

Improvement in Survival of People Living with HIV/AIDS and Requirement for 1st- and 2nd-Line ART in India: A Mathematical Model

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Predictions on the future number of individuals who will require second-line antiretroviral therapy (ART) (among the individuals who are currently infected with HIV and future possible new infections) have not been generated since the initial estimates made by the World Health Organization for Treatment 2.0. As part of the preparatory activity to assist the National AIDS Control Organization (NACO) in India for the fourth phase of the National AIDS Control Program (NACP IV) (2012-2017), mathematical models were developed describing the survival dynamics in people living with

HIV on first-line antiretroviral therapy (ART-1),¹ second-line antiretroviral therapy (ART-2),² and No ART in those who are not detected by the system. Since the launch of the free second-line antiretroviral therapy (ART-2) to people living with HIV/AIDS (PLHIV) in India during 2008 [1], there has been a slow recruitment into ART-2 until the end of 2010 (with an anticipated ART-2 number around 2,000). NACO, the apex body of the government of India, announced in November 2010 that it will provide ART-2 to all the first-line ART individuals who are currently enrolled either in government programs or in private centers [2] when they become eligible for the treatment.

As part of a model explaining the trends in AIDS-related mortality and incidence [3], we have constructed a submodel for understanding the survival trends in PLHIV receiving first-line and second-line ART during the next phase and beyond in India [4]. Model analysis reveals that from 2013 onwards the number of people eligible for ART-2 could gradually increase to around 100,000, with a concurrent decline in individuals who are eligible

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¹First-line therapy is given when the count of CD4/ml reaches below 350 in an individual who has been detected with HIV.

²Second-line antiretroviral therapy is given to HIV-infected individuals who have developed drug resistance to first-line therapy.

for ART-1 (peak attained in 2012 at above one million) if case detection remains at current levels. We project that there will be 0.6 million PLHIV on ART-1 by the end of 2011. At the end of the NACP IV period (i.e., 2017), the number of eligible PLHIV on ART-1, ART-2, and No ART will be around 0.49 million, 96,000, and 91,000 respectively. Our submodel takes into consideration parameter values for the incubation period with and without ART from the references listed in the recent UN population perspectives [5]. Instead of two years [5] of mean survival after AIDS without ART, we have adopted four and a half years as the mean survival period without ART. Sensitivity analysis was performed on two key parameters: namely, recruitment rate of ART among people eligible for first-line, and rate of development of resistance to the first-line therapy (see Figure 1). The values in the legends in Figure 1 are annual recruitment rates into ART-1, and legends in Figure 2 are rates of development of resistance to the first-line ART. We have also generated model-based output based on two years mean survival after AIDS without ART for the period 2007–2017, which we have not presented in this short communication but have shared with senior officials at NACO. Care and support systems in the recognized government centers need strengthening in the wake of new ART-2 projections to facilitate accurate diagnosis of resistance. It is important to build on the success of the third National AIDS Control Program, NACP III (2007–2012), and address the emerging issues such as second-line ART during the fourth phase of the program. If the present level of recruitment to ART-1 is sustained during the next phase, there will be around 69,000 people who will be cumulatively eligible for ART-2 by the end of 2017. The model took into account the dynamic interaction of ART-1 and ART-2 on the pool of eligible PLHIV and the impact on survival within the PLHIV pool. Such modeling schemes are new to the literature; hence we could not draw any comparative conclusions on the number of second-line ART people during NACP IV. These results have implications not only for India but for other countries—for example, Brazil, Nigeria, Russia, etc.—which have successful first-line therapy and are initiating second-line therapy.

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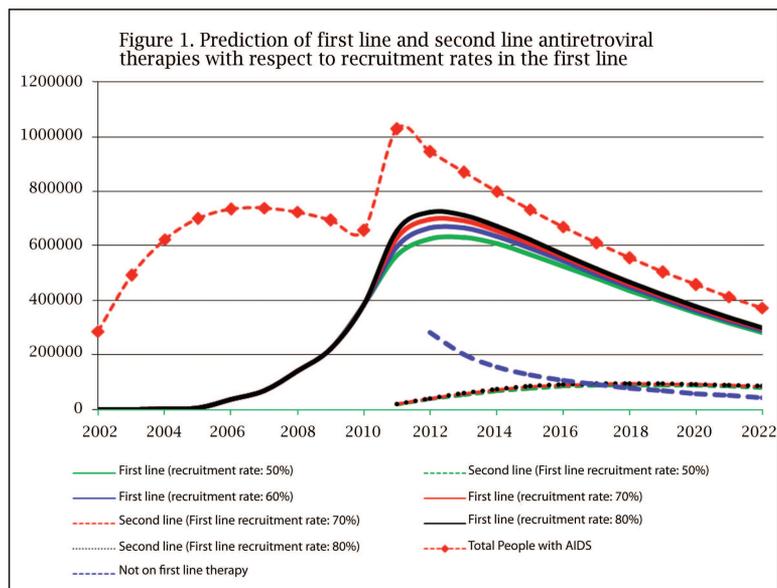


Figure 1.

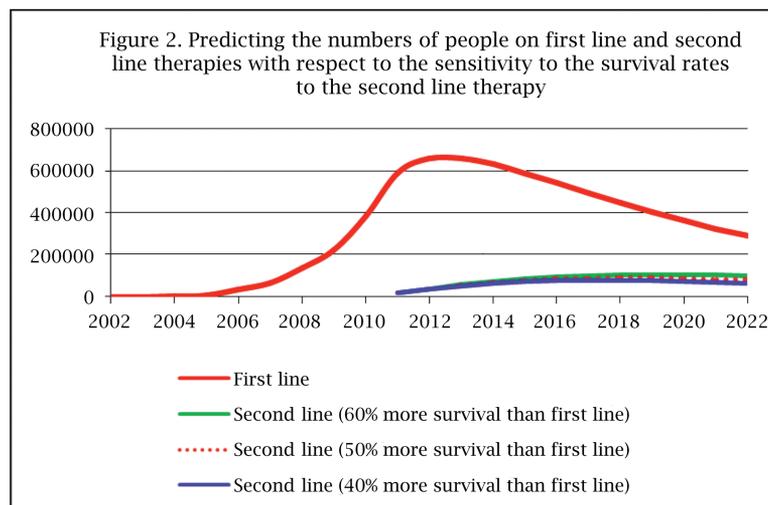


Figure 2.

and corrections from Professors Vidyanand Nanjundiah and Nilanjan V. Joshi, Indian Institute of Science, Bangalore, helped to improve clarity in earlier drafts. Dr. Cynthia Harper, Oxford, read the paper for English language before final revision and assured us that everything was all right. We are indebted for their valuable time.

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2. National Guidelines on Second-Line ART for Adults and Adolescents, NACO report (2011), <http://www.nacoonline.org/upload/Care%20&%20Treatment/NACO%20guidelines%20for%20second%20line>

Table 1: Parameters.

Parameter	Description	Value	Reference
α_1	Mean incubation period during pre-ART period	9.2 years	1
δ_1	Mean survival period among AIDS without treatment	2, 4.5 years	2, Assumption
p_1	Annual rate of recruitment in ART-1	58.67 %	**
ρ	Annual rate of development of resistance to ART-1	4 %	Assumption
δ_2	Mean survival period among AIDS individuals with ART-1	9.5 years	3
δ_3	Mean survival period among AIDS individuals with ART-2	5.2 years	4
r	Annual growth rate of people living with HIV	-0.03	*

* Calculated as weighted rate of decline in last three years

** Calculated from model output and actual data

20ART%20April%202011.pdf (browsed on 14 September 2011).

3. ARNI S. R. SRINIVASA RAO, THOMAS KURIEN, SUDHAKAR KURAPATI, BHAT RAMESH, and P. K. MAINI (2011), working paper in progress, earlier version of the draft paper was prepared as input for the preparatory process for the Fourth Phase of National AIDS Control Program, NACP-IV (2012-17), National AIDS Control Organization (NACO), Department of AIDS Control, Ministry of Health and Family Welfare, government of India.
4. A dynamical model was developed with flow of infected people to the AIDS compartment due to disease progression, and then a proportion of them were recruited to the ART-1 compartment. Due to resistance, a proportion of people on ART-1 will move to ART-2. The results were presented to government officials during July-August 2011. Modeling equations and descriptions appear in the appendix.
5. United Nations, Department of Economic and Social Affairs, Population Division (2006), World Population Prospects: The 2007 Revision.

Appendix

We have developed a mathematical model for predicting the number of people who are eligible for ART-1 and ART-2 and who will be on ART-1 and ART-2 beginning in 2011 in India. We carried out the modeling in two phases: in the first phase we estimated the number of individuals who developed AIDS after HIV infection and the number eligible to receive ART-1 after subtracting annual deaths before people were ready to be given therapy. The modeling equations for describing the process are:

$$\begin{aligned} \frac{dX_1}{dt} &= rX_1 - \alpha_1 X_1, & \frac{dX_2}{dt} &= \alpha_1 X_1 - \delta_1 X_2, \\ \frac{dX_3}{dt} &= \alpha_1 X_0 - p_1 X_3 - \delta_1 X_3, \\ \frac{dY_1}{dt} &= p_1 X_3 - \rho Y_1 - \delta_2 Y_1, & \frac{dY_2}{dt} &= \rho Y_1 - \delta_3 Y_2. \end{aligned}$$

Here X_1 is the number of infected people before developing AIDS, X_2 is the number of people who have full-blown AIDS in the scale-up period, X_3 is the number of people who have full-blown AIDS after removing annual recruited people on ART-1

and annual deaths without ART-1, Y_1 is the number of people on ART-1, and Y_2 is the effective number of people on ART-2. After we projected X_1 values for the predominantly No ART period, we used the model below for projections of the number of people on ART-1 and ART-2 during post ART scale-up years, i.e., from the middle of NACP III years and for the NACP IV period.

The parameter descriptions and values are provided in Table 1. Reciprocals of the parameter values are used in the model wherever the parameter has units in time.

References for Appendix

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3. J. STOVAR et al. (2006), Projecting the demographic impact of AIDS and the number of people in need of treatment: Updates to the spectrum projection package, *Sexually Transmitted Infections*, Vol. 82, Suppl. 3, iii, 45-50.
4. Monitoring of Antiretroviral Therapy in Resource-Limited Settings: Discussion (http://www.medscape.com/viewarticle/726673_4) (browsed on 6 July 2011).