

Building a Durable Response to HIV/AIDS: Implications for Health Systems

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Abstract: The remarkable rise in investments for HIV control programs in 2003–2010 enabled an unprecedented expansion of access to HIV services in low-income and middle-income countries. By the end of 2010, more than 5.2 million people were receiving antiretroviral therapy (ART), which transformed HIV infection, once a death sentence, into a long-term illness. The rapid expansion in the number of persons receiving ART means that health systems must continue to provide acute life-saving care for those with advanced HIV/AIDS although also providing chronic care services to expanding cohorts of more stable patients who are doing well on ART. This expansion also means a transition from an emergency response to the epidemic, characterized by a public health approach, to a more integrated and durable approach to HIV prevention, care, and treatment services that fosters individualized care for those requiring long-term antiretroviral treatment. Yet most low-income and middle-income countries, which have weak health systems, are poorly prepared to make this transition. In this article, we highlight the challenges health systems face in developing a sustained and durable response to HIV/AIDS. The article analyses the readiness of health systems to combine rapid expansion of ART access with long-term treatment and continuity of care for a growing cohort of patients. We argue that effective management of a transition from an emergency AIDS response to long-term programmatic strategies will require a paradigm shift that enables leveraging investments in HIV to build sustainable health systems for managing large cohorts of patients receiving ART although meeting the immediate needs of those who remain without access to HIV treatment and care.

Key Words: AIDS, chronic illness, health systems, HIV, sustainability

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INTRODUCTION

Large-scale investments in HIV programs between 2003 and 2010 led to an unprecedented expansion in access to HIV

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services in low-income and middle-income countries (LMIC). By the end of 2010, more than 5.2 million people were receiving antiretroviral therapy (ART), a 13-fold increase from the 400,000 receiving ART in 2003.^{1,2} Sub-Saharan Africa benefited most from the scale-up, with the number of people receiving ART rising from 100,000 in 2003 to 4 million in 2010.²

Fragile LMIC health systems struggled to cope with the speed and scale of the rapid expansion of treatment, due mostly to poor human resource capacity, weak supply chain management systems, limited capacity for monitoring and evaluation functions, and inappropriate service delivery designs.^{3–5}

The fragility of health systems meant rapid expansion of treatment access could be achieved only with a “public-health approach,” using a limited set of standard treatment regimens.^{6,7} This strategy worked successfully, increasing ART access in LMIC. Between 2004 and 2009, mortality rates from HIV declined by 19%.⁸ ART transformed HIV infection, once a death sentence, into a long-term illness.^{9,10}

The HIV response proved that complex interventions could be delivered at district and community levels using simplified, standardized and nonmedicalized models of care.^{11,12} Yet by the end of 2009, despite this extraordinary achievement, only 36% of the 15 million people estimated to be in need of ART, based on 2010 World Health Organization (WHO) eligibility criteria, were receiving treatment.^{2,13}

EMERGENCE OF A REMARKABLE TRANSITION

The rapid expansion in the number of persons receiving ART highlights a pair of key challenges. At the clinical level, health workers and health systems must continue to provide acute life-saving care for those with advanced HIV/AIDS while also providing chronic services to burgeoning cohorts of more stable patients who are doing well on ART.^{10,11} At the policy and planning level, countries must consider how and whether to transition from an emergency response to the epidemic, characterized by “HIV exceptionalism”—disease-specific programing and a heavy reliance on external technical assistance—to a more integrated and durable approach to HIV prevention, care, and treatment services. Most low-income countries, with weak health systems, are inadequately prepared to make the transition.^{14–16}

LONG-TERM LARGE-SCALE ART PROGRAMS: SIGNS OF SYSTEM STRESS

The rate of retention, or the proportion of patients remaining alive and on ART at various points in time after treatment initiation, is increasingly used as the litmus test

to assess the long-term success of large-scale ART programs.^{2,17} According to reports submitted to the WHO by 38 national LMIC AIDS programs in 2008, the proportion of adult and pediatric patients remaining on treatment averaged 80% at 12 months after treatment initiation, 75% after 24 months, 74% after 36 months, and 73% after 48 months. These figures vary by region, with the best 48-month retention rates achieved in Latin America and the Caribbean (74%) followed by North Africa and the Middle East (78%). Lower retention rates are achieved in Europe and Central Asia (67%), sub-Saharan Africa (67%), and East, South, and Southeast Asia (55%).² These rates are comparable to program data from resource-rich settings, emphasizing the universal challenge of retaining patients in care.

A meta-analysis using data from 22,500 patients initiated on ART in sub-Saharan Africa showed an average of 70% retention 36 months after initiating patients on treatment,¹⁷ although an earlier systematic review found 60% retention at 24 months.¹⁸ In Malawi, retention of patients initiating ART still recorded as “in treatment” dropped from 70% at 24 months to 55% after 48 months.⁸ A retrospective study conducted in a resource-constrained setting in Kenya found that scaling up the ART program by 300% between 2005 and 2007 may have overburdened the system, resulting in low adherence and retention rates.¹⁶

Ensuring that expanding programs have the resources to adequately support adherence and retention, although still scaling up to reach those not yet on ART, presents specific health systems challenges. As countries move from an emergency AIDS response to long-term programmatic strategies, a paradigm shift will be needed to leverage investments in HIV to build sustainable health systems to effectively manage the large cohort of patients receiving ART without losing sight of the immediate needs of those who remain without access to HIV treatment and care.^{19,20}

In this article, we highlight the challenges health systems face in developing a sustained and durable response to HIV/AIDS. The article analyses the readiness of health systems to combine rapid expansion of ART access with long-term treatment and continuity of care for a growing cohort of patients.

UNDERSTANDING THE TRANSITION FROM AN EMERGENCY APPROACH TO A COMBINED HIV RESPONSE

Appropriate access to ART has increased the average life expectancy of an HIV-infected person from 10.5 years in 1996 to 22.5 years in 2005.⁹ Similar gains are possible in resource-limited settings. Analysis of data from Côte d'Ivoire, Malawi, South Africa, and Zimbabwe showed that in the second year of ART, patients who started with high CD4 counts and less advanced disease had mortality rates comparable with those estimated for non-HIV-infected general populations.²¹ Substantial declines in population-level AIDS mortality have been observed in the most affected age groups after ART scale-up in a number of high-prevalence settings: up to 57% decline in a rural district in Malawi,²²

a 50% reduction in Addis Ababa,²³ and an average of 25% drop in KwaZulu-Natal, South Africa.²⁴

Because of limited longitudinal data—the majority of people in LMIC receiving antiretroviral drugs (ARV) typically have 5 years of history on treatment or less—estimating ART's impact on life expectancy is difficult. Yet the long-term needs of patients in LMIC receiving ART are already evident and demand greater attention than have been received to date.

TRANSITION FROM LOW TO HIGH NUMBERS RECEIVING ART

The number of people living with HIV in the world increased by around 20% between 2001 and 2009, with almost 2.6 million new infections in 2009 and 5 patients newly infected for every 2 starting ART.⁸ More than 5 million people are currently receiving ART, and scale-up is likely to continue at the rate of 1 million per year. The adoption of new WHO guidelines will lead to a higher proportion of the population already living with HIV qualifying for treatment over the next decade, mostly in countries where health systems remain frail.^{16,25–27} Between 2003 and 2010, the emergency response, with low numbers of patients receiving ART, has been transformed; large numbers now require long-term care (Fig. 1).

High levels of HIV incidence and prevalence in sub-Saharan Africa will place continued demand on health systems for the next few decades unless there is a step change in prevention of new HIV infections—even in South Africa, which has successfully reduced HIV incidence.²⁸ In Zimbabwe, if all who need treatment gain access by 2010, the numbers in need of treatment would still be 6 times greater by 2030.²⁹

Health systems are struggling to sustain the performance of large-scale HIV treatment programs with increasing needs of patients on ART.^{14–16} A large prospective cohort study of more than 3000 patients in South Africa found that the cumulative probability of losing clients to follow-up was 29.1% after 6 years and that this proportion increased with each

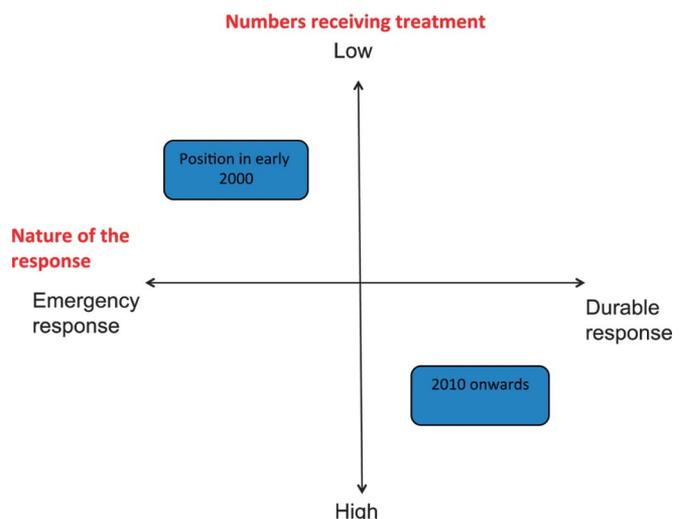


FIGURE 1. Transition from an emergency response to scale up antiretroviral treatment to long-term response to large treatment cohort.

successive year of enrollment. An increasing case load led to increasing waiting times, shorter consultations, reduced opportunities for counseling and adherence support, stretched human resources, and limited capacity to follow-up patients missing appointments.¹⁵

TRANSITION FROM LOW TO INCREASING COMPLEXITY OF CARE

The challenge of providing quality long-term care for patients receiving ART will further increase over time as complexities emerge, including complications of long-term ART; clinical progression of HIV, including cardiovascular, hepatic, and renal diseases and malignancies; ongoing risk of coinfections, including tuberculosis and hepatitis; the effects of aging, as individuals on ART survive for decades.^{10,30–33,34} The growing burden of HIV among adults older than 50^{35,36} will rapidly impact sub-Saharan Africa, where an estimated 3 million people over 50 were living with HIV in 2007, accounting for approximately 14% of all infections in the region.³⁶

In addition, as patients remain on ART for longer periods of time, they are more likely to experience viral resistance to existing combinations of first-line ART regimens, requiring access to more expensive second-line and third-line ARV and increasingly complex laboratory monitoring.^{7,37,38} In many settings, comprehensive HIV care has evolved to include services for endemic infectious diseases such as tuberculosis and malaria; over time, services may expand to include comanagement of other conditions prevalent in the general population, such as chronic noncommunicable diseases and cancers.^{34,38–40}

The confluence of long-term HIV infection, comorbidities, opportunistic infections, and longevity means a rapidly growing number of HIV-infected individuals receiving ART will increasingly need individualized care, with high complexity—in sharp contrast to the public health approach, with its limited set of treatment regimens (Fig. 2).

This transition has implications for health systems. Now, the emergency public health response to increase access to HIV care and treatment services must be combined with

a durable response that provides both acute care services and personalized potentially complex long-term clinical care. This will require additional human resources, more complex clinical and laboratory monitoring, expanded formularies and procurement systems, and enhanced health information systems.^{7,38}

HEALTH SYSTEM BOTTLENECKS PERSIST

The rapid scale-up of HIV interventions exposed the frailty of health systems to effectively mount an HIV response and cope with management of HIV as a long-term illness.^{3,5,11,12,20,26} Most LMIC health facilities still lack key elements needed to provide continuity care,^{11,12} despite investments to strengthen health systems.^{3,41} WHO reports that of 94 countries reporting in 2010, 38% reported at least one or more ARV stockout in health facilities during 2009, compared with 34% of 90 countries in 2008 and 38% of 66 countries in 2007.²

Scale-up of HIV programs in health systems is a dynamic process influenced by the readiness of individuals targeted by new interventions to adopt new interventions, interactions between program components, and interaction between the program and health systems. This complexity leads to diverse causal pathways in the solutions that emerge.⁴² However, there is limited evidence on what works in varied contexts to deliver quality long-term HIV treatment and care^{43,44} although effectively maintaining the trajectory of scale-up.⁴⁵

MANAGING THE TRANSITION: COMBINING EMERGENCY AND DURABLE RESPONSE

Although there is agreement that stronger health systems are needed to achieve improved outcomes in HIV programs, there is much less consensus on how to strengthen health systems.⁴⁶ A number of health system strengthening actions have been used to mount an effective response to the HIV epidemic, including strengthening supply chain management systems to prevent stockouts of ARV and other key medicines; addressing health workforce shortages and the need for new competencies to manage evolving complexities in HIV treatment; enhancing weak and fragmented health information systems; meeting financing needs and preventing high out-of-pocket expenditures that undermine patient retention in care; and reducing significant inefficiencies in service delivery and adverse effects from rapid introduction of suboptimal system designs.^{3,42,47,48} However, there is limited evidence on what works in varied contexts to deliver quality long-term HIV treatment and care^{44,45} while effectively maintaining the trajectory of scale-up.⁴⁶

Although rapid scale-up of the HIV response was achieved with targeted disease programs, provision of long-term care for patients receiving ART will require effective integration of HIV programs into mainstream health systems.^{3,49} However, evidence on effective integration approaches to develop optimal service designs remains weak, as do the evidence on the influence of varied levels of integration and the impact of different service designs on health outcomes. Hence, an effective transition to integrated care is likely to be hampered by major gaps in the existing knowledge base, where a number of key questions remain unaddressed—in particular:

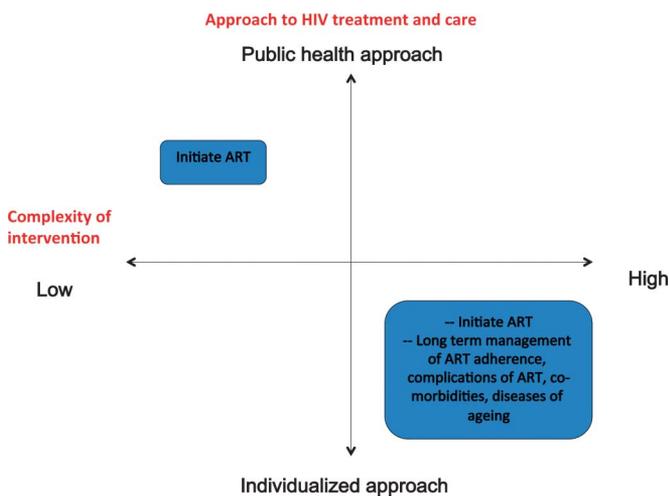


FIGURE 2. Transitioning from a public health approach to managing HIV infection to complex individualized care.

- What are the optimal delivery models that enable effective scale-up of complex interventions (such as long-term ART and combination prevention programs)?
- Which system designs are optimal at different scales to effectively manage the transition that combines emergency and long-term responses?⁴⁸

A lifelong commitment, ART requires patients to adhere diligently to daily medication dosing schedules and make regular clinic visits for continuity care. Yet, in general, adherence has been shown to diminish with time. Operational research is needed to assess the long-term roles of current adherence interventions, such as outreach, directly observed therapy, and the use of expert patients and mobile communication technologies. Interventions that sustain adherence and improve patient retention in care and policy changes designed to reduce socioeconomic, time, and logistical barriers will ultimately contribute to better treatment outcomes.⁵⁰

Health systems can improve patient retention in ART with strategies designed to set up and maintain simple standardized monitoring systems at every ART facility; reliably ascertain true treatment outcomes; lower death rates; ensure uninterrupted ARV supplies; support the use of ART regimens that are simple, nontoxic, and free; decentralize ART clinics and reduce the frequency of visits required of stable patients; lessen indirect patient costs; strengthen ART links between health services and the community; encourage the use of ART services to deliver other critical interventions; promote operational research and development of innovative service delivery models.⁵¹

Substantial inefficiency in existing AIDS programs is of particular concern for long-term sustainability. Although ARV are the single most costly component of an AIDS treatment program, the total of other costs of providing treatment substantially outweigh the cost of drugs.⁸ Significant variation exists in the unit costs of delivering prevention services across facilities operating at the same scale within and across countries⁵² and in the unit cost of treating AIDS patients with ARV.⁵³ As ART programs expand, additional research is needed on the key variables in large-scale treatment delivery models that in combination provide technical efficiency and quality and provide value for money over the long term.

The global economic crisis has provided a stark reminder of the fragility of the gains made and the need to focus on developing strategies for a sustainable response. The economic crisis means flattening of domestic and external financing for global health, including for HIV, against a growing demand for AIDS treatment. The negative effects on the HIV response are felt globally except for East Asia—least affected by the economic crisis. As the recent rate of growth in HIV funding is unlikely to be maintained in the near future the imperative for a paradigm shift to establish a durable HIV response is acute.⁵⁴

CONCLUSIONS

The success of HIV scale-up during the last decade has led to the emergence of a remarkable transition. In addition to large numbers of very sick patients requiring prompt initiation of life-saving ART, health systems now also face a burgeoning

pool of patients enrolled in life-long treatment and care that is likely to grow more complex over time. Two challenges now face national health systems: how to evolve the public health response to accommodate the increasing complexity of long-term care and treatment and how to integrate HIV services into mainstream health programs to ensure a durable response, although confronting persistent health systems bottlenecks and suboptimal and inefficient service delivery designs within a constrained economic environment.

Managing the transition toward sustainable long-term care will require both upstream and downstream adjustments: upstream adjustments to HIV and health system strategies; mapping out priorities, policies, and resource requirements to ensure effective management of the process; and downstream adjustments to delivery models, programs, and operational systems to ensure high-quality services as programs expand.

REFERENCES

1. World Health Organization (WHO). *Progress on Global Access to HIV Antiretroviral Therapy: A Report on "3 by 5" and Beyond*. March 2006. Geneva, Switzerland: WHO; 2006. Available at: http://www.who.int/hiv/progressreport2006_summary_en.pdf. Accessed March 9, 2011.
2. WHO. *Towards Universal Access: Scaling Up Priority HIV/AIDS Interventions in the Health Sector: Progress Report 2010*. Geneva, Switzerland: WHO; 2010.
3. Samb B, Evans T, Atun R, et al. WHO Maximizing Positive Synergies Collaborative Group. An assessment of interactions between global health initiatives and country health systems. *Lancet*. 2009;373:2137–2169.
4. Yu D, Souteyrand Y, Banda MA, et al. Does investment in HIV/AIDS programs help strengthen health systems in developing countries? *Global Health*. 2008;4:8.
5. El-Sadr WM, Abrams E. Scale-up of HIV care and treatment: can it transform health care services in resource-limited settings? *AIDS*. 2007; 21(suppl 5):S65–S70.
6. Gilks CF, Crowley S, Ekpini R, et al. The WHO public-health approach to antiretroviral treatment against HIV in resource-limited settings. *Lancet*. 2006;368:505–510.
7. Bartlett JA, Shao JF. Successes, challenges, and limitations of current antiretroviral therapy in low-income and middle-income countries. *Lancet Infect Dis*. 2009;9:637–649.
8. Joint United Nations Program on HIV/AIDS (UNAIDS). *UNAIDS Report on the Global AIDS Epidemic 2010*. Geneva, Switzerland: UNAIDS; 2010.
9. Harrison KM, Song R, Zhang X. Life expectancy after HIV diagnosis based on national HIV surveillance data from 25 states, United States. *J Acquir Immune Defic Syndr*. 2010;53:124–130.
10. Atun R, Gurol-Urganci I, McKee M. Health systems and increased longevity in people with HIV and AIDS. *BMJ*. 2009;338:b2165.
11. Rabkin M, El Sadr W. Why reinvent the wheel? Leveraging the lessons of HIV scale up to confront non-communicable diseases. *Global Public Health*. 2011;6:247–256.
12. Harries AD, Zachariah R, Jahn A, et al. Scaling up antiretroviral therapy in Malawi—implications for managing other chronic diseases in resource-limited countries. *J Acquir Immune Defic Syndr*. 2009;52:S14–S16.
13. WHO. *Antiretroviral Therapy for HIV Infection in Adults and Adolescents: Recommendations for a Public Health Approach. 2010 Revision*. Geneva, Switzerland: WHO; 2010.
14. Konde-Lule J, Makumbi F, Pakker N, et al. Effect of changing antiretroviral treatment eligibility criteria on patient load in Kampala, Uganda. *AIDS Care*. 2011;23:35–41.
15. Nglazi MD, Lawn SD, Kaplan R, et al. Changes in programmatic outcomes during 7 years of scale-up at a community-based antiretroviral treatment service in South Africa. *J Acquir Immune Defic Syndr*. 2011;56:e1–e8.
16. Unge C, Sodergard B, Ekstrom AM, et al. Challenges for scaling up ART in a resource-limited setting: a retrospective study in Kibera, Kenya. *J Acquir Immune Defic Syndr*. 2009;50:397–402.

17. Fox MP, Rosen S. Patient retention in antiretroviral therapy programs up to three years on treatment in sub-Saharan Africa, 2007–2009: systematic review. *Trop Med Int Health*. 2010;15(suppl 1):1–15.
18. Rosen S, Fox MP, Gill CJ. Patient retention in antiretroviral therapy programs in sub-Saharan Africa: a systematic review. *PLoS Med*. 2007;4:e298.
19. Ullrich A, Ott JJ, Vitoria M, et al. Long-term care of AIDS and non-communicable diseases. *Lancet*. 2011;377:639–640.
20. Samb B, Desai N, Nishtar S, et al. Prevention and management of chronic disease: a litmus test for health-systems strengthening in low-income and middle-income countries. *Lancet*. 2010;376:1785–1797.
21. Brinkhof MW, Boule A, Weigel R, et al. Mortality of HIV-infected patients starting antiretroviral therapy in sub-Saharan Africa: comparison with HIV unrelated mortality. *PLoS Med*. 2009;6:e1000066. Published online April 28, 2009.
22. Floyd S, Molesworth A, Dube A, et al. Population-level reduction in adult mortality after extension of free anti-retroviral therapy provision into rural areas in Northern Malawi. *PLoS One*. 2010;5:e13499.
23. Reniers G, Araya T, Davey G, et al. Steep declines in population-level AIDS mortality following the introduction of antiretroviral therapy in Addis Ababa, Ethiopia. *AIDS*. 2009;23:511–518.
24. Herbst AJ, Cooke GS, Barnighausen T, et al. Adult mortality and antiretroviral treatment roll-out in rural KwaZulu-Natal, South Africa. *Bull World Health Organ*. 2009;87:754–762.
25. Tkatchenko-Schmidt E, Atun R, Wall M, et al. Why do health systems matter? Exploring links between health systems and HIV response: a case study from Russia. *Health Policy Plan*. 2010;25:283–291.
26. Atun RA, McKee M, Drobniewski F, et al. Analysis of how health system context influences HIV control: case studies from the Russian Federation. *Bull World Health Organ*. 2005;83:730–738.
27. Nakanjago D, Kiragga A, Castelnuovo B, et al. Initiating antiretroviral therapy at CD4 counts below 350 cells/ul. What does this mean to HIV/AIDS care programs in Uganda? Presented at: 48th Annual ICAAC/IDSA 46th Annual Meeting; October 25–28, 2008; Washington, DC.
28. Meyer-Rath G, Brennan A, Long L, et al. Total cost and potential cost savings of the national antiretroviral treatment (ART) programme in South Africa 2010 to 2017 [Abstract 16112]. Presented at: 18th International AIDS Conference; July 18–23, 2010; Vienna, Austria.
29. Hallett TB, Gregson S, Dube S, et al. Estimating the resources required in the roll-out of universal access to antiretroviral therapy in Zimbabwe. Cited in: *The Treatment Time Bomb*. London, United Kingdom: All-Party Parliamentary Treatment Group on AID; 2009.
30. Luetkemeyer AF, Havlir DV, Currier JS. Complications of HIV disease and antiretroviral treatment. *Top HIV Med*. 2010;18:57–65.
31. The ART Cohort Collaboration. Causes of death. *Clin Infect Dis*. 2010;50:1387–1396.
32. Deeks SG, Phillips AN. HIV infection, antiretroviral treatment, ageing, and non-AIDS related morbidity. *BMJ*. 2009;338:a3172.
33. Blanco JR, Caro AM, Pérez-Cachafeiro S, et al. HIV infection and aging. *AIDS Rev*. 2010;12:218–230.
34. Palella FJ, Baker RK, Moorman AC, et al. Mortality in the highly active antiretroviral therapy era: changing causes of death and disease in the HIV outpatient study. *J Acquir Immune Defic Syndr*. 2006;43:27–34.
35. Lazarus JV, Nielsen KK. HIV and people over 50 years old in Europe. *HIV Med*. 2010;11:479–481.
36. Negin J, Cumming RG. HIV infection in older adults in sub-Saharan Africa: extrapolating prevalence from existing data. *Bull World Health Organ*. 2010;88:847–853.
37. Gulick RM. Antiretroviral treatment 2010: progress and controversies. *J Acquir Immune Defic Syndr*. 2010;55(suppl 1):S43–S48.
38. Volberding PA, Deeks SG. Antiretroviral therapy and management of HIV infection. *Lancet*. 2010;376:49–62.
39. Kitahata MM, Tegger MK, et al. Comprehensive health care for people infected with HIV in developing countries. *BMJ*. 2002;325:954–957.
40. Mayosi BM, Flisher AJ, Lalloo UG, et al. The burden of non-communicable diseases in South Africa. *Lancet*. 2009;374:934–947.
41. Loubiere S, Boyer S, Protopoulos C, et al. Decentralization of HIV care in Cameroon: increased access to antiretroviral treatment and associated persistent barriers. *Health Policy*. 2009;92:165–173.
42. Atun R, de Jongh T, Secci FV, et al. Integration of targeted health interventions into health systems: a conceptual framework for analysis. *Health Policy Plan*. 2010;25:104–111.
43. Rabkin M, El-Sadr W, De Cock KM. The impact of HIV scale-up on health systems: a priority research agenda. *J Acquir Immune Defic Syndr*. 2009;52(suppl 1):S6–S11.
44. Handford C, Tynan A-M, Rackal JM, et al. Setting and organization of care for persons living with HIV/AIDS. *Cochrane Database Syst Rev*. 2006;3:CD004348.
45. Mutevedzi PC, Lessells RJ, Heller T, et al. Scale up of a decentralized HIV treatment programme in rural KwaZulu-Natal, South Africa: does rapid expansion affect patient outcomes? *Bull World Health Organ*. 2010;88:593–600.
46. Travis P, Bennett S, Haines A, et al. Overcoming health-system constraints to achieve the millennium development goals. *Lancet*. 2004;364:900–906.
47. Atun R, de Jongh T, Secci F, et al. A systematic review of the evidence on integration of targeted health interventions into health systems. *Health Policy Plan*. 2010;25:1–14.
48. Atun RA, Bennett S, Duran A. *When Do Vertical (Stand-Alone) Programmes Have a Place in Health Systems?* Policy Brief. Copenhagen, Denmark: WHO Regional Office for Europe; 2008.
49. DART Trial Team. Routine versus clinically driven laboratory monitoring of HIV antiretroviral therapy in Africa (DART): a randomised non-inferiority trial. *Lancet*. 2010;375:123–131.
50. Buscher AL, Giordano TP. Gaps in knowledge in caring for HIV survivors long-term. *JAMA*. 2010;304:340–341.
51. Harries AD, Zachariah R, Lawn SD, et al. Strategies to improve patient retention on antiretroviral therapy in sub-Saharan Africa. *Trop Med Int Health*. 2010;15(suppl 1):70–75.
52. Marseille E, Dandona L, Marsall N, et al. HIV prevention costs and program scale: data from PANCEA project in five low and middle income countries. *BMC Health Serv Res*. 2007;7:108.
53. Rosen S, Long L, Sanne I. The outcomes and outpatient costs of different models of antiretroviral treatment delivery in South Africa. *Trop Med Int Health*. 2008;13:1005–1015.
54. UNAIDS. Impact of the global financial and economic crisis on the AIDS response. UNAIDS/PCB(25)/09.26. Available at: http://data.unaids.org/pub/InformationNote/2009/20091030_impact_economic_crisis_on_hiv_final_en.pdf. Accessed April 20, 2011.