

The building blocks of “3 by 5”

As national responses to the pandemic accelerate, the most critical elements are becoming easier to identify. First and foremost is ARV therapy, which must be regarded as part of a continuum of care for adults and children infected with HIV. It is initiated only at the point where the course of opportunistic infection and related illnesses – diagnosed via CD4 counts and/or clinical staging – indicates the need for ARV drugs.

To qualify for ARV therapy, an individual must test HIV-positive. Whatever the results of tests, they must be accompanied by pre-test and post-test counselling. For many individuals, the point of entry will be a counselling and testing site at which the client voluntarily opts into the process. However, WHO and UNAIDS recommend that, particularly in key health care settings such as antenatal clinics and TB treatment facilities, counselling and testing be offered routinely.

Testing and counselling underlie many other important processes. If a person is clinically well when first diagnosed with HIV infection, it may be possible to postpone ARV therapy by prompt diagnosis and treatment of opportunistic infections such as TB; and by prophylaxis using simple and safe drugs such as co-trimoxazole to prevent opportunistic infections. In such cases, all that is required are monitoring and basic medical interventions. The individual needs to adopt a healthy lifestyle and be empowered to make informed decisions. This, in turn, requires education.

Early testing has another critically important spin-off, as many people who voluntarily test are found not to be infected and immediately become a prime target for prevention. Many centres are now monitoring people who have been referred from entry points, such as clinics treating sexually transmitted infections and antenatal clinic services rolling out prevention of mother-to-child transmission, or harm-reduction centres for injecting drug users.

The vast majority of people are diagnosed with HIV infection when they are already sick. In many countries, TB is the most common opportunistic infection. This makes TB services an important entry point for ARV therapy programmes. Inpatient hospital wards are another important entry point.

All programmes need an uninterrupted supply of quality medicines and diagnostics, which are essential to identify HIV and to monitor clinical progress. Staff must be trained and the capacity developed to implement ARV therapy. From the outset, an integrated approach is best, because once ARV therapy is initiated, it must be continued for the person’s entire life. Training should involve all relevant types of health care workers: at tertiary and referral centres, district hospitals and health centres. It should also include community workers and adherence supporters.

Standard systems for monitoring the progress of people receiving ARV therapy are critical and should be linked at the facility level to drug supplies, dispensing cards and laboratory records. Regular cohort analysis of registers of people receiving therapy becomes possible as information is extracted for reporting to regional centres and the national programme. From these data, countries can report progress to civil society, all national stakeholders and donors. The data also facilitate regular updates for global reporting, including the impact of treatment on mortality.

HIV testing and counselling

As access to ARV therapy is scaled up, HIV testing and counselling are increasingly recognized by national programmes as the gateway to prevention, care, treatment and support interventions. A key theme being promoted in many countries is “know your status”. Published information and community mobilization programmes, along with toolkits for testing and counselling, have been developed to spread this message.

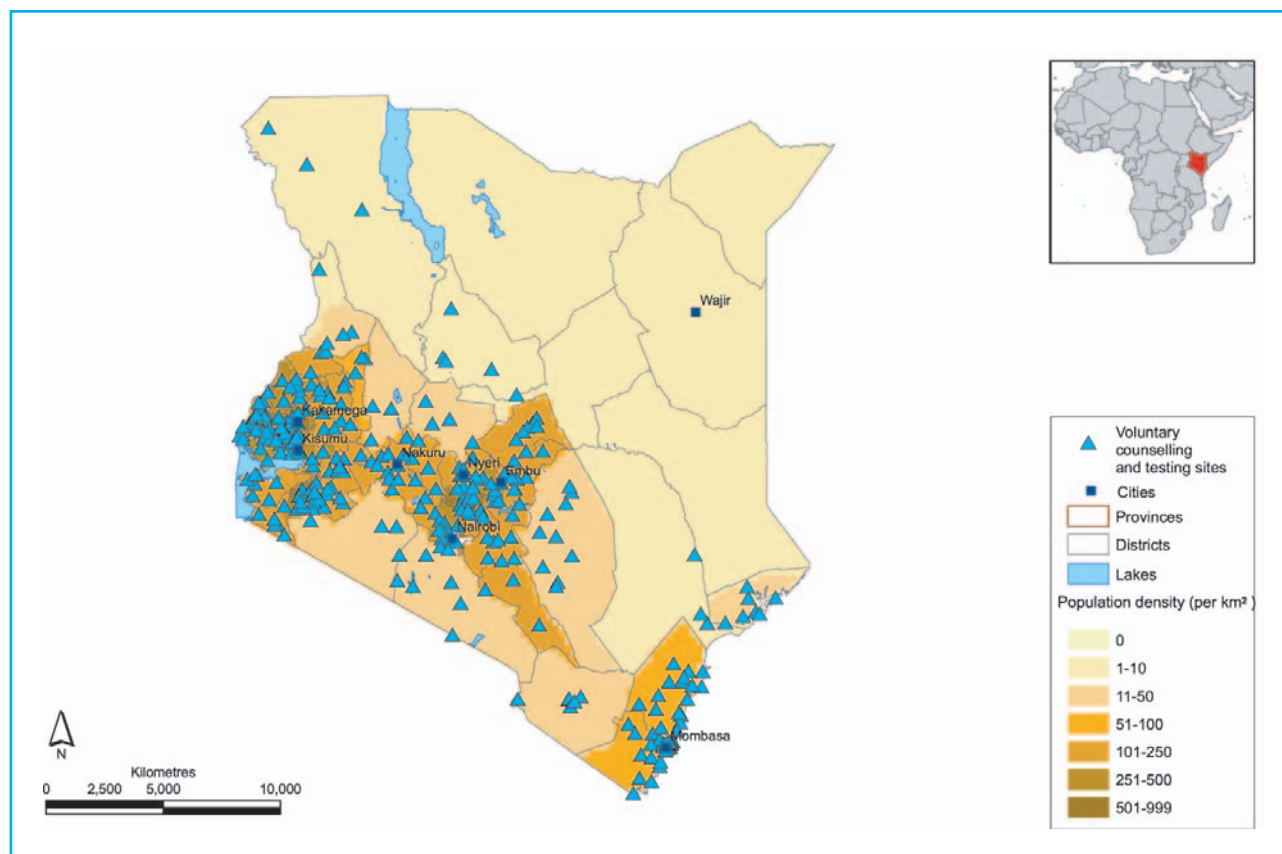
In June 2004, UNAIDS and WHO issued a joint policy statement on HIV testing and produced guidelines for rapid testing in resource-constrained settings.¹³ They also cosponsored, with the United States Government, a consultative meeting on the scaling up of testing and counselling for 18 African countries in Johannesburg,

¹³ WHO and UNAIDS, UNAIDS/WHO Policy Statement on HIV Testing (<http://www.who.int/hiv/pub/vct/en/hivtestingpolicy04.pdf>)

South Africa during November 2004. WHO worked with the International HIV/AIDS Alliance to produce a toolkit for testing and counselling and teamed up with the Global Business Coalition on HIV/AIDS to advocate for scaling up the use of “know your status” toolkits.

There has been considerable progress, with countries such as Botswana, Kenya (Fig. 12) and Lesotho routinely offering this service. Key to this issue is a need to identify how many people have been tested and counselled. This information is not yet available, and highlights the need for standardized reporting systems.

Fig. 12. Location of sites offering voluntary counselling and testing in Kenya, December 2004



Tuberculosis and HIV/AIDS

TB programmes are emerging as an important partner in HIV prevention, treatment and care in resource-constrained settings. Although TB is one of the most common causes of morbidity and mortality among people living with HIV/AIDS, TB is far more than part of the problem, TB programmes can be an important part of the solution.

Many countries have well-established TB control programmes that could, with additional resources, contribute to systems for delivering ARV therapy (Box 3). Both TB and ARV therapy programmes require political commitment, community mobilization to enhance early detection, standard case definitions, quality diagnostic services, standard treatment regimens with adherence support, reliable drug supplies and standardized monitoring systems.

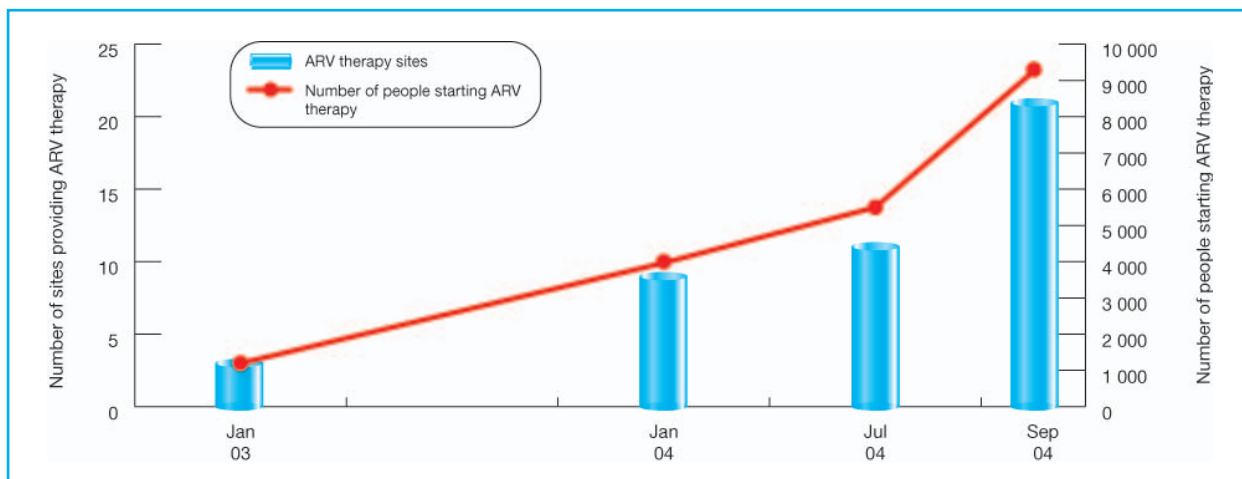
In countries with a high prevalence of HIV infection, up to 80% of people living with TB test positive for HIV, and these TB programmes are increasingly taking responsibility for reducing the impact of HIV and in collaboration with HIV/AIDS programmes are becoming an important partner in the “3 by 5” movement.

Box 3. Building on experience from TB control: Malawi

In Malawi, an estimated 900 000 people are living with HIV/AIDS, and 170 000 need ARV therapy. Malawi’s plan for expanding ARV therapy aims to provide ARV therapy free of user charges to 80 000 people by the end of 2005, exceeding their “3 by 5” target of 68 000, despite annual per capita spending on health of only US\$ 12 and a huge human resources deficit (Fig. 13).

How will Malawi meet its ambitious target? For many years, the country has followed the DOTS strategy for effective TB control. Now, it is applying the lessons learned to accelerate access to ARV therapy. This means standard definitions of who is eligible, simple treatment regimens, reliable drug supplies, treatment supporters to ensure adherence and regular monitoring and evaluation through standardized recording and quarterly reporting. Thus, Malawi intends to maximize uptake and adherence to ARV therapy and minimize drug resistance.

Fig. 13. Number of sites providing ARV therapy and number of people starting ARV therapy in Malawi, January 2003–September 2004

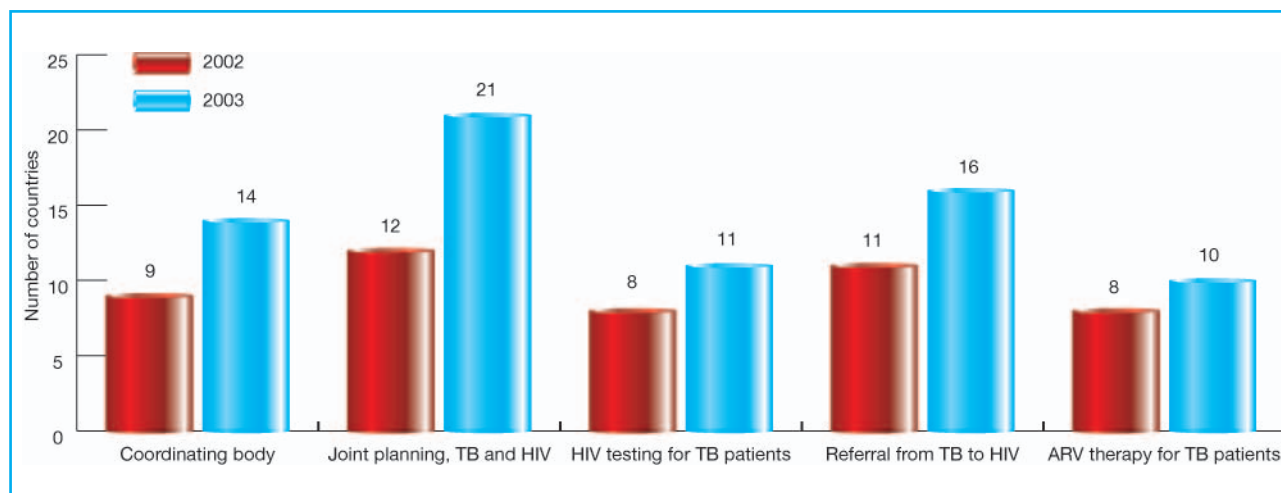


Collaboration between TB clinics and HIV counselling and testing clinics has led to more than 70% of people being treated for TB accepting the offer of HIV testing. Lay counsellors relieve nurses of counselling duties and help to compensate for an acute shortage of nurses. By January 2005, all 44 hospitals in Malawi’s 28 districts will be providing routine HIV counselling and testing for people being treated for TB. As of December 2004, 23 of 59 earmarked sites in the public sector are providing ARV therapy and more than 9000 people are receiving ARV therapy. Regional TB officers have been trained in ARV therapy and are recording, reporting, monitoring and evaluating for both TB and ARV therapy. New monitoring and evaluation tools for ARV therapy build on the cohort analysis approach also used for TB. Central units of the national TB and HIV/AIDS programmes will work together on analyzing the data collected by the regional officers.¹⁴

A survey of collaborative TB and HIV/AIDS activities of 45 countries with a high burden of HIV-related TB elicited responses from 32 countries (Fig. 14). There was progress in almost every policy area. Ten of the 32 countries now have a policy to provide ARV therapy to people living with TB.

¹⁴ Harries A et al. Monitoring the responses to antiretroviral therapy in resource-poor settings: the Malawi model. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 2004, 98:695–701. Harries A et al. Expanding antiretroviral therapy in Malawi: drawing on the country’s experience with tuberculosis. *British Medical Journal*, 2004, 329:1163–1166.

Fig. 14. Results of a survey of 32 countries with a high burden of HIV-related TB on national policies on collaborative TB and HIV/AIDS activities, 2002 and 2003



Preventing and treating opportunistic infections

HIV weakens people's immune systems and makes them susceptible to infections that can normally be controlled when the immune system is healthy. Prophylaxis with co-trimoxazole, a readily available, low-cost drug, can help prevent many such infections and is recommended for people with HIV infection or AIDS. Prophylaxis with isoniazid, a cheap and safe anti-TB drug, can help prevent active TB from developing. Cryptococcal infection can be prevented and prevented from recurring following initial therapy (secondary prophylaxis) by fluconazole, a widely available antifungal drug.

Some countries, such as Thailand, have made a concerted effort to improve the coverage of co-trimoxazole prophylaxis, the treatment of TB and secondary prophylaxis for cryptococcal meningitis among people living with HIV/AIDS.

In Africa, co-trimoxazole prophylaxis is rarely used. A 2003 survey estimated that 3% of adults and 1% of children living with HIV/AIDS received co-trimoxazole.¹⁵ The results of two recent studies in Uganda (on adults¹⁶) and Zambia (on children¹⁷) prompted WHO, UNAIDS and the United Nations Children's Fund (UNICEF) to modify the current recommendations for co-trimoxazole prophylaxis in children. According to the new recommendations, prophylaxis should be given to all HIV-exposed children from 4–6 weeks of age and to any child identified as HIV-infected with clinical signs or symptoms suggestive of HIV. A follow-up review meeting is planned for early 2005.

Preventing HIV infection among infants

Also high on the priority list is the need to prevent HIV infection among infants, especially preventing mother-to-child transmission. Nevertheless, in 2003 only an estimated 5% of pregnant women in sub-Saharan Africa and 8% globally were offered services for preventing mother-to-child transmission.

Just as TB presents a model for delivery systems, antenatal programmes are key to accelerating access to treatment for preventing mother-to-child transmission. One measure that is proving successful is the choice to routinely offer HIV testing and counselling. Pregnant women are told that HIV tests are standard and are asked if they want to opt out – an approach often used for other standard medical tests.

Primary prevention services, testing and counselling, treatment and support to women living with HIV and their families also need to be expanded.

¹⁵ USAID, UNAIDS, WHO, UNICEF and the Policy Project. *Coverage of selected services for HIV/AIDS prevention, care and support in low and middle income countries in 2003*. Washington, DC, Policy Project, 2004 (http://www.who.int/hiv/pub/prev_care/coverage/en, accessed 31 December 2004).

¹⁶ Mermin J et al. Effect of co-trimoxazole prophylaxis on morbidity, mortality, CD4-cell count, and viral load in HIV infection in rural Uganda. *Lancet*, 2004, 364: 1428–1434.

¹⁷ Chintu C et al. Co-trimoxazole as prophylaxis against opportunistic infections as HIV-infected Zambian children (CHAP): a double-blind randomized placebo-controlled trial. *Lancet*, 2004;364:1865–1871.

Ukraine has shown that the prevention of mother-to-child transmission can be scaled up. The Ministry of Health has a well-developed infrastructure for maternal and child health services that looks set to eliminate new HIV infections in infants by 2010. Using the “routine offer” approach to testing and counselling and with nearly all women consenting to be tested, Ukraine reduced mother-to-child transmission from 28% in 2000 to 10% in 2002.

By June 2004, the Elizabeth Glaser Pediatric AIDS Foundation was supporting programmes for preventing mother-to-child transmission in 17 countries worldwide. Of the more than 90 000 women living with HIV/AIDS who had been identified through the programmes, over two thirds received ARV prophylaxis to prevent transmission to their infants. By December 2004, the Foundation had also provided ARV therapy to nearly 9500 adults and 785 children through its care programmes in four countries.

Columbia University in New York City operates the MTCT-Plus initiative at 13 sites in nine countries: eight in sub-Saharan Africa and one in Thailand. The initiative supports the prevention of mother-to-child transmission and the provision of care, including ARV therapy for women, their partners and their children. Between January 2002 and August 2004, 5540 women and their families had benefited, and 1142 had received ARV therapy. Both the Glaser Foundation and Columbia University programs receive significant funding from the United States President’s Emergency Plan for AIDS Relief.

Prevention and treatment go together

Prevention and treatment must be synergistic, and achieving the “3 by 5” target involves scaling up both. Effective treatment is a form of prevention, albeit imperfect, because it lowers viral loads and decreases the chances of transmitting HIV, even in unprotected sex. In scaling up treatment, the concomitant need to rapidly scale up counselling and testing is a critical entry point for expanding all prevention activities. The more people learn about HIV and AIDS, the better able they are to prevent transmission and to protect themselves from opportunistic infections. If they test negative, they can take measures to protect themselves and their families from getting infected.

As people become better informed, stigma and discrimination decline, making it easier for others to determine their status and thus break the chain of transmission.

There has been relatively little information on how treatment affects prevention in developing countries. In affluent industrialized countries, a recent meta-analysis concluded that people living with HIV/AIDS receiving ARV therapy did not exhibit increased sexual risk behaviour, even when therapy achieved an undetectable viral load. However, people’s beliefs about ARV therapy and viral load may promote unprotected sex. Prevention messages should address these issues.¹⁸

Preparing for treatment

People living with HIV/AIDS and affected communities both have a key role to play in preparing people to begin and stay on HIV treatment over the long term. As the intended beneficiaries of treatment, care and prevention programmes they need to be heard, to be involved in their own health care decisions and to be active participants in developing and implementing long-term programmes. They also need to be supported in their advocacy efforts. Treatment preparedness – encompassing advocacy, literacy and community mobilization for people living with HIV/AIDS and affected communities – is therefore central to the potential impact of any plans, resources and delivery systems for HIV/AIDS treatment. The WHO Preparing for Treatment Programme has therefore made a major financial contribution to the Collaborative Fund for HIV Treatment Preparedness. The Collaborative Fund is structured as a global partnership between the Tides Foundation, the International Treatment Preparedness Coalition, WHO, more than 15 other donors and numerous providers of technical assistance. Its core activity is providing peer-reviewed grants to support HIV/AIDS treatment literacy, advocacy and community mobilization projects in developing countries. Community review panels comprising people living with HIV/AIDS and community-based treatment advocates and educators in each funding region or subregion determine funding priorities, review applications and decide about disbursement.

In addition, the Collaborative Fund undertakes capacity-building efforts in relation to treatment access and preparedness among regional networks of people living with HIV/AIDS, community-based HIV treatment

¹⁸ Crepaz N, Hart TA, Marks G. Highly active antiretroviral therapy and sexual risk behavior: a meta-analytic review. *JAMA*, 2004, 292:224–236.

advocates and educators. The type of support provided varies in each region, depending on the respective needs, capacity and established infrastructure. In addition to providing financial support to the Fund, WHO is supporting a participatory evaluation of the programme's effectiveness which will assist in the design and implementation of future community-driven initiatives.

The Collaborative Fund is a leading example of the principles of the Greater Involvement of People Living with HIV/AIDS (GIPA) applied to a global public health initiative.

AIDS medicines and diagnostics

A reliable source of medicines and diagnostics related to HIV/AIDS is critical to programmes in developing countries. The costs of drugs and diagnostics to people and to countries are still an impediment to scaling up and need to be addressed. The quality of drugs and diagnostics also needs to be assured. Moreover, it is important to ensure an adequate supply of treatments that can make them easier to take and lower their cost, increasing adherence to ARV therapy.

An important part of this effort is WHO's prequalification programme. Prequalification is not a drug regulatory system. WHO does not approve drugs for use in any particular country. That is the role of national regulatory authorities based on the national legal requirements. WHO simply lists those drugs that have been proven to meet existing international standards for quality, safety and efficacy – making them suitable, first and foremost, for procurement by United Nations agencies (see <http://mednet3.who.int/prequal> and http://www.who.int/medicines/organization/qsm/expert_committee/expertcomm.shtml). WHO prequalification is transparent (all relevant information is available in the public domain) and is conducted by highly qualified assessors and inspectors from well-established regulatory authorities including European Union countries, Canada and Switzerland (Box 4). The programme also facilitates training for regulators from developing countries.

The AIDS Medicines and Diagnostics Service (AMDS) has expanded to 16 members and has redefined itself as a network of organizations providing support in procuring and managing supplies of HIV/AIDS drugs and diagnostics. WHO acts as the secretariat, and other partners provide much of the technical support and actually supply the ARV drugs.

AMDS has pursued dialogue and negotiations with the research-based pharmaceutical industry with a view to ensuring adequate supplies of affordable, high-quality HIV/AIDS treatments. One focus is on the tiered pricing system and expanding the lists of countries eligible for low and intermediate prices. Another is on tracking sales to help determine the numbers of people receiving treatment in each country and to help assess needs for accelerating access to treatment.

A clearinghouse for information on ARV drugs and diagnostics, AMDS provides partners with the latest data on patents, registration status and prices and on the discovery, manufacture, availability and cost of new drugs.

The AMDS partners involved in procurement have seen sharp rises in their sales of ARV drugs and diagnostics. The International Dispensary Association has provided ARV drugs worth US\$ 105 million to 21 countries in 2004 – a dramatic increase from only three countries in 2003. UNICEF has provided ARV drugs to 37 countries in the past 18 months. The value of procurement is rapidly increasing from less than US\$ 2 million in 2003 to US\$ 7.5 million in the first three quarters of 2004. UNICEF has been stockpiling ARV drugs since October 2004 to help meet shortages. It has agreements with 22 countries and a stockpile worth US\$ 500 000 to deal with emergencies. The Bill & Melinda Gates Foundation has donated an additional US\$ 250 000 to increase the stockpile. The William J. Clinton Presidential Foundation has negotiated preferential prices for some generic ARV drugs and for some diagnostics and concluded agreements with the World Bank, the Global Fund to Fight AIDS, Tuberculosis and Malaria, UNICEF, the International Dispensary Association and WHO that ensure that the countries and organizations with which they work can access these drugs and diagnostics at preferential prices.

AMDS partners, including WHO and UNICEF, also support the development of principles for national drug regulatory authorities to help guide them through reviewing applications for approval of fixed-dose combination products. WHO has prequalified generic fixed-dose combinations to treat people living with HIV/AIDS in resource-constrained countries. A small multiple-site clinical trial in Cameroon showed very encouraging effectiveness, safety and quality of a generic fixed-dose combination of nevirapine, stavudine and lamivudine.¹⁹ Such studies are vital for continuing to assess the drugs that WHO recommends and that numerous donor agencies purchase.

¹⁹ Laurent C et al. Effectiveness and safety of a generic fixed-dose combination of nevirapine, stavudine, and lamivudine in HIV-1 infected adults in Cameroon: open-label multicentre trial. *Lancet*, 2004, 364:29–34.

Box 4. Ensuring high standards

In late May 2004, WHO removed two of Cipla Ltd's prequalified antiretroviral products from the list of prequalified products. On 9 November 2004, India-based Ranbaxy Laboratories Ltd voluntarily withdrew seven ARV drugs (plus all ARV product dossiers under assessment) from the WHO prequalification list. The following week, another generic antiretroviral manufacturer based in India, Hetero Drugs Limited, also withdrew six of its ARV drugs from the WHO prequalification list.

These de-listings were spurred by WHO inspections of contract research organizations that had carried out bioequivalence studies. In subsequent inspections, the companies found discrepancies in the documentation relating to proof of the products' bioequivalence with originator medicines. The companies also found that the contract research organizations they had used for studies of bioequivalence were not working in compliance with the international guidelines on good clinical practices and good laboratory practices.

WHO has advised its Member States that, in principle, the irregularities found at the contract research organizations do not undermine the proven pharmaceutical quality of the medicines, including their purity and stability, but users should – where possible – suspend the use of the de-listed medicines and switch to other prequalified products. WHO, however, has also recommended the continued use of de-listed products if obtaining alternative prequalified products immediately is difficult. The risk of withholding treatment is higher than that of providing medicines that may or may not be bioequivalent but that have demonstrated quality and safety. A switch to non-prequalified products is not recommended, as WHO has not documented their quality.

On 30 November, WHO reinstated two ARV drugs manufactured by Cipla Ltd on its list of prequalified medicines. Cipla has carried out new bioequivalence studies to confirm that its two ARV drugs are therapeutically equivalent to their brand-name counterparts.

Ongoing WHO inspections of contract research organizations conducting tests on ARV drugs are part of the continuing monitoring process and an integral component of the prequalification project. This work reflects WHO's responsibility to assist countries in promoting safe and effective medicines and improving their quality assurance mechanisms. The current WHO list of prequalified medicines contains 50 ARV drugs, including three double and two triple fixed-dose combination (two or three ARV drugs in one pill) manufactured by Abbott Laboratories, GlaxoSmithKline and Cipla. A number of new ARV drugs – including fixed-dose combinations – are currently in the pipeline for WHO assessment.

AMDS brokers technical support, helping countries build capacity into their supply chains, so supplies move efficiently from central purchase to treatment centres. One way of supplying this support is through regional workshops in procurement and supply management. In December, for example, workshops in Kenya and Cambodia provided training to dozens of participants from almost 20 countries. Another way is to help countries develop procurement and supply management plans. Many countries have developed such plans and expect to have 120 supply managers trained by mid-2005.

ARV drug prices in developing countries

The high cost of ARV drugs remains a barrier to scaling up HIV treatment and care. For first-line treatments, the lowest price available to countries is around US\$ 140 per person per year, but average prices are still at least US\$ 300. Reaching the December 2005 milestone of US\$ 50–200 per person per year will require substantial collaboration by all "3 by 5" partners. Meanwhile, second-line treatments remain prohibitively expensive throughout much of the world. As the contours of the epidemic change, this situation could pose an increasingly serious public health hazard. It is critical that the international community acts now to ensure that the cost of drugs does not pose a barrier to continued improvement in the uptake of and adherence to HIV-related services.

Pricing in Europe and central Asia

Meanwhile, pricing of first-line and second-line treatment remains a concern in eastern Europe and central Asia. Countries that are members of the Commonwealth of Independent States have secured reductions in the prices of ARV drugs. In the Republic of Moldova and Ukraine, for example, governments are buying generic ARV drugs via the International Dispensary Association through their grant from the Global Fund to Fight Aids, Tuberculosis and Malaria. In the Russian Federation, direct negotiations with the research-based industry are ongoing, and at the same time generic ARV drugs are in the process of being registered.

In other countries, prices remain high, severely limiting treatment access. As the number of people with AIDS is relatively low, except for Romania, most people currently receive ARV drugs through the official public health care system. As their numbers grow, the financial burden for purchasing ARV drugs starts weighing heavily.

A meeting of activist organizations in Warsaw established a working group that aims to urge the Health and Consumer Protection Directorate-General of the European Commission to take action. Reducing prices for the 10 countries that joined the European Union in May 2004 is complicated because the provisions of the single market of the European Union have resulted in prices being raised to the levels prevailing in the 15 countries that were members before May 2004. Several meetings have been held to address this issue, and more are planned.

Procurement and supply management

Countries and programmes are rapidly accumulating first-hand experience in procuring ARV medicines. Challenges and potential bottlenecks in procurement and supply management are therefore shifting. During 2005, officials will struggle less with selecting products, identifying suppliers and placing orders than with funding repeat purchases, preserving operational and legal flexibility in the procurement process, forecasting demand based on the uptake of ARV therapy and implementing a robust system for supply management to ensure that health facilities are (re)-supplied in a timely manner. Helping countries to develop an efficient and effective system for procurement and supply management is not only critical to scaling up ARV therapy but also facilitates the treatment of other chronic diseases such as diabetes and hypertension.

Training health workers

As access to ARV therapy expands, a major constraint is the lack of skilled health care workers, ranging from specialized physicians to aides. As many as 100 000 trained health workers may be needed to realize the "3 by 5" targets. WHO's Integrated Management of Adult and Adolescent Illness (IMAI) training modules provide a technically sound approach to shifting essential skills, transferring knowledge and expanding health care teams to embrace laypeople, including people living with HIV/AIDS.

The IMAI modules provide simple guidelines, training materials and educational tools and addresses clinical care, counselling and monitoring of people receiving treatment as well as district coordination of ARV therapy.

Pioneered in Uganda, the IMAI approach fosters new partnerships within and between countries. Workshops and the creation of knowledge hubs nurture local buy-in and exponential growth in the number of professional and lay health care workers (Box 5). This also strengthens the whole health system, as limited human resources are used optimally and care is integrated.

Box 5. A regional knowledge hub in Ukraine

Training for ARV therapy was virtually nonexistent in central and eastern Europe before 2003. In 2003, a grant from the German Gesellschaft für Technische Zusammenarbeit (GTZ) supported WHO and the American International Health Alliance in working with Ukraine's Ministry of Health, the National AIDS Centre, the Kiev Medical Academy of Postgraduate Education, MSF and AIDS Foundation East-West on planning a regional knowledge hub. In January 2004, the Knowledge Hub for the Care and Treatment of HIV/AIDS in Eurasia was established in Kiev, Ukraine. The Knowledge Hub:

- helps develop national HIV/AIDS plans that address needs for human capacity-building;
- develops and implements training programmes with knowledge-based components in educational and clinical settings and skills-based components through on-site mentoring;
- develops online information resources for health care professionals; and
- translates and adapts guidelines, protocols and best practice materials.

The Knowledge Hub was instrumental in building a consensus for Ukraine's national plan for scaling up ARV therapy, with targets of providing ARV therapy to 2000 adults and 100 children in six regions by 2005. The approach is to start by building care teams consisting of a physician, a nurse and a social worker or counsellor. Knowledge-based training will be followed by skills-based training. Since June 2004, the Knowledge Hub has trained 66 caregivers with a grant from the Global Fund to Fight AIDS, Tuberculosis and Malaria and support from the International HIV/AIDS Alliance.

The Knowledge Hub has developed a system for measuring and evaluating the results of the training that includes regular on-site follow-up. Knowledge Hub staff also visit sites to assist with ARV therapy as the first groups of people receiving therapy come through.

The Knowledge Hub is now working towards nationally and internationally recognized certification for physicians, nurses and social workers that take its courses. It plans to extend its training programmes into the Russian Federation in 2006 and is engaged in discussions with other countries.

Because people living with HIV/AIDS tend to become experts in their own illness, they are encouraged to become expert patient trainers in courses for clinicians and aides and to become aides themselves. Those with the aptitude can also assume administrative duties, thus freeing up professional staff.

In Swaziland, for example, eight expert trainers and 12 other IMAI trainers are in place. By August 2004, 32 health professionals from Swaziland's four regions had been trained. IMAI training is also well underway in Eritrea, in the Province of the Eastern Cape in South Africa and in Sudan. Clinical guidelines have been rapidly adapted in Burundi and Senegal, where training is underway. Guidelines are being adapted in Burkina Faso and other French-speaking countries in Africa.

Quality assurance and accreditation

A lack of physical infrastructure and services that meet satisfactory standards remains a problem in most developing countries. The Joint Commission International sets the standards by which health care quality is measured for more than 15 000 health care organizations worldwide. Accreditation includes on-site reviews by teams of Joint Commission International health care professionals at least once every three years.

Some countries already have systems of accreditation but there is no system pertaining specifically to the treatment of HIV/AIDS. Practical, adaptable guidelines for developing accreditation systems are expected to be available by August 2005.

Standard-setting is in no way intended to penalize countries or individual health facilities. Rather, the objective is to introduce a framework for continuously improving quality. This in turn can help to structure a country's approach to scaling up treatment. WHO and the Joint Commission International are developing practical, adaptable guidelines to be used as tools for introducing accreditation systems for HIV/AIDS service delivery. They will also provide technical support to countries or institutions wishing to set up accreditation systems. They will promote and support the development of in-country, regional and international partnerships to encourage the acceptance of and compliance with accreditation standards, to monitor and evaluate application of the standards and to improve them.

Monitoring treatment

Successful ARV therapy can transform HIV/AIDS from a death sentence to a chronic disease. Chronic disease management to keep the person healthy and productive requires regular monitoring and evaluation of clinical condition and adherence to medication.

Ideally, the history of a person living with HIV/AIDS is recorded and available whenever a clinic visit is made. The patient register is one critical component of the record-keeping and monitoring system. Most of the information is used for that person's own benefit; the remainder allows programmes to work properly and to produce the data used to evaluate and improve services at the institutional, national and global levels. Summaries of these data help, for example, with the timely procurement and distribution of drugs and supplies and with measuring progress towards national and global targets. Simplicity is the key to a robust monitoring system, so the system collects the minimum data needed for the care of the person living with HIV/AIDS, for managing the facility and the national system well and for international reporting.

In March 2004, WHO convened a meeting of representatives from the U.S. Government, other bilateral donors and many nongovernmental organizations to agree on a standardized minimum set of data to be collected.

In several countries the monitoring system is building on the TB experience with alterations to accommodate lifelong ARV therapy. Malawi has developed such a system (Box 3).

There are also examples of developing electronic monitoring systems. Brazil has more than 900 ARV therapy sites and uses an Internet-based system to manage the procurement and distribution of drugs and supplies to the sites. Other institutions and organizations have developed computer-based medical record systems, including the Mosoriot Hospital in Kenya, MSF (a software package called FUCHIA) and the United States Government (the CareWare system designed for use with U.S. HIV patients and now used in some clinics in Uganda). In Haiti, Partners In Health has developed an electronic medical record system that uses satellites to communicate with remote sites, track current stocks of drugs and other supplies and estimate future needs, thus proving the feasibility of bypassing weak infrastructure to solve a critical problem.

Drug resistance

HIV mutates frequently during replication in human cells, and some mutations reduce the effectiveness of HIV drugs. If treatment adherence is poor, resistant HIV strains can emerge and lead to treatment failure. However, if ARV therapy regimens are properly designed and delivered and adherence is high, the emergence of HIV drug resistance will be minimized.

There is no evidence to indicate that scaling up ARV therapy in developing countries is making the spread of drug-resistant HIV strains more difficult to manage. The resistance to drugs is no higher than that reported by affluent industrialized countries. Primary HIV-1 drug resistance has remained low in Brazil, where triple therapy was introduced on a large scale in 1995–1996, and in Côte d'Ivoire and Uganda, which introduced ARV therapy in 1998 as part of the Accelerating Access Initiative.

WHO is now focusing on working with countries to set up HIV systems for the surveillance and monitoring of drug resistance. Threshold surveys are planned to determine the level of drug resistance transmission, mostly using specimens left over from HIV surveillance rounds or special studies at sentinel sites, in populations where ARV therapy has been in use informally for several years. The first study has been completed in Mexico. Monitoring of HIV drug resistance will start in populations commencing standardized treatment in two countries in the next few months. In addition, much attention is being paid to building a network of

laboratories that test for drug resistance. Laboratories in Botswana, Côte d'Ivoire, Senegal and South Africa are now involved in a programme for the quality assurance of laboratories involved in monitoring HIV drug resistance in the African Region of WHO.

Operational research

There are no universal models for scaling up the provision of HIV treatment and optimizing prevention programmes at the necessary scale. An evidence-based approach is essential, but the urgency of the task requires innovative approaches. "Learning by doing", of which operational research is a key element, is essential to the process of scaling up. Incomplete evidence must not constrain efforts, and learning from the various initiatives underway requires assessing evidence in real time while treatment programmes are being launched and expanded.

Priority must be given to research that is directly relevant and can be applied widely. There are two core principles. First, research must be multidisciplinary, incorporating clinical, economic, health systems and sociobehavioural elements. Second, ownership of the process must rest with countries. Implementation of operational research studies should be embedded within routine programme activities, whether the initiative originates with local stakeholders or outside partners. WHO, UNICEF, the World Bank, the United Nations Development Programme (UNDP) and other partners have started to work with countries to set priorities for operational research and to develop research proposals.

Home based care

In many highly affected countries, the burden of HIV has fallen squarely on large health facilities. A study in Zambia reported that up to half of all patient-days in medical wards of a central hospital were accounted for by people with HIV-related illness. Home care programmes are therefore a critical component of scale-up efforts, and their expansion is a priority.

Where appropriate, home care can reduce the burden on health systems significantly; for the patient they also have clear advantages. After initiation of ARV therapy, long-term hospitalization is rarely needed. Most HIV-related infections, such as fever and diarrhoea, can be treated at home with support from trained health workers. In many cases, staying at home is the only option since hospital facilities are often remote, making transport and lodging prohibitively expensive.

Another advantage of home-based care is its contribution to the acceleration of prevention efforts. Experience from the TASO programme in Uganda and other locations suggests that counselling and education for people with HIV and their families is both easier and more effective in the home setting. Moreover, well designed home care programmes can reduce isolation and stigma, drawing on social and psychological resources offered by the local community.

Treating children

Children have been tragically neglected in efforts to accelerate access to ARV therapy. Advocacy on behalf of children has been weak, monitoring is limited and, despite proof to the contrary, policy-makers and caregivers are often unconvinced that ARV therapy works for children.

Globally, children under 15 years of age account for an estimated one-sixth of all HIV/AIDS deaths but account for a much smaller proportion of people getting ARV therapy. Few programmes have focused on treating children. An exception is Thailand's national programme, through which 200–300 children per month are enrolled in ARV therapy programmes and children constitute about 8% of the number of people in treatment. In Brazil, where women and children comprise a minority of infected people, about 5% of people being treated are children. MSF reports that 6% of the people it treats in all countries are children.

The exact number of children infected with AIDS is unknown. Rough global estimates are based on estimating the number of women living with HIV/AIDS delivering children and applying a mid-range rate of mother-to-child transmission, assuming breastfeeding is the norm. In 2004, more than half a million children are thought to have died globally from HIV/AIDS.

There is very limited surveillance of HIV status in children; this has not been a priority issue or a component of second-generation surveillance approaches. Surveillance is complicated by the fact that diagnosing infants is not easy. In children under the age of 18 months, HIV can only be diagnosed reliably by special tests. Most children who are born to infected mothers do not have access to these expensive and complex technologies. Standard, widely available HIV tests are based on detecting antibody, which transfers from mother to infant: a positive test under the age of 18 months may represent passive transfer of maternal (positive) antibody rather than true infection in the child. Over half of childhood HIV-related deaths occur in this period; they are largely undiagnosed and uncounted – and therefore invisible.

WHO is proposing the development of criteria for the presumptive diagnosis of HIV/AIDS that will lead to treatment even without definite confirmation. WHO, UNICEF and other partners are proposing a revised definition for HIV/AIDS in children, along with an improved clinical staging system that takes into account the rapid roll-out of programmes for preventing mother-to-child HIV transmission. Meanwhile, WHO is advocating for funding of research programmes to develop better methods of diagnosis.

The WHO clinical staging system for HIV infection and disease in children was developed several years ago and has never been evaluated. Many of the stage 2 and stage 3 clinical events are not specific to HIV infection and there is considerable overlap with HIV-uninfected children. Few laboratories are equipped to conduct CD4 assays, and most have equipment that can only report absolute counts rather than CD4 percentages (this requires much more expensive and complex machines). The recommendations appear too complex for widespread use in a public health approach. The treatment guidelines will be revised and simplified in accordance with new data on the safety and efficacy of different treatment regimens and drug resistance.

Besides improved clinical and diagnostic tools, there is an urgent need for affordable and appropriate paediatric drug formulations. There are very few specific paediatric formulations, and those that exist are often much more expensive than the adult formulations. Many providers break adult tablets into half or even quarters and accept that the drug dose in the broken-up pills may be relatively erratic. Dosing charts based on body weight are complex and not generally easy to use in facilities without specialized paediatric expertise.

Dispensing complex dosing regimens is challenging for the guardian or caregiver, and the volume of drugs needed per month can be considerable. Simpler, more practical approaches to dosing need to be developed (Box 6). UNICEF and WHO have convened the first of a series of consultative meetings to develop new paediatric formulations consistent with the revised treatment guidelines. Better data on HIV/AIDS in children will improve the forecasting of demand for various formulations and assist the pharmaceutical industry in committing to making the necessary products.

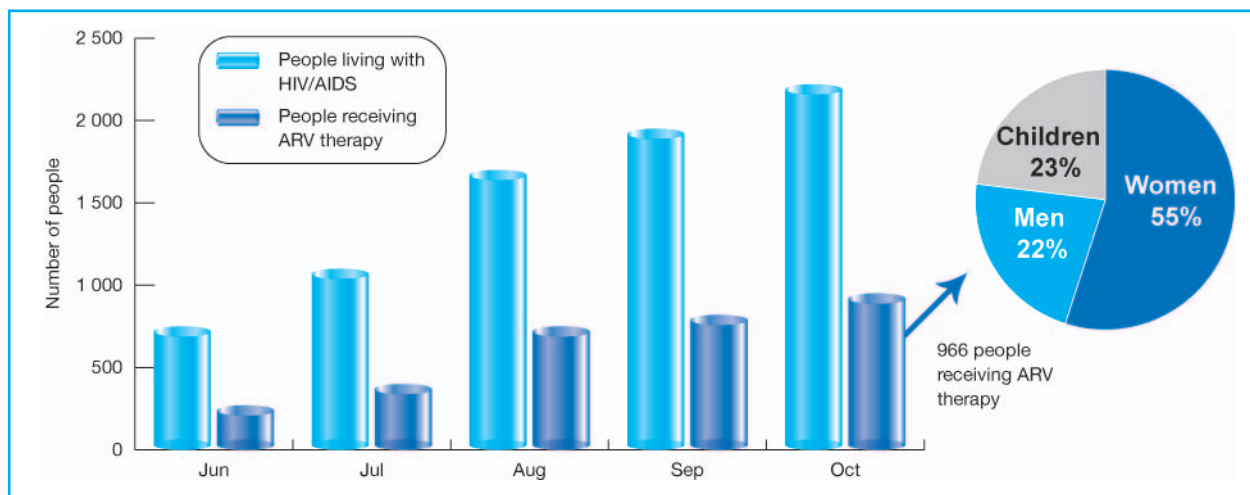
Box 6. A family-centred approach towards HIV care: the ACONDA experience in Abidjan, Côte d’Ivoire²⁰

Côte d’Ivoire has a decade of experience in clinical and therapeutic HIV research. It has become one of the leading countries developing pilot programmes to enhance access to care, including highly active ARV therapy. ACONDA is a nongovernmental organization created in Abidjan by physicians and other health professionals involved in these activities together with the Ministry of Health and the Agence Nationale de Recherches sur le Sida. In collaboration with its partners, ACONDA is now providing comprehensive care and treatment services for families affected by HIV/AIDS in the two most densely populated districts of Abidjan.

In two community-run maternal and child health clinics, 446 pregnant or delivering women living with HIV/AIDS have been enrolled since August 2003. Women of childbearing age are the entry point to build a family care HIV programme. Pregnant women who meet the WHO criteria for ARV therapy for themselves start ARV therapy prior to delivery in accordance with the 2004 WHO guidelines for preventing the mother-to-child transmission of HIV.²¹ A total of 192 women and 27 children in the same families have started ARV therapy. Further, 116 male partners have already accepted being tested for HIV, 64 have been told their HIV-positive serostatus and 33 have started treatment.

In early 2004, the same team rolled out the comprehensive approach to a large government-run primary care hospital with a dedicated HIV clinic for adults and children offering voluntary counselling and testing and the full range of HIV services. Adults and children seeking regular care are the entry point to the HIV care programme. Within six months, 2217 people living with HIV/AIDS have been enrolled, including 1177 women and 338 children. Of these, 966 are now receiving ARV therapy, mostly women and children (Fig. 15). The programme is now being extended to 10 more sites in Greater Abidjan to provide the HIV primary care services and family approach with ARV therapy to at least 10 000 people living with HIV/AIDS by 2008. The initial treatment results are very good.

Fig. 15. Cumulative number of people living with HIV/AIDS enrolled by ACONDA in Abidjan, Côte d’Ivoire, June–October 2004



²⁰ Reported by (alphabetical order): Xavier Anglaret, François Dabis, Bertin Kouadio, Valérie Leroy, Dominique Marchand, Thérèse Ndiri-Yoman, Freddy Perez, Roger Salamon, Catherine Seyler, Besigin Tonwe-Gold and Siaka Touré for the ACONDA-ISPED Team. Fassinou P et al. Highly active antiretroviral therapies among HIV-1- infected children in Abidjan, Côte d’Ivoire. *AIDS*, 2004, 18:1905–1913.

²¹ *Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants*. Geneva, World Health Organization, 2004 (<http://www.who.int/hiv/pub/mtct/guidelines/en>, accessed 31 December 2004).

HIV/AIDS and health systems

Because HIV/AIDS is the first major chronic disease to which many developing countries are responding with large-scale ongoing treatment, it could strengthen many health systems, as a wide range of interventions need to be delivered through different points, public and private, on an ongoing basis. The challenges presented by the pandemic are shared with other health priorities such as TB, malaria and maternal and child health.

Achieving the “3 by 5” target requires a wide range of interventions to be delivered quickly through many public and private delivery points on an uninterrupted basis. Three questions are commonly raised:

- How can major health system constraints be overcome in the short term?
- How can results be sustained in the medium term?
- How can ARV therapy be scaled up not by diverting scarce resources from other health priorities but, instead, by enhancing the delivery of all health services?

Attention is being given to four critical elements that constitute what is known as the HIV/AIDS health system platform:

- a skilled workforce;
- information systems;
- a well-managed and regular supply of drugs and other supplies; and
- fair and sustainable financing systems.

A skilled workforce

A report by the Joint Learning Initiative on Human Resources for Health and Development²² – a consortium of more than 100 health leaders – shows that health workforce development in developing countries has suffered from years of neglect in national and international health policy circles. Nearly all resource-constrained settings are challenged by shortages of health workers, imbalances in skill mix, maldistribution of health workers, a negative working environment and a weak knowledge base. Especially in the poorest countries, the workforce is under assault by HIV/AIDS, emigration and inadequate investment. Mobilizing and strengthening human resources for health is critical to combating health crises.

Information systems

An interim response to the lack of data in many of the countries with the highest burdens of HIV/AIDS is the application of a geographical information system to map the key services in districts: the Service Availability Mapping (SAM) tool. This captures district-level information on HIV/AIDS and other essential health services and on infrastructure, laboratories and human resources (Fig. 16). It can be used to monitor the scaling up of ARV therapy but simultaneously pays attention to the key health system indicators, including geographical equity.

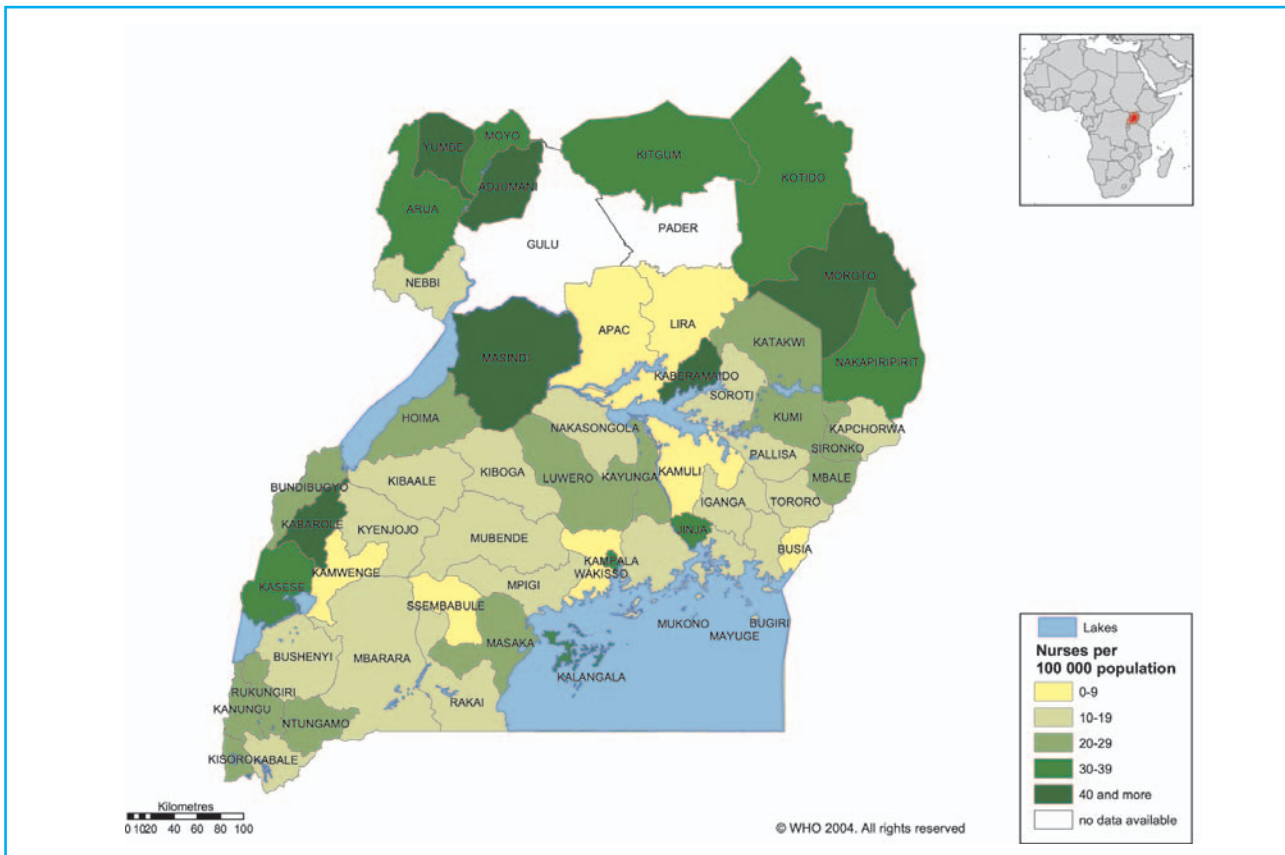
Such short-term solutions need to be linked to more comprehensive efforts to improve health information systems in the poorest countries for the longer term. This is being pursued by the Health Metrics Network, a new international partnership underwritten by the Bill & Melinda Gates Foundation. The Network’s goal is to catalyse the development of country health information systems, thus increasing the availability and use of timely and sound health information to support decision-making at the country and global levels.

Procurement and supply

Even with the impressive reductions in drug prices, ARV therapy is still very costly. In 18 countries in Africa, total health spending is less than US\$ 10 per person per year, including external resources. Countries must have support in creating adequate, fair and sustainable funding mechanisms as well as obtaining additional funds for health. This requires action both on the ground, in the form of material and technical assistance to national, regional, and local health agencies; and internationally, in the form of advocacy and policy designed to increase competition in the markets for pharmaceuticals and other key inputs.

²² Joint Learning Initiative on Human Resources for Health and Development. *Human resources for health: overcoming the crisis*. Cambridge, Global Equity Initiative, Harvard University, 2004 (<http://www.globalhealthtrust.org/Report.html>, accessed 31 December 2004).

Fig. 16. Number of nurses per 100 000 population in Uganda, by district, March 2004



Fair and sustainable financing systems

Countries need the capacity to estimate financial needs and to track the sources and uses of funds. They need to develop plans for financial sustainability that ensure that the health system can cope with extensive scale-up that incurs continuing costs – for the health system and for treatment. In doing so, a key issue under discussion by countries is whether to impose a direct user charge for ARV drugs. Donors need to acknowledge that external funds will remain a critical funding source in the poorest countries for some years to come.

Meanwhile, HIV/AIDS scale-up activities take place within a health and development landscape that includes health reforms, sector-wide approaches to health development, medium-term expenditure frameworks and poverty reduction strategies. Governments, having agreed to all of the Millennium Development Goals related to health, are trying to advance on several fronts at once. Oversight and dialogue are needed to reconcile the competing demands for resources, to avoid excluding vulnerable groups and to reduce duplication and waste. In the field of HIV/AIDS, this has already led to acceptance of the UNAIDS “three ones” approach (see above). Careful attention needs to be given to how HIV/AIDS strategies fit the overall sector strategies and to the potential and actual effects of scaling up on the rest of the health system.

Given the current level of financial scale-up, recipient countries are expected to meet high standards of fiscal accountability. On the other hand, many recipient countries want to tackle HIV/AIDS more effectively but are concerned about how major increases in funds will affect carefully negotiated health policies, expenditure frameworks and fiscal stability. Insistence on accountability and concerns about macroeconomic policy are two sides of the same coin – both hinge on a reciprocal, trusting and respectful relationship between highly affected countries and donors. The cornerstone of this relationship must be a commitment by all parties to the absolute priority of HIV treatment, care and prevention services.