well as the prevalence of unsuppressed HIV, subgroup-specific HIV transmission rates, PrEP coverage and use of needle-exchange programs. We allowed awareness of infection to reduce the probability of transmission even absent treatment by 21%–42%[17]. These relationships are represented by a set of differential equations and solved using the *odeintr* package in R, version 4.0.2[18,19].

Study Setting:

We selected 32 metropolitan statistical areas (MSAs), which included 48 high burden U.S. counties plus Washington DC[2].

Model Calibration:

Within each MSA, we used a Bayesian calibration process to estimate 131 parameters governing subgroups' time-dependent risks of HIV infection, frequency of HIV testing, PrEP uptake, viral suppression, use of injection drugs, and propensities for mixing with other subgroups. This process took prior information on possible values for each parameter derived from the published literature (generally from national or large cohort data, detailed in Table S1), and ran 400,000 simulations in each MSA to identify a set of specific parameter values – for each city – that reproduced 10 calibration targets which summarize the local epidemic[20,21]. These calibration targets included reported diagnoses, estimated number of people with HIV (PWH) aware of their diagnosis, the proportion of PWH in care who are virally suppressed, and the number of individuals receiving a prescription for PrEP (see Supplementary Table S2). The calibration process yielded 1,000 well-fitting simulations for each MSA; we projected these simulations forward to 2030 under different intervention scenarios to estimate the impact of different levels of PrEP uptake on each MSA's HIV epidemic. In order to summarize overall model fit, we calculated mean absolute percentage errors[22] for reported diagnoses and prevalence.

Modeled Interventions:

We modeled PrEP uptake – the proportion of MSM at risk for HIV acquisition in each subgroup of age, race, and intravenous drug use status who are enrolled in a PrEP program in a given year. We conceived of PrEP as both use of a medication which reduces the risk of acquiring HIV and regular clinic follow-up with HIV testing every 3–6 months. JHEEM does not explicitly model the number of those at risk for HIV in a demographic subgroup; instead, PrEP use reduces the number of incident infections in subgroups. For example, having 25% of those at risk in a given subgroup on PrEP would reduce new infections by 25% multiplied by the efficacy of PrEP in that subgroup.

JHEEM estimates time-varying oral PrEP use in different subgroups based on local prescriptions of emtricitabine-tenofovir. Our simulations continued recent increase in PrEP use into the future to project likely PrEP uptake, which increases over time, absent any additional intervention – we refer to this as "base" PrEP uptake. We projected HIV incidence through 2030 under a scenario in which there was no LAI-PrEP and this base uptake was continued as oral PrEP and under a scenario where all base PrEP use was converted to LAI PrEP. We also evaluated six expansion scenarios that included either 10% or 25% "additional" PrEP uptake over and above base uptake; testing combinations of all-oral

additional on top of all-oral base PrEP, all-LAI additional on top of all-oral base PrEP, and all-LAI additional on top of base PrEP converted to all-LAI. We assumed that interventions on PrEP use began to roll out on January 1st, 2023, and scaled up linearly over 5 years, reaching full implementation by Dec 31st, 2027.

The population-level impact of PrEP is influenced by both its effectiveness in preventing HIV infections (percent reduction in acquisition risk per person-day) and the discontinuation rate – the proportion of those on PrEP who discontinue after a given period of time[8]. We defined four model parameters to govern these characteristics, and allowed each parameter to vary randomly across 1,000 simulations: (1) the effectiveness of oral PrEP, (2) oral PrEP discontinuation rate at one year, (3) the relative efficacy of LAI vs oral PrEP, and (4) the relative discontinuation rate of LAI vs oral PrEP at one year. We sampled the first three parameters according to the published literature (see Table 1)[8,10,23]. Because no data yet exist on persistence among those taking LAI PrEP, we allowed the rate of discontinuation for LAI PrEP to range from 1.25 times that of oral PrEP to one-quarter the discontinuation rate for oral PrEP, which allows LAI PrEP to improve on oral PrEP by decreasing discontinuation.

Outcome:

Our primary outcome was the reduction in incident infections in 2030 relative to 2020, calculated as follows:

$$\left[\frac{(I_{2020} - I_{2030})}{I_{2020}}\right] * 100$$

Where I_{2030} is the projected incidence in 2030 and I_{2020} is the projected incidence in 2020. We calculated the mean reduction across 1,000 simulations for each of the 32 cities considered and 95% credible intervals as the 0.025^{th} quantile and 0.975^{th} quantiles.

We conducted a post-hoc secondary analysis to evaluate the impact of LAI-PrEP on racial disparities. In this analysis, our outcomes were the 2030 incidence rate ratios (IRRs) for Non-Hispanic-Black MSM vs. non-Black-non-Hispanic MSM and for Hispanic vs. non-Black-non-Hispanic MSM under potential interventions targeted to all MSM and to Black and Hispanic MSM specifically. We tested an additional intervention of 25% additional LAI uptake on top of base LAI among only Black and Hispanic MSM to evaluate whether it would affect disparities in incidence.

Sensitivity Analyses:

We conducted sensitivity analyses to assess how key parameters governing PrEP affected the projected reduction in incidence as well as the additional reduction gained by using LAI instead of oral PrEP. For the scenario with 25% additional LAI PrEP uptake above a base case of all oral PrEP, we calculated the Spearman rank correlation between the estimated efficacy and persistence of both oral and LAI PrEP and the reduction in incidence for each simulation. We also compared the projected reductions in the 200 simulations with the highest value of each parameter to the 200 simulations with the lowest value. We performed

an analysis on the difference in incidence reduction comparing 25% additional oral PrEP above base case vs. 25% additional LAI PrEP plus conversion of base case PrEP levels from oral to LAI.

To explore what factors influence the impact of LAI PrEP at the city level, we calculated partial rank correlation coefficients (PRCCs) between six key variables and the primary outcome (reduction in incidence over ten years) for the scenario with 25% additional LAI PrEP uptake on top of converting all base PrEP use to LAI. The six variables were (1) the number of newly diagnosed cases relative to the population size in 2019, (2) the prevalence of HIV relative to population size in 2019, (3) PrEP coverage in 2019, (4) the ratio of newly diagnosed patients to HIV prevalence (a rough approximation of transmission) in 2019, (5) the proportion of diagnosed PWH who were virally suppressed in 2019, and (6) and the change in incidence from 2015 to 2019. We calculated the PRCCs by regressing the ranked average outcome across all 1,000 simulations in each city on the ranked average value in each city of each of the six variables[24].

Web Tool:

We constructed a publicly available web tool – www.jheem.org?prep – where users can run custom scenarios for the roll-out of LAI and oral PrEP across populations and visualize model projections for each city and subgroup in detail.

RESULTS:

Simulations reproduced calibration targets well: across all 32 MSAs, the estimated new diagnoses from 2010 – 2018 among MSM differed from reported diagnoses by 520 cases on average (a mean absolute percentage error of 3% Figure S2, ranging from 4% in New York to 18% in Memphis). Estimated prevalence differed by 4,467 cases on average (a mean absolute percentage error of 1% Figure S3, ranging from 4% in New York to 13% in Cincinnati). In the absence of any intervention, base case trends of oral PrEP uptake among MSM varied across MSAs, as well as by age, race, sex, and risk factor. On average, uptake among MSM was 11% in 2020, ranging from 5% in Sacramento to 23% in New York in 2020, and increased by 2% from 2020 to 2023, ranging from 0% increase in Sacramento to 3% in New York City. These levels of oral PrEP, along with current levels of HIV care continuum engagement, yielded a projected reduction in HIV incidence of 19% among MSM from 2020 to 2030 across all 32 cities, ranging from a 2% increase in Sacramento to a 37% reduction in Washington D.C. (Figure 1 and Figure 2, column 1).

Across all cities, switching from oral to LAI PrEP without increasing uptake resulted in a modestly increased incidence reduction of 4 percentage points in both the 10% and 25% uptake scenario (i.e. the difference between Figure 2 columns 3 and 5, and columns 6 and 8). A 10% increase in oral PrEP uptake above base case was projected to reduce incidence by 33% (CrI 19–47%) (Figure 2, column 3) to year 2030, compared to 36% (95% CrI 23–50%) reduction in incidence when the additional 10% uptake was with LAI PrEP (Figure 2, column 4). Similarly, at 25% additional oral PrEP uptake, the projected reduction in incidence across cities was 50% (CrI 38–61%); and at 25% additional LAI PrEP uptake, the incidence reduction was projected at 54% (95% CrI 45–64%) (Figure 2, column 5;7).

The potential effects of scaling up LAI PrEP varied substantially across cities; for example, the projected incidence reduction with 25% additional LAI PrEP usage (above base case oral PrEP) ranged from 38% (CrI 31–51%) in Atlanta to 68% in Seattle (CrI 51–80%) (Figure 2, column 7). Individual city projections are available at www.jheem.org?prep. In a sensitivity analyses, the reduction achievable in a city by scaling up LAI PrEP was not significantly associated with six epidemiological indicators: reported diagnoses, prevalence, PrEP coverage, viral suppression, and the ratio of reported diagnoses to prevalence in 2019, plus the reduction in incidence from 2015 to 2019 (partial rank correlation coefficients ranging from −0.17 to 0.22 Figure S4),

Assumptions about the efficacy and discontinuation rate of oral and LAI PrEP had modest impacts on our projected results (Figure S5). The discontinuation rate of LAI PrEP was most strongly associated with the projected reduction in incidence, with a Spearman correlation (R) of −0.34 in the scenario with 25% additional LAI PrEP uptake above a base case of all oral PrEP. The effects on projected reduction in incidence were lower for efficacy with oral PrEP (R = −.14, discontinuation rate of oral PrEP (R = −0.14), and efficacy of LAI PrEP (R = − 0.001).

In terms of the incremental impact of LAI as compared to oral PrEP, the ability of LAI PrEP to expand uptake and improve persistence over oral PrEP had a stronger effect on HIV incidence than its higher efficacy (Figure 3). In comparing the difference in incidence reduction from 25% additional uptake of LAI PrEP (above base case of LAI PrEP) with 25% additional uptake of oral PrEP (above base case of oral PrEP), we observed that the discontinuation rate of LAI PrEP was strongly associated with this absolute difference (R, = −0.88), compared to LAI efficacy (R = 0.14). When LAI PrEP was assumed to have a discontinuation rate of 25–40% that of oral PrEP, we projected an absolute additional reduction of 9 percentage points (95% CrI 6–14) in HIV incidence (LAI PrEP minus oral PrEP), compared to a 0 percentage point reduction (95% CrI −3–1) when the discontinuation rate of LAI PrEP was assumed to be 104–125% that of oral PrEP. In contrast, this difference was negligible (5 percentage points, 95% CrI 3–7, versus 3, 95% CrI 0–5) if LAI PrEP were assumed to have 75–87% greater efficacy than oral PrEP, versus 5–57%.

Estimated 2019 incidence rate ratios (IRRs) varied across cities, ranging from 1.2 in Seattle to 12.6 in Memphis for Black vs. non-Black-non-Hispanic MSM and 1.3 in Jacksonville to 6.2 in Philadelphia for Hispanic vs. non-Black-non-Hispanic MSM (see Figures S6 and S7). Interventions targeted to all MSM did not substantially change the projected 2030 IRRs, with no more than a 0.5-point decrease. A maximal intervention targeted only to Black and Hispanic MSM which converted all base PrEP from oral to LAI and adding 25% additional LAI PrEP uptake did impact IRRs, with up to a 2.9-point reduction. Under this scenario, 2030 IRRs ranged from 0.7 to 9.7.

DISCUSSION:

We present results from a detailed HIV transmission model on potential impacts of scaling up long-acting, injectable PrEP among MSM in 32 US cities with a high burden of HIV. In the absence of additional interventions, HIV incidence was projected to fall by 19% from

2020 to 2030 across all 32 MSAs. Adding 10% (or 25%) LAI PrEP uptake among MSM across all cities augmented this estimated reduction to 36% (or 54%). The effects varied substantially among individual cities, with incidence reductions as high as 68% in Seattle in a scenario modeling 25% increase LAI PrEP uptake – detailed city-specific projections are available at www.jheem.org?prep. Mixed uptake of oral and LAI PrEP, which may be more realistic, will likely result in effects falling between our all-oral and all-LAI projections. The ability of LAI-PrEP to reduce incidence depended more on its ability to expand uptake and continuation of PrEP than on its greater pharmacologic efficacy compared to oral PrEP.

Nationally, of the 1.1 million adults with indications for PrEP, only 100,000 accessed PrEP as of 2017[5,6]. Approximately 44% of individuals discontinue PrEP within a year of starting it[8]. While the ability of injectable PrEP to increase uptake and persistence is still uncertain, experiences with contraception are informative: the availability of multiple contraceptive modalities increases uptake, and matching women's preferred modality is associated with increased continuation[25].

We projected that, at a given level of uptake, using LAI PrEP instead of oral provided only modest improvements over oral PrEP (4 percentage point difference total across all 32 cities). The magnitude of this improvement depended largely on the degree to which LAI PrEP improved the discontinuation rate relative to oral PrEP, not on the relative efficacy. Thus, the primary potential benefits of LAI PrEP at the population level will likely derive principally from its ability to expand the use of PrEP across the population, rather than pharmacological superiority to oral PrEP. Our projections also illustrate that LAI PrEP is unlikely to change stark racial disparities in HIV incidence unless it is specifically promoted to racial groups with a high burden of HIV. This finding reinforces the need for ongoing efforts to address disparities in awareness of and access to PrEP[26].

Few previous studies have modeled the potential impact of LAI PrEP on local HIV epidemics. Marshall et. al. projected that 35% LAI PrEP coverage would avert 44% of infections in MSM in Atlanta, GA from 2015 to 2024 compared to no PrEP[27]. We conducted analogous simulations and projected a 31% reduction. Maloney et. al. projected that 15% PrEP coverage (half LAI and half oral), would avert 4.3% of infections among MSM in Atlanta over 10 years, compared to all oral PrEP[28]. Under similar conditions, we projected a 13.2 percentage point difference in incidence reduction of compared to base case levels of all oral PrEP. Our compartmental model may not capture all the network effects that Marshall and Maloney's agent-based simulations do; conversely, we also represent the broader population beyond MSM and can examine broader population effects. Our study builds on this literature by extending projections to 32 cities over the coming decade, and by exploring the impacts of incremental gains in coverage and persistence with LAI PrEP.

As with any modelling effort, our results should be viewed in light of several limitations. First, our model does not explicitly represent subgroups' risk for HIV in separate compartments, but instead assumes that both LAI and oral PrEP use are evenly distributed across a demographic subgroup irrespective of specific risk patterns. If the highest-risk individuals in a group are also more likely to start and continue oral or LAI PrEP, our projections will underestimate the impact of PrEP. Conversely, if higher-risk individuals

are more difficult to enroll in a PrEP program, we will overstate the program's effects on transmission. We also cannot examine the impacts of changes in individuals' indications for PrEP over time. Additionally, we do not consider the impact of event-driven PrEP uptake which could be an important mode of oral PrEP usage, and we do not incorporate potential "risk compensation" – where PrEP use may result in increased unsafe sex among PrEP users[29,30]. Second, the discontinuation rate of LAI PrEP in real world situations – a key model parameter – is unknown. We incorporate this uncertainty by simulating a wide range of possible values using a Bayesian process; future empirical studies are needed to provide real-world estimates of this value. Additionally, in focusing on epidemiological impact, we do not provide cost or cost-effectiveness estimates of varying combinations of expanded PrEP use; this remains an important avenue for future investigation. Third, our projections do not take into account the potential impact of the COVID-19 pandemic. Studies from early in the pandemic report decreased use of PrEP, but it is unclear (a) whether this represented decreased coverage for those with indications, or reduced need for PrEP due to less sexual activity and (b) how long these effects persisted[31]. If reductions in PrEP use were short-lived or if they were balanced by reductions in sexual activity, we expect our projections to hold. Future iterations of the model could incorporate additional post-pandemic data as they become available. Lastly, our study focuses on PrEP and does consider the potential impact of other interventions including increased treatment or increased diagnosis of HIV. Modelling the potential impact of these interventions at the national and local level remains an avenue for further investigation.

In summary, PrEP is a critical component in the US strategy to reduce HIV infections. Our city-specific projections from show that LAI PrEP can substantially reduce HIV incidence by increasing PrEP uptake and persistence across at-risk MSM. The effectiveness of expanding PrEP usage will depend on local dynamics of HIV epidemics.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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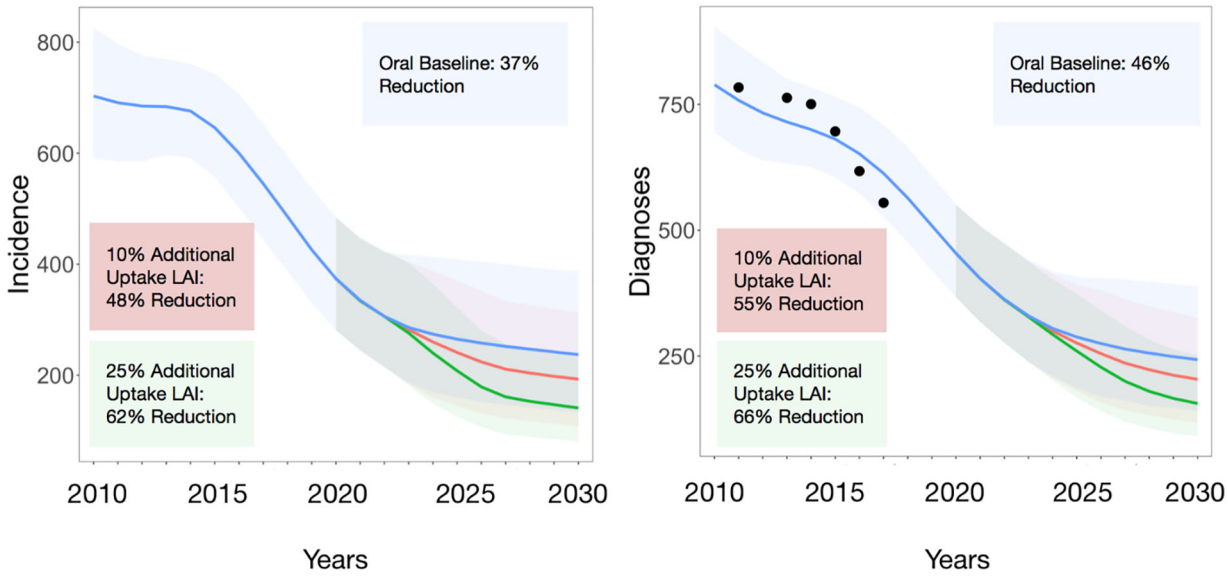

Figure 1. Projected Incidence and Reported Diagnoses of HIV among MSM in the Washington, DC Metropolitan Statistical Area Under Potential PrEP Uptake Scenarios

Lines represent the mean across 1,000 simulations. Shaded regions represent the 95% credible interval. Black circles represent CDC surveillance data for total reported diagnoses among MSM. The “No Intervention” scenario (blue lines) assumes base case levels of oral PrEP uptake, varying across simulations and over time. Base case PrEP levels prior to intervention were projected to be 11% on average in 2020, rising to 13% by 2023. Interventions begin implementation in 2023 and reach full implementation by 2027. The “10% Additional Uptake” scenario (red lines) represents an additional 10% uptake of LAI PrEP – above base case of all oral PrEP uptake – among MSM. The “25% Additional Uptake” scenario (green lines) refers to an additional 25% uptake of LAI PrEP above base case of all oral PrEP. A) Incidence of HIV from 2010–2030 under three uptake scenarios. B) Reported diagnoses of HIV from 2010–2030 under three uptake scenarios. Text boxes refer to the mean across all 1,000 within-simulation incidence reductions under the aforementioned three interventions.

	No Additional Uptake		10% Additional Uptake			25% Additional Uptake		
Additional PrEP Uptake	0%	0%	10%	10%	10%	25%	25%	25%
Type of Additional PrEP	NA	NA	All Oral	All LAI	All LAI	All Oral	All LAI	All LAI
Type of Base PrEP*	Oral	LAI	Oral	Oral	LAI	Oral	Oral	LAI
New York-Newark-Jersey City, NY-NJ-PA	32%	34%	45%	47%	48%	60%	63%	63%
Miami-Fort Lauderdale-Pompano Beach, FL	14%	15%	28%	30%	31%	45%	49%	49%
Los Angeles-Long Beach-Anaheim, CA	9%	10%	20%	22%	22%	34%	38%	39%
Atlanta-Sandy Springs-Alpharetta, GA	13%	14%	28%	30%	31%	46%	50%	50%
Houston-The Woodlands-Sugar Land, TX	20%	20%	32%	34%	35%	48%	51%	52%
Dallas-Fort Worth-Arlington, TX	2%	5%	18%	21%	23%	38%	43%	44%
Chicago-Naperville-Elgin, IL-IN-WI	37%	38%	47%	48%	49%	59%	62%	62%
Washington-Arlington-Alexandria, DC-VA-MD-WV	23%	25%	36%	38%	39%	51%	55%	55%
Philadelphia-Camden-Wilmington, PA-NJ-DE-MD	27%	28%	40%	42%	43%	55%	59%	59%
Orlando-Kissimmee-Sanford, FL	35%	37%	48%	49%	51%	62%	65%	66%
San Francisco-Oakland-Berkeley, CA	25%	26%	38%	40%	41%	54%	56%	57%
Phoenix-Mesa-Chandler, AZ	24%	25%	38%	41%	41%	55%	57%	59%
Tampa-St. Petersburg-Clearwater, FL	16%	17%	36%	39%	39%	56%	61%	61%
Riverside-San Bernardino-Ontario, CA	17%	19%	35%	38%	39%	55%	59%	59%
Detroit-Warren-Dearborn, MI	36%	37%	46%	47%	48%	57%	61%	61%
Baltimore-Columbia-Towson, MD	28%	28%	41%	42%	43%	55%	57%	57%
Las Vegas-Henderson-Paradise, NV	28%	31%	39%	41%	42%	51%	55%	55%
Boston-Cambridge-Newton, MA-NH	35%	36%	47%	48%	49%	60%	63%	63%
San Diego-Chula Vista-Carlsbad, CA	9%	10%	25%	27%	28%	44%	48%	49%
Charlotte-Concord-Gastonia, NC-SC	12%	12%	27%	28%	30%	44%	49%	49%
San Antonio-New Braunfels, TX	11%	12%	28%	30%	31%	47%	51%	52%
Jacksonville, FL	30%	32%	42%	44%	45%	56%	59%	60%
New Orleans-Metairie, LA	24%	24%	36%	38%	38%	51%	54%	54%
Memphis, TN-MS-AR	15%	19%	40%	44%	46%	63%	68%	68%
Seattle-Tacoma-Bellevue, WA	34%	36%	47%	49%	51%	62%	65%	66%
Austin-Round Rock-Georgetown, TX	17%	17%	31%	33%	33%	47%	51%	51%
Indianapolis-Carmel-Anderson, IN	12%	13%	26%	28%	28%	42%	47%	47%
Cincinnati, OH-KY-IN	25%	26%	37%	39%	40%	52%	55%	56%
Columbus, OH	17%	18%	26%	28%	28%	40%	44%	44%
Baton Rouge, LA	-2%	-1%	24%	27%	28%	49%	55%	55%
Cleveland-Elyria, OH	37%	38%	47%	48%	49%	59%	62%	62%
Sacramento-Roseville-Folsom, CA	19%	21%	33%	36%	37%	50%	54%	54%

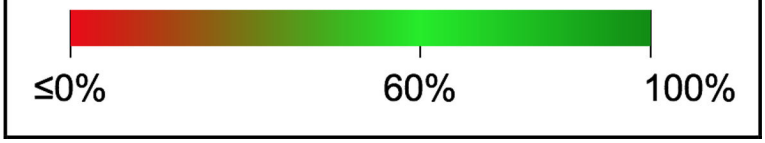

Figure 2. Reduction in HIV Incidence Among MSM from 2020–2030, at Different Levels of Uptake of Oral and Long Acting Injectable PrEP in 32 US Cities

Uptake is defined as the proportion of those at risk for HIV who are enrolled in a PrEP program during a given year. *We have two Base PrEP scenarios of future PrEP use through 2030: one in which there is no LAI PrEP use and oral PrEP uptake continues at the rate it had in the previous 5 years (Oral), and one in which all oral PrEP use is converted to LAI PrEP in 2020 and increases at this same rate (LAI). We report the reduction in HIV incidence among MSM in 2030, relative to 2020 levels, under each scenario. The percentage value in each cell represents the mean reduction across 1,000 simulations, with reductions

ranging from <0% to 100%. In the absence of intervention, base case oral PrEP uptake varies by simulation, city, and time; in 2020, uptake of oral PrEP was 11% across all 32 cities, ranging from 5% in Sacramento to 23% in New York in 2020; by 2023, average uptake across all cities was projected to rise to 13%.

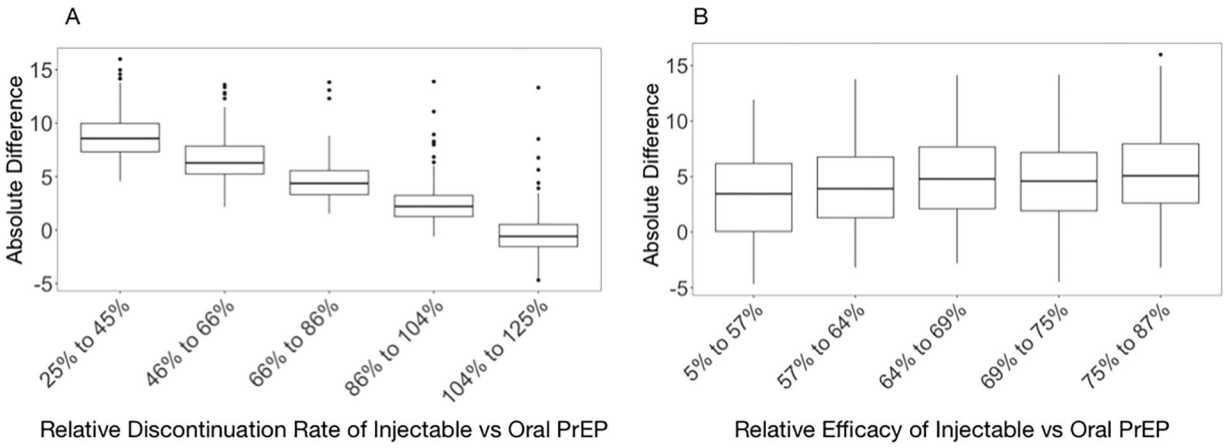

Figure 3: Impact of Relative Efficacy and PrEP Persistence on the Gain in Projected Reduction in HIV Incidence among MSM with Injectable vs. Oral PrEP

For each of the 1,000 simulations per city, we calculated the additional reduction in HIV incidence for long-acting injectable (LAI) vs. oral PrEP by projecting the total incidence among MSM from 2020 to 2030 across 32 cities. We estimated the incremental reduction in HIV incidence from adding 25% uptake of all-LAI PrEP to a base case of all-LAI PrEP and subtracted the incremental reduction achieved from 25% additional uptake of all-oral PrEP with a base case of all-oral PrEP. Panel A shows the additional impact of LAI versus oral PrEP across five quintiles of the relative discontinuation rate on LAI PrEP (versus oral PrEP), whereas Panel B shows this same quantity across five quintiles of relative efficacy. For each group, we present a boxplot of the distribution in additional incidence reduction from LAI PrEP: the horizontal line represents the median reduction, the box represents the interquartile range, the whiskers represent the 95% credible interval, and dots represent outliers.

Table 1.

Key Parameters for Oral and Long-Acting Injectable PrEP

Parameter	Median [Uncertainity Range]	Distribution	Source
Oral PrEP Efficacy *	0.86 [0.64–0.96]	Log-normal	McCormack et al., 2016
Relative LAI PrEP Efficacy **	0.66 [0.38–0.82]	Log-normal	Landovitz et al., 2021
Oral PrEP Discontinuation Rate †	0.45 [041.–0.47]	Normal	Coy et al., 2019
Ratio of Discontinuation Rate for LAI vs Oral PrEP ‡	0.625 [0.25–1.00]	Uniform	*Assumption*

* Efficacy is one minus the relative risk of infection while on Oral PrEP.

** Relative efficacy is one minus the hazard ratio for the risk of infection while on LAI PrEP vs. while on oral PrEP.

† Discontinuation Rate = the proportion of people on PrEP who will discontinue PrEP after one year.

‡ As there are no data to inform the relative rates of discontinuation for LAI vs oral PrEP, we allowed the rate of discontinuation of LAI PrEP to vary between 25–125% of the rate of Oral PrEP discontinuation.