Operational guide for national programmes on the use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants in resource-limited settings

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Contents

Abbreviations and acronyms

3TC	lamivudine
ABC	abacavir
AIDS	acquired immunodeficiency syndrome
d4T	stavudine
EFV	efavirenz
HIV	human immunodeficiency virus
NNRTI	non-nucleoside reverse-transcriptase inhibitor
NRTI	nucleoside reverse-transcriptase inhibitor
NVP	nevirapine
PCR	polymerase chain reaction
PMTCT	prevention of mother-to-child transmission of HIV
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNICEF	United Nations Children's Fund
WHO	World Health Organization
AZT	Azidothymidine

1. Introduction

The WHO comprehensive approach to preventing HIV infection among infants and young children addresses a broad range of HIV-related prevention, treatment, care and support needs of pregnant women, mothers and their children. Reaching the goal of eliminating HIV infection among infants and young children requires providing a standard package of services that includes HIV primary prevention services, antiretroviral drugs for treatment or for preventing mother-to-child transmission (PMTCT), safer delivery practices, counselling on and support for infant feeding and sexual and reproductive health services for women living with HIV. It also includes links to ongoing care and support services.

Provision of antiretroviral drugs plays a critical role within the comprehensive approach. It addresses both PMTCT and maternal treatment needs and therefore ensures the global standard of pregnancy outcome among pregnant women living with HIV. Several projects have also demonstrated that the availability and accessibility of antiretroviral therapy is usually accompanied by increased uptake of counselling and testing, a reduction in stigma and discrimination and enhanced services integration. Providing antiretroviral therapy therefore improves the utilization of other HIV prevention and care services.

Treating pregnant women who require antiretroviral therapy has several benefits. It reduces mortality and morbidity among pregnant women, leads to improved quality of life and substantially reduces the risk of mother-to-child transmission. Reducing mortality among mothers living with HIV reduces the number of AIDS orphans and improves child survival. Any programme-related recommendation or advice provided in the operational guide should therefore be viewed as an integral part of the comprehensive approach.

Although PMTCT programmes started to be implemented as early as 1998 in resource-limited settings, most programmes still focus mainly on strategies for preventing HIV transmission from women living with HIV to their infants using single-dose nevirapine (NVP). Compounded with very low coverage (less than 10% of pregnant women living with HIV receive antiretroviral prophylaxis globally), the use of single-dose NVP, short-course azidothymidine (AZT) or AZT + lamivudine (3TC) alone will not lead to the elimination of HIV among infants as desired due to the relatively lower efficacy compared with highly potent combination regimens. However, single-dose NVP remains a useful option in situations where alternative combinations and longer regimens cannot be implemented. From a public health standpoint, the single-dose NVP approach therefore cannot lead to the attainment of the goals of an HIV- and AIDS-free generation. Further, national programmes face several other challenges such as limited human resources and infrastructure that hamper scaling up; inadequate integration into maternal, newborn and child health services; weak coordination between PMTCT and maternal, newborn and child health (PMTCT is still viewed as a vertical programme); poor follow-up of women and children; weak links with HIV prevention, treatment, care and support; weak monitoring; poor quality of services; inadequate community involvement; weak supply management systems; and lack of access to technologies for early infant testing. All these challenges need to be addressed to achieve the goal of universal access to HIV prevention, treatment, care and support and an HIV- and AIDS-free generation.

The current WHO recommendations for antiretroviral drugs for treating pregnant women and PMTCT in resource-limited settings are based on evidence from randomized controlled trials, high-quality scientific studies for non-treatment-related options, observational cohort data or expert opinion where evidence is lacking or is inconclusive. The current guidelines revise earlier recommendations in 2000 and 2004. One key guiding principle underpinning the recommendations in the revised WHO guidelines is that all pregnant women living with HIV who need treatment should receive antiretroviral therapy for their own health. The guidelines also promote and support more efficacious regimens for those for whom antiretroviral therapy is not yet indicated. This consists of a prophylactic combined antiretroviral regimen comprised of antepartum AZT from 28 weeks or as soon as possible; intrapartum AZT and 3TC plus single-dose NVP; and postpartum AZT and 3TC for seven days for the women. The infant regimen consists of single-dose NVP and AZT for one week. The recommendations also take into account situations where women present late in pregnancy.

The revised guidelines are aligned with the international commitment to universal access to HIV prevention, treatment, care and support services and the Abuja Call to Action: Towards an HIV-free and AIDS-free generation. Additionally, they are harmonized with the WHO guidelines for antiretroviral therapy for adults and children.

The guidelines provide recommendations on:

- drug regimens for women who become pregnant while receiving antiretroviral therapy;
- pregnant women with indications for antiretroviral therapy; and
- antiretroviral prophylaxis for preventing HIV infection among infants.

The advantages of the recommended regimens are as follows.

- Efficacy: in non-breastfeeding settings, the recommended AZT and single-dose NVP regimens (with a tail of AZT + 3TC to reduce the risk of resistance) may achieve transmission rates as low as 2%; in breastfeeding settings, transmission rates of 3–9% have been seen.
- Low level of viral resistance to antiretroviral drugs: the recommended regimens have much lower viral resistance than single-dose NVP and therefore preserves future treatment options for mothers and their children.
- Improved child survival: antiretroviral therapy for mothers who are eligible reduces maternal mortality and morbidity and thereby improves the chances of survival of children born to mothers living with HIV.

Nevertheless, the use of antiretroviral drugs for preventing postnatal transmission in breastfeeding infants is still a subject of research.

WHO and its partners have developed this practical operational guide to help countries develop, revise and implement their guidelines in accordance with the WHO recommendations.

2. Aim and objectives

Aim

The aim of these guidelines is to provide operational guidance on developing and revising national guidelines on antiretroviral drugs for treating pregnant women and PMTCT in accordance with the WHO guidelines and recommendations.

Objectives
Specifically, the document will draw general principles on which to base the effective implementation of national guidelines in accordance with the WHO guidelines and provide practical guidance on the following issues:

- programmatic requirements for adapting the WHO guidelines at the country level; and
- basic steps of adapting the WHO guidelines and introducing or changing over to a new regimen.

3. For whom is this operational guide intended?

This operational guide is a resource to help those supporting and implementing PMTCT programmes in resource-limited settings. It is intended to guide their work in adapting the WHO guidelines on antiretroviral drugs for treating pregnant women and PMTCT. The target audiences for this operational guide are:

- national policy-makers such as national AIDS control programmes, health ministries, managers of PMTCT programmes and their technical working groups, reference groups or task teams;
- nongovernmental organizations and private-sector organizations involved in implementing PMTCT programmes and engaged in developing national policies and strategies for PMTCT; and
- multilateral and bilateral development partners who support the development of PMTCT policy and programmes.

4. How to use the operational guide

The operational guide provides an overview of how policy-makers and programme managers can adapt and deliver the WHO recommendations on antiretroviral drug regimens for treating pregnant women and PMTCT as part of a comprehensive and effective PMTCT programme. It also deals with what needs to be done to adapt the WHO recommendations and provides step-by-step guidance on how to change over to the WHO-recommended regimens.

The operational guide is based on the WHO guidelines on scaling up antiretroviral therapy in resource-limited settings, on antiretroviral therapy for HIV infection among infants and children in resource-limited settings and guidelines on antiretroviral drug regimens for treating pregnant women and preventing HIV infection among infants. It should therefore be used in conjunction with the three documents and other resources related to antiretroviral drugs for resource-limited settings and WHO/UNICEF supply management guides.

5. Recommended regimens for treating pregnant women living with HIV and PMTCT

The WHO recommendations on antiretroviral drug regimens for treating pregnant women living with HIV and preventing HIV infection among infants are based on the most recent scientific information and programmatic experiences. The key principles considered while recommending the regimens include the public health approach, whose foundational tenet is building a programme around a simple common but efficacious regimen suitable for most women and their infants.

To effectively adapt the WHO guidelines, a country needs to decide on regimens appropriate for its setting for treating pregnant women for PMTCT. The WHO-recommended regimens consist of the following:

- antiretroviral therapy for all pregnant women living with HIV who need treatment for their own health; and
- prophylactic regimens comprising antepartum AZT from 28 weeks or as soon as possible thereafter; intrapartum AZT and 3TC plus single-dose NVP; and postpartum AZT and 3TC for seven days for women, with the infant regimen comprising single-dose NVP and AZT for one week.

Some programmes may opt to provide short-course AZT + single-dose NVP but without the tail of AZT + 3TC.

Annex 1 shows a list of drugs WHO recommends for use by pregnant women and infants either for treatment or prophylaxis.

The use of fixed-dose combinations within the recommended regimen such as 3TC and AZT (Combivir®) should be encouraged, as this will reduce the pill burden to the mothers and therefore improve adherence.

5.1. Antiretroviral therapy regimens for treating eligible pregnant women

As with all adults, the principle guiding the treatment of pregnant women is that treatment decisions should be based on their needs and eligibility for antiretroviral therapy. The WHO-recommended criteria for initiating antiretroviral therapy for pregnant women are the same as for non-pregnant women, except that initiating such therapy is recommended for pregnant women who have clinical stage 3 HIV disease and a CD4 cell count below 350 cells per mm^3. Antiretroviral therapy for pregnant women is therefore recommended for:

- all women in clinical stage 4 irrespective of the CD4 cell count;
- women in clinical stage 3 with a CD4 count <350 cells per mm^3, if available; if the CD4 cell count is not available, all women in stage 3 should be treated; and
- women in clinical stages 1 and 2 with a CD4 cell count <200 cells per mm^3.

According to the WHO-recommended guidelines on regimens for adults and adolescents, the recommended first-line antiretroviral regimens for pregnant women are the following:

- AZT + 3TC + NVP and stavudine (d4T) could provide an alternative to AZT; and
- AZT + 3TC + efavirenz (EFV) for women with tuberculosis coinfection.

5.2. Antiretroviral regimen for PMTCT

The recommended prophylactic regimen is:

- for the mother:
  - antepartum: AZT starting at 28 weeks of pregnancy or as soon as thereafter
  - intrapartum: single-dose NVP + AZT + 3TC
  - postpartum: AZT + 3TC for seven days;
- for the infant: single-dose NVP plus AZT for one week.

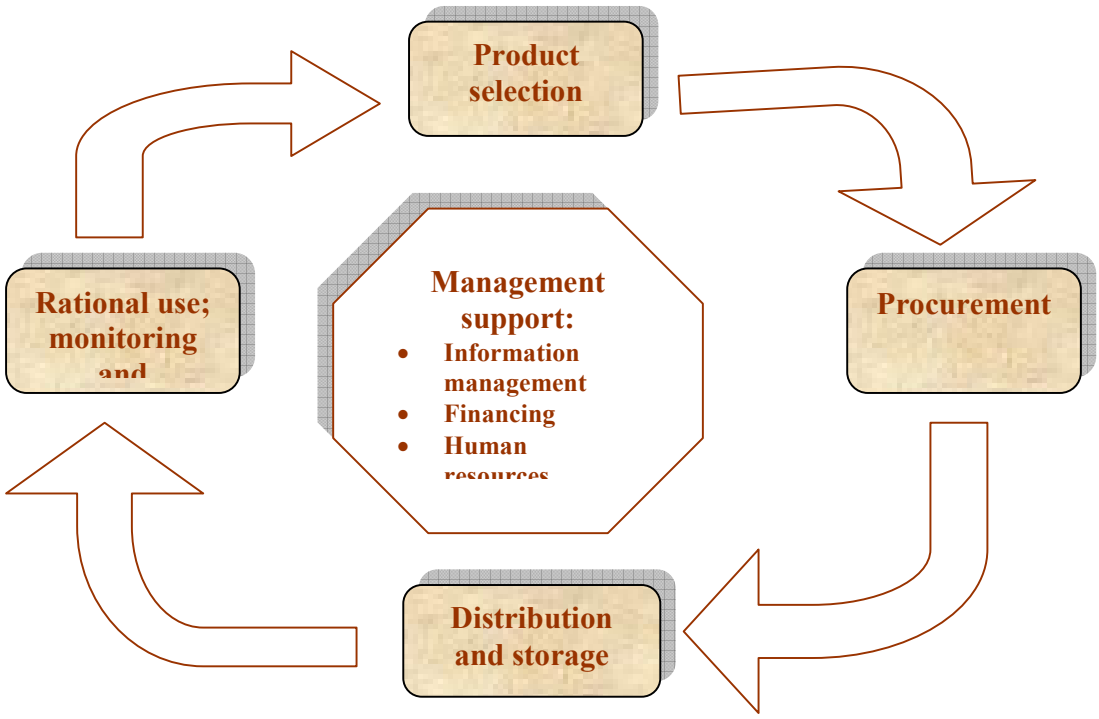
The WHO guidelines describe alternative regimens, including regimens for women seen during labour and infants born to women living with HIV who have not received antepartum or intrapartum therapy or prophylaxis.

6. Managing the supply of drugs for PMTCT

A well-functioning drug supply management system capable of selecting, forecasting, quantifying and delivering needed antiretroviral drugs is a prerequisite for effective delivery of PMTCT services. The management of PMTCT drugs should be viewed as part of essential drug procurement and supply management, supporting the goal of universal access to HIV prevention, treatment, care and support services. Programme managers should therefore consider integrating the supply of selected drug regimens for treating pregnant women and PMTCT into an existing drug supply management system. Integration has the advantage of reducing duplication and the need for additional staff.

6.1. Cycle of PMTCT drug supply management

Fig. 1. Cycle of drug supply management



Source: Operational guide for national tuberculosis control programmes on the introduction and use of fixed-dose combination drugs. Geneva, World Health Organization, 2002 (http://www.who.int/tb/publications/2002/en/index1.html, accessed 29 June 2007).

The aim of the supply management cycle for PMTCT (Fig. 1) is to achieve uninterrupted supply and access to all the necessary drugs and essential commodities. Drug supply management follows a well-recognized cycle in which different components are interlinked. Management support cuts across all the four components of the United Nations comprehensive approach, and the key aspects include financing, information management and human resource management. Management support activities occur at all organizational levels: from the national programme management level to the level at which drugs are dispensed to pregnant women. The components in the cycle are as follows.

- Product selection: the process of establishing a limited list of antiretroviral drugs for PMTCT. The choice of antiretroviral drugs should be based on the agreed national protocol.
- Procurement: the process of acquiring antiretroviral drugs either through purchase or donations. The principle of value for money must be maintained in purchasing antiretroviral drugs for PMTCT. They should be proven good quality and have acceptable expiry dates.
- Distribution and storage: the process of distribution includes: receipt at the port of entry; customs clearance; transport and storage at a central depot; and effective and efficient delivery to the point of use without disruption in supplies.

- Rational use: this entails: correctly determining eligibility for use; ensuring adherence to national standards and guidelines when prescribing, labelling and dispensing drugs; and ensuring that pregnant women adhere to the prescribed regimen.

6.2. Selecting the most appropriate and feasible antiretroviral drug regimens

The national technical working group should be involved in the selection process at the national level. Selection should be based on WHO-recommended regimens for both first-line antiretroviral therapy for treating eligible pregnant women and for PMTCT (Box 1).

Box 1. Factors to be considered in selecting antiretroviral drug regimens for PMTCT

- Feasibility, acceptability and resources available
- The availability of HIV testing and counselling services
- Attendance at antenatal, delivery and postpartum care
- The acceptability and ease of dosage schedules
- The efficacy and safety of various antiretroviral drug regimens, including their potential to compromise future treatment options
- Infant feeding options related to the regimen
- The risk of drug resistance following antiretroviral prophylaxisThe infant component of the antiretroviral regimen
- The impact of postpartum transmission through breastfeeding on long-term efficacy

Antiretroviral therapy and prophylactic antiretroviral drugs comprise just one component of a comprehensive approach to PMTCT. Other operational issues should therefore be taken into account in selecting the regimen of choice. Currently, the key question in most resource-limited countries regarding PMTCT is whether to use single-dose NVP or to change to combination regimens, such as AZT + NVP and AZT + 3TC.

Countries are advised to introduce combination regimens because they are more efficacious in reducing the risk of mother-to-child transmission. However, using single-dose maternal and infant NVP remains a practical although less desirable alternative in situations in which combination regimens are not acceptable or feasible. Provision of single-dose NVP for PMTCT should not be stopped or undermined if a country is not yet able to provide the more complex combination regimen.

6.3. Procurement

Antiretroviral drug procurement should be an integral part of national drug procurement systems. The process includes:

- quantifying drug needs;
- selecting methods for purchasing:
  - selecting reliable suppliers
  - managing tenders
  - ensuring compliance with contract terms; and
- assuring quality.

If there is more than one source of antiretroviral drugs in the country, procurement should be closely coordinated with the government procurement agency to ensure adherence to national antiretroviral therapy protocols and to ensure equitable distribution.

6.3.1. Quantification of drug needs and forecasting

Effectively implementing a drug protocol requires that drugs and other supplies be quantified correctly before implementation. The target number of pregnant women and infants to receive antiretroviral drugs, hence the quantity of drugs to be ordered, should be adjusted based on available funds and the unit cost of the selected regimen.

A phased approach to funding the programme should be adopted, as funds are usually identified and mobilized on an ongoing basis. At any one time funding should be adequate to ensure that the target population does not suffer from any supply interruptions and stock-outs. Two major challenges in forecasting (Box 2) and quantifying drugs are:

- taking into consideration the pace and scale of an expanding PMTCT programme; and
- anticipating the actual demand as opposed to estimating the population needing treatment.

Box 2. Forecasting
A two- to three-year medium-term forecast for drug needs is required to coordinate funding and procurement. The estimate should be based on the target number of pregnant women and infants identified for treatment and PMTCT and the selected regimens for providing that prevention and treatment. However, forecast data should be revised during the course of implementation as experience is gained on the acceptability, tolerability and efficacy of chosen regimes. Subsequent quantification will be based on actual consumption that will be obtained from the logistic management information system.

For detailed guidance on quantification, see Annex 2.

6.3.2. Procurement methods and selecting suppliers

For purchasing antiretroviral drugs, any procurement method used by governments and nongovernmental organizations, such as open tendering, restricted tendering, direct procurement

and competitive negotiations, may be used. The goal of obtaining high-quality antiretroviral drugs at competitive prices from quality-assured suppliers must always be maintained (Box 3).

Box 3. Key elements in purchasing antiretroviral drugs at the country level

- Identifying potential suppliers of antiretroviral drugs – which could be a local distributor or manufacturer or international source.
- Issues of government procurement procedures and donations and donor guidelines should be considered.
- A WHO-prequalified supplier or any other approved source may be used.
- Proper prequalification (evaluation of suppliers' capacity and reputation) and post-contract monitoring helps to eliminate substandard suppliers.
- Registration of selected medicine.
- Patent issues with manufacturers or distributors.
- There should be ongoing assessment of purchasing options, based on price comparison and quality assurance issues. Countries may have to negotiate prices with individual suppliers.
- The contract document should address packaging, labelling and minimum product specification requirements.

6.3.3. Definition of roles and responsibilities in procurement

Table 1 shows the responsibilities of the procurement and programme managers.

Table 1. Responsibilities of procurement and programme managers

National procurement manager	PMTCT programme manager
1. Procuring recommended antiretroviral drugs 2. Ensuring that antiretroviral drugs are registered in both the importing and exporting country 3. Prequalifying the suppliers for quality and reliability 4. Specifying the packaging requirements in contracts with suppliers 5. Monitoring the performance of suppliers 6. Encouraging quality testing for all antiretroviral drugs received	1. Selecting drug regimens for use in PMTCT 2. Accurately quantifying drug needs prior to procurement 3. Coordinating procurement activities with the national procurement manager 4. Training staff on accurate utilization of antiretroviral therapy 5. Interrelating procurement, distribution, rational use and quality assurance

6.3.4. Quality assurance

Quality assurance of products and their sources is a primary concern and must be maintained. The quality of drugs must be maintained throughout production, distribution, storage, dispensing and use. There should be criteria for manufacturers' qualifications, based on internationally recognized guidelines on drug manufacturing practices and quality assurance. Quality inspections and sample testing should be performed in the country. Monitoring quality throughout the procurement system requires considerable technical expertise and equipment, and

adequate resources should therefore be provided to ensure that standards are consistently and satisfactorily met. The drug regulatory authority should be in charge of ensuring the quality of antiretroviral drugs and should monitor quality throughout the procurement chain up to the health facility level. In doing so, they should coordinate with the PMTCT programme manager and heads of health facilities.

6.4. Distribution and storage

Distribution is the process by which procured antiretroviral drugs are received at the port of entry, cleared through customs, and transported from the central warehouse(s) to depots and health facilities. In health facilities, drugs are stored and dispensed to pregnant women and infants. The distribution system should be an integral part of national drug procurement systems.

Box 4. Issues to consider in storing antiretroviral drugs

- Temperature maintenance needs: for the recommended WHO first-line drugs, storage temperature should not exceed 30°C.
- Storage equipment needs: such as racking, pallets, lockable cabinets and handling equipment
- Security measures to ensure security during storage and transport and procedures for monitoring antiretroviral drugs at dispensing facilities. These may entail reinforced storage and elements of logistical procedures for products regulated as dangerous drugs, allowing fewer people to dispense, using countersigning procedures, and returning filled prescription

The purpose of storage is protecting the quality of drugs and their packaging throughout the supply chain and making drugs available for distribution. There should be clear storage guidelines (Box 4).

Distribution can be the role of the central and/or the regional warehouse. Similar to storage, protecting the quality and security of drugs is paramount.

Inventory procedures

The purpose of an inventory control system is to maintain an appropriate stock level of the antiretroviral drugs, avoiding shortages and stock-outs (Box 5). The key questions to address are:

- Who places orders?
- When are orders placed?
- How are orders made?

Box 5. Advice on good stock management

- **Records:** keep good records of the drugs received and distributed from all levels: received at port of entry and distributed to depots; received at depots and distributed to health facilities; and received at health facilities and dispensed to patients.
- **Avoiding wastage:** store antiretroviral drugs in a secure and appropriate environment to avoid pilferage, theft and damage. Rotate stock according to first expired first out and then first in first out principles to avoid loss due to expiry.
- **Avoiding stock-outs:** review the stock level of each drug each time an issue is made. If the stock level is at or below the set minimum, place an order to bring it to maximum level. Maintain adequate buffer stock.

The minimum-maximum inventory control system is recommended: a minimum is set at a high enough level to ensure that the country or facility does not run out of supplies and the maximum is set low enough to ensure that all of the stock fits in the storeroom, and it does not reach its expiration date before being used.

6.5. Drug problem reporting system

A system of antiretroviral drug problem reporting should be established and should entail the following activities:

- recording and reporting tools (forms); and
- guidelines that indicate:
    - the responsible officer for reporting at each levels of the supply chain
    - to whom the report(s) should be sent
    - what actions are to be taken for each anticipated problem.

Reportable problems include: adverse drug reactions, theft, quality problems and recalls by suppliers.

6.6. Monitoring and evaluation

A well-functioning information system provides decision-makers throughout the supply chain, with accurate, timely and appropriate data (Box 6). Data obtained from the information system is used to: make decisions on how much of the drugs should be ordered or resupplied; identify potential supply problems and forecast demand; assist in procurement planning; and identify problems with drugs.

Box 6. Specific questions in monitoring

- What indicators should be collected?
- What methods and design should be used?
- What data should be collected and how to generate the indicators?
- What tools and resources will be necessary? Who will do what and at what level?
- Who will aggregate data?
- What will be the frequency of reporting?
- With whom will information be shared?
- How will the information collected be used?

To avoid reporting disparity between the quantities of drugs distributed and consumed, programme monitoring data should be linked to supply monitoring data. Note that other forms of health information tend to be less sensitive than supply information system, and the type of analysis required differs. Below are proposed indicators for monitoring newly introduced regimens.

- **Amount of stock at hand:** measures the quantity of stock at one point in time for each time the drug is available at the different levels of the system.
- **Average percentage of time each drug is out of stock:** measures the stock management procedures at different level of facilities.
- **Amount of drugs dispensed:** measures the quantity of dispensed during a particular reporting period.
- **Amount of drugs removed from distribution:** measures the extent of wastage of drug. It considers stock removal for any reason other than dispensing (such as damage or pilferage) during a particular reporting period.
- **Number of people receiving therapy:** measures the number of pregnant women and infants on individual medications during a particular reporting period. This is useful for comparing actual consumption and distribution information. The reporting periods for these two measurements should therefore be the same.
- **Number of shifts:** measures the movement from one regimen to another for pregnant women receiving antiretroviral therapy during a particular reporting period.
- **Number of people with severe adverse effects:** measures the extent of problems with severe adverse effects of antiretroviral drugs.

Appropriate data collection tools and an effective recording system should be designed for use at all dispensing facilities.

6.7. Surveillance of drug resistance

Although the antiretroviral therapy programme may largely focus on antiretroviral drug resistance surveillance, the PMTCT programme manager must coordinate closely with the antiretroviral therapy programme, particularly with regard to NVP resistance.

The public health responsibility to protect the future utilization of drugs and the need to minimize the emergence of drug resistance must be recognized and respected. Measures to prevent the emergence of resistance include:

- appropriate antiretroviral drug prescribing and usage;
- ensuring the quality of the dispensed drugs;
- maintaining continuous drug supply; and
- ensuring that the people receiving drugs adhere to them.

The methods commonly used for surveillance for antiretroviral drug resistance include:

- threshold surveys;
- cross-sectional prevalence estimates; and
- prospective monitoring of the people initiating antiretroviral therapy.

Threshold surveys are conducted among newly diagnosed people living with HIV using sentinel surveillance population focusing on those most likely to be recently infected. Tests are done on excess serum from serosurveillance.

It is recommended that antiretroviral drug resistance surveillance be established at the same time that treatment programmes are established and expanding. Threshold surveys are convenient and considered the standardized approach.

7. Programmatic and managerial issues to consider when introducing a new regimen

7.1. The locomotive role of a national plan for scaling up

On its own, introducing more efficacious antiretroviral drug regimens for treatment and prevention cannot attain the goal of an HIV- and AIDS-free generation. More efficacious regimens must be combined with concerted efforts to promote integrated and comprehensive PMTCT programmes while increasing the coverage and uptake of PMTCT services. In this context, efforts to introduce more efficacious regimens should be reviewed, and introduction should follow the framework of the national scale-up plan. Introducing the new regimen should therefore be a component strategy of the overall plan for scaling up PMTCT. Essential for enabling services to be rapidly scaled up is a country-driven scale-up plan with clearly defined numerical targets for service delivery; supply management and monitoring and evaluation components; budgets; and partners' roles and responsibilities. This is a vital component for

refocusing actions to accelerate nationwide implementation and bringing together all stakeholders to invest appropriate and adequate financial and technical resources for implementation.

7.2. Thinking of innovative commodity supply systems for PMTCT

Individually packaged materials for one mother should be considered to improve the efficiency of delivering PMTCT within maternal, newborn and child health settings. This will ensure standardization, improve efficiency and reduce waiting times for mothers. These PMTCT kits should include:

- HIV rapid test kits;
- gloves for examination;
- prepackaged antiretroviral drug courses for PMTCT, including maternal and infant doses;
- condoms; and
- leaflets or other materials for informing, educating and communicating with women and their partners.

7.3. Communities as partners for improving the delivery and uptake of services

Community participation plays an important role in overall PMTCT. Communities will more likely accept PMTCT interventions if they are involved throughout the process, from decision-making to the implementation of services. There is no single view on the role communities can play in health programmes. In the context of PMTCT, communities can play vital roles in reducing stigma and discrimination; educating and mobilizing; supporting mothers in their infant feeding choices; promoting and advocating for HIV testing; and supporting mothers' adherence to their drugs. Strategies for involving communities must therefore be clearly articulated in developing the scale-up plan.

7.4. Linking PMTCT and the scaling up of antiretroviral therapy

Effective and efficient service delivery requires emphasizing an integrated approach. PMTCT programmes and the scaling up of antiretroviral therapy share a unique similarity in the sense that both have the same programmatic, logistical, resource mobilization and community mobilization needs.

In most resource-limited settings at the primary level where most people receive care, health care services are provided in a comprehensive manner, within the same facility and by the same staff.

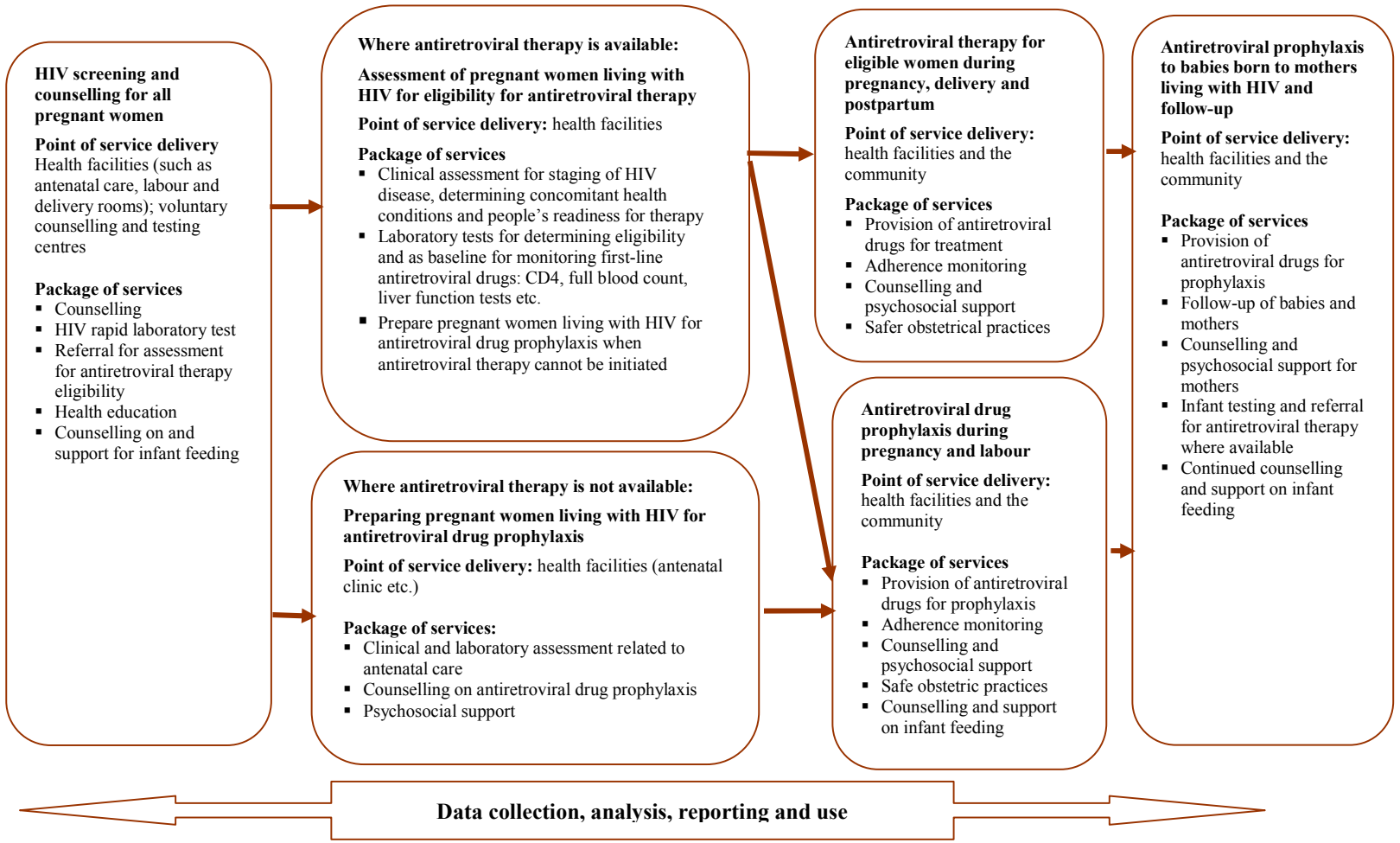
It is therefore imperative that the scale-up of PMTCT programmes and antiretroviral therapy programmes be linked (Fig. 2). Integration should be seen at all levels of the service delivery chain:

- policy development;
- planning;
- management and coordination;

- service delivery;
- community mobilization; and
- following up the people receiving treatment and care.

Although a vertical approach may be a useful option when programmes are initiated and in driving implementation and monitoring, at the central level it is costly and leads to duplication of efforts.

Fig. 2. Package of services needed at the various stages in the process of providing antiretroviral drugs to pregnant women and infants for treatment and prophylaxis



7.5. Requirements

7.5.1. Resources mobilization and allocation

Until very recently, the lack of resources limited HIV screening in antenatal and childbirth settings, and the high price of antiretroviral drugs was a major impediment to scaling up treatment and providing highly efficacious combination antiretroviral prophylaxis. The result has been that most countries currently use single-dose NVP. However, pharmaceutical companies are now offering drugs at significantly lower prices; and the synergistic effects have been recognized of combining short-course AZT or short-course AZT + 3TC with single-dose NVP, resulting in the reduction of long-term transmission to the range of 2% in non-breastfeeding settings and 6–9% in breastfeeding settings. Further, over the years funding opportunities have increased through donor-funded initiatives such as the Global Fund to Fight AIDS, Tuberculosis and Malaria and the United States President's Emergency Plan for AIDS Relief. This improved scenario has led to a general increase in access to antiretroviral therapy. Resource mobilization and allocation continues to be a critical component of successful scale-up and introducing more efficacious regimens. Effort should be made to build on existing funding mechanisms and partnerships to ensure that adequate resources are allocated to scaling up PMTCT and introducing more efficacious regimens.

Development partners should assist countries through sustained advocacy for additional resources and rational allocation of existing resources and work in collaboration to ensure a coordinated approach to funding HIV and AIDS programmes that avoids duplication. Consistent with the multisectoral approach, funding challenges can only be resolved by working in partnership.

Providing the WHO-recommended regimen may have several implications for costs and resources. The areas for resource considerations include:

- improving the health system;
- programme coordination and management;
- high-quality antenatal care and delivery care;
- provider-initiated HIV testing and counselling;
- clinical and immunological assessment of women living with HIV;
- dispensing of antiretroviral therapy for treatment or PMTCT;
- follow-up of infants born to mothers living with HIV;
- drugs, logistics and laboratory monitoring;
- strategic management of human resources through capacity-building and task-shifting;
- equipment and logistics;
- physical infrastructure; and
- health information systems.

7.5.2. Improving the health system

Providing high-quality antiretroviral drugs to pregnant women and infants requires a basic level of maternal, newborn and child health services. These include systems related to programme

coordination and management, antenatal and delivery care, HIV testing and counselling, procurement and supply management and monitoring and evaluation (Box 7).

Box 7. Maternal, newborn and child health service requirements

- Capacity to coordinate and manage programmes
- Quality antenatal care and delivery care
- Capacity to provide HIV testing and counselling and post-test services
- Capacity to assess pregnant women living with HIV for eligibility for antiretroviral therapy
- Capacity to store and dispense antiretroviral therapy
- Capacity to provide adequate follow-up for mothers and infants and ensure adherence
- Capacity to collect and analyse data on programme performance

The introduction of complex regimens does not need to be delayed until all the health system requirements stated above are in place. However, these requirements are important for ensuring high-quality services and sustainable and rapid scale-up. Efforts should therefore be made to build these capabilities.

7.5.2.1. Programme coordination and management

Managing broad participation by key stakeholders requires having coordination mechanisms for all levels of programme management. If possible, these mechanisms should be integrated within national, provincial, district and local structures. It may be advisable to establish task forces and committees to act on behalf of the coordination structures. In general, national coordination structures should bring together: key health departments and programmes involved in PMTCT-related activities; nongovernmental organizations; people living with HIV; and key implementing partners. All the actors involved in these coordination structures should have clearly defined roles and responsibilities. In addition, policies and programmatic guidelines should be in place for smooth implementation.

PMTCT service delivery should emphasize an integrated approach as opposed to a vertical approach. One of the major challenges to the success of PMTCT interventions is the lack of integration with other HIV services. Since mothers of young infants are in frequent contact with the maternal, newborn and child health unit for immunization and other maternal, newborn and child health services, HIV diagnosis, PMTCT prophylaxis and antiretroviral therapy should be integrated to allow for more optimal use of staff and to avoid the stigma that can be a major barrier for young women that need to attend the “HIV clinic”.

7.5.2.2. Quality antenatal care and delivery care

Antenatal care and delivery services are the entry point for high-quality PMTCT. High-quality antenatal care and delivery care services are therefore likely to lead to high-quality PMTCT services (Box 8).

Box 8. Package of services for antenatal care

- Essential antenatal care services, including routine offer of HIV testing and counselling
- Management of malaria in stable malaria areas
- Clinical and immunological assessment of women living with HIV
- Screening for, preventing and treating tuberculosis
- Screening for and managing liver diseases
- Screening for, preventing and managing sexually transmitted infections
- Screening for and managing injecting drug use
- Initiating antiretroviral therapy and antiretroviral prophylaxis for PMTCT
- Co-trimoxazole prophylaxis
- Isoniazid prophylaxis where needed
- Counselling on and support for nutrition
- Counselling on and support for infant feeding

7.5.2.3. Provider-initiated HIV testing and counselling

Before a woman can be offered antiretroviral drugs for treatment or prophylaxis, she must know whether she is living with HIV. HIV testing and counselling therefore comprise a prerequisite for providing PMTCT services. HIV screening should be routinely offered in all antenatal care, delivery settings and postpartum services, including well-child clinics. Good coverage of antenatal care and utilization of delivery care services is required to improve access to HIV testing. HIV testing requires adequate infrastructure to ensure confidentiality; trained human resources to conduct testing and counselling; regular uninterrupted testing supplies; and a community that accepts testing and is involved in promoting and providing services, including post-test services.

7.5.2.4. Clinical and immunological assessment of women living with HIV

The current WHO guidelines emphasize wider availability of CD4 testing to guide decision-making on when to initiate antiretroviral therapy and when to switch and salvage antiretroviral therapy regimens in resource-limited settings. CD4 cell counts and staging are particularly important when deciding whether pregnant women living with HIV should be offered antiretroviral therapy or antiretroviral prophylaxis for PMTCT. Service providers should be able to make clinical assessment for HIV disease staging, especially in settings where CD4 testing is not yet available.

Where available, laboratory tests such as viral load, haematology and biochemistry are of value as a baseline for monitoring people receiving antiretroviral drugs and for decisions on management.

7.5.2.5. Dispensing of antiretroviral therapy for treatment or PMTCT

Most of the recommended PMTCT regimens can be dispensed at the community health level, depending on the following factors:

- the availability of trained personnel;
- the basic drug supply management system, including secure storage; and
- the basic system for capturing and storing patient monitoring data and information.

Inability to deliver these services at these primary health care points will result in continued poor coverage of PMTCT services. Access to health services is therefore a major factor in reaching the majority of pregnant women who need treatment.

Approaches to dispensing drugs to pregnant women may vary from regimen to regimen and operational circumstances. To facilitate the efficient delivery of drugs to individuals, all the drugs necessary for a given time period (such as two weeks) plus a full course of prophylaxis or a month's course of treatment could be put into a package according to required dosage. These packages could be prepared at the health facility level and dispensed during clinic visits. This procedure makes it easier to distribute and monitor the usage of drugs by individuals. For example, in situations in which following up pregnant women living with HIV during pregnancy is difficult or most women deliver at home, drugs and other supplies (gloves and condoms) may be prepackaged and provided to the mother at the time of testing. This may include NVP syrup for the infant, which is packaged in a syringe. It is therefore important to determine the approach for dispensing drugs to mothers and to ensure that the operational implications are taken into consideration.

7.5.2.6. Follow-up of infants born to mothers living with HIV

According to the revised guidelines, follow-up of HIV-exposed infants requires that the infant receive antiretroviral drugs during the first week of life, be followed up for routine care, provided co-trimoxazole prophylaxis and, where available, polymerase chain reaction (PCR) testing be performed at six weeks or serological testing done between 9 and 12 months or later at 18 months. In regions with high HIV prevalence, children and mothers with unknown HIV exposure status should also be offered antibody screening so that they can access relevant services. Given that close to 50% of infants living with HIV in resource-limited settings will die by age 24 months without treatment, early PCR testing should be emphasized as the preferred diagnostic tool, and infant follow-up programmes should strive to carry out PCR testing within the first few months of life to ensure that infected infants have early access to life-saving antiretroviral therapy. In addition, a systematic follow-up system should be built into routine maternal, newborn and child health programmes for HIV-exposed infants and their families. In that regard, national programmes should build institutional systems and human capacity for early diagnosis of HIV among infants, including the use of dry blood specimens.

7.5.2.7. Drugs, logistics and laboratory monitoring

Estimating the cost of implementing national antiretroviral therapy guidelines for PMTCT requires knowing the unit cost of providing antiretroviral drugs to pregnant women and infants. This, in turn, requires information on the targeted number of pregnant women and infants who require antiretroviral therapy and antiretroviral prophylaxis, the planned activities of introducing the new regimen and the actual cost of these activities. The steps in costing the provision of antiretroviral drugs for pregnant women and infants include the following.

1. **Defining the programmatic strategic target**
   To define the strategic target in terms of number of pregnant women and infants who need antiretroviral drugs, the following should be considered:
   - HIV prevalence among pregnant women;
   - the uptake of HIV testing and counselling; and
   - the proportion of pregnant women living with HIV who are eligible for antiretroviral therapy.

2. **Defining the unit cost of each activity component of implementing the WHO guidelines**
   Such activity components include training, laboratory monitoring, monitoring and evaluation, clinical treatment and care. In general, the costs of activity components include both recurrent costs such as training, materials and supplies and capital costs such as infrastructure, medical equipment, vehicles and furniture. However, the cost should be primarily considered for key activities related to developing guidelines, tools, training and key equipment. Item or activity costs can be derived from various sources, such as published lists (such as WHO and Médicins sans Frontières price information on antiretroviral drugs and other essential medicines and diagnostics, existing cost studies and ongoing small-scale projects.).

3. **Calculating the unit cost per pregnant women and infant**
   The unit cost per pregnant woman and infant can be calculated based on the target number of pregnant women who need antiretroviral drugs for prophylaxis and treatment and the cost for the programmatic activities. This is a crucial calculation because the target number of pregnant women and infants to be reached during a particular period can then be determined using the unit cost and the available funds.

7.5.2.8. Strategic management of human resources through capacity-building and task-shifting

The number of skilled personnel should be adequate to carry out the following tasks: counselling, testing, clinical management, drug management and dispensing and adherence management and follow-up. The basic required health workers include: physicians, clinical officers, nurses, midwives, pharmacists, pharmacy technicians, laboratory staff, counsellors and community health workers. Besides their professional training, each health worker needs to undergo training on at least all the developed guidelines and protocols. Additional training on antiretroviral therapy for some should be considered where appropriate and will help support the rolling out of antiretroviral therapy programmes in level one health care clinics and in rural settings.

The selected training strategies should be appropriate, affordable and sustainable. Workshop models away from work stations often contribute to staff shortages and are expensive. Innovative models such as interactive videos and CDs and other in-service models can be used to upgrade staff skills.

Introducing more complex regimens might require some strategic shift in the distribution of tasks at the health facility level, especially with the initiation of antiretroviral therapy among all pregnant women who need treatment. The urgent need to scale up national PMTCT interventions as an integral component of antenatal care and delivery care will require transferring tasks and roles between doctors and antenatal care and delivery care providers. National programmes should consider building the capacity of nurses and midwives in charge of antenatal and delivery care for the clinical and immunological assessment of pregnant women living with HIV and the initiation of antiretroviral therapy. However, this should not compromise the need to ensure the safety and quality of care and can be achieved as long as adequate training of nurses with back-up physician consultation is in place.

7.5.2.9. Equipment and logistics

Equipment for laboratory testing and drug management may need to be installed or improved. Where there is an antiretroviral therapy programme, capacity could be built on drug resistance surveillance.

7.5.2.10. Physical infrastructure

This may be necessary to: improve service delivery space, including laboratory space; improve security of drugs; ensure confidentiality; and create a comfortable environment for patients and workers.

7.5.2.11. Health information systems

Timely and reliable information is essential for managing programmes and the people receiving treatment and care. Setting up an information system requires additional resources, whether it is paper-based or computer-based. For most countries, health information systems will be paper-based while the necessary capacity is developed to integrate computer-based systems.

8. How to introduce and change over to different regimens

Once a country has made the decision to change or introduce a combination regimen within its comprehensive PMTCT programme, several activities (Annex 3) need to be completed to ensure that the change is flawless. A well-thought-out and carefully planned changeover or introduction of the new regimen is therefore essential.

The entire process includes four main phases:

- decision-making;
- preparation phase;
- initial implementation; and
- full-scale implementation.

8.1. Decision-making phase

Before a well-founded decision to switch over or introduce a new regimen is taken, several activities have to be performed and certain information has to be obtained and made available.

It is vital that the involvement, endorsement, commitment and leadership of all parties concerned and key stakeholders be enlisted during the decision-making phase. This should be done through consensus-building mechanisms in which clear justification and the rationale for changing or introducing the new regimen are explained, discussed and agreed upon. Reviewing or formulating relevant policies and strategies for mobilizing resources should also be considered during this phase.

The essential activities the PMTCT programme manager needs to carry out during the decision-making phase are described below.

Activity 1: prepare the information required for making a well-founded decision

- Read and internalize the WHO guidelines and other related documents.
- Collect information from international guidelines and recommendations on justification for the need to change to the new regimens.
- Determine the cost of providing the new regimens per person compared with the current regimens.
- Determine the total cost of providing the new regimens in terms of drugs and the change itself.
- Develop a rationale and justification for the regimen change or introduction based on the local context. This should demonstrate how introducing the regimens would contribute to achieving targets of eliminating HIV infection among infants and young children.
- Analyse the existing country PMTCT policies and guidelines to determine gaps that may hinder the implementation of the WHO-recommended regimen.

Activity 2: consult with the technical working group on specific decision points

- Meet the technical working group and consider the following questions with regard to changing to a more efficacious regimen:
    - Should the country change to the WHO-recommended regimens? Why?
    - Which regimens would be most appropriate for the local context?
    - How will the resources needed for the change be mobilized?
    - How should the change be conducted?
    - Who are the key stakeholders and what role will they play?
    - What key information should be given to the health ministry for decision-making?

Activity 3: seek approval and a decision from the health ministry

- Arrange a meeting with the health ministry officials and present the need to change to more efficacious regimens, including justification and cost and policy implications. Provide a written concept note on the change.
- Agree on the key issues of the change and enlist the commitment of the decision-makers.
- Obtain a decision on the change.

Activity 4: obtain the buy-in and commitment of national stakeholders to the changes

This should be done through a consensus-building meeting with all key stakeholders in which clear justification, rationale and evidence for change is explained, discussed and agreed upon.

The expected outcomes of the decision phase are the following:

- decision to switch from the current regimen (or guidelines) to a new one;
- a firm budget commitment and resource mobilization strategies;
- commitment to integration into existing service; and
- defining the role of various stakeholders.

8.2. Preparation phase

During this phase, detailed planning, resource mobilization and readiness activities are conducted. Preparation begins once decision on switching to new regimens has been made. This is a phase in which the programme manager works closely with the technical working group to ensure that the country is ready to introduce the new regimens.

Under the leadership of the health ministry, the technical working group will drive the technical processes of changing to the new regimens. The membership of the technical working group should include the health ministry; the national AIDS control programme; the national PMTCT programme manager or coordinator; WHO; UNICEF; the United States Centers for Disease Control and Prevention; academic institutions; experienced PMTCT staff; maternal, newborn and child health or reproductive health and antiretroviral therapy programme mangers; and nongovernmental organization and private sector partners.

The purpose of the technical working group is to assist in developing and reviewing PMTCT guidelines, protocols and training packages; assessing the needs and readiness at the national and site levels; and drawing up a detailed implementation action plan, including a training plan and a capacity-building strategy, supply management strategies and infrastructure development strategies. Key activities that need to be carried out during this phase include the following.

Activity 1: informing all stakeholder and health workers about the decision to change to a new regimen

Activity 2: forecasting demand for the new regimen

Deciding on what quantity of the new regimens to procure is the first step in the supply chain. The initial quantity forecasted should be based on the target number of pregnant women and infants, which in turn will depend on the funds available. The first step in forecasting is therefore setting the target number of mothers and infants to be reached.

Activity 3: regimen selection

The role of the technical working group includes selecting feasible and appropriate regimens for the country based on the WHO-recommended options and country circumstances. These should include regimens for treating eligible pregnant mothers as well as for PMTCT (see sections 5.1 and 5.2 for guidance for selection of regimen). The process of selecting

appropriate regimens should fall within the overall process of developing or revising the national PMTCT guidelines or protocols.

Activity 4: assessing the capacity and readiness to provide the new regimen

This is a critical step in gathering information for planning purposes (Box 9). It is conducted to determine the availability and quality of the essential services for the introduction of WHO-recommended regimens and to identify needs for strengthening and improving the critical components of the programme.

Using a well-designed checklist, a countrywide assessment is conducted to determine the gaps that need to be addressed before changing to new regimens.

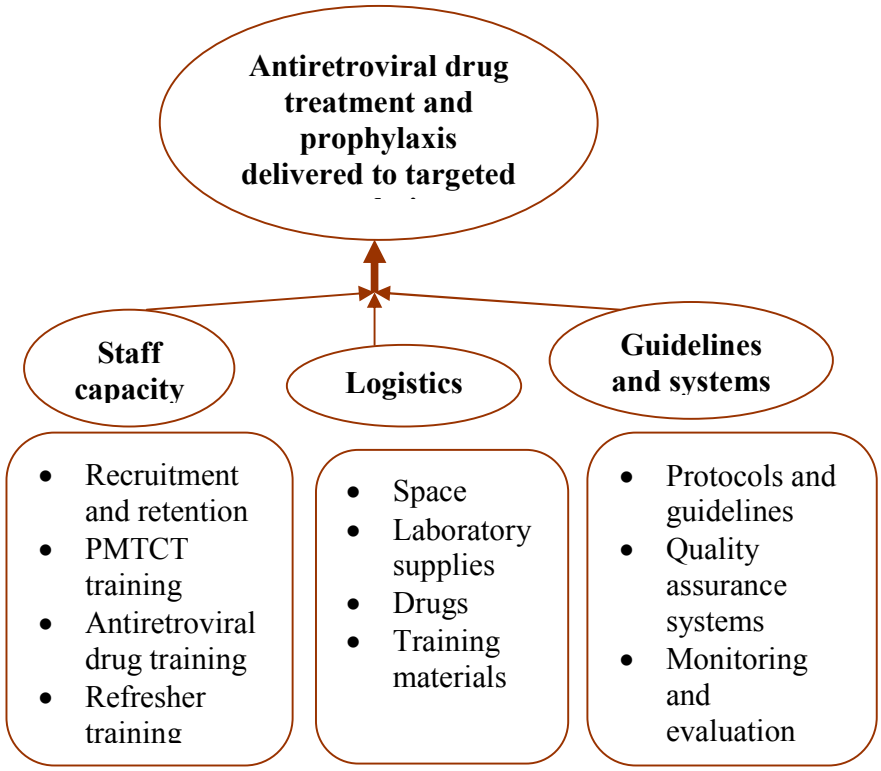
Box 9. Critical areas for assessment

- Additional infrastructure and equipment needs, such as secure storage, air-conditioning, forms and record systems
- Human resources capacity in terms of number, skills and training on HIV and antiretroviral therapy in particular
- Supply management system and capacity
- Management and coordination capacity
- Information management system and capacity
- Existence and coverage of other supporting services such as antenatal care, maternity, testing and counselling, home care, management of opportunistic infections etc.
- Willingness of communities to accept the new regimens

Activity 5: preparing implementation strategies and an action plan

The technical working group, under the leadership of the health ministry, plays a crucial role in preparing the national implementation action plan. The action plan should be a component of the strategy for scaling up, clearly stating objectives, targets, activities, timelines, measurable indicators, budget and responsibilities. Once capacity assessment is completed and the findings are analysed, action planning should follow to direct further action. The action plan may follow the framework in Fig. 3.

Fig. 3. Framework for delivering antiretroviral drugs



Within the identified area, the plan should indicate the targets, objectives, activities, responsible officer, location and implementation partners.

Activity 6: preparing and reviewing the treatment protocol

A new or revised PMTCT drug protocol that reflects changes should be prepared before training. The protocol should indicate what HIV treatment regimens are approved and who is entitled to prescribe. All clinicians should adhere to the approved protocol. The technical working group or its subcommittee should play the lead role in developing the protocol.

Activity 7: developing and revising all relevant guidelines, manuals and tools

Other national guidelines, protocols, manuals and tools relevant to introducing the new regimen need to be revised or developed. These will include:

- the overall national guidelines for the implementation of the PMTCT programme;
- training manuals;
- policies and guidelines governing drugs forecasting, procurement, storage, dispensing and handling old stock;
- guidelines for monitoring and following up the people receiving treatment and care; and
- monitoring and evaluation tools and the record-keeping system.

Activity 8: mobilizing and allocating resources

Additional resources are needed for successfully implementing a change to new regimens. In planning resource mobilization, a country should look at both internal and external sources. Resource mobilization should be an ongoing activity. Countries should be prepared to optimize the available resources. Identifying existing resources (internal and external), identifying gaps, mobilizing and allocating to fill gaps are critical to implementing the guidelines. The budget will guide the additional resources needed.

8.3. Initial implementation phase

There may be several approaches to implementation, but a phased approach is recommended because it gives an opportunity for learning and overcoming major pitfalls.

The most important considerations to make in implementing national guidelines are the availability of financial resources and the adequacy of the health system in terms of human resources, access to services, storage, distribution and infrastructure. Regimens containing AZT and 3TC are more resource intensive and require more skilled staff, storage space and a stringent adherence and follow-up system.

A phased approach could be used to scale up programmes to the national level. In general, most countries might use both single-dose NVP and combination regimens for a time period. Based on the national scale-up plan, a set of criteria will help identify and set minimum requirements for changing to more efficacious combination regimens. Other settings could continue providing single-dose NVP as a background while upgrading their capacity to provide more efficacious regimens.

Once the plans and guiding documents are in place, implementation should start in earnest. The various steps in implementation may overlap or be conducted concurrently. The initial implementation steps include the following.

Activity 1: selecting the health facilities for initial implementation
Facilities should be selected according to the national scale-up plan and based on predetermined criteria such as level of readiness and commitment.

Activity 2: printing new or revised protocols, guidelines and tools
The printed materials should be distributed and made available to all the implementing facilities.

Activity 3: **conducting staff training**
All relevant staff should be oriented on all new guidelines and systems based on the needs assessment. To ensure access to antiretroviral therapy for women living with HIV, antenatal care providers, such as physicians, midwives and nurses, need additional training on the clinical and immunological assessment of women living with HIV for eligibility for antiretroviral therapy and antiretroviral therapy management, particularly during pregnancy. This is in addition to the usual PMTCT training and any other HIV and AIDS training.

Activity 4: improving infrastructure, pharmacy and laboratory logistics

This should be done based on the needs identified during capacity assessment. Although this may be necessary for introducing the new regimens, it should be carried out as part of the national drug management programme activities.

Activity 5: procuring drugs, reagents and other needed supplies
Quantification, registration, authorization for procurement and actual procurement should start early and precede any training and programme intervention, as this may be time consuming and cause delays in implementation.

Activity 6: establishing a drug supply management system
Ordering, distribution, secure storage, inventory maintenance, dispensing and a monitoring and documentation system need to be established. As the new regimens are introduced, interruption in supply and treatment should be avoided by ensuring that the stock of the new regimens is adequate before completely withdrawing the old stock.

Activity 7: implementation
Implementation at the selected sites should begin once all the necessary systems are in place and staff members have been trained. This includes a system for drug management and dispensing, support supervision and mentorship, documentation and monitoring.

Activity 8: **evaluating and documenting the lessons learned from the initial implementation sites**
The initial implementation phase should be evaluated after a predetermined period.

8.4. Full implementation phase

The scaling up of implementation should be based on lessons learned from the initial implementation phase. The activities preceding scale-up include the following.

Activity 1: reviewing the action plan
Based on the results of the pilot phase, the initial plan may be reviewed. If necessary, the guidelines should be revised before full implementation.

Activity 2: selecting additional sites
New sites for scaling up should be selected if a phased approach is the option for scaling up.

Activity 3: preparatory activities for scale-up
These include preparing a schedule for scale-up, mobilizing additional resources, training, improving systems, documentation and supervision.

Activity 4: implementation
Implementation in the next sites should start as soon as the systems are in place. Monitoring and documentation should continue as in the plan.

9. The challenges

While scaling up provision of antiretroviral therapy in the context of PMTCT, a country should expect to face a number of challenges that may impede the implementation of the guidelines. Some of these challenges are inherent to the entire health system and the implementation of PMTCT programmes.

First, in most resource-limited settings the majority of pregnant mothers have not been tested and do not know their HIV status. This greatly hampers access to antiretroviral drugs, as HIV testing is a prerequisite for receiving antiretroviral drugs. Improving access to HIV testing is therefore crucial to successful implementation of the WHO guidelines.

Second, coverage of antenatal care and deliveries by skilled attendants affects the access of pregnant women to all the services related to PMTCT. Most resource-limited settings have very low coverage of antenatal care and deliveries by skilled personnel.

Third, several challenges related to the health system influence effective implementation of the WHO recommendations. These include:

- staff shortages and skills deficits: antiretroviral therapy, information technology, laboratory, counselling and management;
- lack of motivation and functional depletion of existing staff because of many vertical programmes and the associated training burden;
- poor physical infrastructure and lack of equipment are common in most resource-limited settings;
- traditional health care, as the first point of care, often leads to additional delays in seeking services, adherence failure and toxicity problems; and
- systems deficits, such as facility management, accountability, financial management, communication, procurement, monitoring and evaluation, administration and security.

Fourth, new regimens should be introduced in a way that does not cause interruption in supply and treatment, as this may lead to unwanted outcomes. It is therefore imperative that change not start unless enough stock of the new drug(s) is in the country. In addition, stocks of old drugs should be handled with care to avoid wasting resources.

Annex 1. Specification of the WHO-recommended drugs

Drug acronym	Generic name	Trade names	Class	Dosage form and formulation	Package information	Storage conditions
AZT	Azidothymidine	Retrovir®	Nucleoside reverse-transcriptase inhibitor (NRTI)	• Tablet, 300 mg (oral) • Capsule 100 mg, 250 mg • Oral solution or syrup, 50 mg/5 ml • Solution for intravenous infusion	• 100 mg capsules into one pack of 100 capsules • 250 mg capsules into one pack of 40 capsules • 300 mg tabs into one pack of 100 tabs or 60 tabs • 50 mg/5 ml solution into one bottle of 5 ml or 200 ml	• Room temperature below 30°C • Dry environment • Away from direct sunlight
d4T	Stavudine	Zerit®	NRTI	• Capsule 15 mg, 20 mg, 30 mg, 40 mg (oral) • Powder for oral solution, 5 mg/5 ml	• 15 mg capsules into one pack of 56 capsules • 20 mg capsules into one pack of 56 capsules • 30 mg capsules into one pack of 56 capsules or 60 capsules • 40 mg capsules into one pack of 56 capsules or 60 capsules • 5 mg/5 ml solution into one bottle of 5 ml or 200 ml	• Solution should be stored in the refrigerator • Room temperature below 30°C • Dry environment • Away from direct sunlight

3TC	Lamivudine	Epivir® Combivir® (AZT + 3TC)	NRTI	• Tablet, 150 mg (oral) • Oral solution 50 mg/5 ml	• 150 mg tablets into one pack of 60 tablets • 50 mg/5 ml solution into one bottle of 5 ml or 240 ml	• Room temperature below 30°C • Dry environment • Away from direct sunlight
NVP	Nevirapine	Viramune®	Non-nucleoside reverse-transcriptase inhibitor (NNRTI)	• Tablet 200 mg • Oral suspension 50 mg/5 ml	• 50 mg/5 ml suspension into one bottle of 5 ml or 240 ml • 200 mg tablets into one pack of 160 tablets	• Room temperature below 30°C • Dry environment • Away from direct sunlight
EFV	Efavirenz	Stocrin®	NNTRI	• Capsules 50 mg, 200 mg, 600 mg • Syrup 30 mg/ml	• 50 mg capsules into one pack of 30 capsules • 200 mg capsules into one pack of 90 or 30 capsules • 600 mg tablets into one pack of 30 or 10 tablets • 30 mg/ml syrup into one bottle of 180 ml	• Room temperature below 30°C • Dry environment • Away from direct sunlight
ABC	Abacavir	Ziagen®	NTRI	• Tablet 300 mg • Oral solution 20 mg/ml	• 60 tablets in one blister pack • 20 mg/ml oral solution into one bottle of 240 ml	• Room temperature below 30°C • Dry environment • Away from direct sunlight
Fixed-dose combinations						
3TC + AZT	Lamivudine + azidothymidine	Combivir®	NRTI/NRTI	• 150/300 mg	• 60 or 10 tablets in one pack	• Room temperature below 30°C • Dry environment • Away from direct sunlight

3TC + d4T	Lamivudine + stavudine	Coviro LS 40® or Coviro LS 30®	NRTI/NRTI	• Tablets 150 mg/40 mg or 150 mg/30 mg	• 60 or 10 tablets in one pack	• Room temperature below 30°C • Dry environment • Away from direct sunlight
3TC+ d4T + NVP	Lamivudine + stavudine + nevirapine	Triviro® or Triomune®	NRTI/NRTI / NNRTI	• 150 mg/40 mg/200 mg or 150 mg/30 mg/200 mg	• 60 or 10 tablets in one pack	• Room temperature below 30°C • Dry environment • Away from direct sunlight
AZT + 3TC + ABC	Lamivudine + azidothymidine + abacavir	Trizivir®	NRTI/NRTI / NRTI	• 150 mg/300 mg/300 mg	• 40 or 60 tabs in one pack	• Room temperature below 30°C • Dry environment • Away from direct sunlight
AZT + 3TC + EFV	Lamivudine + azidothymidine + efavirenz		NRTI/NRTI / NNRTI	• 150 mg/300 mg/600 mg	• 10 + 5 or 60 + 30	• Room temperature below 30°C • Dry environment • Away from direct sunlight

Annex 3. Summary table of activities

Phase	Main activity	Subactivity 1	Subactivity 2	Subactivity 3	Subactivity 4	Subactivity 5
Decision-making	**1. Prepare the information required for making a well-founded decision**	Consult with the WHO/UNICEF local office or web site to obtain the latest guidelines	Collect information on international guidelines and recommendations	Determine the total cost of providing the new regimen and the cost of providing the new regimen per person compared with the current regimen	Analyse the existing country PMTCT policies and guidelines to determine gaps that may hinder the implementation of the WHO-recommended regimen	Develop a rationale and justification for the regimen change or introduction
	2. Consult with the technical working group on specific decisions	Meet the technical working group and consider the questions related to changing over to a more efficacious regimen	Obtain consensus on the need to change or introduce a more efficacious regimen based on the WHO guidelines			
	3. Seek approval and a decision from the health ministry	Present the need and justification for changing to a more efficacious regimen	Get consent from health ministry decision-makers			
	4. Obtain the buy-in and commitment of national stakeholders to the changes	Hold a national multisectoral stakeholders' workshop to obtain buy-in and commitment to support the regimen change or introduction				

Phase	Main activity	Subactivity 1	Subactivity 2	Subactivity 3	Subactivity 4	Subactivity 5
Preparation	**1. Informing all stakeholder and health workers about the decision to change to a new regimen**	Inform all stakeholders and health workers about the decision and the process that will be followed to introduce the new regimen				
	2. Forecasting the demand for 2–3 years and estimating the quantity required for one year of drugs in the new regimen	Forecast the quantity that will be required for 2–3 years based on the target in the strategic plan as basis for mobilizing resources	Quantify the requirements for the first year based on the available resources	Secure the required funding from government or development partners for purchasing drugs		
	3. Regimen selection	Working through the technical working group, select the regimen for PMTCT prophylaxis and first-line antiretroviral therapy for pregnant women				
	4. Assessing the capacity and readiness to provide the new regimen	Select the assessment team with the help of the technical working group	Develop the methods and instruments for the assessment based on information needs	Make a schedule of field visits and inform the relevant site authority about the visit	Conduct the site assessment	Analyse the information to determine the available resources, gaps and needs
	5. Preparing implementation strategies and an action plan	The technical working groups drafts the implementation plans, including the budget	Present the implementation plan to the health ministry officials for comments and approval	Present the implementation to the broader stakeholders for comments and buy-in	Finalize the implementation plan	Communicate the implementation plan to the health workers and the relevant stakeholders
	6. Preparing and reviewing the treatment protocol	Working through the technical working group, revise the existing treatment protocol according to the selected regimen				
	7. Developing and revising all relevant guidelines, manuals and tools	Working through the technical working group, revise all relevant guidelines, manuals and tools in accordance with the new regimen				

	8. Mobilizing and allocating resources	Identify all resources needed for introducing the new regimen and estimate their cost	Identify all potential sources of resources based on the commitments made	Secure the resources for all activities related to introducing the new regimen	Allocate the resources based on the budget in the implementation plan

Phase	Main activity	Subactivity 1	Subactivity 2	Subactivity 3	Subactivity 4	Subactivity 5
Initial implementation	**1. Selecting the health facilities for initial implementation**	Set the criteria for the selection of the initial sites	Determine the number of initial sites	Select and inform the initial sites		
	2. Printing new or revised protocols, guidelines and tools	Secure the funding	Print and distribute to health facilities			
	3. Conducting staff training	Determine the number of staff members that need training and develop a training plan based on need	Develop and prepare training materials	Determine the training venue and prepare a training calendar or schedule	Conduct training according to the plan and schedule	
	4. Improving infrastructure, pharmacy and laboratory logistics	Determine the specification and the scope of work required for each site	Outsource the infrastructure development	Monitor progress		
	5. Procuring drugs, reagents and other needed supplies	Verify with the drugs regulatory authority the registration status of the drugs in the selected regimen and about the fast track or exemption process	Determine the size of the first order, including the buffer stock	Determine the procurement methods and ensure that they conform to all requirements	Set the procurement calendar for activities such as tendering, contracts, shipment and receipt and payments and monitor the procurement process	Receive stock at the national store, check quantities, contents and packaging and perform quality assurance testing, informing the supplier or manufacturer if there is any discrepancy
	6. Establishing a drug supply management system	Set up procedures for distributing and managing new drugs	Distribute the new drugs to the initial sites and store	Start providing the new regimen to pregnant women	Monitor the implementation of the new regimen	
	7. Implementation	Inform the initial site to start providing the new regimen to newly registered pregnant mothers living with HIV	The selected sites start providing the new regimen			

	8. Evaluation and documentation	Collect data using the agreed protocol	Analyse the data	Make reports on the findings	Disseminate the findings to the relevant stakeholders	
Phase	**Main activity**	**Subactivity 1**	**Subactivity 2**	**Subactivity 3**	**Subactivity 4**	**Subactivity 5**
Full-scale implementation	**1. Reviewing the action plan**	Make a report at the end of the initial phase after a predetermined time period	Revise action plans, procedures and the drug ordering and distribution system based on the findings of the initial implementation			
	2. Selecting additional sites	Select the next sites based on the predetermined criteria in a phased approach	Inform through an introductory seminar			
	3. Preparatory activities for scale-up	Follow the revised action plan				
	4. Implementation	Distribute drugs to the new site and store them	Start providing the new regimen	Monitor and document implementation		