

Strategic Considerations for Scaling Up Antiretroviral Therapy for Children Living with HIV/ AIDS in South-East Asia: Guidelines for Programme Managers



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Strategic Considerations for Scaling up
Antiretroviral Therapy for Children
Living with HIV/AIDS in South-East Asia:
Guidelines for Programme Managers

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Preface

UNICEF and WHO are committed to advance national capacities in South-East Asia to ensure universal access for all age groups, including children, to HIV care and treatment, including antiretroviral treatment (ART). The collaboration between the WHO Regional Office for South-East Asia (WHO/SEARO) and the UNICEF Regional Office for South Asia (UNICEF/ROSA) has included the development and publishing of *Management of HIV Infection and Antiretroviral Therapy in Infants and Children: A Clinical Manual*; clinical and didactic training of paediatricians and other health professionals; and support for governments to develop national strategies, guidelines and time-bound care and treatment scale-up plans.

While there has been significant progress in past years in increasing access for children to ART around the world, a huge gap still remains between the need and the actual response. This is as true for most of the South-East Asia (SEA) Region as for the rest of the world.

This publication is designed to provide practical guidance to national programme managers in South-East Asia and implementing partners in developing and scaling up HIV care and treatment for children based on global and regional experience. Global experiences have highlighted a number of critical success factors, including:

- Paediatric HIV care and treatment has benefited significantly from integration into existing ART programmes as well as within MCH programmes.
- Ensuring access to HIV testing in facilities where sick children are seen and those with HIV are likely to be diagnosed increases programme efficiency.
- Access to virological testing through dried blood spot specimen collection and transport has also been effective in linking HIV-infected children to care and treatment prior to the onset of severe disease or even death.

In preparation for this document, an assessment of the situation of ART services for children in SEA countries was made. A structured, open-ended questionnaire was given to health authorities in SEA countries.

The recommendations made in this document are informed by the findings of the assessment.

WHO/SEARO and UNICEF/ROSA consider it important to mobilize regional and national actions and resources to include children on the care and treatment agenda leading towards universal access and to ensure the commitment of partners in accelerating collaborative action on paediatric ART, care and support. This document identifies the gaps in extension of benefits of ART to children, and discusses the strategies to accelerate the scale-up.

The document presents programmatic steps necessary for roll-out and strengthening of ART services for children. We hope that programme planners, implementers and public health authorities in countries of South-East Asia will find it useful for strengthening ART services for children with HIV/AIDS in their national AIDS and MCH programmes. WHO/SEARO and UNICEF/ROSA will welcome feedback on the document.

Abbreviations

AIDS	Acquired immune deficiency syndrome
ART	Antiretroviral therapy
ARV	Antiretrovirals
AZT	Zidovudine
CHC	Community health center
CSW	Commercial sex worker
DNA PCR	Deoxyribonucleic acid Polymerase chain reaction
ELISA	Enzyme linked immunosorbent assay
FDC	Fixed dose combination
FRU	First referral unit
HIV	Human immunodeficiency virus
IEC	Information, education and communication
IMCI	Integrated management of childhood illness
MCH	Maternal and child health
NGO	Nongovernmental organization
OI	Opportunistic infection
OVC	Orphan and vulnerable children
PLHA	People living with HIV/AIDS
PMTCT	Prevention of mother-to-child transmission
PSM	Procurement and supply chain management
SEA	South-East Asia
TB	Tuberculosis
WBC	White blood cells

1

Background

1.1 HIV burden and access to antiretroviral therapy in SEA Region countries

With nearly half the world's population, Asia is likely to determine the future of the global HIV/AIDS pandemic. Although the HIV prevalence rate is still low in South-East Asia, it is one of the regions with the most rapidly growing HIV/AIDS epidemics globally¹. Because of the large population base and presence of several factors that enhance the spread of HIV, including poverty, gender inequality and social stigma, the South-East Asia Region is likely to increasingly suffer the brunt of the epidemic.

If HIV prevalence rates in China, India and Indonesia increase to numbers similar to those seen in Cambodia and Thailand, the number of people with HIV and AIDS globally would double². Such growth would be devastating for individuals and for the Region's health systems, economies and social fabric.

Fortunately, recent advances in antiretroviral therapy indicate that HIV-infected individuals can lead normal lives. The challenge before all the partners is to enable the public health systems to deliver ART in an equitable manner to the HIV-infected individuals. In the South-East Asia Region, though the access to ART is increasing, the coverage still remains low. Table 1 shows the estimated HIV burden in SEA countries and also the estimated numbers of individuals receiving ART.

Recent data on the estimated number of people receiving antiretroviral therapy, people needing antiretroviral therapy and the percentage coverage in low- and middle- income countries in different regions (December 2003– December 2007) shows that the East, South and South-East Asia

has the second-highest number of individuals who need ART (Table 2). However, only 18% of the estimated numbers of individuals needing therapy were receiving it in 2006³.

Table 1: HIV burden and access to antiretroviral treatment in SEA countries

Country	Estimated number of PLWHA 2006-2007	Adult HIV prevalence in 2007	Estimated number of people ever started ART in public and private sectors (by date)			
			Dec-04	Dec-05	Dec-06	Dec-07
Bangladesh	7 500	<0.1	5	n/a	n/a	178
Bhutan	<500	<0.1	5	6	13	18
DPR Korea	n/a	n/a	n/a	n/a	n/a	n/a
India	2 500 000	0.36	3 500	23 700	55 473	133 020
Indonesia	193 000	0.14	2 500	3 300	6 042	6 653
Maldives	<100	<0.1	0	1	1	1
Myanmar	242 000	0.7	1 500	3 700	5 000	11 100
Nepal	70 000	0.54	75	210	473	1 240
Sri Lanka	4 000	<0.1	25	44	66	107
Thailand	562 000	1.1	52 997	88 261	111 429	133 539
Timor Leste	<100	<0.1	n/a	n/a	n/a	20

Source: National HIV/AIDS programme

1.2 HIV in children and the rationale for scale-up of paediatric ART

The total number of children infected with HIV in East, South and South-East Asia was estimated around 180 000 to 220 000 at the end of 2006. It was estimated that 64 000 (range: 32 000 – 120 000) HIV infected children needed ART in December 2006 and more than 200 000 children need cotrimoxazole prophylaxis. Of those who need ART, around 13 300 children are receiving ART. In other words only 21% of children who need ART treatment⁴ are actually getting it.

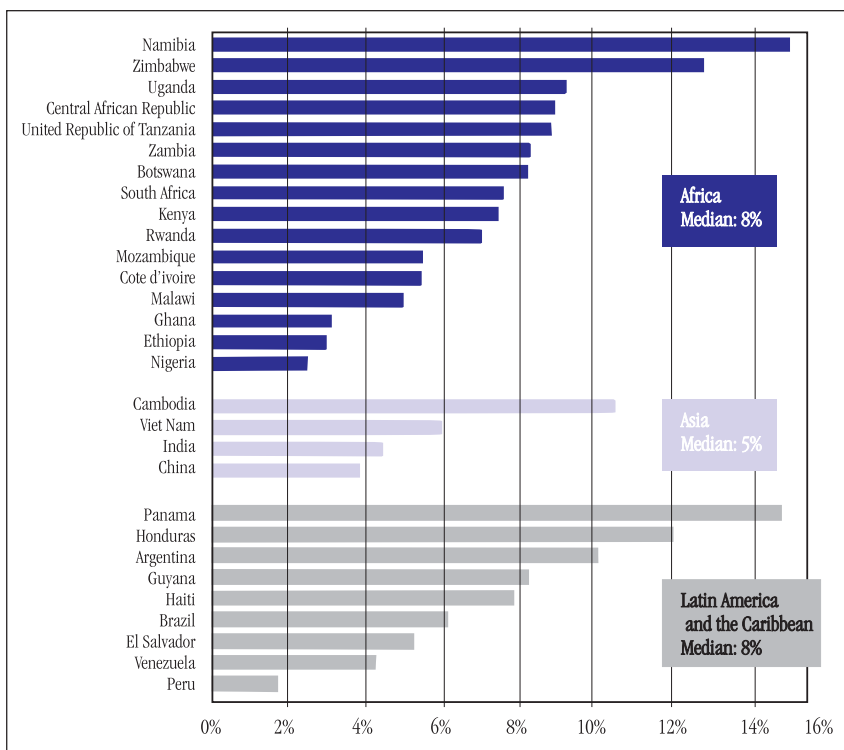
There is limited data on HIV-infected children needing ART and those who are receiving it. Figure 1 shows the percentage of people on

Table 2: Estimated numbers of people receiving and needing antiretroviral therapy, and the percentage coverage in low- and middle-income countries according to region (December 2003 to December 2006)

Geographical region	Estimated number of people receiving antiretroviral therapy, December 2007 (range)	Estimated number of people needing antiretroviral therapy, 2007 (range)	Antiretroviral therapy coverage, December 2007 (range)	Estimated number of people receiving antiretroviral therapy, December 2006 (range)	Estimated number of people needing antiretroviral therapy, December 2006 (range)	Antiretroviral therapy coverage, December 2006 (range)	Estimated number of people needing antiretroviral therapy, December 2003 (range)
Sub-saharan Africa	2 120 000 (1 925 000–2 315 000)	7 000 000 (6 250 000–7 900 000)	30% (24–34%)	1 375 000 (1 280 000–1 470 000)	6 700 000 (5 900 000–7 600 000)	21% (18–23%)	100 000 (75 000–125 000)
Latin America and Caribbean	390 000 (350 000–430 000)	630 000 (550 000–770 000)	62% (51–70%)	345 000 (305 000–385 000)	600 000 (510 000–740 000)	58% (47–68%)	210 000 (160 000–260 000)
East, South and South East Asia	420 000 (375 000–465 000)	1 700 000 (1 300 000–2 100 000)	25% (20–32%)	280 000 (225 000–335 000)	1 600 000 (1 220 000–2 060 000)	18% (14–23%)	70 000 (52 000–88 000)
Europe and Central Asia	54 000 (51 000–57 000)	320 000 (240 000–440 000)	17% (12–22%)	35 000 (33 000–37 000)	260 000 (180 000–380 000)	13% (9–19%)	15 000 (11 000–19 000)
North Africa and Middle East	7 000 (6 000–8 000)	100 000 (70 000–135 000)	7% (5–10%)	5 000 (4 000–6 000)	97 000 (66 000–130 000)	5% (4–8%)	1 000 (750–1 250)
Total	2 990 000 (2 700 000–3 280 000)	9 700 000 (8 700 000–11 000 000)	31% (27–34%)	1 330 000 (1 200 000–1 460 000)	400 000 (300 000–500 000)	22% (19–25%)	400 000 (300 000–500 000)

Source: Towards Universal Access: Scaling-up priority HIV/AIDS interventions in the health sector. Progress report 2008. Geneva, WHO/UNAIDS/UNICEF 2008.

Figure 1: Percentage of people on treatment for HIV infection who are children (in selected countries), June 2006



Source: Progress in scaling up access to HIV treatment in low and middle-income countries, June 2006 WHO/ UNAIDS.

treatment who are children, as at June 2006 in different countries³. It is estimated that in Asia, the median percentage of people on treatment who are children is only 5%⁴. In the South-East Asia Region, Thailand has made significant progress in paediatric ART.

The disease progresses faster in children because of their immunological immaturity. The clinical course of vertical HIV-1 infection is highly variable, but before the widespread use of antiretroviral therapy, two general patterns of survival were described. Approximately 10% to 20% of infected infants experienced rapid progression of disease and died of AIDS-related complication by four years of age. The mean survival time for the remaining 80-90% of infected children was approximately 9-10 years⁵. It is evident that children will need antiretroviral therapy earlier

in the course of disease than adults. But in the absence of specific diagnostic facilities, such as PCR, infants are often not diagnosed and, therefore, deprived of benefit of antiretroviral therapy; many succumb before diagnosis is confirmed.

The efficacy of ART in children is well documented. In the developed countries, many of those treated have now grown into adults, leading a productive life.

One of the most encouraging information from the XVI international AIDS conference in Toronto was the growing body of evidence that HIV treatment can be successfully delivered to children in low resource settings^{6,7,8,9}. Treatment outcomes observed in low-resource settings are similar to those found in Western countries in terms of survival rates, adherence levels and other markers. Use of cotrimoxazole in the absence of ART (Zambia) led to a 45% decline in mortality¹⁰. High two-year survival rates for children placed on treatment (Ivory Coast, Kenya, Thailand, Uganda, and others), and undetectable viral load levels in 75% of 1 370 children placed on treatment at 24 weeks (Uganda) have been reported^{6,7,8,9}.

Even though treatment is very effective and has generally few and time-limited side effects, it is only effective for children who receive it. Unfortunately, most of the HIV-infected children are not being detected early enough. Because of very high mortality for HIV-infected children (50% by age two)¹¹, the fact that median age for treatment initiation is well beyond two years in many countries implies that many children are unable to access life-saving treatment.

1.3 Experience with scale-up

Antiretroviral therapy has transformed HIV-infection into a chronic, manageable disease condition. It has saved millions of lives and more importantly, has improved the quality of life of individuals living with HIV infection. In an effort to scale up and benefit HIV-infected individuals, various campaigns have been launched. The most prominent among these was the “3 by 5” programme¹².

Considerable progress has been made in scaling up antiretroviral therapy. This experience has prompted the international community to promote accelerated action for scale-up. A United Nations

General Assembly resolution adopted on 23 December 2005 requested UNAIDS and its cosponsors to assist in “facilitating inclusive, country-driven processes, including consultations with relevant stakeholders, including nongovernmental organizations, civil society and the private sector, within existing national AIDS strategies, for scaling up HIV prevention, treatment, care and support with the aim of coming as close as possible to the goal of universal access to treatment by 2010 for all those who need it”¹³.

While there has been progress in providing antiretroviral therapy to a large number of HIV-infected individuals, a large proportion of the beneficiaries have been adults. The extent of scale-up for paediatric ART has not been satisfactory. It is generally agreed that 10-15% of all recipients of ART should be children⁴. However, the current figure for children is about 5% in the Region. This highlights the need for more aggressive and rapid scale-up for children.

2

Planning roll-out of ART for children

2.1 Technical and programmatic considerations for scale-up of paediatric ART

There is an interplay of a wide range of technical, programmatic and social reasons for delay in extending the benefits of ART to HIV-infected children. The various obstacles/ barriers are discussed here:

Delay in diagnosis

- (a) **Infants:** The infants at risk of HIV-infection are the ones that are born to HIV-infected mothers. This implies that early identification of at-risk HIV-exposed infants is heavily dependent on the maternal screening programme and the PMTCT programme. In most countries in the Region, the coverage of these screening programmes is inadequate. The available data suggests that except for Thailand, less than 5% of HIV-infected pregnant women receive antiretroviral prophylaxis⁴. The second issue/gap is the need for specific diagnostic tests for HIV-exposed infants under 18 months of age¹⁴. The widely available antibody test cannot be used for confirming the diagnosis of HIV infection in infants of HIV-infected mothers because of presence of maternal anti-HIV antibodies in the infants; these antibodies may persist till about 18 months of age. The diagnosis can be confirmed only by sophisticated virologic tests such as DNA PCR. However, the limited availability of the test leads to delay in diagnosis. In the absence of a diagnosis, the infants are deprived of the benefits of ART.
- (b) **Older children:** Till the time the maternal screening programmes and PMTCT programmes have a wide coverage

and acceptance, most HIV-infected children will continue to be diagnosed only when they exhibit symptoms. The other opportunity for diagnosis may come if another family member is diagnosed to have HIV infection and the children are screened. ELISA testing for anti-HIV antibodies is the mainstay for diagnosis of HIV infection in children older than 18 months age. Health workers have to be sensitized to recognize such opportunities to maximize diagnosis of HIV-infected children.

Inadequate experience in the management of chronic conditions in children

- (a) Management of HIV infection with antiretrovirals has transformed HIV/AIDS into a chronic condition. There is a widely prevailing perception that chronic disorders do not occur in children. In many countries, the experience of health care providers, including paediatricians, is limited in providing care for chronic diseases. The capacity to handle HIV infection, which necessitates a new paradigm of lifelong antiretroviral therapy, introduces complexities both at the health system and health-care provider level.
- (b) In addition, the concern about the adverse effects of medications (felt to be “too strong”) that are given long-term to the child are likely to interfere with successful therapy. The care of a child may also be affected adversely by the fact that other family members/caregivers may also be infected.
- (c) Often, the diagnosis of HIV infection is not disclosed to the child; this again may interfere with the adherence.

Lack of trained individuals to treat children with HIV infection

This is still an issue in many countries in the Region, as physicians and other health workers are not trained in administration of ART. Frontline health workers in many countries are not trained in identifying children likely to have HIV infection.

Lack of paediatric ART formulations

The adult ART programme uses one or two formulations for each ART regimen. This is not possible at present for paediatric ART as the doses of various drugs used in paediatric ART vary with the weight of the child. In order to provide appropriate doses of all three drugs using fixed-dose combinations (FDC), different formulations will be required for several weight bands. In addition, the dose will have to be modified as the child grows. This increases the complexity of paediatric ART. Moreover, in most countries appropriate paediatric formulations are not available as yet. While there has been some experience of using the adult FDC formulations for treating HIV-infected children, there are limitations to this approach. It makes the dosing inaccurate, leading to over- or under-dosing for different drugs in the FDC. Further, there is growing consensus that the adult FDC tablets should not be split into more than two parts. This is based on the fact that the distribution of the three drugs in an FDC tablet is not uniform, and breaking into more than two parts is likely to lead to variations in the doses administered.

Lack of awareness that children do well with ART

While the benefits of ART in HIV-infected adults are well documented and the information widely disseminated, there still is lack of awareness that HIV-infected children do well with ART. As a result of this, the health care workers may not be confident to treat children.

Inadequate health infrastructure to take care of sick children

The success of the ART roll-out is strongly dependent on the quality of health care facilities for sick children, as ART is only one of the important components of HIV care. There has to be enough emphasis on the ability to handle concurrent infections and most importantly to follow up a child lifelong.

In addition, there may be poor access to health-care facilities. In some parts of the Region, this may be due to geographical factors. There is a chronic shortage of health-care workers in most of the countries in

the Region; this is likely to be one of the major bottlenecks in scaling up treatment.

Many of the infected individuals belong to migrant/slum communities. It is a challenge to provide health care services to these individuals.

Social factors

Lack of widespread awareness about the manifestations of HIV infection in children often leads to delayed diagnosis in children. Children may be diagnosed only when they have advanced disease. In view of the potential for discrimination, parents may not disclose their own status, which could help in the child's diagnosis. Children with HIV infection often do not have advocates and activists in the same way as adults.

Economic barriers

While the antiretroviral drugs may be made available by the programme, there still may be economic considerations that may prevent patients from accessing care. Direct costs such as cost of travel to the treatment center, cost of stay, and so on, as well as indirect costs like loss of wages while the parents/guardians are away from work, may prevent access to care.

Programmatic barriers

Lack of sufficient facilities to counsel families and test children are a major barrier to access to treatment. In addition, there are major technical issues in infant diagnosis of HIV infection. Health-care professionals may not be well trained to suspect HIV infection in children and also inadequately trained for managing it. The shortage of health-care personnel in the public sector is likely to worsen this problem.

There may not be enough resources for funding the programme. There will be competition for available funds for other child health programmes.

While the roll-out of services for children may begin as a vertical initiative, there will be challenges in subsequently integrating HIV care and support programmes with the child health programme.

As national efforts for ART are scaled up, it is imperative that efforts be made to include HIV-infected children in the programme. The region has the second-highest number of infected individuals (after sub-Saharan Africa). The same is also likely to be true for children. Specific strategies have to be discussed for extending the benefits to children.

2.2 Principles of a successful roll-out plan for paediatric ART

The critical elements of the scaling up towards a universal access programme are¹⁵:

- (1) It occurs within and builds upon existing processes at all levels.
- (2) Countries drive the process, supported by international and bilateral institutions and donors, in line with the “Three Ones” principles and the recommendations of the Global Task Team. “Three Ones” principles call for the coordination of a national AIDS response around **one agreed AIDS action framework, one national coordinating authority** (including government, civil society, people living with HIV and the private sector) and **one agreed country-level monitoring and evaluation system**.
- (3) It covers the scale-up of a comprehensive and integrated AIDS response, including prevention, treatment, care and support.
- (4) It focuses on finding practical solutions to the main obstacles to scaling up, building on decisions already made.
- (5) The participation of a wide range of stakeholders-especially civil society and people living with HIV-is critical to its elaboration and success.
- (6) It encourages countries to set their own roadmaps – including midpoint targets and milestones-in order to advance toward universal access and to achieve the Millennium Development Goal on HIV/AIDS.

Table 3: Point of delivery of care

	Exclusive paediatric care centres	Existing ART centres
Pros	<ul style="list-style-type: none"> – Involvement of paediatricians/specially trained care-providers – Greater experience in caring for children – Possibly better care 	<ul style="list-style-type: none"> – Directed towards family-based care – Will facilitate rapid scale-up – Easier to manage drug supply chain
Cons	<ul style="list-style-type: none"> – Difficult for family (multiple points of care) – Limited numbers of such facilities may hinder rapid scale-up 	<ul style="list-style-type: none"> – Need for better training of medical personnel for handling paediatric issues – There may be difficulties in child-specific issues like growth and development monitoring

- (7) It utilizes opportunities to develop linkages with existing public health programmes, develops public-private partnerships, and also focusses on the vulnerable section of the society afflicted with HIV/AIDS.

2.3 Strategies for paediatric ART roll-out programme

There could be various strategies for the roll-out plan depending on the location of service delivery points, roles of different institutions, and roles of the public/private sector.

Location of service delivery points

Countries in the Region will have to decide on the location of service delivery points for paediatric ART. These could be all the existing ART centres (in countries where ART centres are being run for the adult population). The other option to consider is establishment of exclusive paediatric ART centres. Table 3 highlights the pros and cons of these approaches.

An alternative could utilize both these approaches. The existing ART programmes could be modified to include paediatric components. The

exclusive paediatric care centres could serve as centres for referral, where children with various problems in management or complications could be referred for expert care.

Linkages of the paediatric ART units with paediatric units in various settings are indispensable, at least in the initial phases of implementation. This will provide necessary support to the ART centres and also facilities for handling any complications and intervening illnesses. It may be desirable that the paediatric units of the hospitals run the paediatric HIV care and treatment services, with support for drug dispensing, supply and other logistics.

While the paediatric ART roll-out may begin as an independent/vertical programme, it will be desirable to work for integration of the same with the child health services/ programmes. The decentralization will prevent the designated treatment sites from becoming overwhelmed.

One concern may be the disparities that exist between the rural and more resourced urban areas. It may be easier to prepare the existing urban hospitals to manage HIV-infected children than reaching out to remote rural areas, where the health-care infrastructure is often poor.

The priorities for individual countries will be dependent on the magnitude of the problem. Even within a country, there may be variation in the prevalence. For example, in India, there are a few high prevalence states where there will be a greater burden of paediatric HIV patients.

It is appropriate that the services are rolled out in phases. The first phase should be targeted at the high-prevalence districts. This phase will also give important lessons in implementation of the programme and also yield information on various problems. The subsequent phases could then be implemented to gradually cover the entire affected geographical region.

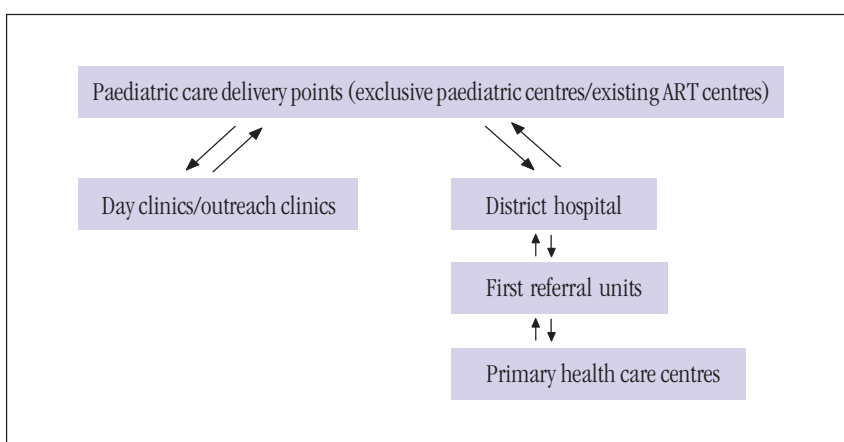
Phases of implementation

Each country will necessarily have to go through development, initiation and expansion phases. Most countries in the Region are either in the development or initiation phase.

(a) Development phase

- (1) Development of tools and strategies for a paediatric ART roll-out
- (2) Extensive training targeted at the ART teams (prescribing doctors, counseling nurses, dispensing pharmacy personnel and laboratory technicians).
- (3) Generation of experiences in developing the necessary strategies that could be used to implement a more rapid scale-up programme.
- (4) Upgrading of physical facilities of selected hospitals and consolidation of the capacities of laboratories in monitoring treatment.
- (5) Defining role of the private sector.

Figure 2: Suggested hierarchy of Paediatric HIV care delivery centres



(b) Initiation phase

- (1) Preparation of health centres to take up more responsibilities in the following phase should be done in this phase.
- (2) Health officers or senior clinical nurses in health centres without health officers should be trained to initiate first-line ARV treatment for uncomplicated cases, in an effort to prepare for the decentralization of ART service delivery to levels lower than the hospitals.

(c) Consolidation and rapid expansion phase

This phase will involve improvement in the quality of services and expanding rapidly to cover the target population.

Every effort should be made to **decentralize** care to make the treatment more convenient and also to ensure better follow-up and adherence. This could be done utilizing the services of district hospitals and primary health care centres.

In the initial stages of expansion it may be prudent if treatment could be initiated at a hospital/district level centre. Once the child stabilizes, then the follow-up could be at a PHC/outreach clinic with periodic review at the main centre. The time schedules for such visits could be decided in each programme.

Once the system gets stabilized and experience accumulates, countries may consider devolving the responsibility of initiation of treatment to the district level. The other levels have the responsibility of referring suspected cases to the appropriate level for diagnosis and initiation of therapy and for monitoring the therapy. These levels should ideally be able to treat minor complications.

Role of private sector needs to be defined

Each country will need to define the role of the private sector in its efforts to scale up the antiretroviral therapy. While the sector plays an important role in health-care delivery in many countries in the Region, there are concerns about affordability for a large proportion of population. In addition, the ability of the sector to deliver chronic care for an infectious disease is not tested. There have been efforts at developing a public – private partnership in the TB control programme. There could be lessons learnt from that experience.

The private sector could play an important role in identification of HIV-infected children and referral. In addition, efforts could be made to support paediatricians/physicians who are interested in providing regular care for HIV-infected children. In such a scenario, the drugs could either be supplied to these practitioners for free dispensing or the ART centres could dispense the drugs prescribed. Mechanisms for accreditation of the private sector need to be developed.

3

Making paediatric ART a reality in national HIV/AIDS programmes: Steps for paediatric ART roll-out

Based on the principles discussed in Section 2.2 and those of the “3 by 5” scale-up, following are the suggested steps/requirements for the paediatric ART roll-out and scale-up.

3.1 Advocacy for paediatric ART services

National policy-makers recognize the potential benefits of antiretroviral treatment to HIV-infected individuals, their families and overall social and economic development. As most of the HIV care and treatment programmes are targeting adults, there is a need to apprise the policy-makers of the magnitude of paediatric HIV infection and convince them of the benefits of antiretroviral therapy in children.

In many countries, programmes for ART in adults are in place. Even in these countries, policy-makers from multiple agencies need to discuss and debate the way forward for the paediatric ART roll-out and scale-up. They will need to be convinced about the benefits of ART in children as often there is a lack of awareness.

The policy-makers may often face some of the following dilemmas:

- (a) Should ART for children take precedence over immunization, management of common childhood illnesses like diarrhoea and acute respiratory infections or other national priorities?
- (b) If so, how should the ART services be funded?
- (c) Where should the paediatric care centres be located?

- (d) Who will be responsible for these services?
- (e) What are the issues about other essential clinical HIV interventions, such as management of opportunistic infections, preventive therapies and palliation?
- (f) How could the paediatric ART programme be linked to and/or integrated with the existing child health programmes?
- (g) What are the various convergence areas that could be strengthened: PMTCT, management of opportunistic infections, follow-up care?

It is important to clarify all these issues. For this, it is desirable that all stakeholders including policy-makers deliberate on such issues in a group to accelerate decision-making.

Finally, the need for making specific budget provisioning for paediatric ART in national HIV/AIDS programmes cannot be overemphasized.

3.2 Creating demand for the services by the community and community preparedness

For the success of delivery of paediatric ART services, development of evidence-based messages for **IEC** (information, education and communication) is required. The key issues to be highlighted here should be advocacy of the child's rights and positive impact of ART on infected children's health and quality of life. This message may be delivered more easily in areas where adults are benefiting from the ART programme. It will be important to dispel the common myths and apprehensions about the paediatric ART programme (particularly about the adverse effects).

Once families of HIV-infected children recognize the benefits of ART, they are generally eager for treatment to begin. However, not all HIV-infected children need or are ready for ART, and in the early stage of programme implementation, there may be limited treatment slots for those who are. It will be necessary to emphasize that not all HIV-infected children need antiretroviral treatment. However, it should be emphasized that all HIV-infected children be enrolled in the programme and followed up regularly to improve their health status and also determine the need for ART as and when needed. Thus, it is critical to define clinical and social

criteria and disseminate the criteria widely. Strict, transparent adherence to the criteria can minimize erosion of community support for ART.

Antiretroviral therapy has made HIV infection a chronic, manageable disease. HIV infection is unique, as it has to be treated for an indefinite period – much longer than the longest therapy for other chronic infections like tuberculosis. This is likely to be a new concept for many communities, especially in the case of children.

It is imperative that programme staff discuss these issues with local stakeholders: parents/guardians of children with HIV infection, district and municipal officials, traditional leaders, health workers, the media and others. This will assist in explaining the planned interventions, forging partnerships and developing plans for joint action.

In areas with high HIV prevalence, parents/guardians of children with HIV infection involved in the programme could communicate eligibility criteria to the broader community; religious leaders could address stigma and discrimination among their congregations; and NGOs providing home-based care could refer clients to ART learning sites.

Mobilizing community organizations and NGOs for supporting the families and children receiving ART is an important step in paediatric ART planning and implementation. Their involvement will help in multiple areas of child health in addition to supporting adherence. They could also provide vital inputs in improving child's nutrition and supporting education.

As there may be multiple community groups/NGOs working in a region, it will be helpful to define roles for various community groups to implement programme components such as home-based care, education and nutrition.

3.3 Improving the ability to identify HIV-infected children

An important challenge in most countries is how to identify the infected children and enroll them in HIV care and treatment programmes. This is

particularly important for younger children because of the high risk of death in HIV-infected children less than two years old. To achieve this, multiple sites need to be defined for screening. These include:

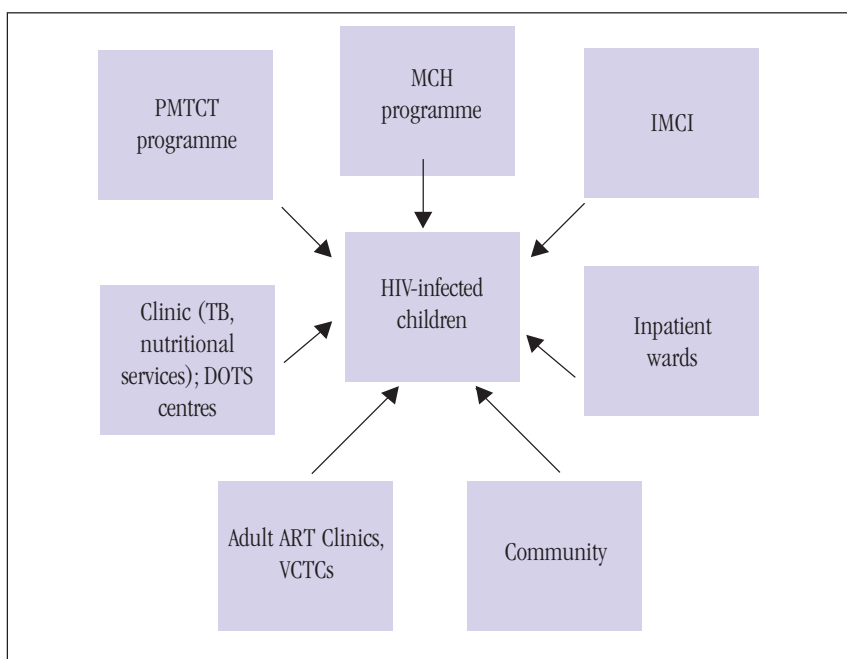
- (a) ***PMTCT programme:*** Early diagnosis of HIV allows health-care providers to offer optimal care and treatment of HIV-infected children, assists in decision-making on infant feeding and avoids needless stress on mothers and families. The increasing efficacy and coverage of PMTCT interventions implies that the majority of children born to HIV-infected mothers will be uninfected (with effective ARV/ART interventions exceeding 90%). Consequently, recognizing those with infection before they become unwell is only possible through routine diagnostic testing, ideally in PMTCT or maternal and child health services. For identifying the infants, it is desirable that universal screening of pregnant women is implemented and the infected mothers enrolled in the PMTCT programmes. For successful implementation of the programme and for the sake of continuity of care, the importance of linkages between PMTCT programme and the paediatric HIV care and treatment programme cannot be overemphasized. This will ensure follow-up of the HIV-exposed infants and appropriate testing of the infants.

Box 1: Clinical conditions that should raise a possibility of diagnosis of HIV infection

- (1) Parents diagnosed/suspected to have HIV infection/AIDS
- (2) Child presenting with opportunistic infections
- (3) Child presenting with recurrent/chronic infections: diarrhoea, pneumonia, etc.
- (4) Child presenting with severe infections
- (5) Severe wasting
- (6) Children with features suggestive of lymphoid interstitial hyperplasia (LIP)

- (b) ***MCH programme:*** This will allow screening of children with risk factors like those with unusual infections or unusual manifestations of common illness. In areas with high prevalence, there may be a benefit in screening all children who come for immunization (it could be done at the time of measles vaccination using a rapid test and the diagnosis then confirmed by a DNA PCR). The health staff will need to be trained in identifying sick children who are likely to have immune deficiency, for example recurrent diarrhoea, chronic diarrhoea, recurrent pneumonia, disseminated TB¹⁶.
- (c) ***IMCI services:*** In countries/districts where an IMCI programme is being implemented, the HIV module of the package could be implemented after adequate reorientation of the health care staff. This will also offer an opportunity to identify the infected children in the community.
- (d) ***Clinic services:*** Available literature suggests that it may be worthwhile screening children with severe malnutrition for HIV infection^{17,18}. In most countries, the prevalence of severe wasting has gone down and one should strongly suspect HIV infection in a severely wasted child. Similarly, there is evidence to suggest high prevalence of HIV infection in children with severe forms of TB, especially disseminated TB and extrapulmonary TB^{19,20}. It is important to screen children who need regular blood transfusions such as those with thalassemia.
- (e) ***Inpatient services:*** Admission of a child to a paediatric ward may provide the health-care personnel an opportunity to diagnose HIV infection. Again, the index of suspicion has to be high.
- (e) ***Adult ART clinics:*** It will be worthwhile to target children of adults who are enrolled in the HIV care/ART clinics for screening. This strategy is likely to have a good yield and may lead to early diagnosis of HIV infection in children.
- (f) ***Children in specific situations:***
 - ***Orphanages:*** These sites are likely to have children whose parents succumbed to HIV disease. Screening of children here may lead to identification of infected children and

Figure 3: Potential sources for identification of HIV-infected children



lead to their enrollment into the Paediatric ART programme.

- *Children of CSWs*: Children of CSWs form a high-risk group and would benefit from screening for HIV infection.

Guidance is available from WHO for provider-initiated HIV testing and counseling in health facilities²¹. As most countries in the Region are experiencing concentrated and low-level HIV epidemics, consideration may be given to the implementation of provider-initiated HIV testing and counseling in the following health facilities or services:

- Health services for most-at-risk populations
- Antenatal, childbirth and postpartum services
- Tuberculosis services

While it is important to identify maximum numbers of infected children, enough attention should be paid to counseling, confidentiality and informed consent by the caregiver.

HIV testing and counseling

Young children and infants are primarily tested in provider-initiated (or parent/caretaker-initiated) contexts rather than through traditional voluntary counseling and testing (VCT) programmes. Given this, issues of consent and rights-based approaches are of particular importance. Settings where child/infant-focused HIV testing and counseling (HTC) need to be made available or accessible include those such as antenatal care or post-PMTCT programmes, orphanages, hospitals and clinics and outreach services. Additionally, access to HTC is needed for children presenting to services *in addition to* HIV or PMTCT programmes, including within services such as TB programmes and nutrition and child health services. This is of particular importance in countries with a high HIV prevalence.

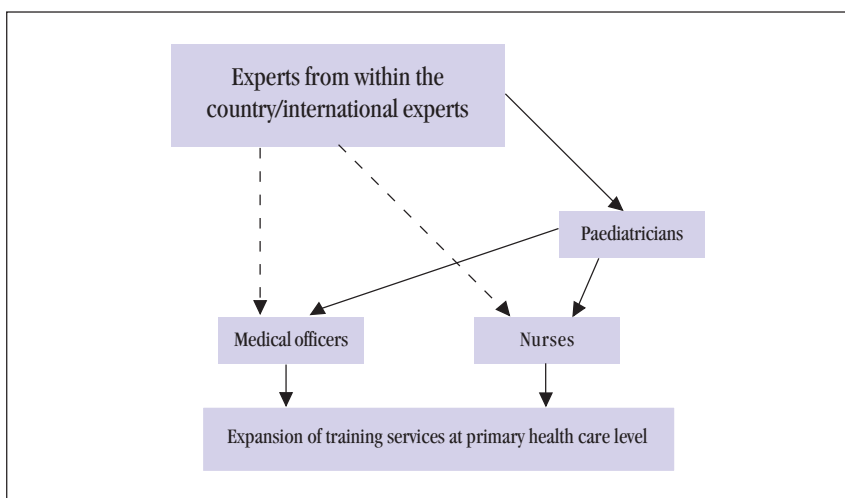
Mandatory testing of children should not be undertaken under any circumstances and governments must protect against such testing. It is neither ethical nor effective as a public health measure and is in violation of the rights of a child and/or their guardian to freely choose or refuse testing, and to have his or her confidentiality and privacy maintained. Additionally, HIV testing and status should not and must not be used to deny other rights to a child or infant (for example, to housing, education or care). Health care providers need to understand when it is their duty to provide HIV diagnostic testing.

Priority areas that should be addressed

- (1) ***Informed consent:*** National HIV and HTC policies and country-level guidance must clearly articulate who may give consent for a child to receive treatment, and at what age a child may give consent for themselves (or for others, as may be the case with child heads of households). Formal legal frameworks should help promote and ensure that HTC is properly provided. Guidance on child-friendly approaches to informed consent need to be elaborated for health-care providers; child-friendly consent forms and protocols should be used to ensure age-appropriate information has been given to, and is understood by, any child to be tested.

- (2) ***Counseling:*** Counseling must be made available for any child undergoing HIV testing, including post-test counseling for both the child and his or her parent(s) or caretaker(s). Appropriate counseling is inseparably linked to HIV testing. Counseling children requires skills that differ from adult and adolescent HIV counselling and providers must have access to adequate training and tools in this area. Age-specific training, materials and guidelines for counsellors and care providers on counselling young children for pre-test, post-test and ongoing counselling are needed. While the training of staff is a costly undertaking, country-level support through technical expertise and materials may be made available by organizations such as the WHO.
- (3) ***Confidentiality, disclosure and informing the Child and/or parent of HIV status:*** Informing the child and parent/caregiver of a child's HIV status also presents challenges to health-care workers and best practices need to be elaborated and understood by those performing counseling. Parameters for confidentiality need to be well defined and understood by all stakeholders. Confidentiality is intimately linked to disclosure, and issues of disclosure and informing young children can be complex. Thus, protocols must be clearly elaborated, and should to maintain confidentiality while also ensuring the best interests of the child. Providers must be clear as to whom, when and how best to inform or disclose a child's HIV status.
- (4) ***Addressing stigma and discrimination:*** Children experience stigma and discrimination based on HIV/AIDS within the family, the community and its institutions, as well as within health-care settings. This can take the form of isolation within families, marginalization amongst peer groups, discrimination within schools, denial of health-care services and social services. Stigma and discrimination need to be addressed for children at each of these levels. Age-appropriate, post-test counseling approaches should be undertaken that teach children and their parents/caretakers to deal with stigma and discrimination. This should include addressing stigma by association where the children of HIV-infected parents are discriminated against.

Figure 4: Training scheme



3.4 Technical expertise

In order to deliver care to HIV-infected children, trained health care personnel such as doctors, nurses, and pharmacists are needed. These personnel will have to be trained in the management of HIV infection in children. The focus could be first on high-burden regions/centres. Depending on the strategy (discussed below), the target population will be paediatricians, physicians manning the ART centres, general practitioners, etc.

To begin with, it may be desirable to train the paediatricians in delivering care and ART to HIV-infected children. They are likely to pick up these skills faster than a general practitioner/medical officer because of their experience in treating children. Thereafter, these trained individuals could help in training other physicians, nurses and other health-care workers.

Some regions/countries may have a shortage of paediatricians. In this setting the care will have to be provided by physicians or graduate medical officers.

Nurses are an indispensable resource in carrying out new responsibilities. In addition to patient triage and adherence counseling, nurses can assume

broader clinical responsibilities with appropriate training, including coordinating care services, managing adverse drug effects and providing leadership for the HIV team, thereby freeing doctors to treat more patients or start ART at more than one clinic.

To address the shortage of nursing staff, it may help to involve nurses at primary health facilities and with community-based services, who often have experience interacting with and caring for people living with HIV/AIDS (PLHA). They can be trained to identify potential candidates for ART, manage side effects and make referrals.

It will be desirable for all cadres of health workers to get hands-on training, in addition to classroom instruction, to prepare them for the rigors of an ART programme.

Standard operating procedures or clinical care protocols, including those defining the schedule for follow up visits and laboratory testing, promote effective clinical management and monitoring of children on ART. In addition, opportunities for case consultation with experienced ART clinicians can be extremely beneficial in building the capacity of providers to manage patients while improving patient care. Case consultation sessions are especially useful when they include the entire team caring for HIV patients. The sessions can be held at regular, predefined intervals. This will also help improve staff motivation.

While building capacity on paediatric ART management, programmes should also strengthen clinical practice in managing HIV disease overall, particularly diagnosis and management of opportunistic infections and other HIV-related conditions. In addition, adherence to standard precautions and appropriate waste management has to be emphasized. The issues of stigma and discrimination also have to be addressed.

It is best for HIV specialists from countries or settings similar to the local context to conduct training. Experience from “developed” countries is valuable, but practicing the science of HIV/ART is strongly impacted by local factors, traditions and belief systems.

Another area to consider for enhancing the country’s capacity to scale-up is pre-service training. This could be delivered to the undergraduate

Table 4: Training requirements

Staff	Training requirements
Infectious disease specialist	<ul style="list-style-type: none"> – Assessing medical condition of severely ill patients – Managing severe ARV therapy side effects – Changing treatment regime when drug resistance occurs – Balancing ARV therapy and treatment taken for other reasons – Managing severe opportunistic infections
Paediatrician/Physician	<ul style="list-style-type: none"> – Assessing general medical condition – Reading and interpreting lab results (HIV, CD4 count, Viral Load, chemical blood tests) – Prescribing ARV therapy and explaining its use – Counseling on ARV therapy and adherence – Detecting and managing moderate opportunistic infections
Nurse	<ul style="list-style-type: none"> – Taking histories – Assessing general patient condition – Providing counseling on HIV testing – Taking, coding, and registering blood samples – Conducting rapid HIV tests, and reading and interpreting results – Providing general counseling on ARV and adherence – Registering ARV drug recipients
Laboratory technician/specialist	<ul style="list-style-type: none"> – Doing CD4 counts and CD4% – Doing viral load tests – Doing chemical blood tests – Doing HIV ELISA tests – Doing HIV rapid tests – Doing HIV DNA PCRs – Doing chemical blood tests – Managing stocks of reagents and lab supplies
Pharmacist	<ul style="list-style-type: none"> – Knowing about ART regime – Storing and distributing ARV drugs and other essential drugs – Managing stocks and ordering ARV and other essential drugs – Assuring drug quality – Establishing measures to minimize drug pilferage – Counseling on ART adherence
Counselor	<ul style="list-style-type: none"> – Conducting HIV test counseling – Conducting general ART counseling – Conducting ART adherence counseling
Nutritionist	<ul style="list-style-type: none"> – Knowledge about the nutritional requirements of HIV infected children – Assessment of dietary intakes – Nutritional counseling and prescription of therapeutic diets

medical and nursing students. The training material will have to be prepared to achieve this. Experience gained in the pre-service training of IMCI could be useful here.

While the training requirements of various categories of staff depend upon the way the health system is organized in a particular country, Table 4 gives the generic training requirements of staff at various levels. This needs to be adapted by the countries depending on the local conditions.

3.5 Capacity building

Technical guidelines

For initiating the paediatric ART programme and also for developing technical expertise in the area, development/adaptation of technical guidelines for paediatric ART are mandatory. WHO guidelines for paediatric antiretroviral therapy in resource limited settings are available now. These include the WHO paediatric ART document and WHO-SEARO clinical manual^{14, 22}. Also guidelines on co-trimoxazole prophylaxis and prevention of mother-to-child transmission are available^{23, 24}. These guidelines will serve as important resource materials.

Clinical guidelines are essential to standardize services at clinics and to facilitate the smooth referral of patients within public facilities and between public and private clinics. Clinicians in both public and private sectors should be supported to adhere to the guidelines. The national guidelines should address the following issues:

- Criteria for children who should start ART
- Selection of the treatment regime for children
- Adherence counseling requirements
- Type and frequency of laboratory tests needed to monitor patients
- Side effect management
- When to shift to second-line treatment protocols
- Referral protocol between different levels within the public sector and between public and private sectors

- Procedures for sending blood samples and results between different levels
- Procedures for registering patients and follow-up

The specific guidelines developed must be simple to understand, have specific “what to do” instructions, be user-friendly and be available where needed, in a language commonly used at the service point. The process of developing national clinical guidelines should include a committee of experts in the following areas: medical, nursing, laboratory, pharmaceutical and counseling.

The countries will also have to finalize the dosing regimen, based on the availability of formulations. Once the formulations are chosen, then specific weight band based dosing guidelines will have to be developed. Some countries in the region have already started this exercise. The Thai programme relies predominantly on adult FDC formulations. India is using the paediatric stavudine-based three-drug FDCs for the roll-out programme²⁵. Pending the availability of paediatric FDCs, it is recommended that experts in the country work together to arrive at consensus on the dosing guidelines. Existing guidelines from WHO and individual countries will be useful. A few generic issues that will need to be addressed include:

- (a) Are the ARV drugs recommended in the guidelines the most appropriate for the country context?
- (b) Is the regimen the most effective choice, based on recent scientific research?
- (c) Are the most appropriate drugs registered in the country?
- (d) Are appropriate formulations for children available in the country?
- (e) Can the programme afford the most effective drugs?
- (f) Do donors or the host government restrict certain drug formulations or generic or branded drugs?
- (g) Are there barriers to import, such as excessive taxes?
- (h) What is the status of monitoring facilities?

It is critical to address such questions early when integrating paediatric ART into existing HIV care and support services. Delaying the process can delay procurement, which will adversely affect the outcomes of children infected with HIV. It is best to select regimens based on scientific data, adapt from international and WHO guidelines and then undertake a process to register the most appropriate drugs for that setting. In addition, the pharmaceutical industry could be encouraged to develop and provide appropriate paediatric ARV formulations.

The task of developing/ adapting the guidelines could be entrusted to a group of experts. It may be useful to involve professional bodies of paediatricians to take a lead in developing such materials.

It is important to realize that care and treatment guidelines- including those relating to Paediatric ART generally reflect the knowledge and treatments available around the time of publication, and therefore, require periodic review and updating. A definite plan for updating should be drawn up at the initial stage itself.

Guidance on role definition – various levels of the health-care delivery system

Each country will have to define the roles for the various levels of the health care delivery system (see Table 5). At the field level, the major contribution could be for early recognition of HIV-infected children and referral, support to the patient and family and ensuring adherence to therapy. At district level, capacity should be built to diagnose HIV infection, initiate antiretrovirals, manage the opportunistic infections and monitor the therapy. At the tertiary/specialized level, diagnostic facilities like HIV-DNA PCR could be provided and expertise developed to manage complicated cases.

Appropriate training material

A key requirement for rapid scale-up of paediatric ART will be the capacity to train necessary numbers of health-care personnel (physicians, nurses, pharmacists and counselors) within a short period of time. For this purpose, each country/region needs to develop appropriate training materials. The

Table 5: Services and level of staffing specific to ART at different levels of the health systems

Level	Primary care/First level	District level	Specialized centre
Services	<ul style="list-style-type: none"> – Suspecting diagnosis of HIV infection in children – Counseling for HIV testing – Rapid HIV testing – Counseling for ART adherence – Clinical assessment – Blood sample – Referral – Registration of ART recipients – Patient follow-up – Basic side-effect management 	<ul style="list-style-type: none"> – All primary level services – HIV ELISA testing – Complete blood counts – Blood urea level – Serum Bilirubin level – Moderate side-effect management 	<ul style="list-style-type: none"> – All district level services – CD4 count – Viral load – Severe side-effect management
Antiretroviral drug dispensing?	No	Yes	Yes
Minimum staffing	Nurse Counselor	Physician Nurse Lab technician Counselor Pharmacist	Infectious disease specialist Physician/ Paediatrician Nurse Lab technician Nutritionist Counselor Pharmacist
Community support	Social worker NGOs	Social worker NGOs	Social worker NGOs

professional paediatric bodies or specialized institutions could take the lead. Some material that has been developed internationally could be adapted for local use. A suggested approach is conducting workshops that have an optimal mix of lectures, case discussions and demonstrations on actual patients. The supplementary material required will be a training manual. To scale up rapidly, training of trainers could be conducted and thereafter these trained faculty could accelerate the training.

Continuing mentorship could provide ongoing training of trained health-care professionals. This will allow newly trained physicians treating children with HIV infection the opportunity to clarify their doubts and increase their competence. Individual programmes could decide on the methods to do this, which should include:

- (a) Periodic visits to the centres by experts on pre-decided dates
- (b) Consultation on cases where problems are encountered in diagnosis or management
- (c) Telephonic consultation with experts

The training materials could include:

- (i) Clinical care manuals
- (ii) Presentation modules
- (iii) Simple tools for drug dosing
- (iv) Web-based learning tools

Pre-service training

It is desirable to include theoretical and practical training for identification of HIV-infected children and their management in the curriculum of undergraduates in respective countries. This should be aligned with the national treatment guidelines for the children.

Trained laboratory personnel and laboratory infrastructure

Children need special investigations for diagnosis and management of HIV infection. The following investigations are required in the management of HIV-infected children:

- (1) Diagnosis of HIV infection in children
 - (a) ELISA test for children older than 18 months – guidelines for this will be the same as that for adults.
 - (b) DNA PCR for children < 18 months born to HIV-infected mothers: As there is passage of antibodies from the HIV-infected mother to a child born to her, ELISA tests cannot be used for diagnosing HIV infection in the

infant. For confirmation of HIV infection, HIV DNA PCR has to be used. This can also be carried out on a dried blood spot sample. The other virologic tests such as viral culture are expensive and require sophisticated methodologies and equipment and hence are not routinely used.

- (2) Initial evaluation of HIV-infected child.: The *laboratory assessment* for infants and children at baseline should include:
 - (a) measurement of CD4 and CD4%, where available
 - (b) hemoglobin measurement in infants and children initiated on zidovudine containing first-line regimens
 - (c) white blood cell count (WBC)
 - (d) pregnancy test for sexually active adolescent girls
 - (e) Screening for TB and malaria (and diagnostic testing where clinically indicated), and for other major treatable HIV coinfections and HIV-related opportunistic diseases as clinically indicated.

- (3) Monitoring of children receiving ART: Laboratory assessment of CD4 values is desirable every six months, or if clinically indicated. The total lymphocyte count (TLC) is not suitable for monitoring of therapy as it does not reliably predict treatment success. Haemoglobin measurement in those infants and children initiated on AZT-containing first-line regimens should be performed during the first few months of treatment. Haematology tests for liver damage (i.e. liver enzymes) are recommended in infants and children receiving nevirapine or coinfecting with hepatitis viruses during the first few months of treatment with these drugs. When choosing other laboratory parameters, clinical symptoms should be taken into consideration for assessing the response to therapy. Some routine monitoring tests may be advisable according to the specific drugs used, however laboratory monitoring of adverse events should largely be directed by clinical symptoms (see Table 6).

Table 6: Laboratory parameters for monitoring infants and children at baseline, prior to ART and during ART

Diagnosis and monitoring laboratory tests		Baseline	Monthly at initiation of 1 st or 2 nd line regimen (weeks 4, 8, 12)	Every 6 months	As required (i.e., symptom-directed)
HIV diagnostic testing: virological and Ab testing		✓	–	–	–
Haemoglobin ^a		✓	✓	–	✓
WBC and differential		✓	✓	–	✓
% CD4 or absolute CD4 cell count ^b		✓	–	✓	–
Pregnancy testing in adolescent girls ^c		✓	–	–	–
Full chemistry (including, but not restricted to, ALT ^d , liver enzymes, renal function, glucose, lipids, amylase, lipase and serum electrolytes) ^e		–	–	–	✓
Diagnostic tests for treatable coinfections and major HIV/AIDS-related opportunistic infections (OIs)	Screening for TB and malaria (basic microscopy; i.e. sputum smear test for TB and thick blood drop smear test for malaria diagnosis) ^f	–	–	–	✓
	Full cerebrospinal fluid (CSF) microscopy (including India ink for cryptococcal meningitis). In adolescents: syphilis and other STI diagnostic tests.	–	–	–	✓
	Diagnostic tests for hepatitis B, hepatitis C serology, bacterial microbiology, and cultures and diagnostic tests and procedures for PCP, Cryptococcus, toxoplasmosis and other major OIs)	–	–	–	✓
HIV viral load measurement ^g	–	–	–	–	✓

Notes for table:

- Haemoglobin monitoring during the first weeks of treatment has been recommended by some experts if AZT is used. However, other experts suggest that the haemoglobin level can be monitored in a symptom-directed approach, particularly for AZT-free regimens.
- Children who are not yet eligible for ART should be monitored with measurement of CD4 every 6 months. For infants and children who develop WHO Stage 2 events, or whose CD4 measurements approach threshold values, the frequency of CD4 measurement can be increased. Measurement of % CD4 is preferred in children <5 years of age.
- Pregnancy testing may be needed for adolescent girls initiating a standard first-line regimen containing EFV.
- The predictive value of pre-emptive liver enzyme monitoring is considered very low by some experts; WHO recommends liver enzyme monitoring in a symptom-directed approach. However, regular monitoring during the first three months of treatment and symptom-directed measurement of liver enzymes thereafter has been considered by some experts for certain children using nevirapine-based regimens, in particular for adolescent girls with CD4 cell > 250 cells/mm³ and infants and children coinfecting with hepatitis B or hepatitis C virus, or other hepatic disease.

- e. Regular monitoring (every six months) of full chemistry tests, particularly lipid levels, liver enzymes and renal function, should be considered for infants and children using second-line drugs.
- f. In general, active TB infection should be excluded in all patients prior to the initiation of ART, as indicated by symptoms, and according to national TB control protocols.
- g. Viral load measurement is currently not recommended for decision-making on initiation or regular monitoring of ART in resource-limited settings. Technology for assessment of viral load can also be used to diagnose HIV infection although it is not yet standardized for this purpose.

(**Source:** WHO. Antiretroviral therapy of HIV infection in infants and children in resource-limited settings: towards universal access: Recommendations for a public health approach. Geneva. 2006).

In addition, in resource-constrained settings, HIV-infected children may have a variety of HIV-related conditions including TB and malaria. Strong laboratory capacity at health facilities helps diagnose and treat these conditions prior to ART initiation, as well as distinguish between drug toxicity and treatment failure after treatment has started. With a moderate investment in laboratory upgrading, community health centres and district-level facilities can conduct most laboratory tests for ART monitoring (Table 7). As part of programme planning, it is crucial to develop an implementation plan to strengthen laboratory services.

There will also be a need to upgrade some of the laboratories to perform HIV DNA PCR for diagnosis in young infants. In children under five years of age, it is important to have % CD4 reports instead of just absolute CD4 counts, as this correlates better with prognosis. Policy-makers should strongly consider upgradation of available equipment to perform such analysis. **If new equipment is being procured, it should be capable of delivering % CD4 reports in addition to absolute CD4 counts.**

There should be efforts to enhance the capacity of the laboratories for diagnosis of opportunistic infections especially *Pneumocystis jiroveci* and fungal infections in children. In most conditions, the needs are same as those for adults.

Though integrating Paediatric ART into existing laboratory services may be relatively easy, it is important to ensure that laboratories can support scale-up. Components of the existing system may be weak or already stressed by the workload. In the push to start, stakeholders may overlook laboratory-related constraints to expansion, especially if there is much to address.

Table 7: Recommended tiered laboratory capabilities for ART monitoring

Diagnosis & monitoring laboratory tests		Primary care level	District level	Regional/Referral level
HIV antibody testing ^a		✓	✓	✓
HIV virological diagnostic testing ^b		–	+	✓
Haemoglobin ^c		+	✓	✓
WBC and differential		–	✓	✓
CD4 (Absolute count and %)		–	✓	✓
Pregnancy testing ^d		+	✓	✓
ALT		–	✓	✓
Full chemistry (including but not restricted to: liver enzymes, renal function, glucose, lipids, amylase and serum electrolytes)		–	–	✓
Diagnostic tests for treatable coinfections and major HIV/AIDS-related opportunistic infections (OIs)	Basic microscopy for TB and malaria (sputum smear for TB and blood film for malaria diagnosis) ^e	+	✓	✓
	Full cerebrum spinal fluid (CSF) microscopy (including India ink for cryptococcal meningitis), syphilis and other STI diagnostic tests	–	✓	✓
	Diagnostic tests for hepatitis B, hepatitis C serology, bacterial microbiology and cultures and diagnostic tests and procedures for PCP, Cryptococcus, toxoplasmosis and other major OIs)	–	+	✓
HIV viral load measurement ^f		–	–	+

Key: ✓ Essential test
+ Desirable, but not essential test
– Not essential test

ALT – alanine transaminase; CSF – cerebrum spinal fluid; WBC – white blood count;
PCP – Pneumocystis pneumonia

- Rapid tests are recommended at primary level and conventional methodologies can be used at district and regional/central levels.
- Virological testing for establishing HIV diagnosis in infants and children under 18 months of age can be performed using dried blood spots (DBS)
- Should be available if AZT is being considered for use.
- Should be available if EFV is being considered for use.
- Referral if microscopy is not available.
- Viral load measurement is currently not recommended for decision-making on initiation or regular monitoring of ART in resource-limited settings. Technology for assessment of viral load can also be used to diagnose HIV infection although it is not yet standardized for this purpose.

Source: WHO. Antiretroviral therapy of HIV infection in infants and children in resource-limited settings: towards universal access: Recommendations for a public health approach. Geneva, 2006.

When the paediatric ART roll-out plan is in the initial stages, there will be intense efforts to identify infected children and enroll them. In such a scenario there will be a need for laboratory diagnosis for a large number of children. In this initial phase, it may be useful to dedicate a few days exclusively for diagnosis in children.

Programme planners need to anticipate equipment needs and address human resource constraints given that the workload of the laboratory will increase significantly with both routine and *ad hoc* testing required for those on ART. **Trained personnel and procedures to ensure quality of results must be in place before roll-out/scale-up.**

3.6 Managerial expertise

The comprehensive nature of HIV/AIDS programmes makes them extremely complex as there are many interrelated dependencies. The ART roll-out plan consists of many components that are complex on their own. However, to create managerial focus, the roll-out of ART stands central in this implementation plan. Expansion of the existing ART services or creation of new delivery sites for paediatric ART will need expert managerial skills. Various areas demanding competence include:

- (a) **Human resources** (*Health-care professionals and allied staff*): There will be a need for managerial experience to make efficient use of the services of the available health-care personnel for delivering ART to children. In addition, opening of new centres will require new staff. The centers' workload has to be identified and the numbers of patients seen should be spaced out equally to improve the clinical care. The roles of the personnel – physician/paediatrician, nurse, counselor, pharmacist, supporting staff – have to be defined. For the existing centres, the staff will have to be motivated to take care of additional workload.
- (b) **Managing drug supplies** (*ensuring that there no periods of stock out*): The key determinant of success of the ART programme is the ability to ensure >95% adherence to the therapy lifelong. This aspect is important to ensure sustained virologic and immune response to ART as has been shown in various studies²⁶. As more than 95% adherence is critical to success of the therapeutic regimen, the supply of drugs has to be ensured at all times, so that children are not sent back without ART. Various factors to be considered are:

- (i) ***Use of multiple formulations:*** Unlike adults, where one or two formulations are used for any regimen, in children there is a need for multiple formulations to deliver antiretroviral drugs in appropriate doses.
 - (ii) ***Dose adjustments for growth of children:*** As the children grow, the dose and the formulations will need to change. There will be a need for regular monitoring of these aspects to ensure that the supplies are maintained.
 - (iii) ***Drug procurement and distribution:*** the programme managers will have to look at the requirements of various drugs that are approved for use by the expert group. The calculations for the drug requirement will need to be modeled and the available packages like SPECTRUM²⁷ could be used for the same. The programme can be downloaded from the site: http://www.unaids.org/en/KnowledgeCentre/HIVData/Epidemiology/epi_software2007.asp. In addition to the issues of timely procurement, the distribution will also have to be streamlined so that there are no periods of stock-out at any of the centers.
- (c) ***Managing patient flow and follow up:*** More than 95% adherence to the therapy is an important determinant of success of the ART programme. One of the determinants of this will be the ability of the treating team to convince the guardians/parents to adhere to the therapy. Patients often avoid coming to health-care facilities that are not perceived as patient-friendly. The programme managers should make efforts to make the clinic visits convenient to the patients and also emphasize the need for a **family-based** approach. If more than one member of the family is infected and needs care/ART, then efforts should be made to evaluate these patients together. There will be a need to think of strategies to ensure adherence to a follow-up schedule. One suggestion could be giving out an appointment for the next scheduled follow-up visit. If staffing permits, then the families could be contacted a day or two before the scheduled visit by the pharmacist/nurse to

remind the patient about the follow-up. A good recording system helps in ensuring follow up. Strategies to improve follow-up may include use of telephone, home visits by a health-care worker, identification of a treatment supporter, etc. However, extreme care should be taken to ensure confidentiality of the families.

- (d) ***Managing laboratory function and supply of diagnostics:***
The laboratories will have to handle the additional workload for diagnosis of HIV infection and opportunistic infections in children. For children younger than 18 months, DNA PCR will have to be arranged. Depending on the national policy, these services may be made available only at some centrally located facilities. The programme should be able to project the demand for additional diagnostic capabilities and be able to meet them as the programme expands.
- (e) ***Programme costs:*** The programme managers will also have to address to the estimation of the cost of the roll-out programme. The costs include:
 - (i) Antiretroviral drug cost
 - (ii) Laboratory costs
 - (iii) Costs for sample transfer
 - (iv) Human resources and training costs
 - (v) Information technology management
 - (vi) Behavioural change communication strategy costs

Setting targets: Depending on the extent of problem, individual programmes will have to define the targets to be achieved in a set time period. For that, reasonable estimates of the extent of the problem are required. Some of these parameters include: number of infected children, geographical distribution and number of children needing ART. Based on these numbers, the targets for different phases could be determined. This will also allow the determination of resources required. Once the targets are decided upon, adequate financial support should be ensured.

Adequacy of facilities to provide health care to children

The national plans to respond to paediatric HIV/AIDS cannot be achieved without adequate focus on improving health-care system capacity. As the paediatric ART programme is rolled out, the number of children accessing care is likely to increase. Extra efforts will be made to improve the identification of HIV-infected children as the programme is scaled up. To ensure credibility of health-care systems, they should be able to take care of such increases in number. Many HIV-infected children may require care for concurrent illnesses, particularly in the early part of enrollment in the HIV care and treatment programme. For this, the overall capacity of health-care systems to manage sick children will need to be enhanced.

3.7 Supplies

For a programme to run successfully, great attention has to be paid to the supply chain management for antiretroviral drugs.

Appropriate paediatric antiretroviral formulations

For initiating ART in children, appropriate paediatric formulations are desirable. The possible options are:

- Syrups
- Tablets of individual drugs
- Fixed dose combination tablets (scored and dispersible)
- Fixed dose combination suspensions/syrups
- Adult fixed dose combinations

Of all these, for logistic reasons, paediatric FDCs (scored and dispersible) are most appropriate. In some countries, different FDC formulations are available for stavudine, lamivudine and nevirapine. It is desirable that all the weight bands are covered using the minimum number of formulations. For example, in India three types of stavudine based three-drug paediatric formulations are available²⁵ as shown in Table 8.

Table 8: Paediatric formulations of stavudine based three-drug combination available in India

	Stavudine	Lamivudine	Nevirapine
FDC 6	6 mg	30 mg	50 mg
FDC 10	10 mg	40 mg	70 mg
FDC 12	12 mg	60 mg	100 mg

At present, no paediatric zidovudine based three-drug formulation is available. However, there is an effort to develop paediatric formulations of combinations of zidovudine, lamivudine and nevirapine.

While syrups increase the dosing accuracy, the volumes that have to be administered increase significantly for a year-old infant and compromise adherence.

Efforts are underway to encourage the pharmaceutical industry to develop and deliver appropriate formulations. If this is not feasible, then the countries should consider import of such formulations.

Recently, WHO has recommended new formulations for three drug combinations of ART for children²⁸. A simplified dosing table for ideal products has been prepared for twice daily dosage. Countries will find this useful to make decisions regarding the most suitable combination depending upon national policy.

Procurement and supply chain management (PSM)

Initial forecasting based on regimens in the national treatment guidelines, ensuring local registration, procurement, storage, distribution and end-user monitoring are major processes in PSM. Attention to drug procurement must come very early in the programme and precede training and other programme interventions. This is increasingly important as the lead time between ordering and receipt of products increases as pharmaceutical firms face exponential increases in ARV orders worldwide.

The forecasting of drug supplies for children is complicated by the need for multiple formulations and frequent changes in the dosing as the child grows.

To guarantee regular drug supply and avoid stock-outs and drug expiry, it is essential to define protocols for drug forecasting, ordering, dispensing and tracking at both the national and health-facility levels. For preventing wastage of drugs due to expiry, care should be taken to ensure a “first in, first out” principle. Pharmacy staff require training on ART, related protocols, functional record-keeping of drug procedures, and systems to minimize drug theft and diversion. Before an ART programme begins, it is important to consider infrastructure needs, such as secure storage space and confidential counseling areas. Records (bin cards, forms and patient records), labels and bottles/cartons are also essential to an effective pharmacy function.

It is possible to integrate ART services into supply and logistic management systems of health ministries in the country. But it is critical to understand each site, identify unique strengths and weaknesses and then collaboratively develop a plan with clearly defined roles, responsibilities and timeframes. It is beneficial to involve different disciplines to build trust and foster understanding of professional roles across departments.

3.8 Monitor and evaluate programme implementation

Ongoing monitoring and evaluation of roll-out programme implementation is an essential component of the plan. The key issues to be monitored should include the number of children enrolled, the follow-up rates, adherence to ART, caretakers’ satisfaction and measures to improve these. In addition, monitoring/auditing of prescriptions for children will be essential, given the complexity of the dosing regimen.

Routine collection and analysis of patient response data is essential to the effective management of children on ART. For example, ARV drugs will be ordered according to the child’s regimen. Thus, it is imperative to know the proportion of children still on a certain regimen, who needs modification of the formulation, who changes one or more drugs, who

ceases treatment, etc. It is also critical to know the type of side effects and drug toxicity experienced by children in order to adjust paediatric ART educational sessions and materials. Further, when regimens fail it means resistance has developed to certain drugs. The frequency of occurrence of such events has to be monitored carefully and efforts should be made to determine whether this was related to poor adherence. Treatment failure has implications not only for the child, but for programme management as well (drug procurement, supply sources, costs, etc.). In the current scenario, most countries have provision for just the first-line regimens. So it is important to invest enough in ensuring adequate use and adherence to the first-line regimen. At the same time, efforts should be made to monitor drug resistance in the HIV. Data on treatment failures may guide the programme managers to decide on the strategy for second-line antiretroviral drugs.

A good patient data management system needs to be developed, where the data of all the patients is transmitted to the central programme coordination agency/team on a regular basis, which can then be periodically analysed. It will be important to decide about the key indicators to be monitored.

Box 3: Suggested monitoring indicators

Improve the ability to identify HIV-infected children

- (1) Percentage of pregnant women who received HIV-testing
- (2) Percentage of HIV-infected women who received antiretrovirals for prevention of MTCT.
- (3) Percentage of infants born to HIV-infected women who are followed up at six weeks age; percentage of such infants who are tested by PCR for HIV infection.
- (4) Percentage of children diagnosed to have TB, who are tested for HIV infection.
- (5) Percentage of HIV-infected children who are enrolled in HIV clinic services.

Training

- (1) Number of staff trained in management of children with HIV infection
- (2) Number of training sessions conducted for different categories of medical staff.

Infrastructure

- (1) Number of treatment facilities offering paediatric ART.
- (2) Capacity to screen for HIV disease in infants and children.

Technical expertise

- (1) Development of guidelines for management of children with HIV infection.

Laboratory

- (1) Number of laboratories that can perform DNA PCR for diagnosis of HIV infection in HIV-exposed infants.
- (2) Number of laboratories that can report on CD4 percentage counts in addition to the absolute CD4 count.

Capacity to sustain high adherence rates

- (1) Continuation of first-line regimen at 6, 12, and 24 months after initiating treatment.
- (2) Survival at 6, 12, 24, and 36 months after initiation of treatment.

3.9 Enhance measures for ensuring high adherence rates

Drug adherence is of paramount importance for the success of ART. Adherence rates of more than 95% have to be sustained lifelong for ensuring sustained control of HIV viral replication. Various strategies will have to be considered to achieve this goal.

- (A) *Appropriate communication before and at start of ART for the child:* The treating team should identify strategies to

facilitate the child's correct adherence (taste, association of pill-taking with regular daily occurrences or game, respect for confidentiality). In an older child, it may be useful to let the child take part in choosing the best way to take medicine regularly. The prescriptions should be explained in simple language to the child's caregiver.

- (B) **Counseling:** Counselors will need appropriate training to communicate the importance of adherence to the family of the child.

While preparing for counseling for adherence, it is important to assess:

- HIV+ parent's own adherence to treatment if s/he is the caregiver
- Caregiver's awareness of risks to the child deriving from incorrect adherence
- Whether the caregiver is anxious that the medication could harm the child
- Caregiver's cognitive capacity to understand the nature of the treatment and importance of adherence
- Older child's awareness of importance of adherence to treatment
- Presence of depression or "giving up" in the caregiver or older child

The caregivers have to be informed that:

- Child's health depends on strict regularity of pill-taking
- ART has possible transitory side effects that vary in duration and severity

At each visit of the child to the ART centre, adherence will need to be assessed and corrective measures suggested, if required. It is useful to assess the adherence to pre-ART treatment; for example, adherence to cotrimoxazole prophylaxis.

- (C) ***Assessment of adherence by the physician/nurse/pharmacist:*** At each visit to the ART centre, the adherence should be assessed. This could be done by a physician, nurse or pharmacist. The responsibility could be assigned, but it will be useful if adherence is assessed by more than one individual. The adherence could be assessed by interview and pill count. If syrups are being used, then measurement of the volumes left can be done. If there is poor adherence, then the possible reasons should be identified and corrective actions recommended.
- (D) ***Community support strategies:*** This could be a critical element of an effective programme. Community-based organizations, NGOs could play an important role in improving adherence.
- (E) ***Maintenance of confidentiality and delivery of quality health care:*** These are important to ensure adherence. It will be desirable to develop simple tools for families and NGOs to improve adherence. If effective monitoring and support systems are in place, illiteracy has a minimal effect on adherence.

3.10 Retaining trained staff

An increase in numbers of patients on ART may create challenges for already overburdened health staff, resulting in fatigue, stress, and decreased morale and motivation. Attrition may result. To maintain a motivated, competent staff, it will be important to address the professional, psychological and financial needs of health workers. This may be beyond the purview of donor-funded development programmes; advocacy with government budget authorities is an option. However, there could be provisions for special educational opportunities for staff working with HIV patients, clinical consultation, positive supervisor feedback and data feedback on mechanisms that recognize progress in reaching more clients and saving more lives. Other incentives include attention to the HIV care needs of infected health providers and their families, and assistance with writing of abstracts and presentations at national and international conferences on adherence.

3.11 Accreditation and quality assurance

It will be rewarding to take steps to ensure the quality of clinical service delivery from the very beginning. Accreditation criteria could be developed to recognize centres that would be authorized to prescribe paediatric ART. The criteria for accreditation could include the presence of basic physical infrastructure, minimum number of qualified personnel with experience in managing children with HIV/AIDS, the ability to ensure follow-up care and support for the families. The criteria should also be applicable to the private sector.

Use of HIVQUAL software may be useful in implementing the quality control programme. It can be used as a tool to facilitate measurement of quality. HIVQUAL offers a simple vehicle for the rapid generation of reports that monitor clinical performance for those patients who have been entered into the database. It will also analyse data for different subpopulation groups, including gender, race/ethnicity, exposure categories, age, viral load, CD4 count and clinic site. Specific features also include randomized sampling of patients in the database for generation of quality reports. More information about HIV QUAL can be accessed at: <http://hab.hrsa.gov/special/hivqualsoftware.htm>.

Quality indicators currently measured in the HIVQUAL project are:

- HIV staging (viral load, CD4 count)
- Antiretroviral therapy management
- Opportunistic infections prophylaxis (PCP, MAC)
- Gynaecological care (pelvic exam with PAP smear, GC culture, chlamydia screening)
- Tuberculosis screening
- Substance use screening
- Specialty referrals (dental, ophthalmology)
- Treatment adherence
- Patient education
- Access to expert HIV care

4

Operations research

Paediatric ART programmes in many countries are still at an early stage, and, in most cases, are limited to pilot and small-scale projects. As access to ART improves, many questions regarding practical implementation will arise. Moving from pilot projects to large-scale implementation adds great logistical, programmematic, and cost complexities to ART services, particularly for low-income countries. Therefore, key operations research is needed to assist resource-limited countries to design cost-effective ART programmes.

Including operations research from the start of programme planning can be instrumental in integrating research within programme implementation. Early discussions on OR will help in refining the research design in the context of programme implementation, in mobilizing resources to conduct research and in increasing acceptability among health workers, programme planners and implementers.

A few suggested areas for operations research:

1. *Efficacy and safety of various treatment regimens*

Country specific studies on efficacy, safety and acceptability of various treatment regimens will help guide future policy directions about the most suitable regimen.

2. *Defining patient adherence determinants*

- When choosing a treatment combination, is there a difference between rates of adherence with less complicated regimens (three times daily vs. two times daily) and regimens that have a lower pill burden?

- How are the rates of adherence affected by using directly observed therapy or adherence counseling?
- For ART to be successful, the social circumstances of patients must be considered, including their family structure, income and availability of transport to clinic.

3. Exploring low-cost patient monitoring alternatives

Flow cytometry for CD4 measurement, and PCR-based viral load testing is difficult to implement in resource-poor countries because of the cost of equipment, consumables, equipment maintenance and staff training and labour. More innovative thinking is required to ensure feasible, sustainable, low-cost monitoring options. For example, using total lymphocyte count (TLC) as a predictor of a low CD4 cell count can be further tested. Another option requiring operations research is the use of low-cost laboratory techniques in combination with clinical assessment (e.g., weight loss, wasting, neurological signs, onset of opportunistic infection).

4. Testing cost-effectiveness and feasibility of decentralized laboratory services

Centralization or decentralization of laboratory tools is an important consideration in a large-scale ART programme. In some cases, tests can be brought to the patient (for example, rapid HIV testing). When the CD4+ cell and viral load test cannot be brought to the patient, centralization of laboratory services provides important cost savings through volume of samples. Transportation of samples from the peripheral clinics to the central laboratories then becomes the limiting factor. Research on this issue needs to consider the availability of suitable blood sample transport mechanisms, the stability of samples, the transport route and the cost of sample transportation, and recommend the appropriate balance between centralizing and decentralizing laboratory tests. An important issue to be evaluated is the feasibility of using of dried blood spots for HIV DNA PCR for diagnosis of infection in HIV-exposed infants.

References

1. UNAIDS / WHO. *AIDS epidemic update: December 2007*. Geneva, 2007. (http://whqlibdoc.who.int/unaid/2007/9789291736218_eng.pdf - accessed 26 May 2008).
2. Human Development Network. *Addressing HIV/AIDS in East Asia and the Pacific*. Washington D.C., The World Bank. 2004.
3. WHO / UNAIDS. *Progress in scaling up access to HIV treatment in low and middle-income countries, June 2006*. Geneva, 2006. Joint fact sheet WHO/UNAIDS/309 August 2006. http://www.who.int/hiv/toronto2006/FS_Treatment_en.pdf - accessed 26 May 2008).
4. WHO / UNAIDS / UNICEF. *Towards universal access: scaling up priority HIV/AIDS interventions in the health sector: progress report, April 2007*. Geneva, 2007. (http://whqlibdoc.who.int/publications/2007/9789241595391_eng.pdf - accessed 26 May 2008).
5. Barnhart HX, Caldwell MB, Thomas P, Mascola L, Ortiz I, Hsu HW, Schulte J, Parrott R, Maldonado Y, Byers R. Natural history of human immunodeficiency virus disease in perinatally infected children: an analysis from the Pediatric Spectrum of Disease Project. *Pediatrics*. 1996 May; 97(5): 710-6.
6. Wamalwa D, Farquhar C, Obimbo E, et al. Adherence and early response to highly active antiretroviral therapy in Kenyan children. Abstract no. TUPE0104. *AIDS 2006 - XVI International AIDS Conference, Toronto. 2006*.
7. Nannyonga M, Morelli E, Atai B, Michelin E., Lain MG, Marinello S, Bettio M, Mazza A, Putoto G, Giaquinto C. Efficacy of HAART in Ugandan HIV-infected children. Abstract no. MOPE0246. *AIDS 2006 - XVI International AIDS Conference, Toronto. 2006*.
8. Raleigh B, Soeung S, Akao K, Te1 V, Gupta J, Khem S, Janssens I B, Zachariah R. Excellent outcomes can be achieved in children on highly active antiretroviral treatment under program conditions in Cambodia: the experience from two hospitals in Siem Reap and Takeo, Cambodia. Abstract no. MOPE0254. *AIDS 2006 - XVI International AIDS Conference, Toronto. 2006*.
9. Chearskul P, Chokephaibulkit K, Chearskul S, et al. Efficacy of highly active antiretroviral therapy (HAART) in Thai Children : Bangkok. Abstract no. TuPeB4446. *AIDS 2006 - XVI International AIDS Conference, Toronto. 2006*.
10. Chintu C, Bhat GJ, Walker AS, Mulenga V, Sinyinza F, Lishimpi K, Farrelly L, Kaganson N, Zumla A, Gillespie SH, Nunn AJ, Gibb DM; CHAP trial team. Co-trimoxazole as prophylaxis against opportunistic infections in HIV-infected Zambian children (CHAP): a double-blind randomised placebo-controlled trial. *Lancet*. 2004 Nov 20-26; 364(9448): 1865-71.
11. Newell ML, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P, Dabis F. Mortality of infected and uninfected infants born to HIV infected mothers in Africa: a pooled analysis. *Lancet*. 2004 Oct 2-8; 364(9441): 1236-43.
12. WHO / UNAIDS. *How will the 3 by 5 initiative deal with HIV drugs resistance?* Geneva, 2003. (http://whqlibdoc.who.int/hq/2003/WHO_HIV_2003.10.pdf - accessed 6 June 2008).

13. United Nations. *Preparations for and organization of the 2006 follow-up meeting on the outcome of the twenty-sixth special session: implementation of the declaration of Commitment on HIV/AIDS*. Resolution adopted by the General Assembly. Resolution No. 60/224. (http://data.unaids.org/topics/ungass2003/a60-l43_2005_en.pdf - accessed 26 May 2008).
14. World Health Organization. *Antiretroviral therapy of HIV infection in infants and children in resource-limited settings: towards universal access: recommendations for a public health approach*. Geneva, 2006. (<http://www.who.int/hiv/pub/guidelines/WHOPaediatric.pdf> - accessed 26 May 2008).
15. UNAIDS. *The road towards universal access: scaling up access to prevention, treatment, care and support - concept paper*. January 2006. Geneva, 2006. (http://data.unaids.org/Topics/UniversalAccess/UniversalAccess_Concept_Jan2006_en.pdf - accessed 26 May 2008).
16. Yarmohammadi H, Estrella L, Doucette J, Cunningham-Rundles C. Recognizing primary immune deficiency in clinical practice. *Clinical and Vaccine Immunology*. 2006 Mar; 13(3): 329-32.
17. Angami K, Reddy SV, Singh KhI, Singh NB, Singh PI. Prevalence of HIV infection and AIDS symptomatology in malnourished children—a hospital based study. *Journal of communicable diseases*. 2004 Mar; 36(1): 45-52.
18. Karande S, Bhalke S, Kelkar A, Ahuja S, Kulkarni M, Mathur M. Utility of clinically-directed selective screening to diagnose HIV infection in hospitalized children in Bombay. *Indian Journal of Tropic Pediatrics*. 2002 Jun; 48(3): 149-55.
19. Shahab T, Zoha MS, Malik MA, Malik A, Afzal K. Prevalence of human immunodeficiency virus infection in children with tuberculosis. *Indian Pediatrics*. 2004. Jun; 41(6): 595-9.
20. Merchant RH, Shroff RC. HIV seroprevalence in disseminated tuberculosis and chronic diarrhea. *Indian Pediatrics*. 1998 Sep; 35(9): 883-7.
21. WHO / UNAIDS. *Guidance on provider-initiated HIV testing and counselling in health facilities*. Geneva, 2007. (http://whqlibdoc.who.int/publications/2007/9789241595568_eng.pdf - accessed 27 May 2008).
22. World Health Organization, Regional Office for South-East Asia, UNICEF. *Management of HIV infection and antiretroviral therapy in infants and children: a clinical manual*. WHO Technical Publication No. 51. New Delhi. 2006.
23. World Health Organization. *Guidelines on co-trimoxazole prophylaxis for HIV-related infections among children, adolescents and adults in resource-limited settings: recommendations for a public health approach*. Geneva, 2006. http://whqlibdoc.who.int/publications/2006/9789241594707_eng.pdf - accessed 27 May 2008).
24. World Health Organization. *Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants in resource-limited settings towards universal access: Recommendations for a public health approach*. Geneva. 2006. http://whqlibdoc.who.int/publications/2006/9789241594660_eng.pdf - accessed 2 June 2008).

25. IAP / NACO. *Guidelines for HIV care and treatment in infants and children*. New Delhi: Indian Academy of Paediatrics, 2006.
26. Bangsberg DR. Less than 95% adherence to nonnucleoside reverse-transcriptase inhibitor therapy can lead to viral suppression. *Clinical Infectious Diseases*. 2006 Oct 1; 43(7): 939-41.
27. USAID-Health Policy Initiative. *A computer program for making HIV/AIDS projections and examining the demographic and social impacts of AIDS: spectrum system of policy models*. Washington, 2007. (http://data.unaids.org/pub/Manual/2007/aim_manual_2007_en.pdf- accessed 27 May 2008).
28. World Health Organization. *Preferred antiretroviral medicines for treating and preventing HIV infection in younger children: report of the WHO paediatric antiretroviral working group*. Geneva, 2008.

While there has been significant progress in recent years in increasing access for children to antiretroviral therapy (ART) around the world, a huge gap still remains between the need and the actual response. This is as true for most of the South-East Asia Region as for the rest of the world. Based on global and regional experiences, this publication is designed to provide practical guidance to national programme managers and implementing partners in South-East Asia for developing and scaling up HIV care and treatment for children.



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