WHO AND THE UK's DEPARTMENT FOR INTERNATIONAL DEVELOPMENT

Provision of antiretroviral therapy in resource-limited settings: a review of experience up to August 2003

Prepared by the Health Systems Resource Centre for the UK Department for International Development in collaboration with the World Health Organisation

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Acronyms and abbreviations

3TC	Lamivudine

AAI	Accelerating Access Initiative
ACAHP	African Comprehensive AIDS Partnerships
AIDS	Acquired immunodeficiency syndrome
ANC	Antenatal care
ANRS	Agence Nationale de Recherches sur le SIDA
ART	Antiretroviral therapy
ARV	Antiretroviral
ATP	Ability to pay
CADRE	Centre for AIDS Development, Research and Evaluation
CBO	Community based organisations
CDC	Centers for Disease Control
CIE	Electricity company of Cote d'Ivoire
CoC	Continuum of care
D4T	Stavudine
DAI	Drug Access Initiative
DALY	Disability Adjusted Life Year
ddI	Didanosine
DFID	Department for International Development
DOTS	Directly observed therapy, short course
EDL	Essential drugs list
EPI	Expanded Programme on Immunisation
EFV	Efavirenz
FHI	Family Health International
GAVI	The Global Alliance for Vaccines and Immunization
GFATM	The Global Fund to Fight AIDS, Tuberculosis and Malaria
HAART	Highly active antiretroviral therapy
HAPAC	HIV/AIDS Prevention and Care
HBC	Home-based care
HIPC	Debt initiative for the Heavily Indebted Poor Countries
HIV	Human immunodeficiency virus
HSRC	Health Systems Resource Centre
IDS	Institute of Development Studies
IHN	Integrated health network
IHSD	Institute for Health Sector Development
IHSG	International Health Systems Programme
JCRC	Joint Clinical Research Centre
JSI	John Snow International
KAP	Knowledge, attitude and practice
LIMS	Logistics management information systems
LPV	Lopinavir
M&E	Monitoring and evaluation
MCH	Maternal and child health
MDR	Multi-drug resistant
MEDS	Mission for Essential Drugs and Supplies
MoHP	Ministry of Health and Population
MSF	Médecins Sans Frontières
MTCT	Mother-to-child transmission
NAA	National Aids Authority
NGO	Non-governmental organisation
NNRTI	Non-nucleoside reverse transcriptase inhibitors
NRTI	Nucleoside reverse transcriptase inhibitors
NVP	Nevirapine
OI	Opportunistic infection
PEP	Post-exposure prophylaxis
PI	Protease inhibitors

PLHA	People living with HIV/AIDS
PMTCT	Prevention of mother-to-child transmission
PRSP	Poverty Reduction Strategy Paper
RTV	Ritonavir
TAC	Treatment Action Campaign
TASO	The AIDS Support Organisation
TB	Tuberculosis
TLC	Total lymphocyte count
TRIPS	Trade-related Aspects of Intellectual Property Rights
UNAIDS	Joint United Nations Programme on HIV/AIDS
USAID	US Agency for International Development
US CDC	US Centre for disease control
US NIH	US National Institute for health
VCT	Voluntary counselling and testing
WTP	Willingness to pay
WHO	World Health Organisation
ZDV	Zidovudine

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EXECUTIVE SUMMARY

Introduction

The prospects for expanded access to antiretroviral therapy (ART) in resource-poor settings have greatly improved as a result of global and national efforts to reduce the cost of antiretroviral (ARV) drugs, growing availability of cheaper generics, and increased financing available from the Global Fund to Fight Acquired Immunodeficiency Syndrome (AIDS), Tuberculosis and Malaria (GFATM), private foundations, corporate initiatives, government budgetary resources, and multilateral and bilateral donors. In addition, there is the prospect of additional financing for ARVs through the US Millennium Challenge Account.

The increase in the affordability of, and financing for, ARVs has resulted in a rapid expansion of programmes providing ARVs and of countries planning to introduce or scale up access to ART (Picazo, 2003). Whilst global organisations, such as WHO and the International Human Immunodeficiency Virus (HIV) Treatment Access Coalition, are supporting country efforts to expand access to treatment through a series of regional consultations exploring opportunities for scale up and lessons learned from pilot initiatives (Kapp, 2002), there is a lack of clear evidence-based information to guide policy makers and planners in resource-poor countries.

This background paper aims to increase understanding of the requirements for introducing and scaling up provision of ART as part of comprehensive HIV/AIDS programmes in resource-poor countries. The paper provides an overview of experience and lessons learned with regard to:

- The feasibility of ART in resource-poor settings.
- The different approaches being taken to delivery of ART.
- The issues to be considered in scaling up ART provision.

The review is based on published and unpublished literature, interviews with key informants, web searches and country information. It also draws on a review conducted by the HSRC and JSI for the Government of Kenya in late 2002 (under the DFID supported HAPAC Project managed by the Futures Group) and a review of the impact of HIV on health systems conducted by HSRC and JSI in early 2003.

Feasibility and impact of ART in resource-poor settings

Pilot studies have demonstrated the clinical feasibility and effectiveness of highly active antiretroviral therapy (HAART) in a range of resource-poor settings, including Cameroon, Cote d'Ivoire, India, Kenya, Malawi, Senegal, South Africa and Uganda. There is limited evidence of the feasibility and effectiveness of HAART outside of these small studies.

These pilots have achieved positive outcomes for patients that compare with those found in patients in rich countries, in terms of decrease in viral load, increase in CD4 cell count, decrease in morbidity associated with opportunistic infections (OIs), and similar rates of side effects. Patients have demonstrated good adherence, and there is limited evidence of the development of resistance. Mascoloni (2002) in an article summarising findings presented at the Barcelona Conference, identified factors contributing to effectiveness as careful preparation and counselling of patients prior to starting treatment, training family members to support patients, local government and community support, and recovery from AIDS illnesses, which strengthens patient commitment. Patients on HAART appear to do better than patients on dual

nucleoside therapy. For reasons of cost, providers or patients in some settings opt for cheaper but less optimal 2NNRTI regimens. Dual nucleoside regimens have limited durability and may promote more rapid emergence of drug resistance.

The impact of HAART in reducing mortality in resource poor settings is variable. There are impressive results from Brazil, where universal access to treatment has reduced HIV-related mortality by 50 per cent since 1996, and median survival has increased from 18 to 58 months. Improvements in survival rates have also been reported from Mozambique, South Africa and India. However, in some African studies, mortality has been higher and this is attributed to late stage of presentation for treatment. For example, in the Médecins Sans Frontières (MSF) pilot in Homa Bay, Kenya, the majority of patients enrolled are in WHO stage 4 or have a CD4 count of less than 50 and the mortality rate is 20 per cent.

ART has been shown to reduce the risk of tuberculosis (TB) by as much as 80 per cent. In Brazil, TB incidence of 8.4 per cent was reduced by 80 per cent with HAART. In South Africa, TB incidence was reduced from 17 per cent to 3 per cent in a group of patients with CD4 counts below 200. However, evidence from countries including Thailand, Botswana and South Africa, shows that HAART alone will not prevent a rise in TB cases among people with HIV. In Botswana, even with a well-managed DOTS programme that has achieved 90 per cent treatment completion rates, TB remains the leading cause of death among people with HIV.

Universal provision of ART in Brazil has also had a positive impact on health service expenditure. An estimated 358,000 hospital admissions were avoided between 1996 and 2002, saving $2.2 billion. Private sector companies, such as the Electricity Company of Cote d'Ivoire (CIE), have reported both health benefits and cost savings as a result of providing ART to employees. In the 2 years following the introduction of comprehensive HIV/AIDS care with ART there was a five-fold increase in company-based voluntary counselling and testing (VCT), 94 per cent decrease in absenteeism, 81 per cent decrease in HIV-related hospitalisations, 78 per cent decrease in new AIDS cases, and a 58 per cent decrease in HIV-related mortality. During this period, the company saved $287,000 from reduced absenteeism, $294,000 in health care costs and $194,000 in funeral costs (Eholie S, 2002; Eholie S et al, in French Ministry of Foreign Affairs, 2002). Evidence is also emerging of the positive social and economic impact of ART on households and communities.

There is considerable debate about whether the introduction of HAART could lead to either a significant increase or decrease in the number of new HIV infections, and the overall impact on behaviour and implications for the spread of the epidemic in developing countries remain unclear. It is feasible that use of HAART could increase the spread of HIV, because treatment increases the length of an individual's life and, hence, the period of time during which they can infect others; the availability of ARVs may increase the possibility that infected and uninfected individuals will take greater risks.

However, in Brazil, where the government has continued to support prevention programmes, there has been no reported increase in unsafe behaviour, and a study in Cote d'Ivoire, which compared people who had access to HAART with those who did not, found that unprotected sex was associated with not being on treatment with ARVs, and concluded that fears that access to ART may result in irresponsible sexual behaviour were not supported by the data. The MSF programme in Khayelitsha, South Africa has reported increased uptake of HIV testing and counselling and increased condom use following the introduction of ART.

Approaches to delivery of ART

National plans and strategies

A number of resource-poor countries have national ART programmes, including Brazil, Thailand and Botswana. Others are developing programmes to provide ARVs through the public health system, in response to increasing demand and availability of resources. Analysis by the WHO in November 2002 of over 90 country HIV/AIDS plans found that more than 60 per cent had incorporated ART into their plans or had defined specific ART coverage targets.

Ministries of Health in some countries, such as Mozambique, Malawi and Kenya, have developed national strategic plans for scaling up of ART. Others, such as Uganda, have focused on service delivery and access to ART, rather than on strategic planning. Other countries are reviewing their legal and policy frameworks. An assessment of access to ART in Latin American and Caribbean countries, which reviewed national AIDS programme reports and published studies on access, found that most countries in the region have or are developing laws to ensure better access, although there are still countries without policies or where policies have yet to be implemented (Chequer et al, 2002).

Experience in Malawi and Kenya indicates that setting clear goals and targets supports the identification of priorities for scale-up. Experience in these two countries, and in Mozambique, also highlights the importance of integrating ART programming into national HIV/AIDS strategic plans and review processes led by multisectoral national AIDS councils or committees, and of ensuring that the scale up strategy is consistent and integrated with the existing health system and wider health sector plans.

In a review of national HIV strategic plans in five sub-Saharan African countries, Alban (2002) highlighted a number of weaknesses in national plans and the priority-setting process: budgets are designed for the purposes of resource mobilisation, so priorities are unrealistic in terms of resource allocation; priority setting is not based on cost or cost-effectiveness considerations and, in practice, real priorities are decided by donors; and the balance between prevention and care is often determined arbitrarily. The key issue facing policy makers is not whether to include ART as part of the care package, but determining the balance of resource allocation between prevention and care interventions and between care interventions.

National strategies for ART provision also need to be considered in relation to aid instruments. The Joint United Nations Programme on HIV/AIDS (UNAIDS) recommends that the main strategies in national HIV/AIDS plans are included in poverty reduction strategy papers (PRSP) and documents of the Heavily Indebted Poor Countries (HIPC) initiative, since addressing the epidemic is central to poverty reduction (UNAIDS and World Bank, 2001). However, in practice, PRSPs do not typically identify specific strategies to address HIV/AIDS except where they feature in health plans, and the different aid instruments, international organisations and sectors involved in the response to HIV/AIDS are not always aligned. Global health initiatives, such as the GFATM, have added another dimension, and there is emerging anecdotal evidence that these initiatives are not always well integrated with national pro-poor priority setting, planning and budgeting processes, including sector frameworks, and may as a result distort these processes.

Models of delivery

National governments are working to coordinate a wide range of ARV providers in emerging national programmes. Different providers in different settings are operating under a variety of management, financing, and logistic arrangements and clinical practices. The rapid emergence of these different approaches to ARV provision makes it difficult for policy makers and planners to evaluate coverage, quality of services and equity impact (Picazo, 2003).

A review of the literature indicates that approaches adopted by the public sector in most countries represent one, or a combination of, three 'models': provincial and regional hospital delivery, district level delivery, and community clinic or community-based delivery. Other key ARV providers are the private sector, through company schemes and private health care facilities and physicians, and the non-governmental organisation (NGO) sector, through international, national and local organisations, including mission hospitals and faith-based networks.

Experience indicates that scaling up care and treatment programmes is best achieved through collaboration and coordination between a mix of providers, including the public sector, private medical providers, private companies, NGOs and community-based approaches. Service delivery approaches need to be appropriate to the national context, the health system and the existing mix of providers.

Kenya illustrates how different service delivery approaches can co-exist in one national ART programme. Plans for national public sector scale up follow the provincial or regional hospital model. The Ministry of Health (MoH) is planning a phased expansion of ART provision, establishing treatment centres in regional and selected high-volume district hospitals. These centres will offer comprehensive care and receive patients from multiple entry points, including prevention of mother-to-child transmission (PMTCT), maternal and child health (MCH) and TB programmes, VCT centres, other hospitals and paediatric clinics. The Family Health International ART pilot learning sites in Mombasa, with multiple entry points to care and treatment, follow the district level model, fostering collaboration between public and private health facilities, NGOs and communities. A US Centre for Disease Control (CDC) project, supporting provision of ART to adults living in the Kibera slums of Nairobi, follows the community clinic approach, offering treatment as a component of comprehensive services through a local clinic and community-based organisations. The Mission for Essential Drugs and Supplies (MEDS) is supporting over 40 faith-based hospitals to provide ART. Treatment in Kenya is also available through private physicians, industry and employers.

Public health sector

Most countries, especially in sub-Saharan Africa, are taking a phased approach to the introduction or scale up of ART through the public sector, starting initially with provision through selected provincial or regional hospitals. For example, Botswana, the first African country to offer ART through the public health system, is rolling out the programme through hospitals in 4 sites, including Francistown General Hospital and other major hospitals. Nigeria started a pilot ARV programme in January 2002 through 25 treatment centres based in Federal tertiary hospitals across the country, and scale up will involve expansion of the programme to 100 health institutions. Senegal is scaling up from pilot programmes to a national ART programme, using major hospitals as the entry point for ARVs and district facilities to manage counselling, OIs, PMTCT, patient monitoring, and referral. In Ghana, ARVs will be made available initially through the two main teaching hospitals, Korle-Bu in Accra

and Komfo-Anokye in Kumasi, and the Atua Agormanya government hospital in the Eastern region. The second phase, providing ARVs through all 10 regional hospitals, will start by mid-2004. A similar approach is planned in Benin, Malawi and Tanzania.

Countries taking, or planning to take, a district approach to delivery include Brazil, China, Lesotho, Mozambique, Rwanda, and Zambia. Brazil's national treatment programme delivers care and treatment through a decentralised network of 900 facilities, 208 VCT centres, and 424 AIDS Drug Dispensing Units located in public hospitals or health centres (Vitoria in WHO/UNAIDS, 2003). In Mozambique, ART will be available through integrated health networks (IHNs), which will provide diagnosis, prevention, treatment and care, links to VCT and PMTCT services, day hospitals for specialised HIV/AIDS care and treatment, home based care, and referral to social and clinical services (Republic of Mozambique, 2003). Zambia's MoH announced a programme to provide ART through the district health system to 10,000 adults by the end of 2002 (AIDSMAP, 2002a). In April 2003, China started to provide free ARVs to people in rural provinces who contracted HIV through government-approved blood collection stations, through county, township and village health facilities. Lesotho, with funds from the GFATM, plans to scale up VCT services in all 10 districts, and provide comprehensive care including ARVs to 50 per cent of those who need them over the next 5 years. Rwanda's plans include increasing the availability of ART and treatment for OIs, with the establishment of 3 VCT centres in each of the country's 39 districts and provision of ARVs and OI drugs to 200,000 people living with HIV/AIDS (PLHA), largely through government facilities.

Non-government and community organisations

In some countries, international, national and local NGOs are at the forefront of providing ARV treatment, through small pilot schemes and community programmes.

MSF, for example, is running pilot programmes in 9 countries in Africa, including Cameroon, Malawi, Mozambique and South Africa, and in Asia and Latin America. Other NGOs providing ART in Africa include the AIDS Healthcare Foundation with clinics in South Africa and Uganda, the Joint Clinical Research Centre in Uganda, the Lighthouse Trust in Malawi, and the Pangaea Foundation in Rwanda and South Africa.

The number of ARV patients cared for varies, with some programmes providing ART for as few as 50-60, while others have 300 or more. Almost all have plans to scale up significantly the number of PLHA reached, although the feasibility of this has yet to be tested. In addition, experience has shown that it is essential that national NGOs and community based organisations (CBOs) involved in providing care and support services and, in some cases, prescribing ARVs, are well informed about ART, and receive training and information to enable them to deliver ART and educate communities effectively.

Faith-based networks are also playing an increasing role. Mission hospitals are major providers of health care in many sub-Saharan African countries, and in Kenya, for example, mission hospitals have emerged as one of the main sources of ART, with around 40 hospitals providing ARVs.

Community-based models, including the potential of programmes that already provide comprehensive HIV/AIDS interventions to deliver and follow up ART and the need to develop tools to assess existing infrastructure and capacity, are being considered in some settings (Arbour, 2002). The small ART programme in a poor rural community in Haiti, documented by Farmer (2002), is perhaps the best-known

example of a community approach. This programme provided directly observed therapy (DOT) with HAART to about 60 patients, resulting in dramatic improvements. In Uganda, TASO is working with CDC to develop a pilot model in rural communities.

Private sector

Even in the poorest countries, ART has been available for some time to PLHA with financial resources through the private health sector. Treatment through the private sector is expensive, ranging from $300 a year in Zambia to $130 a month in Tanzania. High prices are not always a guarantee of quality, as doctors may prescribe according to what patients can afford and what is available on the market, rather than on the basis of biomedical considerations.

Whilst one study in Kenya found that private physician prescribing was consistent with international standards, another study, in Uganda, found that drug regimens and the frequency of monitoring varied considerably. Other studies indicate that monotherapy remains common in the private sector and that unreliable drug supply is leading to intermittent treatment or regimen switching. There is also emerging evidence that ARVs are leaking into formal and informal private sector markets. Limited information is available about ART provision by private health care providers and this area requires further investigation, particularly issues related to quality, consistency of care and the risks that inappropriate prescribing and lack of adherence pose for the development of drug resistance.

Determining the extent to which industry and employers are providing ARVs is difficult, mainly due to issues of confidentiality and reluctance on the part of employees to inform their employer of their HIV status because of concerns about the impact on their job security and career prospects. However, a growing number of private companies, mostly large enterprises and multinational, are starting to provide ART to their employees and, in some cases, spouses and children. Multinationals providing ARVs as part of comprehensive HIV/AIDS care programmes include drinks manufacturers and breweries such as Coca-Cola and Heineken, car manufacturers such as Daimler-Chrysler and Ford, and mining companies such as Anglo American. Larger national enterprises in Africa providing ART include mining companies in South Africa and Botswana, and electricity generating companies in South Africa and Cote d'Ivoire.

There is some evidence from Africa of cost saving for companies, although studies suggest that affordability is more important than cost saving in influencing the decision to provide ART. At the same time as some companies are expanding treatment access, there is also a trend among private sector firms in Africa to shift the burden to households and to government, through practices including pre-employment screening and restructuring and reducing employee benefits. Cost sharing models vary: Coca-Cola expects employees to pay 10 per cent of the cost of treatment, whereas the Bank of Uganda expects employees to pay 50 per cent of the cost of ARVs.

Issues in scaling up ART provision

Selection of beneficiaries

Coverage

In December 2002 WHO estimated that fewer than 1 in 18 people in middle and low-income countries estimated to need ART were on treatment, and that nearly two-

thirds of these were in Latin America and the Caribbean. In sub-Saharan Africa, where an estimated 4.1 million people could benefit from treatment, only 50,000 are on ART.

Eligibility criteria

WHO guidelines for resource-poor settings recommend treatment for people diagnosed with AIDS and people with HIV who have a CD4 cell count below 200 or who fulfil the guidelines based on clinical diagnosis when CD4 is not available. However, in countries where programmes only have the capacity to reach a proportion of those who could benefit from treatment, difficult choices need to be made about who receives ART and additional criteria are required to inform this decision-making process. Clear economic and social criteria, in addition to biomedical criteria, are required to determine eligibility for treatment in contexts where ART will not be available initially to all those who could benefit. Communities need to be aware of eligibility criteria and to understand that not everyone with HIV needs or will benefit from immediate treatment.

MSF in South Africa has established clear eligibility criteria for its 3 HIV/AIDS clinics in Khayelitsha (WHO and MSF, 2003). Patients are only considered for ART if they meet biomedical, adherence and social criteria. The latter includes verifying that the patient lives in the geographical catchment area. Measures to determine that patients are from a defined geographical area are important, given concerns that ART programmes may be overwhelmed in the early stages by patients from outside the area. Preference is also given to patients on the basis of their number of dependants, health status, income, and disclosure and activism.

Equity and priority target groups

Scale up of ART programmes should be informed by equity issues. Policy decisions around equity are just starting to emerge in countries currently planning for scale up. Consideration needs to be given to coverage of the poor, of different geographical areas, of rural versus urban populations, and of specific population groups. More attention also needs to be paid to gender, to ensure that clinical or socio-economic criteria do not disproportionately exclude women with HIV who are not pregnant from accessing treatment, and WHO has expressed concerns at the exclusion of children from many ARV access programmes.

Socio-economic criteria for determining which patients receive free or subsidised ARVs need to be carefully defined, to ensure equitable access. Even at subsidised cost, treatment may not be affordable for the poorest. Experience outside of large-scale national programmes indicates that the poor are the least likely to access ART. For example, in the Drug Access Initiative (DAI) in Cote d'Ivoire, despite efforts to ensure equitable access, poorer people were less likely to access treatment than those who were better off. Ethiopia is planning to start provision of generic ARVs at a cost to patients of $40 a month, a price most people will be unable to pay. Similarly, in Mozambique, the cost of triple therapy has been reduced to around $80 a month since late 2002, but this is still twice the average monthly wage in the formal sector. If a cost sharing approach is adopted, questions about the level of charging, means testing and waiver systems will need to be addressed.

Mozambique and Kenya are two countries following an objective of wide geographical coverage to inform their plans for initial scale up. Examples are also emerging of countries targeting key groups. Priorities identified for free or subsidised provision of ART include people who are ill with serious damage to their immune

systems, extension of strategies for PMTCT to include continued treatment of HIV-positive mothers and, where necessary, of their male partners, post-exposure prophylaxis (PEP) for health care workers exposed occupationally and women and children exposed though rape or sexual abuse, treatment for key public sector workers and for those who are unable to pay. In Botswana, patients with TB, HIV positive women and their spouses and infants will be targeted initially (PlusNews, 2002). Similarly, in Zambia, immediate priority will be given to mothers with HIV identified through sites offering PMTCT, their partners and infants born with HIV (AIDSMAP, 2002a). Kenya's proposal to the GFATM explicitly targets pregnant women who are HIV positive, individuals needing post exposure prophylaxis, including victims of sexual assault and health workers exposed at work.

Criteria for inclusion and free access also need to evolve as the situation changes and more PLHA can be covered, for example, as the price of drugs falls or governments mobilise additional resources.

Health systems

Systems strengthening

There is limited information on the impact of HIV/AIDS on the health systems of developing countries. Available evidence suggests that the HIV/AIDS epidemic is increasing demands on already constrained health systems and undermining the capacity of systems to provide services through attrition of health sector workers. Attempts to address the systemic impact of HIV/AIDS remain fragmented, confined to a few countries, and lacking the support of a coherent policy and resource framework. This will become more critical as countries move towards scaling up ART, since effective and efficient provision of ART will require well-functioning health systems.

Scale up of ART provision has the potential to strengthen systems and improve outcomes for non-HIV related conditions, if investment is used to address infrastructure, human resources and logistics weaknesses. A pilot programme in Thailand is reported to have resulted in a stronger HIV/AIDS service system, more commitment from health workers, greater community involvement and a better referral system (Satasit, 2002). Horizons reported that the introduction of PMTCT in a busy clinic in Lusaka, Zambia had a positive effect on services. The Haiti experience (Farmer, 2002) suggests that improving clinical services can boost staff morale. Conversely, without appropriate investment in systems strengthening, ART programmes could weaken health system capacity and have an adverse impact on other disease outcomes.

There is no shortage of literature identifying system-related challenges to scale up. Key challenges identified by Morrison (2002) include the need for substantially more resources to expand health system capacity, strengthening and integrating prevention activities with treatment; and anticipating and mitigating side effects and the emergence of drug resistance. Reviewing the question of whether African health systems are ready to incorporate ARVs, based on the situation in Kenya, Tanzania and Uganda, Kalibala (2001b) identified issues including equity, maintaining clinical standards, affordable monitoring, access for spouses, emergence of resistance, and how to address ill-equipped and under-resourced health systems and underpaid health workers. Nkengasong (2002) cites the cost of drugs and lack of laboratory infrastructure to monitor the therapy as systems factors that contribute to the limited widespread use of ARV drugs.

Systems issues have impacted on the scale up of ART in many resource-poor countries. In Malawi, the process of increasing the number of patients receiving ART will be slow because of the capacity of the health system to cope with the additional workload, including the monthly monitoring of clients and the impact that this will have on services for non-ARV clients (IRINnews, 15th July 2003). Lack of capacity at some state and municipal departments of health is cited as one of the main challenges to the decentralised approach in Brazil (John Snow Brazil, 2001).

Strategies to support health systems to deliver ART programmes are being developed, based on experience and lessons learned. The Clinton Foundation is working in Rwanda, Mozambique, Tanzania, Haiti, Bahamas, Dominican Republic and with the Organisation of Eastern Caribbean States to build capacity for effective programmes through upgrading health and laboratory facilities, training health personnel, and improving management, patient information and drug distribution systems. Kenya has undertaken a preliminary situational analysis of public and private health infrastructure in terms of its capacity to support a national ART programme at all levels. This has included situational assessments of regional and district facilities identified for roll out, to identify needs and gaps and system strengthening requirements.

Integration of services

It is generally accepted that ART needs to be delivered as part of a comprehensive approach to prevention and care services including VCT, PMTCT, diagnosis and treatment of opportunistic infections and other HIV related illnesses, and other prevention, care and social support services (UNAIDS, 2002).

The WHO strategy for chronic disease management (see Annex 2) in resource-poor countries has been suggested as a model for delivering comprehensive services to people infected with HIV. Integration and coordination of services is an important component of this model, for example, expansion of VCT for women could be achieved through integration into existing antenatal care (ANC), family planning and MCH programmes. However, there are few documented examples of programmes that have integrated ART into the continuum of HIV/AIDS prevention and care or that have addressed the integration of chronic disease care into existing health services in developing countries.

Many countries are attempting to introduce ART following principles of integration with other HIV/AIDS prevention and care services and health service provision more generally. Kenya, for example, is committed to integrating ART into the existing health system instead of setting up new parallel structures, but rather than full integration at lower levels of the system, PMTCT, VCT and TB programmes will act as entry points to regional treatment centres.

Others have also considered the potential of VCT and TB programmes as entry points for ART. The Zambia ProTest project (Terris-Prestholt, 2002) has piloted the use of VCT as an entry point for integrated case management and prevention of HIV-related TB, in order to improve collaboration between health services and community organisations. The Haiti Partners in Health programme has argued that the DOTS approach used for TB treatment can equally be applied to ART (Farmer, 2001b). The Start Study in South Africa, where up to two thirds of patients with TB are co-infected with HIV, has been exploring the use of existing TB DOTS programmes as sites for initiation of ART through a pilot study at the Durban Chest Clinic. However, others have argued that the DOTS approach may be less easily adopted for ART, since TB treatment is time limited, whereas ART is life long, disclosure of HIV status has more

significant implications than disclosure of TB status, and many DOTS programmes are weak. There are also concerns about the risks of cross-infection if people with HIV are exposed to infectious TB patients.

Infrastructure

Adequate infrastructure, including clinical care, laboratory and pharmacy facilities, is needed to deliver ART. Limited health service infrastructure has been identified as a major constraint to scaling up ART in many resource-poor countries. In Mozambique, the current infrastructure is inadequate to meet the demands of a large-scale programme, and the 2003 strategic plan for scale up identified areas that require attention including rehabilitation of facilities, acquisition of equipment, and HIV/AIDS laboratory and blood bank services.

There is a lack of clarity about minimum infrastructure for ART delivery and how to cost this, including taking account of efficiencies of scale. Kenya is one of the few countries to conduct a situation assessment of public health facility infrastructure.

Human resources

Shortage of staff is a major constraint to scale up, affecting capacity to absorb new resources, provide quality ART, and meet cumulative demand for chronic care. In many countries, including those with high HIV prevalence rates, the health sector is facing a crisis in human resources. Inability to recruit and retain an effective, well-motivated, appropriately skilled workforce stems from problems including low pay and morale, poor conditions of work and inadequate management. Shortages of staff are exacerbated by migration to the private sector or other countries and HIV/AIDS-related attrition.

China is experiencing difficulties in providing ART because of the shortage of doctors who can administer ARV drugs; there are fewer than 100 doctors with the necessary training and skills, in a country where an estimated 1 million people in rural areas have contracted HIV through unsafe blood collection procedures (Sui, 2003). The Botswana National AIDS Coordinating Agency (NACA) has identified the need for at least 20 additional full-time doctors to enrol, assess and supervise 10,000 new patients, and a report by McKinsey suggested that Botswana would need an additional 330 nurses to support the planned ART programme. The shortage of pharmacists outside the main hospitals is also a problem (Rollnick, 2002). In Kenya, staffing has been identified as a major constraint to scale up (Ministry of Health, 2003). All 13 hospitals visited during an assessment of facility preparedness were found to be operating below required staff levels, with shortfalls in clinical, laboratory, pharmacy and other critical skills. In Ghana, where phased scale up is planned, specialist training for health professionals on ART and treatment of OIs has started, but there are few doctors, nurses and laboratory technicians with the skills required to deliver the latest HIV/AIDS care. In Tanzania, preliminary evaluation of capacity prior to ARV roll out in the public sector found that there were fewer than 100 specialist physicians in the public sector.

Given this background, countries are trying to find innovative ways to cope. Botswana is planning to train and employ 500 lay counsellors. In Malawi, strategies being considered include reducing the frequency of monitoring visits for stable and adherent patients, prescribing of ARVs by district hospitals but collection of drugs and monitoring at satellite health centres using simplified clinical review guidelines, and developing simple but robust record keeping and drug monitoring systems. Strategies being employed elsewhere, for example in Kenya and Uganda, include

reducing dependence on highly trained physicians and training clinical officers to perform more routine functions associated with the provision of ART.

Training is critical, and must be provided for clusters of doctors, nurses and other health workers, to ensure common messages and approaches. The content and length of in-service training curricula is variable. Guidance on appropriate training is limited, although the Forum for Collaborative HIV Research is promoting collaboration and sharing of experience between organisations conducting training programmes for health and laboratory workers in Africa, to identify factors that contribute to effective training.

There is a need to rethink training strategies and methods to ensure that these are responsive and incorporate continuing education, given the rapidly evolving nature of ART, and that training addresses health worker interaction with patients and with communities. Published information about experience of training community and family care providers to support ARV therapy is limited, although WHO has identified several programmes that are beginning to target these groups.

The public sector also needs the technical and institutional capacity to manage as well as deliver ARVs. Studies indicate that improved staff management would potentially result in substantial increases in staff productivity. In relation to HIV/AIDS, increased emphasis on ARV, VCT or PMTCT require not just appropriate technical skills but also management skills in relation to systems, administration, procurement, logistics, delivery and referral as well as effective links between formal and informal sectors. The issue of management is especially pertinent within the broader contexts of decentralisation and health sector reform. Strengthening management capacity to coordinate, supervise and monitor the scaling up process at all levels is critical.

Drugs and supplies

ARV programmes need a regular and timely supply of quality drugs and supplies at competitive prices. This should also include laboratory reagents and related supplies, and drugs for OIs and other HIV related illnesses. The system must be able to buffer against uncertainties in funding and minimise risks of interrupted supplies, since continuous treatment is critical to minimise the development of resistance. A secure supply chain, with no leakage and interruptions, is also essential alongside strict monitoring of inventory levels and secure storage facilities. There is already an illegal market in ARVs in many countries, and leakage of government-provided drugs could exacerbate the risk of inappropriate use of ARVs and development of resistance. Countries planning scale up need to determine how drugs and supplies will be procured and distributed, and to ensure that related policies covering the public and private sectors, regulations to prevent misuse and counterfeiting, and logistics systems are in place.

Experience in a number of countries has identified particular challenges associated with registration and procurement of ARVs. In many countries, the registration process is slow and complex. Challenges associated with procurement include lack of information to inform drug selection, delays, corruption, and import taxes and duties, the latter adding to the cost of ARVs. While many of the ARVs used in Brazil are produced domestically, some of the most expensive drugs are purchased from abroad, and the continuing high cost of these drugs threatens the Brazilian policy of free distribution of drugs. Procurement of reagents can also be problematic. The Joint Clinical Research Center in Uganda has reported difficulties in importing laboratory reagents that are not produced locally (Nanyumba et al, 2002).

The use of generics for triple therapy can significantly reduce costs. Brazil, India, Thailand and China are all manufacturing generic ARVs. Some countries, such as Kenya, are removing legal barriers to the importation of generics. MEDIMOC, a Mozambican pharmaceutical company, plans to import generic ARVs from Brazil and India, and 10 private pharmacies in Maputo and two in Beira have been authorised to sell generic nevirapine and other ARVs. Other countries are investigating the potential for local manufacture. Ethiopia is encouraging the private sector to produce ARVs and, along with South Africa, is receiving technical support to start producing ARVs. Ghana is also discussing technology transfer for local manufacture, and has identified two local manufacturers and signed an agreement with the Thai government for local production of ARVs.

A recent review of care and support programming by USAID-funded implementing agencies (Synergy Project, 2003) included an assessment of challenges in scaling up delivery of ART. Challenges identified by the JSI DELIVER project, which is involved in logistics management of ARVs in several African countries, and the MSH RPM Plus project, which provides technical assistance on health commodity management for an ART initiative in Kenya, include: weak public sector logistics management systems for most essential drugs; poor storage facilities; weak transportation systems; problematic customs processes; diversion of products; inadequate training; lack of information systems; inaccurate quantification and forecasting (Chandani in WHO/USAID, 2003).

An important issue is accurate estimation of drug requirements. In most developing countries, this is based on consumption rather than morbidity data (Hardon and Hodgkin, 2000). With the trend towards decentralisation, it is critical to provide support at district level for planning and informed decision making about drug requirements, in the context of allocation of drug budget for treatment of other health problems. The National AIDS Programme (NAP) in Brazil introduced a computerised system, SICLOM, in 1998, for control of drugs. Each AIDS Drug Dispensing Unit (ADDU) has at least one computer running the system, and data is sent at the end of each day to the NAP in Brasilia. SICLOM registers distribution of ARVs, helps to maintain adequate stocks of drugs at ADDUs and tracks prescriptions.

Key logistics management issues in scale up (Chandani in WHO/UNAIDS, 2003) include: role of public versus private sector; supportive policy and legal environment; harmonised or standardised procurement; quality assurance and control systems; criteria for quantification and forecasting; standard treatment guidelines and inclusion in essential drug lists (EDL); inventory control system; secure transportation and storage; monitoring prescribing patterns, dispensing patterns, stock levels. JSI DELIVER's lessons learnt with Logistics Management Information Systems (LMIS) indicate that to include ART they need to: be user friendly; have a minimal burden on health workers; be able to provide timely data; be flexible enough to respond to changes in consumption due to patient mobility, regime changes, drug substitution.

Clinical management

Standard guidelines

The WHO 2002 Clinical Guidelines for scaling up ART in resource poor settings have been widely used and have reduced the complexity of treatment and monitoring. Simplified treatment regimens and approaches to monitoring keep down costs and enable more people to access treatment, especially in settings where the personnel and infrastructure required for clinical management and intensive laboratory are not available. Many resource-poor countries are focusing on developing national

guidelines following the WHO approach, and standardised regimens for first and second line treatment and simplified eligibility criteria for initiating ARV therapy and for patient monitoring are being developed at country level.

Ensuring that guidelines are adhered to is a challenge in some settings, especially where there is a range of different service providers. For example, the USAID-funded PHRPlus project, which is working in Zambia and Mexico, noted that some patients are still on mono and dual therapy. Reasons suggested include lack of mechanisms to ensure that national guidelines are enforced, as well as the cost of triple therapy and the low skills and poor training of prescribers.

Alternative treatment regimens

Despite price reductions and standard treatment regimens, HAART remains relatively expensive and complex. The evidence base to support a simplified approach and to develop simplified and cheaper treatment options is being developed.

Colebunders et al (2003), reviewing potential, less costly, alternatives to HAART in resource-poor settings, suggest that structured treatment interruption looks the most promising. One randomised controlled trial found no difference at 36 weeks of treatment in viral load or CD4 count between patients on continuous therapy and patients on 3 weeks on, 3 weeks off treatment. In Thailand, HIV-NAT conducted a study of structured treatment interruption and found that using CD4 cell count to guide the resumption of therapy was just as effective as a 1 week on, 1 week off approach, in terms of preventing clinical illness (Ananworich J et al, 2003). More trials are being conducted to compare HAART with structured treatment interruption. The Development of ART (DART) randomised controlled trial will evaluate structured treatment interruption (3 months on, 3 months off) in Uganda and Zimbabwe (recruitment for 3,000 symptomatic ART-naive adults from 3 sites – 2 in Uganda, 1 in Zimbabwe – started in January 2003), assessing whether structured treatment interruptions can reduce toxicity without compromising efficacy.

Clinical and laboratory monitoring

Monitoring is essential to assess the progress of patients receiving ART. Good quality laboratory facilities with well-trained staff are required to conduct CD4 or viral load testing and basic safety tests for side effects. However, in many resource-poor settings, laboratory services are inadequate. In addition, whilst the price of antiretroviral drugs has fallen, the price of CD4 and viral load tests has not.

Current approaches to support scaled up access to ART in resource-poor settings include strengthening laboratory services, simplifying monitoring, using low-cost alternatives to CD4 tests, negotiating reduced prices of tests and reagents and replacing proprietary agents with cheaper generic alternatives, and developing cheaper new technologies and assays for laboratory monitoring (WHO, 2003).

Some have argued that simplified approaches involving greater reliance on clinical markers, such as weight, and limiting the frequency of CD4 tests to once every 6 months, unless there is serious clinical deterioration, are adequate for individual patient monitoring, and that use of viral load testing should be limited to monitoring for resistance at national referral centres.

New and cheaper technology is being developed. CDC reported in Barcelona (July 2002) that researchers working in Uganda in collaboration with the Ministry of Public Health had found that significantly cheaper CD4 test and viral load monitoring

technology performed effectively and was comparable with standard tests in use (US Department of Health and Human Services, 2002b). Another paper presented at Barcelona reported on a multicentre study in 6 West African countries of the Dynabeads assay, an alternative method of providing CD4 counts. The results were encouraging and the cost per assay is less than US $10. Cytospheres, which have been approved by the US FDA, are easier to use but more expensive at $9 per test, although they only require investment in a light microscope and a haemocytometer. At least 9 studies in Africa have correlated CD4 counts assessed by Cytospheres or Dynabeads with counts measured by flow cytometry. In most, but not all, correlation has been excellent. However, these technologies have some disadvantages. Reading the results is labour intensive and requires trained technicians, so the number that can be done each day is limited. WHO recommends further evaluation of both methods in a multi-centre study before they can be recommended for laboratories in developing countries.

Other technologies under development include affordable, portable CD4 counts using microchips (Rodriguez et al, 2003). Alternative flow cytometry-based methods, and non-flow cytometry-based devices are also in various stages of development (de Wit, 2002). The PanLeucogating (PLG) protocol, a flow cytometry-based system developed by the AffordCD4 Initiative has the potential to reduce the range of reagents used and to improve the accuracy of testing, as well as to reduce the cost. A heat denatured HIV p24 assay is currently being evaluated as an alternative to PCR-based and bDNA-based viral load assays (www.hivforum.org).

Drug resistance

In most countries, resistance testing for individual patients will be difficult to afford and laboratories are not currently equipped to carry out the tests. In such settings, WHO (2002) recommends that consideration be given to using resistance tests as a surveillance tool, for example, to track the acquisition of drug-resistant virus in people who have recently acquired HIV.

The development of drug resistance is commonly cited as a concern with rapid scale up programmes in resource-poor settings. WHO is working with partners to initiate a global HIV drug resistance surveillance programme, which will review prevalence, improve understanding of factors that lead to resistance, and identify strategies to minimise the emergence and spread of drug resistance.

A World Bank meeting in June 2003 concluded that there was no empirical evidence that viral resistance is more of a problem in developing countries than in developed countries, but highlighted concerns about the implications of the current unregulated availability of ARV drugs in developing countries. The meeting concluded that concerns about resistance should not delay scale up, and that the most effective strategy for minimising the development of resistance will be to ensure that distribution of ARVs occurs in the context of practices and procedures that promote rational drug use and encourage patient adherence.

Demand and adherence

Uptake of ART

Making ARVs available is not enough to guarantee access. Uptake of ART, which has been lower than anticipated in some high prevalence settings, is influenced by financial, organisational, physical and social factors.

Many people are not aware of their HIV status, and increasing access to VCT is a vital first step. The availability of treatment with ARVs and for PMTCT has increased uptake of VCT in a range of settings, such as Haiti and South Africa. The Mildmay Centre in Kampala, Uganda conducted a survey to find out why, despite reduced drug prices, uptake of ARVs by patients did not increase. The survey found that limited knowledge and negative attitudes towards ARVs, on the part of health workers and patients, were the main limiting factors. Following efforts to increase health worker knowledge and to use people already taking ARVs to educate others about the therapy, the number of patients increased.

Affordability is a major barrier to accessing treatment in 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 towards the costs of their treatment varies between African countries planning to provide ART. Proposed costs for patients should be based on research on willingness to pay (WTP) or ability to pay (ATP) and assessment of the impact of payment on households. Cost of treatment for OIs may remain an obstacle to access to treatment even for PLHA who receive ART free of charge. Financial contribution of patients to the cost of treatment may also be more problematic where, as in many cases, there is more than one person infected in the household. PLHA covered by private insurance may not request reimbursement because they fear disclosure of their HIV status and discrimination.

Other barriers to access include lack of transport, especially in more remote and rural areas, and stigma and fear of discrimination, which can deter people with HIV from seeking treatment. However, there is also some evidence that the availability of treatment can increase uptake of services, change community perceptions of AIDS and reduce discrimination towards PLHA.

Educating communities about ART, its benefits and limitations, is also an essential step in improving uptake. In the South Africa PMTCT pilots, appointing provincial Community Liaison Officers was an important factor in successful implementation. Education by patients already taking ARVs has also been shown to be an effective strategy, in Uganda for example. Community education is also essential to ensure adherence, dispel unrealistic expectations about ARVs, and avoid increased risk behaviour.

Adherence

Concerns have been raised about whether patients in resource-poor settings will be able to follow the strict treatment regimen required for ART to work effectively, but studies have shown that programmes in resource-poor settings can achieve adherence rates similar to those seen in rich countries (Laurent, 2002; Kityo, 2002). The MSF pilot programme in Khayelitsha, South Africa, for example, has achieved high rates of adherence. Preliminary results from a clinic-based, self-reported evaluation indicate that 89 per cent of patients demonstrate adherence of greater than 95 per cent after 3 months on treatment.

Factors promoting adherence include affordability, patient knowledge, disclosure of status to partners and family, and support, and streamlined regimens that minimise the number of pills patients have to take. Poor clinical management and side effects can adversely affect adherence.

Patients can adhere to strict regimens, provided they receive adequate information and ongoing support. Buddy systems and support groups can play an important role

in treatment compliance. Support from partners, family and community is also crucial. Strategies including ongoing counselling, regular follow-up and home visits, and family involvement have worked well. Programmes that combine all these strategies are most effective. MSF has developed a patient-centred education programme, which combines individual, peer and practical support. And in Brazil, high rates of adherence are attributed to affordability, fixed dose combinations, community participation, involvement of civil society organisations, and support for adherence provided through adherence groups and support houses (Vitoria in WHO/UNAIDS, 2003).

However, more research is required to identify the main barriers to and determinants of adherence, and to identify effective interventions to promote adherence. FHI and Horizons are currently conducting operational research in the pilot project in Mombasa, Kenya to evaluate the effectiveness of community and clinic based approaches to adherence.

Community involvement

A recent WHO and UNAIDS meeting highlighted the need for community preparedness. Experience indicates that uptake and adherence are lower if communities are poorly prepared but, conversely, that working in partnership with PLHA and their families and communities can help to overcome barriers to accessing treatment, especially discrimination and stigma. Planning and budgeting for appropriate training for health providers, and education and capacity building for communities will be critical to the success and sustainability of expanded ART programmes (WHO, 2003).

In Brazil, PLHA groups and other civil society organisations have played a key role in community mobilisation as well as in advocating for the national policy of universal free provision of ARVs. In South Africa, civil society organisations, such as the Treatment Action Campaign, and organisations of PLHA, such as the National Association of People Living with AIDS, have played an important role in educating communities about HIV/AIDS and treatment issues. Preparing communities in this way has been critical for both uptake of, and adherence to, treatment by patients attending the MSF Khayelitsha clinics (WHO and MSF, 2003).

There is growing recognition of the importance of community involvement in deciding who will receive treatment in contexts where ART is not yet available to all, to ensure that decisions are made in a transparent and equitable manner. Programmes in South Africa and Thailand have demonstrated the benefits of involving community members in the selection process.

Affordability and financing

ARV prices

Decreasing drug prices have been a significant factor in enabling governments to provide ART through the public sector. Prices have come down substantially, as a result of increasing competition and availability of generics. As of May 2003, the least expensive brand name combination recommended by WHO for low-income countries cost approximately $675 per person per year and the least expensive generic combination was just under $300 per person per year. Local manufacture and export of generics from Brazil, India and Thailand have made a significant contribution to increased affordability of ARVs in resource-poor countries.

Costing and sustainability

Kumaranayake et al (2002) reports on an economic planning model that costs ARVs and their delivery and strengthening and upgrading of health systems. Applying the model to 83 countries, the author concludes that achieving widespread coverage by 2015 would require additional annual spending of $6.8-9.2 billion for ARV treatment.

Countries with limited public sector budgets and large numbers of PLHA face or anticipate considerable difficulties. ARVs are still expensive, despite price reductions and the increasing availability of generics. Patient contributions in resource-poor settings represent a small proportion of drug costs. Governments will continue to require external aid to provide free or highly subsidised ART. For example, only a few countries of the 19 that have supply agreements in place through the accelerating access initiative (AAI) (Gabon, Barbados, Trinidad and Tobago, Chile, Morocco, Romania) have been able to commit to fully subsidised ARV therapy; the other 13 have been unable to do so due to lack of funds. The Botswana Ministry of Health has indicated that the national ART programme is unlikely to be financially sustainable once Gates and Merck support ends, and is hoping that costs will fall as infection rates decline and fewer people need ARVs (PlusNews, 2002).

However, a recent report (Geffen et al, 2003), which calculated the cost of a publicly funded comprehensive HIV/AIDS response in South Africa, including ARVs and the costs of training and improvement in infrastructure, concluded that this is feasible. By 2015, the most expensive year in the calculation, a package of interventions for prevention, treatment of OIs, and ART would cost 20.3 billion Rand, about 1.74 per cent of GNP. This level of spending would require an increase in public expenditure on health from 3.7 per cent of GNP to 5.4 per cent, with ART representing 99 per cent of this additional cost. There is also potential for the cost of ART to be offset by reductions in cost of treatment of OIs and hospitalisation (South Africa spent $400 million on these in 2001) (National Treasury of the Republic of South Africa, 2001). An analysis of HIV/AIDS expenditure in Senegal to date (Vinard P et al in ANRS, 2003) found that this has not been to the detriment of other health priorities. As a result of the Senegalese Antiretrovirals Access Initiative, the costs of treatment (ARVs, reagents, certain drugs for treatment of OIs) have increased relative to other activities, especially prevention, but have remained below 40 per cent.

Financing mechanisms

Long-term provision of ARVs solely through public sector financing remains an unrealistic scenario in most resource-poor countries, and multi-funding approaches are needed. Many countries introducing ART will need to do so on a cost recovery basis, unless external funding through the GFATM and other sources is identified.

Mugyeni (in French Ministry of Foreign Affairs, 2002) proposes a range of strategies for financing the costs of treatment in resource-poor settings. These include: drug cost reduction (advocacy, negotiation, TRIPS, generic competition, eliminating taxes, procurement strategies, bulk purchase); laboratory monitoring cost reduction (low price alternatives, development of simpler cheaper tests); graduated cost sharing (based on ability to pay) and other out of pocket expenditure (NGO, private); national government exchequer funds; employer treatment schemes; health insurance scheme coverage of ART; social insurance funds; and donor support, including from the GFATM.

Monitoring and evaluation

ART programme M&E

Various authors have identified the need for monitoring and evaluation (M&E) to enable lessons to be learned and applied quickly as countries move from small to large-scale ART programmes. M&E needs to identify programme inefficiencies, obstacles and adverse effects, to address feasibility and cost issues, and to consider ART within comprehensive care. Issues that will require attention in M&E systems, in addition to clinical outcomes, include equity, quality of care, and impact on risk behaviour.

Countries have identified M&E weakness as a constraint to scale up, and a recent WHO/UNAIDS workshop (WHO/UNAIDS, 2003) highlighted the complexity of M&E of ART programmes. The Thai Ministry of Public Health has noted the lack of a standard ART M&E approach that countries can use as a model. Lessons learned from experience to date include the need for simple monitoring systems that are developed step by step and avoid generating an overwhelming amount of data and adding too much to existing workload (Chasombat and Yarnwaidsakul in WHO/UNAIDS, 2003).

Patient monitoring and follow up

The development of integrated systems to track patients, drugs and fees at point of delivery will be essential for scaled up ART programmes. Lessons are being learned from other programmes, such as TB control programmes. For example, MSF is working with the Lighthouse Trust, the national TB programme, and the National AIDS Commission to develop a simple record-keeping system designed for use by health centre staff that will allow a quarterly cohort analysis of ARV clients and enable staff to know at the end of each month if any client has not come to collect their drugs.

Some countries are planning to use traditional paper-based systems, with patient identity or photo cards and health facility registers, to monitor patient drug collection and use, and to follow up patients using community-based workers. Others are exploring the potential to use new technologies, such as patient smart cards and smart card or fingerprint readers, bar-coded drug packaging, and electronic databases to manage patient and drug monitoring. In Brazil, for example, most patients now receive a magnetic card, which must be presented to receive treatment and which helps to track prescriptions. Some countries are considering the potential of computer technology and fixed and mobile telephone-based linkages to provide an efficient and effective system for delivering data from facility-based clinical notes and patient registers to and from central monitoring points.

REVIEW OF EXPERIENCE

1. FEASIBILITY OF ART IN RESOURCE-POOR SETTINGS

1.1 Pilot programmes

Pilot programmes, a selection of which are discussed below, have demonstrated that provision of ART is feasible and clinically effective in a diverse range of resource-poor settings.

The UNAIDS Drug Access Initiative launched a four-country pilot initiative in November 1997, providing drugs for opportunistic infections (OIs) as well as antiretrovirals (ARVs) through approved centres, to develop models to improve access to drugs to treat HIV and OIs. The initial phase was designed to set up the necessary infrastructure and systems on a small but sustainable scale. Participating countries included Uganda and Cote d'Ivoire.

- The pilot initiative in Uganda started in 1998, involving 5 clinics in Kampala and 6 mid-level centres outside Kampala, and training of 183 physicians and health care workers. 905 PLHA (or 0.1 per cent of all PLHA), all with advanced AIDS, have received ARVs and 58 per cent were alive when the programme was evaluated in March 2000. There was an approximately equal split between those started on dual nucleoside and on triple therapy (HAART). The preliminary report for the first 2 years focused on clinical response to treatment and evaluation of drug resistance. Patients who initially received triple therapy, or who were switched to HAART regimens, demonstrated a continued rise in CD4 count and fall in viral load throughout the follow-up period, indicating that HAART was successfully implemented. Patients on the dual nucleoside (or 2NRTI) regimens also showed improvements, but the durability of these regimens is limited.

- The Cote d'Ivoire pilot started in 1998 and involved 6 treatment centres in Abidjan and training of more than 190 physicians and health care workers. Approximately 650 patients were receiving ARVs, either dual nucleoside or triple therapy, depending on what they could afford. Drug costs were subsidised for patients defined as 'needy' – 23 per cent were unemployed and 40 per cent reported having no income – and 53 per cent of patients started therapy with a subsidy (Cote d'Ivoire, 2000). However, the Ministry of Health noted that socio-economic criteria used to define need differed from one centre to another. After 18 months, compliance was relatively high, with 71 per cent of patients still being treated.

The mid-term evaluation of the pilots in Uganda and Cote d'Ivoire (UNAIDS, 2000a) concluded that the rational use of ARVs is feasible in developing countries. It also concluded that the pilots had increased capacity for care and support of PLHA, increased knowledge of ARVs, improved distribution and stock management of drugs, and improved management of OIs. For example, in Uganda, the DAI facilitated the development of the non-profit company Medical Access Uganda Ltd, which was responsible for procurement, management and distribution of ARVs to participating treatment centres.

The Centre Intégré de Recherche Clinical d'Abidjan, Cote d'Ivoire and McGill University, Montréal, Canada conducted a study to examine whether standard triple combination therapy with Combivir and Indinavir was effective in this West African setting. 20 patients were enrolled from October 1999 to January 2000. The difference in CD4 count and viral load between baseline and the end of the study was

statistically significant ($p < 0.05$). The researchers concluded that triple therapy is effective in an urban, West African setting (Diop, 2001).

In 2000, the Government of Senegal established a pilot scheme, making ARVs available in 3 clinics in the capital, Dakar, to symptomatic patients with CD4 counts below 350 and asymptomatic patients with viral load above 100,000. By June 2000, 75 individuals had been treated. The pilot was extended to December 2001 and included a total of 470 patients. There was high reported compliance (88 per cent), limited resistance, and a universal decrease in viral load and increase in CD4 counts (Sow, 2001). After 39 months of follow up, 5 patients had abandoned the treatment and 20 had died. A review conducted by the National AIDS Control Programme with French partners Agence Nationale de Recherches sur le SIDA (ANRS), Institut de Medecine et d'Epidemiologie Africaine, and Foundation d'Espoir, concluded that this pilot study demonstrated the feasibility of use of ARVs in a resource-poor African context as well as the effectiveness and tolerance of these drugs (Sow, 2002; Vinard et al in ANRS, 2003).

Researchers from the YRG Centre for AIDS Research and Education (YRG CARE), Brown University and University of Madras studied survival times and adverse effects of 287 patients receiving ART between June 1996 and June 2001 in Southern India. Study subjects were divided into 4 groups based on CD4 cell count and initiation of ART. The study showed that ARV therapy in patients with advanced disease is feasible and beneficial even in very poor settings (Kumarasamy, 2002).

Médecins Sans Frontières (MSF) assessed the feasibility of HAART in Cameroon, Kenya, Malawi, South Africa, Thailand, Cambodia and Guatemala. Therapy was provided free of charge to patients who were severely immuno-compromised (CD4 count <200) following adherence consultations, and CD4 count was followed up every 6 months. Of the 743 adults included in the study, 61 (8.2 per cent) died, 18 were lost to follow up (2.4 per cent), and 25 (3.4 per cent) interrupted treatment; high rates of adherence were achieved. MSF concluded that ART was feasible in low-income and middle-income settings (MSF and Epicentre, 2002a).

1.2. Positive and negative impacts of ART

Health and health services

The positive impact of ART on HIV/AIDS-related mortality and morbidity has been reported from both pilot and larger scale programmes. Presentations at the Barcelona AIDS Conference in 2002 suggested that rates of toxic side effects in patients in resource-poor settings such as South Africa and Senegal are similar to those in patients in resource-rich settings (Mascoloni, 2002).

Brazil has the most advanced national treatment programme in the developing world following a presidential decree in November 1996 that access to ARVs be made universally available at no cost through the public health system, and the country produces a significant proportion of ARVs in its own generic pharmaceutical industry. As of 2000, nearly 100,000 out of 530,000 people with HIV infection were receiving ART; by November 2002 this had increased to 115,000. HIV-related mortality has fallen by 50 per cent and median survival time has increased dramatically (from 18 months to 58 months among all patients and 84 months among ARV-naïve patients) since 1996 (Marins J et al, 2003), and an estimated 58,000 new AIDS cases and 90,000 AIDS-related deaths were avoided between 1996 and 2002 (Vitoria in WHO/UNAIDS, 2003).

Patients participating in the MSF pilots demonstrated significant improvements in terms of weight gain, cell count and viral load (MSF and Epicentre, 2002a). At MSF South Africa HIV/AIDS clinics in Khayelitsha, patients receive standardised triple therapy regimens (ZDV, 3TC, and NVP or EFV - NVP is used if the patient is pregnant; EFV is used if the patient is taking TB treatment or has abnormal liver function). A preliminary analysis of patients who started treatment between April 2001 and late 2002 included 255 adults without prior ART. Selected outcomes are summarised in the Table below. In addition to these outcomes, incidence of OIs fell and Health-Related Quality of Life (HRQoL) improved. New cases of TB and oral or oesophageal candidiasis, two of the most frequently observed OIs, decreased by two thirds during the first 12 months of ART compared to the period preceding treatment. At the start of treatment, there were significant differences in HRQoL measures between ART patients and a community sample. After 12 months there were no significant differences between these two populations (WHO and MSF, 2003).

Outcomes in patients attending MSF Khayelitsha HIV/AIDS clinics, South Africa

Outcome	**After 6 months treatment**	**After 12 months treatment**
Mean weight gain (kg)	+6.4	+9.3
Proportion of those tested with undetectable viral load levels (<400 copies/ml) *(50 per cent of patients had prior diagnosis of AIDS on initiating therapy)*	91 per cent	84 per cent
Mean CD4 cell count change for those with serial measurements *(Median cell count at baseline 48. Increases were higher in patients with lower CD4 count at baseline)*	+141/mmm	+221/mmm
Proportion surviving *(All deaths among patients on ART were attributed to AIDS; none were attributed to treatment complications. 75 per cent of deaths occurred before 90 days on treatment, mainly due to late initiation of treatment)*	86 per cent	83 per cent

Source: MSF and WHO, 2003

Factors contributing to the success of the MSF Khayelitsha pilot (Kasper et al, 2003) include:

- Affordable drugs – use of imported generics.
- Community involvement – facilitated by giving treatment at primary care level rather than at a large reference hospital.
- Patient involvement – at political (involvement in TAC, challenging politicians views about feasibility of ART in South Africa), community (involvement in support groups for new patients on ART) and individual (educating themselves about adherence) levels.

Key lessons learned include:

- ART can be used safely and effectively in resource-poor settings and by poor people.
- Managing HIV/AIDS patients on ARVs at primary care level is often easier than managing patients not on ARVs due to reductions in OIs.

- Availability of treatment boosts staff morale, because of the shift from care of the dying to helping patients return to good health.
- Synergy between prevention and treatment – the availability of treatment is an incentive to seek VCT to ascertain HIV status.
- Access to ART encourages patients to stay in the medical system – there have been no losses to follow up, in contrast with general experience in this highly mobile township.

Improvements in survival rates have been reported by YRG CARE in India (see Table below), and in patients receiving generic combination therapy in Mozambique (Gialloretti et al, 2003).

Median survival following ARV treatment in southern India

CD4 levels	Survival with ART	Survival without ART
Less than 200	46 months	27 months
200-350	78 months	55 months

Source: Kumarasamy, 2002.

Some pilot studies, for example in Senegal and Kenya, have reported high mortality rates, attributed to late presentation for ART. In Homa Bay, an area of Kenya with an HIV prevalence rate of around 30 per cent, MSF France started a pilot programme in November 2001 and, as of the end of 2002, had provided free ART to 250 patients. The mortality rate of 20 per cent was high, as most patients presented at an advanced stage of disease (WHO Stage 4 or CD4 cell count <50). In the recently initiated FHI pilot project in Mombasa, Kenya, 5 of the first 15 people enrolled have already died, due to late stage of presentation (van Praag, personal communication, 2003). Late initiation of therapy, usually after diagnosis of an AIDS-defining illness, has been identified as an important issue in Uganda, where researchers also reported that ART was ineffective when patients who could not afford to pay both for treatment for OIs and for ART chose to spend their money on ARVs; a substantial minority died from OIs before significant immune reconstitution could take place.

Relatively little data has been published about the benefits of ART for children. A recent French study concluded that provision of HAART to HIV-positive infants in the first 6 months of life prevents the early onset of HIV disease. By 18 months of age only one HAART-treated infant developed an OI, no cases of encephalopathy were recorded, and none died. In the pre-HAART comparison cohort, 6 per cent of infants developed an OI, 12 per cent developed encephalopathy, and 12 per cent died (Faye, 2003). The Mildmay Centre, an out-patient HIV clinic in Kampala, Uganda, is one of the few developing country programmes reported in the literature to have provided ART for children. Between 1998 and 2001, 51 children accessed ART, paid for by their families. By the end of this period, 29 were still receiving treatment and 3 were known to have died (Moss, 2002).

ART can reduce the risk of TB in people with HIV. In Brazil, TB incidence of 8.4 per cent was reduced by 80 per cent. In South Africa, TB incidence was reduced from 17 per cent to 3 per cent in a group of patients with CD4 counts below 200. However, evidence from countries including Thailand, Botswana and South Africa shows that HAART alone will not prevent a rise in TB cases among people with HIV. In Botswana, for example, with a well-managed DOTS programme that has achieved 90 per cent treatment completion rates, TB remains the leading cause of death among people with HIV.

Universal provision of ART in Brazil has also had a positive impact on expenditure on HIV/AIDS-related hospital and ambulatory treatment and care. An estimated 358,000 hospital admissions were avoided between 1996 and 2002, saving an estimated $2.2 billion (Vitoria in WHO/UNAIDS, 2003). The Ministry of Health, Kenya (2002) suggests that proposed out-patient ART provision may benefit patients with non-HIV health problems who are currently being crowded out of the health system and of hospital care in particular.

Private sector companies, such as the Electricity Company of Cote d'Ivoire (CIE), have reported both health benefits and cost savings as a result of providing ART to employees. In 1999, CIE established an HIV solidarity fund, which expanded the company's existing health care package to include ART for workers with HIV. Between 1995 and 1999 HIV was the leading cause of death for employees. In the 2 years following the introduction of comprehensive HIV/AIDS care with ART there was a five-fold increase in company-based VCT, 94 per cent decrease in absenteeism, 81 per cent decrease in HIV-related hospitalisations, 78 per cent decrease in new AIDS cases, and a 58 per cent decrease in HIV-related mortality. During this period, the HIV solidarity fund contributed $217,000 and the company saved $287,000 from reduced absenteeism, $294,000 in health care costs and $194,000 in funeral costs (Eholie S, 2002; Eholie S et al, in French Ministry of Foreign Affairs, 2002).

The DFID HIV/AIDS Knowledge Programme is working with GlaxoSmithKline to develop and analyse mathematical models of the impact of potential patterns of ARV use in developing countries, looking at the impact on mortality, transmission and drug resistance. The models have focused on the stage at which treatment is used and the targeted use of treatment in high-risk groups.

HIV prevention and behaviour change

There is considerable debate about whether the introduction of HAART could lead to either a significant increase or decrease in the number of new HIV infections. For between 50 per cent and 90 per cent of patients, HAART reduces viral loads to levels that are undetectable, and there is some preliminary evidence indicating that those on HAART will be less likely to transmit the virus to others (Forsythe, 2002). It is also feasible that use of HAART could increase the spread of HIV, because treatment increases the length of an individual's life and therefore increases the period of time during which they can infect others, and the availability of ARVs may increase the possibility that infected and uninfected individuals will take greater risks, thereby increasing the likelihood of new infections. However, the overall impact on behaviour and implications for the spread of the epidemic in developing countries remain unclear (Forsythe, 2002).

In Brazil, AIDS case reporting has increased, indicating that the availability of treatment provides an incentive for people to seek HIV testing (Galvao, 2002). The Brazilian government has continued to support prevention programmes, and there has been no reported increase in unsafe behaviour in Brazil.

The MSF programme in Khayelitsha is one of a range of HIV/AIDS initiatives in Western Cape Province. Government initiatives include expansion of VCT sites and youth-friendly clinics, provision of PEP for rape survivors in government clinics, and expansion of PMTCT programmes in public health facilities. These initiatives, together with the availability of ART in the MSF clinics, have significantly increased the uptake of interventions to prevent HIV transmission such as HIV testing and counselling and condom use. The availability of interventions to reduce MTCT and of ART motivates people to seek testing for HIV, promotes openness and reduces

stigma associated with HIV/AIDS. In Khayelitsha district, uptake of VCT increased from fewer than 1,000 HIV tests in 1998 to more than 12,000 in 2002. A 2002 survey of nine sites, including Khayelitsha in South Africa, found that Khayelitsha residents reported the highest levels of male condom use, willingness to use a female condom, willingness to have an HIV test, and desire to join an AIDS club (CADRE, 2002). The availability of ART has also played an important role in community mobilisation against AIDS, encouraging educational initiatives by HIV-positive people who are open about their status, and improved the efficacy and psychological wellbeing of health workers who are able to offer more than treatment for OIs.

However, education is critical to correct misconceptions about ARVs, in particular the idea that these drugs are a cure for HIV/AIDS, and to promote safe sexual behaviour. In Hong Kong, a survey of 2,720 well-educated employees of 20 different businesses found that 56 per cent believed that ARVs can cure AIDS, 28 per cent thought the drugs could eliminate transmission of HIV, and 8 per cent reported that they took fewer precautions than previously because of their belief in the effectiveness of treatment (Abdullah, 2002).

In Benin, some patients thought that once they were on treatment it was no longer necessary to use condoms with their partner (Sehonou in French Ministry of Foreign Affairs, 2002).

Similarly, in Cote d'Ivoire, of several hundred people receiving ART and who had a regular partner, 64 per cent of men and 96 per cent of women had disclosed their status to their partner. All men reported being sexually active; the percentage reporting unprotected sex was 30 per cent among those who had told their partner of their status and 50 per cent among those who had not (Kabore, 2002). However, another study in Cote d'Ivoire, which compared people who had access to HAART and those who did not, found that unprotected sex was associated with not being on treatment with ARVs, among other factors. The researchers reported that fears that access to ART may result in irresponsible sexual behaviour were not supported by the data (Prudhomme et al, 2002). Programmes that have strong community links appear to have noticeably more positive outcomes.

Social and economic impact of HIV/AIDS

Evidence is emerging of the favourable effect of ARV treatment on households and society at large, especially when programmes involve communities. The introduction of scaled-up ARV-treatment programmes has the potential to help reverse the breakdown of family life in high-prevalence, low-income settings, to mitigate the economic impact of the epidemic, as people become well enough to work again, and to reduce the vulnerability of women and children to situations that increase their risk of HIV infection (WHO, 2003).

2. APPROACHES TO DELIVERY OF ART

2.1 National plans and strategies

Plans for scale up

WHO recommends including ART in national HIV/AIDS prevention and control policies that encompass the entire continuum of care. WHO analysis in November 2002 of over 90 country HIV/AIDS plans found that more than 60 per cent had incorporated ART into their plans or had defined specific ART coverage targets. These targets remain low, amounting to approximately 500,000 people on ART by 2005.

An assessment of access to ART in Latin American and Caribbean countries, which reviewed national AIDS programme reports and published studies on access, found that most countries in the region have or are developing laws to ensure better access, but there are still countries without policies or where policies have yet to be implemented (Chequer et al, 2002).

Almost 80 countries have expressed interest in participating in the Accelerating Access Initiative (AAI), a partnership between the UN and 5 pharmaceutical companies, launched in 2000 to make HIV/AIDS drugs and diagnostics more available and affordable in developing countries. The AAI is advocating for price reductions in line with developing country purchasing power and exploring other avenues for reducing ARV costs, including reducing or eliminating import duties and taxes, encouraging patent holders to grant voluntary licences, and pooled procurement. As of May 2002, 39 countries had developed or were developing care plans of action, and 19 countries (Barbados, Benin, Burkina Faso, Burundi, Cameroon, Chile, Congo, Cote d'Ivoire, Gabon, Honduras, Jamaica, Mali, Morocco, Romania, Rwanda, Senegal, Trinidad and Tobago, Uganda and Ukraine) had used these as a framework for negotiating reduced ARV prices with pharmaceutical companies.

There has been progress in regional procurement approaches, in West Africa through ECOWAS, which aims to expand coverage in the region to 400,000 people by 2005, and in the Caribbean through CARICOM, where 7 countries have achieved price reductions of 50 per cent (www.unaids.org/acc_access/contact_group/May2002). In June 2003, 10 Latin American health ministers signed an agreement with manufacturers of brand-name and generic drugs, which will secure reductions of up to 72 per cent in the price of ARVs and up to 60 per cent in the price of reagents used for HIV diagnosis, and a regional policy that stipulates maximum prices for products in all ten countries (www.itacoalition.org).

A number of countries have already started to provide ART. In recent months, many more have announced plans to introduce or scale up provision of ARVs. For example, Chile, which by 2002 had 2,600 patients on ART, 86 per cent of all people meeting criteria in the national guidelines, recently received a substantial grant from the Global Fund for AIDS, Tuberculosis and Malaria (GFATM), which will enable the country to achieve almost 100 per cent coverage, providing ART to 4,200 patients. Selected country plans are described in more detail in the discussion of public sector approaches in Section 2.2.

WHO is organising a series of regional workshops on scaling up access to care and treatment and, for example, at a recent regional workshop for East and Southern

Africa, 17 countries developed plans outlining the process each country will follow in developing, finalising and implementing national programmes for comprehensive care and treatment. The DFID HIV/AIDS Knowledge Programme is collaborating with WHO in the Gates Foundation Build-up Initiative, which seeks to generate the evidence base for ART programmes as they start up or go to scale.

The increase in the number of countries with plans for large-scale public sector distribution is largely due to the availability of additional resources from the GFATM (see Annex 3) and other sources. Following review of two rounds of proposals, the Global Fund has approved a total of $1.5 billion over 2 years to more than 150 programmes in 92 countries. Among the proposals approved by the GFATM during its first round, 20 countries were awarded funds to expand ART: Argentina, Burundi, Cambodia, Chile, Ghana, Haiti, Honduras, Indonesia, Malawi, Moldova, Morocco, Nigeria, Rwanda, South Africa, Senegal, Thailand, Uganda, Ukraine, Zambia and Zimbabwe. However, this literature review has revealed the difficulties in obtaining a complete picture of the availability of global and national resources and of tracking resource flow and allocation (see Annex 2 for available information about selected funding sources). There has been a lack of coordination between different bodies engaged in tracking (UNAIDS, 2003) and a lack of coordination between major donors in resource allocation, resulting in some countries receiving funding from several sources and other countries receiving little or no external support.

National strategies

Ministries of Health in some countries, such as Mozambique, Malawi and Kenya, have developed national strategic plans for scaling up of ART. Others, such as Uganda, have focused on service delivery and access to ART, rather than on strategic planning.

Over recent months, Mozambique has been developing a Strategic Plan for Scaling-Up HIV/AIDS Care and Treatment with the support of the Clinton Foundation and its partner, Health Alliance International, based at the University of Washington School of Public Health and Community Medicine. The Plan, which sets a target for the number of people receiving HIV care and ART during the next 5 years, builds on and is integrated with the Strategic Plan for the Health Sector, which gives equal priority to HIV/AIDS prevention and treatment (Republic of Mozambique, 2003).

Malawi is developing a National HIV/AIDS Policy, a Strategy Framework, a Management Plan, and a 1-year national work plan. The Management Plan will set out priority programming areas and anticipated achievements for the next 5 years, including institutional arrangements, resource requirements, implementation modalities and performance measurement, and aims to cover the mandates and initiatives of all major implementers, including the public sector, which come under the leadership and coordination of the National AIDS Council. The new central HIV/AIDS unit in the Ministry of Health and Population has responsibility for implementation and delivery of the ART programme.

In 2002, the Ministry of Health in Kenya decided to develop its ART programme in a systematic and consultative way, and will finalise its strategic plan by the end of 2003. Extensive preparatory work has been done to ensure that the scale up strategy is consistent and integrated with the existing health system, including the Essential Health Package and decentralisation process, and that standard setting and quality assurance mechanisms are in line with the wider sector development agenda.

Lessons learned from experience in Malawi and Kenya include the importance of setting clear programme goals and the importance of integrating the development of strategic plans for scale up of ART into wider national AIDS strategic plans and review processes led by multisectoral national AIDS councils or committees.

Defining programme goals clarifies government policy and commitment, provides the basis for resource mobilisation, and supports the identification and setting of priorities for scale-up. Malawi has a programme goal of providing ART to at least 25,000 eligible patients within 5 years of the start of the drug delivery system. Other objectives refer to adherence, increases in survival, impact on economic productivity and number of orphans. Following a successful application to the GFATM and the increasing availability of cheaper generic drugs, there are plans to revise the goal upwards. Kenya plans to "*Progressively deliver effective ART, according to standardised regimes, to people with HIV/AIDS in need of treatment, reaching 20 per cent by 2005 and 50 per cent by 2008, so as to increase quality of life and survival by 10 years, reduce HIV-related hospital admissions by 60 per cent and enhance significantly national prevention efforts".*

In Malawi, the National AIDS Council and Ministry of Health and Population are working to ensure that the objectives and plans for the scale up of ART are fully integrated into the National AIDS Council's overall management and work plans. To promote integration into wider strategic plans and processes, Kenya has established an annual review process – the Joint AIDS Programming Review. The first review, which took place in 2002, assessed progress against the National AIDS Strategic Plan and started to build a prioritised financing framework for HIV/AIDS in Kenya. A treatment and care working group also considered the role of ARVs within the National AIDS Programme, identifying indicators, outputs and resources required.

In a review of national HIV strategic plans in five sub-Saharan African countries, Alban (2002) notes that such plans do not always reflect changes in the wider environment, such as ARV price reductions. The review highlighted the need for policy makers to be aware of current levels of coverage and of the costs and benefits of scaling up provision of ART, as well as a number of weaknesses in national plans and the priority-setting process. These weaknesses include: budgets which are designed for the purposes of resource mobilisation, so priorities are unrealistic in terms of resource allocation; priority setting which is not based on cost or cost-effectiveness considerations meaning that, in practice, real priorities are decided by donors; and the balance between prevention and care which is often determined arbitrarily.

For example, at the time of the Alban review, care constituted 30 per cent of the budget in the Zimbabwe Strategic Framework for a National Response to HIV/AIDS (2001-2005). Half of the care budget is allocated for home-based care and support, and 33 per cent for treatment of OIs; no budget is allocated for ART. In contrast, the Zambia National HIV/AIDS Strategic Framework (2001-2003) allocated 33 per cent of the budget for hospital care and 29 per cent for ART. "*Planners felt that 50 per cent of HIV patients should have access to ART by 2003*", based on the assumption that 30 per cent of all HIV-positive persons could benefit from ART and that 50 per cent of these would have access by 2003.

The appropriate role for ART was assessed as part of the appraisal for the Tanzania MAP in early 2003 (Roedde, 2003). Different ministries have developed plans to combat HIV/AIDS. The Ministry of Health budget for HIV strategies in the health sector alone is $208-236 million for the next 5 years, of which approximately $47 million would be for ARVs.

With regard to the balance between prevention and care in national HIV/AIDS strategies and plans, a review of the cost-effectiveness of HIV/AIDS interventions (Creese et al, 2002) shows that preventive interventions are more cost-effective than care interventions, and that TB care and prophylaxis is more cost-effective than ART, even at very low prices (see Table below). The authors conclude that the opportunity cost of introducing ART in a country with an incomplete prevention agenda is high. Alban notes that, from an 'efficiency' perspective, prevention should receive priority in resource allocation until sufficient resources have been mobilised, but that this is not possible, given the need for health systems to provide care for people who are sick and political pressure on governments to introduce ART. Key issues facing policy makers are not whether or not to include ART as part of the care package, but determining the balance of resource allocation between prevention and care interventions and between care interventions. Finally, it must be realised that access to health care and to medicines are increasingly considered essential human rights (www.unaids.org/en/in+focus/hiv_aids_human_rights/related+publications+.asp) and that efficiency and cost-effectiveness considerations should be but one aspect of decision making.

Cost benefits by disability adjusted life years (DALYS)

Intervention	Cost per DALY gained
PMTCT + HAART	$62-87
TB	$68
Female Condoms (medium risk)	$99
Condoms	$1
VCT	$18-22
HAART in DOTS	$140
Family Planning	$150

Expanding access to ART requires a major organisational effort, even when building on existing infrastructure, but government bureaucracy in many countries is not conducive to new management or organisational structures. Many national programmes appear to have under-estimated the skills and capacity required to coordinate and manage scale up.

National strategies for ART provision also need to be considered in relation to aid instruments, and efforts to mainstream HIV/AIDS into these instruments and to ensure that they improve the response to HIV/AIDS. UNAIDS recommends that the main strategies in national HIV/AIDS plans are included in PRSP and HIPC documents, since addressing the epidemic is central to poverty reduction (UNAIDS and World Bank, 2001). However, in practice, the different aid instruments, international organisations and sectors involved in the response to HIV/AIDS are not always aligned.

HSRC (Walford, 2002), in a review of the health-related content of selected PRSPs and interim-PRSPs, found that whilst some countries identify HIV/AIDS as an important issue in the analysis of poverty trends and issues, PRSPs do not typically identify specific strategies to address HIV/AIDS except where they feature in health plans. Exceptions are Malawi, which explicitly refers to the objective of implementing the HIV/AIDS strategic plan in its policy matrix, and Tanzania, which has an explicit budget allocation for HIV/AIDS. This review did not find any literature relating to the role of ART in PRSPs and other aid instruments.

Global health initiatives, such as the GFATM, have added another dimension. There is emerging anecdotal evidence that these initiatives are not always well integrated with national pro-poor priority setting, planning and budgeting processes, including sector frameworks. Harmonisation of global initiatives with national and sectoral pro-poor and HIV/AIDS strategies is essential to strengthen government capacity and systems and to sustainability.

2.2 Public health sector

Approaches to introducing and scaling up public sector provision of ART vary. A review of country experience and plans indicates that these approaches tend to fall into one of three categories or 'models': provincial or regional hospital delivery, district level delivery, and community clinic or community level delivery. Some countries, such as Malawi, are taking a phased approach, starting with provision at provincial or regional hospitals, with plans to expand coverage to district level over time. Examples of national plans and programmes illustrating each model are given below.

Provincial or regional hospital

In January 2002, Botswana started rolling out a public HIV treatment programme through hospitals in 4 sites, including Francistown General Hospital and other major hospitals. As of April 2003, 6,061 patients were enrolled, 4,643 of whom were on HAART. The government had planned to reach 19,000 people by the end of 2002, and to expand the number of sites in order to cover an additional 20,000 each year in the subsequent 4 years of the programme (Rollnick, 2002). The programme involves a collaborative public-private partnership, the African Comprehensive AIDS Partnerships (ACHAP), between the Government of Botswana, Merck and the Bill and Melinda Gates Foundation. Gates and Merck have dedicated US$50 million each over a 5-year period for ACHAP. Other partners include Boehringer-Ingelheim, which has pledged medication for PMTCT, and Unilever, which is contributing expertise in setting up distribution systems and public communication. The KITSO AIDS Training Programme, a collaborative educational initiative between the Ministry of Health and the Harvard AIDS Institute, funded by ACHAP, is training health care providers in ART; this partnership is also undertaking research on the potential hazards of ARV. In 2000, a $4.9 million grant from Secure the Future, a research initiative of Bristol-Myers Squibb, supported the establishment of the Botswana-Harvard HIV Reference Laboratory.

Public sector provision of ARVs started in 2002 in Kenya, with Kenyatta National Hospital, Moi Teaching and Referral Hospital in Eldoret, and provincial facilities in Mombasa and Nakuru providing services. In 2003, the government embarked on a stepwise expansion of ART to establish 15 regional treatment centres, beginning with provincial and selected high-volume district hospitals. Facilities were chosen on the basis of geographical coverage and HIV prevalence, and their readiness to provide ART was assessed through a situation analysis (see Infrastructure in Section 3.2). These regional treatment centres will follow the Comprehensive Care Centre model developed by Kenyatta National Hospital, offering integrated AIDS care and support services, and will act as referral centres receiving patients from multiple entry points, including hospitals, PMTCT and MCH programmes, VCT centres, TB control programmes, and paediatric clinics. The government is planning to provide laboratory equipment for CD4 testing and seed money for revolving ARV drug funds to these regional treatment centres. GFATM funding is being used for training in all provinces (see Human resources in Section 3.2).

The Nigerian government announced in mid-2001 that it would start providing ARVs to 10,000 adults and 5,000 children, after negotiating an agreement with the Indian manufacturer Cipla for provision of a generic triple combination drug at $350 per patient per year. It was anticipated that patients would be asked to contribute around 20 per cent of the cost. The initial government outlay on drugs will to be funded through a $90 million World Bank loan to support Nigeria's Emergency AIDS Action Plan, and diagnostics and monitoring of treatment response by the Ford Foundation (AIDSMAP, 2001). A pilot ARV programme started in January 2002 through 25 treatment centres based in Federal tertiary hospitals across the country. Scale up will involve expansion of the programme to 100 health institutions.

Senegal is scaling up from pilot programmes to a national ART programme, using major hospitals as the entry point for ARVs and district facilities to manage counselling, OIs, PMTCT, patient monitoring, and referral. At hospital treatment centres, medical committees manage enrolment, medical follow up and PEP, and psychosocial support committees manage adherence support, counselling and PLHA clubs. The HIV/AIDS Division of the Ministry of Health is coordinating the programme, with specific national sub-committees responsible for drugs and reagents, PMTCT, and VCT. As of May 2003, 1,350 patients were on treatment and 5 of the country's 11 regions were involved. The programme will be extended to the remaining regions by the end of 2003, and will cover 7,000 PLHA by 2006 (Toure in WHO/UNAIDS, 2003).

At present, the only public source of ARVs in Ghana is through two FHI-designated district hospitals in Manya Krobo district in the Eastern region (see discussion of district approaches below), the region with the highest prevalence rate in the country, where 100 patients are receiving treatment. The current cost of ART from the private sector is between $200 and $300 a month; the daily minimum salary is about $2 (www.irinnews.org). In July 2003, the Ghanaian government announced that it has ordered ARVs to provide treatment for 2,000 PLHA patients over the next 2 years. The drugs will not be 100 per cent free, but the extent to which the government will subsidise the cost to patients is as yet unclear. In the first phase of the programme, ARVs will be made available through the two main teaching hospitals, Korle-Bu in Accra and Komfo-Anokye in Kumasi, and the Atua Agormanya government hospital in the Eastern region, by the end of 2003. The second phase, providing ARVs through all 10 regional hospitals, will start by mid-2004. Plans for supply at the district hospital level have not been discussed in detail, but the Ministry is envisaging that teaching and regional hospitals will act as co-ordination centres (with full laboratory and ancillary service back-up) and district hospitals will act as collection points for drugs (DFID Ghana, personal communication, 2003).

The Thai Ministry of Public Health aims to support 50,000 on treatment by the end of 2004 through an Access to Care Network (www.itacoalition.org; WHO consultation on scaling up HIV/AIDS care, 12th May 2003), implemented through participating hospitals. Currently, 460 hospitals are providing ART, and approximately 6,500 patients are on treatment through Ministry of Public Health facilities.

In late 2001, a national plan for ARVs had been approved by the government in Tanzania to cover private and public facilities, starting with Muhimbili hospital. Patients are likely to be expected to pay for ARVs, and the government will cover the cost of laboratory monitoring. At the time, ARVs were available through private pharmacies at a cost of $130 per month (Kalibala, 2001b). PharmAccess International recently started a pilot project with the Ministry of Defence in Tanzania,

providing access to HAART through DOT to 100 individuals in two military hospitals in Dar-es-Salaam and Mbeya.

The Benin Initiative on Access to Antiretrovirals (Sehonou in French Ministry of Foreign Affairs, 2002), a collaboration between the Government of Benin, the French International Therapeutic Solidarity Fund and the NGO Action Plus AIDS Health, planned to offer ART to 400 patients over 2 years, starting in November 2001, through 3 sites in the city of Cotonou. Since the beginning of March 2002, 50 patients have started on ART. The programme will be expanded to cover 2,000 patients over 3 years, funded by a $6.42 million grant from the GFATM, and negotiations are underway with producers of generic drugs.

To date in Malawi, ARVs have only been available through the private sector, through the Ministry of Health's Lilongwe Central Hospital and Queen Elizabeth Central Hospital in Blantyre, which have been dispensing the drugs through a cost-sharing scheme, and through MSF, which is providing free ARVs in Thyolo district and at the Chiradzulu district hospital (IRIN news 31st July 2003). Using funds from the GFATM, Malawi is planning a phased approach to public sector provision of ARVs, starting with Lilongwe Central Hospital and the Queen Elizabeth Central Hospital, and then expanding the programme to districts that have the essential package of HIV/AIDS care services in place. ARVs will either be free or provided on a cost-sharing basis. The government is also planning to investigate the potential for using a community-based HAART DOT approach.

Uganda has received GFATM funds to increase the number of districts providing VCT and PMTCT services to 56, and to expand the number of hospitals providing ART to 11. Implementing partners include the Ministry of Health and government health facilities, Rakai District, AIDS NGOs, and the Uganda Protestant Medical Bureau. Uganda has 120,000 people with HIV. In 2002, 10,000 had access to ART, and the government aims to treat 30,000 people by 2005. In July 2003, the government announced that it is working on a policy to provide free ART for all public sector workers, with provision for ARVs included in the 2003-2004 budget (Global Business Coalition on HIV/AIDS, 2003a), and is also reported to be working towards a policy of universal free provision in 2 year's time (www.itacoalition.org). PHRPlus is exploring options for expanding ARV delivery in the public and private sector to help policymakers plan and cost a comprehensive and country-specific programme. Pfizer, Inc is reported to have provided a grant to build, equip and operate a new AIDS prevention, treatment and training centre in Kampala, which will also serve as a regional training centre (www.pfizer.com; www.businessfightsaids.org).

District

Brazil, with the most advanced national treatment programme in the developing world, has taken a decentralised approach to delivery of ARVs. The programme involves 900 facilities providing public alternative care services, 208 VCT centres, and 424 sites called AIDS Drug Dispensing Units (ADDUs) located in public hospitals or health centres. To be eligible to receive treatment, patients must be enrolled at the Unit. Public health doctors issue prescriptions and follow up patients. Brazil also has a network of 66 laboratories with the capacity to perform CD4 cell counts, 78 laboratories that can measure plasma viral load, and 14 that can perform resistance testing (Vitoria in WHO/UNAIDS, 2003).

In Mozambique, the government recently approved plans to provide treatment for PLHA. Initially, ART will be provided in 22 integrated health networks (IHNs) to cover 20,000 patients (www.irinnews.org). Phased roll out will proceed in tandem with

expanding human resource and facility capacity. There will be 129 IHNs by 2007, providing nationwide coverage. The IHNs will provide diagnosis, prevention, treatment and care, linking VCT, PMTCT, day hospitals for specialised HIV/AIDS care and treatment, home based care, and referral to social and clinical services. Day hospitals (DHs) will be the principle sites for coordination and management of all components of the IHNs. Approximately 15 DHs, at least one per province, will act as referral, management support and supervision centres, and these will be supplied with CD4 test equipment. Community and nutritional support, as well as adherence monitoring, will be done in conjunction with NGOs (Republic of Mozambique, 2003).

In August 2002, Zambia's Ministry of Health announced that a programme to provide ART through the district health system to 10,000 adults would begin before the end of the year, funded by a grant from the Global Fund. At present, treatment is only available in the private sector at a cost of around $300 a year. The pilot scheme will begin in 8 sites in Lusaka, Ndola, Livingstone, Kasama, Mukinge and St Francis, using generic ARVs procured in bulk. ART will be part of a package of care including treatment and prophylaxis of OIs, provision of food supplements, treatment information, counselling and access to home care, support groups and income generation programmes (AIDSMAP, 2002a).

Preliminary findings from introduction of ART in district-based comprehensive HIV care services in sub-Saharan Africa suggest such an approach to be both feasible and acceptable (van Praag in French Ministry of Foreign Affairs, 2002).

In China, some hospitals in major cities such as Beijing have the capacity to provide ART, but capacity in rural areas is limited. In April 2003, China started to provide free ARVs to people in rural provinces who contracted HIV through government-approved blood collection stations. While the drugs are free, patients must pay for HIV and other tests before receiving treatment, for laboratory tests during treatment, and for management of side effects. The government sees co-payment as a strategy to reduce the waste of drugs and increase sustainability of treatment. So far, 2,870 people in Henan, 420 in Hubei, 200 in Anhui and 60 in Sichuan provinces have started treatment and a programme has just been launched in Hunan province. Unable to afford the cost of purchasing the latest ARVs from international pharmaceutical companies, the government is using a combination of four patent-expired drugs, manufactured in China (including ZDV, ddI and D4T) and two imported innovator formulation drugs (Efavirenz and ZDV/3TC). However, the patent-expired drugs are less effective and have adverse effects; in one province 327 people are reported to have already dropped out of treatment because of serious side effects (Sui, 2003).

In preparation for the expanded treatment programme, the Chinese Ministry of Health has established a national task force and national guidelines, and plans to set up 100 comprehensive care demonstration sites. Treatment will be provided through county, township and village health facilities. There will be an ARV management steering committee and clinical treatment team at county level, and a treatment cooperation team at village level, which together will manage patient selection, treatment provision, follow up and supervision. Weaknesses identified so far include lack of capacity at county level to handle the number of patients, inadequate medical records, and lack of effective mechanisms to promote and monitor adherence.

Lesotho, with funds from the GFATM, plans to scale up VCT services in all 10 districts, and provide comprehensive care including ARVs to 50 per cent of those who need them over the next 5 years. Currently, the government only covers the cost

of OI treatment for 25 per cent of those who need them, and there is only 1 site offering ARVs, to those who can afford to pay.

Burkina Faso, also with funds from the GFATM, will implement a 4-year programme to provide medical treatment for PLHA, including provision of ARVs. The programme includes progressive access to ARVs of 3,600 patients through increasing the capacity of 2 health centres and expansion to additional treatment centres, and expansion of PMTCT prevention from 3 to 11 districts.

Rwanda's plans include increasing the availability of ART and treatment for OIs, training for health workers, VCT and comprehensive care and support, with the establishment of 3 VCT centres in each of the country's 39 districts and provision of ARVs and OI drugs to 200,000 PLHA, largely through government facilities.

FHI is piloting strengthened HIV care and support with a treatment component, and multiple entry points, at district level in Ghana, Kenya and Rwanda (FHI, 2003). By the end of 2003, 500 patients are expected to be receiving ART in the 3 countries.

- In Kenya, FHI is implementing the pilot ART project in Mombasa, with 3 facilities (Port Reiz District Hospital and the Mkomani Bomu and Changamwe VCT primary health care clinics) referring patients to Coast General Provincial Hospital. This model differs to the national model being followed in Kenya, which focuses on strengthening the capacity of regional treatment centres, in that it is strengthening district and sub-district facilities to manage HIV disease and ART.
- In Rwanda, the initial sites for introducing ART include Kabgayi District Hospital, 8 health centres in the rural district of Kabgayi, and the Biryogo Medical and Social Centre, which is in one of the poorest sections of Kigali.
- In Ghana, the pilot is using two approaches, a district comprehensive model in Manya Krobo and Yilo Krobo districts in the Eastern region, and a modified model in the Korle Bu and Komfo Anokye teaching hospitals.

All the sites offer VCT, PMTCT, referral, and support for adherence, and each pilot is fostering collaboration between district public and private facilities, NGOs and communities, to ensure that patients have access to a continuum of care. Lessons learned from implementing these pilot programmes to date include:

- Introducing care and treatment in resource-poor countries requires collaboration and coordination between NGOs and public agencies.
- Critical areas to address are community preparedness, systems to ensure drug security, proper drug administration by clinicians, and strategies to facilitate patient adherence.
- Drug selection and procurement is a process that must start early in programme planning since it requires data, coordination and approvals from government and private sources, both locally and internationally.
- Programmes must address health care workers' concerns about workload and pay, as well as their fears about HIV/AIDS.
- With proper preparation, it is possible to avoid overwhelming sites with demand for treatment.
- Creativity is required to establish referral linkages and to respond to the PLHA needs for services such as home-based care and psychosocial support.
- Once a site has been established, countries can move more quickly to set up multiple sites. Developing locally feasible standards can support efficient replication and scaled-up access to care.
- Financially strained governments must be convinced that treatment is a worthy investment.

The DART trial in Zimbabwe, which is monitoring the HIV epidemic in the rural population where ARVs will be introduced, is setting up the district ARV treatment programme within Manicaland. This is part of a planned network of cohort studies, which WHO is co-ordinating, with a view to monitoring the introduction of ARVs. The study population includes an open cohort of approximately 10,000 individuals in 12 rural communities with limited access to care, where the relationship between HIV and social, demographic and economic variables will be explored.

Community clinic or community

Community-based models, including the potential of programmes that already provide comprehensive HIV/AIDS interventions to deliver and follow up ART and the need to develop tools to assess existing infrastructure and capacity, are also being considered in some settings (Arbour, 2002). In Uganda, for example, TASO is working with CDC to develop a pilot model in rural communities.

In Nairobi, Kenya, the Slum Doctor Programme achieved good results with a model incorporating ART into a home-based care programme targeting slum dwellers. The programme was instituted to follow up patients discharged from Kenyatta National Hospital. Trainers were trained to educate families about caring for the sick and also acted as treatment educators for patients prescribed OI and ARV drugs. They kept a daily tally of medications taken and recorded side effects, which were reviewed weekly by a doctor. Patient progress was monitored by weight gain, absence of OIs, few admissions, clinical improvement, gained appetite and resumption of work. Drug compliance was 100 per cent. The study concluded that a well-coordinated home-based care programme with the family, community and doctor at the centre and use of simple monitoring techniques can incorporate ARVs with good results even without expensive laboratory back up (Obwogo, 2002).

The Kenyan Ministry of Health, CDC and community-based health and AIDS support organisations are implementing a 2-year programme to deliver ART at community level to 500-1,000 adults in the Kibera slums of Nairobi. ART is one component of a comprehensive service, which also includes social services, HIV prevention counselling, screening and treatment for active TB, preventive therapy for TB, and cotrimoxazole prophylaxis for OIs, provided for PLHA and their families through a local clinic and community-based organisations. A clinical officer at a community-based clinic treats patients, with backup from a trained clinician. Patients needing hospitalisation will be managed by the Mbagathi District Hospital. The original plan included limited cost recovery with a charge of KSh 100 ($1.25) for each consultation visit. However, as it soon became clear that even this small amount was hindering adherence and clinic attendance, the programme changed its approach and now charges a one-off fee as a prerequisite for entry into the programme. Adherence, family planning, and prevention of HIV transmission, are supported through intensive patient education and counselling in the clinic and home visits from trained community health workers. Community-based organisations are sensitising communities and community leaders about the programme and ARVs, and will provide community feedback on changes that need to be made to the programme design. After the programme ends in December 2004, CDC will continue to provide support for AIDS treatment and care, including ART, for participants enrolled during the first 2 years.

The AIDS Healthcare Foundation (AHF) provides financial support for ARV provision through community clinics in South Africa and Uganda. In South Africa, the Ithembalabantu clinic is located in Durban, KwaZulu Natal, and the scheme is funded

in conjunction with the Network of AIDS Communities in South Africa (NetCom SA), an NGO based in Durban. Some 100 PLHA are receiving ARVs. In Uganda, AHF, together with the Uganda Business Coalition, supports the Masaka rural health centre ARV pilot, attached to the Masaka Hospital. Some 53 PLHA are receiving ARVs, at an estimated cost of $740 per patient per year.

Some countries are planning a combination of national, district and community models. For example, Burundi plans to provide ARV drugs, OI drugs and psychosocial support to 2,597 new patients, with support from the GFATM, through Bujumbara national hospital, provincial hospitals and community health centres run by the government and NGOs. GTZ is supporting PMTCT in Kinshasa, DRC, and is reported to be planning to support the government in provision of ARVs in government hospitals and health centres in Bas Congo, and in the development of related national guidelines and training.

The Pangaea Global AIDS Foundation has ARV demonstration schemes in Kigali, Rwanda and in South Africa. The Rwanda scheme, known as the Family HIV Care and Support Project, is a joint initiative with the Ministry of Health, the Office of the First Lady, and the Treatment Research AIDS Centre. Based in the Central Hospital of Kigali, with four participating clinics within Kigali, it provides ARV to HIV-positive pregnant women, their partners, and children. The treatment model pairs community health centres with district hospitals to create HIV treatment capability at the community level, with an HIV-trained Rwandan doctor as the primary provider. The South Africa scheme, implemented in partnership with hospitals, university medical institutions and community clinics, is developing and testing models of HIV treatment and care, including access to ARVs. The provincial sites are in KwaZulu-Natal, Gauteng and Western Cape.

In other countries, it is unclear how expanded access to ART will be delivered. In Mexico, for example, where ART has been available to people with social security insurance and a small number of people without insurance since 1996, the Ministry of Health recently announced that it would fund ART for all uninsured people with AIDS by the end of this year. Up to 177,000 people in Mexico are estimated to have HIV, but the number with AIDS is not known. No details were given about eligibility criteria, drugs to be made available or who will supply them (Associated Press, 2003). PHRPlus with the National Institute of Public Health is conducting a study to estimate the incremental cost of scaling up services. In August 2003, the Ethiopian government announced that it will shortly begin distribution of ARVs, but only to those who can afford to pay. The drugs, which have been imported from India, will sell for around $40 per person per month. Sites for distribution have been identified and around 300 health workers trained to deliver the drugs (www.irinnews.org).

2.3 Non-government and community organisations

In some countries, international, national and local NGOs are at the forefront of providing ARV treatment, through small pilot schemes, community programmes, and networks of faith-based organisations. The number of ARV patients cared for varies, with some programmes providing ART for as few as 50-60, while others have 300 or more. Almost all have plans to scale up significantly the number of PLHA reached. It is essential that these organisations are well informed about ART, and receive training and information to enable them to deliver ARVs and to educate communities effectively (International HIV/AIDS Alliance, 2002).

International NGOs

Medécins sans Frontières (MSF) is running pilot programmes in 9 countries in Africa, Asia and Latin America. The pilots are intended to develop a model of care that can be widely adopted by governments and to demonstrate that ART is feasible in primary health care settings and potentially affordable in resource-poor countries, if prices are reduced to the levels offered by generic producers (MSF and Epicentre, 2002b). MSF pilot countries in Africa include Cameroon, Kenya, Malawi, South Africa and, most recently, Mozambique.

In May 2001, MSF, in collaboration with the provincial government, started to provide ART to people with advanced HIV infection at 3 dedicated HIV/AIDS clinics in Khayelitsha, a township in Western Cape Province, South Africa (WHO and MSF, 2003, Kasper et al, 2003). The clinics offer a comprehensive package of services to PLHA, including counselling, support, prophylaxis, treatment of opportunistic infections, ART and referrals where necessary. Currently, the clinics serve over 3,000 PLHA of whom 300 are on ART. Initially, the staff in each clinic included a doctor, a nurse, and a lay counsellor. With increasing patient load and a shift to a nurse-based service model, the clinic teams have been expanded to include an additional nurse and lay counsellor. Generic drugs, procured from Brazil, and laboratory monitoring are free of charge, and adherence and clinical results have been good. The Khayelitsha clinics also run a PMTCT programme. The number of women seeking testing has tripled since the programme started in late 1999. Almost 12,000 women have been tested for HIV and two-thirds of the 2,000 who have tested positive have received ZDV in the 34th week of pregnancy.

In Malawi, MSF is providing hospital-based treatment for AIDS patients, who make up 70 per cent of admissions, at the Chiradzulu district hospital. In May 2001, MSF started to provide nevirapine to HIV positive mothers and, in August 2001, received permission to extend the care of AIDS patients to include ART. The project is currently providing ARVs to around 300 clients and plans to expand this number in 2003. In 2001, MSF also started planning a pilot PMTCT programme in Zimbabwe using nevirapine.

In Cameroon, where ART was available but at a cost of $3,000-$4,000 a year, MSF started a pilot project in a clinic in the capital city Yaounde in January 2001. The estimated cost was $277 per patient per year, but the annual monitoring cost per patient was $455. Patients are charged a nominal fee. The pilot had 133 patients on ART in 2001 but planned to expand this to 2,500 by the end of 2002. In addition to ART, patients also receive treatment for OIs and psychological support.

In November 2002, MSF announced plans to launch a 5-year pilot programme in collaboration with the Mozambican government to provide free ARVs. The programme would cover 350 people in the capital Maputo and 350 people in the northern province of Tete in the first year, reaching a total of 1,500 people by the end of the second year (www.irinnews.org).

The international NGO, Partners in Health, and its local partner organisation, Zamni Lasante, run a small HIV treatment programme in a poor rural community in Haiti. During 1998-2000, the programme provided directly observed therapy (DOT) with HAART to about 60 patients with advanced HIV disease using the pre-existing tuberculosis control infrastructure. A further 40 patients were enrolled in 2001. DOT-HAART was modelled on successful tuberculosis control efforts. Each patient has an *accompagnateur*, often a community health worker, who observes ingestion of pills, responds to patient and family concerns, and offers moral support. The response to

HAART in the initial cohort of 60 patients was dramatic. Side effects were rare and readily managed, and only 6 patients required a change in drug regimen. The programme has changed community perception of AIDS and reduced stigma. This is reflected in an increasing willingness of patients to discuss their HIV diagnosis openly, a 300 per cent increase in demand for HIV testing within the last 2 years and a reduction in patients' complaints about abuse from their families and community (Farmer, 2001a; 2001b).

Farmer reported at the Barcelona AIDS Conference on 'unanticipated challenges' of scaling up. These included: managing concurrent health problems (including OIs); assessing generic drug quality; assuring uninterrupted drug supply (forecasting demand) and storage; maintenance and servicing of laboratory equipment; second-line regimens for drug-resistant HIV; use of fixed dose combinations of ARVs; training for and monitoring rational use of ARVs; management of scarce resources in settings of extreme poverty; effective integration of traditional healers, including birth attendants; and responding to wider issues such as unemployment, lack of food and clean water (Farmer, 2002).

National NGOs and CBOs

The Lighthouse Trust in Malawi started as a community home-based care group in 1997, adding VCT and some clinical services in 2000. The Trust, which combines charitable funding and government support, works closely with the Ministry of Health and Population and most staff are employees of Lilongwe Central Hospital (LCH). The Trust set up a small ARV clinic in 2000, taking a few clients a week. Initially ZDV/3TC was given, later generic ZDV/3TC, both at relatively high cost (approximately $150 per month per patient), and uptake was slow. In October 2001, Malawi negotiated a deal with Cipla for the generic triple therapy Triomune, which is purchased through Central Medical Stores and sold to clients at approximately $30 a month. The programme moved to the Lighthouse in July 2002.

The Lighthouse and LCH have started 1,500 clients on ARVs since the programme began, most during 2002, and currently has almost 1,000 on treatment. Capacity is limited to 2,000 patients on ARVs. Most clients are monitored monthly, but stable and adherent clients from further away are given a 2-month supply at each visit. Despite relatively low retention in the programme, there is little evidence of clinical failure as yet. Clients appear to be adherent whilst on treatment but often discontinue treatment because of financial constraints. A research programme, led by the University of North Carolina, to examine the clinical efficacy of Triomune in this setting has just started, and this should help to identify any development of resistance. A second research programme, in partnership with the Liverpool School of Tropical Medicine, is exploring community KAP and the effectiveness of patient education, particularly with regard to adherence. Lighthouse has developed and is piloting a 'fast track' review for stable HAART clients. This is a questionnaire-based review, designed to be handled by nursing staff, that will enable the programme to scale up of services and shift a proportion of reviews out to health centres (Boxshall, 2003).

Uganda's Joint Clinical Research Centre (JCRC) started to import generic drugs in 2000 and has become their leading distributor in Uganda. JCRC operates an ARV clinic in Kampala; in July 2002, about 180 patients were on ARVs. The clinic prescribes 3 drugs costing US$92 per month. JCRC has plans for scale up to districts (see Perspectives and Practice Uganda Case Study www.who.int/hiv/prev_care/en/Uganda_E.pdf).

The South Africa Medical Association (SAMA) and the Nelson Mandela Foundation are collaborating to support the Tsepang project, the first large-scale civil society ARV initiative in South Africa, raising funds to set up 2 ARV pilot projects in each of South Africa's 9 provinces to provide treatment to 9,000 patients.

In India, YRG CARE is providing ARVs at cost, as well as providing AZT to antenatal women through a subsidised pharmacy. YRG CARE has been providing home-based care and day-care facilities for PLHA since 1994, and in-patient care since 1995 (www.yrgcare.org). It has so far trained 202 health care workers in 5 states in South India and strengthened service delivery by four NGOs (Satish Kumar, 2002).

The involvement of PLHA organisations in programmes is another approach. A pilot PMTCT project in Burundi is working closely with the PLHA association ANSS. ANSS provides support for voluntary counselling and testing, referring positive women to the PMTCT centre, follow up, and peer exchange sessions. These exchange sessions have helped to resolve family problems, reduce stigma, and identify solutions to other implementation problems (Ndayishimiye, 2002).

Mission hospitals

Mission hospitals are major providers of health care in many sub-Saharan African countries. In Kenya, for example, mission hospitals provide approximately 40 per cent of in-patient beds and have emerged as the widest service providers of ARVs. Service provision started in June 2001, after prices of combination ARVs started to fall. Out of 57 hospitals, 25 were providing ARVs in June 2002, and this had increased to 34 by the end of 2002. However, there is no organised network or coordination of ART activities between these hospitals. Drugs, predominantly WHO pre-qualified generic ARVs from Cipla or Ranbaxy in India, are supplied by the Mission for Essential Drugs and Supplies (MEDS). MEDS requires hospitals to have at least 1 doctor trained in the use of ARVs to act as team leader, to have a developed patient tracking system, to undertake not to resell the drugs, and to not mark up drugs above the agreed price. The increasing use of ARVs in the mission hospital sector in Kenya illustrates that scale up can be achieved through NGO networks with minimum quality assurance built in.

2.4 Private sector

Industry and employer schemes

A growing number of private companies – mostly large enterprises and multinational companies – are starting to provide ART to their employees and, in some cases, spouses and children. Examples of private sector schemes are described below.

The private sector has significant potential for increasing access. A review in Kenya (Phillips, 2002) reported that 15-20 large companies, including Tetrapak, BAT, Coca Cola, Standard Chartered Bank, Serena, Delmonte and EverReady Batteries, are offering ARVs. Two parastatals, Central Bank and Kenya Ports Authority, also have ARV programmes and Kenyatta National Hospital offers free treatment to its employees and immediate spouses. But the review also highlighted difficulties in determining the extent to which companies provide ARVs, because of the issue of confidentiality and workers' concerns about the impact on job security and career prospects of informing employers of their HIV status.

Studies have been undertaken by the Futures group for multinational companies considering ARV treatment in Kenya, Burundi and Thailand, along with a literature

review of reasons why companies decided to make such provision. Affordability appeared to be more important than evidence of direct cost savings to the company (Forsythe et al, 2002), although cost saving is often proposed as the main rationale for introducing free treatment.

A recent review in South Africa, conducted by FutureForesight and the Wits Health Consortium, suggests that poorly managed treatment programmes could be doubling the costs to companies. Factors contributing to higher than necessary costs, in particular productivity losses, include starting treatment when employees are already at an advanced stage of disease as a result of low uptake, poor clinical management and follow up resulting in failure to keep employees healthy and a high proportion of patients failing therapy and developing resistance (www.irinnews.org).

It is also important to note that, while many multinationals are expanding treatment access, there is a trend among private sector firms to shift the burden to households and to government, through practices including pre-employment screening, reductions in employee benefits, restructured employment contracts which render workers ineligible for benefits, outsourcing of low-skilled jobs, selective retrenchment and changes in production technologies. Between 1997 and 1999 in South Africa, for example, two thirds of large employers reduced the level of health care benefits or increased employee contributions (Rosen S and Simon J, 2003).

Multinational companies

Coca-Cola Africa, which has 1,200 employees, has been providing ART as part of a comprehensive workplace HIV/AIDS programme to workers with HIV and their dependants since June 2001. In September 2002, the Coca-Cola Africa Foundation, in partnership with GlaxoSmithKline, PharmAccess International and PSI, announced an expansion of the programme to cover employees (and their spouses and children) of its 40 bottlers in Africa; these employ 60,000 people in 54 African countries. Some countries are further ahead than others. Employees of Namibia Beverages, a Coca-Cola bottling company, for example, began receiving the drugs in October 2002 through the company's medical programme. Given the infrastructure challenges, Coca-Cola anticipated that it would take up to 12 months to fully roll out the programme. The Foundation estimates that the expanded programme will cost $11 million a year, of which 50 per cent will be covered by Coca-Cola, 40 per cent by the bottling companies and 10 per cent by employees. Drugs will be sourced from GlaxoSmithKline. (Global Business Coalition on HIV/AIDS, 2002; Coca-Cola News Release, 2003).

Heineken has had an AIDS prevention programme in the Central African Republic for 10 years. In 2001, the company started introducing ARV treatment in its health services for employees, their partners and children, in partnership with PharmAccess International, Rotterdam Institute of Tropical Diseases, Antwerp Tropical Institute, the Bead Group, the PIA Group, and the Global Business Council. The programme started with pilots in Burundi and Rwanda and is being extended to cover 25 breweries in 9 African countries including Nigeria, Congo, Ghana and Democratic Republic of Congo (Global Business Coalition on HIV/AIDS, 2002). In Rwanda, the beer and soft drink company Bralirwa, one of the few private companies in the country to provide ARVs to employees and close family members, has so far provided treatment for 25 of its 1,138 employees. In Burundi, the pilot programme has so far provided treatment for 20 of its 1,221 employees. While take up of VCT has been lower than expected, the experience has demonstrated that treatment is possible within company health care services, but also illustrates the importance of health staff training and support, secure drug supply, supervision and monitoring the

performance of external referral laboratories, and developing a database to streamline patient follow up (www.heineken.com; www.irinnews.org).

The mining company Anglo-American has two subsidiaries in South Africa. Anglo Gold provides ARVs to workers who do not already qualify for treatment under medical aid schemes. Around 18,000 of the company's 90,000 employees are estimated to be HIV positive. Anglo Gold signed a comprehensive agreement with the labour unions in August 2002, which established a joint working group to consider strategic and implementation issues relating to HIV/AIDS. The cost of treatment to the company is around $165 a month per employee (www.angloamerican.co.uk). Also in August 2002, Anglo American and De Beers announced their intention to facilitate and subsidise provision of ARVs to HIV positive employees (Global Business Coalition on HIV/AIDS, 2002). Subsequently, after negotiations with the South African National Union of Mineworkers, De Beers agreed to revise its policy to provide treatment free of charge to spouses or life partners as well as employees. This will be done through a network of accredited medical practitioners in addition to medical facilities available at the mines, and the programme was due to start in July 2003. One challenge still to be resolved is that provision of ART to employees and spouses or life partners outside of company medical facilities is subject to fringe benefit tax, which would make treatment unaffordable for many of the intended beneficiaries. As an interim measure, De Beers has agreed to pay the tax, but intends to raise the issue with the Department of Finance (Global Business Coalition on HIV/AIDS, 2003b).

Also in South Africa, Daimler-Chrysler has an HIV/AIDS programme, which includes treatment delivered by the company's medical teams in its own clinics. ARV is available to the employee, partners, and children. Corporate funds have been set aside to guarantee access to ARVs to employees above the existing medical scheme (www.daimlerchrysler.com). The Ford Motor Company has established an HIV/AIDS workplace programme at its engine plant in Port Elizabeth and assembly plant in Pretoria using corporate funds. On-site VCT was launched in October 2002 and health insurance benefit was aligned to promote disclosure of AIDS status. HIV-positive employees are provided with additional medical cover under the Aid for AIDS Programme, and enrolled under the disease management programme of the company's medical aid scheme.

Barclays Bank has initiated a pilot VCT programme for bank employees and their families in Botswana but, as yet, has not provided ARVs. Unilever in Cote d'Ivoire, which has 1,404 employees in Abidjan, provides free ARVs and treatment for OIs.

Local companies

Anglovaal Mining in South Africa is implementing VCT, wellness management for HIV-positive workers, and provision of ARVs for PMTCT, rape victims, and employees with occupational exposure starting in 2003 (www.avmin.co.za).
Gold Fields, South Africa's second largest gold producer, announced in April 2002 that it would begin providing ARVs to HIV-positive workers through in-house hospitals and clinics. This is an expansion of the company's initial ART programme, which only covered pregnant women, sexual assault victims, and company health workers with occupational exposure to HIV. Gold Fields has 48,000 workers (30 per cent are estimated to be infected with HIV), of whom 1,000 are at the late stage of AIDS (www.journ-aids.org).

In March 2001, Debswana, a mining company in Botswana, and a partner of De Beers, took a decision to provide ARV treatment to its employees with HIV/AIDS,

after testing revealed that a third of its workforce was HIV positive. The company covers up to 90 per cent of the costs of treatment and monitoring for each infected employee and one qualifying spouse nominated by the employee, but expects the government to provide treatment for other partners and their children. The company also decided to establish a trust fund in 2002 to manage the cost of ARVs and related monitoring, funded out of payroll contributions (www.debswana.com).

ESKOM, the South African electricity company, has set aside funds for treating employees and their families and has also developed protocols for management of HIV infected individuals including 6-monthly CD4 testing, PCP prophylaxis where indicated and TB prophylaxis in those with CD4 counts below 300. In Cote d'Ivoire, as described in Section 1.1, the private electricity company, Compagnie Ivoirienne d' Electricité, started offering ARVs to all employees with a medical indication for this treatment in 1999 (Ehoile, 2002).

In Uganda, there are various examples of private sector initiatives (Kalibala, 2001b). These are reported to cover a total of 10,000 patients (see www.who.int/hiv/pub/prev_care/en/Uganda_E.pdf). For example, employees of the New Vision newspaper are treated at JCRC through the UNAIDS DAI. The costs are shared 50:50 between the company and the patients. The company pays for monitoring viral load and CD4 and treatment of OIs. The Bank of Uganda pays 50 per cent of ARV costs for employees and families with HIV. Patients are treated at JCRC, Mildmay and Nsambya through the UNAIDS DAI. Again, the company pays for viral load and CD4 monitoring and OI treatment (Dr Mugyenyi, personal communication).

In March 2003, Transnet in South Africa reported that it had set aside R500 million for a disease management programme for HIV-positive employees, and is implementing a pilot at Spoornet, one of company's divisions. The programme includes VCT, prevention of MTCT, and ARV and OI treatment. It also assesses employee fitness and considers options for redeployment of employees while they are on treatment to other departments where their workload would be lighter (www.journ-aids.org). Border Technikon, an educational institution in Grahamstown, South Africa, provides free student VCT and triple ARV where necessary, until graduation.

There is growing interest in financing of ARV through pharmaceutical benefit management companies and private insurers. For example, the Aid for AIDS medical aid scheme in South Africa was launched in 1998 by Pharmaceutical Benefit Management, an independent managed health care company. It provides, among other things, ARV treatment for private sector employees, with an annual benefit limit for HIV/AIDS-related medication of R25,000 per family. Under this scheme, drug manufacturers agreed to supply dispensing doctors with ARV drugs at best market prices.

Private health care providers

Despite the large number of people accessing ARVs through the private sector, limited information is available about ART provision through private for profit health care providers, and this is an area that requires further investigation.

Mildmay International, with Medical Access Uganda Limited and GlaxoSmithKline, conducted a survey to identify ARV prescribing by private-for-profit medical facilities in Uganda (Sebulime, 2002). The survey showed that ARV prescribing is common in the private medical sector and that drug regimens and the extent of CD4 and viral

load monitoring vary considerably. As a result of differences in costs, and stock-outs, some patients were using alternative sources of ARVs, including pharmacies and donations from relatives abroad. Cost, in particular affordability for patients, was one of the main factors determining the frequency of laboratory monitoring.

The role of private sector providers was also assessed in Kenya (Macharia, 2002). A review of the charts of 300 patients receiving ARV therapy from 5 physicians in the private sector in Nairobi concluded that ARV prescribing was consistent with international standards. Of patients starting ARV treatment, 53 per cent continued their treatment and 32 per cent were still on treatment after 2 years. Mortality was low. The review concludes that efforts to train more practitioners, develop cheaper monitoring tests and further reduce prices for drugs could increase the number of patients treated in the private sector in Kenya.

Concerns have been raised about quality and consistency of care and changes in regimens, especially if clients on treatment move from provider to provider according to their ability to pay and the availability of drugs (Horizons, 2002), and about inappropriate prescribing resulting in the development of resistance. A recent editorial in the BMJ highlights the risk that inappropriate private prescribing poses for the development of drug resistance (Brugha, 2003), quoting a study in Zimbabwe in 2000 which found that 82 per cent of pharmacies stocking ARVs carried a single drug and monotherapy was prescribed to 17 per cent of patients. The author suggests that poor prescribing practice, driven by the cost of drugs, is likely to continue to be the norm wherever differential pricing excludes the private sector.

3. ISSUES IN SCALING UP ART PROVISION

3.1. Selection of beneficiaries

Coverage

As of December 2002, fewer than 1 in 18 of the adults in middle and low-income countries who could benefit from ART were on treatment. The lowest coverage relative to need is in sub-Saharan Africa. Burundi, where only 1,000 of the 90,000 people who need treatment are receiving it, illustrates the gap between ART provision and need (AIDSMAP, 2003).

Coverage of antiretroviral treatment, December 2002 (adults by region)

Region	Number of people on ART	Estimated need	Coverage
Sub-Saharan Africa	50,000	4,100,000	1 per cent
Asia	43,000	1,000,000	4 per cent
North Africa, Middle East	3,000	9,000	29 per cent
Eastern Europe, Central Asia	7,000	80,000	9 per cent
Latin America, Caribbean	196,000	370,000	53 per cent
Total	**300,000**	**5,550,000**	

Source: WHO, 2002

WHO has set a target of 3 million PLHA in developing countries on ART by 2005 (Lancet, 2003b) and, as discussed in Section 2, many countries are planning to expand access to ARVs. However, the scale of these proposed programmes is still likely to be insufficient to meet the needs of all those who could benefit from ART, especially in sub-Saharan Africa. In Zambia, where the government plans to provide ART for 10,000 adults, there are more than 500,000 people with HIV. The Government of Malawi is planning to scale up access to reach approximately 25,000 patients, but there are an estimated 1 million people with HIV in the country, a third of whom may benefit from ART.

Equity and priority target populations

In resource-poor settings where governments can only afford to provide ARVs to a proportion of those who need them, difficult choices have to be made about selection of treatment recipients. Although political considerations will influence decisions, scale up of ART programmes should be informed by wider public debate about equity issues. Consideration needs to be given to coverage of the poor, of different geographical areas, of rural versus urban populations, and of specific population groups such as orphans or street children.

In the DAI in Cote d'Ivoire, despite efforts to ensure equitable access, poorer people were less likely to access treatment than those who were better off (Prudhomme et al, 2002). Galvao (2002), reviewing experience of universal free provision of ARVs in Brazil, highlights the disproportionate rise of HIV infection among the poor and the need to analyse how effectively the public health system provides HIV diagnosis and treatment for the most socially excluded population groups.

In Zambia, $2 million of MAP resources have been budgeted and approved by Parliament for ARV. However, the Network of Zambian People Living with AIDS (NZP+) has expressed concern that the poor and powerless may not be able to access such drugs when they become available (www.irin.org April 1st 2003; www.journa-aids.org). An important lesson learned from experience in Haiti is that the full participation of community health workers is required if HIV prevention and care are to reach the poorest and most vulnerable communities (Farmer, 2002).

Ethiopia recently announced plans to start provision of ARVs, but the drugs, which have been imported from India, will cost patients $40 a month, a price most people will be unable to pay. Similarly, in Mozambique, the cost of triple therapy has been reduced to around $80 a month since late 2002, when an Indian manufacturer began supplying Mozambican pharmacies with cheap generic ARVs, but this is still twice the average monthly wage in the formal sector (www.irinnews.org).

Kenya has given careful consideration to equity issues. Recognising that a fully equitable approach is not feasible with currently available resources, the government has decided to include an element of cost sharing, to select initial target populations to receive ART, and to start provision of ARVs at provincial hospitals. Cost sharing for ARVs will be linked to the existing cost sharing programme and wider health sector reform processes. Work is ongoing to develop practical and equitable means testing and exemption mechanisms and to determine other target groups that will be eligible to receive ARVs when more funding becomes available (reference).

In contexts where services providing free ARVs will only be able to meet a fraction of likely demand, explicit rationing will be more appropriate than ad hoc systems (Boxshall, 2003). Priorities identified for free or subsidised provision of ART in resource-poor settings include people who are ill with serious damage to their immune systems, extension of strategies for PMTCT to include continued treatment of HIV-positive mothers and, where necessary, of their male partners, PEP for health care workers exposed occupationally and women and children exposed though rape or sexual abuse, treatment for key public sector workers and for those who are unable to pay. In Botswana, patients with TB, HIV positive women and their spouses and infants will be targeted initially (PlusNews, 2002). Similarly, in Zambia, immediate priority will be given to mothers with HIV identified through sites offering PMTCT, their partners and infants born with HIV (AIDSMAP, 2002a).

Eligibility criteria

Clear biomedical, economic and social criteria are required to determine eligibility for treatment in contexts where ART will not be available initially to all those who could benefit. Communities need to be aware of eligibility criteria and to understand that not everyone with HIV needs or will benefit from immediate treatment.

WHO guidelines for resource-poor settings recommend treatment for people diagnosed with AIDS and people with HIV who have a CD4 cell count below 200. Where CD4 cell counts are not feasible, people with HIV with symptoms of immune deficiency but no AIDS-defining illness should receive treatment if they have a total lymphocyte count below 1200 cells/mm.

In Zambia, national guidelines on clinical eligibility for treatment will be based on WHO recommendations (AIDSMAP, 2002a). Similarly, in Botswana, patients with a CD4 count of 200 or below, in addition to the priority groups noted above, will be targeted (PlusNews, 2002). In Ghana, the Ministry of Health recommends initiation of

treatment for patients with a CD4 count of less than 250, and a total lymphocyte count less than 1000 (DFID Ghana, personal communication, 2003).

In China, patients are selected according to guidelines issued by the county health bureau. All selected patients will be given a unique code and will have to sign an awareness letter. This letter explains the patient's rights, obligations, possible adverse effects during treatment, involvement criteria, exclusion criteria and medical record forms. Before starting treatment, every patient is given an introduction to ART to ensure they have a clear understanding of the drug regimen.

In Haiti (Farmer, 2001a, 2001b), in the absence of CD4 counts and viral-load testing, inclusion in the DOT-HAART project was based on clinical criteria and basic laboratory data available in most rural clinics. Guidelines used for inclusion were:

- Absence of active tuberculosis.
- Recurrent opportunistic infections difficult to manage with antibacterials or antifungals.
- Chronic enteropathy with wasting.
- Otherwise unexplained and significant weight loss.
- Severe neurologic complications attributable to HIV.
- Severe leukopaenia, anaemia, or thrombocytopaenia.

In the CDC Kibera pilot programme in Kenya, assessment of patient readiness for treatment includes evaluation of understanding of the limitations of ART, actions to take in the event of side effects, and of the fact that long-term funding for the programme is not guaranteed. Patients are asked to give oral consent to treatment, and a health worker documents consent in the medical record.

One lesson learned is the need for flexibility in the biomedical criteria used to initiate treatment. The Kibera programme has changed its criteria to include patients who present without an AIDS-defining illness but who have a history of subjective symptoms such as weight loss, chronic fever, and night sweats. MSF in Malawi started with strict criteria for inclusion of clients including, for example, turning up on time for 3 appointments and bringing a partner or guardian with whom they had shared their status. This has changed as capacity to meet demand has increased, and MSF now uses a clearly defined geographical catchment area, providing drugs to eligible residents of Chiradzulu district, which has a population of 230,000.

Measures to determine that patients are from a defined geographical catchment area are important, given concerns that ART programmes may be overwhelmed in the early stages by patients from outside the area. MSF in South Africa has established clear eligibility criteria for its 3 HIV/AIDS clinics in Khayelitsha (WHO and MSF, 2003). Patients are only considered for ART if they meet the following criteria:

- Biomedical – assessed by a doctor based on disease stage (3 or 4 according to the WHO classification) and CD4 cell count (less than 200).
- Adherence – assessment based on adherence to cotrimoxazole prophylaxis and TB treatment, and regular and punctual clinic attendance (attendance for at least 3 months and on time for the last 4 visits).
- Social – assessed by a community selection committee, based on a home visit to verify that the patient lives in Khayelitsha and has disclosed to at least one person who will act as a treatment assistant, and commitment to long-term therapy and safe sex practices.

In Khayelitsha, preference is also given to patients on the basis of their: number of dependants (a woman with children as opposed to a single man); health status (very sick as opposed to meeting clinical criteria); income (very poor as opposed to being able to afford treatment); and disclosure and activism (open about HIV status and active in community organisations as opposed to refusing to disclose).

In the Benin Initiative (Sehonou in French Ministry of Foreign Affairs, 2002), an eligibility committee, involving government, NGO, PLHA, public and private sector health professional, employers association and civil society representatives, was set up to determine, anonymously, which patients would receive treatment and their financial contribution. A doctor and a social worker assess clinical and socio-economic criteria.

Measures also need to be in place to provide people who do not meet criteria or cannot benefit from ART – including those with concurrent OIs, such as TB, requiring treatment prior to ART, those who cannot tolerate or maintain ARV therapy, and those with terminal illness or who no longer respond to the available regimen – with appropriate treatment, care and support (van Praag in French Ministry of Foreign Affairs, 2002).

3.2 Health systems

Systems strengthening

There has been relatively little analysis of the impact of HIV/AIDS on health systems (JSI and HRSC, 2003). One study, of the impact of HIV on health services in nine regions of Tanzania, found changes in disease patterns (with more people affected by TB, STIs and pneumonia), growing budgetary constraints (resulting from increased admissions, prolonged hospital stays, increased expenditure on drugs, HIV screening reagents and x-rays, exemptions for HIV patients, and the costs of treatment and funerals for health staff), significantly increased burden on staff (resulting from growing demand for diagnosis, laboratory tests, treatment and care), and decreasing human resources (resulting from a governmental freeze on employment, absenteeism for domestic caring responsibilities and funerals, illness and death). The provision of new HIV counselling services was highlighted as an additional pressure on staff time and resources (Malecela-Lazaro et al, 2001).

Another review of the impact of HV/AIDS on health systems reported that, in Botswana up to 80 per cent of adult medical wards, and 33 per cent of paediatric wards had HIV related conditions. There was also an increase in bed occupancy rates, and an increase in hospital length of stay, as well as an increased mortality in clinically suspected HIV/AIDS cases. Septic conditions related to surgery, gynaecology and obstetrics were also reported, as well as high readmission rates. HIV/AIDS cases were complex and required extensive diagnostic investigations, there were large numbers of critically ill patients with limited numbers of high dependency beds and staff. Hospital costs increased due to extensive use of diagnostic services, and drugs. In Kenya, a study of admissions at Kenyatta National Hospital in Nairobi revealed an increase in bed occupancy from 100 per cent in 1992 to 190 per cent in 1997, an increase in HIV and AIDS hospital admissions, but not an increase in length of stay. HIV/AIDS admissions appeared to stabilise at about 40 per cent and over time there has been a decline in presentation of end stage AIDS patients to the hospitals. An increased proportion of hospital bed occupancy is due to HIV/AIDS related illness in developing countries, ranging from 39 per cent in Kenyatta National Hospital in Nairobi, Kenya, to a high of 70 per cent in Burundi. Hospitals in other parts of Africa and in Thailand have HIV/AIDS related bed

occupancy of 50-60 per cent. There is concern that HIV positive patients might be crowding out non-HIV infected patients in hospitals. A longitudinal study in Kenyatta National Hospital found that over a period of time, HIV/AIDS mortality stabilized at 35 per cent, however non-HIV mortality increased from 13.9-23 per cent. One possible explanation is that non-HIV patients are being admitted only when critically ill, thus they are more likely to die. Specific studies to assess the impact of HIV/AIDS on morbidity and mortality of non-HIV infected people at out-patient and in-patient level are needed. A report on hospital admissions in rural South Africa found an increase in total hospital admissions of 81 per cent, an increase in adult TB ward admissions of 360 per cent, and a 43-fold increase in admissions of non-TB AIDS adult cases (HIV/AIDS And Health Systems: Response And Impact, A Review Of The Literature, February 2002).

At the same time as the HIV/AIDS epidemic is increasing demands on already constrained health systems and undermining the capacity of systems to provide services through attrition of health sector workers, it is widely recognised that effective and efficient provision of ART requires well-functioning health systems.

Scale up of ART provision has the potential to strengthen systems and improve outcomes for non-HIV related conditions, if investment is used to address infrastructure, human resources and logistics weaknesses. A pilot treatment programme in Thailand is reported to have resulted in a stronger HIV/AIDS service system, more commitment from health workers, greater community involvement and a better referral system (Satasit, 2002). Horizons reported that the introduction of PMTCT (including VCT, infant feeding counselling, provision of formula, and prophylactic ARVs) in a busy clinic in Lusaka, Zambia had a positive effect on services. Waiting time for ANC clients did not increase and health worker contact time with ANC and non-ANC MCH clients actually increased. Additional personnel conducted 70 per cent of counselling, but did not assist with routine ANC activities. The authors conclude that training for PMTCT may have improved overall service quality and use of health worker time (Levin, 2002). The Haiti experience (Farmer, 2002) suggests that improving clinical services can boost staff morale.

Conversely, without appropriate investment in systems strengthening, ART programmes could weaken health system capacity and have an adverse impact on other disease outcomes. A recent paper presented in South Africa (Barron P, 2003) highlighted the following ways in which scaled up ART programmes could undermine health systems:

- An increase in under-funding of primary care.
  Primary care services make up about 15 per cent of the total public sector health budget in South Africa. Adding on an ART programme, without addressing current under-funding, will exponentially increase under-funding of primary care.
- Increasing inequity.
  There are widespread district inequities in the resources provided for primary care, often with an inverse relationship between health need and resources provided. It is likely that ARVs will be introduced in a selective way based on the capacity to run programmes and those districts with the best services and the most resources will be given extra resources to run ARVs. This will not only increase inequity directly but also indirectly by attracting scarce human resources. Even if ARVs are introduced everywhere, the likelihood is that there will be good care in some areas and inadequate and sub-standard care in the poorer areas.
- Increased rationing of primary care.

The current level of resources available to primary care is insufficient to cope with the volume of patients and the comprehensive basket of services in the primary care package. Introducing ARVs will increase existing ad hoc rationing.

- Curative care will take precedence over prevention.
  With the introduction of a universal free care service, clinics have already experienced increased numbers of patients requiring curative care. This is often provided at the expense of programmes focused on preventive care such as immunisation. The introduction of a high profile ARV programme is likely to exacerbate this situation.
- Decreased quality of care.
  Currently, most of the key targets for immunisation coverage, TB cure rate and VCT provision are not being met. An ART programme could distract attention from these targets. There are many facilities without the necessary infrastructure or back-up systems to provide good quality primary care, let alone more complex ARV therapy. There is also the danger that individuals who receive ARVs with sub-optimal care will be at risk for toxicity as well as increasing drug resistance.
- Inadequate human resource provision will worsen.
  There is a shortage of skilled personnel in the public health sector and this is worst in rural and disadvantaged urban areas that need health workers the most, and that also have the highest HIV prevalence rates. There is no strategic plan to produce the additional doctors, nurses and other health care workers who will be required to manage an ART programme. Recent research by HSRC suggests that over the next 10 years there will already be a shortage of 20,000 nurses in South Africa.
- Increased need for monitoring and evaluation.
  A national ARV programme will require monitoring and evaluation at a number of levels, starting at the facility level, but supervisors of primary care and managers do not have the skills and capacity to do this, and information systems and use of information from these systems is weak in existing programmes, such as TB control and PMTCT.
- Decentralisation process.
  The health system is at a crucial and complex stage in the development of a decentralised health system, with a health bill awaiting the legislative process, and it is likely that it will take the next 3 years to establish the governance and managerial structures. Health managers are likely to be focused on structural issues rather than ARV quality of care issues.

Systems-related issues to be considered in scaled up provision of ART in resource-poor settings are summarised in the box below.

- Adequate physical infrastructure.
- Strengthened and scaled up comprehensive care programmes to accommodate ART that can manage common HIV-related illnesses, OIs and drug side effects.
- Accessible counselling and testing services.
- Available laboratory services to monitor ART.
- Appropriate staffing levels and training of health workers.
- Quality assurance systems for drugs and patient care.
- Community involvement and sensitisation.
- Monitoring and evaluation framework.

There is no shortage of literature identifying system-related challenges to scale up. Key challenges for scale up in resource-poor settings identified by Morrison (2002) include the need for substantially more resources to expand health system capacity,

strengthening and integrating prevention activities with treatment; and anticipating and mitigating side effects and the emergence of drug resistance. Reviewing the question of whether African health systems are ready to incorporate ARVs, based on the situation in Kenya, Tanzania and Uganda, Kalibala (2001b) identified a number of issues to consider in scaling up, including equity, maintaining clinical standards, affordable monitoring, access for spouses, emergence of resistance, and how to address ill-equipped and under-resourced health systems and underpaid health workers. Nkengasong (2002) cites the cost of drugs and lack of laboratory infrastructure to monitor the therapy as systems factors that contribute to the limited widespread use of ARV drugs.

Morales et al (2003) review experience of initial scaling up of access to ART in Chile between 1998 and 2001 in a context where the ability of the public system to subsidise ART was limited by lack of resources and the private sector did not provide cover for ART expenditures, and consider the implications of increased but limited access for the health system and for patients; they identify four key issues:

- Criteria for access to ART in a context of limited resources – health centres defined their own criteria, resulting in a wide variety of approaches to selecting patients to receive ART, and better off patients were more likely to be on treatment than the less well off; drug users were also less likely to receive treatment.
- Transfer of patients from private to public health services – due to better cover, 30 per cent of patients switched to the public health system.
- Financial burden for patients – patients had to pay for the third drug to complete their treatment and used a range of strategies to access ART, including making out of pocket payments and taking out loans; the longer they had waited for ART the more likely they were to be more seriously ill, thereby incurring higher health expenses, breakdown in supply also meant they occasionally had to purchase their drugs privately.
- Distribution of ART – due to the complexity of the distribution process, stocks frequently ran out, leading to interruptions in treatment.

Actions subsequently taken in Chile to address these problems are: improvement of the medical decision-making process, with the creation of an advisory committee to manage the prescription of ART and therapeutic changes; improvement of coordination and planning of negotiation with industry, with a yearly schedule for procurement and fixed negotiation rounds; and reduction of the number of stakeholders involved in drug procurement, management, logistics and distribution.

Systems issues have impacted on the scale up of ART in many resource-poor countries. In Malawi, according to the National AIDS Commission, the process of increasing the number of patients receiving ART will be slow because of the capacity of the health system to cope with the additional workload, including the monthly monitoring of clients and the impact that this will have on services for non-ARV clients (IRINnews, 15th July 2003). In Botswana, the launch of the national treatment programme was delayed in 2002. According to the programme manager, the start date was unrealistic given the system's capacity and the time required to enrol people diagnosed with HIV and to sensitise the public (PlusNews, 2002). Lack of capacity at some state and municipal departments of health is cited as one of the main challenges to the decentralised approach in Brazil (John Snow Brazil, 2001).

A pilot programme to implement PMTCT in South Africa, implemented in 18 sites, covering 193 facilities, demonstrated that it was feasible to introduce PMTCT into routine PHC activities, but that success varied depending on the effectiveness of the

provincial health department and the functioning of local health services (Hilderbrand, 2002). The Dominican Republic initiated a scaled up integrated package of PMTCT interventions in May 2000 and, as of November 2001 had implemented the programme in the main hospitals of 12 provinces. Low numbers of voluntary counselling sessions and inadequate numbers of HIV rapid tests were the two main obstacles identified (Perez Then, 2002).

The main priorities for systems strengthening identified at a recent WHO/UNAIDS workshop on strategic information for ART programmes (WHO/UNAIDS, 2003) were:

- Standardisation of monitoring and evaluation practices.
- Strengthening health and logistics management information systems.
- Assessment of human resource needs and capacity for ART programmes.
- Assessment of individual and community preparedness.
- Strengthening HIV/AIDS disease staging and surveillance.

Hardon and Hodgkin (2000) proposed the following framework to increase access to ART:

- Ensuring rational selection and use of HIV-related drugs (identifying needs at different levels of care, evidence-based guidelines, improved surveillance as basis for quantifying requirements).
- Ensuring improved affordability (increasing competition and price transparency, feasibility of joint procurement and revolving funds, using voluntary and compulsory licensing provisions, R&D to develop more affordable regimens, fiscal measures to reduce prices).
- Ensuring increased and sustainable financing (increased international commitment, sustainable national level financing, discouraging non-sustainable donations and pilot initiatives).
- Strengthening the capacity of health services to provide care (training, strengthening essential drugs programmes, developing workable models for integration into existing primary and secondary care).

Strategies to support health systems to deliver ART programmes are being developed, based on experience and lessons learned. The Clinton Foundation is working in Rwanda, Mozambique, Tanzania, Haiti, Bahamas, Dominican Republic and with the Organisation of Eastern Caribbean States to build capacity for effective programmes through upgrading health and laboratory facilities, training health personnel, and improving management, patient information and drug distribution systems (**www.clintonpresidentialcenter.com/AIDS_in_country_work.html**).

For example, the 2003 strategic plan for scaling up in Mozambique, prepared with Clinton Foundation support, includes strengthening the overall provision of health services to ensure sustainable provision of high quality HIV/AIDS and other critical care as a goal. It notes that improvements in physical facilities and strengthening of systems for distribution of drugs and blood supply safety will serve not only to ensure high quality HIV/AIDS care but also to enhance care for all diseases. There are plans to use Clinton Foundation funds to address a range of systems issues, including refurbishment of medical facilities, purchase of equipment, expansion of human resource capacity, increased salaries for clinical staff, training of new personnel, building management capacity, strengthening financial management and audit, and programme evaluation.

Kenya is taking careful account of systems issues in developing its strategic plan for a scaled-up ART programme, to avoid increasing pressure on already over-burdened

public health services. The government commissioned a preliminary situational analysis of public and private health infrastructure and its capacity to support a national ART programme at all levels, including identifying regional and district systems strengthening requirements. To inform the situational assessment, the Ministry of Health identified basic service, personnel and infrastructure needs for ART delivery. The findings are being used to plan essential system strengthening activities required for provision of comprehensive HIV/AIDS care and treatment (Ministry of Health, Kenya, 2003).

A review of Zimbabwe's health sector capacity to manage ART (Noguera et al, 2003) made recommendations for clinical service initiation and expansion. These include: appoint a national ART programme manager within the AIDS and TB unit, to support sites initiating and expanding ART services; develop clear protocols for patient selection and screening, ARV prescribing, monitoring and management, adherence support, management of side effects and treatment failure, and for coordination with other programmes such as TB control; introduce ART initially in sites with existing HIV-related out-patient care services; establish standard basic site requirements to ensure full readiness for provision of ART; establish site specific and national quality assessment monitoring programmes; actively engage private sector practitioners and company medical staff in planning.

Various strategies are being explored in Malawi, including reducing the frequency of monitoring visits for stable and adherent clients, piloting a distribution system where district hospitals prescribe ARVs but where clients are able to collect drugs from and be reviewed by satellite health centres, piloting simple clinical review guidelines that can be used at satellite facilities, and developing simple but robust record keeping and drug monitoring systems (Boxshall, 2002).

An evaluation of the PMTCT pilots in South Africa by the Health Systems Trust identified a number of factors contributing to successful implementation, which included: dedicated leadership of the provincial programme; community liaison through a Liaison Officer; coordination and availability of a pool of PMTCT expertise; well planned site preparation; selecting sites that are made up of a network of facilities rather than single isolated facilities; recruitment and payment of lay counsellors to take pressure off clinical staff; providing staff with effective support and supervision; providing good quality training that emphasises skills and problem solving, and repeating training to address high staff turnover; ensuring the support of doctors; providing appropriate and private space for VCT; and emphasising that counselling is not just about getting consent for HIV testing (McCoy, 2002).

Integration of services

Comprehensive care

ART needs to be delivered as part of a comprehensive package of services that includes VCT, PMTCT, diagnosis and treatment of opportunistic infections and other HIV related illnesses, and other prevention, care and social support services (UNAIDS, 2002). The 2000 mid-term evaluation of the UNAIDS DAI pilots concluded that it is not enough just to make ARVs available – comprehensive HIV/AIDS care also requires VCT, prophylaxis, diagnosis and treatment of TB and other OIs, well-trained and supervised health workers, equipment and supplies, social support and the rest of the continuum of care, including palliative care (UNAIDS, 2000).

The Horizons diagnostic study of PLHA involvement (in Ecuador, Burkina Faso, India and Zambia) showed that while access to treatment is a prime concern for PLHA, it

has to be accompanied by psychosocial support, provision of accurate information and training on issues such as positive living, support group formation and opportunities for involvement in NGOs and CBOs.

Farmer et al (2001a) propose a basic minimum package for provision of HAART, based on their experience in Haiti. This includes HAART with DOT using community health workers, monthly support meetings for people on ART, social support including financial assistance to families, provision of prophylactic ART and breastmilk substitutes to prevent MTCT, and post-exposure prophylaxis for occupational accidents and rape.

Kalibala (2002a) notes that systems for HIV/AIDS care are broader than public and private sector medical services, and suggests that strategies for provision of ART need to consider the role and potential role of home-based care programmes, NGOs and CBOs, support groups and PLHA networks, as well as traditional healers, herbalists and spiritualists. More information about the role of the informal sector and the impact of HIV/AIDS on utilisation of informal health providers is needed, as well as about the knowledge, attitudes and beliefs of informal providers.

Dabis et al (2000) concluded that effective scaling up of PMTCT needs appropriate antenatal, delivery and post-natal care, VCT, short-course ZDV or nevirapine, and suitable alternative feeding, all of which require a well-functioning medical and social system (Kalibala, 2001a). Consideration also needs to be given to integration of PMTCT and delivery of ART to women and children (Synergy Project, 2003).

PAHO and the International Association of Physicians in Health Care have proposed a phased ‘building blocks’ approach, where implementation of basic services provide the foundation for delivering more specialised services. Kitahata et al (2002) suggest that the WHO strategy for chronic disease management in resource-poor countries could provide a model for delivering comprehensive services to people infected with HIV (see Annex 2). Integration and coordination of services is an important component of this model, for example, expansion of VCT for women could be achieved through integration into existing ANC, family planning and MCH programmes. However, with the exception of PMTCT programmes (JSI, 2001), there are few documented examples of programmes that have integrated ART into the continuum of HIV/AIDS prevention and care or that have addressed the integration of chronic disease care into existing health services in developing countries (Gilks in JSI and HRSC, 2003).

Many countries are attempting to introduce ART following principles of integration with other HIV/AIDS prevention and care services and health service provision more generally. Different models of health care delivery will be needed to respond to the needs of different contexts. A description of the northern Thai ARV programme experience stresses the importance of integration into existing health infrastructure and involvement of all key stakeholders, including community based organisations and PLHA, in planning (Srithanaviboonchai, 2002a).

Thyolo district in Malawi is one of the few documented examples of planned integration of ART into a continuum of care. The district has 7 VCT sites and 1 PMTCT site; 2,300 symptomatic and asymptomatic PLHA are supported through home-based care and health centres; TB patients have access to VCT and cotrimoxazole prophylaxis; 1,700 symptomatic HIV patients are registered at the district hospital based HIV/AIDS clinic. The district plans over the next 5 years, under the national scale up programme, to provide access to HAART to at least 50 per cent of people with AIDS, using a simplified clinical protocol and fixed drug combination,

conducting screening and preparation in the home-based care and PMTCT populations, and providing treatment through 2 HIV/ART clinics at two hospitals and decentralised health centres and adherence follow up through guardians and home-based care.

Entry points for ART

Kenya is committed to integrating ART into the existing health system instead of setting up new parallel structures, but rather than full integration at lower levels of the system, PMTCT, VCT and TB programmes will act as entry points to regional treatment centres.

Others have also considered the potential of VCT and TB programmes as entry points for ART. The Zambia ProTest project (Terris-Prestholt, 2002) has piloted the use of VCT as an entry point for integrated case management and prevention of HIV-related TB, in order to improve collaboration between health services and community organisations. Core components are coordination between HIV and TB activities, provision of VCT with TB preventive therapy, outreach and home care services for HIV-related illnesses, but ART is not included as yet. VCT is a logical entry point for HIV care including ART, since it is the essential first step in the diagnostic process, and there is a need to upgrade VCT facilities and staff to identify patients eligible for ART (Horizons, 2002; van Praag in French Ministry of Foreign Affairs, 2002).

The Haiti Partners in Health programme has argued that the DOTS approach used for TB treatment can equally be applied to ART, based on experience in Haiti of DOT-HAART and DOTS Plus for multi-drug resistant (MDR) TB (Farmer, 2001b). The Start Study in South Africa, where up to two-thirds of patients with TB are co-infected with HIV, has been exploring the use of existing TB DOTS programmes as sites for initiation of ART through a pilot study at the Durban Chest Clinic (Jack C, 2002). In 2002 the authors highlighted the need for feasibility to be carefully assessed, and clinical, logistics and training issues to first be addressed. More recently, the Start Study reported on its experience, which indicates that TB DOT programmes can serve as an entry point for identifying patients with HIV and the introduction and monitoring of ART. Once-daily administration of ART and TB therapy has proven to be safe and effective, and the pilot has generated a positive response from staff and patients (Jack et al, 2003).

In Malawi, doctors from the national TB programme have highlighted a number of steps for establishment of a DOT programme for ART. These proposed steps include integration of TB and HIV treatment, in order to avoid adverse drug interactions, increase access to HIV-infected individuals, use existing DOT providers, reduce stigma associated with HIV, support reliable drug supply, and ensure all patients have a monitoring card similar to that used for the DOT TB programme. The proposals also acknowledge that a phased approach will be required, to allow time to pilot the selected triple therapy regimen, define clinical algorithms for monitoring treatment and complications, strengthen infrastructure and train staff in pilot districts, and test the feasibility of integrating ART into the TB programme structure (Harries et al, 2001).

Harries et al (2002), reviewing the potential synergies between HAART and TB control in Africa, highlight the potential for, and limitations of, using TB control programmes to deliver ART. Arguments for include: the structure used to deliver and monitor anti-TB treatment could be a model for delivery of ART, using an adaptation of the five key elements in TB control; building on existing infrastructure would be cost-effective; national TB programmes have experience in long-term patient care,

support and monitoring; DOT for both anti-TB treatment and HAART could be administered by the same provider; and adverse reactions could be managed holistically.

However, arguments against include: the likely huge demand for HAART could potentially overwhelm TB services, and even good DOTS programmes are finding it difficult to cope with the increasing number of TB patients resulting from the HIV epidemic; there are serious concerns about the risks of cross-infection if people with HIV are exposed to infectious TB patients and about the spread of resistant TB; and the stigma associated with HIV/AIDS may be transferred to TB, reducing uptake of TB services. Others have also argued that the DOTS approach may be less easy to adopt for ART than is sometimes suggested, since TB treatment is time limited whereas ART is life long, disclosure of HIV status has more significant implications than disclosure of TB status, and many DOTS programmes are weak.

Directly observed treatment also draws heavily on human resources. This is increasingly being recognised by TB programmes, which are expanding approaches to involve church group volunteers, people who previously received treatment and women's organisations, among others, as treatment supporters (WHO, 2003).

An assessment in Trinidad and Tobago found that, while most PLHA were willing to take a strict lifelong regimen of ARVs, the majority did not want a nurse visiting them at home to give medications. Home visits would only be acceptable if the PLHA was too sick to go to the clinic and the nurse was not in uniform. DOT involving health workers would therefore not be an appropriate option to improve adherence for these patients (Jack N, 2002).

In South Africa, the HIV/AIDS and TB programmes collaborate on policy formulation, advocacy, health education, training, community mobilisation, operational research and surveillance, rather than service delivery. At district level there are joint teams, VCT is offered to TB patients and TB screening to HIV positive patients, cotrimoxazole prophylaxis is provided to HIV positive TB patients, and the teams ensure that TB DOT supporters provide HIV education, condoms and VCT promotion, and that home-based carers provide DOTS.

Infrastructure

Adequate infrastructure, including clinical care, laboratory and pharmacy facilities, is needed to deliver ART. Limited health service infrastructure has been identified as a major constraint to scaling up ART in many resource-poor countries. In Mozambique, the current infrastructure is inadequate to meet the demands of a large-scale programme, and the 2003 strategic plan for scale up identified areas that require attention including rehabilitation of facilities, acquisition of equipment, and HIV/AIDS laboratory and blood bank services. In Botswana, there are only 2 government referral hospitals, in Gabarone and Francistown, and most health care is delivered through local clinics that offer only basic services.

There is a lack of clarity about minimum infrastructure for ART delivery and how to cost this, including taking account of efficiencies at scale. Kenya is one of the few countries to conduct a situation assessment of public health facility infrastructure. The assessment identified a number of infrastructure constraints to scale up at provincial and district level. Some facilities were found to have inadequate physical infrastructure and to require expansion and upgrading for effective delivery of ART programmes. Infrastructure issues to be addressed include the design and arrangement of laboratory and pharmacy space, in the latter case to support drug

counselling. Although laboratory equipment was available in most facilities to support basic tests needed in an ART programme, capacity to perform CD4 tests was lacking and service agreements were not generally in place (Ministry of Health, Kenya, 2003; JSI and HRSC, 2003).

Human resources

Staff shortages

Human resource issues are a major constraint to scale up, affecting capacity to absorb new resources, provide quality ART, and meet cumulative demand for chronic care. In many countries, including those with high HIV prevalence rates, the health sector is facing a crisis in human resources. Inability to recruit and retain an effective, well-motivated, appropriately skilled workforce stems from problems including low pay and morale, poor conditions of work and inadequate management. Shortages of staff are exacerbated by migration to the private sector or other countries and HIV/AIDS-related attrition. For example, South Africa's Chris Hani-Baragwanath Hospital, the site of an ARV research project, is reported to be facing a severe shortage of nurses, as many have left to work in the UK and have not been replaced.

In Lusaka, Zambia there is high HIV prevalence in midwifes (39 per cent) and in nurses (44 per cent). In Southern Zambia the mortality rates among nurses rose 0.5 per cent per year through the 1980s to 2.7 per cent in 1991 due to HIV/AIDS. The World Bank and the Malawi government report a rising death toll among health workers of 3 per cent in 1997, a 6-fold increase in levels before the epidemic. In South Africa TB incidence among staff increased resulting in absenteeism and high treatment cost. In countries with high seroprevalence and generalised epidemics there was increased absenteeism related to employees providing care for ill relatives and attending funerals (HIV/AIDS And Health Systems: Response And Impact, A Review Of The Literature, February 2002).

A recent press report highlighted the difficulties China is experiencing in providing ART because of the shortage of doctors who can administer ARV drugs. There are fewer than 100 doctors with the necessary training and skills, in a country where an estimated 1 million people in rural areas have contracted HIV through unsafe blood collection procedures. The lack of suitable doctors is also partly responsible for patients stopping treatment when they experience side effects (Sui, 2003).

The Botswana National AIDS Coordinating Agency (NACA) has 10 doctors working full time on HIV/AIDS in the main hospital in Gabarone and 5 at each of the other hospitals. It has identified the need for at least 20 additional full-time doctors to enrol, assess and supervise 10,000 new patients, and the government is seeking to recruit doctors from overseas. However, language is an important issue; already 90 per cent of doctors in Botswana are foreign and do not speak Setswana. A report by McKinsey suggested that Botswana would need an additional 330 nurses – there are currently approximately 4,400 – to support the planned ART programme. Nurses in rural clinics do not have time to counsel every HIV/AIDS patient, so the NACA is planning to train and employ 500 lay counsellors. The shortage of phamacists outside the main hospitals is also a problem, and existing pharmacy technicians will need training to manage ARV supplies and distribution (Rollnick, 2002).

In Kenya, staffing has been identified as a major constraint to scale up (Ministry of Health, 2003). All 13 hospitals visited during an assessment of facility preparedness were found to be operating below required staff levels, with shortfalls in clinical, laboratory, pharmacy and other critical skills. There is also an imbalance in

deployment, with facilities near Nairobi having better staffing levels. The majority of hospitals were found to have adequate staff to initiate ART provision, but will quickly need additional staff as patient numbers increase.

In Ghana, where phased scale up is planned, specialist training for health professionals on ART and treatment of OIs has started, but there are few doctors, nurses and laboratory technicians with the skills required to deliver the latest HIV/AIDS care. In Tanzania, the NACP estimates that an additional 10,000 medical, nursing, pharmacy and laboratory staff will be required to roll out ARV provision (Personal Communication, Swai, 2003).

In Malawi, plans in Thyolo district to manage ' in addition' a maximum of 700 patients during the first 6 months of treatment at the district hospital based HIV/AIDS clinic indicate the scale of human resource requirements (1 receptionist, 2 consultation units staffed by 1 nurse and 1 clinical officer, 2 ART units each with a nurse counsellor, and 1 data entry technician to manage the patient archive and database) (Teck in WHO/UNAIDS, 2003).

Given this situation, WHO is currently assessing human resource requirements for public sector scale up, and proposing that ART programmes consider strategies to identify core treatment tasks and related skills training needs and to reduce reliance on highly-trained physicians by devolving routine aspects of treatment and care to other health workers. In some countries this may already be happening. For example, modelling by Kurowski et al of human resources for health in Tanzania and Chad suggests that some tasks and activities are carried out by less highly qualified staff, and that surpluses of staff with lower skills compensate for deficits of staff with higher skills. However, this has implications for quality of care, health worker morale, and legal liability (JSI and HRSC, 2003).

The national ARV programme in Uganda plans to adopt a similar approach for the expansion phase to be supported by the Global Fund. Under its public health and primary care model, physicians will play the lead role in assessing PLHA, initiating or switching therapy, managing serious conditions and supervising staff. However, clinical officers, nurses and counsellors, including those based in primary care settings, will routinely follow up ARV therapy – including counselling and the initial diagnosis and treatment of common opportunistic infections. In taking this decision, Uganda built on the experience of its own community AIDS service organisations and experience in other countries that have adopted similar approaches, aided by standardised ARV regimens and simplified monitoring procedures (WHO, 2003).

A recent WHO and UNAIDS meeting identified the need for better data about human resources, including information about staff numbers, skills and use of time, to inform training and determine optimal task distribution between different levels of facilities and between health services and communities (Greesch in WHO/UNAIDS, 2003; WHO, 2003). Similarly, Kinoti and Tawfik argue that the extent to which health service personnel have been trained in counselling and testing, PMTCT, management of opportunistic infections and provision of ART needs to be more clearly determined (JSI and HRSC, 2003).

Quantitative investigations are required to estimate the impact of HIV/AIDS on morbidity and mortality in health care workers, to plan future human resource requirements. Information on health worker knowledge attitudes, beliefs and perceptions about HIV/AIDS is needed to inform training. Training also needs to ensure that health care workers have accurate information about HIV/AIDS, clinical management, the real occupational risk of HIV/AIDS and universal precautions.

Qualitative work is also needed to assess the psychological impact of HIV/AIDS care on health workers, to design programmes to support them.

Training

Staff training is a significant issue. Few staff in Kenya have received training in HIV management, and the Ministry of Health plans to use Global Fund resources for training of trainers in every province, focusing on physicians, clinical officers, laboratory and pharmacy technicians, and nurse-counsellors. Training is also an issue in the private sector. Working Group 5 of the Commission on Macroeconomics and Health noted that only 30 per cent of private physicians prescribing ARV had received any training in ART (JSI and HRSC, 2003).

Most programmes in developing countries have relied on in-service training for the introduction of ARV therapy. The current content of in-service training curricula is highly variable. For example, current HIV/AIDS training programmes range from 1 week in Uganda for all physicians, nurses, laboratory technicians, pharmacists and counsellors based in hospitals and health centres to a suggested minimum of 3 months for clinical officers in Kenya. Guidance on appropriate training is limited, although the Forum for Collaborative HIV Research is promoting collaboration and sharing of experience between organisations conducting training programmes for health and laboratory workers in Africa, to identify factors that contribute to effective training (www.hivforum.org). The Pangaea Global AIDS Foundation, a non-profit affiliate of the San Francisco AIDS Foundation, is managing a project to build a centre of excellence for clinical training and treatment in Uganda

There is a need to rethink training strategies and methods to ensure that these are responsive and incorporate continuing education, given the rapidly evolving nature of ART, and that training addresses health worker interaction with patients and with communities. Published information about experience of training community and family care providers to support ARV therapy is limited, although a working group convened by WHO under the umbrella of ITAC has identified several programmes that are beginning to target these groups.

Finally, clinical management is not the only aspect of scaling up ART with human resource implications. Effective programmes will also require staff with the skills to manage planning, procurement, logistics and referral in the context of decentralisation and health sector reform.

Drugs and supplies

ARV programmes need a regular and timely supply of quality drugs and supplies at competitive prices. This should also include laboratory reagents and related supplies, and drugs for OIs and other HIV related illnesses. The system must be able to buffer against uncertainties in funding and minimise risks of interrupted supplies, since continuous treatment is critical to minimise the development of resistance. A secure supply chain, with no leakage and interruptions, is also essential alongside strict monitoring of inventory levels and secure storage facilities. There is already an illegal market in ARVs in many countries, and leakage of government-provided drugs could exacerbate the risk of inappropriate use of ARVs and development of resistance. Countries planning scale up need to determine how drugs and supplies will be procured and distributed, and to ensure that related policies covering the public and private sectors, regulations to prevent misuse and counterfeiting, and logistics systems are in place (Chandani in WHO/UNAIDS, 2003).

In a recent review of care and support programming by USAID-funded implementing agencies (Synergy Project, 2003), challenges identified by the JSI DELIVER project, which is involved in logistics management of ARVs in several African countries, and the MSH RPM Plus project, which provides technical assistance on health commodity management for an ART initiative in Kenya, included: weak public sector logistics management systems for most essential drugs; poor storage facilities; weak transportation systems; problematic customs processes; diversion of products; inadequate training; lack of information systems; inaccurate quantification and forecasting (Chandani in WHO/USAID, 2003). Key lessons learned are:

- Selection of drugs – Countries need to develop appropriate essential drug lists and standard treatment guidelines to guide product supply, and to plan for possible toxicity and resistance to first-line drugs by selecting second-line options.
- Forecasting, quantification and procurement – Simplified regimens are important, since use of many ARVs makes forecasting, quantification and procurement very complex. Forecasting, quantification and procurement should be based on periodic and consistent monitoring of ARV consumption and take into consideration health service capacity, enrolment of patients and infrastructure and equipment requirements. Harmonised or standard procurement is advisable. Decisions about the quantity of ARVs imported should be based on storage capacity and the capacity of the system to deliver the drugs. Importing large quantities may result in wastage if drugs cannot be stored properly or used before their end of their shelf life.
- Registration and importation – Drugs must be registered with the national drug regulatory authority before they can be imported; this process can take considerable time.
- Inventory management and distribution – Strict monitoring of inventory levels, secure storage and transportation are essential to minimise pilfering and leakage. Collect baseline data on logistics system performance and capacity and ensure that logistics management information systems are in place before distribution of ARVs begins.
- Logistics management information systems (LMIS) need to be user friendly, involve minimal additional work for health workers, provide timely data, and to be flexible enough to respond to changes in consumption, due to patient mobility, regime changes or drug substitution. Systems need to be in place for quality assurance of drugs, and to monitor prescribing and dispensing patterns as well as stock levels.
- Training – Training health managers and service providers in ARV management is as important as training in clinical management and service delivery.
- Coordination and funding – Governments and donors funding ART programmes need to be clear about the scope and duration of funding, roles and responsibilities, and issues such as drug selection and management. Donors should be prepared to provide funding to ensure proper management and distribution of ARVs. Governments should identify alternative sources of funding to ensure uninterrupted supplies of ARVs if a donor decides to phase out funding.
- Management systems – Vertical systems are stronger but create multiple fragmented logistics, duplication of effort, and effective strategies are required for integration of systems and to strike appropriate balance between rapid parallel systems and long-term system building.

Forecasting, quantification and monitoring

An important issue is accurate estimation of drug requirements. In most developing countries, this is based on consumption rather than morbidity data (Hardon and

Hodgkin, 2000). With decentralisation, it is critical to provide support at district level for planning and informed decision making about drug requirements, in the context of allocation of drug budget for treatment of other health problems, and an appropriate balance of expenditure on prevention and care for HIV, and types of care, for example, treatment of OIs, palliative and home care.

To address this, the National AIDS Programme (NAP) in Brazil introduced a computerised system, SICLOM, in 1998, for control of drugs. Each AIDS Drug Dispensing Unit (ADDU) has at least one computer running the system, and data is sent at the end of each day to the NAP in Brasilia. SICLOM registers distribution of ARVs, helps to maintain adequate stocks of drugs at ADDUs and tracks prescriptions. It automatically checks prescriptions issued by doctors to establish whether they fall within national guidelines, and data is used to determine where further training for health providers is needed. Also in Brazil, with the support of PAHO, CDC is starting to evaluate ARV use in 3 health facilities in Rio de Janeiro, with a focus on patterns of use, investigation of whether patients are receiving medications according to national guidelines, and analysis of data collected through ARV surveillance systems.

Logistics and distribution

JSI has developed the ARV Drug Supply Chain Assessment Tool for use in Zimbabwe (www.jsiuk.com), which allows a comprehensive system-level assessment of the performance of the supply chain for ARVs and other related supplies. It is intended to help gather information on the flow and management of ARVs and related products in a country; confirm optimal use of resources in expanding availability; identify areas in need of improvement; collect baseline data to monitor performance over time; and monitor the continuous availability of drugs and supplies at service delivery points. The tool covers product selection, forecasting, supplier pre-qualification and selection, procurement, quality assurance, receipt and storage, distribution, rational use and management and coordination.

The Noguera et al (2003) review of Zimbabwe's health sector capacity also made recommendations for logistics management, including: develop and implement an effective logistics management system for all HIV-related products at central and site levels; establish a new HIV logistics section within the Ministry of Health with a clear mandate to coordinate logistics for all HIV commodities; implement a manual or automated LMIS to capture essential logistics data and track product use in the system; establish mechanism and procedures to coordinate product requirements and institute medium to long-term procurement planning for commodities with donors.

Uganda is reported to be taking an approach that includes: integrated procurement, storage and distribution under National Medical Stores; establishing a separate LMIS for ARVs with a view to integration into national LMIS in the longer term, including linking the LMIS with the HMIS and M&E; and accreditation of private pharmacies contingent on data provision.

In China, ARVs are managed by the county CDCs, which record delivery, divide the drugs into packages of 2-week dosages, and provide these to health facilities for distribution to patients.

PharmAccess International has identified difficulties in safe and appropriate storage of drugs, especially the lack of refrigeration for drugs that require it in peripheral facilities and in patients' homes.

Registration, procurement and local manufacture

Experience in a number of countries has identified particular challenges associated with registration and procurement of ARVs. While economic difficulties are the main reason for limited access to ARVs in Thailand, the relatively slow registration process for newly available anti-HIV drugs and the passive attitude of some local pharmaceutical company representatives are also factors (HIV-NAT, 2002). The experience of HIV-NAT is that, if clinical studies are initiated in collaboration with pharmaceutical company headquarters, local subsidiaries are forced to take a more pro-active import approach. In addition, local data and experience generated can help pharmaceutical companies facilitate the registration of new agents.

An initiative by PharmAccess International to provide ARVs to Kenya, Uganda, Senegal and Cote d'Ivoire experienced a number of difficulties including length of time taken for funds to be transferred and disappearance of some drug shipments in transit and at the airport; it took 12 months to solve these and other logistical problems. The EC has also been forced to take steps to prevent ARVs sent to developing countries being intercepted and re-sold in Europe.

In Brazil, initial purchase of ART drugs was managed by CEME, the Ministry of Health Medicine and Drugs Centre. However, CEME was disbanded because of charges of corruption against its managers and directors, and management of ART distribution has been decentralised to the National STD/AIDS programme. The programme has established an AIDS committee, which is responsible for identifying and recommending new ARVs for procurement. However, this committee too has been subject to pressure from international pharmaceutical companies to include new ARV drugs in the Ministry of Health approved list. As a result, the Ministry had decided to replace the committee members on an annual basis (John Snow Brazil, 2001).

UNAIDS reported that the 19 countries that have concluded supply agreement with the Accelerating Access Initiative (AAI) have moved to waive import taxes and duties on drugs used in HIV/AIDS treatment (UNAIDS 2002). However, costs remain high compared with generics and, in some countries, such as Kenya, the drugs are only being made available under the AAI to private hospitals and NGOs due to concerns over the lack of accountability and a patient tracking system in the public sector.

Access to Quality HIV/AIDS Drugs and Diagnostics, a UN initiative managed by WHO, aims to assist developing countries with procurement by providing accurate and up-to-date product information. As of March 2002, WHO had evaluated 40 products from 8 branded and generic manufacturers and identified a list of 11 ARV and 5 OI drugs that met WHO standards, and a further 13 suppliers and 100 products were under review (www.who.int/medicines/).

The use of generics for triple therapy can bring the costs as low as $295 a year (UNAIDS, 2002), a significant cost saving on branded products. Certain countries are removing legal barriers to the importation of generics. In mid-2002, Kenya enacted the Industrial Properties Act to remove legal barriers to the importation of generics, a major step forward and is only the second Act of its kind in sub-Saharan Africa. Currently several branded and a few generic ARVs are fully registered for use in Kenya. However, formal registration of most of the generic ARVs is pending approval by the Poisons and Pharmacy Board (PPB); currently these are being imported under the AAI waiver system until the PPB completes the registration process. A second significant development in Kenya was the inclusion of ARVs (4 NRTIs, 2 NNRTIs and

5 PIs, including all drugs required for the recommended national regimens) on the National Essential Drug List in September 2002 (Ministry of Health, Kenya, 2003).

MEDIMOC, a Mozambican pharmaceutical company, plans to import generic ARVs from Brazil and India, and 10 private pharmacies in Maputo and two in Beira have been authorised to sell generic nevirapine and other ARVs. The number of distributors is expected to increase in future, but these must be authorised by the provincial health directorates.

Brazil, India, Thailand and China are all manufacturing generic ARVs. In China a number of policy initiatives have been taken including: waiving imported ARV drug tariffs; fast tracking all ARVs for registration by the State Drug Administration; and licensing 2 domestic companies to manufacture 4 off-patent generic ARVs (Desano is manufacturing ddI, d4T and NVP, and Northeastern Pharmaceuticals is manufacturing ZDV). Some African countries are investigating the potential for local manufacture. Ethiopia is encouraging the private sector to produce generic drugs, and is one of only 2 African countries – the other is South Africa – to receive technical support to start producing ARVs (IRINnews, 5th August 2003). Ghana is discussing technology transfer for local manufacture, and has identified two local manufacturers and signed an agreement with the Thai government for local production of ARVs. The government is taking a multi-faceted approach to ARV provision in Ghana, using funding from the Global Fund to procure drugs and considering ways to procure generics at lower prices, alongside exploring options for local manufacture.

A recent article in the Lancet (Galvao, 2002), reviewed the issue of access to ARVs in Brazil, including government strategies for acquisition and the logistics of drug distribution. While many of the ARVs used in Brazil are produced domestically, some of the most expensive drugs are purchased from abroad, and the continuing high cost of these drugs threatens the Brazilian policy of free distribution of drugs.

Procurement of reagents can also be problematic. The JCRC in Uganda has reported difficulties in importing laboratory reagents that are not produced locally (Nanyumba et al, 2002).

3.3 Clinical management

Standard guidelines

WHO has produced guidelines for scaling up ART provision in resource-poor settings, which address issues such as when to start therapy, recommended first-line and second-line regimens, and regimens for pregnant women, children and TB patients, in addition to recommendations for promoting adherence, monitoring resistance, and clinical and laboratory monitoring of ART use (WHO, 2000; 2002a). Simplified treatment regimens and laboratory monitoring, and the inclusion, since April 2002, of 12 ARVs in the WHO Model List of Essential Drugs (WHO, 2002), have significantly reduced the complexity of treatment.

Despite this, there are areas where additional clinical research, to inform use of ART in resource-poor settings, is required (see Annex 1) (Rabkin, 2002). A key issue is the point at which ART is initiated. WHO recommends that in resource-limited settings adolescents and adults at stage 4 of disease progression should start treatment regardless of CD4 count. Where lymphocyte count can be assessed, people with stage 2 or 3 disease should also be offered treatment. Where CD4 tests are available, all HIV infected people with cell counts less than 200 should be offered

treatment. However, there are several AIDS case definitions in use, not all of which are harmonised with the definition of stage 4 in the WHO stages of disease progression. Some, for example the CDC definition, require intensive diagnostic evaluation to establish an AIDS diagnosis, which is not feasible in many resource-poor settings. The use of different definitions in different countries means that treatment approaches vary. WHO and UNAIDS have identified a need for congruence, both for clinical and surveillance purposes (WHO/UNAIDS, 2003).

In addition, some clinicians have questioned international guidelines, which are based on data from clinical trials in developed countries and recommend starting patients on ARV drugs with AIDS-related symptoms or very low CD4 cell count. They argue that these guidelines may be less useful in settings where most HIV-associated morbidity and mortality is due to infections that occur in patients with CD4 cell counts above 200, and maintaining a healthy lifestyle, including access to good nutrition and medical care, is not feasible for most individuals with HIV infection, highlighting the need to look critically at the potential benefits of starting treatment earlier (Mwanakasale, 2003; Reynolds, 2003).

National guidelines on standardised first-line and second-line regimens, eligibility criteria for starting ARV therapy, and patient monitoring are essential, to assist planning of drug procurement, limit the number of drugs to manage, predict patterns of resistance, simplify training of health care providers using standard clinical management protocols and education of patients, and develop simple and effective monitoring and evaluation systems. CDC is developing standardised treatment regimens, criteria for initiating and changing therapy, and simplified laboratory monitoring using alternatives to CD4 and viral load tests (AIDSMAP, 2002).

Although experience has shown that it is feasible to follow standardised treatment regimens in resource-poor settings, ensuring compliance with guidelines can be a challenge. For example, the USAID-funded PHRPlus project noted that, contrary to national guidance, some patients in Zambia and Mexico are still on mono and dual therapy, and identified reasons including lack of mechanisms to enforce national guidelines, cost of triple therapy and poor prescriber training and skills.

More specific considerations in selecting first-line therapy in resource-poor settings include cost, availability, generic formulations, food restrictions, resistance, adherence, PMTCT, cold chain, future options, drug interactions, prevalent OIs, pregnancy, drug hypersensitivity, hepatotoxicity, co-infections, and DOT programmes. In areas with high TB prevalence, it is also important to consider the number of pills patients need to take for both TB and HIV treatment, drug interactions (for example, the anti-TB drug rifampicin induces liver enzymes that the body uses to break down some anti-HIV drugs, resulting in reduced levels of ARV drugs in the body, which may lead to drug resistance), increased likelihood of side effects in patients taking several drugs and the difficulty in working out which drug is responsible when side effect profiles overlap.

Clinical guidelines need to describe how to manage adverse events. In China, patients who have adverse effects will first seek help from village doctors or the city or provincial medical team (it is provincial policy to send medical teams from provincial and city levels to township and village levels to provide medical service for poor villagers) via the village clinic. For those patients with serious side effects, village doctors will report to the county CDC, which will decide whether or not to stop treatment.

Maximising the benefits of HAART also requires that patients have access to prevention and treatment of OIs. Uganda, Cote d'Ivoire and Senegal are among the African countries to have introduced national policies for prevention of OIs along with the introduction of ARVs (UNAIDS, 2002).

Alternative treatment protocols

Despite price reductions and standard treatment regimens, HAART remains relatively expensive and complex. Colebunders et al (2003), reviewing potential, less costly, alternatives to HAART in resource-poor settings, suggest that structured treatment interruption looks the most promising. One randomised controlled trial found no difference at 36 weeks of treatment in viral load or CD4 count between patients on continuous therapy and patients on 3 weeks on, 3 weeks off treatment. In Thailand, HIV-NAT conducted a study of structured treatment interruption and found that using CD4 cell count to guide the resumption of therapy was just as effective as a 1 week on, 1 week off approach, in terms of preventing clinical illness (Ananworich J et al, 2003).

More trials are being conducted to compare HAART with structured treatment interruption, including the multi-centre Strategies for Management of ART (SMART) study in the US and Australia, and a similar study in Cote d'Ivoire. The Liverpool School of Tropical Medicine is leading a consortium of researchers in the Development of ART (DART) randomised controlled trial to evaluate structured treatment interruption (3 months on, 3 months off). Recruitment started in January 2003 and 3,000 symptomatic ART-naive adults from 3 sites (2 in Uganda, 1 in Zimbabwe) with CD4 <200 cells will receive 3-drug ART (first-line and second-line) and be followed for up to 5 years (Kityo, 2003). The London School of Hygiene and Tropical Medicine also reports on a proposal to trial continuous versus interrupted ART among mineworkers in South Africa (Grant, 2002).

Following its pilot ARV programmes in Yaounde, Cameroon and Guatemala City, Guatemala, which started in 2000, MSF Switzerland concludes that increasing access to treatment outside capital cities will require simplification of treatment protocols so that ARVs can be provided at local treatment sites, as well as clear guidance on strategies such as interrupted treatment (Calmy, 2002). Strategies will be needed for DOT for structured treatment interruption, such as blister packs that include placebos or vitamins for the time periods when patients are not supposed to take ARV drugs. MSF has also highlighted the need for affordable and appropriate drugs for paediatric use and, in particular, for paediatric fixed dose combinations (MSF, 2003a; 2003b).

HIV-NAT also studied the feasibility of dose reduction of two NRTIs, as an approach that could reduce treatment costs (UNAIDS, 2000b). A retrospective cohort analysis of patients treated between 1995 and 1999 in Chiang Mai, Northern Thailand, found that dual combination therapy, considered to be sub-optimal by WHO, was associated with a 57 per cent reduction in the death rate among people with advanced HIV, relative to those who received no therapy. The authors highlight the dilemma for physicians in resource-poor settings of treating a smaller number of patients with optimal therapy or a larger number with sub-optimal therapy, while the gap between the cost of HAART and dual regimens remains so great (Pathipvanich P et al, 2003).

Other potential alternatives include use of less expensive drugs, such as hydroxyurea or chloroquine, and boosting ARVs with less expensive drugs, for example, allopurinol increases didanosine levels and ketoconazole boosts indinavir

levels, but there is insufficient evidence to support the use of these approaches (Colebunders et al, 2003).

Clinical and laboratory monitoring

Monitoring is essential to assess the progress of patients receiving ART. Good quality laboratory facilities with well-trained staff are required to conduct CD4 or viral load testing and basic safety tests for side effects – WHO recommends, if possible, haemoglobin or haematocrit tests to check for anaemia, white blood cell count, and liver function tests to look for early signs of damage to the liver. However, in many resource-poor settings, laboratory services are inadequate. The Zambian Ministry of Health has stated that monitoring will be difficult because there are only 2 centres for CD4 and viral load testing in the country (www.irin.org April 1st 2003; www.journa-aids.org).

In addition, whilst the price of antiretroviral drugs has fallen, the price of CD4 (approximately $25) and viral load (approximately $150) monitoring tests has not. Many countries, and patients, cannot afford these tests in addition to the cost of ARVs (Nkengasong, 2002). In Uganda, for example, fewer than 30 per cent of clients accessing ART through the Joint Clinical Research Centre (JCRC) could afford to pay for CD4 and viral load monitoring (Atwiine, 2002; Weidle et al, 2002).

Current approaches to support scaled up access to ART in resource-poor settings include strengthening laboratory services, simplifying monitoring, using low-cost alternatives to CD4 tests, negotiating reduced prices of tests and reagents and replacing proprietary agents with cheaper generic alternatives, and developing cheaper new technologies and assays for laboratory monitoring (WHO, 2003).

In Brazil, the Ministry of Health established in 1997 a network of public laboratories to provide CD4 and viral load testing for patients free of charge. A computer system, SISCEL, gathers information from public laboratories and tracks test results and changes in CD4 and viral load for use by clinicians. The MSF Switzerland pilots in Yaounde and Guatemala City concluded that efforts to improve access to laboratory monitoring will be required to support scaled up provision of ART outside these capital cities. The evaluation of the UNAIDS DAI pilots reached a similar conclusion, noting that there is a need to improve the feasibility and sustainability of laboratory monitoring.

Some have argued that simplified approaches involving greater reliance on clinical markers, such as weight, and limiting the frequency of CD4 tests to once every 6 months, unless there is serious clinical deterioration, are adequate for individual patient monitoring, and that use of viral load testing should be limited to monitoring for resistance at national referral centres. The MSF South Africa pilot (WHO and MSF, 2003) focuses on assessing the clinical status of patients receiving ART, every week for the first 2 weeks, then every 2 weeks until the end of the second month, then every month. Once patients are stable on therapy, they are assessed every 2 months. Where necessary, laboratory tests are done by National Health Laboratory Services centres. The DART study is assessing the feasibility and effectiveness of clinical monitoring with and without CD4 counts and laboratory monitoring for toxicity (Kityo, 2003). The Perinatal HIV Research Unit of the WITS Health Consortium in Johannesburg, South Africa has been awarded a $21.3 million grant over 5 years by the US Institute of Allergy and Infectious Diseases, and will evaluate simple, inexpensive methods to monitor disease progression and the effectiveness of ART (US Department of Health and Human Services, 2002a).

Flanigan et al (2002) propose total lymphocyte count (TLC) as a possible surrogate for CD4 cell count in resource-limited settings. Cheaper but less accurate indication of CD4 count can be obtained using TLC, and can be done by most laboratories in developing countries. However, to date TLC has mostly been used to decide whether or not to initiate therapy rather than to judge the success or failure of treatment.

The Forum for Collaborative HIV Research, which met in April 2002 and involves WHO, USAID, CDC, ANRS, Rockefeller Foundation, PharmAccess International, the diagnostic industry and a range of research programmes, is working to support transfer of diagnostic and monitoring technology to resource-poor settings, including tracking new developments and facilitating clinical validation and acceptability of alternative technologies (www.hivforum.org). The Forum has established working groups on viral load and CD4 assays to set priorities for further research and create a network of test sites in developed and developing countries. WHO has initiated research and field-testing of cost-effective and simple tools (Vercauteren, 2002), and CDC reported in Barcelona that researchers working in Uganda in collaboration with the Ministry of Public Health had found that significantly cheaper CD4 test ($5.00) and viral load monitoring ($30.00) technology performed effectively and was comparable with standard tests in use (US Department of Health and Human Services, 2002b).

The gold standard for CD4 count is flow cytometry, but this requires a cytometer. The cost of this equipment (approximately $35,000), the annual maintenance contract (approximately $6,000 a year) and reagents (approximately $12 per test), is too expensive for many countries.

The most affordable way of quantifying CD4 cells is by manual technologies, using synthetic beads and microscopy. Currently the most efficient methods for low-volume applications are Dynabeads and Cytospheres. Dynabeads cost $3 per test and need an investment of $750 for a magnet and mixer. The original technology also requires an expensive immunofluorescence microscope, costing $7,500, but alternatives include use of alternative staining techniques compatible with light microscopy or purchasing a device, costing $1,800, that converts a light microscope into a fluorescent microscope. A paper presented at Barcelona reported on an ANRS multi-centre study of Dynabeads in 6 West African countries. The results were encouraging and the cost per assay was less than US $10.00 (Hopkins HIV Report, 2002). Cytospheres, which have been approved by the US FDA, are easier to use and cost $9 per test, although they only require investment in a light microscope and a hemacytometer. At least 9 studies in Africa have correlated CD4 counts assessed by Cytospheres or Dynabeads with counts measured by flow cytometry. In most, but not all, correlation has been excellent. However, these technologies have some disadvantages. Reading the results is labour intensive and requires trained technicians, so the number that can be done each day is limited. WHO recommends further evaluation of both methods in a multi-centre study before they can be recommended for laboratories in developing countries.

Other technologies under development include affordable, portable CD4 counts using microchips (Rodriguez et al, 2003). Alternative flow cytometry-based methods, and non-flow cytometry-based devices are also in various stages of development (de Wit, 2002). The PanLeucogating (PLG) protocol, a flow cytometry-based system developed by the AffordCD4 Initiative has the potential to reduce the range of reagents used and to improve the accuracy of testing, as well as to reduce the cost. Uptake of this technology by the South African National Health Laboratory Services (NHLS) reduced the cost from $24.00 to $8.30 per CD4 test. Negotiations between

NHLS and manufacturers of viral load kits have also resulted in a slight decrease in the cost per test to $45.00.

A heat denatured HIV p24 assay is currently being evaluated as an alternative to PCR-based and bDNA-based viral load assays. This assay has excellent sensitivity and specificity in diagnosing infection with HIV-1 sub-type B, and has performed well as a clinical monitoring tool and a correlate of disease progression; establishing its assay's value in people infected with non-B viruses is a priority (www.hivforum.org).

Drug resistance

Resistance testing is important both for individual patients and for surveillance. Trials have shown that prescribing based on treatment history, the only realistic alternative, is inferior to resistance testing. As of November 2002, in Brazil, the laboratory network had 60 physicians trained to provide a reference service, and the Ministry of Health had acquired 6,000 test kits to be used in people experiencing treatment failure, with a viral load above 5,000, on ARV combinations that include at least one protease inhibitor (PI) (Dantas, 2002). However, in most countries, resistance testing for individual patients will be difficult to afford and laboratories are not currently equipped to carry out the tests. In such settings, WHO (2002) recommends that consideration be given to using resistance tests as a surveillance tool, for example, to track the acquisition of drug-resistant virus in people who have recently acquired HIV.

The development of drug resistance is a key concern in the context of scaling up access to ART in resource-poor settings. In the Uganda DAI pilot, resistance testing was performed on 44 specimens from 30 patients, 14 on 2 NNRTIs and 16 on HAART. Resistance to NNRTIs, especially 3TC, was common, which is expected when it is used outside of triple therapy, but was less so for NRTIs or PIs. The regimes used for the most part were not HAART as the third drug required was not affordable for most patients, and more patients on the more affordable regime developed drug resistance, indicating that use of 2 NNRTIs may promote more rapid emergence of drug resistance (Weidle, 2001; Weidle, 2002). At the XIII International AIDS Conference, high levels of genotypic and phenotypic resistance to one or more ARV drugs in a cohort of 68 patients being treated under the DAI were also reported from Cote d'Ivoire. Results of the genotypic analysis revealed that 57 per cent of samples contained resistance mutations, most frequently to ZDV and 3TC. The phenotypic analysis indicated 40 per cent of samples had resistance to any one NRTI.

At the 9th Conference on Retroviruses and Opportunistic Infections, Miller et al (2002), from the Innovir Institute in Johannesburg, South Africa, reported on the significant prevalence of drug-resistant HIV-1 in southern Africa, despite previously low rates of ARV use. They reported genotypic test results on 120 patients from South Africa (87), Botswana (31), and Zimbabwe (2) who were failing ART. Thirty were failing their first HAART regimen and 90 were no longer responding to subsequent therapies. The results were: 15 samples (11 per cent) – no recognised resistance mutations detected; 11 samples (8 per cent) – resistance to 1 class of antiretroviral agents (ARV) detected; 104 samples (77 per cent) – resistance to 2 or more classes. There is also some evidence, for example from the Uganda HIVNET 012 trial, that mothers can rapidly become resistant to nevirapine used for PMTCT (JSI, 2001) although, in July 2003, based on the final report (March 2003) of the reassessment of the HIVNET 012 trial and further research in South Africa which has confirmed the safety and efficacy of nevirapine, WHO reconfirmed its support for the use of nevirapine for PMTCT (www.who.int/reproductive-health/rtis/nevirapine.htm).

However, a World Bank meeting in June 2003 (Provision of ARV therapy in resource-limited settings: challenges of drug resistance and adherence) concluded that there was no empirical evidence that viral resistance is more of a problem in developing than in developed countries. In Brazil, the prevalence of resistance has increased as access to ARVs has expanded, but rates of resistance are considerably lower than in developed countries. In 2001, 6.6 per cent of new infections involved drug-resistant strains, a third to a half of rates reported in the US and Western Europe. The Brazilian government-sponsored national Network for Drug Resistance Surveillance collects samples from treatment-naïve people in 21 cities from 9 states. A study of recently infected people from 13 VCT centres found low rates of primary infection with resistant virus. Among isolates analysed, 2.2 per cent were found with primary PI mutation and 2.4 per cent with primary NNRTI mutation (Mascoloni, 2002).

In contrast, there is increasing evidence of transmission of resistant strains of HIV in the developed world. In the US, 50 per cent or more of ARV-treated patients exhibit viral resistance, and 5-15 per cent of newly infected patients in the US and Western Europe have resistant virus, attributed to sub-optimal therapy in the pre-HAART era. The results of a recent 17-country study of drug resistance mutations in 1,633 patients in Europe found that 10 per cent of newly diagnosed patients were resistant to at least one ARV (Das, 2003).

The Bank meeting concluded that concerns about resistance should not delay scale up and that the most effective strategy for minimising the development of resistance will be to ensure that distribution of ARVs occurs in the context of practices and procedures that promote rational drug use and encourage patient adherence (www1.worldbank.org/hiv_aids/WHOIATCMeeting.asp).

WHO has established the Global HIV Drug Resistance Surveillance Network to assist countries in monitoring, review resistance prevalence, improve understanding of factors that lead to resistance, and identify strategies to minimise the emergence and spread of drug resistance (www.who.int/hiv/strategic/mt300703/en/).

Various studies are already being conducted to monitor resistance. For example, the Adult Antiretroviral Treatment and Resistance Study in Botswana, established in 2000 to: compare the time to virological failure between randomised groups of patients initially receiving 1 of 4 HAART regimens; compare the time to significant drug resistance between randomised groups of patients initially receiving 1 of 4 HAART regimens; fully characterise the genotypic patterns of resistance under selective drug pressure in HIV-1C infected individuals and compare these to HIV-1B primary and secondary resistance mutations; compare the time to virological failure and significant drug resistance between randomised groups of patients initially receiving 1 of 2 adherence strategies (the current Botswana standard-of-care adherence strategy and the current Botswana standard of care plus community-based directly observed therapy); and evaluate the time to development of treatment-related toxicity as measured by a clinical event or a laboratory-determined adverse event among all treatment groups.

Promising advances in diagnostic techniques for monitoring resistance have recently been reported: using different assay techniques to measure replication capacity (Mo et al, 2003) and using a single genome sequencing approach (Kearney et al, 2003).

Review of experience indicates that strategies to minimise the development of resistance include: strengthening health systems and human resource capacity; identifying standardised treatment regimens of fixed-dose therapies and drug

combinations that minimise resistance; identifying and implementing strategies to improve the quality and effectiveness of ARV treatment programmes, promote patient adherence and actively involve patients, families and communities; supporting the development and implementation of simplified clinical monitoring and measures to monitor ARV resistance; and improving regulation of the availability of ARVs in developing countries. It is also particularly important to ensure reliable drug supply to avoid the problems seen early on in Gabon and Cote d'Ivoire where erratic supply resulted in high levels of drug resistance (Reynolds et al, 2003).

3.4 Demand and adherence

Uptake of ART

Expanding the supply of ARV drugs alone will not achieve increased access to ART. Even where ART is available and there are many people with HIV, demand is sometimes lower than expected and many patients start treatment when they are at an advanced stage of disease. Barriers to uptake (UNAIDS/WHO/Alliance, 2002) are:

- Organisational – for example, attitudes of health workers, lack of staff, drugs and supplies, confusing procedures, corruption.
- Physical – for example, lack of transport, distance to health facilities, lack of access to VCT.
- Social – for example, stigma and discrimination, lack of knowledge, denial and misinformation.
- Financial – for example, poverty, cost of drugs, user fees and other charges, cost of transport, lack of medical insurance schemes.

Programmes aiming to scale up access to ART will need to address these barriers, and to encourage people to come forward earlier for diagnosis so that treatment can be started sooner.

Horizons report that, in a PMTCT programme in Zambia, misconceptions about ARVs and rumours that the drugs harm or kill an unborn child resulted in some women refusing to take ARVs after they have brought them home from the clinic. In one clinic in Kenya, several women returned the drugs because of opposition from their husbands (Horizons, 2001).

A review of the needs of home-based care clients in Malawi noted that only 26 per cent knew their HIV status (van Praag, 2001). The author concludes that, without effective public education and wider access to VCT, uptake of ART will be limited.

In Malawi, only upper middle class patients who could afford to pay $35 a month were able to access ARV medication when it first became available in October 2001 (Hosseinipour et al, 2003). Uptake at the Lighthouse ARV clinic was slow to start with, and this was attributed in part to the high initial cost of drugs.

In Uganda, the average cost of the triple regimen in the DAI was the equivalent to the salary of the highest paid government official. 60 per cent of patients enrolled were men. During the pilot period, the cost of a month's therapy for 2 NRTIs was $214-406; for HAART including a NNRTI $440-660; and for HAART including a PI $531-708. Although drug prices in dollar terms reduced or remained stable during the pilots, the costs to patients increased due to currency devaluation. High costs excluded the poor and women, who tend to be disproportionately poor. Until recently, only patients who could afford to pay – an estimated 10 per cent of PLHA – have had

access to treatment in Uganda, and doctors have had to turn away patients who cannot afford to pay (www.irinnews.org).

There has been little research to assess how treatment is paid for, and what impact this has on households. One of the few studies conducted, in Senegal, where drugs prices are lower and subsidies are available, reported that paying for ARVs took up 14 per cent of household income (Sylla, 2000).

The Mildmay Centre in Kampala, Uganda conducted a survey to find out why, despite reduced drug prices, uptake of ARVs by patients did not increase. The survey found that limited knowledge and negative attitudes towards ARVs, on the part of health workers and patients, were the main limiting factors. Following efforts to increase health worker knowledge and to use people already taking ARVs to educate others about the therapy, the number of patients increased from 102 in 1999 to 416 in 2001. Compliance with therapy and routine check ups for viral load and CD4 counts also improved. Increased awareness resulted in the formation of a support group, which shares experiences, provides mutual treatment support, and educates others in the community (Tumusiime, 2002).

In Botswana, a key concern of the National AIDS Coordinating Agency is low uptake by pregnant women, a priority target group for the national treatment programme. Contributing factors include stigma associated with HIV/AIDS and women who do not breastfeed, and the unequal status of women, who need permission from husbands, parents or in-laws to seek HIV testing or other medical care. A study in Cote d'Ivoire found that only 151 of 754 positive women availed themselves of PMTCT services at 3 community-based antenatal clinics, and the authors recommended investigation of missed opportunities and the potential for community mobilisation (Ekouevi, 2002).

In Nigeria, where uptake of ARVs is reported to be poor, advocacy groups have identified stigma associated with an HIV diagnosis as a significant barrier. The experience of International HIV/AIDS Alliance partners indicates that discrimination, including by health workers, deters people from seeking care, even when ART is available, and highlights the need for interventions to tackle discriminatory attitudes and to help PLHA fight stigma (International HIV/AIDS Alliance, 2002). However, there is also some evidence that availability of treatment can help to reduce stigma and discrimination. As one patient involved in the MSF pilot programme in Malawi reported in Barcelona, treatment 'is the best tool against stigma', as people do not reject you when you look and feel better (Minandi, 2002).

Private sector firms have also found that uptake of ART among employees is often poor, because of concerns about the impact on employment rights of disclosing HIV status to the company. The International HIV/AIDS Alliance and the Futures Group Policy Project report cases of employees covered by private company insurance schemes choosing not to request reimbursement for similar reasons. Involving private insurance companies and other financing schemes and providing them with information about the cost of AIDS-related care and sensitisation on management of confidentiality, establishing legal referral centres to address concerns about employment rights, and developing human rights indicators to evaluate programmes are some of the strategies proposed by USAID-funded implementing agencies, based on experience in a range of countries (Synergy Project, 2003).

An International HIV/AIDS Alliance needs assessment of access to treatment in India, Zambia and Cote d'Ivoire (International HIV/AIDS Alliance, 2001) concluded that increasing uptake requires strategies that:

- Reduce stigma and discrimination.
- Provide ARVs in the context of comprehensive care and a continuum of care.
- Promote appropriate attitudes, skills and behaviours in treatment providers and beneficiaries.
- Provide accurate and accessible information.
- Involve PLHA and their families and communities.

Adherence to treatment

Good adherence to ART is essential to achieve sustained suppression of viral replication and to prevent the onset of resistance. Concerns have been raised about whether patients in resource-poor settings will be able to follow the strict treatment regimen required for ART to work effectively, but studies have shown that programmes in resource-poor settings can achieve adherence rates similar to those seen in rich countries (Laurent, 2002; Kityo, 2002), in some cases without interventions to support patient adherence.

An assessment of the Uganda DAI pilot reported an adherence rate of 88 per cent, based on self-reported data collected from 221 patients (Weidle et al, 2002). A recent study (Orrell et al, 2003) in South Africa found good rates of adherence among 289 patients, many of whom were living in extreme poverty, enrolled in ARV trials at a government hospital in Cape Town. Adherence of 90 per cent was maintained by 63 per cent of patients, despite the fact that there were no interventions to support patient adherence. The authors note that limited access to ARVs in South Africa may have been an important motivating factor.

However, in most programmes, measures have been taken to promote adherence. The most effective programmes appear to be those that employ a combination of simplified and affordable treatment regimens, and patient education and support (including directly observed therapy) (Rabkin, 2002). In Brazil, for example, high rates of adherence are attributed to affordability, fixed dose combinations, community participation, involvement of civil society organisations, and support for adherence provided through adherence groups and support houses (Vitoria in WHO/UNAIDS, 2003).

The MSF pilot programme in Khayelitsha, South Africa, has achieved high rates of adherence. Preliminary results from a clinic-based, self-reported evaluation indicate that 89 per cent of patients demonstrate adherence of greater than 95 per cent after 3 months on treatment. This is attributed to use of simplified and standardised regimens that minimise the number of pills the patient has to take, dosages and the risk of side effects, and steps to ensure that patients fully understands the treatment and have a good support system. To help promote adherence, MSF only provide a month's supply of ARVs to patients at each clinic visit and treatment candidates must attend the clinic for 3 months before starting ARVs. Most are receiving prophylaxis for TB or PCP, so health workers can assess their pill taking habits. Workers also visit patients at home to ensure family support. MSF has developed a patient-centred education programme, which combines individual, peer and practical support:

- Individual support – all patients who enrol are required to identify a treatment assistant, usually someone living in the household, who is aware of the patient's status and is willing to assist with medication as necessary. Lay counsellors in the clinics are available to help patients develop an individual adherence plan. If there are serious problems with adherence, a nurse or counsellor visits the patient at home.

- Peer support – twice a month, the clinics host support groups for patients on ART. This enables patients to discuss barriers to adherence, side effects, disclosure and other psychosocial issues that affect them. A counsellor runs regular adherence sessions during the support group meetings.
- Practical support – patients are given pillboxes and drug identification charts, daily schedules, diaries and educational materials explaining the benefits and risks of ART.

In the MSF pilot programme in Chiradzulu, Malawi, adherence support involves trained counsellors, adherence plans, a treatment assistant (usually someone living in the household of the PLHA), and ARV support groups, which allow discussion of barriers to adherence, adverse events, disclosure and other psychosocial issues (WHO, 2003). The patient from this programme, quoted earlier, reported that he has not missed one dose of his treatment. He attributed this both to the time taken by staff to explain how the drugs work, possible side effects, and the importance of strictly following the treatment regimen, and to participation in a PLHA support group. Group members explain how to cope with side effects to new patients, collect drugs for patients who are too sick to come themselves, and help to ensure that those who cannot tell their families about their HIV status take their drugs (Minandi, 2002).

MSF in Cameroon visits patients once a month when treatment begins and then as often as necessary to foster adherence. A pharmacist dispenses enough pills for a week and verifies adherence by interview at each visit.

The International HIV/AIDS Alliance, reporting on a study of PLHA involvement in Burkina Faso, Ecuador, India and Zambia, also highlighted the important role of support groups in promoting ART literacy and adherence to treatment, and of involving PLHA with first-hand experience of ART as treatment educators. For example, one PLHA group in Ecuador, which has a good working relationship with local hospitals and doctors, provides advice about the medications, dosages, and side effects to people starting on treatment. The Alliance concludes that the involvement of PLHA, in educating communities and patients, promoting openness, and providing counselling and psychosocial support, will be a critical component of scaling up ART provision

Early indications from the Botswana programme are that few patients have difficulty adhering to ARV regimens. The programme uses a ‘buddy system’ where each patient is encouraged to form a special bond with someone who makes sure they take their medication (Rollnick, 2002). Similarly, in Thailand, strategies that have helped to promote adherence include training people with HIV as peer educators, and integrating peer support through PLHA groups and day centres into clinical services (Srithanaviboonchai, 2002b).

In a pilot project in Rio Grande do Sul, Brazil, participation by pregnant women taking ARVs in weekly meetings of a ‘Group of Adhesion’ was found to increase adherence to treatment, and 90 per cent of those attending the meetings showed improvement in CD4 and viral load measurements (Rosa, 2002). Women attending Kenyatta Hospital in Kenya, are given a timetable that they mark each time they take a tablet to help them to adhere to their ARV regimen; they are also asked to return with their drugs to check adherence. In Zambia, where many women give birth at home, traditional birth attendants (TBAs) have been enlisted to help ensure women get their labour dose of ARV. TBA births are registered at the health centre, where a health worker checks that the woman received her dose of ZDV (Horizons, 2001). Horizons recommends several practical steps to promote ARV use for PMTCT: sensitising communities; stressing the benefits for mothers; training TBAs and using the birth

registration system to monitor use of ARVs outside health facilities; training labour and delivery staff; and strengthening links between ANC and delivery care.

The AIDS Healthcare Foundation, stresses three factors that enhance ARV adherence: on-site support by NGOs, ongoing education by peers who are also in ARV therapy; and involvement of family members before and during treatment (Mascoloni, 2002).

A high pill burden is associated with poor adherence (Dansburg et al, 2003), and adherence may be more difficult for patients who are on both ART and anti-TB treatment and have to take a large numbers of pills. In Senegal, a small study assessed the feasibility of a once-a-day HAART regimen (combining ddI, 3TC and EFV) in ARV-naive patients with advanced immune deficiency. 40 HIV-1 infected patients were treated over 24 weeks. Of the 23 patients who reached week 24, all but one had a significant decrease in viral load. The researchers concluded that a simple once-a-day HAART regimen might help increase adherence in developing countries. Further evaluation of long-term efficacy is ongoing (Landman, 2001).

To promote adherence, treatment regimens need to meet the following criteria (AIDSMAP, 2002):

- Small number of pills – pill taking is not common in some countries, where there is a preference for receiving medicine by injection.
- Simple once or twice daily dosing schedule that fits with daily life – for example, in contexts where people do not eat three times a day., and systematic review of studies investigating adherence for other chronic conditions showed that adherence is significantly better with twice rather than thrice daily dosing.
- Ease of storage – for example, in contexts where refrigeration is not widespread and disclosure of status is an issue.
- Constancy of drug supply – reliable supplies are essential for individual adherence.

Fixed-dose combinations, which reduce the number of tablets taken to one twice a day or three once a day, are increasingly available on the market. Accelerating access to these simplified regimens in resource-poor countries will facilitate the achievement of high rates of adherence.

Lack of financial resources is a significant barrier to adherence in settings where patients have to pay for, or contribute towards the cost of, treatment. In Malawi, the Lighthouse Trust has experienced difficulties in enforcing payment from clients, and lack of funds is almost always the reason cited by clients for discontinuing therapy (Boxshall, 2002). In Uganda, the JCRC centre reported that poverty was a significant barrier to adherence, and an assessment of the DAI pilot, where patients were fully responsible for treatment costs, found that financial barriers were the reason for non-adherence in 33 per cent of cases (Weidle et al, 2002). When counsellors at the Mildmay Centre in Kampala talked to 100 ART defaulters to identify the reasons, they found that 60 per cent defaulted because of poverty (Bakunda, 2002). Many providers in Uganda reported that patients interrupted therapy during a brief period of severe currency devaluation in May 1999 (Weidle, 2002). A study in Botswana found that the main barriers to adherence were financial (44 per cent) (Hopkins HIV Report, 2002)

In contrast, analysis of the pilot programme in Senegal found high adherence among patients that receive ART free of charge, with 91 per cent adherence over 24 months from November 1999 to October 2001 among 164 patients and no missed doses

reported during the 69 per cent of the months of follow up (median 10 months). With the four-fold decrease in prices in November 2000 and wider access to 100 per cent subsidy, lack of resources has become a rare cause of non-adherence. (Diop, 2002; Taverne, 2002).

Poor management is a factor in poor adherence. Indian researchers from Mumbai reported on 200 patients previously treated with ARVs by other doctors, whose treatment had been seen to 'fail'. Only 10 per cent, all of whom had been on 'protease sparing regimens', had adhered properly to their regimen, 32 per cent were illiterate, and only 10 per cent had received any counselling before starting treatment. More than half had interrupted treatment because of claims of miracle cures by traditional healers. Dual drugs had been used by 70 per cent, monotherapy by 23 per cent, incorrect doses in 80 per cent of cases, and in 61 per cent ARVs were given without treating OIs that were present (Saple et al, 2002).

Adverse effects are also associated with poor adherence. The Thai Ministry of Health pilot programme in Northern Thailand found that, of the 243 patients who discontinued treatment, 101 had done so due to adverse events, especially nausea, dizziness, vomiting, diarrhoea and headache. Counselling patients about potential side effects, how to cope with minor adverse effects and what to do if there are serious reactions, and effective management of side effects, should be an essential component of ART programmes (Srithanaviboonchai, 2002b).

A number of other factors contribute to poor adherence or treatment interruption. In Uganda, poor adherence was associated with inaccessibility of drugs as well as low monthly income and inability to purchase drugs (Tusiime J et al, 2003). Other reasons given by ART defaulters at the Mildmay Centre were related to gender and culture (15 per cent), lack of disclosure to spouses, children or employers (13 per cent), lack of understanding (7 per cent), loss of hope (3 per cent), and side effects (2 per cent). As a result, ART counselling and awareness has been strengthened (Bakunda, 2002). In the assessment of the DAI pilot, other reasons given for non-adherence were 'adverse effects' (17 per cent), 'did not think medicines were working' (6 per cent), 'did not understand directions' (5 per cent), and 'too many pills' (4 per cent) (Weidle et al, 2002).

Other barriers identified in the Botswana study were stigma (15 per cent), migration (10 per cent), side effects (9 per cent) and lack of food (7 per cent) (Hopkins HIV Report, 2002), while in the Orrell study, where treatment was free, factors associated with poor adherence were youth, three times daily dosing, and language. Patients whose home language was not English were less adherent, possibly because dosing instructions were given in English by hospital staff.

3.5 Community involvement

Preparedness and mobilisation

Uganda and Cote d'Ivoire have explicitly involved community members in pilot programme design through participation in the advisory boards of the DAI (WHO, 2003). Community preparedness for the availability of ART determines how people understand ARV treatment, their health-seeking behaviour and the acceptability of treatment.

Experience indicates that uptake and adherence are lower if communities are poorly prepared but, conversely, that working in partnership with PLHA and their families and communities can help to overcome barriers to accessing treatment, especially

discrimination and stigma. However, health providers are often unaccustomed to sharing responsibility with communities in this way and have few incentives and little time to work in partnership; and communities may lack the necessary structures and understanding to engage in dialogue with health professionals. Planning and budgeting for appropriate training for health providers and education and capacity building for communities will be critical to the success and sustainability of expanded ART programmes (WHO, 2003).

A recent WHO and UNAIDS meeting also highlighted the need for community preparedness, emphasising that, unless approaches are informed by local conditions and understanding of community culture, beliefs and behaviours related to illness, programmes could face unanticipated community responses, for example, misconceptions and rumours, resulting in sub-optimal uptake and adherence (Obermeyer in WHO/UNAIDS, 2003).

In 1999, the Population Council and International Center for Research on Women assessed community views in Botswana and Zambia to identify effective mechanisms for enhancing community involvement in PMTCT efforts (Rutenberg, 2002), and the Council's Horizons Project also documented responses to the introduction of PMTCT in Kenya and Zambia. Key issues identified included lack of understanding about pregnancy, stigmatisation of PLHA, influence of partners and other family members on decisions about uptake of PMTCT services, and the cultural importance of breastfeeding. Recommendations highlight the importance of:

- Formative community research using participatory methods.
- Integrated communication strategies that include education, counselling, behaviour change and social mobilisation.
- Interventions to reduce stigma.
- Social support for women, including support groups and capacity to make independent decisions.
- Participatory monitoring and evaluation.

It is also important to work with community organisations, PLHA groups, and those who influence knowledge and care seeking, such as traditional healers, private practitioners, pharmacists and the media.

In Brazil, PLHA groups and other civil society organisations have played a key role in community mobilisation as well as in advocating for the national policy of universal free provision of ARVs. In South Africa, civil society organisations, such as the Treatment Action Campaign, and PLHA have played an important role in educating communities about HIV/AIDS and treatment issues. HIV-positive volunteers working for the Campaign's project *Ulwazi* (knowledge) conduct activities in schools, clinics, churches and workplaces to raise awareness, provoke discussion, reduce stigma, and promote disclosure. Preparing communities in this way has been critical for both uptake of, and adherence to, treatment by patients attending the MSF Khayelitsha clinics (WHO and MSF, 2003).

Communication activities are critical to raising awareness and promoting community involvement. A regional consultation held by UNICEF and PAHO in Mexico in 2002, which reviewed experience of communication support for PMTCT, identified the need for a strategic and sustained approach to communication, for communication to target a wide range of audiences including community leaders, and for integration with other communication strategies.

Selection of beneficiaries

As ARV programmes are established in high-prevalence settings, it will not be feasible to provide treatment initially to all PLHA who could benefit. It is also important that communities are aware that not all those with HIV will meet eligibility criteria so that they understand why some people are refused treatment. There is growing recognition of the importance of community involvement in deciding who will receive treatment in contexts where ART is not yet available to all, to ensure that decisions are made in a transparent and equitable manner.

Programmes in South Africa and Thailand have demonstrated the benefits of involving community members in the selection process.

In the MSF pilot programme in Khayelitsha, South Africa, a committee of community members, PLHA, and clinicians unrelated to MSF reviews anonymous information about candidates and decides whether or not they will be enrolled, based on medical, adherence and social criteria. Community involvement in the selection committee has helped to reduce the risk of nepotism influencing decisions about who receives treatment and to increase community support and ownership of the programme.

Community advisory boards, made up of people with HIV, NGOs and CBOs, are involved in deciding which PLHA receive free ARVs and CD4 testing in Northern Thailand. Enrolment is based on an anonymous review of medical records by a panel of 4 health workers and 4 community representatives, with criteria including no prior ART, CD4 below 400, and symptomatic disease. This approach has helped to engage the community in supporting adherence to treatment and monitoring the programme as it expands (Srithanaviboonchai, 2002b).

3.6 Affordability and financing

ARV prices

Decreasing drug prices have been a significant factor in enabling governments to provide ART through the public sector. Prices have come down substantially, as a result of increasing competition and availability of generics. As of May 2003, the least expensive brand name combination recommended by WHO for low-income countries cost approximately $675 per person per year and the least expensive generic combination was just under $300 per person per year.

Local manufacture and export of generics from Brazil, India and Thailand have made a significant contribution to increased affordability of ARVs in resource-poor countries. In Brazil, the cost per patient of ARV therapy has fallen substantially since universal free provision was introduced in 1996, largely as a result importing or producing generics and using the threat of compulsory licensing to obtain drugs from pharmaceutical companies at more affordable prices (Rosenberg, 2001; Bastos et al, 2001). Brazil has also recently launched an initiative to provide free ARVs for 1,000 PLHA in El Salvador, Guyana, Dominican Republic, Colombia, Paraguay, Namibia, Burundi, Kenya, Burkina Faso and Mozambique. Brazil's government will spend US$1 million on the project, providing 100 patients in each country with drugs for a year. The 10 countries' governments will pay for treatment thereafter.

In 1992, Thailand committed to supply ARVs free to low-income patients. Although an interim review in 1995 concluded that the policy was not affordable (Gilks, 2001),

this year, it was announced that Thailand's Government Pharmaceutical Organisation is to begin production of a 3-drug combination tablet that will cost only $27 per month, a 75 per cent reduction in the cost of treatment with d4T, 3TC and nevirapine compared with current prices.

The Indian generic manufacturer, Cipla, sells a combination of ARVs in the form of a single pill that includes zidovudine, lamivudine and nevirapine (or alternatively, stavudine, lamivudine and nevirapine) for $29 per month.

By April 2003 in South Africa, MSF had cut the cost of ART to $536 per patient per year by using generic drugs and reducing the price of laboratory tests. MSF started to source generic ARVs from the Brazilian state manufacturer FarManguinhos in January 2002. To ensure these drugs met national standards, MSF sought and received authorisation from the South African Medicines Control Council (MCC). The cost per patient per day was $1.55, half that of the lowest price offered by proprietary companies to government ($3.00 per patient per day). Later in 2002, the cost of this Brazilian combination fell further, to $1.08 per patient per day. More recently, MSF received MCC authorisation to source drugs from other manufacturers, increasing the prospects of reducing the costs still further.

Oxfam conducted a study of generic competition, price and access to ARVs, using Uganda as a case study (Oxfam, 2002). Two significant events had improved access since 2000. First, 5 drug companies agreed to reduce the price of some ARVs under the UNAIDS scheme and, second, the JCRC started to import low-cost generics from India, increasing the number of patients it was able to treat. The paper concludes that generic competition is crucial, reducing the price of patented medicines dramatically; that relatively poor people will buy life-saving medicines, but make enormous sacrifices to do so; that there is a the need for systematic and transparent tiered pricing and to maximize the use of TRIPs. (After 2005, countries like Uganda will no longer be able to import generic versions of newly-patented drugs, because generic-producing countries like India will no longer be able to export them.)

Luchini and colleagues (2003) analysed ARV prices in Brazil and 13 African countries, looking at different models of procurement: Accelerated Access Initiative (bilateral negotiations at international level) – Benin, Botswana, Burkina Faso, Congo, Gabon, Kenya; multilateral decentralised process of negotiation at country level – Brazil, Malawi, Nigeria; and a combination of Accelerated Access Initiative and competitive negotiations – Burundi, Cameroon, Cote d'Ivoire, Mali, Togo. They concluded that, while there has been a significant decrease in ARV source prices, this is variable depending on the drug, and that while international support for negotiation has been positive, increased competition remains the main driving force for price reductions. Pressure on pharmaceutical companies has also played a part. In response to pressure, GlaxoSmithKline recently cut the price of ZDV/3TC by almost half, to 90 cents a day, for 63 developing countries including all those in sub-Saharan Africa (IATC, 2003).

An analysis of additional tests, procedures and out-patient visits associated with the provision of HAART concluded that the cost ranged from $70 per month to $140 per month. The World Bank estimates the cost at $67 per month, and Harvard, in estimating global costs, calculate non-drug HAART costs to be about $40 per month, although this would not allow for a full complement of tests to be performed. In practice, Brazil estimates that non-drug costs are about $30 per month (Forsythe, 2002).

Costing and sustainability

Kumaranayake et al (2002) reports on an economic planning model that costs ARVs and their delivery and strengthening and upgrading of health systems. Applying the model to 83 countries, the author concludes that achieving widespread coverage by 2015 would require additional annual spending of $6.8-9.2 billion for ARV treatment, (additional costs for prevention and care would total $8.8.7 and $5.8-7 billion respectively). Infrastructure costs are 17 per cent of prevention, 63 per cent of care and 25 per cent of ARV totals.

Countries with limited public sector budgets and large numbers of PLHA face or anticipate considerable difficulties. Only a few countries of the 19 that have supply agreements in place through the AAI (Gabon, Barbados, Trinidad and Tobago, Chile, Morocco, Romania) have been able to commit to fully subsidised ARV therapy; the other 13 have been unable to do so due to lack of funds.

Application of the AIDSTREATCOST model, designed to assist countries planning to introduce ARVs in the public sector to estimate the cost and resources required (Kombe and Owen, 2003), in Zambia and Uganda found that implementation would be constrained by a shortage of human resources, especially laboratory technicians and counsellors. For example, to achieve 4 per cent uptake of VCT would require 15 per cent of the entire public sector laboratory workforce in Zambia and 20 per cent of the entire public and private sector laboratory workforce in Uganda. The total cost per patient per year was estimated at $532 in Zambia and $619 in Uganda, with ARVs representing 50 per cent of this cost in Zambia and 63 per cent in Uganda, and laboratory monitoring tests representing between 30 per cent and 45 per cent of the total. Average per patient OI treatment costs would be around $25 per year. If a more basic monitoring protocol were adopted (fewer CD4 and viral load tests), Zambia could provide ARVs to 19 per cent more patients and Uganda to 10 per cent more. Both countries are relying on a 2-year Global Fund grant to purchase ARVs. It is not clear where the funding will come from to sustain treatment provision for patients already on ART or to provide treatment for the projected 100,000 new cases of AIDS a year in both countries over the next 5 years.

The Botswana Ministry of Health has calculated the cost of medications, counselling and testing at $600 per patient per year (Rollnick, 2002). Over 5 years, with 20,000 patients being added to the programme each year, the total cost would be around $180 million. The Gates Foundation and Merck have each committed $50 million over 5 years, with Merck supplying the ARVs indinavir and efavirenz, and the government meeting the remaining costs. However, the government has indicated that the programme is unlikely to be sustainable once Gates and Merck support ends, and is hoping that costs will fall as infection rates decline and fewer people need ARVs (PlusNews, 2002).

The Kenyan Ministry of Health budget is approximately Ksh 14 billion. If all patients who could potentially benefit from ARVs received treatment at 2002 prices, the drug costs alone for the standard brand combination regimen would be about Ksh18 billion and KSh5.7 billion for the generic equivalent (Permanent Secretary, Ministry of Health, personal communication, 2002).

A review of the costs of providing ART in Mexico found, not surprisingly, that total costs are substantially higher under HAART and treatment costs are higher for patients in the advanced stage of illness and in their last year of life. ARVs were the

main cost, representing 75 per cent of total treatment costs. Hospital costs decreased but out-patient and monitoring costs increased as patients switched to triple therapy; out-patient visits were the second largest contributor to total treatment costs. The authors conclude that governments need to be realistic about the human resource and laboratory capacity requirements for scaling up HAART, and to prepare for the shift in care and treatment patterns from in-patient to out-patient with the introduction of HAART (Bautista et al, 2003).

Modelling the costs of different ART scenarios in India including, for example, providing ART for HIV-positive mothers and their partners and providing ART for people below the poverty line, Over et al (2003) estimate that costs would range from $177 million to $744 million per year, with the least expensive option comprising 59 per cent of the health budget and the most expensive comprising 62 per cent of the health and social welfare budget combined.

However, a recent report (Geffen et al, 2003), which calculated the cost of a publicly funded comprehensive HIV/AIDS response in South Africa, including the costs of training and improvement in infrastructure, concluded that this is feasible. South Africa spends 8.8 per cent of GNP on health, and 3.7 per cent of GNP on health in the public sector. By 2015, the most expensive year in the calculation, a package of interventions for prevention, treatment of OIs, and ART would cost 20.3 billion Rand, about 1.74 per cent of GNP. This level of spending would require an increase in public expenditure on health from 3.7 per cent of GNP to 5.4 per cent, with ART representing 99 per cent of this additional cost. Decosas also notes that the calculation did not take account of the cost of not responding, and concludes that a 50 per cent increase in the budget for public health care over 12 years is not only feasible but desirable (Decosas, 2003). There is also potential for the cost of ART to be offset by reductions in cost of treatment of OIs and hospitalisation (South African spent $400 million on these in 2001) (National Treasury of the Republic of South Africa, 2001).

An analysis of HIV/AIDS expenditure in Senegal to date (Vinard P et al in ANRS, 2003) found that this has not been to the detriment of other health priorities. As a result of the Senegalese Antiretrovirals Access Initiative, the costs of treatment (ARVs, reagents, certain drugs for treatment of OIs) have increased relative to other activities, especially prevention, but have remained below 40 per cent (it is important to note that patients pay towards drugs for OIs, examinations and hospitalisation). However, the distribution of spending is likely to change dramatically following planned expansion and decentralisation of patient management during 2003-2006 from 1,777 to 6,982 PLHA, with additional funding provided from the World Bank and GFATM, representing 40 per cent and 16 per cent of the total budget respectively. Approximately half of the cost of purchase of ARVs will be covered by Bank financing, with the other half covered by the government, which will also pay for the bulk of reagents. The provisional public spend is considerably higher than current drug purchases by the Ministry of Health. Budgets are based on a yearly ARV treatment cost of $700-1,000 per patient. This cost could be halved by use of generics, but this would require changes in prescribing habits and a generic supply chain. There are also concerns about the capacity to cope of the National Supply Pharmacy, and impact on management and supply of other drugs and supplies; by 2006, total ARV and reagent orders will represent almost 50 per cent of current total orders.

A study modelling of non-drug costs of scaled up ART delivery in Botswana found that most of these costs would fall more sharply as the volume of work increases than they would in a higher wage setting, concluding that pilot programmes in Africa

will generally provide over-estimates of the cost of larger programmes (Ramanathan, 2002).

Financing mechanisms

Long-term provision of ARVs solely through public sector financing remains an unrealistic scenario in most resource-poor countries, and multi-funding approaches are needed. Many countries introducing ART will need to do so on a cost recovery basis, unless external funding through the GFATM and other sources is identified for certain target groups. Even in Thailand, a middle-income country, the government is considering a combination of co-payment, out of pocket expenditure and health insurance programmes.

Mugyeni (in French Ministry of Foreign Affairs, 2002) proposes a range of strategies for financing the costs of treatment in resource-poor settings:

- Drug cost reduction (advocacy, negotiation, TRIPS, generic competition, eliminating taxes, procurement strategies, bulk purchase).
- Laboratory monitoring cost reduction (low price alternatives, development of simpler cheaper tests).
- Graduated cost sharing (based on ability to pay) and other out of pocket expenditure (NGO, private).
- National government exchequer funds.
- Employer treatment schemes.
- Health insurance scheme coverage of ART
- Social insurance funds.
- Donor support, including GFATM allocation.

In Kenya, the Ministry of Health is remodelling the National Health Insurance Fund as a mandatory national social health insurance scheme, with a particular focus on targeting poor people, improving the drug supply and incorporating traditional medicine into the national health care system. It is hoped that the new scheme will be able to cover care and support for HIV/AIDS, including ART. A new revenue stream from a levy on sales of tobacco, alcohol and related products is also being considered. As of the end 2002, only one company in the private insurance sector in Kenya was covering treatment for HIV/AIDS. All other private sector insurance schemes exclude HIV and other chronic diseases.

The current limited public sector provision of ART in China is subsidised by the government through the routine budgets for HIV/AIDS prevention and care provided by the Ministry of Finance. The government is discussing external support for ART with agencies including the Global Fund, US NIH, US CDC, Project Hope and Amfar, and considering the possibility of universal free provision and strategies for future financing including cost sharing mechanisms.

In Ethiopia the government is looking at ways to increase supply and reduce the cost of ARVs, through financial support from the Global Fund and procurement of generic drugs (IRINnews, 4th August 2003).

CIE in Cote d'Ivoire operates a cost-sharing arrangement with its 3,700 employees, paying 100 per cent of health care costs and then seeking 20 per cent co-payment from the worker. In some cases, the company covers 100 per cent of costs if the worker is unable to repay the 20 per cent. The new HIV fund required the workforce to increase their monthly contribution to the health care fund. Contributions are related to salary levels so, for example, a technician on $298 a month would pay $1.3

each month to the solidarity fund (Eholie S et al, in French Ministry of Foreign Affairs, 2002).

3.7 Monitoring and evaluation

ART programme M&E

Van Praag (in French Ministry of Health, 2002) identifies the need for monitoring and evaluation (M&E) to enable lessons to be learned and applied quickly as countries move from small to large-scale ART programmes. M&E needs to identify programme inefficiencies, obstacles and adverse effects, to address feasibility and cost issues, and to consider ART within comprehensive care. Specific studies may be needed to consider issues such as impact on prevention, behaviour and health services in general. Getting the balance right between monitoring through existing health information management systems and meeting the need for specific monitoring of ART interventions will be critical.

A recent WHO/UNAIDS workshop on strategic information for ART programmes (WHO/UNAIDS, 2003) highlighted the complexity of M&E of ART programmes. Systems need to be designed to take account of factors including the lifelong continuous therapy, variety of treatments, toxicity, treatment failure in some cases; to track drug stocks, ARV prescriptions, expiration of drugs through efficient patient and facility records; and to monitor adherence and understand factors facilitating and impeding adherence. M&E systems also need to identify suitable outcome measures, since different measures of effectiveness used at present include patient survival, quality of life, reduction of HIV transmission, and containment of drug resistance.

In Senegal, the government has identified M&E weakness as a constraint to scale up, and highlighted the need to strengthen M&E skills, develop tools, set up M&E sub-units at regional level, and make better use of existing data and systems (Toure in WHO/UNAIDS, 2003).

Thailand has highlighted the lack of a standard ART M&E approach that countries can use as a model. The national programme is trying to keep the monitoring system simple, using essential markers (weight, CD4, status of treatment; continuing on treatment, changing regimens, termination of treatment, loss to follow up, death). The programme has developed standard tools (including for monitoring satisfaction of PLHA and relatives with clinic service and information received; adherence and reasons for non-adherence, care provider confidence, skills and difficulties), registration and reporting systems, and uses site visits. Evaluation focuses on all components of programme management, drug adherence, and economic implications. A key lesson learned is to develop M&E step by step to avoid generating an overwhelming amount of data and adding too much to the existing workload (Chasombat and Yarnwaidsakul in WHO/UNAIDS, 2003).

The Tanzania MAP is proposing to use care and support indicators to track the percentage of people receiving ART and increases in facilities providing services. However, equity is a concern, since there is no prioritisation of target groups or mention of the socio-economic status of those receiving treatment (Roedde, 2003).

Programme evaluation of the Kibera slum pilot will include measurements of the numbers of people enrolled, acceptability, tolerability, and adherence to antiretroviral treatment, response to therapy, and the development of drug resistance.

Quality of care and quality assurance is an important issue. In Brazil, with the support of PAHO, CDC is starting to evaluate ARV use in 3 health facilities in Rio de Janeiro, with a focus on patterns of use, investigation of whether patients are receiving medications according to national guidelines, and analysis of data collected through ARV surveillance systems.

To address concerns that introducing ART will be at the expense of prevention efforts, and could adversely affect risk behaviour, prevention indicators included in national monitoring frameworks (for example, percentage of young people aged 15-24 years reporting condom use with non-regular partner) should allow any adverse effects on prevention to be tracked.

Patient monitoring and follow up

The development of integrated systems to track patients, drugs and fees at point of delivery has been identified as essential for scaled up ART programmes.

In Malawi, MSF and Thyolo district health services are proposing an approach to M&E that uses the GFATM targets as outcome indicators, takes a similar approach to that used by the national TB programme, uses a paper-based system with a patient identity card ('health passport'), patient master card (for registration of monthly treatment outcome, functional status, side effects and adherence),and a drug security form. The programme also plan to use an electronic database for monthly and cumulative reporting and patient summaries.

MSF is working with the Lighthouse Trust, the national TB programme, and the National AIDS Commission to develop a simple record-keeping system designed for use by health centre staff that will allow a quarterly cohort analysis of ARV clients and enable staff to know at the end of each month if any client has not come to collect their drugs. The system will be piloted at the Lighthouse clinic and if successful will be used by MSF at the Chiradzulu hospital.

The Lighthouse Trust is planning to learn from the DOT experience of the TB programme, and envisages a guardian-based DOT scheme for ART, which will be piloted early in 2003. The Trust is also considering how to use its links with the community to follow up patients who drop out of treatment, including using community home-based care volunteers, and this is the approach proposed by the National AIDS Commission in their proposal to the Global Fund. However, there are concerns that this will be labour intensive and could undermine other home care activities. An alternative approach being considered is to develop the role of Health Surveillance Assistants to include follow up of ART clients, but this will require Ministry of Health commitment and additional funding to support training.

In China, each patient has a register card with his or her photo. There are 2 copies of the card, kept at the county CDC and village clinic respectively. Each high prevalence village has a drug delivery form, which records all patients living in this village. When a patient comes to the clinic to collect their drugs, the health worker checks the photo in the register card and the patient signs.

However, traditional facility-based systems using paper records may not be adequate to monitor patients with a chronic disease on long-term treatment, and new methods and technologies may be required. Fingerprint readers, smart cards and smart card readers are examples of technologies that could provide patients with a unique, robust, non-transferable ID with clinical and prescription data. Lighthouse in Malawi is already planning to use some of these technologies, Kenya is considering use of

smart card technology (WHO/UNAIDS, 2003) and, in Brazil, most patients now receive a magnetic card, which must be presented to receive treatment and which helps to track prescriptions.

Some countries are also considering the potential of fixed and mobile telephone-based linkages to provide an efficient and effective system for delivering data from facility-based clinical notes and patient registers to and from central monitoring points. South Africa is proposing to introduce a pilot national ART register, with web-based data from the ART programme linked to drug supply (at a minimum including ID number, clinical stage, current drug prescriptions) and to laboratory and pharmacy data (CD4 and viral load monitoring, drug monitoring). Proposed register outputs include: patient retention, drug switching patterns, survival, drug accountability, and laboratory outcomes.

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AIDSMAP www.aidsmap.com
AusAID www.ausaid.gov.au
Botswana Adult Antiretroviral Treatment and Resistance Study
www.bhp.org.bw/research/tshepo.htm
Clinton Foundation HIV/AIDS Initiative www.clintonpresidentialcenter.com/AIDS
Center for Global Development www.cgdev.org
Coca-cola www2.coca-cola.com
DFID www.dfid.gov.uk
Family Health International www.fhi.org
Gates Foundation www.gatesfoundation.org
Global Business Coalition on HIV/AIDS www.businessfightsaids.org
Global Fund for AIDS, TB and Malaria www.globalfundatm.org
Harvard AIDS Institute www.aids.harvard.edu
Health Alliance International www.washington.edu/haiuw
Health Systems Trust www.hst.org.za
www.hivnat.org
Horizons www.popcouncil.org/horizons/horizons.html
www.globalhealth.org
International AIDS Economics Network www.iaen.org

International AIDS Society www.ias.se
International HIV Treatment Coalition www.itacoalition.org
International Antiretroviral Therapy Evaluation Centre www.iatec.com
International Council of AIDS Service Organisations www.icaso.org
International HIV/AIDS Alliance www.aidsalliance.org
John Snow Inc and DELIVER Project www.jsi.com www.deliver.jsi.com
Joint Clinical Research Centre, Uganda www.jcrc.co.ug
Kaiser Family Foundation www.kff.org
Medecins Sans Frontieres www.msf.org
National AIDS Trust www.nat.org.uk
PAHO www.paho.org
Pangaea Global AIDS Foundation www.pgaf.org
Partners in Health www.pih.org
Policy Project www.policyproject.com
Synergy Project www.synergyaids.com
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Annex 1

Key clinical research questions

When should treatment be started?
- Is there a clinical advantage in starting ART in asymptomatic patients with CD4 count above 200?
- Are there cheaper and simpler methods of measuring CD4 cell count?
- Are there cheaper and simpler methods of measuring viral load?
- Are there other laboratory markers that could guide decisions about when to start ART?
- In the absence of laboratory data, are clinical criteria sufficient to guide decisions about when to start ART?

How should treatment be monitored?
- Is laboratory testing for effectiveness and toxic effects necessary every 3-4 months or is less frequent testing appropriate?
- What is the minimum laboratory monitoring needed to ensure safety and effectiveness?
- Are there less expensive but equally effective methods of monitoring effectiveness of ART?
- Would use of clinical variables (weight gain, quality of life, decreased frequency and severity of complications) be adequate to assess treatment success or failure?

How should drugs be selected?
- Can ART be safely prescribed by non-physicians using standard regimens and structured clinical algorithms?
- What are the most appropriate first-line regimens for resource-poor settings?
- How should treatment failure be defined?
- When should ART be stopped or changed?
- Are structured treatment interruptions, pulse therapy or treatment-to-safety strategies safe and effective?

Source: Rabkin et al, BMJ.

Key operational research questions

Health systems
- What is the appropriate mix of care interventions in settings with resource constraints?
- What factors make for effective service delivery?
- What is needed to improve skills and motivation of providers?
- Where and at what level of the health system can ART be provided? What are minimum requirements for a basic standard of quality care?
- What is the role of different service delivery models?
- How can the potential of private providers be maximised?

Adherence
- What factors contribute to adherence to ART and treatment for OIs?
- What is the impact of comprehensive care programmes on adherence?
- How does use of non-medical providers affect adherence?

Equity and accessibility
- What criteria should be used to select recipients? How are they developed and enforced?
- What are the needs of different groups and who can best meet these needs?
- Should some high-risk groups or specific occupational groups, such as health workers, receive priority?

Community involvement
- What processes promote meaningful involvement? What is the impact of involvement?
- What are community preferences for accessing treatment?
- What is the effect of involving PHA?
- What is the effect of comprehensive programmes that treat families rather than individuals?

Cost
- What are the most feasible and effective models for resource mobilisation, risk pooling, insurance, community resource mobilisation?
- What is the range of costs and cost-effectiveness for different treatment options?
- What proportion of costs can user fees cover? What is the WTP and ATP of clients?
- What are the implications of costs of treatment for families?

Source: Horizons, 2002

Annex 2

WHO strategy for comprehensive chronic disease care in the developing world

- Shift emphasis from acute episodic care to provide continuity of care with planned visits and regular follow up.
- Develop health policies, collaboration, legislation, and health care financing to support comprehensive care strategies.
- Emphasise delivery of services at primary care level to assure broadest access to effective care.
- Develop effective communication and referral systems between primary, secondary and tertiary levels of health care.
- Centre care on the patient, educate patients about their disease so the can become active participants in care and promote adherence to long-term treatments.
- Link care to community resources; provide education and support to family and community members to assist in care.
- Emphasise prevention.
- Monitor and evaluate the quality of services and long-term patient outcomes.

Annex 3

Global and country funding for HIV/AIDS and ART

This Annex provides a summary of current funding and support from selected global, multilateral, bilateral, and private sources, based on a review of web-sites, in order to indicate countries which have, or are likely to have resources for scaled up provision of ART and, where this information is available, planned approaches to scaling up.

It is not a comprehensive overview, since this was not feasible in the time available for this review and other organisations, such as UNAIDS, are taking the lead in identifying resource requirements and tracking resource mobilisation. However, the review highlights:

- Difficulties in obtaining a complete picture of resource requirements for scaling up ART, and of the availability of global and national resources.
- Difficulties in tracking resource flow and allocation, and lack of coordination between different bodies engaged in tracking (UNAIDS, 2003).
- Lack of coordination between major donors in resource allocation, resulting in some countries receiving funding from several sources and other countries receiving little or no external support.

Total global funding

Global funding for HIV/AIDS in resource-poor countries has increased from just over $300 million in 1999 to almost $3 billion in 2002, largely due to additional resources mobilised through the Global Fund for AIDS, Tuberculosis and Malaria (GFATM). UNAIDS estimates that total global spend on HIV/AIDS in 2003 will be $4.7 billion ($1.6 billion: international aid, $1 billion: other international sources, including the GFATM, $1 billion: domestic government expenditure, $1 billion: household expenditure). Despite increases in funding, there is a considerable gap between resources available and resources required. UNAIDS estimates that $10.5 billion a year will be required by 2005.

Global Fund for AIDS, Tuberculosis and Malaria

As of December 2002, donors had pledged $2.1 billion to the GFATM. In 2003, the US made a commitment to contribute to provide $1 billion a year to the Fund if EU and G8 partners match this with an annual contribution of $2 billion. In early June 2003, France, Germany, Italy and the UK promised African leaders that the EU would commit $1 billion to the Global Fund.

Following review of two rounds of proposals, the Global Fund has approved a total of $1.5 billion over 2 years to more than 150 programmes in 92 countries. However, the GFATM faces a lack of money, with an estimated shortfall of $500 million for 2003, and of $3 billion for grants through to the end of 2004.

Among the proposals approved by the GFATM during its first round, 20 countries were awarded funds to expand ART: Argentina, Burundi, Cambodia, Chile, Ghana, Haiti, Honduras, Indonesia, Malawi, Moldova, Morocco, Nigeria, Rwanda, South Africa, Senegal, Thailand, Uganda, Ukraine, Zambia and Zimbabwe. See Table A1 for summary of current grants awarded to countries in sub-Saharan Africa.

Table A1

GFATM-funded ARV and related programmes in sub-Saharan Africa 2002-2003

Country	$ million (2 years)	PMTCT		ARV and OI drugs	
		Included	No. of HIV+ve mothers on nevirapine	Included	No. of HIV+ve patients on ARV
Benin	11.3	Yes	n.a.	Yes	n.a.
Botswana	18.6	Yes	n.a.	-	-
Burkina Faso	7.3	Yes	n.a.	Yes	3,600
Burundi	4.8	Yes	400 mothers	Yes	2,597
Central African Republic	8.2	Yes	n.a.	Yes	n.a.
Cote d'Ivoire	26.9	Yes	n.a.	Yes	27,000 by year 5
Ethiopia	55.4	Yes	n.a.	No	n.a.
Ghana	2.8	Yes	600 mothers and infants per year	Yes	2,000
Guinea	4.8	Yes	n.a.	Yes	4,358 by 2007
Kenya	36.7	Yes	n.a.	MTC spouses, HIV+ve health workers	n.a.
Lesotho	10.6	Yes	n.a.	Yes	50% of those who need it by year 5
Liberia	7.7	n.a.	n.a.	Yes	n.a.
Malawi	41.8	Yes	70%	Yes	25,000
Mozambique	29.7	Yes	20,000 infants	Yes	20,000
Namibia	26.1	Yes	n.a.	Yes	n.a.
Nigeria	26.5	Yes	n.a.	Yes	10,000 adults 5,000 children
Rwanda	8.4	Yes	167,000 mothers and infants	Yes	200,000
Senegal	6.0	Yes	n.a.	Yes	n.a.
South Africa	41	Yes	n.a.	Yes	n.a.
Swaziland	29.6	Yes	n.a.	Yes	n.a.
Tanzania	5.4	AIDS component still to be signed			
Togo	14.2	Yes	n.a.	Yes	n.a.
Uganda	36.3	Yes	n.a.	Yes	n.a.
Zambia	42.6	Yes	n.a.	Yes	n.a.

Source: Proposal summary 'fact sheets', Global Fund website

Benin $11.348 million for first 2 years, covering both HIV/AIDS and TB, to include HIV prevention, VCT, PMTCT, and access to ARVs. Benin has an ARV access initiative and has negotiated price reductions with the pharmaceutical industry. Currently, only 430 AIDS patients are on ARVs.

Botswana $18.58 million for first 2 years, to recruit and train, scale up prevention programmes, and strengthen AIDS treatment, care and support.

Burkina Faso $7.26 million for first 2 years, to provide medical treatment for HIV+ve people, including provision of ARVs. The 4-year programme includes progressive access to ARVs of 3,600 patients by increasing the capacity of two health centres

and expansion to additional treatment centres, and expansion of PMTCT prevention from 3 to 11 districts.

Burundi $4.8 million for first 2 years ($8.7 million over 5 years), to provide ARV drugs, OI drugs and psychosocial support to 2,597 new patients, and expand PMTCT to 400 women. Agencies implementing the ARV programme include Bujumbara national hospital, provincial hospitals and community health centres run by the government and NGOs.

Central African Republic (CAR) $8.2 million for 2 years, to scale up VCT, provide access to ARVs, and expand PMTCT. CAR has an estimated 30,000 AIDS cases and 240,000 with HIV. ARV access through national programme, with detailed plans on negotiation for reduced prices, establishment of an eligibility committee, and treatment protocols.

Chile $13.6 million over 2 years, including increasing provision of ARV therapy ensuring 100% access to treatment.

Cote d'Ivoire $26.9 million for first 2 years, to expand VCT, PMTCT, and provide ARVs. By year 5, 27,000 (nearly 20% of current patients) are expected to be on ARVs, and 100% of regions will have services for PMTCT.

Ethiopia $55.4 million for first 2 years, to scale up VCT, clinical management of MTCT, clinical management of HIV (excluding ARVs), home-based care, and prevention of nosocomial infection.

Ghana $2.8 million for first 2 years ($14.2 million over 5 years), to increase VCT coverage in 16 additional VCT centres, expand PMTCT in 20 additional centres in 10 regions, provide ARVs to 2,000 patients, and establish comprehensive care for PLHA in the 14 districts of the country.

Guinea $4.8 million, to expand PMTCT, strengthen blood safety, support prevention programmes, and expand access to ARV from current 120 patients to 4,358 patients by 2007. Guinea has an estimated 6,000 AIDS cases and 139,000 with HIV.

Kenya $36.7 million for first 2 years, to scale up VCT (reaching 1 million after 5 years), provide ARVs to mothers, infants and spouses, and to health workers with HIV, and expand care and support services.

Lesotho $10.56 million for first 2 years, to scale up VCT services in all 10 districts, provide comprehensive care, including ARVs (to 50% of those who need them by year 5), and expand PMTCT to 18 health service areas.

Liberia $7.66 million for 2 years, to introduce ARVs and OI drugs, provide care and support, promote blood safety, train government health workers on ARV. Liberia has an estimated 246,000 adults and children with HIV.

Malawi $41.8 million for first 2 years ($284.1 million over 5 years), to establish 27 VCT sites and 15 outreach points, provide nevirapine to 70% of pregnant women, ARV and OI drugs to 25,000 HIV+ve patients at the end of 5 years, and care and support to 22,000 chronically ill patients.

Mozambique $29.69 million for first 2 years, to fund comprehensive programme of prevention, care and support using government, NGO, and community structures. Plans by end of 5 years to increase VCT clinics to 50, establish 22 clinics to treat

20,000 patients with ARVs and OI drugs, expand PMTCT to provide nevirapine to 20,000 newborns.

Namibia $26.1 million for 2 years, to include VCT, PMTCT, and ARV treatment.

Nigeria PMTCT: $8.7 million for first 2 years ($27.4 million over 5 years), to establish PMTCT centres of excellence; ART: $17.8 million for first 2 years ($41.8 million over 5 years), to establish 100 ARV centres, following pilots in 25 centres in 2002, providing generic drugs for 10,000 adults and 5,000 children. Government is working with drug companies to begin manufacture of ARVs in 2003.

Rwanda $8.4 million for first 2 years ($14.6 million over 5 years) for HIV and TB, including increasing availability of ART and treatment for OIs, training for health workers, VCT and comprehensive care and support. Plans to establish 3 VCT centres in each of the country's 39 districts, provide PMTCT services to 167,000 pregnant women and their infants, provide ARV and OI drugs to 200,000 PLHA. Treatment will be undertaken largely in government facilities.

Senegal $6.0 million for first 2 years ($11.7 million over 5 years), to expand VCT, access to ARVs, PMTCT, psychosocial support, and behaviour change.

South Africa $41 million over 2 years ($72 million over 5 years) for prevention and treatment of HIV/AIDS and TB, including $27 million for the Enhanced Care Initiative, providing a continuum of care, including ARV therapy, in Kwazulu Natal.

Swaziland $29.63 million for 2 years, to expand VCT, PMTCT, ART, OI treatment, social and legal support, orphan support, and behaviour change.

Togo $14.2 million for 2 years, to provide ART to HIV/AIDS patients who meet eligibility criteria, provide social support to PLHA, introduce PMTCT, improve blood safety, promote safe sex in young people and sex workers, involving government, private sector and NGOs.

Uganda $36.3 million for first 2 years ($51.9 million over 5 years), to increase districts with VCT services to 56, increase hospitals providing ART to 11, increase districts with PMTCT programmes to 56. Partners include Ministry of Health and government health facilities, Rakai District, AIDS NGOs, and Uganda Protestant Medical Bureau. Uganda has 120,000 people with HIV; only 10,000 currently have access to ART.

Zambia $42.6 million for HIV/AIDS and TB for 2 years, to Central Board of Health and Churches Health Association of Zambia, including provision of ART through district health system (8 facilities) intended to cover 10,000 adults, and ARVs for PMTCT through CHAZ facilities.

Announcements have also been made in 2003 about Global Fund grants to be awarded to the following non-African countries: Bulgaria, Cambodia, Cuba, East Timor, Haiti, India, Indonesia, Moldova, Philippines, Romania, Thailand, Ukraine, Western Pacific Islands.

World Bank MAP

The World Bank MAP makes available $1 billion for HIV/AIDS programmes in Africa and $155 million for programmes in the Caribbean. The MAP supports ART in countries in two ways:

- Strengthening health infrastructure, including the development of guidelines.
- Purchase and distribution of ARV drugs and supplies, where they can be administered safely, effectively, ethically and in a sustainable manner.

Sub-Saharan African countries approved to receive MAP funding as of March 2003, with a total commitment of $611.8 million, were Benin, Burkina Faso, Burundi, Cameroon, Cape Verde, Central African Republic, Eritrea, Ethiopia, Gambia, Ghana, Guinea, Kenya, Madagascar, Nigeria, Senegal, Sierra Leone, Uganda and Zambia. Caribbean countries approved to receive MAP funding as of November 2002 were Barbados, Dominican Republic, Grenada and Jamaica.

US government

In 2003, the US announced a 5-year $15 billion Emergency Plan for AIDS Relief. Funding will begin with $2 billion in 2004, and increase thereafter. The $15 billion includes an additional $1 billion annual commitment to the GFATM, conditioned on the Fund showing results. This initiative, which represents a tripling in US funding for HIV/AIDS, covers three areas:

- Prevention of 7 million new infections through VCT, condoms and abstinence education.
- Treatment with ARVs for 2 million people.
- Support and care for 10 million PLHA and AIDS orphans.

Like the World Bank MAP, the US initiative targets Africa and the Caribbean, and the 14 countries with the highest HIV prevalence that will receive most of the funding are Botswana, Cote d'Ivoire, Ethiopia, Kenya, Mozambique, Namibia, Nigeria, Rwanda, South Africa, Tanzania, Uganda, Zambia, Haiti and Guyana (Lancet, 2003a).

Pharmaceutical companies

Drug companies involved in ARV provision in sub-Saharan Africa include Abbott, Boehringer-Ingleheim, Bristol-Myers Squibb, CIPLA, GlaxoSmithKline and Merck.

Abbott's Step Forward Fund has entered into a partnership with the Government of Tanzania to improve access to ARV and drugs for OIs, and improve capacity in the public sector. Covering multiple hospitals and laboratories, it includes training of health workers and laboratory personnel in VCT and ARV treatment, creation of a national reference and teaching centre at Muhimbili National Hospital, strengthening zonal hospitals to ensure people's access to VCT, and creation of a national task force for policy issues, formulation of clinical guidelines, and establishment of procurement and distribution system for ARVs (http://www.businessfightsaids.org/).

Boehringer-Ingelheim's VIRAMUNE (nevirapine) Donation Program was announced in July 2000, under which the company would offer nevirapine free-of-charge for a period of 5 years to developing countries (www.viramune-donation-program.org). Eligible countries include 46 countries in sub-Saharan Africa.

Table A2

Drug company schemes providing ARVs and OI drugs

Drug Companies	Countries	Indication of scale	Indication of cost
Abbott (Step Forward Fund)	Tanzania (Muhimbili and zonal hospitals) (ARV and OI drugs)	n.a.	n.a.
Boehringer-Ingelheim	Lesotho (nevirapine)	n.a.	Free up to 5 years
Bristol-Myers Squibb (Secure the Future)	Botswana, Lesotho, Namibia, South Africa, Swaziland	$100 million	"Below cost" for 5 years
	Burkina Faso, Cote d'Ivoire, Mali, Senegal	$15 million	"Below cost"
CIPLA Ltd	Cameroon, Kenya, Malawi, Mozambique, South Africa, Uganda	MSF ARV pilots	CIPLA sells to MSF at $350 per patient per year; drugs are distributed free to patients
GlaxoSmithKline	22 African countries	n.a.	n.a.
Merck (Enhancing Care Initiative)	Senegal, South Africa	n.a.	n.a.
Pfizer (Diflucan Partnership)	14 African countries in East and Southern Africa (OI drugs)	n.a.	Free of charge

Source: Picazo, 2003.

Bristol-Myers Squibb's Secure the Future programme is a 5-year, $100 million partnership with South Africa, Botswana, Namibia, Lesotho and Swaziland to manage HIV/AIDS in women and children (in March 2001, $15 million was added for Senegal, Cote d'Ivoire, Mali and Burkina Faso). It makes the ARVs didanosine and stavudine available "below cost" under the global ACCESS partnership with UNAIDS.

CIPLA Ltd, an Indian company, uses a three-tiered pricing scheme: commercial wholesalers pay $1,200; governments $600; and MSF $350 per patient per year. CIPLA offered in February 2001 to sell MSF a generic version of a combination consisting of lamuvudine, stavudrine, and nevirapine, provided that the drugs are given to eligible patients at MSF clinics free of charge. The discounted MSF price is far cheaper than the original price of $10,000-12,000. (Patents remain a contentious issue, however, since Bristol-Myers Squibb holds the patent on stavudrine, GlaxoSmithKline on lamivudine, and Boerhringer-Ingelheim on nevirapine.)

Gilead Sciences announced in December 2002 that it would sell its ARV drug Viread at cost, approximately one tenth of its retail price, to 68 developing countries, offering the drug at $475 per person per year (www.iatcoalition.org).

GlaxoSmithKline has made arrangements with 22 African countries for the supply of preferentially priced ARVs (Benin, Botswana, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Congo Brazzaville, Cote d'Ivoire, Eritrea, Gabon, Guinea Conakry, Kenya, Mali, Namibia, Nigeria, Rwanda, Senegal, South Africa, Tanzania, Togo and Uganda), and is also involved in clinical trials in 19 African countries to assess the most appropriate use of ARV in resource-poor settings.

Merck's Enhancing Care Initiative provides support in Senegal and KwazuluNatal, South Africa to enhance the care of PLHA; ARVs are not specifically mentioned (www.merck.com). Merck is also a partner in the African Comprehensive AIDS Partnership with the Government of Botswana and the Gates Foundation.

Pfizer's Diflucan Partnership programme provides this drug for fungal OIs free to Botswana, Kenya, Ghana, Haiti, Lesotho, Mozambique, Namibia, Rwanda, South Africa, Swaziland, Tanzania, Uganda, Zambia and Zimbabwe. Patients enrolled in the programme receive Diflucan for as long as they need it. The programme also includes patient education, provider training (11,000 health care providers have been trained), educational materials, and ongoing monitoring and support. Pfizer's partners are Axios International, International Dispensary Association, Interchurch Medical Assistance, and International Association for Physicians in AIDS Care (www.diflucanpartnership.org).