

Strategies for the Scale-Up of Antiretroviral Therapy in South Africa through Health System Optimization

Pierre M. Barker,^{1,3} C. Joseph McCannon,¹ Nupur Mehta,² Cathryn Green,¹ Michele S. Youngleson,¹ Justin Yarrow,¹ Brandon Bennett,¹ and Donald M. Berwick¹

¹Institute for Healthcare Improvement, Cambridge, and ²Brigham and Women's Hospital, Boston, Massachusetts; ³University of North Carolina, Chapel Hill

In the face of the massive burden created by human immunodeficiency virus/acquired immunodeficiency syndrome and other infectious diseases, developing nations must find ways to rapidly begin treatment for infected persons. Although infusions of personnel, supplies, and diagnostics would make a major contribution to expanding the capacity to treat these diseases, the lack of these resources creates a long-term challenge, and there is a need for additional approaches to spread effective interventions that can leverage existing resources and the much-needed infusions of new resources. This article describes one such approach—applied in several forms in South Africa—that aims to significantly increase the number of patients receiving antiretroviral therapy.

BACKGROUND

Barring the development of an effective vaccine or a radical decrease in disease transmission rates, the developing world—particularly sub-Saharan Africa—faces the bleak prospect of having to manage a staggering burden of HIV/AIDS in its population for at least the next 20–30 years. Although some countries—notably, Zimbabwe [1], Kenya [2], and Uganda [3]—are reporting a slow decline in the number of new cases of HIV infection each year, infection rates in many countries, including those in South Africa, continue to increase [4]. Because individuals are usually asymptom-

atic and do not require antiretroviral therapy (ART) for 7–10 years after infection [5], even successful prevention strategies will not soon result in a meaningful decline in the need for highly active ART (HAART). To rapidly increase access to HAART for a significant fraction of their population, developing countries must devise strategies to quickly spread access to ART that can succeed within the constraints of limited resources and rudimentary health infrastructures and to fully leverage badly needed new resources as they become available.

A major impediment to the treatment of AIDS was removed after HAART prices were dramatically decreased at the turn of the century [6]. International initiatives like the World Health Organization's "3 by 5" campaign [7] and a significant infusion of external donor funding emerged concurrently, which triggered country-wide HAART campaigns throughout the developing world. Countries have since reported examples of notable increases in access to ART, which has saved thousands of lives [8–12], although no nation has yet achieved complete coverage of its infected population. In addition, many developing countries' programs have resulted in inequitable distribution of HAART services, with rural areas being the most disadvantaged [13]. Treatment programs, often jointly managed by national

Potential conflicts of interest: none reported.

Presented in Part: The Realities of Antiretroviral Therapy Rollout: Challenges to Successful Programmatic Implementation, Durban, South Africa, October 2006.

Financial support: this work is supported by the Institute for Healthcare Improvement and by funds supplied through grant subcontracts with local partner organizations (United Nations Children's Fund [UNICEF] and President's Emergency Plan for AIDS Relief funding through the Wits Paediatric HIV Group and Reproductive Health Research Unit at the University of Witwatersrand, and UNICEF funding through the Centre for Rural Health at the University of KwaZulu-Natal). Supplement sponsorship is detailed in the Acknowledgments.

Reprints of correspondence: Dr. Pierre M. Barker, Pulmonary Medicine and Allergy, Dept. of Pediatrics, University of North Carolina at Chapel Hill, Chapel Hill, NC (pierre_barker@med.unc.edu).

The Journal of Infectious Diseases 2007;196:S457–63

© 2007 by the Infectious Diseases Society of America. All rights reserved.

0022-1899/2007/19611S3-0003\$15.00

DOI: 10.1086/521110

government structures and outside agencies (nongovernmental organizations, donors, etc.), have pursued several approaches to expanding treatment rapidly in developing countries. These approaches include provision of external personnel, infusion of drugs and supplies, renewal or new construction of care and treatment centers, strengthening of infrastructure, and building the local capacity of health systems through training of health workers [14].

These interventions have been effective in addressing the immediate needs of the epidemic and, together, have saved many thousands of lives. Because these countries face a long-term fight against the HIV pandemic, new approaches that result in durable strengthening of local health systems will be required to provide long-term, country-wide, sustainable HIV/AIDS care for millions of patients in need. Limited resources, particularly shortages of medical personnel, supplies, and infrastructure, are often, appropriately, described as major barriers to expansion of HIV/AIDS care [15]. However, these are long-term deficiencies that are unlikely to be addressed in time to save a generation of patients infected with HIV. Here, we describe a successful model of scale-up of HIV/AIDS care in the South African state health system that focuses primarily on the optimization of existing health infrastructure rather than on the addition of human and physical resources.

The South African government has sought to provide a comprehensive program for HIV/AIDS care, including HAART, since early 2004 [16]. The program initially focused on single sites within each health district, or “local service areas.” As of September 2006, 213,828 adults and children had started receiving HAART in the state and private sectors of the South African health system [17]. Although the actual number of people who started receiving treatment is impressive, the rate at which the program has grown relative to need has been slow. In its third year, the program is projected to start HAART in approximately one-sixth of the 600,000 additional HIV-infected patients who are estimated to need HAART initiated each year [18]. The Institute for Healthcare Improvement (IHI) projects in South Africa are attempting to show that the goals of (1) finding and treating all who need ART and (2) preventing perinatal HIV transmission can be greatly accelerated through optimization of the current resources at hand in the state health system.

A POSSIBLE APPROACH: HEALTH SYSTEM OPTIMIZATION

Since August 2004, the IHI has collaborated with a number of academic and nongovernmental organization partners and local departments of health in South Africa to support expansion of the state HIV/AIDS program in rural and urban settings. In all cases, we have focused on the task of redesigning the health system to provide access for all HIV-infected patients who need

HAART within a geographic area. In all projects, we have worked with partners who have provided training and medical expertise, and, in some cases (the Gauteng and Western Cape projects), partners have provided additional field-tested medical personnel. The approach, which focuses on the scale and pace at which lean models of care and treatment can be spread, relies on several improvement strategies that have been used successfully in previous IHI-supported projects in the developed world and, more recently, in health care settings in the developing world.

The IHI methods are grounded in operations research and management science, well-established fields that have, for >90 years, combined the disciplines of statistics, psychology, systems engineering, and iterative learning, to have major impact across countries and industries [19]. This science seeks to design systems for maximum effectiveness, efficiency, and adaptability and to actively disseminate the best models at the most rapid rate possible. Within health care, IHI has, for >15 years, systematically applied this science to first design or identify evidence-based interventions and then quickly spread them through networks of facilities [20]. In regional and national projects in developed nations like the United States and United Kingdom [21, 22], as well as in emerging and developing economies like Russia [23] and Rwanda [24, 25], IHI and its partners have sought to spread ideas and improved results for patients, often having a very broad and deep impact. Core properties of many of these projects include

- explicit and ambitious aims, approached with optimism;
- explicit time frames for spreading improvements;
- improvement of the health system within existing care resources;
- participative management and development of learning networks;
- crisp measurement and focus on outcomes; and
- local capability-building for sustainability.

APPLICATION

To prevent designated treatment sites in South Africa from becoming overwhelmed, and to manage logically a burgeoning tuberculosis epidemic, HIV/AIDS care needs to be quickly devolved from its current loci, which are often stand-alone, tertiary facilities, and integrated into the rest of the health system. A common strategy in IHI's South African projects has been to actively recruit all health care facilities (primary, secondary, and tertiary) in a defined geographic area into a network of sites that can act as an interdependent system and can together provide comprehensive HIV/AIDS care in a specific area.

In some cases, IHI and its partners have started working at once with all sites in a given district, whereas, in others, we have developed a stepwise approach with increasing “waves” of clinics joining the network. IHI has adapted its Breakthrough

Series Collaborative model, in which networks of health care facilities come together at regular intervals to set common aims, to learn more about improvement science and methods, to share ideas and results, and to jointly identify and solve problems [26].

IHI and its partners support involved teams as they test innovations at the point of care and iteratively apply and locally adapt successful strategies. This participative strategy has been a major factor in accelerating “buy-in” and revitalization of demoralized staff who are overburdened with the sheer volume of care and disempowered by a traditional “top-down” approach to health care improvement. In some instances—especially those in which a lack of specific personnel, supplies, or space truly is the “choke point” in a series of linked processes—the systems improvement approach we have applied is not alone sufficient to completely optimize outcomes, but participants are, nonetheless, making major improvements, as is described below. In most cases, we also work closely with our partners, who provide complementary training in medical skills, medical content, and, in some instances, targeted medical staff to overcome episodic shortages in the HIV/AIDS care pathway.

A major driving factor for improved care is the establishment of outcome goals that are closely tied to the common aim of providing access to HAART for all the people who need treatment in the district or defined area. For HIV-positive patients with compromised immune systems, delay in the initiation of treatment results in unnecessary deaths; every 6 months spent on the waiting list claims the lives of as many as 22% of people waiting on that list [27], and the majority of patients who present with an AIDS-defining illness can expect to be dead in <18 months without HAART [28]. A crucial first step is for the participants in the collaborative network to define the gap between the current monthly HAART initiation rate and the rate that would ensure treatment for all patients in need. A common aim emerges and becomes a rallying point to obtain buy-in for the changes to the system necessary to reach those goals. Thereafter, the participatory approach to identifying obstacles to reaching that goal and designing potential solutions to overcome the obstacles promotes local ownership of the responsibility for HIV/AIDS care.

After initial learning sessions that bring together teams from different levels of the local health system (primary, secondary, and tertiary) to set aims and chart their course of action, a 1- or 2-person facilitation team from IHI, its partner organization, or both visits the clinics to support continuous improvement activities. The clinic teams work on rapid-cycle improvement strategies directed at overcoming obstacles to reaching their agreed goals. As the project matures, the specific focus of each facility or group of interlinked facilities moves to different parts of the HIV/AIDS care and treatment process map. The partic-

ipating group identifies bottlenecks and opportunities for improvement on an ongoing basis. Successfully tested strategies are packaged as high-leverage “change concepts” for use by all facilities in the network and, particularly, by those newly joining the collaboration, to accelerate the spread of effective models of HIV/AIDS care and treatment. For example, the interactions among primary care, secondary care, and tertiary care units in providing HAART were not well established, particularly because initial HAART care was focused on the larger referral centers. Knowledge and confidence about the appropriate role for each type of facility grew significantly in the course of this work, and we introduced these successful strategies—change concepts—to the larger network of participating facilities over time.

A major goal of IHI’s projects is to transfer health care system improvement skills to our academic and nongovernmental organization partners, along with representatives of the local health system. To achieve this aim, we train project managers and health system managers in operations research and management science through on-site coaching while also facilitating intensive formal training at US and South African workshops.

PROJECTS IN SOUTH AFRICA

Rural Projects

IHI and its partners are currently supporting HIV/AIDS care and treatment programs across 2 rural districts in South Africa, each with significantly different resources available.

Umkhanyakude District (KwaZulu-Natal). In Umkhanyakude District in northern KwaZulu-Natal, IHI and its local partner, the Centre for Rural Health at the University of KwaZulu-Natal, have strengthened a preexisting, loose-knit network of subdistrict hospitals and their referring clinics through learning sessions, site visits, and development of a district-wide e-mail list to facilitate electronic discussion. This district has pioneered the initiation of HAART and long-term care of patients receiving HAART at primary care clinics. Without addition of medical staff, the rate of new HAART initiations increased by 4-fold over 18 months to provide HAART to ~7000 people. During this rapid scale-up, clinics documented high (>85%) rates of viral load suppression. The principal support provided by IHI and its partners was to spread successful innovations among the subdistrict hospitals; encourage local, rapid-cycle testing of solutions for obstructed care; and work with the district office to facilitate collection and feedback of clinic-specific data for improving health care. IHI and the Centre for Rural Health have also been invited to support a district-wide program in the adjacent district of uThungulu. We expect that this will be a rapidly spread program, in which successfully tested innovation will be implemented through the district by introducing improvement methods and building a formal

learning network through application of the Breakthrough Series approach.

Mhlontlo District (Eastern Cape). IHI is collaborating with the Regional Training Center at Walter Sisulu University and the district health office in the Eastern Cape province to support the Mhlontlo District's HIV/AIDS care and treatment program. Although ART initiations are restricted to 4 of the 25 health care sites there, an expanding collaborative network has resulted in the participation of local primary care clinics in testing, patient preparation, and provision of long-term care for those receiving HAART, creating capacity for more initiations at the ART sites and providing convenient local HIV/AIDS management for most of the district's HIV-infected inhabitants. Led by the district office, improvement teams from the clinics meet together at monthly intervals to set goals, discuss innovations and logistics of HIV/AIDS care, plan tests of change, and share process and outcomes information. IHI and its local partner facilitate improvement meetings and undertake targeted site visits. Early on, the ART program quickly trebled its rate of monthly ART initiation (from 12 to 35 people/month) and improved HIV testing and CD4 cell count determination (from 0% in September 2005 to >70% after March 2006) among antenatal clinic attendees. These improvements have been sustained over many months, although further progress has been stalled by the removal of 1 of 3 doctors in this district of 200,000 inhabitants.

Urban Projects

Cape Town Metro (Western Cape). The Western Cape project has been supported by the nongovernmental organization Absolute Return for Kids and by local health departments (City of Cape Town and Western Cape Province). IHI started system improvement activity in this region at a large, overcrowded tertiary care site that was seeing both adult and pediatric patients with HIV infection. The initial focus was on improving clinic efficiency, applying rapid-cycle improvement methods, and using advanced access and flow design principles. A stated aim of the ART clinic at the tertiary care site was to assist in the devolution of ART care to secondary care and primary care sites. IHI then worked with local partners to scale up ART care within a secondary care hospital and at a community health clinic. Shortly thereafter, several referring primary care clinics were brought into the network with a Breakthrough Series project that integrated the sites into the overall aim of complete ART access in the area. These clinics are currently engaged in removing obstacles to case finding (particularly patients coinfecting with *Mycobacterium tuberculosis*), retention of HIV-positive patients in care, and efficient preparation of patients for HAART. Within a few months, we observed a doubling of referrals of patients for HAART initiation from these sites.

Johannesburg Pediatric Collaborative. Initial IHI support

for a single site (Harriet Shezi Clinic at Chris Hani Baragwanath Hospital) has expanded, in partnership with the Wits Paediatric HIV Group [WPHG] at University of Witwatersrand, to include a Breakthrough Series Collaborative comprising 3 tertiary care hospitals, 2 district hospitals, 5 community health care centers, and 7 primary care clinics. The goal of the Collaborative is to ensure that at least 15% of all patients treated in the accredited ART sites are children. In this project, which covers most of the units treating children in the greater Johannesburg area, there are no waiting lists for children needing HAART. This has led to a very focused drive to develop novel processes that result in increased case finding, from diagnosis of infection in HIV-exposed newborn infants to clinical detection of older HIV-infected survivors presenting in children's wards and outpatient clinics.

In the first 9 months of the program, the 3 hospital-based clinics have shown significant increases in the numbers of children referred to their clinics from inpatient wards. More recently, the Collaborative was expanded to include additional primary care referral sites that will identify HIV-exposed infants at the 6-week immunization check, as well as their siblings born to HIV-positive mothers. Our partners (WPHG) provided pediatric HIV/AIDS training and supplemental medical personnel to the clinics and, after intensive coaching by IHI in systems improvement methods, are now independently managing all aspects of the improvement program.

Adult collaborative in Johannesburg. In partnership with the Reproductive Health Research Unit of the University of Witwatersrand and the City of Johannesburg Department of Health, a collaborative learning network of tertiary care, secondary care, and primary care sites has evolved over the past 2 years, aiming to accelerate the rate of ART initiation for new patients. Currently, HAART is dispensed at the tertiary care and secondary care sites, which are becoming overwhelmed by the workload. The principal purpose of engaging feeder primary care clinics is to improve case finding, particularly in tuberculosis clinics, and to downshift diagnostic and preparatory services from secondary care to primary care clinics, thereby creating more capacity for initiating HAART at the secondary care and tertiary care sites. Initial efforts in the tertiary care center resulted in increased efficiencies, with a consequent increase in the capacity for initiating HAART in new patients. After working down the backlog of new referrals, attention focused on referring clients back to the secondary care site. The secondary care site, in turn, has become overwhelmed by the HAART caseload. The Primary Care Collaborative, comprising 6 feeder clinics and the secondary care site, was started in August 2006 to relocate the task of testing and preparation of patients for HAART to primary care sites and to increase case finding. Early results show a 20-fold increase in CD4 cell count testing in HIV-positive adults (from 20 per month to

Table 1. High-leverage innovations: system improvement methods by teams of local health care workers from participating facilities yielding specific innovations at different points in the care and treatment process.

Category	Intervention
Case finding	
Recruitment of inpatients	<ul style="list-style-type: none"> “Opt-out” testing of patients in medical and surgical wards Visits from ART clinic team to pediatric wards weekly
Recruitment of outpatients	<ul style="list-style-type: none"> Training of outpatient staff to recognize primary indicators of AIDS in children
Coordination of HIV/TB care	<ul style="list-style-type: none"> Prioritization of patients with TB for available counseling resources “Opt-out” and group counseling for HIV testing of patients with TB “bundled” with TB clinic entry visit processes Immediate CD4 cell count determination if HIV test results are positive Eligible patients with TB managed as cohort on separate day for HAART
Pre-ART care	
Reduction of steps for pre-ART care	<ul style="list-style-type: none"> Immediate CD4 cell count determination if HIV test results are positive; multiple processes at same visit (e.g., counseling, laboratory testing [CD4 cell count, syphilis, sputum Pap smear testing], clinical staging)
Feedback of CD4 cell count results to clinics from laboratory services	<ul style="list-style-type: none"> List of patient results faxed from central laboratory to clinic weekly
Judicious use of guidelines for HAART eligibility	<ul style="list-style-type: none"> Nurse designated to triage interventions and follow-up on the basis of CD4 cell count result Increased reliance on clinical judgment of health workers who know clients well (e.g., defer home visit if logistic impediments exist)
Early counseling for HAART preparation	<ul style="list-style-type: none"> Primary pre-ART counseling occurs at point of referral for ART and not at the first “ART clinic visit”
Engagement of primary care clinics in preparation of patients for HAART	<ul style="list-style-type: none"> Primary care clinics engage in recruitment, testing, and preparation of patients for HAART (VCT, CD4 cell count determination, counseling)
ART care	
Engagement of local clinics in HAART initiation and long-term care of patients receiving HAART	<ul style="list-style-type: none"> Primary care clinics are supported to initiate HAART through outreach from district hospital teams Patients are referred back from secondary and tertiary HAART initiation sites to primary care clinics for long-term HAART care
PMTCT	
Case finding and processing of HIV-positive mothers	<ul style="list-style-type: none"> “Opt-out” testing of mothers attending antenatal care Same-visit CD4 cell count determination for mothers who are HIV positive Rapid referral of mothers with CD4 cell counts <200 cells/mm³ for HAART
Case finding and processing of HIV-positive infants	<ul style="list-style-type: none"> PCR testing linked to the first immunization visit
Coordination of maternal and infant HIV care	<ul style="list-style-type: none"> Infant and maternal medical records are combined and held by mother Key maternal and infant HIV care information is duplicated in maternal and infant records Maternal CD4 cell count determination is performed every 6 months at immunization/infant clinic at infant’s visit

NOTE. ART, antiretroviral therapy; HAART, highly active ART; PCR, polymerase chain reaction; PMTCT, prevention of mother-to-child transmission; TB, tuberculosis; VCT, voluntary counseling and testing.

370 per month) in the first 2 months of the project, and a sharp increase in referrals for HAART is expected.

LESSONS AND HIGH-LEVERAGE INTERVENTIONS

The main lesson learned through this work is that health systems improvement methods can provide a viable and potentially sustainable approach to rapid scale-up of HIV/AIDS services in a country like South Africa. Although the lack of medical personnel and medical infrastructure is undeniably a formidable and rate-limiting barrier to effective care in many developing countries, much can be done to optimize existing resources in these settings. Although South Africa has much better resources than many of the other countries struggling with the epidemic and has allocated significant internal resources to manage the epidemic, we have seen some of the greatest improvements in treatment outcomes in areas that have resource levels similar to surrounding sub-Saharan states (e.g., in Mhlontlo District, which has 1 doctor for every 100,000 inhabitants). The primary resources that we bring are systems knowledge and optimism that comprehensive HIV/AIDS care, including HAART, can largely be achieved through optimization of the existing health system.

At many sites, the application of improvement methods also empowers clinic staff, leading to a palpable change in morale; where staff were once despondent and overwhelmed, they have become enthusiastic and willing to try new strategies. Notably, this change has been more evident in the rural areas, where clinic staff are more connected to their patient base and less restrained by the heavy bureaucracy that characterizes the urban areas. As with all collaborative networks, a number of the clinics have seen no improvement or have resisted introduction of changes, although IHI and its partners remain optimistic that they will adopt successful ideas and interventions in time [29]. The critical determinant of the likelihood of successful system improvement in a particular clinic is the extent of buy-in to the process by senior leadership (in particular, clinic managers and senior nursing staff). Without their endorsement, sites rarely make progress, and front-line providers are not empowered to generate the highly useful, locally appropriate interventions, documented in table 1, that can rapidly transform outcomes.

CONCLUSION

The scale-up of HAART programs in developing countries will require multiple different interventions to strengthen the existing fragile health infrastructures of many countries. Although the initial global response has been focused on external provision of personnel, drugs, and supplies; renewal or new construction of care and treatment centers; and training of health workers, rapid

and sustained benefit can be achieved through application of methods to strengthen existing health infrastructures.

Several pilot projects in rural and urban settings across South Africa have demonstrated rapid expansion of capacity for treating people with HIV/AIDS by optimization of existing health systems. Although the South African health system has better resources than many other systems in the developing world, improved outcomes were seen across a spectrum of resource levels, and some of the greatest improvements were seen in the rural areas with the fewest resources. The lessons learned in this country are applicable to a variety of settings. Undoubtedly, a lack of trained personnel, adequate drug distribution, and functioning clinics hinders the establishment of effective HAART programs in developing countries, but the strengthening of existing health systems, in conjunction with the struggle to garner more resources, should be given serious consideration as an intervention that is likely to yield long-term improvement in HIV/AIDS care. This broad system-strengthening approach will also allow better integration of HIV/AIDS programs into the rest of the health system.

The current experience with rapid expansion of these pilot projects to include all tiers of the health system across broad geographic regions holds promise that this approach can result in an exponential increase in the capacity to treat all people with HIV/AIDS in a large area. By use of methods that have been successfully employed in developed countries [30], it is possible that a rapid increase in coverage could result in effective, high-quality HIV/AIDS care for all who need it across an entire province or country.

Acknowledgments

Supplement sponsorship. This article was published as part of a supplement entitled "The Realities of Antiretroviral Therapy Rollout: Challenges to Successful Programmatic Implementation," sponsored by the Harvard Medical School Division of AIDS, the Harvard University Center for AIDS Research, and the Harvard Initiative for Global Health.

References

1. Mahomva A, Greby S, Dube S, et al. HIV prevalence and trends from data in Zimbabwe, 1997–2004. *Sex Transm Infect* 2006; 82(Suppl 1): i42–7.
2. Cheluget B, Baltazar G, Orege P, Ibrahim M, Marum LH, Stover J. Evidence for population level declines in adult HIV prevalence in Kenya. *Sex Transm Infect* 2006; 82(Suppl 1):i21–6.
3. Green EC, Halperin DT, Nantulya V, Hogle JA. Uganda's HIV prevention success: the role of sexual behavior change and the national response. *AIDS Behav* 2006; 10:335–46.
4. World Health Organization. Global AIDS epidemic continues to grow. Available at: <http://www.who.int/hiv/mediacentre/news62/en/index.html>. Accessed 31 August 2007.
5. Jaffar S, Grant AD, Whitworth J, Smith PG, Whittle H. The natural history of HIV-1 and HIV-2 infections in adults in Africa: a literature review. *Bull World Health Organ* 2004; 82:462–9.

6. Badri M, Maartens G, Mandalia S, et al. Cost-effectiveness of highly active antiretroviral therapy in South Africa. *PLoS Med* **2006**; 3:e4.
7. Jong-wook L. Global health improvement and WHO: shaping the future. *Lancet* **2003**; 362:2083–8.
8. Stringer JS, Zulu I, Levy J, et al. Rapid scale-up of antiretroviral therapy at primary care sites in Zambia: feasibility and early outcomes. *JAMA* **2006**; 296:782–93.
9. Ferradini L, Jeannin A, Pinoges L, et al. Scaling up of highly active antiretroviral therapy in a rural district of Malawi: an effectiveness assessment. *Lancet* **2006**; 367:1335–42.
10. Wester CW, Bussmann H, Avalos A, et al. Establishment of a public antiretroviral treatment clinic for adults in urban Botswana: lessons learned. *Clin Infect Dis* **2005**; 40:1041–4.
11. Koenig SP, Leandre F, Farmer PE. Scaling up HIV treatment programmes in resource-limited settings: the rural Haiti experience. *AIDS* **2004**; 18(Suppl 3):S21–5.
12. Coetzee D, Hildebrand K, Boule A, et al. Outcomes after two years of providing antiretroviral treatment in Khayelitsha, South Africa. *AIDS* **2004**; 18:887–95.
13. Egger M, Boule A, Schechter M, Miotti P. Antiretroviral therapy in resource-poor settings: scaling up inequalities? *Int J Epidemiol* **2005**; 34:509–12.
14. Kline MW. Perspectives on the pediatric HIV/AIDS pandemic: catalyzing access of children to care and treatment. *Pediatrics* **2006**; 117:1388–93.
15. Kim JY, Farmer P. AIDS in 2006—moving toward one world, one hope? *N Engl J Med* **2006**; 355:645–7.
16. Government of South Africa. Operational plan for comprehensive HIV and AIDS care, management and treatment for South Africa. 19 November **2003**. Available at: <http://www.info.gov.za/otherdocs/2003/aidsplan.pdf>. Accessed 3 August 2007.
17. Statement on World AIDS Day issued by GCIS on behalf of The Presidency. 30 November **2006**. Available at: <http://www.doh.gov.za/mediaroom/index.html>. Accessed 3 August 2007.
18. Actuarial Society of South Africa. ASSA2003 AIDS and demographic model. Available at: <http://www.assa.org.za/aids/content.asp?id=100000449>. Accessed 25 October 2006.
19. Berwick DM. Continuous improvement as an ideal in health care. *N Engl J Med* **1989**; 320:53–6.
20. Berwick DM. Eleven worthy aims for clinical leadership of health system reform. *JAMA* **1994**; 272:797–802.
21. Shafer TJ, Wagner D, Chessare J, Zampello FA, McBride V, Perdue J. Organ Donation Breakthrough Collaborative: increasing organ donation through system redesign. *Crit Care Nurse* **2006**; 26:33–48.
22. Oldham J. *Sic evenit ratio ut componitur: the small book about large system change*. Chichester, United Kingdom: Kingsham Press, **2005**.
23. Abdallah H. Assessing the economic impact of the new system of care for arterial hypertension in Tula Oblast, Russia. Operations research results 2(13). Bethesda, MD: Quality Assurance Project, for the U.S. Agency for International Development (USAID), **2002**. Available at: <http://www.qaproject.org/pubs/pubstitleindex.html>. Accessed 25 October 2006.
24. Furth R, Gass R, Kagubare J. Quality Assurance Project (QAP). Rwanda human resources assessment for HIV/AIDS scale-up. Phase 1 report: national human resources assessment. Operations research results. Bethesda, MD: Quality Assurance Project, for the U.S. Agency for International Development (USAID), **2005**. Available at: <http://www.qaproject.org/pubs/pubstitleindex.html>. Accessed 25 October 2006.
25. Berwick DM. Lessons from developing nations on improving health care. *BMJ* **2004**; 328:1124–9.
26. The Breakthrough Series: IHI's collaborative model for achieving breakthrough improvement. IHI Innovation Series white paper. Boston: Institute for Healthcare Improvement, **2003**. Available at: <http://www.ihl.org/IHI/Results/WhitePapers/whitepapersindex.htm>. Accessed 31 August 2007.
27. Badri M, Lawn SD, Wood R. Short-term risk of AIDS or death in people infected with HIV-1 before antiretroviral therapy in South Africa: a longitudinal study. *Lancet* **2006**; 368:1254–9.
28. Post FA, Badri M, Wood R, Maartens G. AIDS in Africa—survival according to AIDS-defining illness. *S Afr Med J* **2001**; 91:583–6.
29. Rogers EM. *Diffusion of innovations*, 4th ed. New York: The Free Press, **1995**.
30. McCannon CJ, Schall MW, Calkins DR, Nazem AG. Saving 100,000 lives in US hospitals. *BMJ* **2006**; 332:1328–30.