AIDSTAR-One | CASE STUDY SERIES May 2011

From Paper to Practice

Implementing the World Health Organization's 2010 Antiretroviral Therapy Recommendations for Adults and Adolescents in Zambia

Dana Greeson

HIV and child health supplies provided at a health clinic in Livingstone, Zambia (December 2009).

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In 2002, the World Health Organization (WHO) first published guidelines for a public health approach to scaling up antiretroviral therapy (ART) in resource-limited settings. These guidelines were simplified in 2003 and revised in 2006. In October 2009, WHO led a multidisciplinary committee of HIV treatment experts to further revise and update the guidelines. Their recommendations were packaged as *Rapid Advice: Antiretroviral Therapy for HIV Infection in Adults and Adolescents* and were disseminated in late November 2009.

The key messages that emerged from these recommendations are earlier initiation of ART, the use of less toxic treatment regimens, and an expanded role for laboratory monitoring, including both CD4 testing and viral load (VL) monitoring (WHO 2009). Table 1 lists eight key *Rapid Advice* recommendations. The full revised guidelines, *Antiretroviral Therapy for HIV Infection in Adults and Adolescents: Recommendations for a Public Health Approach* (2010 version), were released in July 2010.

The WHO committee of experts that developed the recommendations agreed on a set of guiding principles for countries revising their national HIV treatment guidelines. Principal consideration was given to the need for public health interventions that "secure the greatest likelihood of survival and quality of life for the greatest numbers of people living with HIV." It further emphasizes that "the individual rights of [people living with HIV] should not be forfeited in the course of a public health approach" (WHO 2009, 4). The four guiding principles for countries revising their treatment guidelines are as follows:

This publication was produced by the AIDS Support and Technical Assistance Resources (AIDSTAR-One) Project, Sector 1, Task Order 1.
USAID Contract # GHH-I-00-07-00059-00, funded January 31, 2008.

- **Do no harm:** When introducing changes, preserve access for the sickest and most in need.
- **Ensure access and equity:** All clinically eligible people should be able to enter treatment services (including ART) with fair and equitable distribution of treatment services.
- **Promote quality and efficiency:** Ensure delivery of the highest standards of care within a public health approach so as to achieve the greatest health impact with the optimal use of available human and financial resources.
- **Ensure sustainability:** Understand the long-term consequences of change with the vision of providing continued, life-long access to ART for those in need.

Recently, many countries have begun to assess the feasibility of revising their national guidelines to reflect the new WHO recommendations. Côte d'Ivoire, Malawi, Nigeria, Tanzania, and Zambia have undertaken feasibility studies, including cost analyses, to assess the impact of adopting the new guidelines. These studies have demonstrated that many countries face significant challenges as they move to incorporate the recommendations into their national treatment protocols, including ensuring the availability of resources to support increased patient loads, improving supply chain management capacity, providing sufficient human resources, and building in-country consensus around protocol changes.

After the 2009 release of WHO's *Rapid Advice* for HIV treatment in adults and adolescents, Zambia launched a broad-based effort to update its national treatment protocols. The Ministry of Health (MOH) succeeded in creating an efficient and inclusive review and revision process for the guidelines, which they began implementing in 2011.

TABLE 1. WHO RAPID ADVICE KEY RECOMMENDATIONS

1.	Start ART in all patients living with HIV who have a CD4 count of less than 350 cells/mm^3, irrespective of clinical symptoms.
2.	Start one of the following regimens in ART-naïve individuals eligible for treatment. • Zidovudine (AZT) + lamivudine (3TC) + efavirenz (EFV) • AZT + 3TC + nevirapine (NVP) • Tenofovir (TDF) + 3TC or emtricitabine (FTC) + EFV • TDF + 3TC or FTC + NVP
3.	Start ART in all individuals living with HIV with active tuberculosis, irrespective of CD4 cell count.
4.	Start ART in all individuals living with both HIV and hepatitis B virus who require treatment for their hepatitis B infection, irrespective of CD4 cell count or WHO clinical stage.
5.	Start ART in all pregnant women living with HIV and a CD4 count of less than 350 cells/mm^3, irrespective of clinical symptoms.
6.	Where available, use viral load to confirm treatment failure. • Where routinely available, use viral load every six months to detect viral replication. • A persistent viral load above 5,000 copies/mL confirms treatment failure. • When viral load is not available, use immunological criteria to confirm clinical failure.
7.	A boosted protease inhibitor (PI/r) plus two nucleoside analogues are recommended for second-line ART. • For second-line ART, atazanavir/ritonavir (ATV/r) and lopinavir/ritonavir (LPV/r) are preferred.
8.	National programs should develop policies for third-line therapy that consider funding, sustainability, and equitable access to ART.

Source: WHO 2009.

The Response to HIV in Zambia

Zambia has an estimated 12.9 million inhabitants and a gross national income per capita of U.S.$960 (The World Bank 2009). The most recent Zambian Demographic Health Survey indicates that 14 percent of Zambians between 15 and 49 years of age are living with HIV (Central Statistical Office et al. 2009). However, demographic and regional variation across the country reveals a more complex picture. For example, among women, HIV prevalence is 16 percent, compared to 12 percent among men. For adult women, prevalence peaks at 26 percent in the 30 to 34 age group, which is four times the rate among women aged 15 to 19 and approximately twice the rate observed among women aged 45 to 49. HIV prevalence in urban areas is twice that of rural areas (20 percent versus 10 percent, respectively). HIV prevalence also varies considerably by province, ranging from the highest prevalence in Lusaka (21 percent) to the lowest in North-Western and Northern (both 7 percent). Prevalence in urban antenatal clinics is approximately 25 percent, and an estimated 28,000 infants are born infected with HIV annually.

Rapid increases in HIV funding in the early 2000s led to a major scale-up of all HIV activities in Zambia, with treatment consistently accounting for more than half of all HIV spending. The Zambian national ART program began in 2004 with support from the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) and other stakeholders. Major stakeholders and their relationship (if any) to PEPFAR are listed in Box 1.

In 2004, the national ART program was initiated with the establishment of the first ART clinics, co-located on the premises of existing primary health care centers in the Lusaka urban district. By March 2010, the national HIV program had grown significantly, totaling 232 centers in all provinces (see Figure 1), with over 320,000 patients enrolled in care and 277,355 patients receiving ART. At the end of 2009, the national ART program was reaching over 68 percent of adults in need of ART (Republic of Zambia 2010).

The Zambian national ART guidelines were first developed in 2003 based on WHO guidelines. These were revised in 2007 according to the new WHO guidelines and have recently undergone a second revision catalyzed by the July 2009 release of the WHO *Rapid Advice Guidelines: Antiretroviral Therapy for HIV Infection in Adults*

BOX 1. STAKEHOLDERS IN ZAMBIA'S NATIONAL ART PROGRAM

PEPFAR agencies
- U.S. Agency for International Development
- Department of Defense
- U.S. Centers for Disease Control and Prevention, Department of Health and Human Services

PEPFAR partners
- National HIV/AIDS/STI/TB Council
- Clinton Health Access Initiative
- Centre for Infectious Disease Research in Zambia
- Zambia HIV/AIDS Prevention, Care and Treatment Partnership
- Churches Health Association of Zambia
- Faculty of General Practitioners and Private Sector
- JHPIEGO
- John Snow, Inc. and the USAID | DELIVER PROJECT
- Supply Chain Management System

Other stakeholders
- Konkola Copper Mines Hospital
- Médecins Sans Frontières
- School of Medicine, University of Zambia
- University Teaching Hospital
- World Health Organization
- Japanese International Cooperation Agency

Figure 1. Map of Accredited ART Sites in Zambia

Source: Geographic Information System

and Adolescents and the subsequent July 2010 release of the updated WHO *Antiretroviral Therapy for HIV Infection in Adults and Adolescents: Recommendations for a Public Health Approach*.

Guideline Revision Process

In January 2010, the Zambian MOH called an initial meeting to compare the new WHO recommendations with the current national treatment guidelines. The National AIDS Council; other relevant not-for-profit organizations (e.g., the Centre for Infectious Disease Research in Zambia; the Zambia HIV/AIDS Prevention, Care and Treatment Partnership; John Snow, Inc.; Japanese International Cooperation Agency); private companies, including Konkola Copper Mines; the University Teaching Hospital; the Zambian Defense Force; and other stakeholders, including the PEPFAR team, were invited. Private sector representatives were also invited to all meetings; participants from several pharmaceutical companies and a large mining company attended. Private practitioners were also invited but did not attend the initial meetings.

At this initial meeting, participants reviewed and discussed each of the revised WHO recommendations. The review committee felt strongly that each recommendation should be considered individually for its appropriateness, feasibility, and acceptability within the Zambian context. The MOH initiated and led this review process (for more details, see the Evidence Considered section).

The scientific evidence supporting the guideline changes was not in contention. The issue that led to debate among committee members was the significantly increased cost of implementing guideline changes, because even the old eligibility criteria were expected to create a funding gap for the national treatment program in the next few years. A second area of contention was the impact that the recommendations would have on the public health system's capacity to deliver high-quality HIV care and treatment, and the potential cost to other areas of HIV spending due to additional ART-related expenditure.

The MOH held additional meetings with key stakeholders to discuss the cost implications, both human and financial, of the recommended guideline changes. Official adoption of the new guidelines took place at the end of 2010. Figure 2 displays a timeline mapping the overall meeting process.

Cost concerns: The major costing concerns include new, more expensive drug regimens; additional testing for VL and hepatitis B (HBV); increased patient numbers; the ability of existing systems to absorb increased patient numbers; the expected increased demand on human resources; and space constraints. The specific changes anticipated to significantly impact cost were:

- Withdrawing the less expensive stavudine (d4T)-based regimens and replacing these with more expensive tenofovir (TDF)- or abacavir (ABC)-based regimens.

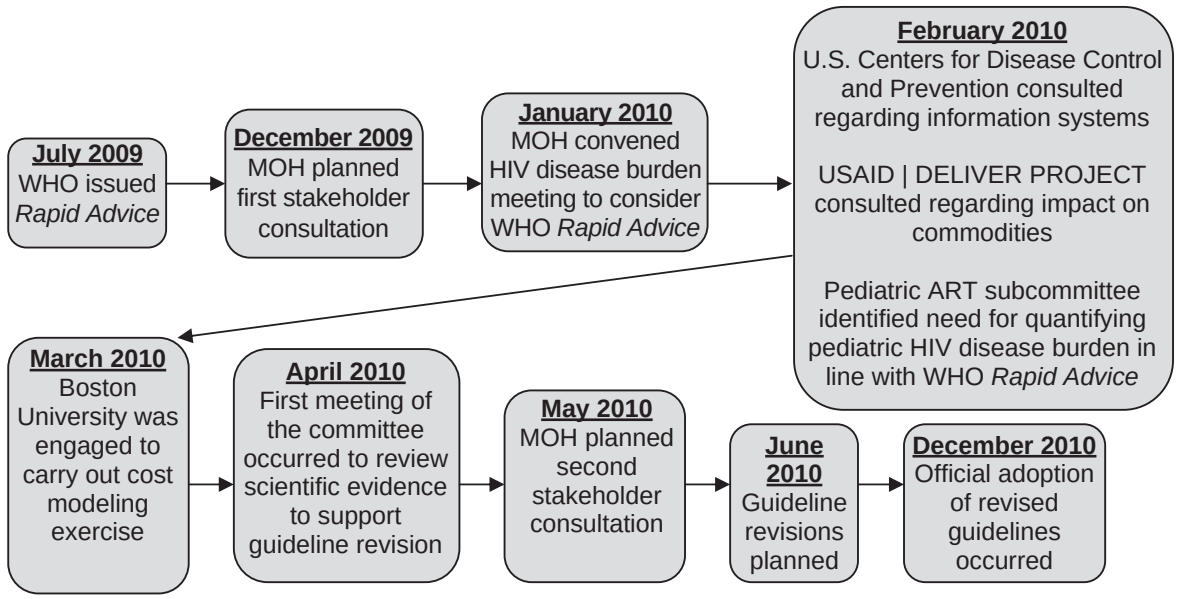
- Increasing the CD4 threshold to 350 cells/mm^3 for ART initiation.
- Providing ART to all patients with active tuberculosis (TB) and HIV.
- Making a third-line regimen available to patients who require it.
- Identifying and treating all patients co-infected with HIV and HBV.
- Treating all HIV-positive partners in serodiscordant relationships.

Cost forecasting: The Supply Chain Management System (SCMS) Project, led by John Snow, Inc., provided cost estimates of each guideline change (discussed subsequently). In addition, the MOH asked Boston University (BU), which previously conducted costing assessments for the national ART program as part of an ongoing operational research project, to perform a broad national-level costing and analysis as part of the National Health Strategic Plan. BU has proposed adapting South Africa's national cost modeling for use in Zambia. The model will provide costs for the national treatment program (antiretroviral [ARV] and non-ARV drugs, visits costs, laboratory costs, and so on) under different scenarios for new treatment guidelines over the next five years. Findings are expected in the first half of 2011.

Quantification and Logistics

The USAID | DELIVER PROJECT, implemented by John Snow, Inc., and a group of clinicians and pharmacists provided support to the MOH for quantifying HIV commodities, including drugs and laboratory supplies, based on the new guidelines. Partner organizations provided current estimates of patient numbers, drug regimens, and projected number of new patients in need of ART. Site-level consumption data were also used. The team used a two-pronged process to evaluate the standard equipment needs and actual consumables based on existing demand, then projected the increased resource needs based on the new CD4 cutoff suggested in the guidelines (< 350 cells/mm^3). This

Figure 2. Timeline of the Zambia Guideline Revision Process



projection assumed an increase in some laboratory supplies (e.g., VL), but also a potential reduction in others. For example, CD4 testing rates were reduced assuming CD4 count was only to be used at baseline visits and would be replaced by VL going forward.

The team used a service statistics-based forecast methodology for the laboratory reagent quantifications. This method relies on actual consumption data for estimating and forecasting quantities. The team reviewed and translated the number of tests conducted per facility per year into product required. For ordering purposes, it was agreed that laboratory supply projections would remain unchanged for the remainder of 2010 because of an expected lag in the impact of the new guidelines. For ARVs, the team used a morbidity methodology based on the number of patients expected to be on treatment each year. It was assumed that current stocks would be sufficient to absorb any small increases experienced in the early phases as the new guidelines were rolled out.

The software used for these quantification exercises was Quantimed. The forecast requirements were input into Pipeline software for costing and procurement planning. These software packages were endorsed by the MOH for use in national quantification exercises in early 2010.

Evidence Considered

Recommendation 1. Start ART in patients living with HIV who have a CD4 count of < 350 cells/mm^3, irrespective of clinical symptoms: The committee reviewed the available literature, which reported marked improvements in post-ART initiation mortality and morbidity associated with raising the threshold CD4 count to 350 cells/mm^3. Studies from both resource-rich and -poor settings supported this recommendation. The review committee agreed that the recommendation was likely to decrease morbidity and mortality in Zambia. However, they also recognized that the revision would increase the patient load.

The MOH asked partners to provide estimates of the increase in patients requiring ART under the revised cutoff. These estimates suggested that an additional 70,000 patients would require treatment immediately. The SCMS Project, which provides logistics and supply chain management support to the Zambian government, provided an estimate of the additional costs that would be incurred. The total additional costs calculated were estimated to reach between U.S.$800,000 and $1,000,000 over the next five years. This takes into account the anticipated costs of additional drugs and laboratory testing.

The MOH estimated that existing stock would be sufficient to cover the additional drug needs up to the end of the 2010 calendar year. Thereafter, funding pledged to the MOH is expected to fall short of the amount necessary to purchase additional stock. Funding sources to purchase additional drugs are expected to either phase out or flat-line in 2011. However, the MOH is committed to mobilizing resources to meet the needs of the increased patient load and decided to adopt this new recommendation and mobilize resources to cover the increased costs. They applied for a Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) Round 10 grant to support increased ARV procurement, and the application was approved with an overall grant budget of approximately U.S.$260 million (GFATM 2011).

Recommendation 2. Start one of the following regimens in ART-naïve individuals eligible for treatment:

- Zidovudine (AZT) + lamivudine (3TC) + efavirenz (EFV)
- AZT + 3TC + nevirapine (NVP)
- TDF + 3TC or emtricitabine (FTC) + EFV
- TDF + 3TC or FTC + NVP

In 2007, Zambia switched to TDF-based first-line therapy. However, approximately 40 percent of patients remained on the d4T-based first-line therapy. The 2009 recommendations recommended a more aggressive approach: rapidly wean patients off d4T and transition them to TDF.

After the SCMS Project conducted a comprehensive cost analysis, it was agreed that the transition from d4T to TDF-based regimens should be done over a period of four years (up to the start of 2015), because this was believed to be the most appropriate time period over which to absorb the increased costs of the switch. National guidelines developed in 2007 when TDF was first introduced guided the switching process. This guidance for switching patients to TDF was also included in the recently revised treatment guidelines. To promote a smooth transition, health care workers and lay counselors received training in the use of these switching guidelines and appropriate patient counseling combined with targeted media messaging.

Recommendation 3. Start ART in all individuals living with HIV with active TB, irrespective of CD4 cell count: The review committee read the published literature and consulted in-country specialists and experts regarding the feasibility of instituting this recommendation. It was anticipated that an additional 30,000 to 50,000 patients would be eligible for ART based on these criteria. Because Zambia relies on rifampicin-based antituberculosis therapy, additional costs would be incurred due to both the increased number of patients requiring treatment and the use of more costly EFV. While the cost challenges were acknowledged, it was decided that earlier ART initiation in patients with active TB would likely lead to better treatment outcomes. This recommendation was adopted, and all patients with active TB would initiate ART within two to four weeks after starting TB treatment.

Recommendation 4. Start ART in all individuals living with both HIV and HBV who require treatment for their HBV infection, irrespective of CD4 cell count or WHO clinical stage: Treatment sites in Zambia do not routinely screen patients living with HIV for HBV, nor does the national program currently have the systems in place to conduct widespread HBV screening. There are limited data on HBV prevalence in persons living with HIV in Zambia. However, crude data based on blood bank statistics suggest an estimate of an additional 10,000 patients who may need treatment (Mphahlele et al. 2002). It was acknowledged that adopting this recommendation would result in additional costs for HBV testing and increased drug costs for the treatment of both HIV and HBV patients. However, the review committee agreed that HBV/HIV co-infection is important enough to include HBV testing in the revised guidelines. The most recent quantification exercise has quantified reagents for HBV testing beginning in the second half of 2011.

Recommendation 5. Start ART in all pregnant women living with HIV who have CD4 count < 350 cells/mm^3, irrespective of clinical symptoms: Zambia raised the CD4 threshold for pregnant women from 200 to 350 cells/mm^3 in 2009. This recommendation was already in place in Zambia, and therefore the review committee did not discuss it in depth.

Recommendation 6. Where available, use VL to confirm treatment failure: VL testing is already available on a limited basis to patients in Zambia, as determined by a VL algorithm that detects patients presumed to be failing treatment. VL testing costs about U.S.$27 per sample and is only available in a few areas of the country. Currently, the cost of VL testing is covered almost exclusively by partner organizations. To avoid unnecessary testing and preserve limited resources, only patients who are obviously experiencing clinical or immunological failure receive VL testing. While the committee

recognized the limitations of this algorithmic approach, it decided that the program should continue with this approach and readdress the issue later in the year. This is largely due to the prohibitive costs of VL testing combined with limited access to countrywide VL laboratory capacity.

Recommendation 7. A boosted protease inhibitor (PI/r) plus two nucleoside analogues (NRTIs) are recommended for second-line ART: Historically, lopinavir/ritonavir (LPV/r) has been the only boosted protease inhibitor (PI) available in sub-Saharan Africa. It therefore follows that LPV/r has been the recommended second-line PI since 2005 and will remain so in the revised guidelines. However, Zambia has recognized the potential clinical importance and cost savings of atazanavir/ritonavir (ATV/r). The combination of ATV/r costs U.S.$355 per patient per year, while LPV/r costs U.S.$440 per patient per year (Clinton Health Access Initiative 2010). Given the anticipated cost savings of ATV/r, a gradual transition from LPV/r to ATV/r is planned as soon as the drug has been registered and becomes available locally. To avoid confusion among care providers, the new guidelines will briefly mention ATV/r but will not yet recommend the combination as second line. Once available, guidelines will be updated so that ATV/r will be recommended as an alternative to LPV/r, and appropriate provider training will be scheduled.

Recommendation 8. National programs should develop policies for third-line therapy that consider funding, sustainability, and the provision of equitable access to ART: The national ART program is now in its seventh year and, as of February 2010, has already identified over 300 patients who potentially require third-line treatment. Third-line drugs are available in Zambia but are not supplied by the MOH. Therefore, the third-line regimen is only available to patients who can afford these costly drugs. In the absence of WHO recommendations on third-line drugs, Zambia has drafted preliminary guidelines. The current recommended third-line drugs are raltegravir and darunavir/ritonavir with either TDF/FTC or AZT/3TC. Genotyping is required before any patients are considered for third-line regimens. Because funding is not currently available, expanding access to third-line ART is on hold. However, the MOH has established a third-line Advanced Treatment Centre (a Center of Excellence at University Teaching Hospital) that has the technical expertise and appropriate diagnostics to monitor patients who are able to pay for third-line regimens.

Implementation

In December 2010, Zambia finalized its revised HIV treatment guidelines to incorporate the most recent WHO recommendations. The original revision committee, with additional support from academic institutions, including the University of Maryland and the University of Alabama, are currently developing an orientation package that highlights the changes compared to previous guidelines. A one- to two-day training of trainers is planned with partner organizations and the MOH. Each district/province has an identified trainer/mentor who will be trained. Mentors are primarily medical officers.

Following training, a staggered implementation of the new guidelines is planned. This will be completed over a relatively short timeframe (approximately 6 weeks) and rolled out district by district using both MOH trainers and partners. This will allow a comprehensive ongoing assessment of the process to be carried out and will also allow for the gradual scale-up and strengthening of associated systems (e.g., logistics). More frequent delivery of drugs, increased storage capacity, and didactic trainings will be accompanied by onsite clinical mentoring and updated pocket guides. These reference materials will contain updated

standard operating procedures, revised treatment guidelines, and standardized job aids.

All 72 districts in Zambia will be targeted. The relevant district health management teams will be responsible for inviting key clinicians from each site. Trainings will be repeated in high-density areas where needed, but all districts will receive a minimum of one training. National coverage for training on the new guidelines is likely to take two to three months. The costs of these trainings will be split between the cooperating partners, the sites, and the MOH. A formal assessment of the implementation process is planned after 6 to 8 months.

Currently, routine indicators are monitored on a quarterly basis for all sites. Indicators will be adjusted to represent the new guidelines. Some examples of adjusted indicators include the number of patients eligible and receiving treatment according to the revised CD4 cutoff, the number of patients on a TDF-based first-line regimen, the number of patients receiving a PI-based second-line regimen, and the number of patients on third-line drug regimens.

Additionally, the MOH has reviewed the software for inventory management in order to link it with Smartcare, the national electronic patient tracking system. This will allow a direct link between the clinic and the pharmacy so that patient numbers and consumption data can be electronically integrated, allowing for more accurate quantification and accountability at the clinic level. Once the ARV logistics system evaluation is complete, these upgrades will be fully implemented.

Dana Greeson

HIV testing and counseling room at a health clinic in Livingstone, Zambia (December 2009).

What Worked Well

Trust built on inclusion and transparency: A policy of open discussion and transparency among policymakers, program managers, implementers, and partner organizations has built a foundation of trust and resulted in a strengthened, unified approach to combating HIV in Zambia, as exemplified by the most recent guideline revision process. A variety of stakeholders were invited to participate in the revision committee, including personnel from teaching hospitals, the private sector, nongovernmental organizations, and those working in pharmacy and logistics/supply chain management.

Identifying stakeholders for the committee: To ensure that the appropriate people were at the table, representatives who had the expertise and could commit to attending the meetings were identified early in the planning process. Engagement of financial managers and costing experts was also critical during the debate on the feasibility of guideline changes. In addition, incorporating a mix of policymakers, program managers, and clinical personnel on the committee increased the likelihood of successful roll-out and implementation of the new guidelines.

Refining the review process: Following the large group discussion, a small core group of reviewers developed the first draft of the guidelines. This dramatically decreased turnaround time. Using email for informal correspondence and official memorandums from the permanent secretary for formal communication allowed for the rapid adoption and dissemination of

policy (even if final guidelines and other documents have taken longer to adopt and disseminate).

Ensuring accurate data: The availability of reliable data was also important. Real patient numbers are essential for forecasting drug and laboratory supplies. Robust software is extremely helpful when taking into consideration varying drug regimens and large numbers of patients. Partners need to work very closely with the MOH to ensure that numbers are accurate. This prevents both drug stockouts and underutilization of drugs, which avoids waste due to expiration.

Implementing task-shifting: Task-shifting has been extremely successful in Zambia. Over 1,000 lay counselors have been trained to assist with filing, adherence counseling, and patient flow. In several pilot sites, lay counselors have been trained to perform vital sign assessments, including height, weight, blood pressure readings, and temperature charting. Also, the General Nursing Council has introduced a year-long nurse practitioner course that qualifies nurses to prescribe ARVs and manage stable patients.

Challenges

Limited community participation: As mentioned previously, in 2007, Zambia switched to TDF-based first-line therapy and began weaning patients off d4T. To support this transition, the MOH coordinated a series of media releases, including public television and print announcements, about the phase out of d4T. The announcements emphasized that the transition would be gradual and that concerned individuals should visit their health providers and discuss the matter before switching any of their drugs. The MOH also reassured asymptomatic patients who were on d4T that the switch, while necessary, was not a matter of utmost urgency. However, the media campaign failed to include messages from community leaders (including traditional and religious leaders), civil society, and people living with HIV, which may have broadened its reach. In addition, community acceptance of guideline changes might have been greater had there been more community engagement starting in the early stages of the revision process.

Communication difficulties: Lack of formal communication from WHO headquarters or the Zambia Country Office alerting the MOH to the upcoming release of the *Rapid Advice* hampered the early stages of the revision process, forcing the MOH to handle multiple media requests and public queries at short notice.

Lack of clarity for some recommendations: The WHO recommendations suggested "progress in reducing use of d4T" but provided little guidance on how to phase out the drug. More guidance in terms of how urgently this should be done would have been helpful to health care providers as they implemented the new guidelines. Also, the WHO recommendation that third-line regimens be developed and implemented provided little guidance on how to obtain these drugs or what to use for countries inexperienced in this area.

Balancing costs and results: As in many developing countries, financial and human resources remain a huge challenge. However, the MOH is committed to providing patients with the care and treatment they require, and recognizes the benefits to both the individuals and the population of earlier, more aggressive therapies. Relying on cheaper first-line regimens may decrease upfront costs but is likely to result in a much higher level of toxicity and more complicated resistance patterns that render second-line options less effective. Identifying patients living with HIV early and achieving virologic suppression remain an important part of the National Prevention with Positives strategy. This strategy was recently introduced in order to shift the focus from treatment toward prevention. It is a comprehensive approach that includes a push toward testing of partners, active screening for and management of sexually transmitted infections, family planning counseling and provision of services, and treatment adherence.

Recommendations

The most recent WHO recommendations provide guidance to countries looking to update their national HIV treatment guidelines. Each recommendation should be assessed carefully for acceptability, relevance, and appropriateness to the local setting.

Understand the costs: Implementation of new guidelines is often a costly process that should be considered from various perspectives. The cost burden may be "front heavy" when, for example, increased costs incurred early in the program may be justified or balanced by lower costs, such as improved patient outcomes, at a later point. Similarly, hidden costs should be considered, including the cost of increasing 1) the number of health care providers in order to screen newly eligible patients, 2) HIV commodity storage and distribution requirements, and 3) renal function (creatinine) testing due to broad-scale use of TDF, as well as the cost of printing new guidelines.

Handle the transition with care: The process for phasing out the older ART regimens and phasing in the newer drugs should be handled carefully. In Zambia, new drugs are added to the monthly ordering forms and facilities receive help with their initial orders. The MOH and partners then carefully monitor drug stocks to ameliorate the high risk of stockouts during the phase in/phase out period.

Establish an ongoing guideline review process: In the ever-changing field of HIV treatment, it is likely that recommendations will be updated or changed regularly. Establishing an annual guideline review process would significantly streamline any revisions and ensure that new WHO recommendations are automatically incorporated into country guidelines. Having a standing guideline review committee would also minimize costs and time associated with the guideline review process. Additionally, health providers and patients should receive clear and concise information because frequent alteration of recommendations may cause uncertainty. Hard copies of guidelines need to be clearly labeled and dated. New documents should state clearly that "these guidelines replace the previous guidelines dated X."

Increase professional staff: Based on the experiences of the MOH, it is important to address the challenge of limited human resources by increasing the number of professional and lay staff available within the health system. This would involve such activities as increasing the number of health care workers being admitted into nursing colleges, medical schools, and affiliated institutions; providing more attractive incentives for medical staff, particularly those in rural areas; and formalizing any cadres of lay health care workers through development of terms of reference, salary scale, and training and mentoring.

Future Programming

In December 2010, Zambia finalized its revised HIV treatment guidelines to incorporate the most recent WHO recommendations; these revised guidelines are currently being printed. The MOH plans to officially endorse, disseminate, and implement these revised guidelines in 2011 according to the implementation plan detailed in this case study. An in-depth costing of the new guidelines is under way to explore resource implications for different guideline scenarios over the next five years. ■

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ACKNOWLEDGMENTS

The AIDSTAR-One team wishes to thank the following partners for providing input and guidance in development of this case study: USAID/Washington, especially Robert Ferris and Tom Minior; USAID/Zambia; Ministry of Health, Zambia; National AIDS Council; PEPFAR; Centre for Infectious Disease Research in Zambia; FHI/Zambia Prevention Care and Treatment; John Snow International and USAID | DELIVER PROJECT and SCMS Project; University Teaching Hospital; the Clinton Health Access Initiative; Catholic Relief Services; Churches Health Association of Zambia; and Boston University.

RECOMMENDED CITATION

Bolton, Carolyn, Stephanie Topp, Victoria Rossi, and Bisola Ojikutu. 2011. *From Paper to Practice: Implementing the World Health Organization's 2010 Antiretroviral Therapy Recommendations for Adults and Adolescents in Zambia*. Case Study Series. Arlington, VA: USAID's AIDS Support and Technical Assistance Resources, AIDSTAR-One, Task Order 1.

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