

BMJ Open Epidemiological impact of achieving UNAIDS 90-90-90 targets for HIV care in India: a modelling study

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ABSTRACT

Objective: Recent UNAIDS '90-90-90' targets propose that to end the HIV epidemic by 2030, 90% of persons living with HIV (PLWH) worldwide should know their diagnosis, 90% of diagnosed PLWH should be on antiretroviral therapy (ART) and 90% of PLWH on ART should be virally suppressed by 2020. We sought to quantify the epidemiological impact of achieving these targets in India.

Methods: We constructed a dynamic-transmission model of the Indian HIV epidemic to project HIV infections and AIDS-related deaths that would occur in India over 15 years. We considered several scenarios: continuation of current care engagement (with early ART initiation), achieving 90-90-90 targets on time and delaying achievement by 5 or 10 years.

Results: In the base case, assuming continuation of current care engagement, we project 794 000 (95% uncertainty range (UR) 571 000–1 104 000) HIV infections and 689 000 (95% UR 468 000–976 000) AIDS-related deaths in India over 15 years. In this scenario, nearly half of PLWH diagnosed would fail to achieve viral suppression by 2030. With achievement of 90-90-90 targets, India could avert 392 000 (95% UR 248 000–559 000) transmissions (48% reduction) and 414 000 (95% UR 260 000–598 000) AIDS-related deaths (59% reduction) compared to the base-case scenario. Furthermore, fewer than 20 000 (95% UR 12 000–30 000) HIV infections would occur in 2030. Delaying achievement of targets resulted in a similar reduction in HIV incidence by 2030 but at the cost of excess overall infections and mortality.

Conclusions: India can halve the epidemiological burden of HIV over 15 years with achievement of the UNAIDS 90-90-90 targets. Reaching the targets on time will require comprehensive healthcare strengthening, especially in early diagnosis and treatment, expanded access to second-line and third-line ART and long-term retention in care.

INTRODUCTION

The advent of antiretroviral therapy (ART) in the past two decades has significantly advanced the treatment and prevention of HIV worldwide.¹ Rapid expansion of ART access to provide early treatment to all

Strengths and limitations of this study

- We constructed a dynamic-compartmental model that incorporates HIV risk status, HIV transmission and disease progression, and engagement in care to model HIV prevalence and incidence in India.
- We quantified the epidemiological benefits of achieving recent UNAIDS 90-90-90 targets by 2020 in India and excess transmissions and mortality that would occur with delayed achievement.
- We are unable to provide financial implications of achieving such targets, as costs of healthcare strengthening (especially to improve retention in care) are unknown.

persons living with HIV (PLWH) has been identified as a key step in addressing the AIDS epidemic at a population level.^{2–6} As such, UNAIDS recently proposed the ambitious Fast-Track ('90-90-90') treatment targets, where, by 2020, 90% of PLWH worldwide should know their diagnosis, 90% of these people should be on ART and 90% of these individuals (ie, 73% of all PLWH) should be virally suppressed, as a means to eliminate HIV as a public health threat by 2030.⁷

Despite recent advances in HIV diagnosis and treatment, many low-income and middle-income countries face significant obstacles in reaching the 90-90-90 goals.⁸ In India, home to the third largest absolute burden of HIV worldwide, less than one-third of PLWH are currently virally suppressed, due to suboptimal diagnosis, treatment and retention in care.^{9–12} While implementing recent guidelines for early initiation of ART continue to remain a high-priority health intervention, other areas for improvement include increasing HIV awareness as well as decreasing the stigma and other sociocultural barriers that preclude many from seeking therapy and engaging in long-term care.^{13–17}

The potential impact of achieving the 90-90-90 targets on the Indian HIV epidemic has yet to be described. We thus constructed a dynamic-transmission model to quantify new HIV infections and AIDS-related deaths over the next 15 years. In particular, we quantified the excess HIV transmissions and mortality that would occur if India delayed the healthcare strengthening necessary to reach these targets. Finally, we show that comprehensive healthcare strengthening in all aspects of HIV care is required to ultimately achieve the UN goal of eliminating HIV as a public health threat by 2030.

METHODS

We used the Johns Hopkins HIV economic-epidemic model to project HIV prevalence, incidence, AIDS-related deaths and care continuum dynamics in India over a 15-year time horizon. Full details of the model are published elsewhere.^{18 19} Briefly, our dynamic-compartmental model divides India's adult population (15–64 years) by sex, HIV infection status and HIV risk-profile (heterosexuals, men who have sex with men, people who inject drugs, female sex workers and high-risk men). HIV transmission is incorporated through sex (heterosexual and male homosexual) and needle sharing. HIV disease progression is dependent on viral suppression status. We also incorporated health system engagement by explicitly modelling rates of HIV screening and linkage to care, ART initiation, ART resistance, and disengagement and re-entry in care. Our model tracks usage of ART regimens, with switches made based on treatment failures and side effects (with rates of such events derived from published literature). We report on the percentage of PLWH on each of these regimens at various time points in our simulations. Model parameters, including HIV transmission probabilities and rates of engagement in care, were calibrated to reflect published epidemiological data on HIV prevalence, incidence and care continuum engagement in India between 2007 and 2011 (the last year for which there were complete epidemiological data).^{10 20 21}

In our base-case scenario, we implemented recent guidance recommending ART initiation irrespective of CD4 count.¹³ We then modelled a scenario in which the 90-90-90 targets would be achieved by 2020. To determine the parameter set that would result in achievement of these targets, we iteratively increased model inputs influencing care continuum dynamics until each individual step along the care continuum matched desired outcomes (table 1). For example, to achieve the first 90, we increased screening rates among the general population (testing every 5 years) and high-risk groups (annual testing) until 90% of PLWH were aware of their serostatus by 2020. We additionally projected epidemiological outcomes of the Indian HIV epidemic if achievement of the targets (as a whole) was delayed until 2025 and 2030. In these two scenarios, we assumed continuation of the base-case scenario until 2020 and 2025,

respectively, at which point we incorporated the comprehensive healthcare strengthening required to reach 90-90-90 targets. We also considered a scenario where India continues a policy of deferred ART initiation at $CD4 \leq 350$ cells/mm³ at current rates of care engagement (see the Results section). We conducted probabilistic uncertainty analysis by simultaneously varying all parameter values by Latin Hypercube sampling over specified ranges and report 95% uncertainty ranges (URs). There are limited data describing the sensitivity ranges for the input parameters for our model. As such, the inputs for the sensitivity analysis were varied widely and largely based on the authors' experience from working in India, in conjunction with published literature.

RESULTS

Assuming adoption of recent guidance for early ART initiation (ie, initiation irrespective of CD4 count) in the current HIV care continuum, we project that 794 000 incident HIV cases (95% UR 571 000–1 104 000) and 689 000 AIDS-related deaths (95% UR 468 000–976 000) would occur in India by 2030 (table 2). Implementation of early ART policies has minimal impact on achieving 90-90-90 targets at current rates of care engagement. At current rates of HIV screening, linkage and retention in care, we estimate that 72% of PLWH diagnosed with HIV would be on ART, and only 76% of PLWH on ART would be virally suppressed by 2030.

Reaching UNAIDS 90-90-90 targets by 2020 would result in a drastic reduction of the HIV epidemic in India. If 90-90-90 were achieved, we estimate that 392 000 new HIV infections (48% reduction; 95% UR 248 000–559 000) and 414 000 AIDS-related deaths (59% reduction; 95% UR 260 000–598 000) could be averted by 2030. Additionally, fewer than 20 000 new HIV infections (95% UR 12 000–30 000) in 2030 would occur if India reached these targets on time. In this scenario of increased care engagement, we project that 26% of PLWH in India would require post-first-line regimens by 2020, and more than half of HIV-infected individuals on ART would require second-line and third-line regimens by 2030.

Delaying achievement of the Fast-Track targets resulted in markedly excess HIV transmission and mortality. With a delay of 5 years (ie, reaching targets by 2025 instead of 2020), India would incur an extra 211 000 HIV infections and 201 000 AIDS-related deaths by 2030 than if targets were reached on time. Furthermore, delaying fulfilment of 90-90-90 targets until 2030 (ie, delay of 10 years) resulted in marginal epidemiological benefits over 15 years compared to the base-case scenario (ie, implementation of early ART initiation alone). Specifically, with this additional delay, we project 709 000 HIV transmissions (95% UR 501 000–893 000) and 617 000 AIDS-related deaths (95% UR 406 000–789 000) over 15 years; this translates to only 11% and 10% reductions in infections and deaths, respectively, over continuation of current care engagement (with early ART initiation).

Table 1 Key model parameters

Variable	Value	Sensitivity analysis	References
HIV care continuum dynamics used in base-case scenario			
Percentage HIV testing in past 12 months among general population	3.2%	1–7.5%	22
Per cent HIV testing in past 12 months among high-risk groups	17–31.8%	5–60%	22
Percentage of newly diagnosed HIV patients with early linkage to care*	50–80%	25–100%	10 23
Per cent of PLWH in care who become lost to follow-up yearly	15–19.5%	10–39%	10 11 24 25, assumption
Median time spent lost to follow-up before return to care	3 years	2–4 years	10 11 24 25, assumption
Percentage of PLWH who develop resistance to first-line ART after disengagement	25%	10–50%	26, assumption
Per cent of PLWH on ART who develop resistance to ART	7–10% yearly	2–30% yearly	11 27 28
Median time after ART failure before treatment modification	1.25–2 years	8 months—20 years	27 28
Median time after linkage to care before initiation of ART (irrespective of CD4 count)†	3 months	2–6 months	13
HIV care continuum dynamics used in 90-90-90 scenario			
Per cent HIV testing in past 12 months among general population	20%	15–25%	Calibrated
Per cent HIV testing in past 12 months among high-risk groups	100% (ie, annual)	80–100%	Calibrated
Per cent of PLWH in care who become lost to follow-up yearly	10–13%	7.5–16.25%	Calibrated
Median time spent lost to follow-up before return to care	1 year	8–15 months	Calibrated
Median time after ART failure before treatment modification	4 months	2–6 months	Calibrated
Median time after linkage to care before initiation of ART (irrespective of CD4 count)	3 months	2–6 months	Calibrated

*Patients without early linkage (ie, linkage within 3 months of diagnosis) could still engage in care at a later time.

†We modelled ART initiation rates based on recent guidance that recommends initiation of ART irrespective of CD4 count, though this may not reflect current policies in India.^{13 29 30} We thus conducted in our sensitivity analysis an alternative scenario in which India would continue a policy of deferred ART initiation (at CD4 \leq 350 cells/mm³; see the Results section).
ART, antiretroviral therapy; PLWH, persons living with HIV.

DISCUSSION

Recent UNAIDS ‘90-90-90’ treatment targets call for rapid scale-up of access and usage of ART over the next 5 years in an effort to eradicate the global HIV epidemic by 2030.⁷ Our results show that achieving these targets on time—by 2020—can more than halve the epidemiological burden of HIV in India over 15 years, through substantial reductions in total incident cases and AIDS-related deaths. Fewer than 20 000 HIV infections would occur in 2030 if these targets were reached in the next 5 years, an 84% reduction when compared to the 120 000 infections that occur per year currently.³¹ Notably, our results suggest that even if achievement of the targets is delayed, the substantial reduction in yearly transmissions by 2030 would still occur—as long as the targets were eventually reached. Delaying fulfilment of the targets, however, would result in significantly excess total infections and mortality over 15 years, demonstrating the urgent need for comprehensive healthcare strengthening in India.

Despite updated guidelines for earlier ART initiation at higher CD4 counts, India currently continues a policy of deferred ART initiation at CD4 \leq 350 cells/mm³.^{13 29 30}

Even in our base-case scenario, which assumes early ART initiation irrespective of CD4 count, our model projects that nearly half of PLWH aware of their serostatus will fail to achieve viral suppression by 2030—well short of current UNAIDS targets. Our modelling process demonstrates that despite its clear epidemiological benefits, earlier initiation of ART is necessary but not sufficient to achieve the Fast-Track targets by 2020. Our results are in contrast to previous studies suggesting that achieving 90-90-90 targets has a similar epidemiological impact as implementation of early ART initiation (at CD4 \leq 500 cells/mm³) in sub-Saharan countries.³² This finding is likely explained by the fact that these countries, like India, experience significant attrition in HIV care that we explicitly accounted for in our modelling approach.³³ Ultimately, early ART initiation addresses only one aspect of the care continuum, and without other improvements in care engagement (particularly early diagnosis, access to alternative regimens and long-term retention in care), its benefits are largely lost.

Current data suggest that a large portion of PLWH in India cannot access and gain the full benefits of earlier treatment due to infrequent HIV testing and late

Table 2 Key model outputs

	Incident cases	AIDS deaths	New HIV infections in 2030
Current care engagement (with implementation of early ART guidance)*	794 000 (95% UR 571 000–1 104 000) (reference)	689 000 (95% UR 468 000–976 000) (reference)	46 000 (95% UR 29 000–71 000) (62% reduction from current yearly incident cases†)
90-90-90 by 2020	415 000 (95% UR 289 000–588 000) (48% reduction)	280 000 (95% UR 194 000–404 000) (59% reduction)	19 000 (95% UR 12 000–30 000) (84% reduction from current yearly incident cases†)
90-90-90 by 2025‡	583 000 (95% UR 479 000–715 000) (27% reduction)	488 000 (95% UR 379 000–623 000) (29% reduction)	21 000 (95% UR 14 000–31 000) (83% reduction from current yearly incident cases†)
90-90-90 by 2030‡	709 000 (95% UR 501 000–893 000) (11% reduction)	617 000 (95% UR 406 000–789 000) (10% reduction)	24 000 (95% UR 14 000–32 000) (80% reduction from current yearly incident cases†)

*We assumed initiation of ART irrespective of CD4 count as per recent international guidance. In our sensitivity analysis, we modelled a scenario where India does not implement these recommendations and continues a policy of deferred ART initiation (at CD4 ≤ 350 cells/mm³). In this scenario, we project that 979 000 new HIV infections and 754 000 AIDS-related deaths would occur over 15 years, with 57 000 new HIV infections in 2030.

†Relative reduction compared to 120 000 yearly HIV infections currently.³¹

‡We modelled scenarios of delayed achievement of 90-90-90 targets by 5 or 10 years by assuming that improvements begin in 2020 or 2025, respectively. Model inputs to achieve these scenarios were calibrated to achieve 90-90-90 outcomes by 2025 and 2030, respectively. ART, antiretroviral therapy; PLWH, persons living with HIV.

presentation to care.^{19 20} We found that with annual HIV screening for high-risk groups and testing every 5 years for the general population (a strategy shown to be cost-effective in India even as an isolated intervention), 9 out of 10 PLWH could achieve and maintain awareness of HIV status by 2020 and beyond.³⁴ In the context of achieving 90-90-90 targets, improved screening would likely yield even greater epidemiological benefits and improved cost-effectiveness, as newly diagnosed individuals would rapidly integrate into care and achieve viral suppression. However, even after initiation of ART, many Indians face delays in detection of viral failure and subsequent treatment modification to alternative ART regimens, as only nine laboratories are qualified to cover viral load testing requests for all of India.⁹ As such, nearly half of PLWH in low-income Asian countries—including India—remain on failing regimens even 1 year after detection of treatment failure.²⁷ By comparison, to achieve 73% viral suppression by 2020, our model necessitated that PLWH were transitioned to second-line therapies on average within 4 months of viral failure. Moreover, one in five HIV-infected Indians in care becomes lost to follow-up, with only half eventually returning to care.^{11 25} Achieving 90-90-90 targets in our model required a significant improvement over these care-engagement dynamics. Specifically, we were able to reach the target outcomes when <10% of PLWH dropped out of care annually, with at least half returning to care by 1 year. Ultimately, our results highlight the need for comprehensive efforts to strengthen the HIV care continuum in India, in conjunction with

immediate ART access for all PLWH irrespective of CD4 count.

While it has seen exponential growth in the past decade, India's ART programme faces numerous challenges in the coming years. Access to second-line ART is limited compared to first-line ART: of the three-quarter million Indians currently on ART, only 10 000 are on a second-line regimen.⁹ Second-line ART regimens also cost up to six times more than first-line therapies.³⁵ Furthermore, India's ART programme is currently facing widespread drug shortages due to recent bureaucratic changes and budget cuts, threatening to interrupt therapy for many.³⁰ Our results suggest that an increasing proportion of PLWH will require postfirst-line regimens in the next 5 years if India reaches 90-90-90 targets, even with optimal engagement in HIV care minimising opportunities for viral failure. India must urgently set aside bureaucratic differences and restore full funding to its ART programme—with a particular emphasis on increasing second-line and third-line ART availability and affordability—if it is to reach the Fast-Track targets on time.

Our findings in India echo those of UNAIDS on the drastic effect of achieving 90-90-90 targets in the Asia/Pacific region, though our projections of relative epidemiological impact are somewhat more modest when accounting for real-life gaps and cycles of care engagement.⁷ Furthermore, in our base-case scenario, we assumed early ART initiation policies in India, as such guidelines are likely to be implemented in the coming years. Given the potentially optimistic assumption of this

policy change, our model may actually underestimate the true epidemiological benefit of achieving the 90-90-90 targets. However, this difference in projections was reduced in our sensitivity analysis when we modelled a scenario where India continued a policy of deferred ART initiation.

Our model has several limitations. As there are a multitude of healthcare interventions that India can institute to reach the Fast-Track goals, the sets of parameters we defined in our various scenarios are likely not unique. However, we used the same iterative approach when arriving at the parameter sets for each scenario, thus minimising any inconsistencies. Our modelling approach does not take into account mid-course variations in the programmatic strategies for healthcare strengthening, as such growth patterns are likely non-linear and thus not predictable. Additionally, we used published national estimates for HIV prevalence, incidence and care engagement to calibrate the model and generate outcomes for India as a whole; we are unable to comment on geographic heterogeneity given lack of complete data at a local and regional level. Finally, we were unable to provide the financial implications of reaching the 90-90-90 targets, as the costs for comprehensive healthcare strengthening (especially costs related to improved retention in care) are not known.

In conclusion, by achieving the UNAIDS Fast-Track targets on time, India can reduce the epidemiological burden of HIV by half and experience fewer than 20 000 new HIV infections in 2030. This substantial reduction in HIV incidence by 2030 will likely occur even if India delays reaching the targets by 10 years, but at the cost of significantly excess overall transmissions and deaths. Comprehensive healthcare strengthening—with earlier diagnosis and treatment, increased access to alternative ART regimens and improved long-term retention in care—is required if India is to reach the 90-90-90 targets by 2020.

Contributors MVM and MS conceived and designed the study; MVM performed experiments with contributions from MS; MVM analysed and interpreted the data; MVM and MS wrote the manuscript with contributions from AG. All authors contributed to interpretation of results and critically reviewed and edited the manuscript.

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