HIV/AIDS SERVICE DELIVERY PROGRAMS

OVERVIEW AND INSIGHTS FOR SUPPLY CHAIN MANAGERS

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Abstract

Delivering effective and quality HIV/AIDS services requires a comprehensive national HIV/AIDS program that ensures a functional and efficient supply chain for the commodities needed by each service delivery component. In order to create programs that can ensure the uninterrupted availability of product, logistics advisors should be aware of difficulties facing HIV/AIDS service delivery in resource-limited settings. The document aims to improve the logistician's understanding of the essential elements of a comprehensive HIV/AIDS program and how the different components relate to each other; how changes in services in each component can affect demand, uptake, or services in another, and the need for products in each; and how, where and when different services are provided and managed within the health system.

CONTENTS

TABLES

ACRONYMS

ABC	abstain, be faithful, use condoms
ABC	abacavir
AIDS	acquired immunodeficiency syndrome
ANC	antenatal care
ART	antiretroviral therapy
ARV	antiretroviral
BCC	behavior change communication
BCG	Bacillus Calmette-Guerin (vaccine for tuberculosis)
CDC	Centers for Disease Control and Prevention
CHCT	couple HIV counseling and testing
CNS	central nervous system
CSW	commercial sex worker
DBS	dried blood spot
ELISA	enzyme-linked immunosorbent assay
FDC	fixed-dose combination
FHI	Family Health International
FI	fusion inhibitor
GDP	gross domestic product
GI	gastrointestinal
HAART	highly active antiretroviral therapy
HBC	home-based care
HCT	HIV counseling and testing
HCW	health care worker
HIV	human immunodeficiency virus
IDU	intravenous drug use(r)
JSI	John Snow, Inc.
KS	Kaposi's sarcoma (cancer)
MSM	men who have sex with men
MTCT	mother-to-child transmission
NGO	nongovernmental organization
NRTI	nucleoside reverse transcriptase inhibitor
NNRTI	nonnucleoside reverse transcriptase inhibitor
NVP	nevirapine
OGAC	Office of the Global AIDS Coordinator
OI	opportunistic infection
OPC	oropharyngeal candidiasis

OVC	orphans and vulnerable children
PCP	pneumocystis carinii pneumonia
PCR	polymerase chain reaction
PEP	post-exposure prophylaxis
PEPFAR	President's Emergency Plan for AIDS Relief
PI	protease inhibitors
PLWHA	people living with HIV/AIDS
PMTCT	prevention of mother-to-child transmission
RNA	ribonucleic acid
STI	sexually transmitted infection
STD	sexually transmitted disease
TB	tuberculosis
TLC	total lymphocyte count
TT	tetanus toxoid
UNAIDS	Joint United Nations Programme on AIDS
UNICEF	United Nations International Children's Emergency Fund
USAID	United States Agency for International Development
VL	visceral leishmaniasis
VCT	voluntary counseling and testing
WHO	World Health Organization

ACKNOWLEDGMENTS

PREFACE

Public health service delivery encompasses activities implemented using service delivery models tailored to local, regional, and national policy and program contexts and needs. The process of designing, implementing, and evaluating service delivery includes a cycle of assessment, implementation, revision of the design, and further monitoring and evaluation.

In the case of HIV/AIDS programs, the process takes into account specific factors related to the epidemic in a country. In addition, program success is influenced by factors such as provider attitudes toward people living with HIV/AIDS and the accessibility, affordability, and acceptability of prevention, care, and treatment services.

Government ministries and donors at the national level are challenged to support service delivery at the facility and community levels. This support entails policies, strategies and guidelines, monitoring and evaluation plans, and approaches to build human capacity to deliver services that are supported by a secure supply chain for program drugs and commodities.

Service delivery is not possible without a comprehensive national HIV/AIDS program that ensures a functional and efficient supply chain for the drugs, supplies, and commodities needed by each service delivery component. The commodities range from condoms and test kits to drugs for pain management. It is critical that there be a coordinated program across levels of the public health care system including primary health care clinics, community health centers, district hospitals, and regional and tertiary health institutions.

It is also critical that supply chain personnel working in HIV/AIDS programs, as well as those who supervise them, understand the natural history of HIV disease, its effect on individuals and communities and the demands that challenge service delivery and national programs. This document is designed to provide logistics advisors with specific background information on HIV/AIDS and service delivery in resource-limited settings, but it is not intended to provide a comprehensive overview of HIV/AIDS programs and services. Rather, this document focuses on those elements that will assist advisors in providing a foundation for understanding the context in which supply chains must be developed—from design through implementation and monitoring. Thus, supply chains can be agile and can respond to the requirements of rapidly expanding HIV/AIDS programs and, ultimately, can ensure uninterrupted product availability.

The document aims to improve the logistician's understanding of the following areas:

- what the essential elements of a comprehensive HIV/AIDS program are, and how the different components relate to each other
- how changes in services in each component can affect demand, uptake, or services in another, and what the need is for products in each
- how, where, and when different services are provided and managed within the health system.

This document draws from a variety of resources, including JSI's domestic and international experience in HIV/AIDS service delivery and clinical care, as well as from a compilation of best practices and lessons learned from a variety of organizations that are working in HIV/AIDS program support and service delivery. Other references that provide more detail include the World Health Organization's (WHO's) *Scaling Up Antiretroviral Therapy in Resource-Limited Settings: Treatment Guidelines for a Public Health Approach* and Family Health International's *Strategies for an Expanded and Comprehensive Response (ECR) to a National HIV/AIDS*

Epidemic: A Handbook for Designing and Implementing HIV/AIDS Programs and *HIV/AIDS Care and Treatment: A Clinical Course for People Caring for Persons Living with HIV/AIDS.*

1. BACKGROUND

HIV/AIDS is a complex infectious disease that is now at the pandemic stage. While it is not possible to provide a thorough understanding of the disease in a brief document, some basic facts about HIV/AIDS are critical to understand if one is to support programs for people living with HIV/AIDS (PLWHA). The following overview focuses on the basic facts logistics advisors and managers should be familiar with if they are to assist programs in acquiring and developing supply chains that will manage HIV/AIDS commodities.

A. OVERVIEW: THE HIV/AIDS EPIDEMIC

As of 2005, 40.3 million people worldwide were living with HIV, up from an estimated 37.5 million in 2003. More than 3.0 million people died of AIDS-related illnesses in 2005; of those, more than 500,000 were children. According to the most recent reports, the steepest increases in HIV infections have occurred in Eastern Europe and Central Asia (25 percent increase to 1.6 million) and East Asia. But sub-Saharan Africa continues to be the most affected globally—with 64 percent of new infections occurring there, or more than 3.0 million people (UNAIDS 2005).

According to UNAIDS, more than 1.0 million people in low- and middle-income countries are now living longer and better lives because they are on antiretroviral treatment (ART). An estimated 250,000 to 350,000 deaths were averted this year because of expanded access to HIV treatment. Commenting on the potential enhanced effect of integrating prevention and treatment, the 2005 report emphasizes that a comprehensive response to HIV and AIDS requires the simultaneous acceleration of treatment and prevention efforts with the ultimate goal of universal access to prevention, treatment, and care.

The words *HIV* and *AIDS* can be confusing because both terms describe the same disease. It is useful to think of AIDS as advanced or severe HIV disease. A person with AIDS has an immune system so weakened by HIV that the person usually becomes sick from one of several opportunistic infections or cancers such as these illnesses: PCP (a type of pneumonia), KS (Kaposi's sarcoma), wasting syndrome (involuntary weight loss), memory impairment, or tuberculosis. If someone with HIV is diagnosed with one of the opportunistic infections (even if the CD4 count is above 200), he or she is said to have AIDS. AIDS usually takes time to develop from the period in which a person first acquires HIV—usually between 2 to 10 years or more. After the person has been diagnosed with AIDS, she or he is always considered to have AIDS, even if that person's CD4 count goes up again, if he or she should recover from the disease that defined the AIDS diagnosis, or both.

Drugs exist to prevent or treat opportunistic infections, but only antiretroviral (ARV) drugs will decrease the viral load, thereby allowing the immune system to rebound. Once started, a person with HIV/AIDS needs the drugs for the rest of his or her life.

The goals of a comprehensive program for HIV/AIDS in a country include reducing HIV transmission, reducing AIDS morbidity and mortality, improving the quality of life for PLWHA, and lessening the impact of the epidemic in affected locations and populations.

First, although this document, and this section in particular, focus primarily on the health sector's response to HIV/AIDS, it is important to recognize that HIV is not only a health-sector problem but also a multisectoral problem requiring a population approach rather than an individual approach to promoting good health. Second, the social environment has been acknowledged to have a significant effect on individual and population health status.

B. HIV/AIDS SERVICE DELIVERY

The components of a comprehensive HIV/AIDS service delivery system should address needs along a continuum of care. That continuum ranges from supplying community education for risk reduction through care and treatment, to providing psychological and physical comfort to people who are dying of AIDS, and to mitigating the effect of the epidemic in a community. Services are designed for a country and then adapted to specific geographic locales as policymakers take into account the stage of the epidemic, the available resources, and the community preferences.

In general, people with HIV infection need comprehensive services along a continuum from the point of infection through testing, treatment, and palliative care. The services that they need change over the course of their illness. A component of a comprehensive continuum of care that meets the needs of community members—from the time they want to know their HIV status through a period of terminal illness—includes the following components:

- behavior change communications (abstain, be faithful, use condoms [ABC], and so on) and condom social marketing for prevention

- voluntary HIV/AIDS counseling and testing services—both provider and client initiated

- prevention of mother-to-child transmission

- post-exposure prophylaxis

- psychosocial support

- clinical care and treatment, including the prevention and management of opportunistic infections, symptom management, and antiretroviral therapy

- nutritional assistance

- community-based services

- home-based care.

A comprehensive national HIV/AIDS program supports the delivery of those components of care through the following program components (FHI March 2005):

- strategic planning

- technical strategies

- administration and resource management

- nongovernmental organization (NGO) involvement

- human capacity development

- costing and use of resources

- managing the supply chain for commodities

- measuring for impact.

The components of a comprehensive program range from those interventions directed at the primary prevention of HIV, to those aimed at providing psychological and physical comfort for people who are dying of AIDS and at mitigating the impact of the epidemic in a community. The interventions are based on the needs of members of the community at different times in their lives, such as when they are not infected but want to know their status or when they are infected and need care and treatment. Figure 1 illustrates the services needed for various members of a community.

Figure 1. Standard Care Services for HIV/AIDS

			Palliative Care		
			Home-Based Care		
	Prevention of Mother-to-Child Transmission		Antiretroviral Therapy		
	Post-Exposure Prophylaxis	Opportunistic Infections and Related Illnesses Diagnosis, Treatments, Preventive Therapies			
	Psycho-Social and Spiritual Support				
	Individual and Family	Care Providers	Bereavement		Orphans
HIV Counseling and Testing, VCT					
Prevention STI Services, Behavior Change Communication, Education on Universal Precautions					
Uninfected People	Exposed People	People Living with HIV	People Living with AIDS	Terminally Ill and Beyond	

HIV/AIDS programs depend on continuous supplies of commodities; this is achieved through well-functioning supply chains that ensure these supplies are available where and when needed. Services require care that is supported by community outreach and education, adequate laboratory infrastructure, and effective supply chain management. Clients need education and outreach to contemplate and accept HIV counseling and testing, which also must be in place. A counseling and testing or prevention of mother-to-child transmission (PMTCT) program cannot exist without trained providers, HIV test kits, a variety of essential drugs, and lab facilities. If clients test negative for HIV (meaning they are not infected), there is a need for continued support to ensure they remain HIV negative. This support involves access to sound and balanced information, support in decision making about abstinence, faithfulness, and condom use, and access to an affordable supply of condoms.

An effective, comprehensive HIV/AIDS program must be able to guarantee simultaneous availability of services and products for HIV/AIDS prevention, diagnosis, counseling, and treatment. Developing a supply chain that can manage the thousands of different health commodities required to provide a comprehensive range of HIV/AIDS-related services can be challenging, particularly because patients have a vastly increased chance of developing drug-resistant HIV if their ART regimens are interrupted by stockouts or for other reasons. In addition, if insufficient or poor quality lab reagents are available to perform CD4 or other tests to tell clinicians if the patient's immune status is at the point where ART is indicated, then the delay in initiation might mean that the patient dies before getting ART. It can also mean that the patient's status has declined, thus decreasing the impact of treatment once it is started.

C. NATIONAL GUIDELINES AND POLICY DEVELOPMENT

HIV/AIDS programs operating in a resource-constrained environment are best designed by using a public health approach for prevention, care, and treatment activities, tailored to reflect the local resource environment. Countries trying to treat large populations of people with HIV on limited budgets should use a public health approach to identify the most effective and affordable approaches to diagnosis, testing, care and treatment of people with HIV/AIDS. Implementation of these approaches requires the dissemination of standardized policies and guidelines, which must be developed on the basis of careful assessment and the input of key stakeholders in decision making.

D. NATIONAL ART PROGRAM NEEDS

When assessing the national antiretroviral therapy (ART) program in any country, it is important to discuss all program components. This is independent of the fact that there are many countries in which these programs are organized as vertical programs. For example, PMTCT, voluntary counseling and testing (VCT), home-based care (HBC), and tuberculosis (TB) sites operate separately from ART delivery sites. The design of the supply chain for any of the items used to deliver those services will depend on the source of the commodity and on how, when, and where the commodity is used. Within the Ministry of Health, or national systems, each service delivery component frequently depends on the same supply chain. Thus, an assessment of one component of the system is a reflection of the other.

Programmatically, the components of the program must work together. HIV counseling and testing sites and ART sites are a clear example. It is possible for a country to train health care providers about managing AIDS patients and using ART and to have a sufficient stock of antiretroviral drugs (ARVs) at a given point in time. However, if the residents of the community in which the prepared facility resides are not participating in a counseling and testing program, they will not know that they are HIV infected and will not seek treatment in a timely manner. Therefore, to effectively scale up ART services in a country, all services that are complementary to ART—including HIV counseling and testing, plus treating opportunistic infections (OIs)—must also be expanded or widely available.

E. RELATIONSHIP BETWEEN EPIDEMIOLOGY AND PROGRAM NEEDS

Several factors affect the demand for services in a country and, thus, the requirements for HIV/AIDS commodities. Those factors include the HIV prevalence; the identification of infected groups; and the reach of the current HIV testing, care, and treatment services.

For example, in the majority of sub-Saharan Africa, the epidemic is considered to be a mature one that affects the general population. Transmission is primarily heterosexual, and prevalence tends to be higher than in other parts of the world. In contrast, across Central Asia and Eastern Europe, for example, the epidemic is concentrated or limited to special risk groups (men who have sex with men [MSM], sex workers, and intravenous drug users [IDUs]. There is a low overall prevalence of HIV/AIDS among the general population in those areas.

Obtaining accurate data regarding numbers of infections and numbers of people with HIV who need treatment is a challenge in this type of epidemic because many of the risk groups engage in illegal behaviors, which results in a reluctance to get a test for HIV or to disclose either risk or HIV status.

Examples of factors that influence the nature of the HIV/AIDS epidemic in a country—and thus the program and services that are available—include the following:

• HIV prevalence, which refers to the number of people who are infected with HIV. Because it indicates how widespread the epidemic is in a given population, it affects all other program demands.

- Cases of AIDS, which refers to the number of people who have HIV in a specific country and who have progressed to the stage of HIV called AIDS, in which they experience a set of signs and symptoms, infections, and conditions.

- Number and type of HIV counseling and testing (HCT) services available, which refers to how many different models of HCT exist (for example, VCT, PMTCT, and so on). It determines where and how many HIV test kits and related supplies will be needed.

- Number of ART sites, which determines the number of antiretroviral drugs (ARVs), drugs for symptomatic relief, and drugs to prevent and treat OIs that will be needed.

- Number of pregnant women each year, attendance rates at antenatal clinics, and number of PMTCT programs, which determines the number of pregnant women who might need the services of a PMTCT program, including test kits, ARVs for mothers and babies, and other medical supplies. These data can be obtained from Demographic and Health Surveys (DHS) and from country data on fertility, average number of children, and attendance at antenatal care (ANC) clinics. In some countries, women are unlikely to come for services, while in others attendance is high.

- Number of home-based care programs, which influences the demand for all related supplies and drugs for symptom relief.

The usefulness of prevalence data in estimating the number of people likely to progress to AIDS and, therefore, needing treatment varies with the type of epidemic in a country. In countries such as those in sub-Saharan Africa, where the virus is spread largely through heterosexual transmission among the general population, estimating the numbers of people infected with HIV is relatively simple. The prevalence of HIV among pregnant women attending ANC clinics is—after some adjustments for age, sex, and urban and rural distribution of the population—applied to all adults in the country to get a national estimate of people living with HIV.

However, in countries where the bulk of HIV infections are concentrated within populations whose behavior puts them at especially high risk of contracting and passing on the virus, estimates that are based on prevalence among women at antenatal clinics are likely to be inaccurate. Men who have sex with men and male drug injectors do not get pregnant. Therefore, if they make up a large proportion of those infected with HIV, antenatal-based estimates will miss a significant part of the epidemic.

Individuals wishing to make accurate estimates of HIV infection in concentrated epidemics, moreover, must take a different approach. First, they must decide which population groups are likely to be most at risk of contracting HIV in their national situation because of their sexual or drug-taking behavior. Second, they must estimate how many people in the country engage in each of those high-risk behaviors. They must next consider whether anyone else is exposed to HIV infection by those who engage in such behaviors, even though the exposed people do not themselves engage in any high-risk behavior. They may also wish to consider whether a significant number of people who once engaged in high-risk behavior (and may have been infected with HIV at that time) have since moved out of those groups—for example, either by leaving sex work or by giving up drug injection. Certainly, they must have an idea of the prevalence of HIV infection within each of the population groups at high risk (UNAIDS/WHO 2004).

It is generally thought that in higher prevalence countries with generalized epidemics, about 10 percent to 20 percent of HIV-positive individuals in the population are ART eligible, and all are likely to need drugs for OI prophylaxis and treatment. Other factors that are unique to a country or community that affect uptake of HIV/AIDS care and treatment services include the level of stigma, the number of treatment sites, and the risk behaviors that result in HIV infection.

Stigma influences the number of people willing to seek HIV testing and treatment. The fact that there will be significant delays in seeking care when there are situations of high stigma and low accessibility means that those with AIDS who need treatment at a given point in time might be a higher percentage of the total population than the percentage in a situation in which people seek treatment more promptly.

If there are few treatment sites or if people do not know or like the sites that exist, they might also delay seeking care. If the people who are infected are involved in illegal activities such as sex work or injecting drug use, there will probably be delays in seeking both testing and care as a result of the potential personal risk involved. If treatment is delayed, for any of those or other reasons, a higher proportion of HIV-positive individuals who do finally seek care is likely to need treatment at the time of entry into care.

Some country experience and treatment reports, plus anecdotal evidence, suggest that about 10 percent to 20 percent of HIV-infected people who are seeking care in a context such as sub-Saharan Africa will need ART, whereas this figure might be as high as 30 percent to 50 percent in another context, such as in Central Asia or Eastern Europe. In those regions, sentinel surveillance is not useful as an estimate of the number of HIV-infected people. Rather, documentation of those who have tested HIV positive at testing sites can be a guideline for ART needs.

Because of gross underreporting of HIV infections and cases of AIDS in many countries (for example, people with AIDS documented instead as having pneumonia or TB), local data might not be valid enough to provide a sound basis for quantification. However, the data do provide a sense of the trend of the epidemic in that country. When one reviews the data for quantification, for example, it is useful to keep in mind that stigma can play a significant role in reducing uptake of services. In addition, stigma around treatment may be more of a barrier in countries with concentrated epidemics. Thus, when one estimates numbers of AIDS cases, it is important to factor in potential uptake rates of both testing and treatment on the basis of issues such as stigma and access to treatment.

Another way to determine numbers requiring ART is by looking at service statistics data on attendance rates for the three most frequent opportunistic infections. Once patients are on ART, the number of opportunistic infections decreases as the immune system rebounds. However, in programs where ART has not yet been introduced or where it is available on a very limited basis, service statistics related to treatment of OIs can supplement prevalence data, because those data can be used as a proxy for people requiring treatment. Moreover, service statistics for OI treatment might also be difficult to obtain because many programs are still relatively new, and the data are usually incomplete.

Another issue to consider in quantification is when to estimate the need for changes to first-line regimens. In sub-Saharan Africa, current estimates are that patients who do not experience adverse reactions or toxicity to first-line regimens will take between three and five years before they need to switch to the second-line regimen. However, reactions or side effects resulting from some drugs in the first-line regimens will require a switch of one of the first-line regimen drugs; current estimates are that about 15 percent of patients on most first-line regimens will need to switch at least one drug.

When one looks at national program needs for post-exposure prophylaxis (PEP), certain factors—such as the current number of reported occupational exposures and data showing whether those reporting occupational or other exposures accept offers of PEP—can form the initial basis for estimates of need. In some countries, PEP is being offered to victims of rape, and estimates would be needed regarding the level of predicted usage in those cases.

A sample tool for estimating program numbers is illustrated in table 1, using local HIV/AIDS data for different subpopulations and different HIV/AIDS service components (FHI 2004–2005).

TABLE 1. ILLUSTRATIVE HIV COUNSELING AND TESTING PROJECTIONS TO ENROLL 450 PEOPLE LIVING WITH HIV/AIDS (PLWHA) IN THE ART PROGRAM

This equation allows you to calculate the number of HIV tests needed to identify and treat a target number of HIV positive people. This equation allows you to forecast the need for HIV tests for the general population and various high risk groups. Known variables required: 1) Target number to receive ART (as dictated by proposal/goal), 2) Estimated population of HIV positive people (or population x prevalence rate), 3) HIV prevalence in general population and among high risk populations, and 4) the CD4 treatment guidelines of the country.

A	B	C	D	E	F	G	H	I	J	K
Target number to receive ART (CD4 < 200)	Total estimated no. of HIV positive persons that need to be identified via testing to reach 450 people on ART	Prevalence in general population*	Test refusal rate	Total no. of people who need to be tested	% (annual) refusing treatment	Adjusted Number of HIV tests needed	Number of HIV tests needed for IDU (prevalence 38.4%)	Number of HIV tests needed for CSWs (4.2%)	Number of HIV tests needed for Seasonal migrant laborers	Number of HIV tests needed for MSM (x3)
450	2,700	0.5	0.1	5,940	0.10	6,534	3,267	653	3,267	2,178

Explanation	* This is an example only, and does not reflect actual HIV prevalence or situation in Nepal.
Column A	The target number of people to receive ART in a designated geographic area or region.
Column B	Formula=sum(A5*6). Not all people who are HIV positive are ready to start ART. This formula is used to calculate the total number of PLWHA who would need to be tested to reach 450 people with CD4 count 200 or lower. The example uses initiation criteria of CD4 < 200. This is determined by multiplying the target number to receive ART by 6. Use the number 6 as a multiplier when using CD4 guidelines < 200. (When using CD4 < 250, multiply by 5, and when using CD4 < 350, multiply by 4.)
Column C	The HIV prevalence level found in the target population.
Column D	The test refusal rate for HIV testing is estimated at 10%. The test refusal rate is likely to be higher for high risk groups. To the extent possible, this number should be based on experience with the target population. If unknown, it is better to overestimate to ensure an adequate supply of tests.
Column E	Formula=sum((B5/C5)*1.10. To determine the number of HIV tests needed for the general population, divide the number of HIV tests needed to generate the required number of persons with CD4 < 200 by the HIV prevalence in the general population, and then multiply that number by 1.10 to compensate for the 10% refusal rate.
Column F	Based on evidence, the percent who refuse treatment for one reason or another is estimated at 10%.
Column G	The adjusted number of HIV tests needed is determined by multiplying the number of HIV tests by 1.1 to compensate for the 10% treatment refusal rate.
Column H	Formula=sum((B5/(C5*2))*1.1)*1.1. To determine the number of HIV tests needed for STI clients, divide the number of people who need HIV tests according to CD4 guidelines by the HIV prevalence in the general population X 2, and then multiply that number by 1.10 to compensate for the 10% testing refusal rate. Finally, multiply the total by 1.10 to compensate for the 10% treatment refusal rate.
Column I	Formula=sum((B5/(C5*10))*1.1)*1.1. To determine the number of HIV tests needed for commercial sex workers, divide the number of HIV tests according to CD4 guidelines by the HIV prevalence in the general population X 10, and then multiply that number by 1.10 to compensate for the 10% testing refusal rate. Finally, multiply the total by 1.10 to compensate for the 10% treatment refusal rate.
Column J	Formula=sum((B5/(C5*2))*1.1)*1.1. To determine the number of HIV tests needed for the uniformed services, divide the number of people who need HIV tests according to CD4 guidelines by the HIV prevalence in the general population X 2, and then multiply that number by 1.10 to compensate for the 10% testing refusal rate. Finally, multiply the total by 1.10 to compensate for the 10% treatment refusal rate.
Column K	Formula=sum((B5/(C5*3))*1.1)*1.1. To determine the number of HIV tests needed for MSM, divide the number of people who need HIV tests according to CD4 guidelines by the HIV prevalence in the general population X 3, and then multiply that number by 1.10 to compensate for the 10% testing refusal rate. Finally, multiply the total by 1.10 to compensate for the 10% treatment refusal rate.

Source: Family Health International October 2004–September 2005.

2. PREVENTION, CARE, AND TREATMENT: HOW THEY ARE ADDRESSED IN A COMPREHENSIVE HIV/AIDS PROGRAM

This section addresses the main aspects of a comprehensive HIV/AIDS program in somewhat more detail than did the introductory section on HIV/AIDS programs.

A. LOGISTICAL IMPLICATIONS OF HIV/AIDS PROGRAMMING TRENDS

In an HIV/AIDS epidemic, a challenge facing donors, policymakers, and program managers is to retain a balanced focus on all components of programs. With limited resources and the pressure of advocacy concerns at any given time, there is often a shift from one area of need to another. Recently, there have been aggressive efforts to redress the fact that treatment for PLWHA in resource-constrained countries was virtually ignored for the first 20 years or more of the epidemic. With the advent of global programs such as WHO's 3 × 5 initiative; the President's Emergency Plan for AIDS Relief (PEPFAR); and the Global Fund for HIV/AIDS, TB, and Malaria, antiretroviral treatment has taken center stage. While this is a significant accomplishment for the global community of people infected and affected by HIV, the heavy focus on ART poses a program-matic challenge as the other components within the program fight for attention and resources. It is important for supply chain managers to be aware of current and future trends in programming, because shifts in priority for services will require corresponding changes in demand for commodities.

B. HIV PREVENTION

As treatment programs expand, there has been a risk of diverting attention from the continuing need for prevention programs. The success of treatment programs depends on the success of prevention efforts. Other-wise, programs will be overwhelmed with ever-escalating demands for care and treatment.

Meeting the prevention needs of communities facing HIV/AIDS is a complex challenge. There are three primary modes of HIV transmission:

- sexual: male-to-female, female-to-male, male-to-male, and female-to-female

- parenteral: blood transfusion, intravenous drug use (IDU), needle sharing, needle stick accidents

- perinatal: in utero, during labor and delivery, and postpartum during breastfeeding.

Worldwide, sexual transmission is the predominant mode. However, in Asia and Eastern Europe and in subpopulations on other continents, IDU exceeds sexual transmission as the primary mode of transmission.

Prevention programs require the use of behavior change communications, access to condoms and clean needles and syringes, contextual interventions, and programs to prevent mother-to-child transmission, which includes counseling and testing, plus antiretroviral drugs.

Susceptibility to HIV infection is related to a wide range of social factors such as poverty, culture, gender relations, and lack of education. HIV prevention programming requires strategies and interventions that support behavior change, access to services, a supportive environment, and positive social norms. Core public health services should be organized so that HIV prevention services are delivered at all levels of the system.

Effective prevention can substantially reduce the number of new infections and, therefore, ultimately will lead to a reduction in the number of people who will need treatment. To be effective, prevention programs use behavior change communication strategies that consist of many types of activities, which might include mass media, peer education, local drama, and so on. Programs need to deliver clear and locally tested messages using different channels. They need to tailor messages to the target audience and to deliver them at a high level of intensity over time. The messages must be accurate, consistent across media, and meaningful to the audiences they seek to reach. U.S. donors, in particular, are emphasizing promotion of abstinence, faithfulness, and condoms. Condom programs are the most dependent on commodities and, therefore, are of greatest relevance to supply chain management programs. Ensuring that condoms are accessible, acceptable, and affordable to those who need them is a challenge that must be met if prevention efforts are to be successful.

C. HIV COUNSELING AND TESTING

As an adjunct to prevention interventions, HIV counseling and testing is considered a powerful prevention tool. It is hypothesized that if a person knows his or her HIV status, then a greater likelihood exists that there will be an effort to decrease the risk of transmission to another person. In addition, as people attend services that include counseling, the overall level of knowledge about HIV in a community will increase.

HIV counseling and testing form a critical entry point for many other HIV/AIDS services, including care and treatment, as shown in table 2 .

TABLE 2. HIV TESTING AND COUNSELING

Promote planning for future orphan care and will preparation	Ease acceptance of serostatus and coping	Provide access to ARV treatment	Promote and facilitate behavior change	Provide access to interventions for preventing mother-to-child transmission
		HIV Testing and Counseling		
Normalize HIV/AIDS and reduce stigma	Facilitate referral to school and peer support	Increase access to family planning services, including condom provision	Promote access to early medical care for opportunistic infections and STIs, and to ARVs and preventive therapy for tuberculosis	

Source: WHO 2005b.

Although service delivery approaches may differ within and between countries, the recommended public health approach for scaling up HIV counseling and testing (HCT) remains the same: the test is voluntary (the client has the right to refuse), the client must give informed consent, the results are kept confidential, the test is accompanied by counseling, and the quality of the HCT is ensured. (FHI 2005).

Several models of counseling and testing are used in different settings, including freestanding clinics, integrated sites, mobile test units, home-based care programs, and so on. Examples of models include the following (Source: CDC/GAP 2005):

- **Voluntary HIV Counseling and Testing (VCT)** gives clients an opportunity to confidentially explore their HIV risks and to learn their HIV test result. VCT services can be provided in freestanding sites or imbedded within other facilities, such as health centers, workplace settings, and military facilities. The target audience is individuals who are interested in knowing their HIV status and learning how to reduce their risk. The focus of the counseling sessions is on risk assessment; risk reduction; partner referral; and linkages to care, treatment, and support.

- **Couple HIV Counseling and Testing (CHCT)** allows sexual partners to learn their HIV status together as a unit. It is offered at VCT sites but may also be offered in other settings as well, such as prenatal clinics. CHCT is an important intervention because as many as 30 percent of couples in high HIV prevalence countries are serodiscordant, i.e., one partner is infected with HIV and the other is not. Counseling sessions focus on discussing risk issues and concerns; risk reduction; and linkages to care, treatment, and support.

- **Provider-initiated HIV counseling and testing** takes place in clinical settings—such as in medical wards and in TB and sexually transmitted infection (STI) clinics—for the purposes of HIV diagnosis and clinical care management. Pre- and post-test counseling sessions focus on recommending and offering the HIV test, obtaining informed consent, using the test results to make medical care decisions or recommendations, and providing appropriate referrals. Provider-initiated HCT is a relatively new phenomenon and has replaced the practice of providers testing for clinical diagnosis without any counseling of the client, or sometimes even without the client's consent.

- **Testing and Counseling for Prevention of Mother-to-Child Transmission of HIV** occurs in prenatal and labor and delivery settings for the purposes of learning a pregnant woman's HIV status and, if necessary, providing a PMTCT intervention. Pre- and post-test counseling sessions focus on recommending and offering the HIV test; obtaining informed consent; using the test results to make decisions about PMTCT; and providing appropriate referrals for follow-up care, treatment, and support.

WHO further recommends that four types of testing be clearly distinguished. In countries following such guidelines, there are implications for logisticians, including the calculation of tests needed by TB and STI clinics, a new area of emphasis in counseling and testing programs.

1. **Voluntary Counseling and Testing.** Client-initiated HIV testing to learn HIV status provided through VCT remains critical to the effectiveness of HIV prevention. UNAIDS and WHO advocate for the effective promotion of knowledge of HIV status among any population that may have been exposed to HIV through any mode of transmission. Pre-testing counseling may be provided either on an individual basis or in group settings with individual follow-up. UNAIDS/WHO encourage the use of rapid tests so that results are provided in a timely fashion and can be followed up immediately with a first posttest counseling session for both HIV-negative and HIV-positive individuals.

2. **Diagnostic HIV Testing.** Such testing is indicated whenever a person shows signs or symptoms that are consistent with HIV-related disease or AIDS. The test aids clinical diagnosis and management, including HIV testing for all TB patients as part of their routine management.

3. A Routine Offer of HIV Testing by Health Care Providers (i.e., provider initiated). This offer should be made to all patients who—

- are assessed in a sexually transmitted infection clinic or elsewhere for a sexually transmitted infection (The test will facilitate tailored counseling using the knowledge of HIV status.)

- are seen in the context of pregnancy (The test will facilitate an offer of antiretrovirals for prevention of HIV transmission.)

- have potential for mother-to-child transmission

- are seen in clinical- and community-based health service settings where HIV is prevalent and antiretroviral treatment is available (injecting drug use treatment services, hospital emergencies, internal medicine hospital wards, consultations, etc.) but who are asymptomatic.

4. Mandatory HIV Screening. UNAIDS and WHO support mandatory screening for HIV and other blood-borne viruses of all blood that is destined for transfusion or for the manufacture of blood products. Mandatory screening of donors is required before all procedures involving transfer of bodily fluids or body parts.

Advances in HIV testing technology have made simpler and cheaper means of rapid HIV diagnostic tests more available, thereby enabling HIV counseling and testing services to become more widely available and affordable. This advanced technology, in turn, has helped ensure that user-friendly, appropriate HIV tests and supplies are available at lower-level health facilities, thus enabling the expansion of HIV counseling and testing services in general and of VCT services in particular. An effective supply chain to manage and ensure continuous availability of HIV tests and supplies is and has been a critical element in enabling expansion of HIV counseling and testing services.

Commodities for HIV testing and counseling services may include the following:

- HIV test kits

- automated analyzers (e.g., enzyme-linked immunosorbent assay [ELISA] readers)

- reagents and controls

- centrifuges

- refrigerators

- test tubes, racks, timers, pipettes, and other laboratory consumables

- commodities for specimen collection (e.g., vacutainers, lancets, needles, syringes, and plasters)

- commodities for universal precautions (e.g., disposable gloves, bleach, cleaning supplies, sharps disposal containers for needles and lancets, and waste disposal bags for blood-contaminated materials)

- safe drinking water and cups

- information materials for training and education

- male and female condoms.

Relevant to quantification are the following insights from the WHO Toolkit:

- HIV testing and counseling services are best supported through approaches that are based on integrated HIV/AIDS care, treatment, support, and prevention.

- The rate of HIV testing and counseling uptake may become inextricably linked with access to ARV treatment, as individuals may be encouraged to find out their HIV status if they have access to better treatment options.

- Rapid scaling up of care also requires a diversification and expansion of HIV testing and counseling services linked to clinical care and antenatal care (ANC) settings.

Implementation of HIV testing and counseling entails various approaches, including the following:

- Use of HIV rapid tests in low-volume settings, or those situated away from provincial treatment centers, and in areas of high prevalence and vulnerability to HIV.

- Diversification of sites where testing and counseling can be provided. This diversification implies, for instance, the availability of rapid testing in areas with greatest representation of vulnerable populations (e.g., STI or reproductive health care services, TB services, and IDU services) and in nonclinical areas where prevention may be optimized (e.g., antenatal care and services for young people).

- Outreach and mobile initiatives may be necessary to improve access to HIV testing and counseling among hard-to-reach groups (e.g., IDUs, sex workers, and young people). Although there may be different approaches to service delivery both within and between countries, the principles of the recommended public health approach for scaling up HIV testing and counseling should be common to the varying approaches.

An issue that has received less attention than it merits is the diagnosis of HIV infection in infants under 18 months of age. Although the HIV tests that are used for adults are acceptable in infants above a certain age, which is being further defined at present, the usual antibody tests are not valid in infants. Infants born to HIV-positive mothers have about a 35 percent chance of acquiring HIV during pregnancy, labor and delivery, or breastfeeding. When they are born, they have the HIV antibodies passed from the HIV-infected mother, but they may not, in fact, be infected themselves. Until 18 months or perhaps as early as 9 months, it is not possible to test for the virus itself using currently available HIV tests, except by use of polymerase chain reaction (PCR) tests. Those tests require very sophisticated laboratory capability in terms of equipment, special room setups, and trained personnel.

Many resource-constrained countries have only one laboratory in the country that is capable of doing PCR. One new technique that is increasingly used involves dried blood spots that are transported to such a lab. The required commodities vary from those for the usual HIV antibody tests. It is important for logisticians to be in communication with policymakers who develop HIV testing strategies, because all plans to use this technology—be it dried blood spot PCR or the usual PCR (direct testing of the blood specimen from the baby)—should be included in supply chain management and planning to ensure the availability of a sufficient quantity of PCR reagents. As a recent example, some countries' governments declared a policy of universal access to PCR testing for all infants, which resulted in an unexpected high demand for infant testing and PCR reagent stockouts.

Widespread access to treatment could bring millions of people into health care settings, thus providing new opportunities for health care workers to deliver and reinforce HIV prevention messages and interventions. Improved access to HIV testing provides an entry point to both prevention and treatment services; it also

provides a unique opportunity to identify and target the infected, vulnerable, and uninfected with more appropriate interventions.

Just as prevention programs are unlikely to achieve full impact in the absence of treatment, so too is the impact of treatment programs reduced if vigorous prevention efforts are absent. Without effective prevention, the number of people requiring care and treatment will grow each year. As more and more people are kept alive with ART, the treatment burden will become enormous unless effective prevention reduces the number of people becoming newly infected. Prevention makes treatment affordable, and treatment can make prevention more effective.

D. PREVENTION OF MOTHER-TO-CHILD TRANSMISSION

Nearly 2,000 babies are born with HIV each day because their HIV-infected mothers do not get the treatment needed to stop transmission (WHO 2004a). *PMTCT* is the term used to describe programs and interventions that are designed to reduce the risk of mother-to-child transmission (MTCT). Such programs are especially valuable because most HIV-infected children acquire the infection through MTCT, which can occur during pregnancy, labor and delivery, or breastfeeding.

PMTCT programs are built around four pillars:

- primary prevention of HIV infection among women and their partners

- prevention of unintended pregnancies among HIV-infected women

- prevention of HIV transmission from HIV-infected women to their children

- provision of treatment, care, and support for women living with HIV/AIDS, their children, and their families.

To accomplish these pillar goals, a PMTCT program encompasses the following components:

- family planning

- HIV testing and counselling

- antiretroviral treatment for prevention of MTCT

- safer delivery practices

- safer infant-feeding practices.

In addition, the program must develop strong linkages so that the mother who is HIV positive and her child are followed after delivery for care and treatment. At present, many programs are not designed to ensure that mothers and their infants are monitored for HIV symptoms and treatment needs after delivery of the baby. Antenatal care (ANC) centers can and should serve as entry points to care and treatment services, including ART for women who need it. In most ANC settings, an HIV test is routinely offered, and some country programs require pre-test counseling of the mother. In other settings, an "opt-out" approach is adopted where women are asked specifically whether they do or do not want to be tested for HIV. Evidence has shown that routine testing or an opt-out approach is more successful in ensuring HIV counseling and testing for pregnant mothers than is an "opt-in" approach.

Short-term ART is an effective and feasible method of preventing MTCT of HIV. Initially, a complicated regimen was used, until studies showed that a single dose of nevirapine given during labor, followed by a dose for the child, was just as effective as the regimen. Recently, however, the concern has been focused on the possible emergence of nevirapine resistance for mothers exposed to single-dose nevirapine and then enrolled on a nevirapine-containing ART regimen later. Recent data also show that a combination of zidovudine (AZT) and nevirapine (NVP) can be more effective with less risk of resistance. Therefore, some countries, where it is feasible, are beginning to use this combination.

To ensure provision of a minimum package of care in ANC centers, programs need to provide many more products than just these two antiretroviral drugs. See appendix 2 for a detailed list.

Additionally, to be the most effective, PMTCT interventions should make a concerted effort to publicly acknowledge that both mothers and fathers have an impact on transmission of HIV to the infant. Emphasis should be placed on making sure both partners are aware of the importance of safer sex throughout pregnancy and breastfeeding. Both partners should be tested and counseled for HIV, and both partners should be made aware of—and provided with—PMTCT interventions to the greatest extent possible.

E. POST-EXPOSURE PROPHYLAXIS

The accidental or unintended exposure to HIV infection can be treated with post-exposure prophylaxis (PEP), if recommended by a physician. PEP for HIV is the use of antiretroviral drugs as soon as possible after a high-risk exposure to HIV to reduce (but not to eliminate) the possibility of HIV infection. PEP is a four-week program of two or three ART medications taken several times a day.

Treatment should be started promptly, preferably within the first several hours after an exposure. It should be administered within 48 hours of a high-risk exposure (not to exceed 72 hours). After 72 hours, PEP is considerably less effective in preventing HIV infection. Therefore, the sooner PEP is administered, the more effective it is.

According to the Centers for Disease Control and Prevention (CDC), effectively delivering PEP after high-risk exposures requires prompt evaluation of patients and consideration of biomedical and behavioral interventions to address current and ongoing health risks. This evaluation should include determination of the HIV status of the potentially exposed person, the timing and characteristics of the most recent exposure, the frequency of exposures to HIV, the HIV status of the source, and the likelihood of concomitant infection with other pathogens or negative health consequences of the exposure event.

A 28-day course of highly active antiretroviral therapy is recommended for people who have had non-occupational exposure to blood, genital secretions, or other potentially infected body fluids of a person known to be HIV infected when that exposure represents a substantial risk for HIV transmission and when the person seeks care within 72 hours of exposure (e.g., in the case of rape). When indicated, antiretroviral PEP should be initiated promptly for the best chance of success. No evidence indicates that any specific antiretroviral medication or combination of medications is optimal for use as PEP, and protocols differ from one country to the other.

Some countries are using two-drug regimens for "low-risk" exposures and three-drug regimens for "high-risk" exposures. Some are using AZT+3TC with or without NVP. Others use d4t+3TC with or without NVP. Some countries are using a protease inhibitor, such as indinavir, as the third drug for high-risk exposures.

In the United States, certain preferences exist for drugs and combinations, including efavirenz and lamivudine, or emtricitabine with zidovudine or tenofovir (as a nonnucleoside-based regimen). Another preferred regimen

includes lopinavir/ritonavir (coformulated in one tablet as Kaletra®) and zidovudine with either lamivudine or emtricitabine. Different alternative regimens are possible as well (CDC January 2005).

For occupational exposure, health workers usually start taking medications within a few hours of exposure. Usually the exposure is from a "needle stick." Such exposures occur when a health care worker accidentally gets jabbed with a needle containing potentially HIV-infected blood.

In the past few years, community activists and researchers began asking why PEP should not be automatically administered after HIV exposures in cases such as rape or when a condom breaks during sexual intercourse. In most developing country programs, exposures such as those that are not directly related to an occupational setting are not addressed in the national treatment guidelines and are still in a stage of debate.

F. CARE AND TREATMENT

The purpose of HIV/AIDS care and treatment programs is to ensure equitable access to diagnosis, medical care, pharmaceuticals, and supportive services; to reduce morbidity and mortality from HIV/AIDS and related complications; to promote prevention opportunities within care, treatment, and support clinical encounters; and to improve the quality of life for adults and children living with HIV/AIDS and their families.

Providing HIV/AIDS care to people living with HIV and AIDS and to their families requires a broad range of services that includes not only medical care and treatment, but also supportive services to ensure adequate nutrition; psychological, social, and daily living support; and prevention messages wherever the opportunity arises. The following components form a comprehensive package of care and treatment services:

- medical and nursing care (counseling and testing; prophylaxis of OIs; treatment of OIs and HIV-related illnesses; TB control; STI management; management of HIV disease and ART; palliative care; access to HIV-related drugs; PMTCT services; clinical HIV/AIDS care for mothers and infants; support systems, such as labs and drug management systems; nutritional support; health education; adequate universal precautions; and PEP)

- psychological support (services to meet emotional and spiritual needs)

- socioeconomic support (material and social support to ensure that nutritional and daily living needs are met)

- support for orphans and vulnerable children

- involvement of PLWHA and their families in service design and evaluation

- respect for human rights and legal needs.

Care and treatment are part of a continuum of care and should be linked to other HIV/AIDS interventions. In addition to the commodities, there is a need for laboratory support, supply chain management, and services and training of the staff and patients.

The care that is needed by the members of a community begins with prevention of HIV infection and includes different services for community members depending on their needs at different points in time. Programs best serve the community if they include components along a continuum of care (as depicted in figure 1).

If a client tests HIV positive, the client will need counseling and psychosocial support about issues such as how to tell a spouse, a child, or other family members about the diagnosis; where to get treatment; and how

to deal with the feelings associated with a diagnosis of HIV. This client demands support from the system, his or her family, and the community, as well as referral to social and medical services. At the time he or she requires prevention or treatment of OIs, the health system will again require trained staff, supplies, and drugs.

A unique feature of HIV disease that distinguishes it from the problems that public health has been addressing in resource-constrained countries for years is that it is a chronic disease. Public health programs are much more accustomed to addressing acute illnesses. HIV care requires a chronic disease management approach. In brief, the principles of chronic case management include the following:

- the patient and health provider must work together as a team.

- care requires regularly scheduled visits to monitor disease status and treatment effects.

- care providers need care and support to prevent burnout.

- treatment is lifelong, so motivation and adherence are critical.

G. TREATMENT OF OPPORTUNISTIC INFECTIONS

The prevention and treatment of OIs plays an essential part in the management of AIDS. There are a few OIs that occur most frequently in PLWHA. In some "high-prevalence" countries, it is recorded that about 80–90 percent of all TB cases are co-infected with HIV (WHO 2005c). This high co-infection rate means that the majority of HIV/AIDS patients will likely have some form of TB—pulmonary or extra pulmonary. Regardless of type, the treatment protocol is the same.

The second most frequent OI is oral or esophageal candidiasis. From a supply chain perspective, again, it is important to understand that treatment is frequently the same regardless of location (oral, esophageal, etc.) of the fungal infection.

The third most frequent infection is PCP (pneumocystis carinii pneumonia). Around 40 percent of patients develop PCP if not on ART (WHO 2005a). A more detailed description of common opportunistic infections can be found in appendix 3.

Some opportunistic infections, such as oral candidiasis, pulmonary TB, and herpes, can be treated when a minimum level of health infrastructure is present. Diagnosis can be made by symptoms or by use of a simple microscope. Another point to keep in mind is that after treatment, and in the absence of ART, such infections can and often do recur, so that patients experience several episodes of an infection.

For OIs such as malignancies, toxoplasmosis, or cryptococcus infections, data are usually only available at the tertiary-level facilities. Those infections are less frequent; they occur at the advanced stage of AIDS and cannot be diagnosed without sophisticated equipment and a highly specialized cadre. Once diagnosed, individuals should be put on lifelong treatment, but usually they do not live longer than a year. Treatment for those conditions often requires specialized drugs, which may not be routinely available at district hospitals and lower-level health facilities. Some of those drugs (e.g., gancyclovir) can cost more than ARV drugs and thus can be prohibitively expensive to patients.

For persons with such infections, there is a need to provide for a number of additional "support medications," such as painkillers, iron substitutes, folic acid, Imodium for diarrhea control, etc. The majority of drugs for treating opportunistic infections are basic essential medicines that should be routinely maintained at district hospitals and primary health care facilities. Those drugs are also used in routine clinical practice and in non-AIDS related cases. They are almost never a part of vertical AIDS programs.

Drugs for TB are usually managed under a national TB program. Because of the public health risks associated with uncontrolled spread of TB, the program is traditionally a vertical one, with dedicated funds for procurement and separate procedures for managing commodities.

H. PROVISION OF ANTIRETROVIRAL THERAPY

Making ART available and widely used at the global level is one of the largest efforts that the international community has ever taken to reduce human suffering caused by an incurable communicable disease. Although ART is not a cure, when used effectively it can decrease illnesses resulting from HIV, decrease AIDS-related mortality, improve quality of life, and decrease risk of transmission. However, providing treatment for those in need on such a large scale has significant challenges, and it is critical that all people involved should be ready to share and learn from their own experiences and from those of others. This approach will help to facilitate the expansion of effective treatment for people who need it sooner rather than later. By instituting large-scale treatment programs while continuing strong prevention efforts in communities, and by reaching both those who are still HIV negative and those who are already infected, the goal is to stop the spread of HIV while providing effective life-prolonging treatment for PLWHA.

There are several essential elements of an effective ART program, including the following:

- country preparedness

- community preparedness

- effective care systems, including sufficient numbers of trained providers, rational guidelines, and accessible sites and services

- adequate site physical capacity

- referral systems and linkages

- patient adherence support

- health management information systems

- quality laboratory systems

- reliable access to appropriate ARVs

- ongoing monitoring, evaluation, and quality management to ensure effective care.

1. Program Issues: Access and Uptake. Putting ARVs into pharmacies does not guarantee that PLWHA will be able to access care and treatment. Many factors determine whether people in a community will seek care at a site that offers ART. Those factors include the fee policies of the clinic, access to testing, stigma in the community toward those infected with HIV, transportation, and many other issues. In addition, community awareness of the availability of ARVs and knowledge about their effectiveness and about how to access them are also critical.

Affordability is a major barrier to accessing treatment in the contexts where patients are expected to pay for all or some of the costs of treatment. Provision of ARVs and related diagnostic and monitoring tests free of charge increases uptake of ART. The extent to which patients will be expected to pay for the lab tests, or the drugs, or both, influences not only their first access to ART but also their ability to continue once they are placed on treatment. Cost of treatment for OIs and laboratory tests may remain an obstacle to access to treat-

ment even for people living with HIV/AIDS who receive ART free of charge. A required financial contribution from patients toward the cost of treatment may be even more of a barrier when more than one person in a household is infected.

Ensuring that people with HIV/AIDS can afford medicines, including ART, is critical. Although ART has fallen in price to U.S. $140 per year, this amount is still too expensive for people living on the equivalent of U.S.$1–2 per day. Evidence suggests that in Africa about 10 million people face impoverishment and about 27 million face severe financial hardships caused by the costs of health care. Countries with low GDP, high HIV prevalence, weak health infrastructure, and limited resources cannot expect to build a large-scale ARV program in the short or medium term without external assistance

Evidence suggests that the availability of treatment can go beyond helping the individual patient. ART programs increase uptake of services such as counseling and testing, PMTCT, and prevention education. Treatment can also change community perceptions of HIV/AIDS and PLWHA. People who were previously a burden on their families can go back to work and can contribute to the community. Hopelessness in communities overwhelmed for years by people dying of AIDS can be turned to hope as they see that people who were wasting are now gaining weight, look years younger, and are interacting actively with their families and in the community. Such changed perceptions can lead to a decrease in the stigma associated with HIV and to an increase in the willingness to talk about HIV and, thus, perhaps to improve prevention efforts as hope increases and as dialogue becomes less threatening.

However, it is also important to realize that the capacity of many ARV programs is still smaller than the population in need of immediate treatment. Particularly in high-prevalence settings, programs are not able to meet demands for treatment to all of those who can benefit. A number of approaches to set priorities for treatment have been tried, including community education and involvement of PLWHA in program design, committees to review patients needing treatment, and a push to expand sites beyond the initial ARV clinics. In addition, because many PLWHA do not yet need ARVs, additional community and consumer education on clinical criteria for ARV (such as CD4 counts) and on the role of healthy lifestyles is also important to ensure that people understand who is eligible and who can wait.

Therefore, assistance at the site and program level will need to focus on capacity building to increase treatment at the site, to expand treatment to other clinics, and to ensure that there are adequate funds for an uninterrupted supply of appropriate ARVs, lab reagents, and OI drugs. For example, one-time donations are not sufficient for most ART programs.

2. ARV Drugs and Patient Management Issues. Antiretroviral drugs inhibit the growth and replication of HIV at various stages of its life cycle. They do not eradicate ("cure") HIV, and so they currently need to be taken for life. Response to treatment is measured both through lab tests and through clinical examination and history. Success is defined as increasing the CD4 cell count (a marker of improving the immune system), decreasing the HIV viral load (the amount of HIV found in the blood) ideally to below the level of detection, and improving health (such as gaining weight) and decreased illnesses and morbidity related to HIV. When used in an appropriate combination of at least three ARVs, the medications can be very strong. However, success is limited in the real world by challenges related to the drug's side effects, the need for near-perfect adherence, and the risk of the virus developing resistance to one or more of the ARVs.

Four main classes of antiretroviral medications are currently used to treat HIV and AIDS, with multiple types of ARVs within three of the four classes (see table 3). Those classes are—

1. nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs)

2. nonnucleoside reverse transcriptase inhibitors (NNRTIs)

3. protease inhibitors (PIs)

4. fusion inhibitors (FIs) (which are not available currently as an oral medication).

TABLE 3. TYPES OF ARV DRUGS (GENERIC AND U.S. BRAND NAME, AS OF MARCH 2006)

NRTIs	NNRTIs	PIs	FIs
Abacavir (ABC, Ziagen®)	Efavirenz (EFV, Sustiva®)	Amprenavir (APV, Agenerase®)	Enfuvirtide (T20, Fuzeon®)
Didanosine (ddI, Videx®)	Delavirdine (DLV, Rescriptor®)	Indinavir (IDV, Crixivan®)	
Lamivudine (3TC, Epivir®)	Nevirapine (NVP, Viramune®)	Lopinavir/Ritonavir (LPV/r, Kaletra®)	
Stavudine (d4t, Zerit®)		Nelfinavir (NFV, Viracept®)	
Zalcitabine (ddc, Hivid®)		Ritonavir (RTV, Norvir®)	
Zidovudine (AZT, Retrovir®)		Saquinavir, soft gel (FTV, Fortovase®)	
Tenofovir (TDF, Viread®)		Fosamprenavir (Lexiva®)	
Emtricitabine (FTC, Emtriva®)		Atazanavir (ATV, Reyataz®)	
		Tipranavir (TPV, Aptivus®)	

NRTIs inhibit the HIV enzyme reverse transcriptase, which is essential for viral replication. These drugs are structurally similar to nucleosides (building blocks of RNA). When inserted in place of the natural nucleoside, they block replication of the virus. A combination of two NRTIs forms the backbone of all current first-line combinations included in the WHO guidance and in other treatment guidelines.

NNRTIs (or "non-nukes") also block reverse transcriptase but through a mechanism different from the NRTIs. The non-nukes are also very potent, but viral resistance can develop through a single change in the viral RNA, which knocks out the entire class. This resistance can even occur after a single dose, if given without other ARVs (e.g., single-dose nevirapine for PMTCT).

Protease inhibitors obstruct the enzyme required to cut the viral proteins before final virus assembly. PIs are also very potent; for many of them, resistance takes longer to develop than it does for NNRTIs. They have a number of characteristics that complicate their use, including side effects, drug interactions, and cost and need for a cold chain for some PIs. In resource-limited settings, these drugs are largely reserved for second-line treatment of individuals for whom first-line treatment is no longer working.

Fusion inhibitors bind to HIV and prevent the virus from infecting healthy cells in the body. As of now, FIs are used in drug-resistant cases as a salvage therapy.

The use of ARVs requires a system that supports providers and patients to ensure near-perfect (>95 percent) adherence. This requirement is because studies have shown that lower rates of adherence are more likely to result in the virus developing resistance to the ARVs currently being used. In addition, this resistance can weaken or even eliminate the potency of other ARVs from the same class ("cross-resistance"). Multiple barriers

exist to adherence, including drug side effects, cost of treatment, access to the clinic, fear of disclosure if family or friends see the ARVs, and many others.

Side effects and toxicities related to ARVs not only threaten adherence, but also can be life threatening, thereby requiring a change in the ARV that is the cause. Side effects can occur early in treatment (e.g., rash caused by nevirapine) or can be delayed (such as lactic acidosis, neuropathy, and changes in body shape).

(a). **Current guidelines on what and when to start.** WHO has produced guidelines for scaling up ART provision in resource-poor settings. The guidelines address issues such as when to start therapy; what the recommended first-line and second-line regimens are; and what the regimens are for pregnant women, children, and TB patients. In addition, there are recommendations for promoting adherence, monitoring resistance, and monitoring the clinical and laboratory use of ART. Simplified treatment regimens and laboratory monitoring and the inclusion, since April 2002, of 12 ARVs have significantly reduced the complexity of treatment.

(i). *When to start ART.* The decision to start antiretroviral treatment is based on weighing the potential benefits of treatment (decreasing risk of death and illness, improving health status) and the risk of disease progression with the toxicities and costs of ART. Therefore, not everyone with HIV needs ART currently, although most will eventually need to start treatment. In resource-limited settings, the decision to start is based on clinical assessment and, where available, on CD4 counts. Those factors determine if therapy should be started or can be or should be delayed. Most of the countries have in their guidelines additional specified "eligibility criteria," and those criteria must be considered along with individual patient readiness for starting treatment and for making a lifelong commitment to taking ARVs. In the case of infants and young children, "patient" readiness refers to readiness of the responsible person who will be administering the ARV.

WHO recommends that—in resource-limited settings—the adolescents and adults who have had an AIDS-defining condition (as defined by the WHO stage 4) should start treatment regardless of CD4 count. Where CD4 counts are available, any person who has a CD4 cell count of <200 cells/mm³ should also be started on treatment. In the absence of access to CD4 cell counts, using a total lymphocyte threshold in combination with the presence of symptoms (WHO stages 2 or 3) will also provide indications to start ART. Some individual countries have modified those criteria, and one should be familiar with such recommendations when working in that area. The newest draft of WHO's clinical staging guidelines is an important reference (WHO 2006b).

National guidelines exist for standardized first-line and second-line regimens, eligibility criteria for starting ARV therapy, and patient monitoring. The guidelines are essential to assist planning of drug procurement, to limit the number of drugs to manage, to predict patterns of resistance, to simplify training of health care providers by using standard clinical management protocols, to educate patients, and to develop simple and effective monitoring and evaluation systems. Although experience has shown that it is feasible to follow standardized treatment regimens in resource-poor settings, ensuring compliance with guidelines can be a challenge. (See table 4.)

TABLE 4. WHO GUIDELINES FOR INITIATION OF ART

The following are a summary of current WHO guidelines for initiating ART:

• WHO Stage IV of HIV disease (clinical AIDS), regardless of CD4 count

• WHO Stages I, II, or III of HIV disease, with a CD4 count below 350/mm

• WHO Stages I, II, or III of HIV disease, with a CD4 count below 350/mm

Source: Adapted from WHO 2003.

> *(ii). What to start.* Guidelines also exist on what combination of ARVs should be started ("first-line"). The guidelines are based on a combination of efficacy and toxicity data, cost, availability, and the need to be able to plan for second-line treatment for patients for whom first-line treatment has failed. In addition, guidelines specify when—and with what—ARV switches should occur for toxicity, drug interactions, or other conditions. For patients who have already been on ARVs, clinicians should obtain the client's ARV history before choosing a regimen. Other considerations include other medications that the patient is taking, current (or planned) pregnancy, and history of toxicity with prior ARVs.
>
> Recommendations are that ART should always be initiated with at least three drugs, including two NRTIs in combination with a PI or an NNRTI. Studies are still ongoing to evaluate the role of triple NRTIs, although initial results have been disappointing. Fixed-dose-combination drugs have been created to decrease the number of tablets or capsules that a patient has to take. In addition, as new research continues to expand understanding of how best to use and sequence ARVs, these recommendations are likely to change
>
> The most commonly and currently recommended first-line regimens in resource-limited settings as of March 2006 include those shown in table 5.

TABLE 5. COMMONLY RECOMMENDED FIRST-LINE ART REGIMENS

Stavudine+Lamivudine		Nevirapine
OR	PLUS	OR
Zidovudine+Lamivudine		Efavirenz

Drug considerations and logistics implications when choosing an ARV regimen include the following:

• cost

• availability of a formulation

• frequency of side effects and toxicities

• frequency of dosing

• dietary restrictions

- storage requirements (particularly cold-chain needs)

- prior ARV exposure

- frequency of opportunistic infections (particularly TB)

- prevalence of liver disease (hepatitis B and C)

- other medications (particularly TB drugs)

- existence of a fixed-dose combination.

    ART treatment is not the only life-prolonging effort. Prevention and treatment of opportunistic infections is critical, and such actions rely on the availability of drugs such as cotrimoxazole and fluconazole. In addition, maintaining a healthy lifestyle, including access to good nutrition and medical care, is also important but remains a challenge for many individuals with HIV infection.

(iii).When to change ARVs. There are a number of situations in which one or all of the drugs in an ART regimen need to be changed. The most common cases include the following:

- Need to change a single ARV

    – Toxicity: change the most likely causative agent.

    – Drug interaction: change the specific ARV (e.g., for TB treatment containing rifampin, change nevirapine to efavirenz).

    – Pregnancy: change from efavirenz (teratogenic).

- Need to change the entire regimen

    – Treatment failure: change to second-line treatment or salvage regimens.

(a). Side effects and toxicity. Patients on ART regimens may develop signs of drug intolerance or toxicity. If this toxicity is linked to a single drug in the regimen, then that drug can be discontinued and replaced with a substitute according to the national protocol. This toxic reaction can constitute a medical emergency (such as severe rash with nevirapine or lactic acidosis) and must be done quickly.

If side effects are not life threatening but are intolerable enough to compromise adherence and if a specific agent cannot be identified, then switching the entire regimen may be appropriate. One of the challenges in rapidly scaling up ART in resource-limited settings and in instituting wide-spread usage of triple fixed-dose combinations as the first-line regimen is the identification of the specific drug in the regimen that is responsible for side effects.

(b). Switching to Second-Line Regimens. Treatment failure is defined as the following:

- *Clinical failure:* By definition, clinical failure is the progression of disease with the development or recurrence of opportunistic infections or malignancy occurring three months or more after the initiation of the therapy. Clinical events that occur within three months or at initiation may result from a strengthening of the immune response to recognize infections that were present before ART (known as the immune reconstitution syndrome).

- *Immunologic failure:* This failure is represented by an inadequate CD4 count increase, or a significant drop from peak CD4 counts, or return to pre-ARV-baseline or lower CD4 counts.

- *Virologic failure:* This is demonstrated by the failure to suppress viral replication to below levels of detection or return of detectable viremia after suppression.

In general, virologic failure occurs initially, followed by a drop in CD4 counts (immunologic failure) and then by disease progression (clinical failure). The ability to detect the different types of failure will depend on lab capacity.

If a patient should switch his or her regimen because of treatment failure, then the switch should be from the original first-line combination to a completely new standardized second-line regimen. The choice will depend on the ARVs included in the first-line treatment, the availability and cost of second-line ARVs, the supply chain implications, and other factors.

Table 6 gives the list of possible second-line regimens according to current WHO recommendations, but it will likely be updated soon.

TABLE 6. ALTERNATIVES FOR SECOND-LINE ART REGIMENS

Regimen	
TDF+ddI+LPV/r	TDF+ddI+LPV/r
ABC+ddI+LPV/r	TDF+ddI+NFV
TDF+ddI+SQV/r	ABC+ddI+NFV
TDF+ABC+LPV/r	

3. Special Populations. Provision of ART also must be considered within the context of special populations, for whom the general guidelines may not be appropriate. These include tuberculosis patients, pediatric patients, and pregnant women.

(a). **Tuberculosis patients.** In areas with high TB prevalence, it is also important to consider the potential for drug interaction, the overlapping toxicities, and the challenges to adherence, which are based on the number of pills that patients need to take for both TB and HIV treatment. The anti-TB drug rifampicin induces liver enzymes that the body uses to break down some anti-HIV drugs. This breakdown results in reduced levels of ARV drugs in the body, which may lead to drug resistance. Therefore, most guidelines have specific recommendations regarding the choice of ARVs and the timing of ART initiation in patients who are starting or are already on TB treatment.

(b). **ARVs in the pediatric population.** In many country programs, pediatric ART provision lags significantly behind the provision of ART to adults. The reasons are many. Diagnosis of HIV in infants and children, especially those under 18 months of age, is difficult (as described earlier). Challenges include having access to appropriate testing, ensuring that all exposed infants are tested, and overcoming stigma and fear among parents and other care providers through education and community outreach.

In addition, for children who present with illness, the mother may be reluctant to test her infant or child if she has not addressed her own HIV status.

Other factors—besides diagnosis—that have resulted in limited treatment for children include the cost and lack of availability of pediatric ART formulations, as well as the inadequate numbers of trained providers who can prescribe, manage, and support children with HIV and their families. The lack of fixed-dose combinations (FDCs) is also an obstacle for good treatment adherence, as well as supply chain and storage implications of liquid formulations. A major challenge for supply chain managers is to estimate changing needs as children grow. Pediatric treatment includes the need to redose children frequently as they gain weight, as well as the need for multiple formulations as children become able to swallow pills and so are changed away from the more-expensive and more-difficult liquids.

WHO has also developed guidelines on when to start treatment for infants and children. Those guidelines include the clinical criteria for infants and children with confirmed HIV infection:

- WHO stage 4. Treat all children irrespective of CD4.

- WHO stage 3. Treat all children irrespective of CD4. In children >18 months of age, this treatment can be guided by CD4, when available.

- WHO stage 2. Treatment depends on the CD4 count and the percentage of total lymphocyte countCD4/TLC guided.

- WHO stage 1. Treat only if n = meets CD4 count or CD4 percentage criteria.

- Treat all children under 1 year of age.

- The clinician should discuss the risks and benefits of a treatment regimen that involves HIV-infected children and their caregivers, thereby allowing them to make an informed decision regarding initiating therapy. If the potential risks outweigh the benefits, then treatment may need to be deferred.

 (c). **Pregnancy.** A number of ARVs are contraindicated in pregnancy because of teratogenicity or toxicities. Efavirenz should not be used in women who are pregnant or are planning on becoming pregnant because of risks of birth defects. The combined use of DDI and D4T is also not recommended for pregnant women because of higher risks of fatal liver toxicity. Finally, the use of nevirapine as part of multidrug ART to prevent MTCT is not recommended for women who are starting treatment with CD4 cell counts of >250 because of increased risk of liver toxicity.

> **The Scale of the Health Workforce Crisis**
>
> - The World Health Organization estimates that one million more health workers are needed in sub-Saharan Africa to deliver the health Millennium Development Goals.
>
> - In Bangladesh, 40 percent of doctors are absent from large clinics, while the rate rises to 74 percent at smaller health centers that have a single doctor.
>
> - In 2001, Chad had only 205 doctors to treat a population of more than 8 million.
>
> - In Mali, there were only 1,785 nurses and midwives in 2001 for more than 12 million people.

4. **When Second-Line Treatment Fails.** A patient's best chance of good clinical outcomes is when the first-line treatment is successful. A second-line regimen is typically less effective because the virus may have developed resistance to this class of drugs. If the second line of drugs fails, then salvage therapy may have to be considered. Salvage regimens are expensive, and their clinical benefit may be limited. In many resource-limited settings, those regimens are not available. Some data suggest that continuing a failing second-line

regimen may still offer some clinical and survival advantage, but this approach needs to be weighed against toxicity, cost, and overall access to second-line treatments. This area is where research is clearly needed within resource-limited settings to determine appropriate management and to develop cheaper and more-accessible salvage therapy options.

I. PALLIATIVE CARE

Definitions of palliative care have varied over time. Emphasis in the past has focused on care to provide comfort to patients needing what people in the United States term *hospice care*. The U.S.-funded PEPFAR program recently expanded its definition to one that says that palliative care is—

> … patient and family-centered care. It optimizes the quality of life of adults and children living with HIV through the active anticipation, prevention, and treatment of pain, symptoms, and suffering from the onset of HIV diagnosis through death. Palliative care includes and goes beyond the medical management of infectious, neurological, or oncological complications of HIV/AIDS to comprehensively address symptoms and suffering throughout the continuum of illness. The means by which this is achieved will vary according to stage of illness but always with the understanding that quality of life involves clinical, psychological, spiritual, and support care (Office of the Global AIDS Coordinator 2005).

The WHO definition says that "Palliative care is an approach which improves the quality of life of patients and their families facing life-threatening illness, through the prevention, assessment and treatment of pain and other physical, psychosocial and spiritual problems" (WHO 2006a).

The goals of palliative care are to provide support and care that make life comfortable for patients throughout all phases of the disease so they can live as fully and comfortably as possible. The underlying principles include the following:

- management of symptoms

- psychosocial support

- teamwork and partnership

- appropriate ethical considerations

- realistic goals that will sustain hope.

The course of HIV/AIDS is highly variable and unpredictable with a wide range of possible complications, rates of progression, and survival. Some patients remain free of serious symptoms for a long time, while others experience periods of increasing dependency with episodes of acute illness or suffer non-life-threatening complications throughout their illness.

The medical management of people with AIDS is a balance between acute treatment and trying to control symptoms. Most people at the end stage of AIDS suffer from many symptoms, including pain. There is often strict legal control on analgesics such as codeine and other opiates. In many countries, the analgesics can be prescribed only by doctors. A balance is needed between, on the one hand, increasing access to adequate pain relief for people with AIDS and, on the other hand, careful supervision and record keeping of prescription of opiate analgesics.

In some countries, home-based care (HBC) programs use a so-called home care package. These packages contain consumables such as gloves, aprons, disinfectants, painkillers, Nystatin for oral thrush, and Imodium

tablets for diarrhea. Other countries designate a central place where HBC workers can get goods as they need them, according to their clients' household needs; in this way, there is less wastage than in pre-packaging kits of goods that might not be used or might expire. Some country programs occasionally receive donations of the needed supplies.

See appendix 4 for a more detailed list of commodities used for provision of palliative care.
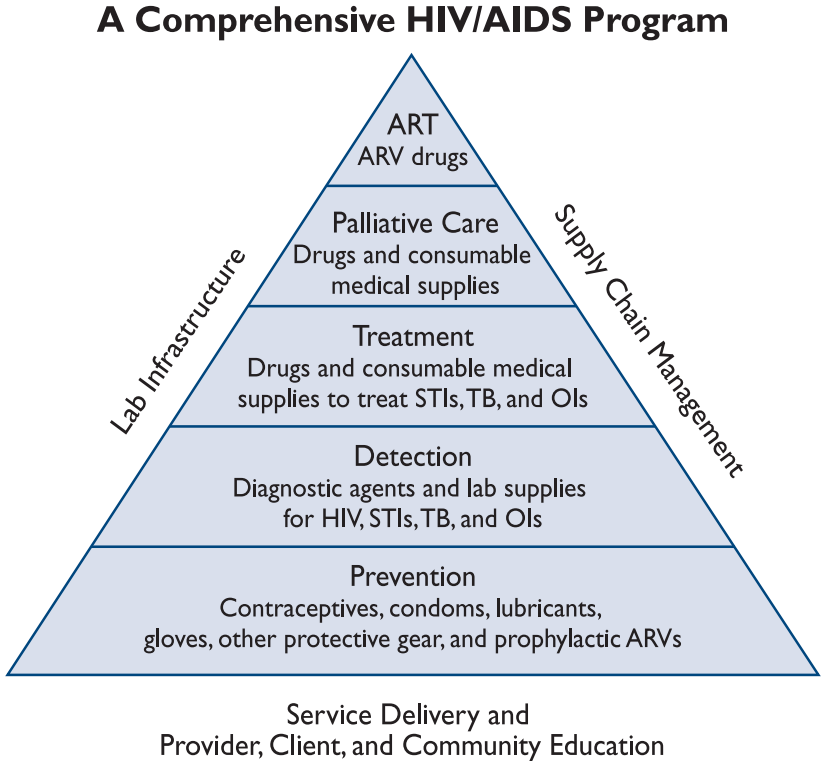
3. HIV/AIDS SERVICE DELIVERY: CRITICAL ELEMENTS AND CHALLENGES

The pyramid in figure 2 presents another framework for depicting the continuum of care and the need for comprehensive services within HIV/AIDS programs. Specifically, it illustrates the types of commodities needed to support HIV/AIDS prevention, care, and treatment services. The pyramid does not imply that one category is more important than another; rather, it reflects loosely the order in which the various commodities have been made available. It, in turn, follows the order in which HIV/AIDS programs historically have been implemented. The pyramid starts at the base with condoms and other products for prevention, followed by test kits for HIV testing and drugs for treatment of STIs, PMTCT, and palliative care, and finally ending with the antiretrovirals that are needed for the widespread scale-up of ART. For each category, there are associated human resource requirements and needs for laboratory reagents and consumables. An effective national program needs all of those types of commodities. Each constituent program—whether it be treatment, care, or prevention—will not need them all, but will need, at the very least, to be able to refer clients to where those clients can obtain them. The package is simply illustrative; it would be impossible to note exactly all of the commodities needed.

Figure 2. A Comprehensive HIV/AIDS Program

A Comprehensive HIV/AIDS Program

ART
ARV drugs

Palliative Care
Drugs and consumable
medical supplies

Treatment
Drugs and consumable medical
supplies to treat STIs, TB, and OIs

Detection
Diagnostic agents and lab supplies
for HIV, STIs, TB, and OIs

Prevention
Contraceptives, condoms, lubricants,
gloves, other protective gear, and prophylactic ARVs

Lab Infrastructure

Supply Chain Management

Service Delivery and
Provider, Client, and Community Education

Currently, three main challenges are common to HIV/AIDS programs in resource-poor settings, regardless of the nature of the epidemic: human resources, infrastructure, and resources.

The first major challenge, *the human resource crisis*, is a global issue in many resource-constrained countries and is not a new challenge. A shortage of trained medical personnel is a chronic problem that is worsened by civil conflict, failing economies, poor wages, difficult working situations, and HIV/AIDS itself. The risk is that—in high-prevalence countries—the presence of a growing AIDS epidemic makes the situation worse by requiring increased work from health personnel, who might themselves be infected or who might have family members at home for whom they must care in their after-work hours. Health care workers often are responsible for stigmatizing patients with HIV/AIDS, making it harder for the patients to disclose their HIV status and to get the care and treatment they need. In addition, care for the caregiver is a critical need for those working in HIV/AIDS service delivery.

In low-prevalence settings, there is often no shortage of medical personnel, but there is a reluctance on their part to provide HIV/AIDS services. Although some Eastern European countries have more medical doctors per population size than are really required, the personnel needed to provide care and treatment for HIV/AIDS patients are inadequate for the demand. As discussed already, these settings consider HIV/AIDS a disease of marginalized groups. As a result, few health personnel are educated on the basic principles of HIV/AIDS prevention, care, and treatment. Some countries even have "special doctors" who do C-sections on HIV-positive women, and those who perform the C-sections get paid extra for their work.

A second major challenge in delivering HIV/AIDS services is the *lack of an adequate health infrastructure.* In some settings, the issue is as basic as a non-existent water supply. In others, those supporting the setting up of HIV counseling and testing sites have found it necessary to provide for the renovation of rooms that provide privacy for counseling sessions. Laboratory infrastructure is a key issue. Ideally, people starting on ART would have a CD4 count to assess the status of their immune system and to determine the need for ART. A viral load is a commonly ordered test in developed countries, but it is often unavailable in all but the most-sophisticated referral hospitals in the most resource-constrained settings. There is a huge challenge to keep delivery of ART up to the standards when the necessary infrastructure is absent.

The third challenge is *financial resources.* Although recently in much greater supply, funds are often channeled and managed in ways that make it difficult to launch and sustain programs that must provide lifelong treatment to people living with HIV/AIDS. Very often, funds are not flowing in as a budget line item but are coming as a one-time donation, or as a three- to five-year program, or as a part of the country's recurrent rather than development budget. ART delivery requires an uninterrupted drug supply; sustainability of long-term funding for ARVs is at the core of any functioning ART program.

4. THE IMPORTANCE OF SUPPLY CHAIN MANAGEMENT FOR HIV/ AIDS PROGRAMS

In addition to the challenges of human resources, infrastructure, and funding, supply chain management is a critical aspect of HIV/AIDS service delivery that can "make or break" a national program. Policymakers and program managers have realized that implementing effective supply chain strategies can play an important role in minimizing challenges associated with HIV/AIDS program and ART scale-up, including:

- Risk of emerging drug resistance among patients, due to supply interruptions or procurement of poor-quality drugs. Once there is drug resistance and the resistant virus is transmitted within a population, the long-term durability of the affordable first-line drug regimens is lost.

- Leakage of ARV drugs from the public sector into the private sector or to other countries, thus disrupting pricing patterns, impacting forecasting and donor support and, again, increasing the likelihood of drug resistance among patients, if prescribed or used improperly.

- Increased expense to programs that already lack sufficient funds for buying and delivering drugs for essential health problems.

Therefore, paramount to the long-term success of ART programs is recognition on the part of international and national leaders of the lifelong nature of ART and therefore of the need to sustain a continuous supply of quality drugs and services, or to ensure *commodity security* for ARV drugs. To ensure the uninterrupted availability of all HIV/AIDS commodities at service delivery points for the medium to long term—a condition referred to as commodity security—there must be a functioning supply chain that manages the continuous flow of quality products from manufacturer to port of entry and through the in-country distribution system to the consumers. HIV/AIDS commodity security will exist when every person has reliable access to quality medicines and other essential health products whenever she or he needs them.

A robust supply chain not only delivers products, it also helps program managers determine what types of products are needed, where and when they are needed, and in what quantities they are needed. Unfortunately, competing priorities for scarce funding often result in insufficient financial, human, and technical resources for public health supply chains. Consequently, supply interruptions caused by damage, expiry, poor management, and chronic shortages are common. At this time of unprecedented expansion of HIV/AIDS programs, it is important that commodity security and supply chain issues are addressed early in the planning stages of program implementation and scale up.

PREVALENCE AND TREATMENT OF HIV DISEASE SYMPTOMS

Symptom	Prevalence	Treatment
Pain	52%	Paracetamol
Tiredness	50%	Multivitamins
Sleep disturbance	37%	Diazepam
Mouth sore	33%	Nystatin
Sadness	32%	Counseling
Weight loss	31%	Multivitamin
Nausea	28%	Metoclopramide
Fever	27%	Paracetamol
Cough	27%	Codeine
Depression	24%	Haloperidol
Diarrhea	24%	Imodium
Skin problem	24%	Calamine
Pruritus	23%	Cortisone cream
Respiratory problem	22%	Antibiotics/antitusics
Vomiting	20%	Metoclopramide

Source: Larue et al. 1997.

COMMODITIES NEEDED TO PROVIDE PMTCT SERVICES

COMMODITIES NEEDED TO PROVIDE PMTCT SERVICES WITHIN THE CONTEXT OF A WHO RECOMMENDED SCHEDULE FOR MOTHER AND CHILD CARE

When?	What happens in terms of intervention?	Implications for supply planning
Antenatal visit 1 Between 16 and 34 weeks	• HIV/STD counselling • Promotion of condom use • HIV testing • Syphilis screening • TT Immunisation • Anaemia prophylaxis • Malaria prophylaxis as needed	Ensure access to/ availability of: • Condoms • HIV tests/consumables needed in testing • Syphilis test/consumables needed in testing • Vaccine/ consumables for administration • Iron and folate supplements • Malaria prophylaxis if needed
Antenatal visit 2 Two weeks after the first ante-natal visit, between 18 and 36 weeks	• Syphilis treatment • Confirmation of HIV positive tests • Post-test counselling • Consent for ARV prophylaxis/initiation of treatment for HIV positive women if eligible • HIV positive women referred to support groups and services • Promotion of exclusive breast-feeding to all pregnant women with HIV • Infant feeding counselling for HIV positive mothers	Ensure access to/ availability of: • Antibiotics for STD treatment • HIV tests for confirmation and tie breakers • Consumables needed in testing • ARVs for ART as needed
Antenatal visit 3 34- 36 weeks	• Initiation of ARV treatment if eligible/prophylaxis if regimen recommended includes a pre-natal component • Counselling and testing of partner	Ensure access to/ availability of: • ARVs for ART as needed • ARVs for PMTCT as needed • HIV tests/consumables needed for testing
Labour/delivery	• Intra-partum ARV component • Avoidance of unnecessary invasive procedures • Universal precautions	Ensure access to/ availability of: • ARVs for PMTCT • Basic midwifery pack
Immediate post-partum	• Support to infant feeding (as per choice of the mother) • BCG, polio 0 • Family planning, promotion of condom use	Ensure access to/ availability of: • Vaccines as per schedule • ARVs for ART as needed

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OVERVIEW OF SELECTED OPPORTUNISTIC INFECTIONS (OIs)

CANDIDIASIS

There are two main types of candidiasis: localized disease (of the mouth and throat, or of the vagina) and systemic disease (of the esophagus, and disseminated disease). The mouth and throat variant (oropharyngeal candidiasis or OPC) is believed to occur at least once in the lifetime of all HIV-infected patients. Occurrence of the vaginal variant is common among healthy, adult women and is unrelated to HIV status.

While OPC is not a cause of death, it causes oral pain and makes swallowing difficult. The main symptom of OPC is creamy white lesions in the mouth that can be scraped away. The symptom of esophageal candidiasis is pain in the chest that increases with swallowing and causes difficulty in swallowing. Disseminated candidiasis causes fever and symptoms in the organs affected by the disease. Localized disease can be treated at first with relatively inexpensive drugs such as nystatin, miconazole or clotrimazole. Systemic candidiasis requires treatment with systemic antifungal agents such as fluconazole, ketoconazole, itraconazole, or amphotericin.

HERPES SIMPLEX AND HERPES ZOSTER

Herpes simplex virus infection (which causes sores around the mouth and genitals) and herpes zoster virus infection ('zonal' herpes or shingles) are not life threatening but can be extremely painful. Both can cause encephalitis, which can be life threatening. Treatment with acyclovir is only marginally effective in herpes zoster but it is sometimes dramatic in HIV-associated herpes simplex with extensive ulceration. This medicine makes the herpes outbreaks last for less time and less intensity, but it does not cure genital herpes.

CRYPTOCOCCOSIS (CRYPTOCOCCAL MENINGITIS)

Cryptococcal infection is caused by a fungus that primarily infects the brain. Systemic mycoses such as cryptococcosis probably cause about 5 percent of all HIV-associated deaths worldwide. Cryptococcosis most often appears as meningitis and occasionally as pulmonary or disseminated disease. Cryptococcal meningitis is the most frequent systemic fungal infection in HIV-infected persons. Without treatment, life expectancy is probably less than a month.

Cryptococcosis is relatively easy to diagnose. However, its treatment (either amphotericin B with or without flucytosine or in mild cases with oral fluconazole) and secondary chemoprophylaxis are often impossible in developing countries because of high cost and limited availability of the drugs required.

TUBERCULOSIS

Tuberculosis is a bacterial infection that primarily infects the lungs. Tuberculosis is the leading HIV-associated opportunistic disease in developing countries. For people who are dually infected with HIV and TB, the risk of developing active tuberculosis is 30-50 fold higher than for people infected with TB alone. And because mycobacterium can spread through the air, the increase in active TB cases among dually infected people means:

- more transmission of the TB germ

- more TB carriers

- more TB in the whole population.

Tuberculosis is harder to diagnose in HIV-positive people than in those who are uninfected. The diagnosis of TB is important because TB progresses faster in HIV-infected people. Also, TB in HIV-positive people is more likely to be fatal if undiagnosed or left untreated. TB occurs earlier in the course of HIV infection than do other opportunistic infections.

A proper combination of anti-TB drugs achieves both prevention and cure:

- Effective treatment quickly makes the individual noncontagious. This prevents further spread of the TB germ.

- The directly observed treatment strategy recommended by WHO treats TB in HIV-infected persons as effectively as it treats those without the virus. A complete cure takes 6 to 8 months and uses a combination of antibiotics. In addition to curing the individual, it also prevents further spread of the disease to others. This is why treating infectious cases of TB has important benefits for society as a whole. Isoniazid preventive therapy is recommended as a health-preserving measure for HIV-infected persons at risk of TB. TB prophylaxis has been shown to increase the survival of HIV-infected persons at risk of TB.

CRYPTOSPORIDIOSIS AND ISOSPORIASIS

Cryptosporidiosis (crypto) and isosporiasis are both caused by parasites. These diseases are easily spread by contaminated food or water, or by direct contact with an infected person or animal. Both crypto and isosporiasis cause diarrhea, nausea, vomiting and stomach cramps. In people with healthy immune systems, these symptoms do not last for more than about a week. However, if the immune system is damaged, symptoms can continue for a long time. Diarrhea can interfere with the absorption of nutrients, and this can lead to serious weight loss.

To confirm diagnosis of either disease, the stool is normally checked for parasites and their eggs. There is no drug treatment that clears up or cures crypto. For isosporiasis, TMP-SMX (trimethoprim-sulfamethoxazole) is the recommended drug of choice.

KAPOSI'S SARCOMA

HIV-associated Kaposi's sarcoma causes dark blue lesions, which can occur in a variety of locations including the skin, mucous membranes, gastrointestinal tract, lungs, or lymph nodes. The lesions usually appear early in the course of HIV infection. Treatment depends on the lesions' symptoms and location. For local lesions, injection therapy with vinblastine has been used with some success. Radiotherapy can also be used, especially in hard-to reach sites such as the inner mouth, eyes, face, and soles of the feet. For severe widespread disease, systemic chemotherapy is the preferred treatment.

LEISHMANIASIS

Leishmaniasis is transmitted by sandflies. The most serious of its four forms is visceral leishmaniasis (VL) (also known as kala azar) which is characterized by irregular bouts of fever, substantial weight loss, swelling of the spleen and liver, and anemia (occasionally serious). Recently, there has been an increase in overlapping of VL and HIV infection. Treatment with pentavalent antimony is relatively expensive, partly because of the cost of the drugs but also because hospital admission is recommended (in milder cases, trained health workers can

administer the injections or infusions at a patient's home). Even with optimal survival time with this co-infection, average survival time is only 12 months.

PCP

Pneumocystis carinii pneumonia (PCP) is caused by a parasite that infects the lungs. PCP is the most frequent HIV-associated opportunistic infection in industrialized countries but appears to be less frequent in Africa. The symptoms are mainly pneumonia along with fever and respiratory symptoms such as dry cough, chest pain, and dyspnea. Definitive diagnosis requires microscopy of bodily tissues or fluids.

Severe cases of PCP are initially treated with trimethoprim-sulfamethoxazole (TMP-SMX) or clindamycin and oral primaquine. Mild cases can be treated with oral TMP-SMX throughout. With both of these regimens, toxicity (notably allergic-type reactions) often requires changes in therapy. Prevention of PCP is strongly recommended for HIV-infected persons with significant immune compromise wherever PCP is a significant health problem for HIV-infected persons, and also after their first episode of PCP. Preventing and treating PCP need not be very expensive: use of non-brand generic products can reduce the cost of drugs for TMP-SMX prophylaxis.

ILLUSTRATIVE LIST OF COMMODITIES FOR PALLIATIVE CARE

Condition	Treatment Drug or Other Commodity
Pain killers	• Aspirin, paracetamol, indomethacin, and ibuprofen • Codeine or dehydrocodeine • Morphine, pethidine, and fentanyl
Diarrhea	• Loperamide or codeine • Oral rehydration solutions
Nausea, vomiting, anorexia, and weight loss	• Prochlorperazine for mild nausea • Metroclopramide for nausea caused by gastrointestinal disturbance • Haloperidol in case of nausea caused by central nervous system (CNS) disorder • Systemic antifungal in case of oral and esophageal candidiasis • Metronidazole in case of gingivitis • 1% gentian violet in case of mouth ulcers
Cough and shortness of breath	• TB treatment • PCP treatment • Antibiotics and fungicides for treatment of bacterial and fungal upper respiratory infections and pneumonia • Treatment for Kaposi's sarcoma, lymphoma, and interstitial pneumonitis • Morphine and codeine for reduction of sense of breathlessness
Anxiety	• Bezodiazepines
Fever	• Paracetamol • Aspirin • Ibuprofen
Skin problems	• Antihistamines or topical steroids • Opioids for severe itching
Brain impairment	• Haloperidol • Chlorpromazine

continued

Condition	Treatment Drug or Other Commodity
Nonmedical items used while nursing people with late stage of AIDS	• Bed pan • Gloves • Household bleach • Cutlery, bed linen • Washing powder • Liquid soap, betadine • Buckets

SECTIONS FROM REVISED WHO CLINICAL STAGING AND IMMUNOLOGICAL CLASSIFICATION OF HIV/AIDS, PLUS CASE DEFINITIONS OF HIV AND RELATED CONDITIONS

TABLE 5.1 WHO CLINICAL CLASSIFICATION OF ESTABLISHED HIV INFECTION

HIV-associated Symptomatology	WHO Clinical Stage
Asymptomatic	1
Mild symptoms	2
Advanced symptoms	3
Severe/very advanced symptoms	4

Source: WHO 2006b.

TABLE 5.2 PROPOSED REVISED WHO CLINICAL STAGING OF HIV/AIDS FOR ADULTS AND ADOLESCENTS WITH CONFIRMED HIV INFECTION

Primary HIV infection
Asymptomatic
Acute retroviral syndrome
Clinical stage 1
Asymptomatic
Persistent generalized lymphadenopathy
Clinical stage 2
Moderate unexplained weight loss (<10% of presumed or measured body weight)
Recurrent respiratory tract infections (sinusitis, tonsillitis, bronchitis, otitis media, pharyngitis)
Herpes zoster
Angular cheilitis
Recurrent oral ulceration
Papular pruritic eruptions
Seborrhoeic dermatitis
Fungal nail infections
Clinical stage 3
Unexplained[7] severe weight loss (>10% of presumed or measured body weight)
Unexplained chronic diarrhoea for longer than one month
Unexplained persistent fever (intermittent or constant for longer than one month)
Persistent Oral candida
Oral hairy leukoplakia
Pulmonary tuberculosis
Severe presumed bacterial infections (e.g. pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia, excluding pneumonia)
Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
Unexplained anaemia (<8 g/dl), neutropenia (<500/mm^3) and or chronic thrombocytopenia (<50 000/ mm^3)
Clinical stage 4
HIV wasting syndrome
Pneumocystis pneumonia
Recurrent severe presumed bacterial pneumonia
Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration or visceral at any site)
Oesophageal candidiasis (or candida of trachea, bronchi or lungs)
Extrapulmonary tuberculosis
Kaposi sarcoma
Cytomegalovirus infection (retinitis or infection of other organs)
Central nervous system toxoplasmosis
HIV encephalopathy
Extrapulmonary cryptococcosis including meningitis
Disseminated non-tuberculous mycobacteria infection
Progressive multifocal leukoencephalopathy
Chronic Cryptosporidiosis
Chronic Isosporiasis
Disseminated mycosis (extrapulmonary histoplasmosis, coccidiomycosis, penicilliosis)
Recurrent septicaemia (including non-typhoidal salmonella)
Lymphoma (cerebral or B cell non-Hodgkin)
Invasive cervical carcinoma
Atypical disseminated leishmaniasis

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[7] Unexplained refers to where the condition is not explained by other conditions.

Source: WHO 2006b.

TABLE 5.3 PROPOSED REVISED WHO CLINICAL STAGING OF HIV/AIDS FOR INFANTS AND

Primary HIV infection
Asymptomatic (intra peri or post partum)
Acute retroviral syndrome
Clinical Stage 1
Asymptomatic
Persistent generalized lymphadenopathy
Clinical Stage 2
Unexplained persistent hepatosplenomegaly
Papular pruritic eruptions
Extensive wart virus infection
Extensive molluscum contagiosum
Recurrent oral ulcerations
Unexplained persistent Parotid enlargement
Lineal gingival erythema
Herpes zoster
Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis)
Fungal nail infections
Clinical Stage 3
Moderate unexplained malnutrition not adequately responding to standard therapy
Unexplained persistent diarrhoea (14 days or more)
Unexplained persistent fever (above 37.5 intermittent or constant, for longer than one month)
Persistent oral candida (after first 6- 8 weeks of life)
Oral hairy leukoplakia
Acute necrotizing ulcerative gingivitis/periodontitis
Lymph node TB
Pulmonary TB
Severe recurrent presumed bacterial pneumonia
Symptomatic lymphoid interstitial pneumonitis
Chronic HIV-associated lung disease including brochiectasis
Unexplained anaemia (<8g/dl), neutropenia (<500/mm^3) or chronic thrombocytopenia (<50 000/ mm^3)
HIV-associated cardiomyopathy or HIV-associated nephropathy
Clinical Stage 4
Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy
Pneumocystis pneumonia
Recurrent severe presumed bacterial infections (e.g. empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)
Chronic herpes simplex infection; (orolabial or cutaneous of more than one month's duration or visceral at any site)
Extrapulmonary tuberculosis
Kaposi sarcoma
Oesophageal candidiasis (or candida of trachea, bronchi or lungs)
Central nervous system toxoplasmosis (after one month of life)
HIV encephalopathy
Cytomegalovirus infection retinitis or CMV infection affecting another organ, with onset at age over 1 month
Extrapulmonary cryptococcosis including meningitis
Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidiomycosis, penicilliosis)
Chronic Cryptosporidiosis
Chronic Isosporiasis
Disseminated non-tuberculous mycobacteria infection
Acquired HIV associated rectal fistula
HIV associated tumours including Cerebral or B cell non-Hodgkin lymphoma
Progressive multifocal leukoencephalopathy

Source: WHO 2006b.

MAJOR POTENTIAL TOXICITIES OF FIRST-LINE ARV REGIMENS AND RECOMMENDED DRUG SUBSTITUTIONS

Regimen	Toxicity	Drug Substitution
d4t/3TC/NVP	• d4t-related neuropathy or pancreatitis • d4t-related lipoatrophy • NVP-related severe hepatotoxicity • NVP-related severe rash (but not life-threatening) • NVP-related life-threatening rash (Stevens-Johnson syndrome)	• Switch d4t ZDV • Switch d4t TDF or ABC[a] • Switch NVP EFV (except in pregnancy) • Switch NVP EFV • Switch NVP PI[b]
ZDV/3TC/NVP	• ZDV-related persistent GI intolerance or severe hematological toxicity • NVP-related severe hepatotoxicity • NVP-related severe rash (but not life-threatening) • NVP-related life-threatening rash (Stevens-Johnson syndrome)	• Switch ZDV d4t • Switch NVP EFV (except in pregnancy; in this situation switch to NFV, LPV/r, or ABC) • Switch NVP EFV • Switch NVP PIb
d4t/3TC/EFV	• d4t-related neuropathy or pancreatitis • d4t-related lipoatrophy • EFV-related persistent CNS toxicity	• Switch d4t ZDV • Switch d4t TDF or ABC[a] • Switch EFV NVP
ZDV/3TC/EFV	• ZDV-related persistent GI intolerance or severe hematological toxicity • EFV-related persistent CNS toxicity	• Switch ZDV d4t • Switch EFV NVP

[a]Switching off d4t typically does not reverse lipoatrophy but may slow its progression. TDF and ABC can be considered as alternatives, but availability is currently limited in resource-constrained settings. In the absence of TDF or ABC availability, ddI or ZDV are additional alternatives to consider.

[b]PI can be LPV/r or SQV/r. IDV/r or NFV can be considered as alternatives (see text).

Source: WHO 2003.

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