Effect of antiretroviral therapy on retention of people living with HIV in India (2012–2017): a retrospective, cohort study

Shweta Chidrawar,[a,h] Suvarna Sane,[a,h] Megha Mamulwar,[a,h] Shilpa Bembalkar,[a,h] Rachna Thakur,[a] Tarun Bhatnagar,[b] Srikanth P. Tripathy,[c] Shrinivasa B. Marinaik,[c] Damodar Sahu,[d] Subrata Biswas,[e] Shanta Datta,[e] Yogesh Sabde,[f] Rajnarayan Tiwari,[f] Deepak Khismatrao,[a] Bhawani Singh Kushwaha,[g] Anoop Kumar Puri,[g] Chinmoyee Das,[g] and Sheela V. Godbole,[a,*] ART-IE team[i]

[a]ICMR-National Institute of Translational Virology and AIDS Research, Pune, India
[b]ICMR-National Institute of Epidemiology, Chennai, India
[c]ICMR-National Institute of Research in Tuberculosis, Chennai, India
[d]ICMR-National Institute for Research in Digital Health and Data Science, New Delhi, India
[e]ICMR-National Institute for Research in Bacterial Infections, Kolkata, India
[f]ICMR-National Institute for Research in Environmental Health, Bhopal, India
[g]National AIDS Control Organization, New Delhi, India

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Summary

Background India's free antiretroviral therapy (ART) programme was initiated in 2004. People living with HIV who were registered with ART centres (ARTC) were initiated on ART based on the CD4 count cutoffs as per prevailing guidelines. The others with higher counts remained on six-monthly follow up. We estimated retention rates among people living with HIV receiving ART in the programme and their determinants during 2012–2017.

Methods In this retrospective cohort study, the records of people living with HIV aged ≥15 years, registered between April 2012 and March 2017 (reference period) in 81 of 396 ARTC across 33 Indian states were reviewed. 'People living with HIV not on ART' were defined as all those who were registered but not eligible for ART initiation or not started ART through the reference period. 'People living with HIV on ART' were those who were already on ART or initiated on ART as per prevailing guidelines. Relevant data from the clinic records were extracted and analysed for 'Not on ART' and 'On ART' groups separately using life-table method, Cox proportional hazards model to estimate retention probability and potential determinants.

Findings Of 154,154 registered people living with HIV, 82.3% received ART ('on ART') during 2012–2017. Proportion retained was lower among 'not on ART' vs 'on ART' people living with HIV and was statistically significant (71.1% vs 88.9%, $p < 0.001$). Five-year retention probability was 57% for 'not on ART' and 81% for 'on-ART' people living with HIV ($p < 0.001$). The incidence of cases who were lost to follow up was 12.9 and 4.3/100 person-years among 'not on ART' & 'on ART' people living with HIV, respectively. Determinants of becoming lost to follow up (Adjusted HR, 95% CI) included 'being in not on ART' (Adjusted HR: 2.95, 95% CI: 2.85–3.05) 'being male' (1.08, 1.05–1.11); 'having CD4 count 351–500 cells/mm^3' at registration (1.21, 1.16–1.26); and 'having tuberculosis' (1.15, 1.10–1.19).

Interpretation New programmatic strategies for improving retention of people living with HIV in care may benefit by focussing on males, younger ages (15–29 years), CD4 counts during registration, history of or new TB diagnoses and early intervention within the first year.

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Keywords: ART; India; Lost to follow-up; National programme; People living with HIV; PLHIV; Antiretroviral therapy; Retention; AIDS

*Corresponding author. ICMR – National Institute of Translational Virology and AIDS Research (ICMR-NITVAR [formerly ICMR-NARI]), Pune, India.
E-mail address: sgodbole@nariindia.org (S.V. Godbole).
[h]Contributed equally.
[i]Collaborating authors are listed in Acknowledgements.

Research in context

Evidence before this study

We searched PubMed for English-language studies published up to March 4, 2024, that had studied the retention in care for people living with HIV in India. Our searches used the terms "(retention in care) OR (retention in programme) AND (HIV) AND (India)". Very limited evidence is available in India describing the retention rates in the world's second largest free antiretroviral therapy (ART) programme in India. Studies done in the programme run clinics have revealed the need for development of effective retention packages for people living with HIV and strengthening linkages with key populations for improving their retention in programme. Studies done in private clinics in India during 2014 have highlighted a long delay from HIV diagnosis to linkage and further attrition during not on ART and on ART phases.

Added value of this study

We conducted the first impact evaluation of the GoI's free ART programme, for the period 2012–17 which included 396 antiretroviral therapy centres (ARTCs) in absence of a baseline comparator. We analysed retention rates and factors associated with lost to follow up (LFU) among people living with HIV registered at ARTC during financial year 2012–2017 in 81 randomly selected ARTCs across India. There was adequate representation from all the states and different geographical regions. Various parameters of programme performance and impact were assessed keeping in mind the changing ART initiation guidelines of the programme.

Implications of all the available evidence

In large scale free treatment programme implementing treat all, and early linkage to treatment is the key policy and implementation intervention to retain people living with HIV in care. While developing the strategies for improving retention in care for people living with HIV should consider the factors associated with LFU status which were males living with HIV, younger age (15–29 years), CD4 counts at registration >350 cells/mm^3, ever having tuberculosis and being in 'not on ART' care. Other innovative interventions to enhance engagement of people living with HIV with ARTCs are recommended.

Introduction

Government of India's free antiretroviral therapy (ART) programme is the second largest free ART programme in the world.[1] People living with HIV in India receive lifetime free ART through this programme which also includes HIV testing, clinical and laboratory monitoring for treatment initiation and continuation.

India's ART programme, initiated in 2004 at eight centres, expanded significantly, and, 6845 people living with HIV were receiving ART across 25 ART centres (ARTCs) by the end of its first year.[1–3] These centres registered all people living with HIV and followed those who were yet to qualify to receive ART as per prevailing CD4 count cutoffs for ART initiation of ≤200 cells/mm^3 (2004–2009), at six monthly intervals.[4] The programme defined such individuals as people living with HIV 'not on ART' because they were registered but not eligible for ART initiation as per the prevailing CD4 cutoffs. They were called for follow up every six months, till ART was initiated. Once the people living with HIV were started on ART, they were identified as 'On-ART' in the programme and had to visit ARTC for monthly dispensing of antiretroviral (ARV) drugs and 6 monthly CD4 cell count estimations. People living with HIV underwent various procedures like counselling, medical examination, specimen collection for various tests including CD4 and drug dispensing as appropriate during the ARTC visit. The individuals who received ART were also provided adherence counselling.

In the early phase of the ART programme in India, when ART was initiated at CD4 ≤200/mm^3, higher mortality was noted in cases with advanced immunosuppression which highlighted the need for timely diagnosis and ART initiation.[5,6] In the subsequent years, the programme adopted changes in the CD4 guidelines for ART initiation, based on the global evidence supporting reduction in morbidity and mortality with early ART initiation. The CD4 cutoffs for ART initiation were raised to 250 cells/mm^3 or less during 2009–2012 and 350 cells/mm^3 or less during 2012–2016.[6,7] After the release of results from landmark multi-centric international clinical trials, the ART initiation guidelines further raised the CD4 cutoffs to 500 cells/mm^3 or less during July 2016–June 2017.[8] The crucial role of ART in prevention of transmission was established through clinical trials and two different cohort studies. After June 2017, India adopted the 'treat all' policy under which ART was initiated regardless of CD4 count to prevent further transmission of HIV.[1–3]

With these revisions in ART initiation guidelines the number of new cases of people living with HIV requiring ART increased over time and the National AIDS Control Programme (NACP) of India responded by increasing the number of ART centres across the country. Within a decade of the programme, during 2004–2012 there was a massive scale up in the number of ART centres to 355, providing ART to 516,412 people living with HIV. In the subsequent five years an additional 176 ARTCs were initiated and 1,050,326 were receiving ART by 2017.[1–3]

The sustained success of any large-scale long-term treatment programme depends upon regular engagement in care, which is called 'retention in care' (RIC). A key indicator of RIC is people living with HIV lost to

follow up (LFU) after registration at an ARTC. The national strategic plan for HIV/AIDS and STI prepared by National AIDS Control Organisation (NACO) in 2017 reported a 'cumulative' LFU of 10% and 12-month retention on ART at 70%.[3] This is one of the key implementation challenges faced by any free ART programme. LFU among people living with HIV on ART may lead to drug resistance, resulting in the transmission of drug-resistant HIV infection. Resistant HIV infection will impose additional cost to the programme and make the care for people living with HIV difficult. In addition, LFU could result in mortality, although in other cases mortality could be a cause of LFU. In either case, it becomes challenging to count the deaths in the programme and conduct a realistic assessment. Retention of people living with HIV on ART across the continuum of HIV care and maintaining adherence level of ≥95% has been identified as one of the key priorities by the NACP.[9]

The classic ARTCs were in the Medicine department of a Government Medical College or district or subdistrict of any other government hospital based on the prevalence of HIV in that particular area and capacity of that hospital to deliver comprehensive ART related services to people living with HIV. The services included screening of people living with HIV for ART initiation, monitor patients in not on ART Care and initiate ART as and when they become eligible, monitoring and managing side effects of ART, CD4 testing and supply of antiretroviral (ARV) drugs and drugs required for treatment of opportunistic infections.[10]

We conducted the first impact evaluation of the Government of India's free ART programme, for the period 2012–2017 which included 398 ARTC. In this article we analysed retention rates and factors associated with LFU among people living with HIV registered at ARTC during financial year (FY) 2012–2017 (hereinafter referred to as 'reference period') in 81 randomly selected ARTCs across India.

Methods

The impact evaluation of ART under NACP was led by Indian Council of Medical Research-National AIDS Research Institute (ICMR-NARI) and data collection for this study was carried out in collaboration with ICMR-National Institute of Cholera and Enteric Diseases (ICMR-NICED), ICMR-National Institute of Epidemiology (ICMR-NIE), ICMR-National Institute of Medical Statistics (ICMR-NIMS), ICMR-National Institute for Research in Environmental Health (ICMR-NIREH), and ICMR-National Institute for Research in Tuberculosis (ICMR-NIRT).

The study protocol was approved by the institutional ethics committee of ICMR NARI (Approval protocol number NARI -EC-2017 10). Subsequently, the same protocol was also approved by the institutional ethics committee of NACO and all other participating sites (NARI-EC Protocol Number: NARI EC/2017-10). This analysis is based on secondary data and hence informed consent was waived off. This study was conducted from April 2018 to August 2020.

Sampling of ARTC

The type of ARTC, its geophysical location and burden of people living with HIV at ARTC were used as criteria for stratification before sampling. NACO had provided a list of 396 ARTCs and it was decided to extract data from 20% ARTCs. There were five types of treatment centres for people living with HIV under NACP in India viz. classic ARTC, public private partnership (PPP) ARTC, Centre of Excellence (CoE Adult), ART plus centre and paediatric Center of Excellence (pCoE). Though PCoE is for treating paediatric patients, adults also visit the PCoEfor routine care. We had selected 20% of the ARTCs from each type.

An ARTC established in collaboration with a private partner (as a part of their corporate social responsibility with the same functions as ARTC in a government setup) was called PPP ARTC.

CoE additionally provided second line and alternative first line ART, training, research and mentored the other ART centres linked to them. It also housed the State AIDS Clinical Expert Panel (SACEP) responsible for assessment of patients with suspected treatment failure to first line ART for initiation of second line ART.[10]

ARTC plus was an upgraded ARTC where in addition to routine services of ARTC second line ARV drugs were also supplied as per eligibility. pCoE were supposed to directly provide quality care to HIV positive children and also build capacity of other ARTCs in their respective regions for the same.[11]

Considering the first criterion of stratification as the type of ARTC, 20% of ARTC were selected randomly from each of the three types (2/10 CoE, 1/5 PCoE, and 2/13 PPP ARTCs). Thus, from 33 states or Union Territories (UT) of India as of 2018, 81 ARTCs were selected for secondary data extraction (Fig. 1).

Databases

We extracted data using standard tools from patient records (white card) with a unique identification number ('not on ART' number or ART number) maintained at the ARTC. The record is updated by counsellors, medical officers, nurses, and lab technicians for each person living with HIV during their scheduled visit at the ARTC. The record captures demographics, family history, (completed at baseline) and history of illness, laboratory test results, adherence, ART details, comorbidities and also describes the 'status' of the person living with HIV at latest visit to ARTC as not on ART or alive on ART or LFU or death.

Data was extracted from other secondary data sources, the computerised databases of the NACP namely

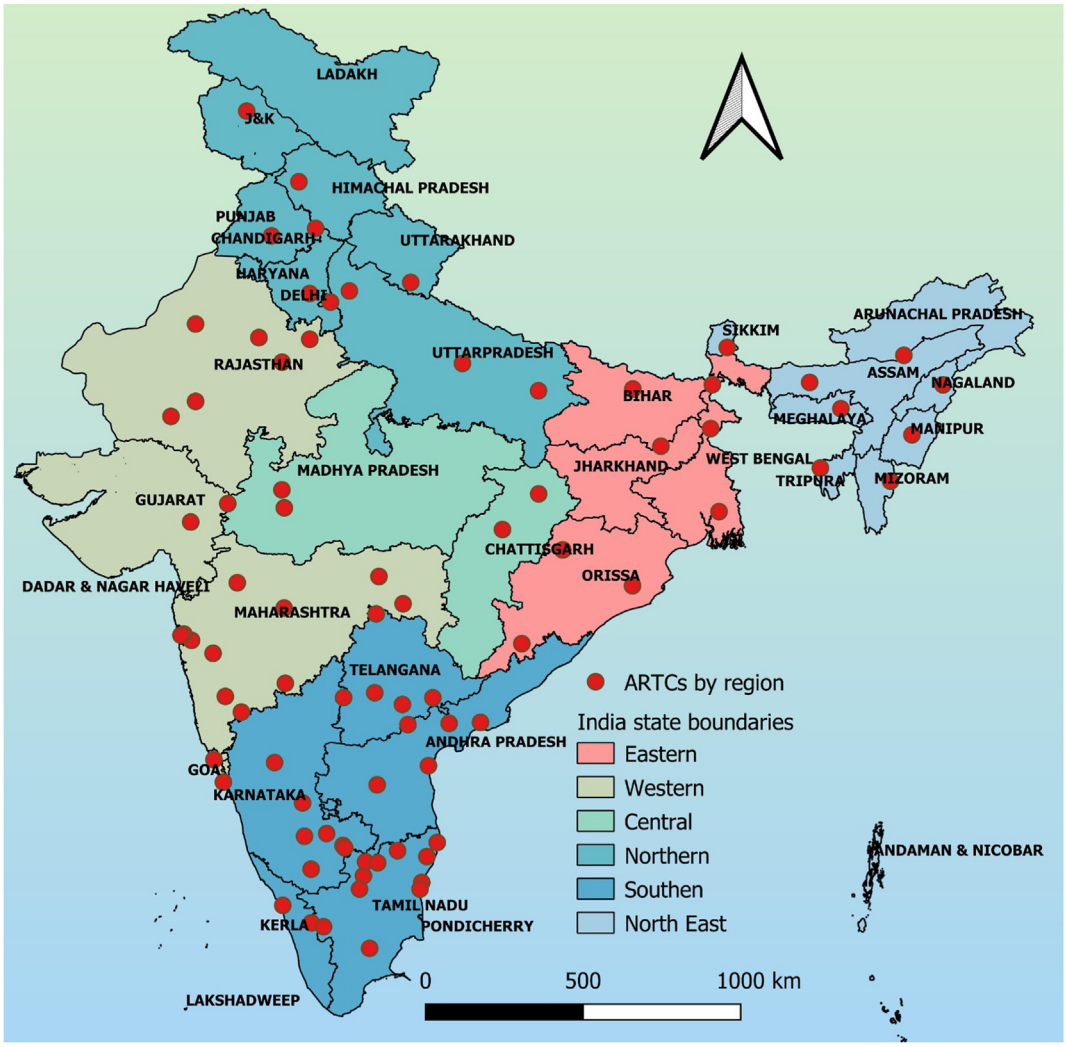

Fig. 1: **Location map of 81 selected centres in India for secondary data extraction under impact evaluation study.**

Inventory Management System (IMS) and Master Line List (MLL).[2] IMS is a SQL (structured query language) based online system and MLL an Excel based database are maintained by ARTCs.

Data collection

A structured tool was developed to extract data from clinical records of people living with HIV maintained at ARTC and was named as secondary data extraction (SDE) tool. Data were extracted for reference period for all registrations of people living with HIV (from April 1, 2012 to March 31, 2017, and their follow ups till March 31, 2018) at the selected 81 ARTCs of India by trained investigators or interns. Data entry, cleaning and merging was done centrally at the lead institute by the study team and the final dataset was called as SDE database. Incomplete records were excluded.

Development of dataset for analysis

A comprehensive dataset was developed by merging SDE data set with the two existing complementary datasets in the programme, IMS and MLL to get a rich data set with all essential variables. Data merging was done using the unique identifiers 'not on ART' number, ART number and ARTC code. Other variables providing crucial information such as ART start date, age, gender, status of person living with HIV, baseline CD4 date, baseline CD4 value, latest CD4 date, latest CD4 value, education, and occupation were compiled during the merging process.

'People living with HIV not on ART'- were defined as all those who were registered but not eligible for ART initiation and had never initiated ART through the reference period. 'People living with HIV on ART'- were the ones who were already on ART or initiated on ART

during the reference period as per prevailing guidelines. These guidelines included CD4 cutoff values, AIDS defining illness, and pregnancies.

Lost to follow-up (LFU) - based on the programme definition, The 'people living with HIV not on ART' were labelled as LFU when they missed two consecutive scheduled visits and were then untraceable. 'People living with HIV on ART' who missed scheduled visits for 3 consecutive months and were untraceable, were considered as LFU. All those who remained in the programme, without being LFU are labelled as 'Retained participants'. 'LFU status' was considered as an event for 'time to event' analysis. In this analysis, we have presented retention rates, calculated as the complement of the LFU probability (i.e., retention = 1 – LFU probability). The last available date attended by the people living with HIV at ARTC for any procedure was considered for the last follow-up (FU) date for calculation of retention.

The duration of follow up was calculated as difference between dates of registration and last visit for 'people living with HIV not on ART' and difference between dates of ART initiation and last visit for 'people living with HIV on ART'.

All people living with HIV were included in the analysis as long as they were alive and remained in the

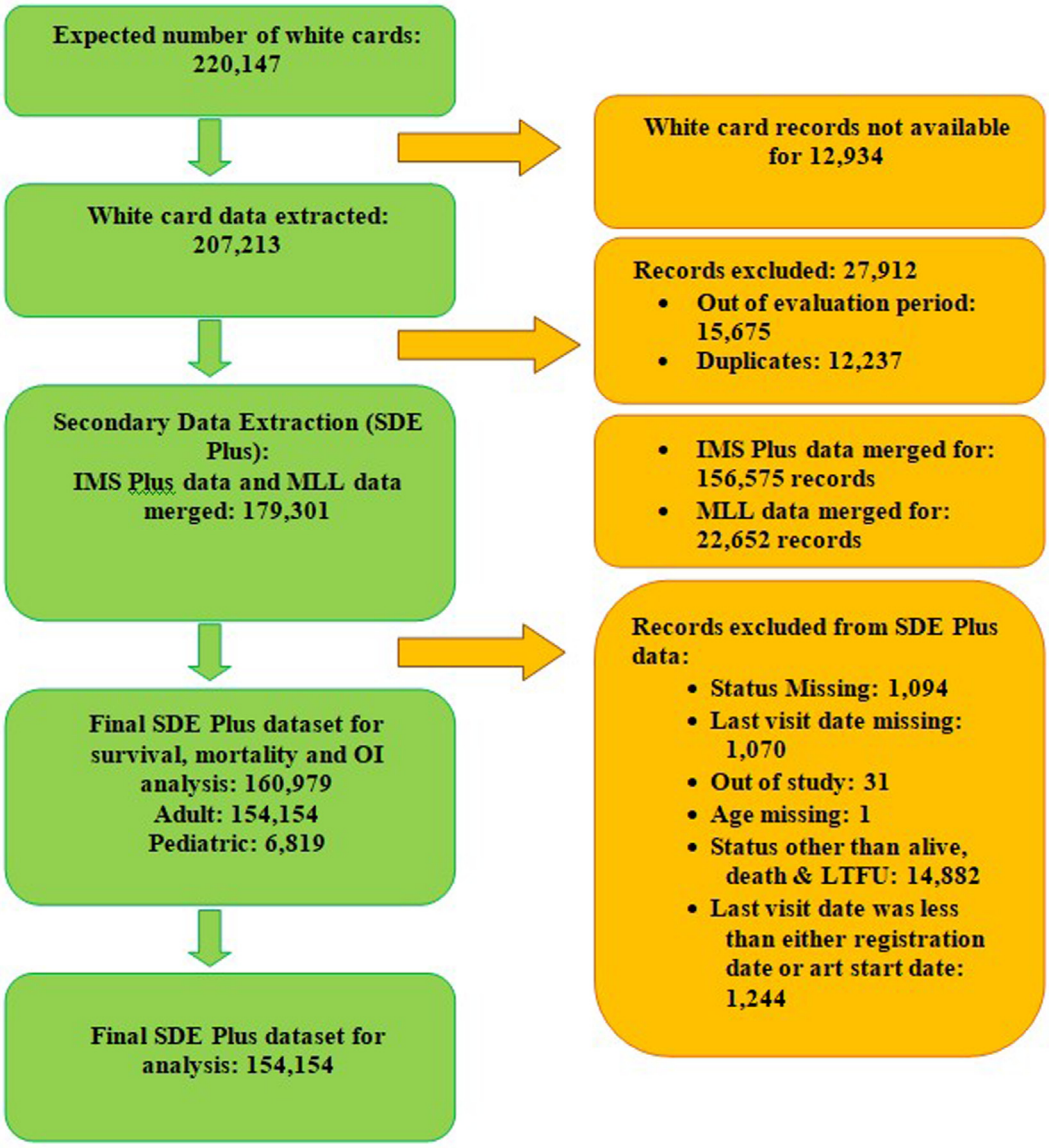

Fig. 2: Steps for creating dataset for analysis.

Characteristic	Not on ART [n = 27,318] % (n)	On-ART [n = 126,836] % (n)	Overall [n = 154,154] % (n)
Gender			
Men	59.3 (16,191)	54.1 (68,653)	55.0 (84,844)
Women	40.0 (10,940)	45.6 (57,804)	44.6 (68,744)
Transgender	0.7 (185)	0.3 (372)	0.4 (557)
Data missing	2	7	9
Age at registration			
Median (Min-Max)	35 (28, 43)	36 (30, 45)	36 (30, 45)
15–29	29.3 (8006)	22.5 (28,533)	23.7 (36,539)
30–44	47.4 (12,960)	51.1 (64,867)	50.5 (77,827)
45–59	18.8 (5138)	22.0 (27,957)	21.5 (33,095)
≥60	4.4 (1214)	4.3 (5479)	4.3 (6693)
Education			
Did not receive formal education	47.6 (11,316)	39.2 (45,524)	40.7 (56,840)
Primary school	26.6 (6327)	27.4 (31,759)	27.2 (38,086)
Secondary school	22.0 (5227)	27.5 (31,943)	26.6 (37,170)
College and above	3.8 (899)	5.8 (6786)	5.5 (7685)
Data missing	3549	10,824	14,373
Marital status			
Married	61.8 (11,705)	66.6 (65,728)	65.8 (77,433)
Widow	16.3 (3097)	17.9 (17,694)	17.7 (20,791)
Single	15.8 (2998)	10.1 (9940)	11.0 (12,938)
Divorced/separated	5.7 (1072)	5.1 (5028)	5.2 (6100)
Live in	0.4 (81)	0.3 (328)	0.3 (409)
Data missing	8365	28,118	36,483
CD4 count at registration (cells/mm^3)			
Median (Min-Max)	403 (1–1782)	237 (1–1797)	255 (1–1797)
≤200	27.8 (6318)	42.9 (46,692)	40.3 (53,010)
201–350	12.6 (2855)	28.2 (30,722)	25.5 (33,577)
351–500	25.7 (5826)	15.0 (16,368)	16.9 (22,194)
>500	33.9 (7702)	13.8 (15,056)	17.3 (22,758)
Data missing	4617	17,998	22,615

ARTC: antiretroviral therapy centres; ART: antiretroviral therapy.

Table 1: **Characteristics of people living with HIV registered in 81 ARTCs.**

programme within their respective groups. Although people living with HIV with outcomes labelled as 'death' or 'transfer out' to another ART centre as per clinical care requirement were not excluded but censored in the analysis.

Statistical analysis

This analysis was done on people living with HIV whose age at registration was ≥15 years. Baseline characteristics were defined by ART status. Incidence of LFU was calculated per 100 person-years. Life table approach was used for the cumulative probability of LFU (retention = 1 – LFU probability). Cox proportional hazards model was used for investigating association between time for LFU and predictor variables. Hazard Ratios (HR) were calculated, and statistical significance was considered when p value <0.05. Data were analysed using IBM SPSS 24.0. Transgender people living with HIV were excluded from the dataset for time to event analysis because of smaller numbers.

Role of the funding source

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Results

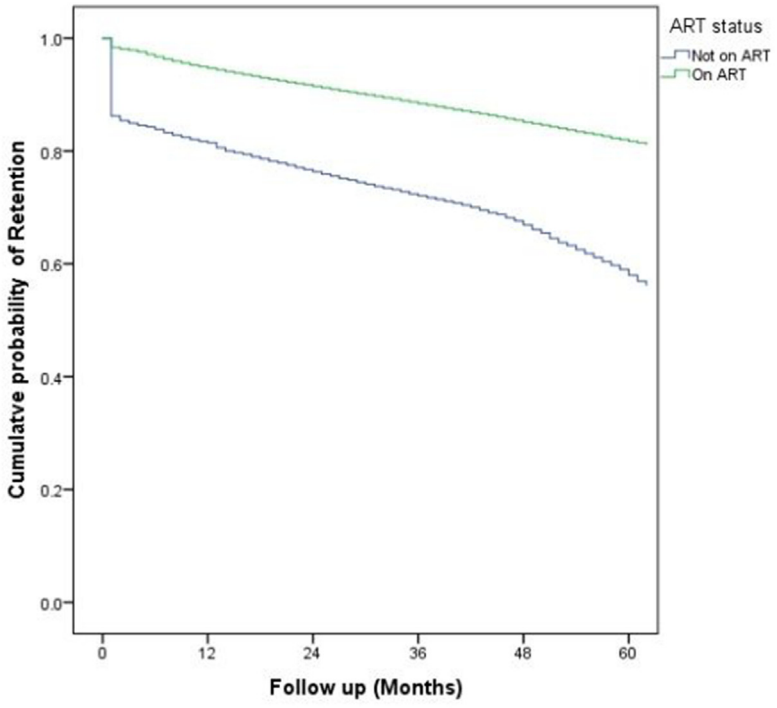
Of 154,154 records of people living with HIV from 81 ARTCs in 33 states or UT of India (Fig. 2) which were analysed, 82.3% people living with HIV were on ART and 17.7% had never been initiated on ART during the reference period. Overall, 55% were men, 44.6% women, and 0.4% transgender. Median age (Q1, Q3) was 36 (30, 45) years, median CD4 count (Q1, Q3) at registration was 255 (123, 421) cells/mm^3. Around 41% were people who did not receive formal education, 65.8% were married, 65.8% had CD4 count ≤350 cells/mm^3 at registration and 19.6% ever had a diagnosis of tuberculosis (TB) during the reference period of the study (Table 1).

People living with HIV not on ART

One-year retention probability was 81%, five-year retention probability was 57% and the probability of retention reduced each year by 4–9% (Fig. 3). Five-year retention probability was less than 50% when CD4 count at registration was between 351 and 500 cells/mm^3. Incidence of LFU was 12.9 per 100 person-years and their proportion was 28.9%. Proportion of LFU was more among women (30.9%) and transgenders (37.8%) as compared to men (27.5%). LFU proportion was 33.8% among those with 15–29 years age at the time of registration. Among those who were LFU and aged 15–29 years, adolescents (15–19 years) were 5.4%. LFU was maximal at CD4 counts >350 cells/mm^3. In the presence of TB as a comorbidity, the proportion of LFU was higher (Table 2).

People living with HIV on ART

One-year retention probability for 'on ART' group was 94% which became 81% at the end of five-years. The probability of retention was reduced each year by about 3–4% (Fig. 3). Five-year retention probability was more than 80% at CD4 ≤200 cells/mm^3 (Fig. 4). During most



	Time (months)	0	12	24	36	48	60
Pre-ART	Population at risk	27,318	18,129	13,849	10,023	5,822	2,626
	Events	3627	192	71	293	69	46
On-ART	Population at risk	126,836	101,492	73,261	50,998	31,182	13,582
	Events	2052	288	203	137	91	39

Fig. 3: **Cumulative probability of retention by antiretroviral therapy (ART) status.**

of our study period ART was initiated when CD4 was below 350 cells/mm^3. Incidence of LFU was 4.3 per 100 person-years and their proportion was 11.1%. LFU proportion was 13.6% among those with age 15–29 years at the time of registration. Among those who were LFU and aged 15–29 yrs, the LFU proportion among adolescents (15–19 yrs) was 7.5%.

When we analysed the LFU who were 15–29 yrs of age it was noted that 7.5% of them were in adolescents (15–19 yrs).

Among people living with HIV 'on-ART', the proportion of LFU, was higher among men (11.6%) and transgenders (14.8%) as compared to women (10.5%), was lower in the age group 30–59 years. LFU was

Characteristic	Not on ART (n = 27,318)		On-ART (n = 126,836)	
	Lost to follow-up % (n)	Retained % (n)	Lost to follow-up % (n)	Retained % (n)
Overall	28.9 (7906)	71.1 (19,412)	11.1 (14,094)	88.9 (112,742)
Gender				
Men	27.5 (4460)	72.5 (11,731)	11.6 (7965)	88.4 (60,688)
Women	30.9 (3376)	69.1 (7564)	10.5 (6073)	89.5 (51,731)
Transgender	37.8 (70)	62.2 (115)	14.8 (55)	85.2 (317)
Age group (years)				
15–29	33.8 (2710)	66.2 (5296)	13.6 (3879)	86.4 (24,654)
30–44	29.1 (3766)	70.9 (9194)	10.4 (6751)	89.6 (58,116)
45–59	23.3 (1199)	76.7 (3939)	10.0 (2798)	90 (25,159)
≥60	19 (231)	81 (983)	12.2 (666)	87.8 (4813)
CD4 count/mm^3 at the time of registration				
≤200	17.7 (1116)	82.3 (5202)	10.2 (4746)	89.8 (41,946)
201–350	30.8 (879)	69.2 (1976)	13.0 (3986)	87 (26,736)
351–500	40.6 (2367)	59.4 (3459)	10.2 (1676)	89.8 (14,692)
>500	32.4 (2495)	67.6 (5207)	9.0 (1351)	91 (13,705)
Ever had tuberculosis (at or after registration)				
Yes	25.2 (761)	70.6 (17,159)	12.9 (3522)	89.4 (89,039)
No	29.4 (7145)	74.8 (2253)	10.6 (10,572)	87.1 (23,703)

Note: The frequencies may not match with overall numbers in case of missing data.

Table 2: **Characteristics of lost to follow-up by antiretroviral therapy (ART) status.**

highest when CD4 count at registration was between 201 and 350 cells/mm^3. The proportion of LFU among people living with HIV 'on-ART' was higher among those who ever had TB during the reference period (Table 2).

Risk factors for LFU

People living with HIV 'not on ART' had three times greater possibility of being LFU as compared to the people living with HIV 'on-ART' (Adjusted HR: 2.95, 95% CI: 2.85–3.05). Men were more likely to be LFU as compared to women (Adjusted HR: 1.08, 95% CI: 1.05–1.11). If a person living with HIV had CD4 at registration between 350 and 500 cells/mm^3 then the possibility of being LFU was 21% (Adjusted HR: 1.21, 95% CI: 1.16–1.26). If a person living with HIV ever developed TB during the reference period considered for the analysis, then they had 15% more possibility of being LFU (Adjusted HR: 1.15, 95% CI: 1.10–1.19) (Fig. 5).

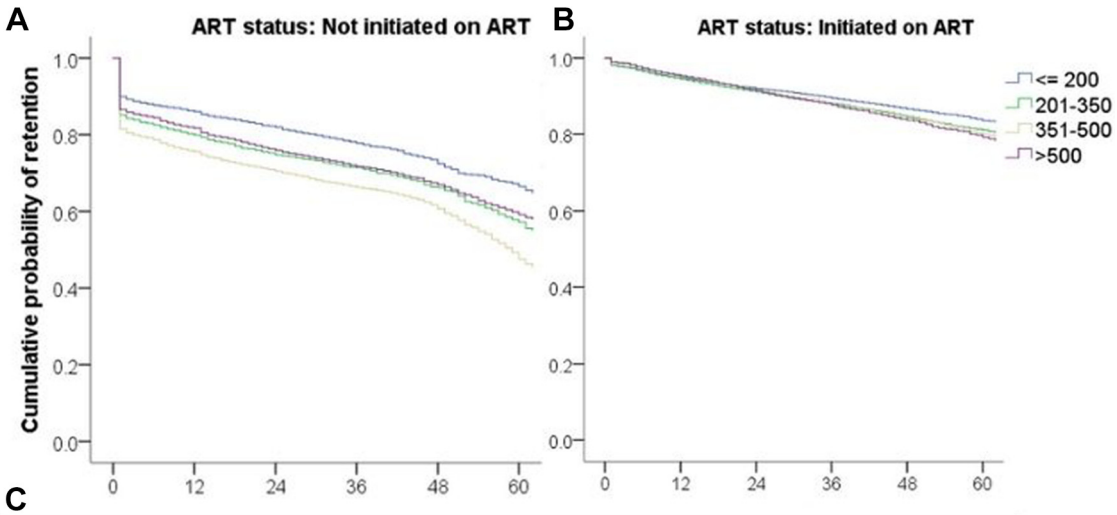
Discussion

The success of any large-scale free long term treatment programme is dependent on retention of patients in care. It is thus one of the key priorities for India's free ART programme which is the second largest such programme in the world.[1] This article, which is part of the first impact evaluation of India's free ART programme, assessed the retention probability among people living with HIV in care, based on ART status during 2012–2017. Our study highlights that antiretroviral treatment was the single largest determinant of retention in care. Among people living with HIV who were 'not on ART', the retention probability reduced from 81% at one year to 57% at the end of five years. On the other hand, people living with HIV 'on-ART' were better retained and with a one-year retention probability of 94% which reduced to 81% at the end of five years. Our study generates important evidence for retention in HIV care prior to HIV eligibility for which limited evidence is available, especially regarding long term retention rates and sociodemographic determinants.[12] Their retention was similar to that of people living with HIV 'not on ART' at the end of one year.

India's NACP adopted the 'treat all' strategy since July 2017. This intervention was anticipated to improve the clinical outcomes for people living with HIV in terms of increase in CD4 count, viral load suppression, reduction in opportunistic infections, and reduction in risk of transmission to sero-negative partners.[13] There were 25% LFU in 2017–18 and 2018-19 among those who were alive and were on ART and it has reduced to 11% in 2022–23.[14]

However, it would be good to pre-emptively develop strategies for retention, identifying people living with HIV who are likely to become LFU such as younger people living with HIV, those who ever had TB, and males, for greater attention from the beginning. These factors related to LFU status highlighted by our study, also reiterate the finding from a cohort study done in India in 2013.[15] Once such people living with HIV are identified, targeted retention efforts for them can be designed. Based on the findings from our study, it is recommended to introduce innovative interventions to retain people living with HIV in the first year itself because the probability of LFU was maximum in the first year. A study conducted in a programme clinic in India suggested 3 monthly CD4 count estimation at least during the first 12 months of registration to improve retention among people living with HIV 'not on ART'.[16] A tertiary HIV care centre in Chennai, India reported an overall dropout rate was 38.1 per 100 person-years—the majority of the drop outs occurred within 6 months from registration.[17] In current context in India, after adoption of 'treat all' strategy, further research is recommended to identify factors for improving retention and design relevant strategies at least for first year following ART initiation as supported by multiple evidences from India.

In addition, reduction of time to ART initiation may be a useful intervention.[18] A study from Mozambique suggested reduction of unnecessary visits to ARTC before and after ART initiation as an intervention to improve retention. However, in our paper, one of the important factors that differentiated the two groups was that people living with HIV 'on ART' had more frequent



C

CD4 count		Not initiated on ART							On ART				
Time (months)			12	24	36	48	60		12	24	36	48	60
≤ 200			0.90	0.85	0.81	0.72	0.66		0.98	0.92	0.89	0.86	0.83
201-350			0.79	0.74	0.71	0.65	0.56		0.94	0.91	0.88	0.84	0.81
351-500			0.75	0.70	0.66	0.59	0.46		0.95	0.91	0.88	0.85	0.80
>500			0.81	0.75	0.71	0.66	0.58		0.95	0.91	0.87	0.84	0.79
Time (months)		0	12	24	36	48	60	0	12	24	36	48	60
≤ 200	Population at risk	6,318	2,958	2,106	1,499	870	426	46,692	36,929	27,662	19,651	12,224	5,515
	Events	573	23	16	8	10	6	846	92	43	47	29	10
201-350	Population at risk	2,855	1,888	1,458	1,112	674	332	30,722	26,762	20,584	14,627	9,351	4,197
	Events	410	16	4	7	8	9	590	82	66	33	33	18
351-500	Population at risk	5,826	4,161	3,428	2,512	1,486	603	16,368	13,317	7,968	5,117	2,766	948
	Events	1068	48	19	10	29	16	183	33	28	9	9	2
>500	Population at risk	7,702	6,060	4,683	3,441	2,084	971	15,056	9,449	5,849	3,676	1,987	689
	Events	1032	82	24	12	19	11	167	24	32	17	5	3

Fig. 4: Cumulative probability of retention by CD4 (CD4 counts in cells/mm^3) at registration. A) Among people living with HIV who were not initiated on ART. B) Among people living with HIV who were initiated on ART. C) Data table showing the cummulative probability of retention.

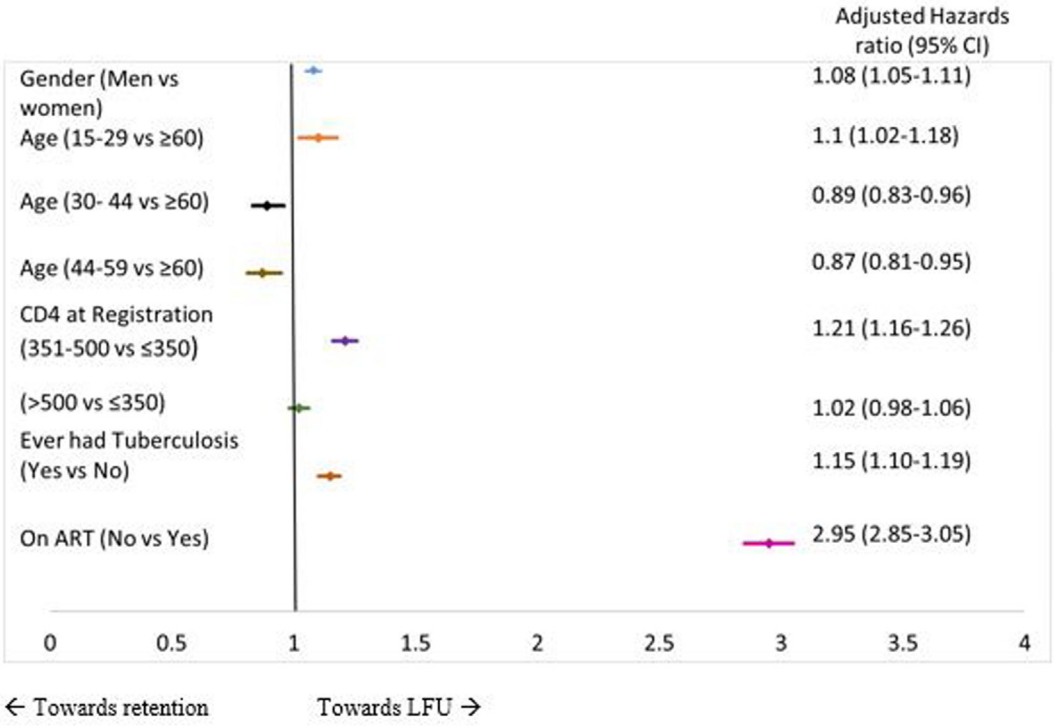


Fig. 5: **Forest plot showing factors associated with lost to follow-up. (Age in years; CD4 counts in cells/mm^3; in ART: antiretroviral therapy)**.

visits for antiviral drug pickup but that also meant that they had more frequent contact with care teams and received more counselling and probably developed better rapport. The same study also suggests other interventions like integrating various services needed by a person living with HIV during their visit to ARTC and redirecting resources to the people living with HIV who are in most need of those resources as useful for improving retention in care,[19] however this analysis does not address those factors.

Thus, the programmatic strategies for improving retention may include reducing the gap between two consecutive visits to ART centre before initiation of ART in the 'treat all' era. A study in low resource setting showed that ensuring the availability of all investigations and their reports needed for ART initiation at one place and a hassle-free immediate initiation of ART after the diagnosis of HIV could be crucial in improving retention.[20] Counter intuitively, a study in Zimbabwe reported that people living with HIV with CD4 count >350 cells/mm^3 was a factor associated with LFU where ART was initiated within 7 days following HIV diagnosis.[21]

One of the challenges and limitations we faced was the extent to which death could have been a reason for LFU. Additionally, death could be either the cause or the result of LFU. Development of notifications to health care staff regarding death of a registered people living with HIV would help to improve programme records and reduce proportion of missing or incomplete records which are assumed as LFU. Developing coordination within and between public health care delivery services, private healthcare providers, and community stakeholder involvement can be some of game changer strategies for improving retention.[22]

The probability of LFU increased subsequently after the first year by 4–9% among people living with HIV 'not on ART' and 3–4% among people living with HIV 'on-ART'. Hence good rapport of the site staff with the people living with HIV could be a key intervention. In the last few years, the NACP has developed various strategies for tracking LFU particularly involving communities of people living with HIV. In addition, differentiated care has been a strategy that has been adopted. Others have suggested developing Community ART Groups by involving peers.[23,24] Specific support groups, use of community stakeholders, grass root health workers for easy dispensing of ART is effective in reducing the travel cost, time and loss of daily wages for people living with HIV.[22] However, some of these need to be studied in a feasibility mode.

Various studies conducted in India (including ours) and other countries reported 'being male' as one of the predictors for LFU.[21,25–28] In India, male adults are often

sole bread winners for the family. Loss of daily wages while attending ARTC could be one reason for LFU among larger proportion of males. Additionally, in India's largely sexually and injecting drug use (IDU)-driven epidemics, men were affected before women and were likely to be sicker and/or acquire TB. In our analysis the median CD4 count at registration among those who were LFU and 'not on ART' was 436 cells/mm^3 and it was 246 cells/mm^3 among those who were 'on ART'. Studies conducted across different Asian and African countries, including ours, have reported that younger people living with HIV were more likely to be LFU as compared to older people living with HIV.[26–28]

In this study, ever having TB during the study reference period was found to be one of the reasons for LFU. The diagnosis of TB leads to increase in pill burden for people living with HIV 'on-ART', side effects of TB treatment, deterioration in quality of life resulting in increase in frequency to visit multiple health care facilities explaining the reason for increase in LFU in such cases. Intensive targeted counselling for people living with HIV diagnosed with TB for improving their adherence and retention in care would be useful.

It has been noted that the incidence of TB among people living with HIV 'on-ART' is higher in the first six months immediately after initiation of ART as a part of immune reconstitution inflammatory syndrome (IRIS).[29] TB can also occur as an opportunistic infection due to a delay in initiation of ART among people living with HIV who have a low CD4 count. Therefore, it is important to initiate ART immediately after diagnosis and screen the people living with HIV regularly for TB even when they are 'on-ART'.[30]

Probability of LFU was less than 50% among people living with HIV 'not on ART' whose CD4 count at registration was between 351 and 500 cells/mm^3. A study conducted in the southern state of Karnataka reported four in 10 individuals not on ART care were LFU within one year of registration.[31] During our study period, most of the time ART was initiated below 350 CD4 cell/mm^3 which might have resulted in occurrence of any opportunistic infection or death (due to delay in initiation of ART) leading to LFU status. HIV care clinics in the private sector from India have also noted a long delay from HIV diagnosis to linkage as one of the factors responsible for attrition during not on ART phase.[32]

Government of India's free ART programme has introduced the test and treat policy since July 2017 so it might reduce the probability of LFU. It has been reported that policies supporting expansion of ART uptake such as fast-track ART initiation on the day of diagnosis and drug dispensing, differentiated service delivery models for ART and support through health care providers and community stakeholders may improve retention in HIV care.[33,34]

Few deaths among people living with HIV might not have been reported to the programme and get counted as a LFU case in absence of up-to-date contact information. Lack of updated contact information of people living with HIV is also problematic when that case becomes LFU. As a result, the records remain incomplete or missing. Missing records were also encountered during analysis of this study and is a limitation of this study. Therefore, contact information of people living with HIV and their caretakers or their family members should be enquired during every visit so that updated information will be helpful to trace people living with HIV if they are LFU. Involvement of family members and community-based organisations as primary sources of support has been found to be an important factor for improving retention in care in India.[35] Digitisation of records of people living with HIV at ARTC is essential and will be useful in developing inbuilt monitoring and evaluation systems. A recently upgraded system is likely to fill this need and make a difference in India. Such systems can give regular feedback to the programme implementation and necessary modification can be done based on real-time data.

However, we reiterate that the duration of retention for pre-ART (not on ART) people living with HIV group, was calculated from the date of registration to the date of the last visit. For the 'on-ART' group, the period during which people living with HIV were not eligible for ART prior to the date of ART initiation was not included in the analysis and the retention period was defined as the time from ART initiation to the last visit. This distinction in the timeframes used to estimate retention in the programme was critical for addressing potential bias stemming from the longer duration of care experienced by the pre-ART group until their eligibility for ART initiation.

New programmatic strategies for improving retention of people living with HIV in care may benefit by focussing on males, younger ages (15–29 years), CD4 at registration, history of or new TB diagnoses and early intervention within the first year. Intensive adherence counselling and additional support is recommended to people living with HIV and with TB to ensure retention in the programme. Though India has already adopted the 'treat all policy', findings from our study generate significant evidence on other retention strategies and key lessons for other countries where this policy is not yet adopted. In large scale free treatment programme implementing treat all, and early linkage to treatment is the key policy and implementation intervention to retain people living with HIV in care.

Contributors

SC: Conceptualisation, data management, data analysis, writing original draft, manuscript review and approval; SS: Data management, data analysis, writing original draft, manuscript review and approval; MM: Conceptualisation, writing and editing original draft; SB: Data management, data analysis, writing original draft, manuscript review and approval; RT: Data management, data analysis, manuscript review and approval; TB, SPT, DS, SB, SD, YS, RT, DK, BSK, AKP, CD: Regional project coordination, manuscript editing, manuscript review and approval; SVG: Conceptualisation and methodology, reviewing and

finalising the manuscript, overall project coordination. All authors have read and agreed to the published version of the manuscript.

Data sharing statement

The data underlying the results presented in the study are available from the National AIDS Control Organisation, Ministry of Health & Family Welfare, Government of India.

Editor note

The Lancet Group takes a neutral position with respect to territorial claims in published maps and institutional affiliations.

Declaration of interests

We declare no competing interests.

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ART-IE Study Team

Writing group

ICMR – National Institute of Translational Virology and AIDS Research (NITVAR): Sheela Godbole (Director, Director & Scientist G); Dr. Megha Mamulwar (Scientist 'C'); Ms. Suvarna Sane (TO, 'C'); Ms. Shilpa Bembalkar (TO, 'B'); Ms. Shweta Chidrawar (Study coordinator, Data Manager & Statistician); Rachana Thakur (Data Coordinator); Dr. Deepak Khismatrao (Project manager).

ICMR-National Institute of Epidemiology, Chennai: Dr. Tarun Bhatnagar (Scientist E).

ICMR-National Institute for Research in Tuberculosis, Chennai: Dr. Srikanth P. Tripathy (Ex Director-in-charge & Scientist G); Dr. Bhavani P K (Scientist D); Dr. Shrinivasa B M (Scientist B).

ICMR-National Institute of Medical Statistics, New Delhi: Dr. Damodar Sahu (Scientist F).

ICMR-National Institute of Cholera and Enteric Diseases (NICED), Kolkata: Dr. S Dutta (Director & Scientist G); Subrata Biswas.

ICMR-National Institute for Research in Environmental Health, Bhopal: Dr. Rajnarayan R Tiwari (Director & Scientist G); Dr. Yogesh Sabde (Scientist E).

National AIDS Control Organization (NACO): Dr. Chinmoyee Das (National consultant, CST); Bhawani Singh Kushwaha; Anoop Kumar Puri.

Implementation group

ICMR – National Institute of Translational Virology and AIDS Research (NITVAR): Dr. Raman Ganagakhedkar (Ex-Director in charge, Director in charge & Scientist G), (Current affiliation-Distinguished Professor, Faculty of Medical & Health Sciences, Symbiosis International (Deemed University), Pune); Dr. Samiran Panda (Ex-Director, Director & Scientist G); Dr. Smita Kulkarni (Scientist 'G'); Dr. Manisha Ghate (Scientist 'F'); Dr. Radhika Brahme (Scientist 'C'); Mr. Rajesh Yadav (PTO); Mr. Amit Nirmalkar (TO, 'B'); Mrs. Shradha Gurav (TO, 'A').

Consultants: Prof. DCS Reddy; Dr. Yujwal Raj.

ICMR-National Institute of Epidemiology, Chennai: Dr. Manoj Murhekar (Director & Scientist G); Mr. K. Boopathi (Senior Technical Officer).

ICMR-National Institute of Medical Statistics, New Delhi: Dr. M. Vishnu Vardhana Rao (Director & Scientist G); Prof Dr. Arvind Pandey (Ex-Director, Director & Scientist G); Dr. Saritha Nair (Scientist D).

Institute of Economic Growth, Delhi: Dr. Indrani Gupta (Professor); Ms. Avantika Ranjan (Research assistant).

Facilitating group

Dr. Naresh Goel (Deputy Director General); Dr. R. S. Gupta (Ex-Deputy Director General); Dr. Manish Bamrotiya (Ex-National consultant, CST); Dr. Neha Garg (Associate consultant, CST).

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