Access to Antiretroviral Therapy for Adults and Children with HIV Infection in Developing Countries: Horizons Studies, 2002–2008

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SYNOPSIS

The Access-to-Treatment research initiative of the Population Council's Horizons program undertook 11 projects across Asia and sub-Saharan Africa from 2002 to 2008. The projects included a variety of cross-sectional exploratory studies, situation analyses, and longitudinal randomized, controlled intervention studies that examined service delivery, community awareness, health-seeking behaviors, adherence, cost, and other factors affecting treatment for adults and children infected with human immunodeficiency virus (HIV). This article summarizes the key findings and lessons learned from these projects, and examines cross-cutting issues such as stigma, quality of life, and sexual-risk behaviors among people living with HIV and acquired immunodeficiency syndrome on antiretroviral therapy. The article concludes with recommendations for evidence-based programming and future research around treatment for both children and adults.

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More than 60 million people have been infected with human immunodeficiency virus (HIV), and 20 million have died since acquired immunodeficiency syndrome (AIDS) was first described in 1981.^{1,2} Treatment with antiretroviral therapy (ART) became widely available in developed countries in 1996, but access in developing countries lagged until advocacy and generic competition drove down prices in 2002.² Although a handful of countries such as Brazil, Thailand, Senegal, and Botswana were providing ART for adults through public-sector health facilities as early as 2000, treatment programs in most other developing countries were not established until 2002 or later. ART services for children were initiated much later and continue to be limited. The introduction of treatment programs in low-resource settings raised questions about readiness of health systems, quality of service delivery, capacity of human resources, and ability of individuals to adhere to the programs, for which relevant evidence from developing country contexts did not yet exist.

In light of these issues, the Horizons program convened a meeting of international experts in 2001 to prioritize research questions around access to ART and the operational challenges related to the introduction of therapy in developing-country settings.³ The resulting Access-to-Treatment research initiative was launched in 2002 and has spawned 11 projects (Figure) across Asia and sub-Saharan Africa examining service delivery, health-seeking behaviors, adherence, cost, and other factors affecting treatment for adults and children infected with HIV. This article summarizes the key findings and lessons learned from these projects, and examines issues such as stigma, quality of life, and sexual-risk behaviors among people living with HIV and AIDS (PLHA) on ART. The article concludes with recommendations for evidence-based programming and future research around treatment for both children and adults.

IDENTIFYING PROBLEMS AND GAPS

Patient retention and adherence

Horizons initially undertook exploratory studies to investigate gaps in programs that were planning to or had already initiated ART services. These studies identified patient retention and adherence to treatment as major challenges for scale-up. A 2002 situation analysis of the newly implemented national ART program in 15 hospitals in five northern provinces of Thailand documented a dropout rate of 30% in the first six months of the program,⁴ primarily because of side effects and lack of ongoing support. Types of nonadherence included

missing doses, not taking medications on time, and not following treatment instructions.

A 2004 study of PLHA in India found adherence to be significantly lower among patients with severe depression and among those receiving free ART compared with patients in the private sector who paid out-of-pocket for treatment. The study also revealed that patient knowledge about their medications was low, highlighting the need for better patient education prior to initiating ART and ongoing adherence support thereafter.^{5,6}

Gaps in provider training

Gaps in provider training, confidence, and competency also emerged as important barriers to service delivery. In Thailand, a majority of ART providers (i.e., doctors, nurses, and counselors) reported difficulties in counseling on medication side effects, and nearly half of the doctors reported difficulties in diagnosing and managing side effects and medication interactions, despite receiving intensive training.⁴ A health-care worker survey in three Kenyan provinces revealed knowledge gaps and low confidence regarding pediatric HIV diagnosis protocols, medication management, management of comorbidities, vaccination in symptomatic children, prevention of mother-to-child transmission (PMTCT), and counseling.⁷ Horizons researchers also identified a lack of standardized or coordinated training for health-care workers on the management of pediatric HIV in South Africa, where most doctors and nurses reported receiving no formal training in ART and relied upon self-directed study from books and online courses.⁸

Integration with other health services

Horizons researchers documented minimal integration of HIV prevention, care, and treatment services, and weak links between services. In South Africa, a 2002 situation analysis of direct and ancillary HIV/AIDS services in 98 health facilities in KwaZulu-Natal, a province where adult HIV prevalence was 30%, revealed that less than one-third of the women receiving antenatal care were counseled on HIV, sexually transmitted infections, and PMTCT; only 42% of community health centers and 17% of clinics provided PMTCT services; and only one-half of the facilities offered voluntary counseling and testing for HIV.⁹ Lack of integration also was reported between ART and tuberculosis (TB) services.¹⁰ A study exploring current practices in pediatric ART rollout at 16 sites in five South African provinces found that the majority of children receiving ART were referred from community clinics when sick or from inpatient wards; less than 2% of children

Figure. Sample characteristics and study designs of Horizons' Access-to-Treatment study projects, 2002–2008

Study title and country	Year(s) of study	Target population	Sample size (n)	Type of study	Sampling methodology	Key findings
Reproductive health services in KwaZulu-Natal, South Africa: a situation analysis study focusing on HIV/AIDS services ^a	2002–2003	Adults infected with HIV	98 health facilities 418 clients 299 health-care providers	RSA descriptive	Simple random sampling of health facilities Convenience sampling of respondents	Integration of reproductive health into ANC services was limited. Availability of PMTCT services to ANC clients was limited to a few centers. Facilities had basic services to treat STIs but lacked laboratory facilities to test for STIs, including HIV. Critical weaknesses in training, supervision, client education, and key program elements remained for many FP services. Comprehensive counseling addressing HIV, STIs, and FP was not provided.
Exploring current practices in pediatric ARV rollout and integration with early childhood programs in South Africa: an RSA ^b	2005	Children infected with HIV	16 ARV programs 126 caregivers 74 health-care workers	RSA descriptive	Convenience sampling	Lack of standardized/coordinated training for health-care workers on management of pediatric HIV. Referral links between pediatric HIV and PMTCT services were weak. Space constraints, human resource shortage, lack of clinical capacity, and “fear of treating HIV-infected children” were key barriers for health-care workers.
Exploring models of delivering ART and integration of ART with TB services in South Africa ^c	2006	Adults infected with HIV	14 health facilities 262 PLHA 43 health-care providers	RSA descriptive	Convenience sampling	Lack of integration among HIV care, ART, and TB services was documented. Referrals were made to other centers for accessing TB or ART services, which posed a problem for clients. Health-care providers received training relevant to services provided—without overlap between HIV and TB. Distance from ART/TB services was a key barrier to accessing services for clients. Women were more likely to access both ART and TB services compared with men.
Formative assessment of the acceptability of an m-DOT strategy to promote adherence to ART among PLHA in Mombasa, Kenya ^d	2002	Adults infected with HIV	38 PLHA	Qualitative descriptive	Purposive sampling	Acceptability of an m-DOT strategy was high. PLHA preferred a clinic-based, m-DOT approach due to confidentiality concerns, risk of stigma associated with home visits, and beliefs that clinic visits afforded access to better quality care.

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Figure (continued). Sample characteristics and study designs of Horizons' Access-to-Treatment study projects, 2002–2008

Study title and country	Year(s) of study	Target population	Sample size (n)	Type of study	Sampling methodology	Key findings
Operations research around the introduction of ARVs in the management of HIV-infected individuals in Mombasa, Kenya ^{e,k}	2003–2006	Adults infected with HIV	234 PLHA	Prospective randomized, controlled study (two arms)	Quota sampling with randomized assignment	DAART was effective in increasing adherence during the intervention period compared with standard care. The beneficial effect was not sustained in the post-intervention phase. DAART strategy was feasible and acceptable. Significant improvements in BMI, immunologic and virologic functions, and depression scores were observed. Stigma declined significantly over time. Self-reported sexual-risk behaviors (multiple partners and unprotected sex) declined significantly over 12 months of follow-up. Unprotected sex continued to be reported with regular partners.
Healthy start pediatric HIV study: a diagnostic study investigating barriers to HIV treatment and care among children in Kenya ^l	2007	Children infected with HIV	1,180 caregivers of children aged <15 years 103 health-care workers	Descriptive	Cluster sampling of households Convenience sampling of health-care workers	Caregivers demonstrated low knowledge of pediatric HIV and treatment options. Attitudinal barriers to pediatric treatment were widespread, and stigma prevented caregivers from accessing care. Cost was an additional barrier to seeking pediatric treatment. Health-care workers cited service-side barriers: gaps in HIV knowledge, insufficient training, lack of confidence in pediatric HIV diagnosis protocols and ARV drug management, space constraints, and staff shortage.
Community education and referral: supporting adherence to ART and prevention for PLHA in Zambia ^m	2004–2006	Adults infected with HIV	1,200 community members 500 PLHA on treatment	Prospective pre- and post-intervention control evaluation	Cluster sampling of community members from households Quota sampling of PLHA	HIV knowledge increased similarly over time in intervention and comparison sites. Between 25% and 37% of study participants had undergone HIV testing; the increase was significant only at the Ndola intervention site. Women received testing significantly more than men. Partner disclosure increased significantly at both the intervention and comparison sites in Lusaka but remained unchanged in Ndola. High levels of adherence to ART were reported from all sites. There were significant reductions in internalized stigma among people on ART in Lusaka. Although community stigma decreased over time at both intervention and comparison sites, it remained an important barrier to accessing care.
Assessment of adherence to treatment and sexual-risk behavior among HIV-positive patients receiving ART: a diagnostic study in India ^{n,o}	2004	Adults infected with HIV	310 PLHA on treatment	Descriptive	Quota sampling	High levels of adherence were reported by study participants overall. Adherence was significantly lower among patients with severe depression and those receiving free ART compared with patients paying out-of-pocket for treatment.

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Figure (continued). Sample characteristics and study designs of Horizons' Access-to-Treatment study projects, 2002–2008

Study title and country	Year(s) of study	Target population	Sample size (n)	Type of study	Sampling methodology	Key findings
A diagnostic operations research to inform the national initiative on improving access to treatment, care, and support for HIV-positive women and their families in India ^a	2005–2006	Pregnant or postpartum (<24 months) women infected with HIV	315 females infected with HIV	Descriptive	Convenience	Integration of HIV services into reproductive health and ANC was limited, and service provision focused on single issues without addressing HIV risk. Less than one-third of the HIV-positive women were informed about testing for CD4 cell counts and ART. Less than one-half of the children born to HIV-positive women were tested for HIV. Future fertility intentions were not explored, and high levels of unmet FP needs were documented. Linkages among ANC, PMTCT, and ART care and support programs were weak.
An RSA of the provision of highly active ART to people living with HIV/AIDS by the Ministry of Public Health's Access to Care Project in northern Thailand ^a	2002	Adults infected with HIV	15 ART clinics 120 PLHA	RSA descriptive	Purposive sampling	Gaps in health-care worker knowledge and ability to manage HIV disease and ART were documented. Nearly one-third of the patients dropped out of the ART program after six months, mostly due to side effects. Lack of follow-up support for patients to manage their treatment was reported.
Reducing dropouts and increasing adherence rates among PLHA on ART in northern Thailand ^a	2004–2007	Adults infected with HIV	45 hospitals 753 PLHA	Randomized, controlled study (three arms)	Convenience sampling of facilities with random assignment to groups Quota sampling of PLHA	Patient dropout rates were lower in the peer-support and enhanced adherence-counseling intervention groups compared with standard care. Self-reported adherence was high in all three groups. Patients in the intervention arms demonstrated higher self-efficacy, greater improvements in quality-of-life scores, and greater decreases in internalized stigma scores.

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^bMichaels D, Eley B, Ndhlovu L, Rutenberg N. Exploring current practices in pediatric ARV rollout and integration with early childhood programs in South Africa: a rapid situation analysis. Horizons Final Report. Washington: Population Council; 2006. Also available from: URL: <http://www.popcouncil.org/pdfs/horizons/sapedssa.pdf> [cited 2008 Mar 10].

^cNdhlovu L, Maphanga T, Madikizela L, Rutenberg N. Exploring models of delivering antiretroviral therapy and integration of ART with TB services in South Africa. Horizons Final Report. Washington: Population Council [forthcoming].

^dSarna A, Hawken M, Kaai S. Acceptability of a modified directly observed therapy approach to improve adherence to antiretroviral therapy. Horizons Research Summary. Washington: Population Council; 2004.

^eHorizons/Population Council; International Centre for Reproductive Health; Coast Province General Hospital, Mombasa, Kenya. Adherence to antiretroviral therapy in adults: a guide for trainers. Nairobi: Population Council; 2004.

^fMunyao P, Sarna A, Luchters S, Geibel S, Shikely K, Mandaliya K, et al. How feasible is a DAART strategy to promote adherence to ART? Lessons from Mombasa, Kenya. Horizons Research Update. Nairobi: Population Council; 2005.

^gSarna A, Luchters S, Geibel S, Chersich MF, Munyao P, Kaai S, et al. Short- and long-term efficacy of modified directly observed antiretroviral treatment in Mombasa, Kenya: a randomised trial. J Acquir Immune Defic Syndr 2008;48:611-9.

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Figure (continued). Sample characteristics and study designs of Horizons' Access-to-Treatment study projects, 2002–2008

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- ²Sarna A, Luchters S, Kaai S, Munyao P, Geibel S, Shikely K, et al. Does being treated with HAART affect the sexual risk behavior of people living with HIV/AIDS? Insights from Mombasa, Kenya. Horizons Research Update. Nairobi: Population Council; 2005.
- ³Sarna A, Luchters SM, Geibel S, Kaai S, Munyao P, Shikely KS, et al. Sexual risk behaviour and HAART: a comparative study of HIV-infected persons on HAART and on preventive therapy in Kenya. Int J STD AIDS 2008;19:85-9.
- ⁴Luchters S, Sarna A, Geibel S, Chersich M, Munyao P, Kaai S, et al. Sexual risk behaviors of HIV-positive persons receiving ART in Mombasa, Kenya: longitudinal study findings. Horizons Research Summary. Nairobi: Population Council; 2007.
- ⁵Kiragu K, Schenk K, Murugi J, Sarna A. If you build it, will they come? Kenya healthy start pediatric HIV study: a diagnostic study investigating barriers to HIV treatment and care among children. Horizons Final Report. Washington: Population Council; 2008.
- ⁶Samuels F, Simbaya J, Sarna A, Geibel S, Ndubani P, Kamwanga J. Engaging communities in supporting HIV prevention and adherence to antiretroviral therapy in Zambia. Horizons Research Summary. Washington: Population Council; 2008.
- ⁷Sarna A, Gupta I, Pujari S, Sengar AK, Garg R, Weiss E. Examining adherence and sexual behavior among patients on antiretroviral therapy in India. Horizons Final Report. Washington: Population Council; 2006. Also available from: URL: <http://www.popcouncil.org/pdfs/horizons/indiaart.pdf> [cited 2008 Mar 10].
- ⁸Sarna A, Pujari S, Sengar AK, Garg R, Gupta I, Dam J. Adherence to antiretroviral therapy and its determinants amongst HIV patients in India. Indian J Med Res 2008;127:28-36.
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- ¹⁰Panpanich R, Sornchai P, Suwanteeerangkul KJ, Thamthitwat S, Sounthisombut P. A rapid situation analysis of the Access to Care Project in northern Thailand. Horizons Final Report. Washington: Population Council; 2004. Also available from: URL: <http://www.popcouncil.org/pdfs/horizons/thaisituationanalysis.pdf> [cited 2008 Mar 10].
- ¹¹Sarna A, Weiss E. Current research and good practice in HIV and AIDS treatment education (UNESCO and WHO, 2007) [cited 2008 Jan 15]. Available from: URL: <http://unesdoc.unesco.org/images/0014/001497/149722E.pdf>
- HIV = human immunodeficiency virus
- AIDS = acquired immunodeficiency syndrome
- RSA = rapid situation analysis
- ANC = antenatal care
- PMTCT = prevention of mother-to-child transmission
- STI = sexually transmitted infection
- FP = family planning
- ARV = antiretroviral
- ART = antiretroviral therapy
- TB = tuberculosis
- PLHA = people living with HIV/AIDS
- m-DOT = modified directly observed therapy
- DAART = directly administered ART
- BMI = body mass index

were referred from PMTCT programs.⁸ A study of HIV-positive pregnant and postpartum women in three high-prevalence Indian states found that less than one-third of the women had been informed about testing for CD4 cell counts, and only 18% were informed about the availability of ART during antenatal care. Of the women with living children, 44% reported that none of their children had been tested for HIV.¹¹

Community awareness

Uptake of ART services depends on community awareness about HIV and availability and accessibility of services. Horizons researchers conducted a community survey of primary caregivers of children in three Kenyan provinces selected because of high HIV prevalence and the availability of pediatric HIV care services.⁷ The study found that while caregivers understood the basics of HIV in adults, knowledge about HIV infection and symptoms in children was low: only half of the caregivers could name three symptoms indicative of pediatric HIV infection. Although the majority of caregivers were aware of treatment options for children infected with HIV and believed that these children could live into adulthood, less than two-thirds of the caregivers knew where to access HIV testing and treatment services for children.⁷ Health-care costs (e.g., transport, consultation fees, and medications) and HIV-related stigma were additional barriers to seeking care. A community intervention is being developed by study partners to raise awareness, encourage people to get tested and have their children tested, and link people to care as necessary.

Confidentiality and stigma concerns

Horizons researchers found that concerns about confidentiality and fear of stigma influence the design of services to promote adherence to treatment. Acceptability of a modified directly observed therapy (m-DOT) to promote adherence to ART was assessed among people infected with HIV accessing services in coastal Kenya.¹² Researchers explored the acceptability of home visits by health-care workers vs. clinic visits among PLHA and the preferred frequency of clinic visits per week, as well as the preferred cadre of health-care workers for home visits. The majority of PLHA interviewed expressed a preference for clinic-based m-DOT, citing confidentiality concerns and risk of stigma within the community associated with home-health visits, and the belief that clinic visits afforded access to qualified health-care workers and the sense of personal control offered by visiting the clinic instead of being visited at home. Clients felt that community health-care workers (not dressed in uniforms) were the preferred cadre

for home visits. As a result of these findings, researchers designed and implemented an intervention study to evaluate the effectiveness of clinic-based, directly administered ART (DAART) in Kenya.

FIRST EFFORTS TO IMPROVE THERAPY ADMINISTRATION

M-DOT for ART

In Kenya, Horizons researchers conducted one of the first randomized, controlled studies of a clinic-based DAART intervention as a strategy to increase adherence to ART. The intervention consisted of clinic visits twice a week for the first 24 weeks, during which patients met with DAART nurses who observed medication ingestion, dispensed medications for the time between visits, performed pill counts, and provided individualized adherence support. Non-DAART patients received standard, monthly in-clinic follow-up, including adherence counseling and routine health care.¹³ The study found that DAART was feasible and effective in promoting adherence during the intervention period (proportion with >95% adherence: DAART, 92% vs. non-DAART, 80%), but these effects were not sustained after the intervention.^{14,15} Horizons researchers found DAART to be particularly beneficial in the first 24 weeks in patients with moderate or severe depression. Study findings raised further questions about the best way to optimize DAART and whether it is most effective among a subgroup of adults at risk for nonadherence.¹⁵

Adherence counseling and peer education

In Thailand, Horizons researchers, in partnership with Chiang Mai University, conducted a randomized, controlled study to evaluate interventions to promote ART adherence and reduce dropouts at 45 hospitals across four northern provinces.¹⁶ Hospitals were assigned to three groups: (1) enhanced adherence counseling, including patient education, side-effect management, and integration of medication into daily life; (2) enhanced adherence counseling plus peer education at clinic and home visits; or (3) standard care consisting of routine counseling and clinical follow-up. The study found that enhanced counseling with and without peer involvement was effective in reducing dropouts compared with standard care after 12 months of treatment, and that the peer intervention served to significantly increase patients' self-efficacy in adhering to ART after 12 months of treatment.¹⁶

AIDS Community Education and Referral Strategy

While interventions designed to increase adherence and decrease risk behaviors are important, effective

community-level interventions may also influence positive outcomes for individuals. The AIDS Community Education and Referral Strategy in the Zambian cities of Lusaka and Ndola represents one such effort. The intervention aimed to raise community awareness of HIV; strengthen community-based PLHA support groups by incorporating traditional healers, church groups, and home-based care services; establish referral mechanisms between health facilities and the community; and utilize volunteer peer-support workers at clinics.¹⁷

While few significant differences were found, it is likely that an unrelated clinic-based adherence program introduced in the comparison sites by another organization diluted the effects. However, the study raises questions about the intensity of interventions required to bring about community-level change. Despite these limitations, the study has contributed to the understanding of the positive roles different groups (e.g., traditional healers, home-based care workers, and positive networks) can play in addressing HIV and how to link clinic services and community activities.¹⁷ These findings were used to inform a similar intervention in Uganda in 2007.

RELATED ISSUES

Stigma and ART

Horizons researchers nested observational studies within intervention studies to examine change in HIV-related stigma among PLHA receiving ART. These studies used an adapted HIV-stigma scale covering four domains: personalized stigma, disclosure concerns, negative self-image, and concern with public attitudes.¹⁸ Common themes from Horizons studies in Thailand,¹⁶ Zambia,¹⁷ and Kenya¹⁹ showed that stigma decreased over time on ART. For example, in Kenya, the proportion of patients receiving ART and reporting moderate to high stigma declined from 73% prior to initiating ART to 56% after 12 months of treatment. In addition, internalized stigma appeared to be higher among female patients compared with male patients prior to initiating ART in Kenya¹⁹ and Zambia.¹⁷

Quality of life and ART

Perceived quality of life is a proxy for effectiveness of medication regimens; if HIV is effectively controlled, individuals have an increased sense of well-being and are able to re-engage in routine activities. Horizons researchers documented significant increases in quality-of-life measures over time. In Thailand, significant improvements were observed in mental and physical health scores during the 12 months following counsel-

ing for adherence and peer support.¹⁶ In Kenya, significant improvements occurred across general health perception; physical, social, and cognitive functioning; pain; mental health; energy; and fatigue.

Gender and ART

Horizons researchers did note gender differentials in patient populations: more than 60% of Kenyan and Zambian patients and more than half of the Thai patients were female.^{15–17} Interestingly, about one-third of the female participants in Kenya and Zambia were widows, suggesting that some women might access treatment after the death of their spouses. It also is possible that women, who often contract HIV infection from their male partners/spouses, access treatment much later and only when symptomatic. No gender differentials in adherence were documented.

Sexual-risk behavior and ART

Researchers have expressed concern that effective treatment and concomitant increases in well-being and sexual activity could lead to an increase in unprotected sex among PLHA. Horizons researchers found no evidence of increased sexual-risk behavior (i.e., multiple partners or unprotected sex) in Kenya,^{20–23} Thailand,²⁴ Zambia,¹⁷ and India.⁵ For example, in Kenya, the proportion of sexually active participants who reported unprotected sex with an unknown or HIV-negative partner declined from 50% at baseline to 28% after 12 months on treatment. However, unprotected sex is still prevalent, underscoring that the risk of HIV transmission remains, particularly with regular partners.

FOLLOW-ON NEEDS

Methods and measures

Horizons researchers used a diverse range of research methodologies and study designs in their Access-to-Treatment portfolio (Figure). They used validated measures and scales frequently, particularly pertaining to adherence,²⁵ depression,²⁶ and quality of life.^{27,28} A team of expert psychologists and social scientists adapted some scales to more accurately reflect the local cultural context, and translations and back translations were pretested before application. In the absence of a gold standard, measuring adherence accurately is a challenge, especially in settings with limited resources. It is recognized that patients often overstate self-reported adherence and underreport missed doses.^{29,30} Adherence studies often require that clinic staff take over measures such as pill counts and self-reports as a part of clinical management. Specialized training for interviewers to ensure consistent and accurate data

collection with regard to these techniques is essential. Newer methods to improve data-collection methods and tools need to be explored.

Horizons partners at Chiang Mai University have developed a computer-based program to increase the accuracy of pill counts as a result of the study; such methods need to be evaluated. The use of audio computer-assisted self-interviewing has been used in other Population Council studies addressing sensitive topics and could be applied to treatment research to improve accuracy of self-report of adherence. Sample selection of HIV-infected patients is often challenging, as PLHA cannot be identified or reached in communities for reasons of confidentiality. Horizons researchers often have had to use convenience or quota sampling to overcome this problem.³¹

Provider training

The Horizons program was among the first to implement intervention studies on adherence in developing countries. The evidence base provided by Horizons' early exploratory studies has greatly contributed to the design, strengthening, and scale-up of ART services. Horizons researchers identified training gaps and lack of provider confidence across several studies. Most treatment programs provide one-time, intensive provider training at their start. The importance of ongoing, need-based, and interactive training for providers cannot be overemphasized, particularly for trained pediatric infectious disease providers. Training materials developed by Horizons, such as the adherence counseling manual used in Kenya,¹³ are important in this endeavor and have since been adapted by programs in Zambia, Tanzania, South Africa, and Russia.

Human resource shortages in Africa are well documented,² and some treatment programs are run by clinical officers and nurses instead of medical doctors. Expert consultation is needed as treatment regimens become more complicated. Future research will be needed to evaluate models of training programs with ongoing mentoring and access to specialist services. As in other sectors, sustainability of interventions after initial funding ends is a challenge for both programs and researchers. For example, peer volunteers or community health workers often play a key role in enhancing service delivery, but may require some form of compensation to continue delivering interventions.

Defining best practices

Horizons' research has highlighted the lack of integration of HIV testing and TB, PMTCT, maternal health, and ART services. Program managers and departments of health have used this information, for example, in

South African program planning efforts. In Kenya, the Kenya Network of Women with AIDS is developing interventions to increase community awareness of pediatric HIV and treatment. Efforts to integrate HIV prevention, care, and treatment services require evaluation to identify best practices and successful models for scale-up. As programs race toward universal access to ART, it is imperative to explore new approaches to service delivery while simultaneously strengthening health systems and monitoring quality of services.

DAART as a strategy to promote adherence was first documented after a successful community-based m-DOT intervention in Haiti using *accompagnateurs* or community health workers.^{32,33} DAART has been evaluated largely among PLHA at risk of nonadherence, such as injection drug users,^{34–36} incarcerated patients,^{37,38} and, to a limited extent, the general population.^{39,40} Horizons has added to the scientific evidence by rigorously evaluating clinic-based DAART in a resource-limited setting. Given that improvements in adherence were not sustained beyond the DAART intervention, further research is needed to determine the optimum duration of the intervention and ways to sustain its effects. Population Council researchers are developing a study to evaluate DAART among nonadherent clients—a population for whom this resource-intensive intervention might prove most beneficial.

HIV programs have long used HIV-positive peers in the developing-country context for prevention, social support, and, to a limited extent, treatment-related activities; however, none has evaluated a peer-based adherence-support intervention. The Thailand Horizons study was one of the first to show that such interventions are effective in increasing adherence, raising self-efficacy, lowering self-stigma, and improving quality of life, compared with standard care. This intervention has been introduced widely across the country with Global Fund assistance. It is recognized that such interventions are costlier than the traditional standard of care, and current scale-up of ART programs may exclude such ancillary services. Still, Horizons' work in Kenya and Thailand shows the value of ancillary services (e.g., DAART and peer education and support).

Targeted population issues

The Horizons studies began as ART programs first rolled out and most patients presented with advanced HIV disease—a factor that undoubtedly stimulated adherence. As the epidemic matures, programs are increasingly managing patients on long-term treatment with emerging evidence of poor adherence.⁴¹ It is inevitable that patients in resource-poor settings

will experience side effects and conditions associated with long-term ART (e.g., lipodystrophy and diabetes), as has been documented in western countries.^{5,42-44} Second-generation adherence studies in developing countries will need to examine these factors, as well as viral resistance, and their intersection with quality of life and stigma. For example, lipodystrophy might serve as an identifier for HIV-positive individuals in the community, resulting in stigma and discrimination.

Although the Horizons studies provide no evidence of an increase in sexual-risk behavior among PLHA on treatment, unprotected sex in regular-partner relationships is prevalent, and the risk of HIV transmission is still a concern. Treatment programs need to emphasize risk reduction, condom use, and partner testing. Council researchers are developing a prevention-with-positives intervention to integrate prevention and treatment services in Kenya to address these issues.

Despite intense recent attention to pediatric treatment, access to treatment for children infected with HIV is still lagging behind that for adults.^{1,45} Priority areas for research include evaluation of interventions to increase diagnosis of HIV among children and to facilitate early treatment for children infected with HIV. Horizons is supporting community interventions to increase uptake of pediatric HIV testing and treatment services in Kenya, and the Population Council is working in South Africa on a family-centered approach to expand HIV testing of children at risk and provide pediatric care and treatment. Adherence interventions for pediatric populations need to be developed and evaluated in the African context as more children infected with HIV receive treatment. Age also is an important consideration, as adherence issues will differ among young children, adolescents, and emancipated minors. While work on this topic has occurred in the West, it may not be immediately translatable to sub-Saharan Africa.

Despite global efforts to provide access to HIV treatment in low- and middle-income countries, only 28% of the estimated 7.1 million adults in need of treatment were receiving ART in 2006;¹ this figure is even lower among infected children. With expanding ART provision in developing countries, research on health service delivery and social behaviors is required. Horizons has made a major contribution to the body of scientific evidence on access-to-treatment issues, answered key research questions, and provided directions for next steps.

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