

Situational analysis of HIV in India and approach to the use of lenacapavir for pre-exposure prophylaxis in high-risk groups

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Abstract:

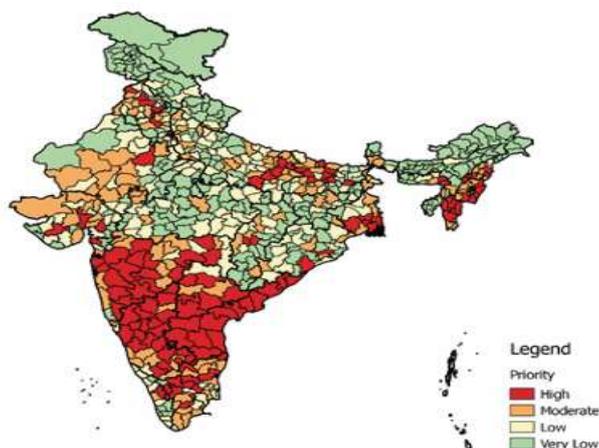
As per 2023 data, India has the 2nd largest HIV epidemic in the world (6.3% of the global PLHIV). National prevalence among adult population remains low (0.20%). India has significantly reduced the annual incidence by 44.23% (global decline-38%) between 2010-2023 and deaths have declined by 79.26% (global decline-51%). Though the country shows a low adult prevalence, its 9-43 times increased among high-risk groups. This is mainly attributable to factors like increased intravenous drug abusers in North Eastern states, increased female sex workers in Southern states, larger and denser urbanized areas, stigma and lack of awareness, and disparities among the states with respect to HIV testing, treatment and prevention strategies. The situational analysis identified an increase in HIV prevalence among the key and vulnerable population when compared to the national average. NACO has also reported 144 high burden districts in India with a prevalence of >1% in 2019. Among the key population with PLHIV, the ART coverage varies between 28-58.7%. Knowledge about HIV prevention practices was reported to be 26.17%. Hence, PrEP can be considered as an additional effort to the existing services to end the epidemic by 2030. Hence, this study explains an approach to the use of lenacapavir for pre-exposure prophylaxis in high-risk groups in high-burden districts of India

Situational Analysis of HIV in India:

As of April 2025, the population of India is estimated to be approximately 1.46 billion accounting to 17.78% of the world's population ranking the highest and majority is contributed by rural sector, with 37.08% contributed by urban dwellers. Immigrants from the bordering countries further add to the population. Though there has been a decline in the growth rate since 1960, it still remains steady at 0.89% since 2023. The total fertility rate has also declined to 1.9 and approximately 68.02% of the population belongs to the 15-64 age group. Its geographically and culturally diverse, which influences the population density. Higher population density is observed across the Indo-Gangetic plain and urban localities in the states, whereas its lower in North Eastern states and rural areas. Shift from rural to urban population leads to urbanization and immigration challenges, competition for the existing resources and jobs causing outpacing supply, exploitation in the labor market, hazardous working conditions and discrimination. All these exacerbate the regional disparities with wealth accumulating in the urban areas, creating urban slums. This leads to poor standard of living, poor access to healthcare facilities and disparity observed among various socio-economic groups with marginalized groups facing higher health risks and psychological stress causing anti-social activities. There are also topographical challenges observed, which impact the healthcare infrastructure development and management. The government has allocated \$11.50 billion during 2025-26 towards healthcare expenditure, but there is always a gap in addressing the challenges due to a large population requiring government support to meet out its healthcare expenses.

As per 2023 data, India has the 2nd largest HIV epidemic in the world (6.3% of the global PLHIV). National prevalence among adult population remains low (0.20%). India has significantly reduced the annual incidence by 44.23% (global decline-38%) between 2010-2023 and deaths have declined by 79.26% (global decline-51%). Though the country shows a low adult prevalence, its 9-43 times increased among high-risk groups namely female sex workers (1.8%), prison inmates (1.9%), male who have sex with men (3%), hijra/transgender (3.8%) and people who inject drugs (9%). Its 4 times higher in single male immigrants (0.89%) and 5 times higher in long distance truckers (1%). There is also regional variation in ANHI ranging between 76.1% in Andhra Pradesh to 524% in Tripura during 2010-2023. Its higher North eastern states excluding Assam, Telangana, Karnataka, Delhi, Maharashtra, Puducherry, Punjab, Goa and Tamil Nadu. This is mainly attributable to factors like increased intravenous drug abusers in North Eastern states, increased female sex workers in Southern states, larger and denser urbanized areas, stigma and lack

of awareness, and disparities among the states with respect to HIV testing, treatment and prevention strategies.



Priority level	Description	Number of Districts	Epidemic Burden
High	Adult prevalence of $\geq 1\%$ or PLHIV size of ≥ 5000	144	63% of PLHIV, 49% of new infections and 55% of PMTCT need
Moderate	Adult prevalence of 0.4% - $< 1\%$ or PLHIV size of 2500 - < 5000	155	21% of PLHIV, 27% of new infections and 25% of PMTCT need
Low	Adult prevalence of 0.20% - $< 0.40\%$ or PLHIV size of 1000 - < 2500	180	12% of PLHIV, 16% of new infections and 14% of PMTCT need
Very Low	Adult prevalence of $< 0.20\%$ or PLHIV size of < 1000	256	4% of PLHIV, 8% of new infections and 6% of PMTCT need

Fig1: District level burden of HIV as in 2019

HIV response has evolved with NACP becoming one of world largest HIV prevent-detect-treat policies. Phase I(1992-1999) focused mainly on awareness generation, sero-surveillance and blood safety component, Phase II(1999-2007) focusing on launch of direct interventions of prevention-detection-treatment with capacity building in the states. Phase III(2007-2012) decentralized the program management to district level. Phase IV(2012-2017) was a period of consolidation and enhanced government funding which was extended(2017-2021), in which “Test & Treat” policy was launched and complemented by universal HIV-viral load testing for PLHIV on ART and “Mission Sampark” to bring up lost-to-follow up cases on ART. Inter and Intrastate systems were improved by leveraging IT systems and various initiatives like community ART and multi-month dispensation were undertaken. Currently NACP is under Phase V(2021-2026) which aims to end HIV epidemic in the country by 2030 and reduce AIDS related mortalities by 80% in 2025-26. The motto of this phase is “Breaking Silos, building synergies”, having 95-95-95 target and dual aim of preventing vertical transmission by 95%, elimination of HIV stigma and promoting universal access to quality STI/RTI services to at-risk and vulnerable population.

External support: UNAIDS enhances and promotes the existing services by working closely with NACO and State AIDS control societies, civil societies, academia and private sector. AusAID works with UNAIDS and has a dedicated program for HIV/AIDS in North East India. German AID-GTZ works in the states of Himachal Pradesh, Maharashtra and West Bengal for “harm minimization” in vulnerable groups. BMGF has been actively involved to scale up prevention and intervention in 6 highly prevalent states. Clinton Foundation trained private doctors, provided CD4 machines and technical consultants to NACO. GFATM has allocated \$500 billion (2023-2025) towards TB and HIV programs and provides financial and technical support for prevention, treatment and care programs in vulnerable population. However, almost 80% of the contributions are made by the GOI through MoHFW-ART centers across the country providing free prevention, testing and treatment services and advanced services like hospitalization and opportunistic infection care.

India has outperformed the global targets with respect to HIV incidence, prevalence and mortality. India’s ambitious target of 80% reduction in ANHI by 2026 was not achieved as there is difficulty in reaching marginalized population, stigma and discrimination and pitfalls in services to at-risk population. There has been gaps in testing and prevention strategies. Moreover, the antiretroviral drug lenacapavir, approved for

PrEP is yet to be launched in India. There is also a need for strengthening coordination among implementation agencies, for improving HIV testing and treatment services among pregnant women, addressing “bridge populations” and focus on reaching these groups through targeted awareness programs and IEC activities, increased access to testing and prevention and treatment services. All these efforts can help achieve the 95-95-95 target.

Recommendation:

Lenacapvir vaccine roll-out for PrEP in high burden districts of India-a strategy to end HIV by 2030

Key gaps: The situational analysis identified an increase in HIV prevalence among the key and vulnerable population when compared to the national average. NACO has also reported 144 high burden districts in India with a prevalence of >1% in 2019. Among the key population with PLHIV, the ART coverage varies between 28-58.7% Knowledge about HIV prevention practices was reported to be 26.17%. Hence, PrEP can be considered as an additional effort to the existing services to end the epidemic by 2030.

Rationale: PrEP aims to reduce HIV incidence among high-risk individuals with an efficacy of 90% and 70% through sexual contact and intravenous drug abuse respectively.

Major currently available PrEP medications, formulated as FDCs:

1. Tenofovir disoproxil fumarate(TDF) 300mg+emtricitabine(FTC) 200mg-1 tablet daily or on demand 2-1-1
2. Tenofovir disoproxil fumarate(TDF) 300mg+Lamivudine(3TC) 300mg-1 tablet daily
3. Tenofovir alafenamide(TaF) 25mg + emtricitabine(FTC) 200mg-1 tablet daily
4. Cabotegravir(CAB-LA)- single dose of 600mg 1 month apart for 2 consecutive months and then every 2 months- intra muscular in the gluteal region
5. Oral Cabotegravir-30mg 1 tablet daily

Group	HIV PrEP Medications		
	TDF-FTC	TAF-FTC	Cabotegravir
Men who have sex with men	Recommended	Recommended	Recommended
Women who have sex with men	Recommended	Not Recommended	Recommended
Men who have sex with women	Recommended	Recommended	Recommended
Persons who inject drugs	Recommended	Not Recommended	Not Recommended
Men who take on-demand HIV PrEP	Recommended	Not Recommended	Not Recommended
Adolescent boys weighing ≥35 kg	Recommended	Recommended	Recommended
Adolescent girls weighing ≥35 kg	Recommended	Not Recommended	Recommended

Fig2: Indications of PrEP medications

The overall evidence conveys effectiveness is directly proportional to adherence which is influenced by adverse events like start-up symptoms that subside eventually. Long term usage showed decline in renal function and bone mineral density. There are also issues with non-adherence associated PrEP failure and infection with wild type and drug-resistant forms (M184V and K65R mutations).

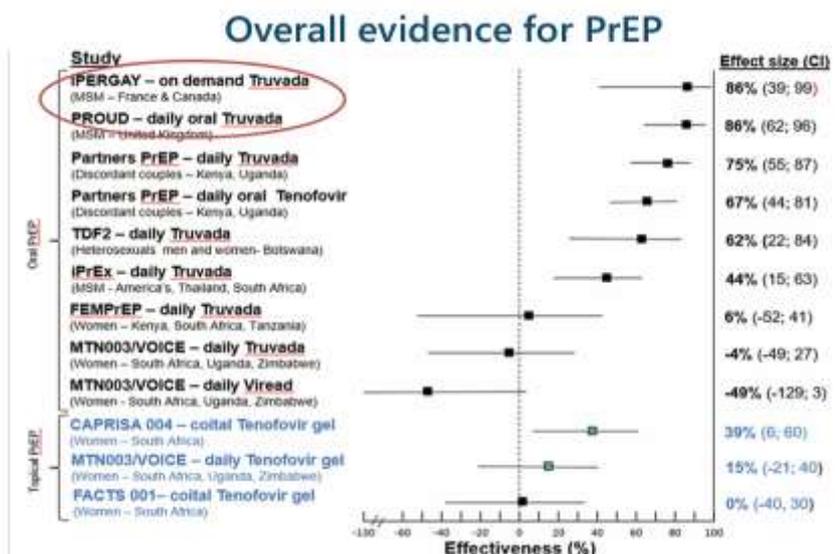


Fig 3: Effectiveness of PrEP medications and its association with adherence

Lenacapavir, a capsid inhibitor used as antiretroviral medication, preventing viral replication and shedding, obtained FDA approval in October 2024 to be used as a longer acting injectable PrEP vaccine, with 96-100% efficacy when compared to other PrEP medications for all high-risk individuals and geographically diverse population, when administered twice yearly, can be a potential candidate to be rolled-out in LMICs national HIV PrEP strategies.

Student and Women organizations play a vital role in improving health outcomes by raising awareness, promoting health education, assist establishment of health clinics, policy advocacy and thereby provide equitable access to essential health services. They serve as crucial support system for at-risk, vulnerable and marginalized population in issues related to maternal and child health, reproductive rights and mental health.

Aim: To evaluate the effectiveness and acceptability of twice yearly lenacapavir injection in preventing HIV incidence in high burden districts and assessing the feasibility of engaging student and women organizations for integrating community-based approaches- In India

Objectives:

Primary Objective: To assess the efficacy of lenacapavir injection (twice yearly) as PrEP in HIV high burden districts of India

Secondary objectives:

1. Assess the acceptability considering adherence and preferences
2. Explore the feasibility of integrating student and women organizations into the PrEP program
3. Assess the potential barriers and facilitators to successful PrEP implementation

Study design: A quasi-experimental pre-post study is conducted across the 144 HIV high burden districts of India as per 2019 NACO report and the cohort is followed for a period of 1 year

Study Population: Consenting at-risk population residing for atleast 1 year in the designated high burden districts potentially including people ≥ 15 years of age, MSM, transgender, FSW and iv-drug abusers.

Study methods with period and timelines: 5 years

Year-1: Preparatory and Planning Phase: IEC and other regulatory approvals for study protocol with annexures will be obtained along with HR recruitment and training. The state HR will establish partnership with SAWO followed by training and capacity building after KAP assessment of these volunteer groups, who will assist the study team to sensitize the community and create awareness in their designated districts. The team assisted by the volunteer groups will map the district boundaries and households after identifying optimal access routes.

Year-2,3: Household enumeration, baseline visit and 2nd dose: A door-door survey and line-listing of all household members will be done by the volunteer groups and the state team screen the household members to identify eligible population for the study. The volunteer groups then visit to interview the eligible population for assessing their contact information, baseline demographic data, bio-behavior related to HIV after obtaining consent. Each participant is assigned an UID and data is electronically captured on electronic database like RedCap, monitored by the state study team remotely. The state medical officer will administer the 1st dose of lenacapavir injection after assessing the baseline HIV symptoms/status. If found sero-positive, the patient is referred to the district healthcare facility for ART initiation. The date of 1st vaccination is recorded on the database. A reminder for the 2nd dose of vaccination is made to the participants after 6 months by volunteers through phone calls and confirm their date of visit within the prescribed week as per their convenience. If found non-responsive on phone calls, the volunteers visit the household in-person to remind and refer the participants for the 2nd dose.

Year-3,4: Follow up visit and endline assessment: The volunteers visit the study participants 1 year after 2nd dose for behavioral survey and refer them for HIV testing and close-out activities to the central state study team.

Year-5: Final evaluation: Conduct a comprehensive evaluation of the lenacapavir PrEP program in terms of effectiveness and feasibility, volunteer sustainability, data analysis and report writing, peer-reviewed publications and dissemination of findings followed by policy briefing to inform the policy makers about the results.

Data analysis plan:

Data quality assurance and confidentiality: A bimonthly monitoring visit is conducted by the study team to review correctness, completeness and compliance with the study protocol. The data is stored in secure servers to ensure confidentiality.

Data analysis: The qualitative variables will be summarized using mean and SD for continuous variable, frequencies and percentages for categorical variables. The mean scores of KAP of volunteers from pre and post-training will be calculated and compared using paired T-test. HIV incidence is calculated in the pre- and post-intervention period. Vaccine efficacy is calculated using Cox's proportional hazards model, time-

to-event analysis, survival analysis. Sub-group analysis of the same variables is considered. Association between vaccine efficacy and adherence is calculated using Odds ratio. Potential confounding factors like concurrent use of other prevention methods, STI status, comorbidities are considered and the efficacy is adjusted using multivariate regression modelling. Incremental cost-effectiveness ratio (ICER) per QALY gained by the intervention will be calculated by dividing the differences in total costs between vaccine and ART to determine whether the intervention is less-cost more-effective or more-cost less-effective.

Ethical Considerations: IEC approved documents are translated to the local language for circulation to the state teams. A written consent will be obtained from the literate participants and in case of illiterate participants, the thumb impression will be obtained after explaining contents of the PIF and study procedures along with the signature of an impartial witness and assent will be obtained from the participants aged 15-18 years of age at the time of enrollment. An honorarium of Rs.1000/month and mobile recharge of Rs.800/quarter is provided to all participating volunteers after obtaining volunteer consent.

Indicators for Monitoring and Evaluation: **Vaccine:** Participation rate, coverage rate, percentage of participants who received 2 doses, sub-group analysis of coverage rate, HIV incidence rate after 1 year of complete vaccination, dropout rates, percentage of adverse events, percentage of vaccine wastage, pre-and post-intervention assessment of HIV incidence

Volunteer groups: number trained, percentage of recruitment, percentage of retention, demographics, total hours contributed, no: of household surveyed by each, no: of participants identified by each, no: of events organized and attended by each, satisfaction and feedback surveys, testimonials from beneficiaries, pre- and post-intervention assessment of awareness.

Expected Outcomes:

1. Higher efficacy, safety, feasibility, impact, acceptability and sustainability of lenacapavir as long-acting injectable PrEP in high-HIV burden districts when compared to other PrEP strategies
2. Reduction in HIV incidence in high-burden districts during post-intervention phase
3. Potential barriers and facilitators to vaccine adherence
4. Increase in the PrEP awareness, knowledge and uptake with the help of community volunteers and digital technologies
5. Expected decrease in ICER of vaccine when compared to ART

Conclusion:

This study will contribute to a deeper understanding of lenacapavir role in HIV prevention in resource limited settings. By involving community-based organizations, the study seeks to ensure that the program is culturally appropriate, sustainable and impactful in reducing HIV incidence and consider thereby integration into the national program.

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