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**From “3 by 5” to Universal Access**

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**CHECK AGAINST DELIVERY**

As I reflect on this world so radically different from 25 years ago, three years post-SARS, I am struck by the inevitability of change if science and public health are to maximally impact on the HIV pandemic and universal access is to mean something tangible. Much has changed in the world since AIDS was identified in 1981, since we learnt about combination therapy in Vancouver 10 years ago. And, if the benefits of antiretroviral treatment are to spread and be sustained, more, across many areas of our response to AIDS, will need to change.

The World Health Organization is the international agency that sets norms, standards, and policy for global health. Experience with antiretroviral scale-up has taught that a strong health sector is essential for a comprehensive response to HIV/AIDS. Universal access will require that the health sector play a central role, one far stronger than the sector that was eroded by Africa's impoverishment over the past two decades, by the pessimism around AIDS of the 1990s, or by misinterpretation that a multisectoral response meant medicine and public health were less important. In this presentation I will review treatment scale-up, discuss the role of the health sector in working towards universal access; and conclude with some cautionary comments about the future.

I wish to acknowledge Dr Lee Jong-Wook, Director General of the World Health Organization, who died unexpectedly in May this year. He was responsible for "3 by 5", the WHO/UNAIDS call to action in late 2003 to place 3 million persons in low and middle income countries on antiretroviral therapy by end 2005. Although the target was not met, implementing partners deserve great credit and "3 by 5" helped change the landscape for HIV/AIDS treatment internationally for ever.

Of the global total of 38.6 million persons living with HIV, approximately 6.8 million in low and middle income countries currently require antiretroviral therapy. WHO estimates that by end June, 2006, some 1.65 million persons in need were accessing ART, for an overall coverage of 24%. Coverage by region ranged from 5% in North Africa and the Middle East, and 13% in Eastern Europe, to 75% in the Caribbean and Latin America. While the 76% still untreated represents a predominantly empty glass, trends in scale-up have nonetheless been encouraging in the areas with the most people with HIV. In sub-Saharan Africa, over a million people are now on treatment, a 10 fold increase since

December 2003, Africans now representing 63% of all treatment recipients. In Asia, a more than 3-fold increase has occurred in 2 years. At least 20 low and middle income countries are treating over 50% of their citizens in need.

Equity of access can be viewed in different ways. This slide shows numbers of persons in need receiving and not receiving treatment by region. Although a majority of people on therapy are African and sub-Saharan Africa has the second highest coverage after Latin America and the Caribbean, sub-Saharan Africa still accounts for 70% of the world's unmet treatment need.

There seems no systematic bias against women in treatment access. In this slide the horizontal bars depict the percentage of treatment recipients in selected low and middle income countries who are women, and the red bars the estimated percentage of all HIV infections that are in women. In most settings, including in Africa, the proportion of ART recipients who are women corresponds closely to the proportion infected, and in some settings exceeds the proportion expected. Such generalizations do not address gender and other aspects of access, such as quality of care and support, including for adherence.

An estimated 800,000 children below the age of 15 require antiretroviral therapy, the vast majority in Africa. Information on treatment access for children is scarce, and these limited data may be best case scenarios. Children account for approximately 14% of AIDS deaths but for only about 6% of recipients of antiretroviral therapy in low- and middle income countries, and we must conclude that scale-up has so far left children behind. There is also a crisis concerning prevention of mother-to-child transmission, an early focus of increased donor support and of antiretroviral drug research. Less than 10% of HIV-infected pregnant women in low and middle income countries are benefiting from antiretroviral prophylaxis, despite virtual elimination of pediatric HIV disease in the industrialized world.

There is particular inequity of treatment for drug users. In Eastern Europe and Central Asia, injecting drug users, a majority of them men, account for over 70% of HIV-infected persons and of treatment need. However, only about a quarter of treatment recipients in this region are drug injectors. It is probably no coincidence that regions and countries where treatment coverage remains lowest and scale-up has been most modest, are the same ones where injecting drug use accounts for most HIV infections.

Meaningful comment on equity of treatment access will require more extensive data relating to time, place, and person - rapidity of scale-up; its geographic distribution, including in relation to type of epidemic and urban versus rural coverage; and populations served, such as drug users, sex workers, specific occupational groups, and refugees. In the meantime, an urgent priority is improving access to antiretroviral therapy for children, especially in sub-Saharan Africa, and for injecting drug users everywhere.

Treatment scale-up has been funded through the US President's Emergency Plan for AIDS Relief; the Global Fund to Fight AIDS, Tuberculosis, and Malaria; the World Bank; other bilateral donors, and pharmaceutical companies through contributions such as the Accelerating Access Initiative. The best-price scenario of around \$130 per person per year for a first-line, generic antiretroviral drug regimen is not universally available. The cost of first-line regimens in middle-income countries remains a barrier to access, as does the price of second-line regimens, pediatric formulations, and diagnostics in nearly all countries. Additional obstacles include the slow pace of registration of medicines in many countries, the imposition of tariffs and taxes on drugs and diagnostics by some recipient governments, and suboptimal use of flexibilities afforded by the TRIPS Agreement.

The best data on treatment outcomes are from special studies. The ART-LINC and ART Cohort Collaboration examined survival in over 27,000 patients from developing and industrialized settings. CD4+ response and viral suppression were similar in both environments. Overall mortality at 1 year was 6.4% in low income settings, approximately 3.5 times higher than the 1.8% one year mortality in high income settings. Mortality was 4.3 times higher in low income settings in the first month, but fell to a ratio of 1.5 during months 7-12. Importantly, this high mortality in the first month for low income settings was still 40-60% lower than that in historical, untreated cohorts.

To maximize benefit, WHO's public health approach places emphasis on initiating therapy for patients with stage III and IV disease, rather than insisting on CD4+ based decision making; if CD4+ testing is available, all persons with counts below 200/cu mm should be treated, and therapy should be considered for those with counts below 350/cu mm. Experience now gives us a broader perspective. In most developing country programs, the majority of patients have late stage disease - in the ART-LINK study, approximately half had a CD4+ count below 100 per cubic mm. when initiating therapy; almost three quarters of deaths were in people whose initial count was less than 100 per cu mm; and over 80% of mortality occurred in the first 4 months. People are receiving therapy too late to get the full benefit ART can offer.

The ART-LINC study also found a 75% lower mortality in treatment programs offering free access, and a meta-analysis of published literature associated free provision of treatment with increased probability of sustained viral suppression. Other studies have associated requirement to pay with non-adherence, which is a major risk factor for drug resistance. WHO and its partners in the HIVResNet program are monitoring drug resistance in populations on treatment and implementing surveillance for the transmission of drug resistant mutants. Areas in green on this map indicate countries participating in such resistance surveys from which first data will be available later this year.

Special effort is required to ensure coordination between HIV/AIDS and tuberculosis programs in low and middle income settings, especially in Africa, if tuberculosis is not to be the Achilles heel of ART scale-up. Patients on ART remain vulnerable to tuberculosis, as indicated by elevated incidence and recurrence rates, and in patients initiating ART

distinguishing between incident tuberculosis, unrecognized prevalent TB, and immune reconstitution inflammatory syndrome is challenging.

From this review, five clear priorities emerge if we are to reduce HIV/AIDS mortality: first, to scale up HIV testing so that persons with HIV infection, including TB patients, are diagnosed earlier; second, to ensure that all patients diagnosed as HIV-positive benefit from a minimum package of care that includes tuberculosis screening and treatment or preventive therapy, co-trimoxazole prophylaxis, and other simple interventions, including in places where antiretroviral treatment is not yet available; third, to ensure that all those with WHO stage III and IV disease receive ART as early as possible, since they are at the greatest risk of dying; fourth, to strengthen laboratory capacity for CD4+ testing, allowing earlier initiation of therapy on immunologic criteria; and fifth, to define HIV/AIDS treatment as a global public good requiring the abolition of user fees at the point of care. A three-and-a half times higher death rate after one year in resource-poor compared with industrialized countries is not acceptable. These priorities require changes in approach to how we diagnose and treat HIV if we are not to squander the benefits of ART.

In June of this year, member states of the United Nations expanded the commitment by leaders of the G8 in 2005 by pledging to come as close as possible to universal access to prevention, treatment and care for all who need it by 2010. By legitimizing the aspiration and right of anyone, irrespective of geography, status or wealth, not to acquire or die from HIV, "3 by 5" helped lay foundations for this promise by the G8 and the world community. Public health agencies like WHO must now help countries translate this political, aspirational target into health goals at country level.

So what should now be the focus of our efforts? WHO has defined five strategic directions for the health sector's contribution to universal access: these are expanding HIV testing and counselling; maximizing prevention; increasing access to treatment and care; strengthening health systems; and investing in strategic information.

Prevention and care are inextricably linked. With treatment reducing mortality but HIV incidence unchanged, the prevalent pool of HIV and AIDS will continue to increase, as shown here for the United States. It is HIV incidence that will write the history of treatment, determining whether we will approach universal access or be condemned to an ever widening treatment gap as the prevalent pool of persons with HIV expands beyond any feasible treatment target. We cannot treat our way out of this epidemic. Debate around prevention has been frequently contentious, sometimes divisive; our best recourse is to listen to science, epidemiology and the communities most affected. One key area, underserved to date, is provision of prevention services for people living with HIV, diagnosed in the millions through the scaling up of treatment programs.

A lesson from "3 by 5" was that the biggest obstacle to treatment scale up is the frailty of health systems - including human resources, physical infrastructure, laboratory capacity, procurement and supply systems, fiscal management, and the whole clinical and public health complex required to manage and deliver services. Universal Access will require

health systems strengthening to become as high a political priority as ART access itself did some years ago. A public health approach emphasizing simplification, standardization, delegation, and decentralization of delivery of prevention and treatment services will be necessary. We should not allow division by the false dichotomy between horizontal health systems strengthening and more vertical HIV treatment and prevention scale-up. Both are necessary and can be mutually reinforcing.

The term strategic information encompasses epidemiology and surveillance, monitoring and evaluation, and operational research. To ensure accountability and assess progress, WHO, with partners, will report annually on the health sector's work towards universal access, assessing availability, coverage, and impact of programs delivering key health sector interventions; the first report should be delivered late this year. Strategic information should evaluate and guide our efforts, learning from the past to shape the future.

The final issue is HIV testing and counselling. While calling for urgent expansion of different models of testing, WHO reaffirms its commitment to basic standards in all contexts: respect for human rights, consent and non-coercion, confidentiality, counselling and information, and policy and legal frameworks to prevent discrimination. The fact that 21 years after the HIV test was introduced only about 10% of infected persons worldwide know their status is an indictment of our commitment to public health and to affected communities, whose most basic rights, life and health, are compromised by the unforgiving natural history of undiagnosed and untreated HIV infection. And as the data indicate, too often, treatment delayed is treatment denied. Encouragingly, increased uptake of client-initiated voluntary counselling and testing has occurred in many settings, including through innovations such as mobile services and outreach. New approaches include family testing and counseling delivered door to door in rural Uganda, and a universal know your status campaign in Lesotho.

Current debate is around the additional, different approach of provider-initiated testing and counselling in health care settings, such as Botswana's policy, introduced in early 2004, of routine HIV testing for all patients at medical visits unless they explicitly refused. Kenya published guidelines in late 2004, advising that HIV testing be performed in clinical settings in the same way other tests are conducted, with simplified pre-test information, emphasis on post-test counselling for HIV-infected persons, and informed consent defined as the right to decline.

In a study of 1200 adults in Botswana, Weiser and colleagues found a majority supported routine testing, believed it would increase access to therapy, and would reduce adverse events. 98% of persons who were actually tested reported no adverse outcomes or regret. Principal reasons for not being tested were fear of knowledge of serostatus and not considering oneself at risk, reminiscent of findings in the industrialized world.

In this changing environment of universal access, WHO and UNAIDS continue to consult and will issue guidance later this year. Global guidance must be tailored to local settings, but some basic principles apply. Provider-initiated testing and counselling

should only be introduced in the context of national plans for scale-up of prevention, treatment, care, and support. Patients must have information about HIV and testing; have a genuine opportunity to decline the routine recommendation of a test; receive their test results; and be linked to appropriate services. Implementation must be monitored to evaluate positive and negative outcomes. Testing leading to punitive action such as imprisonment of infected drug injectors is a violation of human rights. At the same time, the status quo of preventable, undiagnosed, end-stage immunodeficiency as the typical first indicator of HIV infection is incompatible with universal access or with WHO's accountability for setting standards in global health.

In closing, I thank the many colleagues who have directly or indirectly contributed to this talk. We face unusual opportunity and choice, but also vulnerability. Opportunity, because funding and political support have never been as high; vulnerability, because we have to deliver or risk losing credibility and support. If we do not show meaningful impact in the coming few years, including - perhaps especially - with prevention, it will be difficult to sustain funding and donor interest in the face of other global priorities that will inevitably emerge - other infectious agents, security issues, the environment. We cannot stand still but must continuously re-examine how we approach HIV/AIDS, harnessing the evolving forces of science, public health and activism to bear down on this health crisis.