Closing the Gap to Zero HIV Transmission: Modelling the Impact of Long-Acting Injectables (LAI) in United Kingdom (UK)

P347

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Key Takeaways

- **Current strategies alone are unlikely to achieve England's HIV targets: Under continuation of current care and scale up of PrEP, annual HIV diagnoses remain above 2,000 and the lifetime costs associated with new acquisitions are projected to exceed £27 billion.**
- **Scaling up LAI PrEP could substantially reduce HIV transmission: Increasing LAI PrEP uptake, particularly when combined with switching individuals with low oral PrEP adherence, was projected to avert up to 23,515 HIV acquisitions by 2040 and achieve the HIV Action Plan target by 2037.**
- **Combined strategies could accelerate progress towards achieving the national HIV targets: Switching both virally suppressed and unsuppressed people from daily oral ART to LAI ART, alongside increased diagnosis rates, increased averted acquisitions to 25,177 and brought the HIV Action Plan target forward to 2035.**
- **LAI strategies could deliver long-term economic value: LAI PrEP and combined LAI PrEP/ ART strategies achieved a positive long-term ROI across all modelled scenarios.**

Plain Language Summary

- Current approaches may not be enough to meet England's HIV Action Plan targets[1], with new HIV acquisitions and their associated lifetime healthcare costs remaining substantial.
- Expanding PrEP use through long-acting injectable PrEP could prevent many new HIV acquisitions, particularly when offered to people who have difficulty taking daily oral PrEP consistently.
- Combining the use of long-acting prevention and treatment with increased HIV diagnosis could further reduce new acquisitions and help England reach its HIV policy targets sooner.
- Long-acting strategies could also provide long-term economic value, as the costs of implementation may be offset by savings from preventing HIV acquisitions and associated lifetime care costs.

Introduction

- England has made substantial progress toward achieving the UNAIDS 95-95-95 targets and committing to ending new HIV transmissions in England by 2030.[1] However, further reductions in HIV acquisition will require continued investment in innovation across both prevention and treatment.
- Long-acting injectable (LAI) PrEP and antiretroviral therapy (ART) may address limitations associated with adherence and persistence to daily oral regimens.[2-5] Understanding the population-level health and economic consequences of scaling up these interventions is important to inform future HIV prevention and treatment strategies.
- This study evaluated the epidemiological impact and return on investment (ROI) of an integrated scale-up of LAI PrEP and LAI ART in England.

Methods

We developed a compartmental dynamic HIV transmission model calibrated to UK Health Security Agency (UKHSA) surveillance data for England.

Model Overview

The model design followed established approaches for characterising HIV disease care and outcomes; the structure of the US Centers for Disease Control and Prevention's (CDC's) HIV Optimization and Prevention Economics (HOPE) model, which has regularly been used for evaluating population health and epidemiological outcomes for HIV[6-8], was used as the basis for the modelling approach in our study:

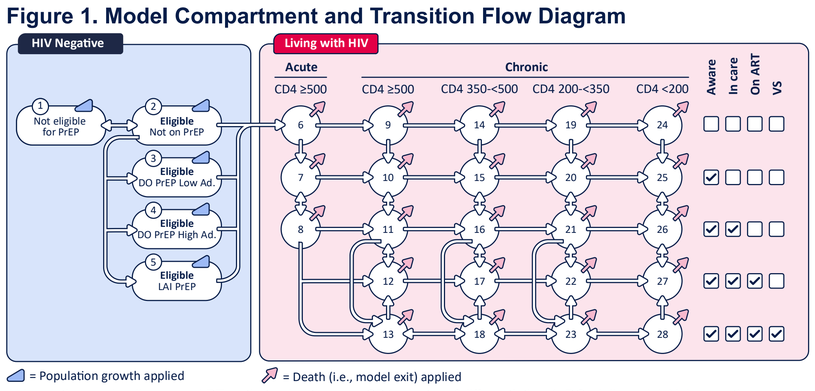
- The deterministic model stratified the population aged 15 years and older by acquisition risk and represented people with HIV across acute and chronic disease stages and established continuum of care steps.
  - Alongside, cluster of differentiation 4 (CD4) stratifications captured disease progression and enabled application of stage-specific risks and costs.
- The use of daily oral PrEP was included considering low (0-3 pills/week) and high (≥4 pills/week) adherence groups, with alternative protection levels; acquisition costs were also aligned to pill usage (**Table 1**).
  - PrEP protection levels for each adherence group and the percentage of individuals with low vs. high adherence was based on the iPREX open-label extension study.[9] These were used to derive the effective protection levels across the daily oral PrEP compartments - the effective protection level modelled was 59.5%.
- The protection level for individuals receiving LAI PrEP was assumed at 92%, based on an indirect comparison of LAI cabotegravir vs. no PrEP among men who have sex with men and transgender women.[10]
- A schematic diagram of the model compartment structure and transition flows is shown in **Figure 1**.

Table 1. Model Cost Inputs

Cost Group	Parameter	Cost	Source
(Projection Period) Annual Cost Inputs			
PrEP – Acquisition	Daily Oral – Low adherence group	£102	BNF. TDF/FTC (245mg/200mg); mean of 1.5 pills per week assumed.[11]
	Daily Oral – High adherence group	£373	BNF. TDF/FTC (245mg/200mg); mean of 5.5 pills per week assumed.[11]
	LAI	£7,671	BNF. Apretude 600mg/3ml & Apretude 30 mg tablets (list price)[12]; 30-day oral lead in assumed for 50% of individuals.
PrEP – Administration	Daily Oral	£0	-
	LAI	£104	Jones 2024[13], assuming 30 mins Band 5 Nurse time for visit 1 and 2, 20 mins all subsequent visits.
PrEP – Monitoring	Daily Oral	£1,103	Brady (BHIVA/BASHH)[14]; Jones 2024[13]; NIHR[15,16]; NHSE 2022;[17]; NICE TA1106[5]
	LAI	£1,255	
Treatment – Acquisition	Daily oral	£9,164	BNF. Basket cost based on 2025 market share data.[18]
	LAI	£9,984	BNF. Vocabria 600mg/3ml + Rekambys 900mg/3ml & Vocabria 30 mg tablets + Edurant 25 mg tablets (assuming 30-day oral lead in for all individuals). Mean annual cost calculated over the average treatment duration.
Treatment - Administration	Daily Oral	£0	-
	LAI	£71	PSSRU. Unit Costs of Health and Social Care 2024; Assuming 15 mins Band 5 Nurse time, per the NICE TA757. Six administrations per year; 7 visits in year 1 and 6 in all subsequent years.
Background Disease Management	CD4 ≥200 - Undiagnosed	£2,239	Beck 2011[19] ART naïve values assumed for Undiagnosed considering non-HIV medication and day ward and inpatient day costs; excl. costs for outpatient care and CD4+ tests and other procedures.
	CD4 ≥200 - Diagnosed, Not on ART	£3,701	
	CD4 ≥200 - Diagnosed, on ART	£5,789	
	CD4 <200 - Undiagnosed	£6,442	
	CD4 <200 - Diagnosed, Not on ART	£8,601	
	CD4 <200 - Diagnosed, on ART	£9,146	
End of Life Care	Excess Costs in Final Months of Life	£14,102	Moeremans 2010[20]
Societal	CD4 ≥500	£3,486	Rodríguez-Sánchez 2022[21] (reduction in employment rates); ONS. Annual Earning & Employment Rate Estimates for 2024.[22,23]
	CD4 350-<500	£8,062	
	CD4 200-<350	£8,062	
	CD4 <200	£11,221	
Discounted (1.5% annually) Lifetime HIV Cost Estimates			
Healthcare system (ART & other resource use)		£350,559	Healthcare system: Basket cost for daily oral ART (see annual value above); other resource use based on Ong 2019[24]
Societal		£140,230	Societal: assumed 40% of system costs, based on Trapero-Bertran 2014[25]
Total		**£490,789**	Mean treatment duration: 43 years based on Ong 2019[24]

Abbreviations: ART, antiretroviral therapy; BNF, British National Formulary; CD4, cluster of differentiation 4; PrEP, pre-exposure prophylaxis; ONS, Office for National Statistics; TDF/ FTC, Tenofovir disoproxil fumarate/Emtricitabine.

Figure 1. Model Compartment and Transition Flow Diagram



Abbreviations: Ad, adherence; ART, antiretroviral therapy; CD4, cluster of differentiation 4; DO, daily oral; LAI, long-acting injectable; PrEP, pre-exposure prophylaxis; VS, virally suppressed.
Numbers represent the compartment indexes in the model.

Epidemiological Calibration and Economic Outcomes

- The model was calibrated to 2017–2024 UKHSA surveillance and published epidemiological data[26-28] using stochastic parameter sampling, as previously described.[29] Calibration targets included HIV prevalence, annual new diagnoses, UNAIDS 95-95-95 indicators (HIV diagnosis, treatment uptake, and viral suppression), and mortality among people living with HIV.
- Net cost benefit was calculated as cumulative lifetime costs avoided through averted HIV acquisitions minus intervention costs. Return on investment was calculated as the ratio of cumulative lifetime costs avoided to additional intervention costs. All future costs were discounted at 1.5% annually. Further methodological details and cost inputs have been previously reported.[29]

Model Scenarios

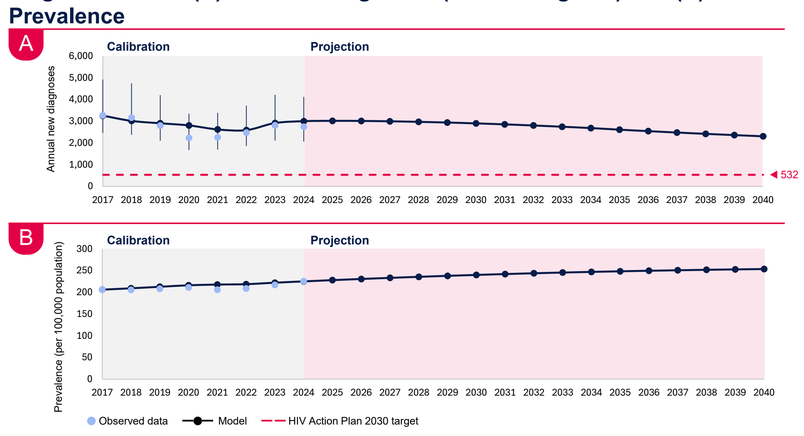
We compared new acquisitions, prevalence, new diagnoses (first in England), and person-years of viraemia (PYV) from 2024–2040 across current care and LAI PrEP/ART scenarios. PYV captures direct effects of treatment switching and indirect effects from reduced transmission.

- Current care provision was projected assuming daily oral PrEP uptake continued to increase annually by 1% of the eligible population from the 2024 level (47.86% of an estimated 232,223 eligible individuals) until 2034. This background increase was applied across all scenarios.
- On top of current care provision, scenarios explored LAI PrEP scale-up, switching of individuals with low adherence from daily oral to LAI PrEP, switching of people virally suppressed on daily oral ART to LAI ART, and increased HIV diagnosis rates, alone and in combination.
- Exploratory viraemic-switch scenarios assumed that 25% of individuals on daily oral ART with viraemia in 2024 switched to LAI ART annually, reaching 75% by 2027; thereafter, the switched population was maintained, accounting for mortality. These assumptions will be refined as further clinical evidence becomes available.

Results

Model predictions based on the calibrated transition rates closely replicated the target data for key endpoints, including number of new diagnoses (**Figure 2A**) and HIV prevalence (**Figure 2B**).

Figure 2. Model Calibration. Model-Predicted Versus Observed/Calibration Target Values for (A) New HIV Diagnoses (First in England) and (B) HIV Prevalence



Epidemiological impact of LAI PrEP and ART

Increasing LAI PrEP uptake was projected to progressively reduce HIV diagnoses and transmission (**Figure 3; Table 2**).

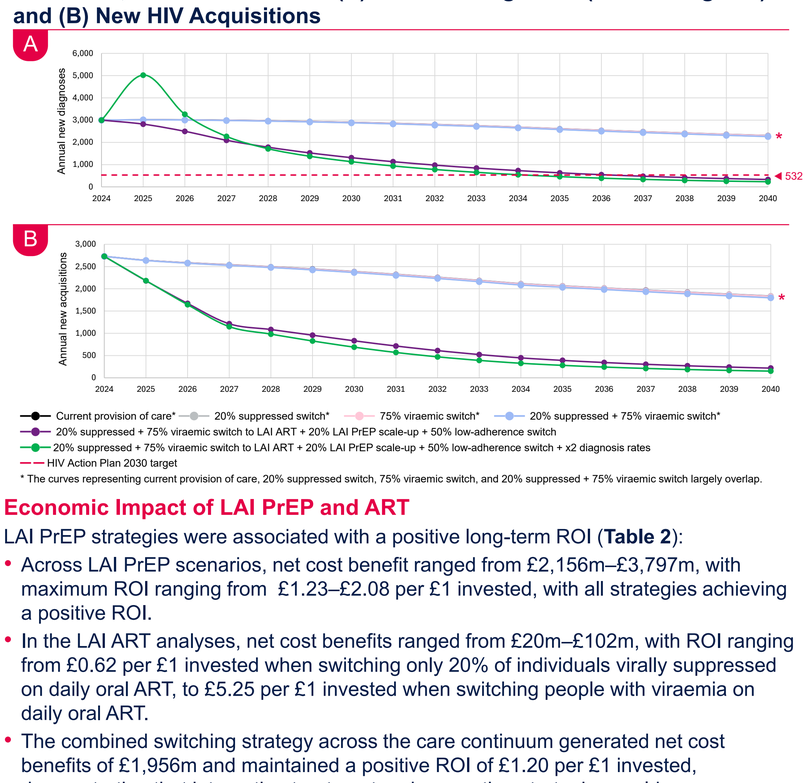
- Scaling up LAI PrEP to 20% of the overall PrEP-eligible population was projected to avert 18,940 acquisitions between 2025 and 2040.
- At 20% LAI PrEP uptake, additionally switching 50% of individuals with low adherence to daily oral PrEP increased the projected number of averted acquisitions to 23,515, with the HIV Action Plan target reached in 2037.

Figure 3. Projected Epidemiological Outcomes Under LAI PrEP Scenarios, 2024–2040. Annual (A) New HIV Diagnoses (First in England) and (B) New HIV Acquisitions

Exploratory LAI ART scenarios showed the greatest impact when combined with LAI PrEP strategies (**Figure 4; Table 2**):

- Switching 20% of individuals who are virally suppressed on daily oral ART to LAI ART was projected to avert 332 acquisitions and 2,609 PYV; switching 75% of individuals with viraemia on daily oral ART averted 49 acquisitions and 298 PYV. Combining both switches averted 380 acquisitions and 2,894 PYV.
- Combining ART and PrEP strategies increased the projected impact to 23,642 averted acquisitions and the Action Plan target was reached in 2037.
- Considering increased diagnosis rates further increased the impact to 24,880 averted acquisitions and brought achievement of the HIV Action Plan target forward from 2037 to 2035.

Figure 4. Impact of Exploratory LAI ART Scenarios on Projected HIV Outcomes, 2024–2040. Annual (A) New HIV Diagnoses (First in England) and (B) New HIV Acquisitions



* The curves representing current provision of care, 20% suppressed switch, 75% viraemic switch, and 20% suppressed + 75% viraemic switch largely overlap.

Economic Impact of LAI PrEP and ART

LAI PrEP strategies were associated with a positive long-term ROI (**Table 2**):

- Across LAI PrEP scenarios, net cost benefit ranged from £2,156m–£3,797m, with maximum ROI ranging from £1.23–£2.08 per £1 invested, with all strategies achieving a positive ROI.
- In the LAI ART analyses, net cost benefits ranged from £20m–£102m, with ROI ranging from £0.62 per £1 invested when switching only 20% of individuals virally suppressed on daily oral ART, to £5.25 per £1 invested when switching people with viraemia on daily oral ART.
- The combined switching strategy across the care continuum generated net cost benefits of £1,956m and maintained a positive ROI of £1.20 per £1 invested, demonstrating that integrating treatment and prevention strategies could preserve favourable economic outcomes while enhancing population-level impact.

Table 2. LAI PrEP and LAI ART Scenarios Projected Over 2025-2040

Scenario*	HIV Target Met (year)	Inter-vention Costs (£m)	Averted Acqui-sitions	Averted Costs (£m)	Net Cost Benefit (£m)	Max ROI**
Scenarios (%LAI PrEP Scale-Up / %Low-Adh Switch to LAI PrEP)						
20% / 0%	No	5,498	18,940	9,296	3,797	£1.69
20% / 50%	Yes (2037)	9,385	23,515	11,541	2,156	£1.23
Explorative Scenarios Including %VS Switch / %Viremic Switch to LAI ART						
0% / 0% / **20% / 0%**	No	265	332	163	102	£0.62
0% / 0% / **0% / 75%**	No	5	49	24	20	£5.25
0% / 0% / **20% / 75%**	No	268	380	186	82	£0.69
20% / 50% / **20% / 75%**	Yes (2037)	9,647	23,642	11,603	1,956	£1.20
20% / 50% / **20% / 75%** + x2 diagnosis rate	Yes (2035)	9,763	24,880	12,211	2,448†	—†

Abbreviations: adh, adherence; ART, antiretroviral therapy; LAI, long-acting injectable; PrEP, pre-exposure prophylaxis; ROI, return on investment; VS, virally suppressed.
*Scenario-specific uptake levels were gradually implemented over 2025–2027, reaching target levels in 2027.
**Values >1 indicate a positive ROI.
†The net cost benefit excludes the additional costs associated with doubling the diagnosis rate. ROI was therefore not estimated for this exploratory scenario.

Limitations

- The lifetime cost estimation assumes all new acquisitions are diagnosed and receive treatment, which will result in a degree of overestimation. However, as most people who acquire HIV will receive a diagnosis in their lifetime, this is not expected to be significant; lifetime cost inputs reflect mean treatment durations for diagnosed individuals based on English surveillance data.[24]
- The model evaluates the overall setting population and implicitly assumes transmission risk behaviours remain constant in the future. Changes in risk behaviour over time may result in alternative outcome projections but conclusional differences are not expected.
- Many diagnoses reported for England have previously been diagnosed abroad. Only diagnoses first occurring in England were considered, due to uncertainties regarding future migration trends and to ensure results reflect local transmission.
- Reductions in PYV may provide additional individual health benefits and influence long-term healthcare costs, which may not be fully captured in the economic analysis.
- Exploratory analyses of switching individuals on daily oral ART with viraemia to LAI ART were conducted whilst awaiting evidence from ongoing clinical studies, which will provide additional data to inform this strategy.

Conclusions

- Current strategies alone are unlikely to achieve HIV targets, with annual HIV acquisitions remaining above 2,000 and substantial lifetime costs associated with new acquisitions.
- Scaling up LAI PrEP could substantially reduce HIV transmission: increasing uptake and switching individuals with low adherence to daily oral PrEP could avert >23,000 acquisitions and achieve the Action Plan target by 2037.
- Increasing HIV diagnosis and engaging people into care could further accelerate progress, bringing achievement of the Action Plan target forward by approximately 2 years when combined with LAI Tx scale-up strategies. This exploratory scenario assessed the epidemiological impact of increased diagnosis rates; further research is needed to evaluate implementation strategies, associated costs, and ROI.
- Beyond its individual clinical value in supporting viral suppression, our exploratory findings suggest that LAI ART could complement LAI PrEP to further reduce HIV acquisitions, deliver population-level and economic benefits, and accelerate progress towards the HIV Action Plan targets.[1]

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