

Lenacapavir: impact and cost-effectiveness of scale- up for South Africa's HIV response.

SANAC National Roundtable on Lenacapavir Access and Sustainability
14 October 2025

Lise Jamieson¹, Leigh Johnson², Jeffrey W. Imai-Eaton^{3,4}, Gesine Meyer-Rath^{1,5}

(1) Health Economics and Epidemiology Research Office (HE²RO), Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; (2) Centre for Integrated Data and Epidemiological Research, School of Public Health, University of Cape Town, Cape Town, South Africa; (3) Center for Communicable Disease Dynamics, Department of Epidemiology, Harvard TH Chan School of Public Health, Boston, MA, USA; (4) MRC Centre for Global Infectious Disease Analysis, School of Public Health, Imperial College London, London, United Kingdom; (5) Department of Global Health, Boston University School of Public Health, Boston, Massachusetts, USA





Conclusions: LEN cost-effectiveness

- **At \$40 PPPY, LEN is more cost-effective than oral TDF/FTC scale-up, even at the same total cost**
- **LEN can substantially reduce the number of new HIV infections**
- **LEN can accelerate progress towards ending AIDS and end AIDS 7-10 years earlier than scaling up oral TDF/FTC**
- **For these impacts, we need to initiate 1-2 million people on LEN every year, for an additional cost of R650-R1500 million per year**
- **Cost-effectiveness of LEN distribution to FSW > LEN to MSM > LEN to pregnant and breastfeeding women or AGYW**

Background: Why lenacapavir?

- **6-monthly lenacapavir (LEN) injection has shown superior effectiveness** in preventing HIV infection
 - PURPOSE-1 and PURPOSE-2 trials revealed a **100%** (cisgender women) and **96%** (cisgender men and transgender and gender non-binary individuals who have sex with men) **reduction in HIV acquisition** compared to TDF/FTC (*Bekker 2024, Kelley 2025*)
 - **TDF/FTC is 65%-85% effective** in preventing HIV infection compared to no PrEP (*Hanscom 2016, Fonner 2016, Baeten 2012*)
- Global Fund announced a \$29 million donation towards LEN, funded through re-prioritisation of existing commitments and covering ~500,000 person-years on LEN in a roll-out in 2026-27
- We modelled the impact of LEN and TDF/FTC scale-up in South Africa and evaluated the cost-effectiveness over the current baseline.
- We further evaluated the impact of different subpopulation targeting strategies for the LEN donation to optimize for maximum impact

Cost effectiveness of national lenacapavir scale-up

Methods for national LEN scale-up

- Using Thembisa 4.8, we model the **impact and cost-effectiveness** of the scale-up of LEN and TDF/FTC, over a 20-year period (2026-2045)
- We modelled a package of PrEP to AGYW, female sex workers (FSW), pregnant/breastfeeding women (PBFW), men who have sex with men (MSM), and other heterosexual men
- **Scenarios**
 - **Baseline:** current TDF/FTC roll-out continues into future; initiation numbers: ~600k-900k/year
 - **TDF/FTC scale up**
 - doubled initiation rates compared to baseline + 41% coverage of PBFW; initiation numbers: ~1.2m-2.3m/year
 - **LEN conservative**
 - same initiation rates as TDF/FTC scale-up + 41% coverage of PBFW; initiation numbers: 600k-2.4m/year
 - average duration on LEN: 12 months (MSM), 6 months (women, other men)
 - **LEN optimistic:**
 - double initiation rates + 54% coverage of PBFW; initiation numbers: 900k-4.3m/year
 - average duration on LEN: 24 months (MSM), 12 months (women, other men)
 - Under LEN scenarios, TDF/FTC continues at current baseline coverage

Costing inputs

- Ingredients-based costing from the **provider's perspective (South African government)**
- Cost of all options includes lowest staff cadre (nurse-led), demand creation and training, as well as lab monitoring, consumables, equipment and overheads
- Costs presented in 2025 ZAR, undiscounted

	LEN	TDF/FTC
Drug price	\$40 or R729/PPPY for injections \$17 or R155/loading dose (one-time) (recently announced agreement)	\$41 or R739 PPPY (current generic prices)
Dose dispensed	2x 463mg/1.5mL injection 1200mg loading dose day 1-2 of initiation	300/200mg (30 tablets)
Frequency	at initiation and 6-monthly	at initiation, month 1 and 3-monthly
Methods of costing provision	trial protocols, adjusted for public sector implementation	guidelines, implementation and demonstration projects

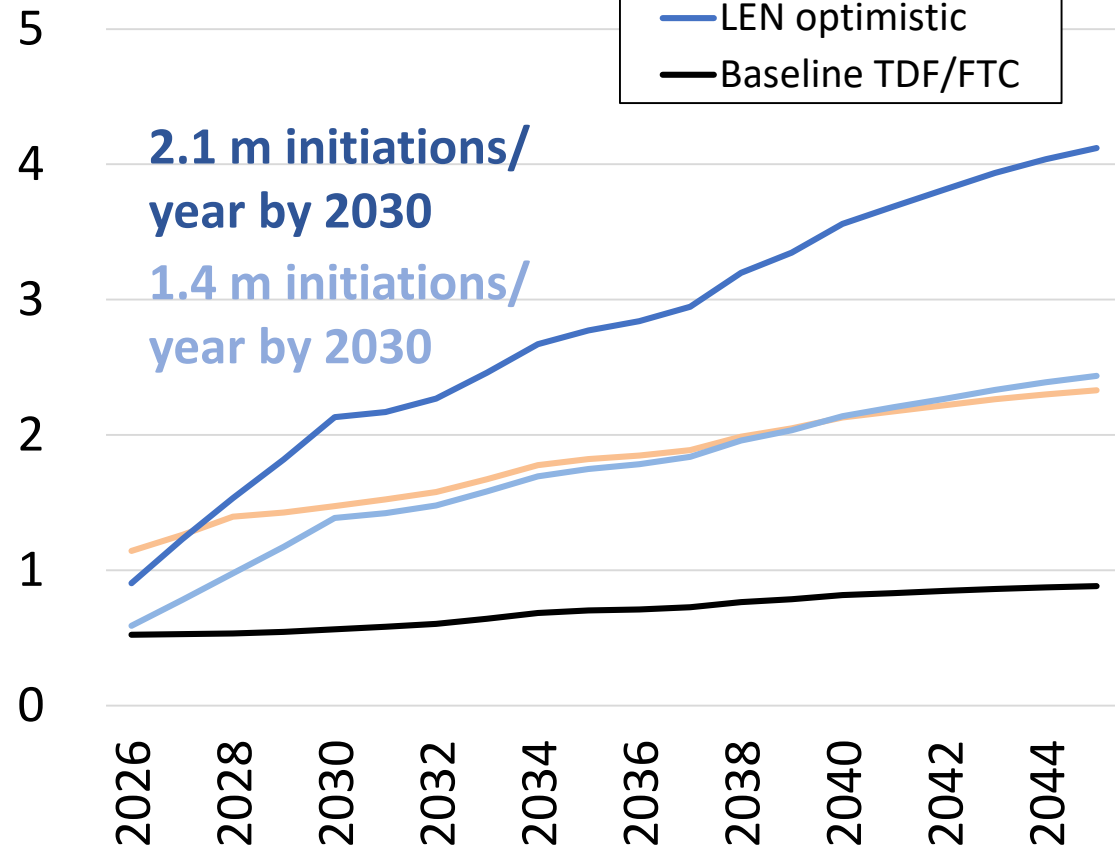
Key model assumptions

	Baseline (current TDF/FTC)	TDF/FTC scale up	LEN scale up scenarios	
			Conservative	Optimistic
			<i>Same initiation rates as TDF/FTC scale-up; 6-12m duration</i>	<i>Doubled rates of TDF/FTC scale-up; 12-24m duration</i>
Duration on PrEP	3 months (women, other men), 6 months (MSM)	3 months (women, other men), 6 months (MSM)	6 months (women, other men), 12 months (MSM)	12 months (women, other men), 24 months (MSM)
Coverage of TDF/FTC and LEN	<i>11% FSW 10% MSM 7% AGYW 0% pregnant women 0.2% other men</i>	<i>22% FSW 21% MSM 16% AGYW 41% pregnant women 0.5% other men</i>	<i>40% FSW 28% MSM 31% AGYW 41% pregnant women 1% other men</i>	<i>65% FSW 49% MSM 51% AGYW 54% pregnant women 3% other men</i>
Effectiveness	65%-85%	65%-85%	99%	99%
Tail (months)	N/A	N/A	6	6
Cost of PrEP per user (full service incl drug)	R1050 (women, other men), R1318 (MSM)		R1100-R1180 (women, other men), R1550 (MSM)	R1570-R1670 (women, other men), R2500 (MSM)

Number of initiations and LEN doses

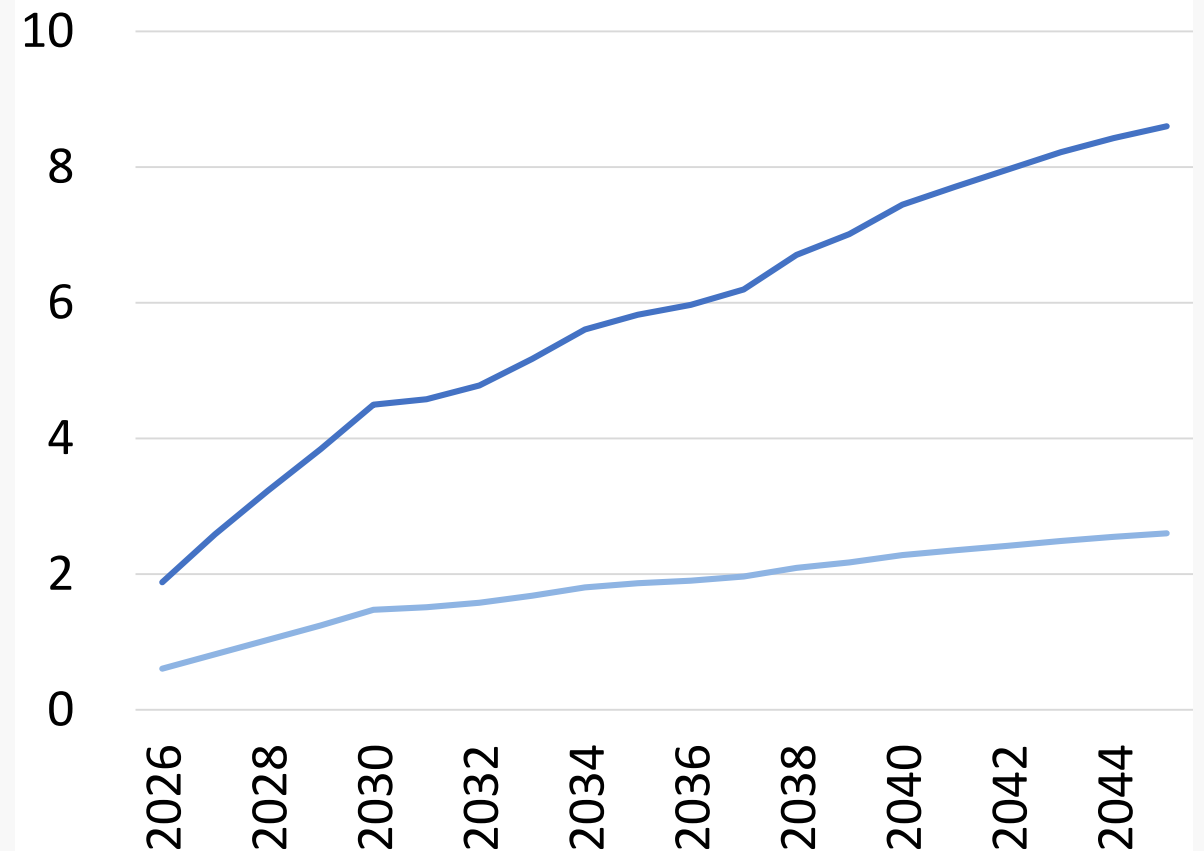
Number of initiated

millions



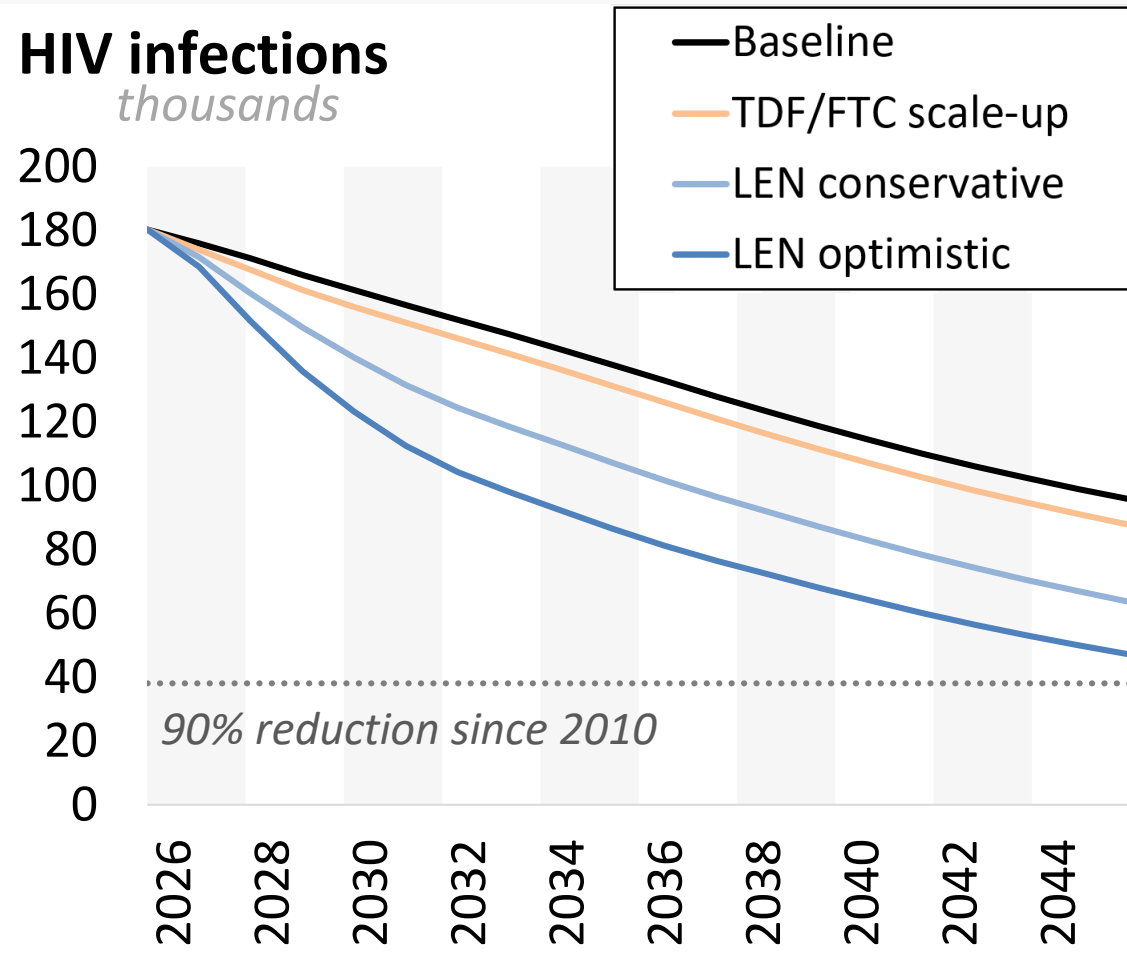
Number of LEN doses

millions



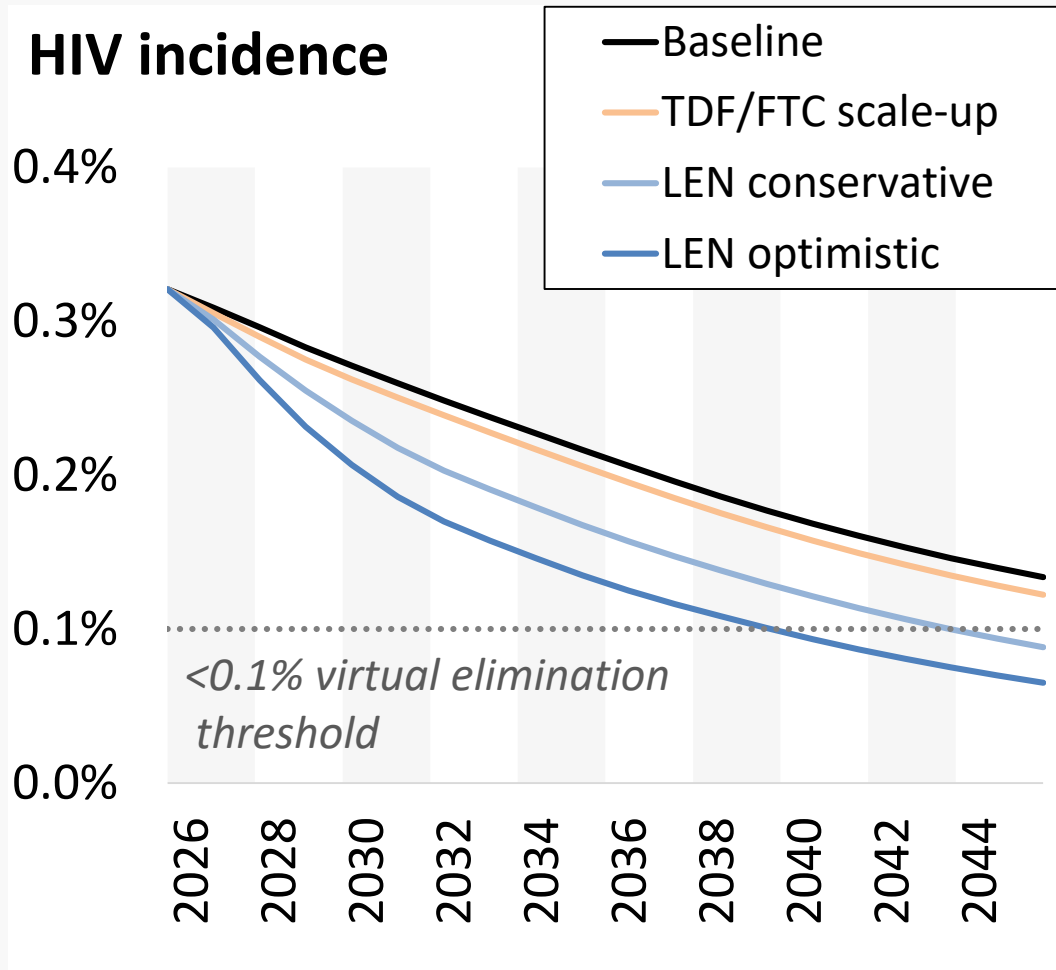
*dose=6-monthly dose

Results: Impact on new HIV infections



- Currently, we have an estimated 180,000 new HIV infections annually, set to reduce over the next 20 years
- LEN could reduce HIV by an average of
 - 32,200 infections/year (conservative; *1.4m initiations/year on LEN by 2030*)
 - 51,700 infections/year (optimistic; *2.1m initiations/year on LEN by 2030*)
- TDF/FTC scale-up would avert an average of 8,000 infections/year

Results: Impact on HIV incidence



- Current total HIV incidence in 2025 (entire population) is estimated at 0.32% (*all ages*)
- LEN could reduce incidence to <0.1% (virtual elimination threshold towards ending AIDS) by
 - 2039 (conservative)
 - 2043 (optimistic)
- TDF/FTC scale-up only reached this threshold in 2050

Results: 20-year impact and cost-effectiveness

Scenario	Cost of the HIV programme (ZAR)	New HIV infections	Life years lost due to AIDS	Incremental cost effectiveness (ZAR)	
	Total cost, billions (% over baseline)	Number, millions (% averted over baseline)	Number, millions (% saved over baseline)	Cost/infection averted	Cost/life year saved
Baseline	738	2.72	19.89		
TDF/FTC scale up	759 (3%)	2.60 (4%)	19.74 (1%)	R180,513	R148,368
Lenacapavir					
Conservative	763 (3%)	2.21 (19%)	19.29 (3%)	R48,575	R41,935
Optimistic	802 (9%)	1.88 (31%)	18.90 (5%)	R76,558	R64,994

- LEN could **substantially reduce expected HIV infections and deaths**, averting 19-31% of new infections and 3-5% of life years lost, over 20 years, compared to baseline
- **LEN offers strong value for money**, with an incremental cost of only R48,575–R76,558/infection averted (vs. R180,513 for TDF/FTC) and R41,935–R64,994/life year saved (vs. R148,368 for TDF/FTC).

Results: Budget impact

Conservative LEN scale-up					
	2025/26	2026/27	2027/28	2028/29	2029/30
Clients	590,000	780,000	980,000	1,170,000	1,390,000
Doses	360,000	570,000	1,030,000	1,240,000	1,470,000
+GF donation	+500,000	+500,000			
Total cost*	R427 m (+1%)	R658 m (+2%)	R1,167 m (+3%)	R1,402 m (+4%)	R1,655 m (+5%)
Optimistic LEN scale-up					
Clients	910,000	1,230,000	1,530,000	1,820,000	2,130,000
Doses	1,630,000	2,340,000	3,230,000	3,840,000	4,500,000
+GF donation	+500,000	+500,000			
Total cost*	R1,257 m (+4%)	R1,816 m (+5%)	R2,601 m (+7%)	R3,087 (+9%)	R3,610 m (+10%)

*Total cost includes the cost of drugs (injections, loading dose), staff, labs, consumables, equipment, and other overheads;
EXCLUDES cost of doses covered by Global Fund donation

Optimising lenacapavir donation for impact

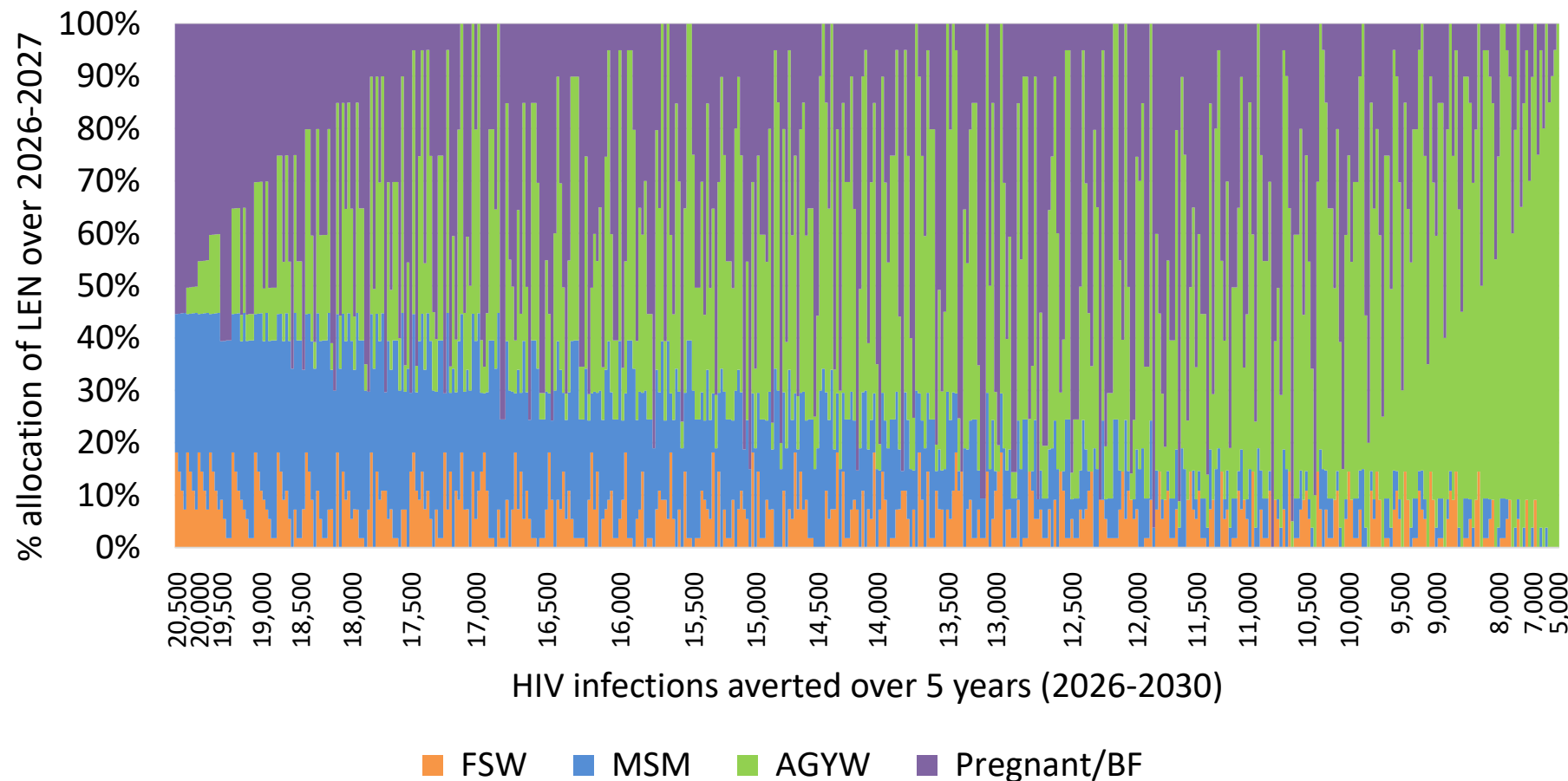


Methods for LEN donation subpopulation optimisation

- **Baseline:** current TDF/FTC roll-out continues into the future; initiation numbers: ~600k-900k/year
- We capped the LEN initiations over 2026 and 2027 combined at 500,000, assuming zero new initiations from 2028 onwards
- Assumed 1-year duration (2 injections) for each subpopulation
- Modelled 490 different combinations of LEN distribution between AGYW, FSW, PBFW, and MSM
- **Maximum population coverages:**
 - FSW (60% coverage $\approx$ 45,000 initiations/year)
 - MSM (30% coverage $\approx$ 93,600 initiations /year)
 - PBFW: up to 250,000 per year ($\sim$ 20% coverage)
 - AGYW: up to 250,000 per year ($\sim$ 4% coverage)
- Modelled 5-year impact (2026-2030) on HIV infections (to include the impact on secondary infections averted)

Impact on HIV infections averted over 2026-2030

More HIV infections averted



- For highest impact, target:
 - PBFW
 - MSM
 - FSW
- There is room for targeting AGYW and still have a moderate-high impact
 - However, >80% of doses would still need to go towards PBFW, MSM, FSW

10 highest impact distribution scenarios

HIV infections averted (2026-30)	% of LEN allocated to target population			
	FSW	MSM	AGYW	Pregnant/BF
20,554	18%	26%	0%	55%
20,554	14%	30%	0%	55%
20,522	11%	34%	0%	55%
20,422	7%	38%	0%	55%
20,260	18%	26%	5%	50%
20,258	14%	30%	5%	50%
20,223	11%	34%	5%	50%
20,121	7%	38%	5%	50%
20,000	18%	26%	10%	45%
19,996	14%	30%	10%	45%

Moderate impact distribution scenarios

HIV infections averted (2026-30)	% of LEN allocated to target population			
	FSW	MSM	AGYW	Pregnant/BF
20,554	18%	26%	0%	55%
18,756	18%	26%	30%	25%
18,742	14%	30%	30%	25%
18,698	9%	30%	15%	45%
18,696	11%	34%	30%	25%
18,630	5%	34%	15%	45%
18,609	0%	34%	0%	66%
18,581	7%	38%	30%	25%
18,561	2%	38%	15%	45%
18,561	2%	38%	15%	45%
18,435	7%	27%	0%	66%

10 lowest impact distribution scenarios

HIV infections averted (2026-30)	% of LEN allocated to target population			
	FSW	MSM	AGYW	Pregnant/BF
20,554	18%	26%	0%	55%
7,038	0%	4%	86%	10%
6,984	9%	0%	91%	0%
6,749	0%	0%	75%	25%
6,663	0%	4%	91%	5%
6,398	0%	0%	80%	20%
6,279	0%	4%	96%	0%
6,085	0%	0%	85%	15%
5,759	0%	0%	90%	10%
5,385	0%	0%	95%	5%
5,003	0%	0%	100%	0%



Conclusions: LEN cost-effectiveness

- **At \$40 PPPY, LEN is more cost-effective than oral TDF/FTC scale-up, even at the same total cost**
- **LEN can substantially reduce the number of new HIV infections**
- **LEN can accelerate progress towards ending AIDS and end AIDS 7-10 years earlier than scaling up oral TDF/FTC**
- **For these impacts, we need to initiate 1-2 million people on LEN every year, for an additional cost of R650-1500 million per year**
- **Cost-effectiveness of LEN distribution to FSW > LEN to MSM > LEN to pregnant and breastfeeding women or AGYW**



Conclusions: LEN donation

- Given the limited LEN donation amount from the Global Fund, PBFW, MSM and FSW should be targeted first: ***highest impact scenario → 55% to PBFW, 26% to MSM and 18% to FSW***
- While LEN distribution to AGYW could result in substantial reductions in HIV, most LEN (>80%) should be prioritised to other key populations (KPs) to maximise epidemic impact.
- **However**, it is important to balance impact vs feasibility – effectively reaching KPs may require different delivery models outside government primary health centres
 - AGYW and PBFW may be a good initial avenue for creating demand for LEN among people **who will benefit the most** (Phase 1)
- During initial implementation, monitoring *who* initiates LEN and their associated risk levels will be essential to update assessments of value for health resources and guide future expansion strategies

Acknowledgements

Special thanks to:

Leigh Johnson

Gesine Meyer-Rath

Jeffrey W. Imai-Eaton

Funding:

Bill & Melinda Gates Foundation INV-063625 (Project Langanisa)

Contact: ljamieson@heroza.org

