Adoption of the 2015 World Health Organization guidelines on antiretroviral therapy: programmatic implications for India

Bharat Bhushan Rewari1, Reshu Agarwal2, Suresh Shastri3, Sharath Burugina Nagaraja4, Abhilakh Singh Rathore5

1World Health Organization Country Office for India, New Delhi, India, 2Formerly National AIDS Control Organisation, New Delhi, India, 3State TB Cell, Revised National Tuberculosis Control Programme, Bangalore, India, 4Employees’ State Insurance Corporation Medical College and PGIMSR, Bangalore, India, 5National AIDS Control Organisation, New Delhi, India

Correspondence to: Dr Sharath B Nagaraja (sharathbn@yahoo.com)

Abstract

The therapeutic and preventive benefits of early initiation of antiretroviral therapy (ART) for HIV are now well established. Reflecting new research evidence, in 2015 the World Health Organization (WHO) recommended initiation of ART for all people living with HIV (PLHIV), irrespective of their clinical staging and CD4 cell count. The National AIDS Control Programme (NACP) in India is currently following the 2010 WHO ART guidelines for adults and the 2013 guidelines for pregnant women and children. This desk study assessed the number of people living with HIV who will additionally be eligible for ART on adoption of the 2015 WHO recommendations on ART. Data routinely recorded for all PLHIV registered under the NACP up to 31 December 2015 were analysed. Of the 250,865 individuals recorded in pre-ART care, an estimated 135,593 would be eligible under the WHO 2013 guidelines. A further 100,221 would be eligible under the WHO 2015 guidelines. Initiating treatment for all PLHIV in pre-ART care would raise the number on ART from 0.92 million to 1.17 million. In addition, nearly 0.07 million newly registered PLHIV will become eligible every year if the WHO 2015 guidelines are adopted, of which 0.028 million would be attributable to implementation of the WHO 2013 guidelines alone. In addition to drugs, there will be a need for additional CD4 tests and tests of viral load, as the numbers on ART will increase significantly. The outlay should be seen in the context of potential health-care savings due to early initiation of ART, in terms of the effect on disease progression, complications, deaths and new infections. While desirable, adoption of the new guidance will have significant programmatic and resource implications for India. The programme needs to plan and strengthen the service-delivery mechanism, with emphasis on newer and innovative approaches before implementation of these guidelines.

Keywords: access, AIDS, antiretroviral therapy, HIV, India

Background

Globally, there is a huge momentum for and commitment to expansion of access to antiretroviral therapy (ART) services.1 It is evident from recent studies that early use of ART results in better, long-term clinical outcomes for people living with HIV (PLHIV), as well as an improved broad public health outcome in terms of prevention. The therapeutic and preventive benefits of ART are now well established.2 Worldwide, there has been a steady decline in the incidence of, and mortality related to, HIV. New HIV infections and AIDS-related deaths have decreased dramatically since the peak of the epidemic, with an estimated 36.9 million people living with HIV, 2.0 million new HIV infections and 1.2 million deaths globally in 2014.3 The current focus is on the Sustainable Development Goals (SDGs),4 wherein the world is committed to ending the AIDS epidemic as public health threat by 2030.5 In 2014, the Joint United Nations Programme on HIV/AIDS (UNAIDS) launched the 90–90–90 target, that, by 2020, 90% of all PLHIV will know their HIV status; 90% of all people receiving ART will have viral suppression.5 Although multiple strategies need to be devised to tackle this phase of the AIDS epidemic, the provision of HIV treatment and care for all who need it is central.5

India has the third-highest burden of HIV worldwide, with an estimated 2.1 million PLHIV, which accounts for 6% of the global burden.6 The continued efforts by the National AIDS Control Programme (NACP) in India resulted in a nearly 66% decrease in new HIV infections in the country, between 2000 and 2011.7 Over the last decade, the scaling up of ART services in low- and middle-income countries has saved an estimated 4.2 million lives and 0.8 million child infections.8 In 2003, the World Health Organization (WHO) recommended ART for all those in WHO-defined clinical stages 3 and 4 and those with a CD4 count of ≤200 cells/mm3.9 However, the 2010 revision of these guidelines recommended increasing the threshold for ART initiation to a CD4 count of ≤350 cells/mm3 for all PLHIV who are coinfected with tuberculosis (TB) or hepatitis B virus (HBV), irrespective of their CD4 count.10 In 2013, in its first-ever consolidated guidelines on the use of antiretroviral drugs, WHO recommended raising the threshold...
for initiation of ART to a CD4 count of ≤500 cells/mm³. The recommendations were based on new scientific evidence from the Strategies for Management of Antiretroviral Therapy (SMART) trial and the HIV Prevention Trials Network (HPTN) O02 study. There was also a recommendation for initiation of ART irrespective of CD4 count in certain special groups, such as PLHIV who also have active TB disease or HBV infection with severe chronic liver disease, pregnant and breastfeeding women, children aged under 5 years, and those living in a sero-discordant relationship, to reduce HIV transmission to uninfected partners. In 2015, with the availability of newer scientific evidence from the TEMPRANO (Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa) and START (Strategic Timing of AntiRetroviral Treatment) trials, WHO recommended initiation of ART for all PLHIV, irrespective of WHO clinical staging and CD4 cell count.

Currently, the NACP in India is implementing the 2010 WHO ART guidelines, where all PLHIV with CD4 counts ≤350 cells/mm³, or with TB coinfection or evidence of active hepatitis, are initiated on ART, and children aged under 5 years are initiated on ART irrespective of their CD4 count. In addition, as partial implementation of the 2013 WHO guidelines, all pregnant and breastfeeding women, and children aged under 5 years, who are HIV positive are also eligible for ART. India has also adopted provision of a single pill of tenofovir disoproxil fumarate + 3TC (lamivudine) + EFV (efavirenz), as recommended in the 2013 WHO guidelines. India has, in principle, agreed to adopt the 2013 WHO guidelines for adults for initiation of ART at a CD4 count ≤500 cells/mm³ and is in the process of rolling out implementation.

However, with further revision of the ART guidelines by WHO in 2015, it is important to understand the impact of the additional number of patients on the existing health system and to plan for the required logistics for sustainable delivery of the required services. New recommendations will also have implications for service delivery, which involves an essential additional requirement for antiretroviral drugs, human resources and finances. In view of this, this study aimed to estimate the number of PLHIV who will be additionally eligible for ART on adoption of the 2015 ART guidelines and the implications for the national programme in India.

Provision of antiretroviral therapy in India

India has a heterogeneous HIV epidemic that is highly concentrated geographically in six states, and socially in vulnerable populations, with an estimated national adult prevalence of 0.26% (lower and upper uncertainty bounds: 0.22%, 0.32%) in 2015. The total number of PLHIV in India was estimated at 2.12 million (lower and upper uncertainty bounds: 1.71 million, 2.65 million) in 2015. The delivery of care and treatment services for people living with HIV/AIDS is provided through ART centres. All PLHIV diagnosed at testing centres are referred to the nearest ART centre for registration, where they are assessed for ART eligibility based on WHO clinical staging, CD4 counts and certain conditions. If they are assessed as being eligible for ART according to national guidelines, they are initiated on treatment. The ART centres have been established mainly at tertiary-care hospitals (medical colleges/district or subdistrict hospitals) in the public sector, and all the services of patient management are integrated with the general health system. The NACP supports human resources, CD4 testing, antiretroviral drugs and drugs for management of opportunistic infection. Further, in states with a high prevalence of HIV, the ART services are decentralized to link ART centres, which are established at subdistrict hospitals to improve accessibility for patients. Some well-performing high-load ART centres have been upgraded and designated as centres of excellence and ART-plus centres, to provide second-line ART drugs. All the ART-related services like diagnosis of HIV, assessments of CD4 counts, and ART drugs are provided to patients free of charge. In India, there are more than 880 000 PLHIV receiving ART at 512 ART and 1080 link ART centres.

Methodology

This cross-sectional study involved retrospective review of records and reports routinely recorded under the NACP. The study population was all PLHIV registered at the ART centres for HIV care under the NACP up to 31 December 2015. The data were extracted from electronic databases maintained in ART centres for PLHIV. The data source included pre-ART registers, ART registers, patients’ treatment cards maintained at each of the ART centres routinely for monitoring and evaluation, and the monthly progress report submitted to the National AIDS Control Organisation India (NACO). The key variables recorded were pre-ART numbers, age, sex, baseline CD4 count at the time of registration (for new PLHIV registered during the last year) and the last available CD4 count (for PLHIV already registered in pre-ART care).

The data abstracted from the electronic databases were analysed to estimate the number of PLHIV who would additionally become eligible for ART. The data were already present in electronic format and were analysed using Microsoft Excel. The necessary approval for analysis of data and projections was obtained from NACO. Since this was a retrospective review of existing programme data and did not involve any direct patient interaction, individual informed consent was not required. Personal identifiers in the data were not redacted.

Review outcomes

As of December 2015, nearly 1.17 million PLHIV were registered in active HIV care under the programme, of which 0.92 million were registered for ART care, while 250 865 were registered for pre-ART care. A person living with HIV is said to be on active pre-ART care, if he or she is not on ART but has undergone CD4 counts in the last year. For the purpose of analysis, the study only considered those who were in active pre-ART care under the programme; those patients reported as deceased, lost to follow-up, or opted out of the programme in pre-ART care were excluded.

Estimates were made to assess the impact of implementation of the revised 2015 WHO guidelines on ART service delivery at two levels, (i) the immediate increase in the number of PLHIV requiring ART as a result of individuals already registered in active pre-ART HIV care under the programme; and (ii) the recurring annual increase in the number of PLHIV requiring ART, of those newly registering under the programme.
Estimates for the immediate increase in the number of people living with HIV needing antiretroviral therapy

In addition to those treated under the programme, all PLHIV who are in active pre-ART with a CD4 count ≥350 cells/mm³ and ≤500 cells/mm³ become eligible for ART according to the 2013 WHO guidelines,¹¹ and all PLHIV irrespective of CD4 count become eligible for ART according to the 2015 WHO guidelines.¹⁶

Out of the 250 865 PLHIV in pre-ART care at December 2015, 135 593 had a CD4 count ≤500 cells/mm³ and thus became eligible according to the 2013 WHO guidelines (see Box 1).¹¹ Another 100 221 would be eligible if the recommendation in the 2015 WHO guidelines to “treat all” is adopted,¹⁶ thereby moving all PLHIV who are in pre-ART care to ART.

Estimates for the recurring annual increase of new enrolment of people living with HIV in the programme

The trend in the number of PLHIV registered under the programme suggests that nearly 0.18 million become newly registered in HIV care in India every year. In 2015, a total of 0.179 million were registered for HIV care, although the eligibility could be assessed for only 0.162 million for whom a baseline CD4 count was done. Of the total registrants, 0.107 million (59.7%) were eligible for ART at the time of enrolment, according to the 2010 WHO guidelines (CD4 count <350 cells/mm³).¹⁰ Therefore, if the newer WHO criteria were implemented, the remaining 0.07 million of the total 0.179 million would become eligible for treatment. Based on the known proportions of baseline CD4 counts, new eligibility would be attributable for an estimated 0.028 million (15.8%) due to the 2013 WHO guidelines (CD4 count ≤500 cells/mm³);¹¹ for 0.030 million (16.8%) due to the 2015 WHO guidelines (CD4 count >500 cells/mm³; see Box 1);¹⁶ and for 0.014 million (7.7%) PLHIV whose ART CD4 counts cannot be determined for various operational reasons.

Overall estimated increase

The projected numbers of eligible PLHIV who will be eligible for ART, according to the 2013¹¹ and 2015¹⁶ WHO guidelines for the next 3 years, are shown in Table 1.

Box 1. Data and estimates for the numbers of people living with HIV

<table>
<thead>
<tr>
<th>Distribution of CD4 count of HIV-infected people already registered in pre-ART care in India, 2015 (n = 250 865)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• ≤500 cells/mm³: 135 593 (54.0%)</td>
</tr>
<tr>
<td>• &gt;500 cells/mm³: 100 221 (40.0%)</td>
</tr>
<tr>
<td>• Unknown: 15 051 (6.0%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CD4 count of HIV-infected people registered annually in HIV care, 2015 (n = 179 211)²</th>
</tr>
</thead>
<tbody>
<tr>
<td>• &lt;350 cells/mm³: 107 021 (59.7%)</td>
</tr>
<tr>
<td>• 350 to ≤500 cells/mm³: 28 285 (15.8%)</td>
</tr>
<tr>
<td>• &gt;500 cells/mm³: 30 105 (16.8%)</td>
</tr>
<tr>
<td>• Unknown: 13 800 (7.7%)</td>
</tr>
</tbody>
</table>

²Numbers extrapolated from PLHIV for whom a baseline CD4 count was done.

Table 1. Estimated numbers (millions) of people living with HIV who would be eligible for antiretroviral therapy using revised WHO CD4 criteria

<table>
<thead>
<tr>
<th>Year</th>
<th>WHO guidelines 2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010¹⁰</td>
<td>0.92</td>
<td>1.03</td>
<td>1.13</td>
<td>1.24</td>
</tr>
<tr>
<td>2013¹¹</td>
<td>—</td>
<td>1.19</td>
<td>1.33</td>
<td>1.46</td>
</tr>
<tr>
<td>2015¹⁶</td>
<td>—</td>
<td>1.35</td>
<td>1.53</td>
<td>1.71</td>
</tr>
</tbody>
</table>

Discussion

Adoption of the 2015 WHO guidelines on ART¹⁶ would be a pivotal step towards universal access for treating and preventing HIV in India. The country may expect a significant additional number of PLHIV at the existing ART centres, on adoption of the 2015 guidelines.¹⁶ In addition, nearly 0.070 million will be added annually each year, over and above the current pace of enrolment, if the newer criteria are implemented. A patient on ART takes it for life; hence, the NACP will have to ascertain the availability and sustainability of funding. It is expected that the benefits of implementation of the 2015 guidelines will outweigh the upfront investment needed and have the potential to change the course of the epidemic in the country.

The HIV modelling consortium used multiple mathematical models on data sets from five countries, including India, to assess the impact and cost effectiveness of implementation of newer guidelines, and found that it would be beneficial.¹¹ For India, the costs from the health-system perspective of extending eligibility to all PLHIV were modelled as US$ 131–241 per disability-adjusted life-year averted, which was classified as “very cost effective”.¹¹

There are several programmatic implications of adoption of these guidelines. First, there will be a marginal increase in the workload at ART centres. However, since the HIV epidemic is concentrated in six high-prevalence states and among vulnerable populations, the workload at ART centres is unlikely to increase in a uniform manner. The distribution of additional PLHIV requiring ART will be higher in ART centres that already have higher load. Differential indicators and strategies for service delivery will need to be adopted to strengthen the existing ART centres to match the workload. To avoid congestion at ART centres, the following strategies may be adopted: (i) giving 3 months’ drug stock at a time to PLHIV who are clinically stable; (ii) giving patients scheduled appointments and calling them on a fixed date and time of the month; and (iii) integrating ART services into the general health system. Expansion of decentralized delivery of services via “closer-to-home” link ART centres, a model currently employed in high-prevalence states, may also help in mainstreaming ART services. Implementation of the above strategies would resolve the additional human-resource requirements and streamline the procurement, supply and delivery of drugs to the patients.

Secondly, there should be a sustainable and continued supply of logistics. Robust procurement and supply-management systems are needed to ensure continued supply of ARV drugs, diagnostics and other commodities across various levels of programme implementation. A real-time supervisory mechanism to monitor the supply-chain management of logistics needs to be established for improvement of the programme. In addition to drugs, there will be a need for additional CD4 tests and tests of viral load.

Implementation of the above strategies will require robust supply and delivery systems. There will be a need for additional CD4 tests and viral load tests.
Thirdly, the programme will also need to gear-up to take care of the changing needs of PLHIV on such long-term ART, for example, by providing adherence support, chronic care and checks for drug resistance, as well as other future options for ART for cases of treatment failure. Development of novel tracking mechanisms to keep a tab on pre-ART patients will decrease the likelihood of loss to follow-up. The national programme should prioritize operational research to evaluate the newer approaches and provide feasible solutions to deliver quality services under the programme. Critically, there is a need to strengthen monitoring and evaluation mechanisms. A framework to expand and strengthen HIV testing and counselling is also needed, to engage those who are difficult to reach and bring people who need treatment into the continuum of care.

Fourthly, it is crucial for any health programme to engage with other stakeholders and line departments. There is an absolute need to optimally link HIV interventions with other partners, such as the medical services of large employers like the railway and defence department, as well as the private sector, to increase coverage, optimize resources and ensure long-term sustainability for the programme. It is clear that early initiation of ART will decrease morbidity and mortality; this opportunity should be utilized to engage with health-insurance providers and HIV should be covered under insurance schemes.

To conclude, in view of the benefit to patients, as well as considering the long-term vision of the programmes, the adoption of newer guidelines is of utmost benefit to PLHIV, as well as for achievement of the larger goal of the NACP. However, the programme should plan and strengthen its delivery mechanism, with emphasis on newer and innovative delivery approaches before progressing to implementation.

The study has some limitations. The concluded implications are based on the available programme data and current trends. The newer initiatives being taken by the programme to increase testing and HIV diagnosis, aiming towards the vision of 90–90–90, and also to improve patient retention within the HIV-care system, have not been taken into consideration in the estimated data.

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