

The Global Fight Against HIV/AIDS, Tuberculosis, and Malaria

Current Status and Future Perspectives

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Abstract

HIV/AIDS, tuberculosis, and malaria are 3 major global public health threats and cause substantial morbidity, mortality, negative socioeconomic impact, and human suffering. Despite the significant increase in financial support and recent progress in addressing these 3 diseases, important obstacles and unmet priorities remain. Disease-specific interventions have had a considerable impact on improving health systems. However, despite considerable investment, weak health systems, inadequate human resources, and poor laboratory infrastructure continue to be major obstacles to expanding health services. Health system strengthening should be addressed in an integrated approach that includes HIV-, tuberculosis-, and malaria-specific interventions. Investment in strategic information and public health laboratory network capacity strengthening are key actions to expand services to successfully address those diseases in heavily impacted countries.

HIV/AIDS, tuberculosis (TB), and malaria are 3 major global public health threats that undermine development in many resource-poor and some transitional settings. Throughout the world, close to 5 million people die every year of these illnesses, with substantial humanitarian, economic, and social impact, which is still not fully measured. The objective of this article is to briefly review the epidemiology of these diseases, describe key interventions, and highlight priorities and challenges to overcoming these diseases at global level.

The Global Impact of HIV/AIDS

Apart from the human suffering caused by these 3 diseases, HIV/AIDS in particular has the potential to impact negatively on the socioeconomic development of individual societies because of the associated high adult mortality in some countries, especially in sub-Saharan Africa. Despite the progress made in the response to HIV/AIDS during the last decade, the HIV pandemic remains one of the most serious challenges to global health and probably will continue to be one of the leading causes of death and disability in the world for the next decades. Since the initial description of HIV as the causative agent of AIDS, more than 60 million people have been infected with the virus, and more than 25 million people have died.¹

International mobilization to combat HIV/AIDS has increased substantially since the Millennium Development Goals (MDGs) were defined in 2000 (<http://www.un.org/millenniumgoals/>). The 2001 UN General Assembly Special Session Declaration of Commitment on HIV/AIDS marked the beginning of significant change in the scope of the HIV/AIDS response.² This declaration was followed by a

substantial increase in political commitment, social mobilization, and financial resources, witnessed in 2003 by the launch of World Health Organization's (WHO's) "3 by 5" initiative³ and the announcement of the United States' "President's Emergency Plan for AIDS Relief" (PEPFAR). These initiatives committed to dramatic scale-up of HIV/AIDS treatment, care, and prevention, including, crucially, access to antiretroviral treatment (ART) throughout the developing world. Although the 3 by 5 target of 3 million living in low- and middle-income countries receiving treatment by the end of 2005 was reached 2 years later than hoped, the collective experience demonstrated that it is feasible to address the HIV pandemic in resource-limited settings using public health principles and a comprehensive approach that encompasses HIV prevention, treatment, and care and that such an approach impacts on morbidity and mortality.^{4,5}

One of the most important achievements of 3 by 5 was to catalyze sustained support for the AIDS response, in particular the subsequent commitment by leaders of the G8 to work toward universal access to necessary HIV/AIDS services.⁶ These universal access goals were subsequently endorsed at the United Nations General Assembly High Level Meeting on AIDS in September 2006.⁷

WHO and UNAIDS recently released new estimates of the magnitude of the global HIV epidemic and the resources needed to confront it.⁸ At the end of 2007, approximately 33 million people were living with HIV globally, with a global adult prevalence of about 0.8%, stable since 2001, but declining somewhat in Africa. Two patterns characterize the epidemiology of HIV/AIDS at a global level: (1) generalized, high prevalence epidemics that are sustained in the general population and where substantial mother-to-child transmission occurs, almost exclusively in the sub-Saharan Africa region but affecting selected countries elsewhere, such as Haiti and Papua New Guinea; and (2) otherwise, concentrated, low-prevalence epidemics that mostly affect risk populations such as injecting drug users, commercial sex workers, and men who have sex with men.¹

Sub-Saharan Africa remains the most heavily affected region of the world, accounting for approximately two thirds of all incident and prevalent HIV infections and three quarters of all AIDS deaths. Almost 90% of children with HIV are African. Approximately 60% of adult HIV infections in sub-Saharan Africa are in women, the incidence being especially high in adolescents and younger women. The impact of the epidemic in Africa has been evident with reduced life expectancy by as much as 2 to 3 decades in the most heavily affected countries of southern Africa, disrupted family and demographic structures, and huge increases in orphanhood. An especially important aspect of the public health impact of HIV/AIDS has been the secondary epidemic of TB, most severe in southern Africa where rates of HIV infection are highest.

By December 2007, it was estimated that almost 3 million HIV-infected people were receiving ART in low- and middle-income countries, representing approximately 31% of the estimated 9.7 million people currently in need of treatment.⁹ There has been a substantial expansion in access to key health sector interventions such as HIV testing and counseling, prevention of mother-to-child transmission, and ART. Coverage of antiretroviral prophylaxis in HIV+ pregnant women for prevention of mother-to-child transmission in low- and middle-income countries, for example, increased from 9% in 2004 to 33% in 2007. By the end of 2007, 200,000 children were estimated to be receiving maintenance ART.

This progressive expansion of ART coverage and other interventions is leading to measurable impact on the HIV epidemic and its related direct costs. The mortality associated with HIV and related diseases has declined during the past 2 years, and much of this must be attributable to ART. Global HIV incidence likely peaked in the late 1990s and has gradually declined since then. Some of this decline is likely the result of interventions rather than the natural history of the epidemic itself. Nevertheless, despite the important progress in treatment and prevention, the number of persons affected by the disease is still rising, with about 2.5 million new infections and 2.1 million deaths in 2007.⁹ Stable or even declining HIV incidence applied to an expanding population means that although incidence and prevalence may have peaked, for example in Africa, the absolute number of people living with HIV may continue to increase.

The prevention and treatment of pediatric HIV remains challenging, despite recent encouraging trends. HIV-related disease is an important cause of morbidity and mortality in infants and children in countries with generalized HIV epidemics, particularly in southern Africa. More than 90% of infections in infants and children result from mother-to-child transmission. It should be noted that in the absence of any intervention, about 20% to 45% of infants born to HIV-infected mothers become infected. The risk of transmission can be reduced to well under 5% with use of proven interventions. Globally, according to the most recent estimates, there are 2.1 million children living with HIV, encompassing 420,000 new infections in children (almost 17% of all new infections globally) and 290,000 deaths in 2007. In many countries, the mode of prevention and treatment programs for infants and children remains that of pilot initiatives, often funded and implemented by outside partners and organizations. National HIV/AIDS programs must ensure they take into account the needs of children and their families and address the associated logistical and financial gaps.

In working toward universal access, WHO has prioritized 5 strategic directions for HIV/AIDS work in the health sector: increasing knowledge of HIV serostatus; maximizing the health sector's contribution to HIV prevention;

accelerating the scale-up of HIV treatment and care, including for neglected populations such as injecting drug users and children; strengthening and expanding health systems to address HIV/AIDS and other conditions; and investing in strategic information to guide a more effective response. Consistent with the reinvigorated commitment to primary health care, WHO recommends a public health approach to the design and provision of services for HIV prevention, care, and treatment.⁵ This entails standardized and simplified approaches, including recommendations for first- and second-line therapy; decentralization of service provision; task shifting strategies to optimize the use of available human resources; simplified clinical decision making; involvement of community members and people living with HIV in managing and designing programs and delivering services; and use of strategies to minimize costs, including the use of generic fixed-dose combination medicines and alternative laboratory technologies to diagnose and monitor treatment.

New estimates of the financial resources required for a comprehensive response to HIV/AIDS were released in November 2007.¹⁰ Resources needed to scale up prevention, treatment, and support programs will grow from \$10 billion in 2007 to \$35 billion in 2010 and will reach \$41 billion by 2015.

Experience to date has shown that weakness of health systems and infrastructures is a major obstacle to the delivery and sustainability of scaled up programs.¹¹ A potentially harmful debate has opened up about whether disease-specific programs help or hinder systems strengthening, and this is an important topic for operational research and targeted evaluation. In the same way that pitting prevention against treatment scale-up was a harmful and false dichotomy, so we must ensure that this new argument does not detract from the wide gap in treatment and prevention access that still exists internationally. A commitment to achieve universal access to HIV/AIDS prevention, treatment, care, and support must be coupled with determination to address health system weaknesses, ensuring both approaches are mutually reinforcing.

The Global Impact of TB

TB is the second most common infectious cause of death worldwide, especially in Asia and sub-Saharan Africa. Globally, 9.2 million new cases and 1.7 million TB-associated deaths occurred in 2006. The majority of these cases occurred in Asia, but the highest population rate has been observed in Africa where the prevalence of HIV infection is at its highest. According to WHO, approximately 700,000 cases and 200,000 deaths related to TB occurred in the HIV+ population worldwide in 2006.¹² The WHO African region, which represented only 12% of the world's total population in 2006,

harbored around a third of all new TB and 85% of all HIV+ new TB cases and was also the region where about a quarter of all estimated people with TB were also positive for HIV infection. In 2006, more than 50% of all reported new cases of TB in sub-Saharan Africa that were tested for HIV were found to be HIV+. Globally, there was an estimate of 500,000 cases of multidrug-resistant TB in 2006. These cases were unevenly spread, with 27 countries (of which 15 are in Eastern Europe) accounting for 86% of the total.

Outside the dramatic situation of TB-HIV coinfection in Africa, elsewhere, with exception of the European region where rates are approximately stable, the number of new cases of TB per capita appears to have been falling globally since 2003. However, in 4 WHO regions, the total number of new TB cases continues to rise globally owing to population growth.

Considering this scenario, scaling up effective HIV/AIDS and TB strategies, including collaborative TB-HIV interventions,¹³ is one of the most important public health challenges faced by Africa today. Ensuring that these programs are effective and decrease HIV-TB-related morbidity and mortality will be the key factor in their success. The Stop TB Strategy is the WHO's recommended approach to reducing the burden of TB in line with global targets (<http://www.who.int/tb/strategy>). Considered as the basis of TB control, the strategy has 6 major components: directly observed treatment, short course (DOTS) implementation; addressing TB/HIV, multidrug-resistant (MDR) TB, and other challenges; contributing to health system strengthening; engaging all care providers; empowering TB patients and communities; and enabling and promoting research. To date, progress obtained with the Stop TB Strategy has been mixed. Some components of the strategy, such as the detection and treatment of new TB cases in DOTS programs, have provided encouraging results, with rates of case detection for new smear-positive cases reaching more than 60% in 2006 (compared with the target of at least 70%) and the treatment success rate improved to just below the target of 85%. However, progress in the implementation and planning of other parts of the strategy has been less, with a need for scaling up and improvement of TB-HIV collaborating activities; more ambitious planning at the country level for treatment of patients with MDR or extensively drug-resistant (XDR) TB; and advocacy, communication, and social mobilization activities.

Regarding financial resources, available funding for global TB control in 2008 reached \$3.3 billion, up from less than \$1 billion in 2002. Nevertheless, the gap between the available and required resources is estimated to be \$1.1 billion.¹² This is mainly due to the higher funding requirements for more effective collaborative TB-HIV activities, in diagnosis and more aggressive management of MDR and XDR TB, and implementation of other activities of the overall Stop TB Strategy to meet the MDGs.

However, as observed with the HIV/AIDS pandemic, laboratory capacity is a major barrier to dealing with this disease, particularly with HIV-associated and drug-resistant TB, requiring a massive effort with associated human resources, capital investments, and biosafety needs. An integrated public health laboratory approach will be necessary to address the dual threat of HIV and TB. As part of the laboratory strengthening of HIV and TB programs, there is an urgent need for improved TB diagnostics, including external quality assurance and strengthened smear-microscopy services. In addition, given the difficulties with diagnosing TB in people living with HIV, HIV and TB programs will need to work together to scale up access to culture and drug sensitivity testing to quickly and accurately diagnose people living with HIV and MDR or XDR TB.

The Global Impact of Malaria

Malaria is endemic in 109 countries and continues to cause between 189 and 327 million clinical episodes of illness each year, with at least 881,000 associated deaths. Around 60% of these cases and more than 91% of deaths occur in sub-Saharan Africa, where malaria is the leading cause of morbidity and mortality in children younger than 5 years and pregnant women. Constituting 10% of the overall disease burden, malaria places a substantial strain on health services and costs Africa about \$12 billion in lost production each year. Furthermore, malaria consumes around one fourth of household incomes in most African endemic countries, reducing access to preventive interventions and lifesaving services.¹⁴

As observed with TB, the major burden of malaria occurs in sub-Saharan Africa and Asia, where a significant overlap with HIV infection also occurs. HIV infection is also associated with an increased frequency of clinical malaria and parasitemia.¹⁵ This association tends to become more pronounced with advancing immunosuppression and could have important public health implications for sub-Saharan Africa.¹⁶ However, the prevalence of malaria and HIV and the extent of geographic overlap vary widely within each region, even in countries with a high prevalence of both infections. Transmission of malaria and HIV can also result from inadequate blood transfusion practices and, for HIV, the use of unsafe injections.¹⁷

Global progress has also been made in malaria control with the adoption of effective interventions that are programmatically simpler than those recommended for HIV and TB: improved access to diagnostics and artemisinin-containing combination therapy for promptly diagnosed acute illness; vector control through use of insecticide-treated bed nets or indoor residual spraying; and use of intermittent preventive therapy in pregnancy. An international

partnership coordinated by WHO, UNICEF (United Nations Children's Fund), United Nations Development Programme, and World Bank—Roll Back Malaria—is targeted to halve the prevalence and deaths associated with this disease by 2010 in comparison with the levels at the beginning of the century (<http://www.rbm.who.int/>). Integrated interventions for malaria control have demonstrated dramatic impact at a community level in some studies, following an integrated introduction of artemisinin-containing combination therapy and insecticide-treated bed nets.

Annual funding for malaria control has increased at least 10-fold during the last 15 years, now approximating \$600 million annually.¹⁸ Millions of these long-lasting insecticidal nets and fixed-dose combination antimalarial treatments have been procured annually worldwide. However, the Global Fund for Tuberculosis, AIDS and Malaria estimates that resources will have to increase to more than \$3.5 billion annually by 2010 to meet the Abuja Declaration and MDGs for malaria control targets.¹⁹

Obstacles, Uncertainties, and Priorities to Fight HIV/AIDS, TB, and Malaria in the Future

Despite the progresses in the management of these 3 diseases, important obstacles, uncertainties, and unmet priorities remain. For HIV, many programs fail to use and integrate available prevention and treatment interventions at large scale—with condom use and cotrimoxazole prophylaxis, for example—or ignore local epidemiology and sociocultural factors when allocating resources. An extraordinary and special effort is required in the face of the HIV pandemic in sub-Saharan Africa, where just 8 countries with an adult HIV prevalence of more than 15% are responsible for more than 35% of the current estimated burden of global AIDS deaths.⁹ Only about 10% to 20% of people living with HIV in Africa know they are infected. In addition, it is increasingly being recognized that TB-related morbidity and mortality threaten progress in scaling up HIV care and treatment services. In April 2008, WHO convened a meeting of experts who concluded that the “Three I’s for HIV/TB”—isoniazid preventive therapy, intensified case finding for TB, and infection control for TB—should be an essential aspect of providing HIV services. The priority interventions for the health sector, including scaled up testing and counseling, preventing mother-to-child transmission, progressive expansion of treatment access, and the Three I’s for TB/HIV, offer the opportunity to normalize HIV and reduce stigma, rather than forever citing stigma as an insurmountable barrier to the right to life and health.¹¹

Priorities for TB include the further expansion of DOTS and addressing MDR and XDR disease as a matter of urgency.

This highlights the huge problem of infrastructure, for without laboratory capacity, drug resistance cannot be tackled because it cannot be diagnosed. TB, like HIV/AIDS, reminds us of the need for public health humility. Despite the meeting of program targets, the incidence of TB in some settings stubbornly refuses to decline. Conversely, in some settings, TB is in decline but other determinants seem more important than drug treatment programs. Similarly for HIV/AIDS, the natural history of the epidemic itself can obscure or override prevention effects, especially if weak, but such observations should make us redouble our efforts, not be discouraged.

Malaria is perhaps the “lowest hanging fruit” of these 3 diseases in which increased and sustained investments could lead to very rapid impact. It may also be the disease for which new technologies may be most applicable. There are early indications from several countries in Africa that this renewed effort at malaria control is beginning to have an effect, but additional tools, including a highly effective vaccine, are needed.

However, common themes extending to HIV, TB, and malaria are the need to adopt interventions according to local epidemiology and to invest in strategic information, particularly weak for malaria.²⁰ Another common element to these 3 public health problems is the urgent need to strengthen laboratory capacity to expand access to diagnosis and adequate management of HIV, TB, and malaria. Although the increased funding availability provides an opportunity for laboratory strengthening, unless efforts are made to simplify, standardize, and coordinate this process to support a public health approach in a comprehensive manner, there is a real risk that this investment in laboratory strengthening will not lead to efficient, effective, and sustainable services that strengthen national health services. WHO, as the UN agency responsible for global public health, is committed to supporting the strengthening of laboratories, in support of national health responses.

Finally, the lessons from the 3 by 5 HIV initiative, Stop TB Strategy, and Roll Back Malaria partnerships are that weak health systems, inadequate human resources, and poor laboratory infrastructure are the major obstacles to scale-up of services. Integrated care and prevention and health systems and human resources strengthening require universal access to drugs, diagnostics, and simplified laboratory tools. The international community cannot lose the enormous ground that it has gained in the last years.

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