Elizabeth Glaser Pediatric AIDS Foundation

December 2012
Vol. 3 | Issue 1

Haba Na Haba
Technical Bulletin

Spotlight On…

The Role of Research in Achieving Virtual Elimination of HIV Infection in Children: An EGPAF Perspective

Photo credit: James Pursey

When the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) was founded in 1988, the majority of HIV/AIDS research was focused on adult populations. A range of questions regarding the unique pathways of mother-to-child transmission (MTCT) of HIV and the distinct medical challenges facing infants and children living with HIV had yet to be answered. In the years that followed,

continued

Welcome!

Welcome to the Elizabeth Glaser Pediatric AIDS Foundation's technical bulletin, *Haba Na Haba!*

This publication provides a dynamic forum for the routine sharing of technical information and promising practices with our fellow colleagues and extended family of partners and like-minded organizations around the world. Each issue of ***Haba Na Haba*** highlights a topic of particular importance to the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF). The highlighted topic for this issue is the **Role of Research in Achieving Virtual Elimination of HIV Infection in Children**.

What Does *Haba Na Haba* Mean?

The name of the bulletin, *Haba Na Haba* ("little by little"), is borrowed from the Swahili proverb ***haba na haba, hujaza kibaba*** ("little by little fills the pot") and was chosen to reflect the often incremental nature of progress in our field. As the experiences described on the following pages demonstrate, the smaller efforts of every one of us are the essential "ingredients" for mounting a strong and united global response to HIV and AIDS.

Feedback is welcomed from all readers, and contributions are accepted from all EGPAF staff. Please send your questions, comments, or content submissions to techbulletin@pedaids.org.

Spotlight On… *(continued)*

Elizabeth Glaser's tenacity helped ensure that children were not forgotten as scientists began to unravel the mysteries of this new pandemic.

More than two decades later, scientific and medical discoveries regarding prevention of mother-to-child transmission (PMTCT) of HIV and HIV care and treatment have contributed to extraordinary advances in the prevention and treatment of HIV infection in children. Pediatric HIV research has taught us how to prevent HIV infection in infants, how to diagnose infant HIV infection early, and how use of early antiretroviral (ARV) therapy and prophylaxis against opportunistic infections can dramatically improve the survival of children living with HIV. Yet the pace of progress in reaching all infants, children, and adolescents with critical HIV prevention and treatment interventions is still considerably slower than progress in reaching adults. Elizabeth's fight must continue until we reach the goal that Ebube Sylvia Taylor, an 11-year-old HIV-exposed but uninfected Nigerian girl, articulated in 2010 to world leaders gathered in New York: "No child should be born with HIV; no child should be an orphan because of HIV; no child should die due to lack of access to treatment."[1]

Scientifically we know that PMTCT interventions, when delivered effectively, can prevent transmission of HIV from mothers to their children. The last decade has seen a rapid scale-up of these interventions across the developing world, leading to a decrease in the number of new pediatric HIV infections annually, from a peak of 570,000 in 2003 to 330,000 in 2011.[2,3] Despite these reductions, there is only partial cause for celebration. Each new infection represents a missed opportunity for prevention; each child living with HIV will require lifelong antiretroviral therapy (ART) and will face a series of daunting challenges before she or he reaches adolescence and, eventually, adulthood.

Continued pediatric HIV-related research remains essential both to prevent MTCT and to ensure the healthy survival of infants with HIV. Research has a particularly critical role to play in achieving the targets outlined in the 2011 UNAIDS *Global Plan Towards the Elimination of New HIV Infections Among Children by 2015 and Keeping Their Mothers Alive*.[1] The solutions to the often complex challenges associated with pediatric HIV infection are in many cases inherently different from those

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

1981

- The first five cases of a "rare pneumonia" are identified in men who have sex with men in Los Angeles, followed by diagnoses of a "rare cancer" seen in Los Angeles, New York, and San Francisco; these are the first cases of what would be named (in 1982) acquired immunodeficiency syndrome (AIDS).
- Elizabeth Glaser receives a transfusion with seven pints of HIV-infected blood following the birth of her daughter, Ariel. Elizabeth unknowingly transmits the virus to her daughter through breastfeeding.

addressing HIV infection in adults. It is therefore vitally important that resources be devoted to research that specifically addresses prevention and treatment of pediatric HIV. Pediatric HIV research remains chronically underfunded, with issues affecting pediatric populations often being overlooked by the scientific community. To address this gap, a vigorous and continuous cycle of advocacy is required, first to secure funding for research addressing HIV in pediatric populations and later to ensure that the evidence generated from these studies is used to drive national pediatric HIV policies and program implementation strategies.

EGPAF as Research Advocate

Since it was founded nearly 25 years ago, EGPAF has been a tireless advocate for increased pediatric HIV research funding and policies that support research benefiting children living with and affected by HIV. Recently, EGPAF successfully advocated for operations and implementation research funding to be included in the second phase of the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) and continues to voice its support for the inclusion of children in HIV vaccine trials. EGPAF also supported the inclusion of a pediatric leadership group during the restructuring of the National Institutes of Health (NIH) National Institute of Allergy and Infectious Diseases (NIAID) HIV clinical trials network[4] and has engaged in advocacy with members of the U.S. Congress to promote the needs of children in the drug development progress through reauthorization of the Best Pharmaceuticals for Children Act and the Pediatric Research Equity Act. Additionally, EGPAF Ambassadors—young people living with or affected by HIV—have served on several panels and research community advisory boards to share their experiences and support the need for pediatric-focused research.

Defining the Pediatric HIV Research Agenda

Research of all varieties—from basic and clinical to operations research—is essential for strengthening existing interventions, closing knowledge gaps, and identifying new and promising courses of action. Despite significant advances in our understanding of the virology, immunology, and pathogenesis of HIV infection and access to more sophisticated research tools, there are still significant gaps in our understanding of MTCT and HIV infection in children. For example, in the absence of antiretroviral drugs (ARVs), why do 60% of infants born to HIV-positive mothers remain HIV-free despite continuous exposure to the virus during breastfeeding?[5] Answering questions like this one could unlock new means of preventing vertical HIV transmission, including more effective drugs and, ideally, a vaccine that could be used in children as well as adults. Lessons learned in the laboratory can lead to the development of new interventions or diagnostic tests that must then be evaluated in real-world clinical settings. Once new interventions and tools are discovered, figuring out how to best deliver them to the populations that stand to benefit is the key to achieving desired outcomes. Research plays an essential role throughout the discovery and implementation of new approaches.

There have been several international scientific consultations in recent years aimed at identifying priority research areas benefiting women and children affected by HIV, efforts in which EGPAF has played a significant role. In 2009, the United Nations Children's Fund (UNICEF), the World Health Organization (WHO), and the Joint United Nations Programme on HIV/AIDS (UNAIDS), in collaboration with George Washington University and EGPAF, held an expert technical consultation on operations research. The goal of this consultation was to identify the highest-priority operations research questions that would support the rapid national scale-up of PMTCT and pediatric HIV care, support, and treatment programs. Participants identified 20 priority research questions in the areas of PMTCT; pediatric care, support, and treatment; integration of PMTCT and maternal, neonatal, and child health services; and health systems strengthening.[6] Following this consultation, EGPAF participated in similar national-level consultations with ministries of health in India and Mozambique.

In 2010, the International AIDS Society (IAS) conducted a landscape analysis and consultation that resulted in the release of a consensus statement entitled, "Asking the Right Questions: Advancing an HIV Research Agenda for Women and Children."[7] This statement was recently updated with a list of priority clinical research questions for PMTCT and pediatric treatment, and IAS went on to secure funding for research in these priority areas from ViiV Healthcare through the CIPHER (Collaborative Initiative for Pediatric HIV Education and Research) program, efforts in which EGPAF was closely involved.[8] EGPAF also helps shape the pediatric HIV research agenda through its participation in the PEPFAR Scientific Advisory Board, the Inter-Agency Task Team on Children and

continued

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

1984

- Human immunodeficiency virus (HIV) is identified as the cause of AIDS.
- U.S. Health and Human Services Secretary Margaret Heckler declares that a vaccine against HIV will be available within two years.
- Elizabeth Glaser gives birth to her son, Jake, and unknowingly transmits HIV to him in utero.

HIV and AIDS (IATT), and national PMTCT and ART technical working groups in EGPAF-supported countries.

Priorities for Pediatric HIV Research

Presented here are some key considerations for those engaging in pediatric HIV research within the various research disciplines.

Basic Science

Studying HIV-positive mother / HIV-exposed infant pairs in which HIV transmission does and does not occur provides a unique opportunity to explore basic immunology, virology, and neonatal immunity questions that can advance our scientific knowledge about HIV transmission. Basic science research conducted in pediatric populations in parallel with studies in adults can accelerate the acquisition of critical knowledge toward the eventual development of effective HIV vaccines. ARVs were shown to provide significant protection against MTCT of HIV long before studies of pre- and post-exposure ARV prophylaxis with comparable regimens showed protection against heterosexual HIV transmission in adults. Similarly, an HIV vaccine may be found to be effective in protecting breastfeeding HIV-exposed infants from HIV infection before its efficacy is demonstrated in adults. In addition, a vaccine could potentially show short-term efficacy for prevention of HIV infection in infants even if it is not effective in adults with sexual or intravenous HIV exposure.

There has also been a renewed energy around and focus on basic scientific research into the development of innovative strategies to "cure" HIV infection. The NIH, the Foundation for AIDS Research (amfAR), and others have committed significant resources to fund investigators and laboratories engaging in these types of studies; none, however, include infants in their study populations. With the majority of infants infected in the perinatal or postnatal period, interventions delivered during the initial period of acute infection could affect subsequent HIV disease progression and may represent a critical window for the administration of a curative treatment, once available.

EGPAF has been a strong voice in the HIV vaccine development community to ensure that infants are included in the HIV vaccine research agenda. For example, EGPAF, in collaboration with the HIV Vaccine Enterprise, IMPAACT Network, the Vaccine Research Center, and other organizations, will convene a consultation in January 2013 in Kampala, Uganda, to discuss and develop recommendations for the design and implementation of current and future preventive HIV vaccine trials in infants born to HIV-positive mothers.

Going forward, EGPAF will continue its work to advocate for the inclusion of pediatric populations in all manner of innovative basic science research. With resources from the Susie Zeegen Fund for Research, EGPAF will fund a two-year postdoctoral research award (one in 2012, with plans for additional awards thereafter) for an early-career scientist to support basic science research in novel approaches to the understanding of HIV transmission and immune responses to infection. It is hoped that research supported by this award will contribute to the development of effective HIV preventive or therapeutic vaccines or novel approaches toward a "cure" in HIV-infected infants.

Clinical Research

A large part of the clinical research agenda focuses on the development and evaluation of new ARVs or ARV regimen combinations for use in pregnant women as well as in infants and children. Although the number of available ARVs has increased considerably since zidovudine (AZT) was first used to treat HIV infection 25 years ago, only a small proportion of drugs currently in use have been adequately tested in pregnant and postpartum breastfeeding women and in infants and children. Continued development and testing of new drugs and better combinations of drugs to maximize their efficacy, tolerability, and long-term safety—particularly since infants are exposed to maternal drugs in utero—remain priorities for clinical research.

Identification of simple, inexpensive point-of-care products for HIV testing, CD4 counts, viral load measurement, and diagnosis of other HIV-associated conditions (e.g., syphilis, TB, cervical cancer) is another area of active clinical research. The need for point-of-care diagnostics continues to grow as HIV-related services are decentralized from hospitals to lower-level health facilities. EGPAF has stayed abreast of new developments in this area by maintaining close contact with researchers and product manufacturers in order to identify opportunities for field testing new diagnostic technologies before they come to market. This is also an area of active engagement between EGPAF and ministry of health–operated

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

1985

- Ariel Glaser tests positive for HIV infection; Jake and Elizabeth also test positive.
- HIV antibody test for children is developed and approved.

laboratories in several EGPAF-supported countries, with the goal of ensuring that testing of products that particularly benefit women and children is deemed a national priority.

There are several priority clinical research areas that are important to eliminating HIV infection in children and promoting a long and healthy life for HIV-positive children (see Box 1). Although the involvement of many organizations, scientists, clinicians, and donors will be vital to address all these needs, EGPAF is uniquely positioned to make a significant contribution to the clinical pediatric HIV research field through its close collaboration with a range of stakeholders in the countries it supports (see pages 28–31 for a list of current EGPAF-supported research activities).

Implementation Research

The translation of interventions identified as being effective during clinical trials into routine health services in the field is fraught with considerable challenges. Governments, donors, and implementing partners are also more likely to accept and scale up interventions when their impact can be demonstrated. Implementation research is therefore crucial to the development of evidence-based, effective, and scalable interventions that address current barriers to PMTCT and HIV care and treatment service delivery.

Collection of more comprehensive, longitudinal patient-level data is another strategy needed in order for clinicians to effectively manage HIV as a chronic disease and to strengthen pediatric HIV research. Since most settings do not collect these data as part of routine program monitoring and evaluation activities, additional efforts may be needed to generate a sufficiently rigorous evidence base in which programs and policies can be grounded. In addition, data that are routinely generated by programs are often limited to activity descriptions and aggregate quantitative data that lack sufficient depth or breadth to allow a determination of the effectiveness of specific interventions. Prioritizing the collection of high-quality data using sound research methodologies within PMTCT and ART programs will significantly enhance the ability to answer key programmatic questions using the best possible evidence.

Many WHO-recommended PMTCT interventions are based on the extrapolation of data from clinical trials, the results of which may not reflect what is achievable in real-world settings. Use of the most effective drug regimens for PMTCT will have reduced overall impact on national MTCT rates unless challenges relating to health service delivery, access, and uptake can be addressed through the application of evidence-based solutions.[9] These health systems challenges are well documented (e.g., weak commodity systems, limited laboratory infrastructure, poor integration of services, limited human resources, lack of community- or patient-centeredness), but scientific evidence regarding the effectiveness of interventions to address them remains scarce.[3] Rigorous evaluation of PMTCT interventions, such as Option B-Plus, as they are being rolled out will be needed to determine their feasibility, acceptability, effectiveness, and cost so that policymakers, donors, and program managers are armed with the information they need to maximize program outcomes.

In addition to conditions within health systems, a variety of social, behavioral, and structural barriers play a significant role in influencing the demand for and uptake of HIV-related services among individuals and communities.[10] These challenges include women presenting at antenatal care late in gestation; the cost of transport for women in rural areas; the perceived poor quality of services; lack of support from family members; and HIV-related stigma in health care settings and the community.[10–13] To reach the goal of virtual elimination of HIV infection in children, population coverage and uptake of PMTCT services needs to be greater than 90%.[1] Identifying interventions that can effectively increase awareness of and demand for PMTCT and HIV services through implementation research will be another critical step toward eliminating new HIV infections in children.

Encouragingly, there has been growing global awareness in recent years of the need for implementation research aimed at strengthening PMTCT service delivery. PEPFAR, the Global Fund, WHO, the Canadian International Development Agency (CIDA), and other donors have begun focusing on the role of implementation science research in determining how global HIV resources can be used most efficiently and effectively. PEPFAR has made a significant commitment to funding implementation research projects through the NIH, the Centers for Disease Control and Prevention (CDC), and the U.S. Agency for International Development (USAID) and now requires rigorous program evaluations for PEPFAR-funded programs. In the last year, 23 out of 74 PEPFAR implementation science awards (31%) were focused on PMTCT.[14] In addition, the National Institute of Child Health and

continued

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

1987

▶ Zidovudine (AZT) becomes the first drug approved to treat HIV infection among adults.

Box 1. Pediatric HIV Research Priorities: Clinical Research

- Determining the cost-effectiveness of the new regimens and their impact on infant HIV-free survival
- Developing and testing inexpensive point-of-care laboratory diagnostic and monitoring tests (e.g., CD4, HIV viral load, early infant diagnosis) that can be performed in lower-level health facilities
- Evaluating the effectiveness of the revised WHO infant feeding guidelines and their effect on infant growth, morbidity, and mortality
- Determining resistance patterns in HIV-positive women on lifelong ART who initiate during pregnancy and in HIV-infected infants exposed to multiple ARVs in utero and through breastfeeding
- Developing pharmacovigilance systems to rapidly detect any increase in toxicity in HIV-positive pregnant women on ART or their HIV-exposed infants and children after in utero exposure
- Longitudinal follow-up (for longer than 12–18 months) of HIV-exposed children with in utero exposure to newer ARVs to assess long-term safety (e.g., growth in tenofovir-exposed infants and congenital / central nervous system anomalies with use of efavirenz)
- Determining ART adherence rates and identifying simple methods for monitoring adherence among pregnant and postpartum HIV-positive women in clinical care settings
- Testing of candidate HIV-preventive vaccines in infants and adolescents

Human Development (NICHD) recently announced the funding of nine PMTCT implementation science awards that link directly to programs, researchers, and institutions in seven countries receiving PEPFAR support.[15] The Global Fund also encourages applicants to include requests for program monitoring, evaluation, and operations research funding, yet these resources are often underutilized, possibly due to lack of awareness or the absence of research experts within proposal development teams.

Finally, although the pool of resources available for operations research continues to expand, it is still insufficient given the breadth of activities that will need to be carried out in order to achieve virtual elimination of HIV infection in children (see Box 2 for a list of priority areas for implementation research). EGPAF remains an outspoken advocate for the mobilization of additional public and private resources to fund implementation research that will play an essential role in achieving Global Plan targets.

Building Research Capacity Where It Is Most Needed

Answering the key research questions that will get us to the elimination of HIV infection in children and keeping HIV-affected families alive and well will only be achieved through studies conducted in the countries most affected by HIV. Expanding the research capacity in these countries, particularly those in Africa, must go hand in hand with funding of specific research projects. Considerable progress has been made on this front through investments by the NIH HIV Clinical Trials Networks, the NIH Fogarty International Center, the European and Developing Countries Clinical Trials Partnership Program, and other programs focused on increasing local capacity to conduct HIV clinical and vaccine trials across Africa, Asia, and other high-HIV-burden areas. Initiatives supporting local HIV-related research as well as training of local scientists have succeeded in producing world-renowned experts. However, these efforts have mainly focused on academic institutions and specialized centers of research excellence conducting clinical research. Training opportunities in other areas, such as implementation science, program evaluation, social and behavioral science, and laboratory science have lagged behind. Arming ministry of health personnel, program managers and implementers, and clinicians with the research expertise and tools needed to conduct more rigorous studies and program evaluations using sound research methodologies is critical for generating the evidence needed to reach elimination of HIV infection in children.

Conclusion

Although progress has been made in the field of pediatric HIV globally, significant gaps remain that research of all types can play a key role in addressing. We are entering an exciting phase of activities as the global focus on the elimination of new HIV infections in children accelerates. Yet the ambitious targets being set will be reached only through a combination of HIV prevention and treatment strategies supported by a comprehensive and rigorous evidence base. Program implementers and policymakers alike will benefit from being able to make informed choices about the most effective interventions to help them meet their national goals faster and more efficiently. To this end, EGPAF and its numerous partners will continue to engage in advocacy and research on a number of fronts to ensure that pediatric HIV remains at the top of the global research agenda until we succeed in realizing Elizabeth's dream of an HIV-free generation.

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

1988

- Ariel Glaser dies from AIDS-related causes.
- AZT has yet to be approved for pediatric use.
- The Pediatric AIDS Foundation (PAF) is launched by Elizabeth Glaser, Susie Zeegen, and Susan DeLaurentis to raise money for pediatric AIDS research.
- Among PAF's first activities is the hosting of "think tanks" for invited experts to discuss critical pediatric HIV research questions.

Box 2. Pediatric HIV Research Priorities: Operations Research

- Assessing models for creating functional linkages between PMTCT clinics not offering ART services and ART sites so that HIV-positive pregnant women receive the drugs they need
- Identifying factors that facilitate or inhibit utilization of PMTCT services by pregnant and postpartum HIV-positive women and methods for improving service utilization
- Assessing to what extent HIV-positive pregnant women with no signs of illness accept and adhere to ART drugs immediately upon diagnosis, throughout pregnancy, and for life (i.e., Option B-Plus)
- Looking at ways in which current staffing levels and configurations in maternal and child health (MCH) centers can be organized to manage the additional workload brought on by ART/MCH service integration, particularly if all HIV-positive pregnant women are initiated on lifelong ART
- Identifying innovative strategies at the health system, community, and individual levels that can increase PMTCT service retention and minimize loss to follow-up, particularly during pregnancy and the postpartum period
- Determining how best to track women and their infants across services delivery sites (e.g., antenatal care, MCH clinics, HIV clinics) and locations over time to ensure that they receive an uninterrupted continuum of care
- Assessing whether the introduction of mobile clinics in remote and/or poorly served areas is a feasible, efficacious, and cost-effective mechanism for the delivery of HIV care and treatment services to HIV-positive pregnant women
- Identifying new technologies, such as mobile health (mHealth) applications, that can improve the effectiveness of PMTCT and HIV care and treatment programs
- Identifying methods to determine overall PMTCT program effectiveness as measured by MTCT and/or HIV-free survival of children at 18–24 months of age that are feasible and can be implemented in settings with limited infrastructure
- Determining the most effective methods of engaging the community and mobilizing community-led responses to the challenge of eliminating HIV infection in children
- Looking at effective methods of facilitating HIV status disclosure to family members to improve treatment adherence among pregnant women during pregnancy and postpartum

References

1 Joint United Nations Programme on HIV/AIDS (UNAIDS). Countdown to zero: global plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive. http://www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2011/20110609_JC2137_Global-Plan-elimination-HIv-Children_en.pdf. Published 2011.

2 UNAIDS. Together we will end AIDS. http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2012/20120718_togetherwewillendaids_en.pdf. Published 2012.

3 UNAIDS, World Health Organization (WHO), and United Nations Children's Fund (UNICEF). Progress report 2011. Global HIV/AIDS response: epidemic update and health sector progress towards universal access. http://whqlibdoc.who.int/publications/2011/9789241502986_eng.pdf. Published 2011.

4 Dieffenbach C, Handelsman E, Mofenson L. Advancing pediatric, maternal and child health. http://blog.aids.gov/2010/10/advancing-pediatric-maternal-and-child-health.html. Published October 19, 2010. Accessed November 22, 2012.

5 De Cock KM, Fowler MG, Mercier E, et al. Prevention of mother-to-child HIV transmission in resource-poor countries: translating research into policy and practice. *JAMA*. 2000;283(9):1175–1182.

6 UNICEF, WHO, and UNAIDS. Expert consultation on operational research on PMTCT and pediatric HIV CST. http://www.unicef.org/aids/files/OR_Consultation_Report_FINAL2.doc. Published 2009.

7 International AIDS Society. Consensus statement: asking the right questions: advancing an HIV research agenda for women and children. http://www.iasociety.org/Web/WebContent/File/Consensus_Statement_Asking_the_Right_Question_March_2010.pdf. Published 2010.

8 International AIDS Society. Collaborative Initiative for Paediatric HIV Education and Research. http://www.iasociety.org/CIPHER.aspx. Accessed November 22, 2012.

9 Barker PM, Mphatswe W, Rollins N. Antiretroviral drugs in the cupboard are not enough: the impact of health systems' performance on mother-to-child transmission of HIV. *J Acquir Immune Defic Syndr.* 2011;56(2):e45–48.

10 Auerbach JD, Parkhurst JO, Cáceres CF. Addressing social drivers of HIV/AIDS for the long-term response: conceptual and methodological considerations. *Glob Public Health.* 2011;6(Suppl 3):S293–309.

11 Bwirire LD, Fitzgerald M, Zachariah R, et al. Reasons for loss to follow-up among mothers registered in a prevention-of-mother-to child transmission program in rural Malawi. Médecins Sans Frontières, Thyolo District, Malawi. *Trans R Soc Trop Med Hyg.* 2008;102(12):1195–1200.

12 Prevention of mother-to-child transmission of HIV: expert panel report and recommendations to the U.S. Congress and U.S. Global AIDS Coordinator. http://www.pepfar.gov/documents/organization/135465.pdf. Published January 2010. Accessed January 9, 2012.

13 Stringer E, Ekouevi DK, Coetzee D, et al., for the PEARL study team. Coverage of nevirapine-based services to prevent mother-to-child HIV transmission in 4 African countries. *JAMA*. 2010;304(3):293–302.

14 Presentations at the PEPFAR Scientific Advisory Board meeting; October 2–3, 2012; Washington, DC. http://www.pepfar.gov/sab.

15 U.S. Department of State. U.S. Government announces implementation science awards on prevention of mother-to-child transmission of HIV [Media Note]. http://www.state.gov/r/pa/prs/ps/2012/11/201144.htm. Published November 28, 2012. Accessed December 7, 2012.

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

1989

- Pediatric AIDS Foundation (PAF) makes its first research grant, for US$60,000, to Dr. Richard Stiehm of UCLA to study perinatal T-cell responses against HIV infection.
- PAF grants its first Scholar Awards to three scientists, including Dr. Richard Koup of the University of Massachusetts to study HIV-specific immunity and vertical HIV transmission (see profile on page 12).

EGPAF and Research: A Historical Perspective

Jeffrey Safrit, PhD, Director of Clinical and Basic Research (jeff@pedaids.org)

The Elizabeth Glaser Pediatric AIDS Foundation's (EGPAF's) research program has had a rich and varied 25-year history. Starting with our first think tanks organized by EGPAF's three co-founders, Susie, Susan, and Elizabeth, in the late 1980s, we went on to award numerous research grants resulting in significant contributions to the field of HIV/AIDS science. More recently, EGPAF has been supporting operations research activities aimed at strengthening HIV/AIDS program implementation in the Africa region.

In its early years, EGPAF began attracting the brightest scientists to the field of pediatric HIV research by offering small basic research grants for studies that were deemed "too risky" or "too preliminary" to qualify for funding by the U.S. government through the National Institutes of Health. The $10–12 million EGPAF raised from private donations in the years before it received U.S. government funding mostly went toward directly funding basic research.

In addition to its basic research grants, EGPAF has instituted programs over the years to address gaps in HIV/AIDS research, with a particular focus on maternal and child health in an HIV context. Our student intern program funded short-term projects (summer or semester laboratory projects) for college and high school students, while the Scholar Awards program identified young scientists and clinicians just completing their medical or doctoral degrees and provided funding for basic research projects. Some of these early scholars went on to receive further funding from EGPAF and remain active in the field of AIDS research; many have become leaders in their respective fields (see awardee profiles on page 12). Over the last few years, we have been fortunate to be able to establish a pediatric HIV vaccine research program as well as an operations research program that has allowed us to fund external and now internally-led research toward the elimination of pediatric HIV.

It would be impossible to list all the many accomplishments attributed to the 1,100 research awards (representing $78 million in combined funding) EGPAF has given over the years, but I'll provide just a few examples. As the first EGPAF multicenter research study, the Ariel Project contributed to the understanding of the mechanisms of mother-to-child HIV transmission. EGPAF-funded scientists contributed to the evaluation of the effectiveness of early antiretroviral therapy for children and helped decipher the earliest pediatric immune responses to HIV. Several of our Elizabeth Glaser Science Award (EGSA) recipients contributed to the discovery of CCR5 as the second cellular receptor for HIV, a major breakthrough in 1995–96 that has led to the development of new drugs and immune-based therapies for HIV and, most recently, the possibility of a cure. EGPAF research support helped incorporate early gene therapy research into the field. In 2001, EGPAF-funded scientists discovered that viruses capable of avoiding the antiviral immune response can be transmitted from mother to child, uncovering potential reasons for the faster disease progression seen in HIV-infected children compared with adults.

One EGSA recipient developed a model for breast milk transmission of viruses in neonatal macaque monkeys that is being used to evaluate interventions to prevent transmission of HIV during breastfeeding. Other recipients have been examining the role of maternal antibodies against HIV and their protective—or even enhancing—role in breast milk transmission. In Zambia, clinicians supported by EGPAF demonstrated that nevirapine could be safely administered to pregnant women who did not know their HIV status to confer greater protection to their unborn infants. They also were among the first to help establish the real-world effectiveness of prevention of mother-to-child transmission (PMTCT) programs, identifying key actions for improving program outcomes.

In the last two years, EGPAF began to evaluate ways in which mobile technology can improve PMTCT programs, and we are also working toward a better understanding of the roles of nutrition and family planning in HIV care and treatment programs. We have come a long way in 25 years, but we still have much work to do.

The EGPAF research team invites you to enjoy this issue of *Haba Na Haba*, which is aimed at enhancing discussion and generating new ideas for research toward our ultimate goal of virtual elimination of HIV infection in children.

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

1990

▶ AZT is approved for pediatric use by the U.S. Food and Drug Administration.

Evaluating PMTCT Program Effectiveness

Seble Kassaye (skassaye@pedaids.org)

Successes in PMTCT

Mother-to-child transmission (MTCT) of HIV has declined to less than 2% in high-income countries due to implementation of prevention of mother-to-child transmission (PMTCT) services, including combination antiretroviral therapy (ART) administered to a mother during pregnancy and delivery, elective cesarean section among women with persistent elevation in HIV RNA levels at delivery, infant postexposure antiretroviral (ARV) prophylaxis, and infant replacement feeding to prevent breastfeeding-associated transmission of HIV. A national MTCT rate of under 2% is, however, not yet feasible in settings where ARVs and safe alternatives to infant feeding practices are not universally available.

Measuring Program Effectiveness and Impact

The World Health Organization (WHO) PMTCT guidelines were updated in 2010 based on evidence from clinical studies, which demonstrated MTCT rates ranging from 1.7% to 6% in clinical efficacy studies of maternal ART or ARV prophylaxis during pregnancy, and maternal ART or infant ARV prophylaxis during breastfeeding.[1–3] Although most countries quickly adopted the 2010 PMTCT guidelines following their release, measurement of PMTCT effectiveness and impact has lagged, primarily because such an endeavor requires systematic collection of patient-level data from a large segment of the affected population to provide a representative picture of key PMTCT outcomes (including MTCT rates, maternal survival, and infant HIV-free survival).

In the United States, data are captured through a national surveillance system in which name-based reports of new HIV diagnoses are sent to the U.S. Centers for Disease Control and Prevention (CDC), thereby providing an estimate of the number of new pediatric infections annually. While such a robust national surveillance program may not be feasible in resource-limited settings, program evaluations using patient-level data, with linkage of data from mother-infant pairs, can demonstrate PMTCT program effectiveness. In Botswana, where conditions allow for safe infant replacement feeding, a relatively small observational study conducted

Photo credit: Bill McCarthy

in two reference hospitals from 2009 to 2010 demonstrated that use of PMTCT interventions during pregnancy and delivery combined with replacement feeding decreased MTCT to approximately 2.5% among study participants.[2] In South Africa, HIV transmission among six-week-old infants attending immunization clinics in 2010 was estimated at 3.5% through a survey conducted in facilities nationwide.[3] Rwanda's community-based evaluation of the effectiveness of the national PMTCT program among 9- to 24-month-old infants—conducted through household surveys in 2009—demonstrated a 4% MTCT rate, with HIV-free child survival of 91.9%.[4]

These evaluations exemplify some of the approaches under consideration by the international PMTCT Impact and Effectiveness Network, a network led by WHO and CDC to provide guidance as nations plan to assess the effectiveness of their national PMTCT programs in settings where national surveillance programs are not established.[5] Currently, most

continued

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

1992

- Pediatric AIDS Foundation launches its first multicenter research study, the Ariel Project, to investigate the mechanisms of mother-to-child transmission (MTCT) of HIV in the United States.
- Elizabeth speaks at the U.S. Democratic National Convention, bringing national attention to HIV/AIDS and pediatric research needs.

Photo credit: James Pursey

national programs in low- and middle-income countries provide population-level estimates of MTCT, using mathematical models with national program coverage data and transmission estimates from clinical efficacy studies, due to their relatively low cost, among other factors.[6] Although this method is useful for projections and target setting, its accuracy may be challenged by the variable effectiveness of PMTCT interventions when delivered in real-world settings.

One simple method sometimes used to assess a country's MTCT rates is to use national early infant diagnosis (EID) results. As EID testing is often highly centralized, such an assessment is easily achieved. However, these data are not generalizable unless infant HIV testing uptake is very high. Considering that the average EID uptake in low- and middle-income countries is 28%, most settings likely could not use these data to accurately estimate national MTCT rates.[6] Testing uptake declines with increasing age of the infant, further limiting the use of this modality for measuring HIV transmission rates after cessation of breastfeeding when the infant is no longer at risk of breastfeeding-associated HIV acquisition. Another option is to measure HIV prevalence among six-week-old infants seeking immunization services, as uptake of these services is high in most settings. Convenience sampling of infants attending a six-week immunization visit, with testing for HIV exposure by HIV antibody testing and direct viral detection using HIV DNA polymerase chain reaction (PCR), would yield a generalizable estimate of the proportion of infants exposed to and at risk of acquiring HIV, and the proportion who have become infected during pregnancy, delivery, and early breastfeeding. Although conducting such a survey is feasible, as demonstrated by the national effectiveness evaluation in South Africa, the data generated are limited and do not capture MTCT during the lengthy breastfeeding period characteristic of most settings in sub-Saharan Africa.

Recruitment and prospective follow-up of a representative cohort of six-week-old HIV-exposed infants, with HIV testing after termination of breastfeeding, would yield the most accurate estimates of MTCT during pregnancy, delivery, and breastfeeding, in addition to HIV-free survival. Yet this approach is costly, takes longer to complete, and requires intensive resources for longitudinal follow-up of infants (Malawi, which is implementing Option B-Plus of the 2010 WHO PMTCT guidelines, is currently planning such an approach).[7] MTCT can also be evaluated using community-based surveys and laboratory testing. This cross-sectional approach can target infants in older age groups not as well represented in facility-based surveys, as rates of health facility attendance among infants older than nine months are typically lower than for six-month-olds. Challenges to this approach include higher costs associated with hiring survey workers, transportation challenges in reaching a representative

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

1994

- Elizabeth Glaser dies of AIDS-related causes.
- AZT is shown to significantly reduce MTCT in the landmark AIDS Clinical Trials Group (ACTG) 076 study.
- Pediatric AIDS Foundation launches a second multicenter research project, the Long-Term Survivor Study, to examine reasons that some individuals (including children) can remain disease free despite no antiretroviral (ARV) therapy.

population in urban and rural settings, and collecting blood samples for testing in the community setting, with subsequent transportation of samples to centralized laboratories for testing. Another limitation includes survival bias, as HIV-exposed or HIV-infected infants who are no longer alive will not be counted.

Elizabeth Glaser Pediatric AIDS Foundation Activities

The Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) is participating in PMTCT effectiveness evaluations to support the implementation of effective programs helping to achieve the virtual elimination of new pediatric HIV infections in the countries it supports. For example, EGPAF is designing an evaluation to assess PMTCT program effectiveness in Lesotho in collaboration with the Ministry of Health. The evaluation team will conduct a community-based household survey to determine HIV exposure and infection among 18- to 24-month-old infants in three districts to provide a relatively quick assessment of the impact of the PMTCT program. This activity should yield results within six to eight months.

Given the limitations of this approach, a prospective cohort of four- to eight-week-old HIV-exposed infants will also be established to more accurately determine MTCT rates, as well as HIV-free survival. This more extensive evaluation will take approximately three to four years to complete. In addition to the evaluation in Lesotho, the HIV-free survival rate at 18 months of age in a prospectively followed cohort of children born to HIV-positive pregnant women receiving Option B-Plus will be measured in a three-year study in Rwanda. Plans are also under way for an evaluation of the EGPAF-supported national PMTCT program in Zimbabwe. An external evaluation team, led by the University of California, Berkeley, recently completed a baseline evaluation of MTCT and HIV-free survival rates among 9- to 18-month-old infants using a community-based national survey. The survey will be repeated in two to three years to determine the impact of efforts to scale up the revised 2010 WHO PMTCT guidelines on these outcomes.

Conclusion

PMTCT program effectiveness and impact evaluations are critical to determining countries' progress toward virtual elimination of new pediatric HIV infections. The successes documented in high-resource settings clearly demonstrate that virtual elimination of new pediatric HIV infections is feasible. As guidelines evolve with the goal of further reducing pediatric infections, it is critical that we continue to accurately assess the impact and effectiveness of our programs in order to permit course corrections and realignment of national and international policies toward the elimination of new pediatric HIV infections.

References

1 Dryden-Peterson S, Jayeoba O, Hughes MD, et al. Highly active antiretroviral therapy versus zidovudine for prevention of mother-to-child transmission in a programmatic setting, Botswana. *J Acquir Immune Defic Syndr.* 2011;58(3):353–357.

2 Goga AE, Dinh TH, Jackson DJ, for the SAPMTCTE study group. Evaluation of the effectiveness of the national prevention of mother-to-child transmission (PMTCT) programme measured at six weeks postpartum in South Africa, 2010. South African Medical Research Council, National Department of Health of South Africa, and PEPFAR/U.S. Centers for Disease Control and Prevention. http://www.doh.gov.za/docs/reports/2012/pmtcteffectiveness.pdf. Accessed September 20, 2012.

3 Ruton H, Mugwaneza P, Shema N, et al. HIV-free survival among nine- to 24-month-old children born to HIV-positive mothers in the Rwandan national PMTCT programme: a community-based household survey. *J Int AIDS Soc.* 2012;15(1):4.

4 Higashi C. PMTCT impact measurement and EMTCT validation: update on global guidance. Paper presented at: 19th International AIDS Conference; 2012; Washington, DC.

5 M&E Working Group of the Interagency Task Team on Prevention of HIV Infection in Pregnant Women, Mothers, and Their Children and the UNAIDS Reference Group on Estimates, Modelling and Projections. Technical report and recommendations. Presented at: Consultative Meeting on Updating Estimates of Mother-to-Child Transmission Rates of HIV; September 1–2, 2010; Washington, DC.

6 Joint United Nations Programme on HIV/AIDS (UNAIDS). Global report: UNAIDS report on the global AIDS epidemic 2012. http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2012/gr2012/20121120_UNAIDS_Global_Report_2012_en.pdf. Published November 2012. Accessed December 10, 2012.

7 Barr B. Designing a national PMTCT impact evaluation for Option B+ in Malawi. Paper presented at: 19th International AIDS Conference; July 17, 2012; Washington, DC.

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

1995

▶ Highly active antiretroviral therapy (HAART) becomes available with the approval of the first protease inhibitor, leading to dramatic reductions in AIDS-related deaths in the United States and other developed countries.

Where Are They Now? Messages from Two Early EGPAF Research Award Recipients

Richard Koup, MD
Chief, Immunology Laboratory, Vaccine Research Center, National Institutes of Health, Bethesda, Maryland

"That's all very nice, but how will it help my son?" It was 1989 and I had just finished telling Elizabeth Glaser about the research I would be doing as a Pediatric AIDS Foundation Scholar. At the time, I was working in the Department of Pediatrics at University of Massachusetts Medical Center along with John Sullivan, one of the early pioneers in pediatric AIDS research. Together we were studying the effects of HIV on children. It was there that we did the first test tube studies on nevirapine, an antiviral drug that was later licensed and shown to be effective in blocking mother-to-child transmission of HIV.

I moved to the Aaron Diamond AIDS Research Center in New York in 1991 to work on the Ariel Project (named after Elizabeth's daughter, who had recently died from AIDS-related causes). Elizabeth made me realize that while I saw HIV as a scientific curiosity, for her it was a personal battle that would not conform to the typically slow advances of scientific investigation.

I was one of the first recipients of the Elizabeth Glaser Science Award—a truly great honor for me. This award allowed me to conduct research leading to the discovery of the major cellular co-receptor for HIV, as well as a natural genetic mutation in that co-receptor that renders certain individuals almost completely resistant to HIV infection. The pharmaceutical industry was quick to realize the importance of this finding and rapidly developed antiviral drugs targeting the interaction of HIV with this co-receptor, adding to the therapeutic options for both children and adults.

I have also served as an advisor to EGPAF. With Katherine Luzuriaga, I co-chaired the scientific advisory board of the Elizabeth Glaser Science Award and International Leadership Award programs. One of the highlights of this work was an annual meeting of awardees in which basic scientists and international leaders, all of whom were dedicated to pediatric HIV research, convened to review data and brainstorm on research opportunities. These types of meetings, or "think tanks," were started by Elizabeth and her friends and co-founders, Susie Zeegen and Susan DeLaurentis. I realized very early on that when you receive a scientific award from EGPAF, you become part of a family, and the love you receive helps drive your commitment to succeed.

For the last 11 years I have been chief of the immunology laboratory at the Vaccine Research Center (VRC) at the National Institutes of Health, where I have continued to work on scientific projects relevant to EGPAF's goal to virtually eliminate pediatric AIDS. The dedicated team of scientists at the VRC has isolated broadly neutralizing antibodies that will soon be tested for their ability to block transmission of HIV during breastfeeding. The vaccines that are currently being tested in adults are being considered as therapeutic agents in HIV-infected children and adolescents as one arm of a cure strategy. If a vaccine can be made that protects adults from becoming infected with HIV, this will ultimately lead to the elimination of pediatric AIDS.

I have never forgotten Elizabeth's first words to me about her son, and I am grateful for the love and support of the EGPAF family. Together, we are making lasting contributions to the field of HIV research.

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

1996

- EGPAF creates the Elizabeth Glaser Scientist Awards (EGSA) and gives the first five to Dr. Richard Koup, Dr. Mike McCune, Dr. Donald Kohn, Dr. Jerry Zack, and Dr. Yves Riviere. The EGSA would go on to become the most prestigious named award in HIV/AIDS research and would award a total of 36 scientists and clinicians with more than $24 million in research funding over the next 10 years. These individuals would use these awards to leverage more than $250 million in additional research funding.

Philippa Musoke, MBChB, PhD
Department of Paediatrics and Child Health, Makerere University, Kampala, and Makerere University–Johns Hopkins University Research Collaboration, Kampala, Uganda

I received the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) International Leadership Award in 2006 to study the effectiveness of an adult fixed-dose combination (FDC) of antiretroviral drugs when used to treat HIV-positive children in Uganda. At the time, most HIV-positive children in Uganda did not have access to antiretroviral therapy (ART), as only adult FDCs were available and pediatric syrup formulations were too expensive for most families. Our study demonstrated that a generic adult FDC tablet divided according to a child's weight was effective in treating HIV infection in children. More than 75% of the children observed had an undetectable viral load after 96 weeks of ART.

These data were shared at Uganda's national pediatric HIV conference and at the International AIDS Society conference.[1,2] The findings were clear: children do respond to ART, and an adult FDC was effective in treating HIV infection in children when pediatric formulations were not available. In addition, the data were analyzed further and published in peer-reviewed journals, providing useful information for the care and treatment of HIV-infected children in resource-limited settings.[3,4]

The knowledge and skills I gained from this research have enabled me to contribute to the development of national and international guidelines and to train medical students and health workers in a national referral and teaching hospital in Kampala, Uganda. I currently serve as the chairperson of the Uganda Ministry of Health's Pediatric ART Sub-Committee of the National ART Committee and am the acting chair of the National PMTCT Committee.

With funding from EGPAF, Makerere University–Johns Hopkins University Research Collaboration (MU-JHU) has supported the Mulago prevention of mother-to-child transmission (PMTCT) of HIV program since 2000; the program counsels and tests more than 30,000 pregnant women annually. Mother-to-child HIV transmission is currently less than 5% among patients at Mulago hospital.

I was also involved with the National Institutes of Health Division of AIDS landmark studies, HIVNET 012 and HPTN 046, at the MU-JHU clinical research center. HIVNET 012 demonstrated that a simple, inexpensive drug regimen could reduce mother-to-child transmission by 50%. This finding formed the cornerstone for PMTCT in developing countries, including the World Health Organization guidelines for PMTCT, which enabled many developing countries to initiate PMTCT programs.

In 2009, I received an operational research grant from EGPAF to improve postnatal follow-up of HIV-positive mothers and their infants using community lay workers, called "peer mothers." We demonstrated the benefit of peer mothers in improving postnatal follow-up at one rural and three urban hospitals in Uganda.

I am grateful to EGPAF for giving me the opportunity to study the treatment of HIV infection in children, to support implementation and operational research in PMTCT, and to develop expertise that has informed prevention, care, and treatment of pediatric HIV infection worldwide.

References

1 Barlow-Mosha L, Ajuna P, Luttajumwa M, et al. Early effectiveness of Triomune in HIV infected children. Paper presented at: Third International AIDS Society Conference HIV Pathogenesis and Treatment; 2005; Rio de Janeiro, Brazil. Abstract No. WeOa0103.

2 Barlow-Mosha L, Bagenda DS, Mudiope PK, et al. The long-term effectiveness of generic adult fixed-dose combination antiretroviral therapy for HIV-infected Ugandan children. *Africa Health J*; 2012. In press.

3 Musoke P, Barlow-Mosha L, Bagenda D, et al. Response to antiretroviral therapy in HIV-infected Ugandan children exposed and not exposed to single-dose nevirapine at birth. *J Acquir Immune Defic Syndr.* 2009;52(5):560–568.

4 Musoke P, Mudiope P, Barlow-Mosha L, et al. Growth, immune and viral responses in HIV-infected African children receiving highly active antiretroviral therapy: a prospective cohort study. *BMC Pediatr.* 2010;10(56):1–11.

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

1997

▶ The Pediatric AIDS Foundation is renamed as the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) in honor of Elizabeth's passion, dedication, and commitment to helping children and families living with and afftected by HIV and AIDS.

Using Routine Program Data for Research and Evaluation: Key Considerations

Rhoderick Machekano (rmachekano@pedaids.org)

Although the distinction between research and program evaluation is often blurred, these practices differ in a number of important areas, including purpose, goals, target groups, and desired outcomes (see Table 1). Evaluation is the systematic assessment of program processes and/or outcomes with the intent of furthering a program's progress. Research typically takes place in a controlled setting and seeks to gather information to test a hypothesis and produce generalizable findings.

Research and program evaluation share many methodologies but they are designed to answer different types of questions. For example, research might help determine whether a program would produce similar results in a different setting, while program evaluation might help determine whether a program is producing a desired result. Research and evaluation both seek to answer questions through the systematic collection and analysis of data and make use of a variety of data collection methods, including interviews, medical chart reviews, and routine program monitoring and surveillance.

Programs generally collect both qualitative and quantitative data for routine monitoring purposes. Most routinely collected quantitative data are aggregated—for instance, client-level data might be combined and summarized for an entire facility or geographical area. Aggregate data are more widely available than patient-level data and should be used whenever possible to help answer important research questions. However, research activities that use aggregate routine program data must fully consider the strengths and limitations of these data.

Aggregate program data are most useful for descriptive research (i.e., to describe trends over time). If data on two attributes are collected over time, it may also be possible to discern some relational and/or causal patterns between the two, but it will not be possible to arrive at definitive conclusions based on these observations. For example, to examine the effect of a prevention of mother-to-child transmission (PMTCT) program on mother-to-child HIV transmission rates, one could look at a year's worth of quarterly data on the proportion of HIV-positive pregnant women initiating antiretroviral (ARV) prophylaxis and the proportion of HIV-infected infants among HIV-exposed infants over that same period. However, in this instance it would be important to rule out other possible reasons for any observed relational patterns, such as concomitant initiation of early antiretroviral therapy (ART) for HIV-infected infants (which may lead to increased survival, making it appear as if the PMTCT program is less effective due to higher observed numbers of HIV-infected infants) or mothers and children that may have received prior interventions.

The drawback of using aggregate data is that they do not provide detailed client information (e.g., which individuals received ARVs, took their drugs as recommended, etc.). Despite the availability of advanced statistical methods for making individual-level inferences using aggregate data, appropriate interpretation requires specialized skills. Additionally, aggregating data from groups with different characteristics (e.g., health behaviors) can weaken relationships between indicators, possibly rendering them undetectable. Aggregate data are also prone to quality problems resulting from double counting and difficulty in verification. It is therefore important to ensure the quality of aggregate data, to the extent possible, when it is used for research (e.g., through the use of electronic registers with integrated data checks).

When feasible, collection of patient-level data during routine clinical services can help overcome the limitations of aggregate data. Although collection of individual-level data in the context of routine program operations can require an additional investment of resources, use of electronic patient-level databases can help alleviate staff reporting burdens and can strengthen program monitoring and evaluation efforts as well as research.

Summary

Research and evaluation share similar methodologies, and both are heavily reliant on data collection and analysis. However, their intent, or the types of questions they seek to answer, often differs greatly. Individual patient-level data, if available, can greatly enhance both research and evaluation by providing a more detailed, accurate picture of patient outcomes. Aggregate program data can be used for descriptive research and evaluation but are not ideal for exploring relationships between different indicators. Programs should explore the use of electronic patient-level databases, which can yield high-quality patient-level data to enrich both research and evaluation activities.

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

1999

- Nevirapine is shown to reduce MTCT by 50% with single doses given to the mother during labor and to the infant following birth in the landmark HPTN 012 study, led by EGPAF's current vice president of research, Dr. Laura Guay (then with Johns Hopkins University).
- EGPAF begins the Call-to-Action prevention of mother-to-child HIV transmission (PMTCT) program in eight clinics in six countries focused on implementing the HPTN 012 intervention.

Table 1. Differences Between Research and Evaluation

Attributes	Research	Evaluation
Primary purpose	To advance more wide-ranging knowledge or theory, producing *generalizable* knowledge	To provide timely and constructive information for decision making about *particular* programs—judging merit or worth
Questions	Scientific inquiry based on intellectual hypothesis and identified problems—researcher initiated	Responding to the needs of a program—the policy and program interests of stakeholders are paramount
Target groups	Investigator- or research-focused—academic community and policy makers	Client-focused—program managers, implementers, policymakers, politicians, communities, funding agencies
Environment	Controlled setting	Conducted within a setting of changing factors, priorities, and resources
Communicating and reporting outcomes	Scientific journals and conferences	Reports and briefs
Institutional review board requirements	In most cases, depending on study design	Sometimes—case dependent

Photo credit: EGPAF

EGPAF staff attend an EGPAF-led workshop on qualitative research methods in Dar Es Salaam, Tanzania (February 2012)

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

2000

- The 13th International AIDS Conference ("Breaking the Silence") in Durban, South Africa, is the first to be held in a developing country, heightening awareness of the global AIDS pandemic.

Using Qualitative Research to Inform PMTCT Program Improvement

Leila Katirayi (lkatirayi@pedaids.org) and Godfrey Woelk

Qualitative data can help researchers understand the various factors that influence the outcomes of prevention of mother-to-child HIV transmission (PMTCT) service delivery, such as antiretroviral therapy (ART) uptake, adherence, loss to follow-up, and antenatal care attendance. Qualitative research provides the opportunity to explore a topic in more detail by clarifying underlying behaviors, attitudes, perceptions, and culture, and can be used in conjunction with quantitative research. The ordering of these two activities will determine how the qualitative findings can be used (see Box 1). Table 1 provides a detailed overview of the differences between qualitative and quantitative research.

Qualitative studies generate descriptive and in-depth data. Three data collection methods are generally used: observation (e.g., through use of a checklist), in-depth interviews (using open-ended questions and unstructured or semistructured interview guides), and focus group discussions (using a focus group discussion guide). Data collectors should be experienced in using these methods and be familiar with the objectives of the study in order to identify points warranting further questioning.

Box 1. Functions of Qualitative Research When Used in Conjunction with Quantitative Research

Qualitative research ***preceding*** quantitative research can
- explore topics in more depth and/or narrow the focus,
- inform development of research questions, and
- identify potential barriers or facilitators to a proposed intervention.

Qualitative research ***concurrent*** to quantitative research can
- provide perspectives on the why or how of a research question,
- determine the acceptability of a new intervention as it is introduced, and
- corroborate findings with an additional level of data ("triangulation").

Qualitative research ***following*** quantitative research can
- provide a deeper understanding of study findings and
- corroborate the findings with an additional level of data ("triangulation").

Photo credit: James Pursey

Interviews and focus group discussions are often recorded on digital devices and transcribed into large documents for analysis. Once data are transcribed, theme identification and data coding can begin. Software specifically designed for qualitative data analysis is often used to sort through large volumes of data and can simplify the process of identifying subthemes and trends.

EGPAF is conducting a number of qualitative studies that will help inform and strengthen PMTCT service implementation. EGPAF-Swaziland is in the process of analyzing data from a study seeking to understand barriers and facilitators to increasing the number of HIV-positive pregnant women who initiate ART. EGPAF-Mozambique

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

2002

- EGPAF introduces the International Leadership Award, which is given to three up-and-coming researchers in resource-limited settings. Among them is Dr. Philippa Musoke of Uganda to support her research on the care and treatment children living with HIV (see page 13 for more on Dr. Musoke).
- Dr. Jeffrey Stringer of the University of Alabama and Center for Infectious Disease Research in Zambia (CIDRZ) becomes the first EGSA awardee to conduct research in a resource-limited setting.
- President George W. Bush launches the International Mother and Child HIV Prevention Initiative, committing $500 million over five years to reaching HIV-positive pregnant women with ARV prophylaxis to prevent the transmission of HIV to their infants in 14 African countries and the Caribbean.

is in the process of analyzing data from a study exploring facilitators and barriers to HIV-exposed and HIV-infected children receiving care and treatment services in two provinces. EGPAF-Malawi is launching a new study to better understand key gaps and potential solutions in early infant diagnosis and treatment in selected districts. Each of these studies is expected to impart a richer understanding of program implementation gaps and challenges and to help identify potential solutions that will lead to improved HIV prevention, care, and treatment services.

Within the context of health programs, qualitative studies can be used to explore trends in behaviors and practices that inhibit the successful delivery of health services. Understanding program challenges in depth can inform efforts to strengthen service delivery and national policy adoption.

Table 1. Differences Between Qualitative and Quantitative Data

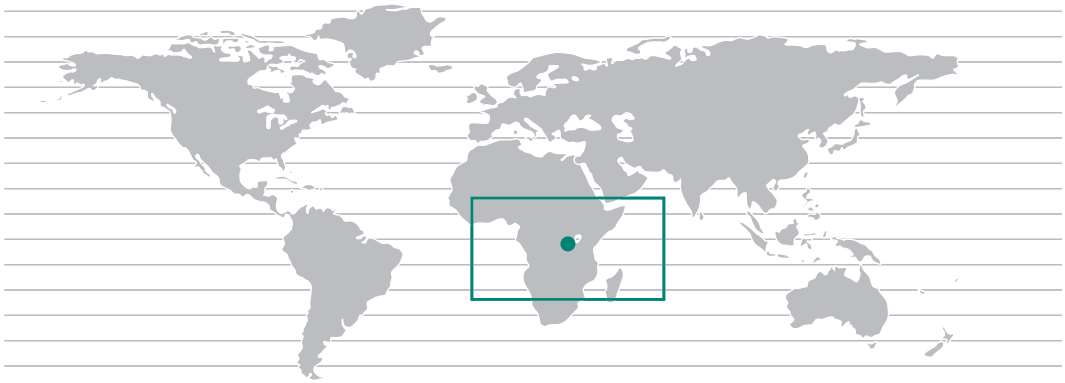
Qualitative	Quantitative
Uses words, pictures, and objects	Uses numbers and statistics
Allows for greater spontaneity	Asks identical questions in the same order
"Open-ended" questions that participants are free to respond to in their own words	"Close-ended" or fixed response categories
Makes minor use of numerical indexes	Reduces data to numerical indexes
Data used for descriptive write-up	Data used for statistical analysis
Evokes responses that are ◦ meaningful and culturally salient, ◦ unanticipated by the researcher, and ◦ rich and explanatory in nature	Allows for meaningful comparison of responses across participants and sites

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

2003

- Nine years after Elizabeth Glaser passes away from AIDS-related illnesses, her vision for pediatric drug research becomes a reality when the U.S. Congress passes the Pediatric Research Equity Act. This new law dramatically increases the number of drugs tested and labeled for use in children.
- During the 2003 State of the Union address, President George W. Bush proposes creation of the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) to make anti-HIV drugs less costly and more widely available to millions of men, women, and children in the poorest regions of the world.

Country Program Notes



RWANDA:

Lessons on Conducting Collaborative Country-Level Research

Paul Dielemans (pdielemans@pedaids.org), Odette Mukandanga, Diane Gashumba, Jill Peterson, Dieudonne Ndatimana, Martha Mukaminega, and Cornelia van Zyl

The Elizabeth Glaser Pediatric AIDS Foundation's (EGPAF's) Rwanda program began in 2000 with provision of technical support to the national prevention of mother-to-child HIV transmission (PMTCT) program. EGPAF has since expanded its support to 47 PMTCT and HIV care and treatment sites in the country, which have provided PMTCT services to more than 250,000 pregnant women and have provided more than 14,000 HIV-positive pregnant women with antiretroviral prophylaxis (as of October 2012).

Background

The government of Rwanda, together with its partners in the national HIV response, is committed to reducing the mother-to-child HIV transmission (MTCT) rate to 2% at 18 months of age by 2015. One of the overarching strategies to achieve this target is to strengthen the integration of HIV and maternal and child health (MCH) services with the aim of reinforcing PMTCT prongs two, three, and four (prevention of unintended pregnancy in women with HIV; prevention of HIV transmission from mother to child; and provision of ongoing care and support to mothers, their children, and families).

During a technical exchange visit to Swaziland in 2009, EGPAF-Rwanda staff witnessed firsthand the country's successful HIV-MCH integration model and

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

2004

- EGPAF becomes a member of the U.S. President's Emergency Plan for AIDS Relief Track 1.0 program. Through this program, EGPAF expands its support to ministries of health for delivery of HIV-related services in more than 5,000 health facilities, setting the stage for EGPAF's intramural implementation research.
- Dr. Tom Hope of Northwestern University and Dr. Grace Aldrovandi of Children's Hospital, Los Angeles, are awarded EGSAs to study how viruses are transmitted from mother to child in utero and during the breastfeeding period, respectively.

brought these ideas back to Rwanda. Over the past two years, EGPAF has supported Rwanda's Ministry of Health (MOH) and the Rwanda Biomedical Center (RBC) to design and pilot a similar model of colocated HIV and MCH services, known as the "one-stop model." This model has been piloted in five EGPAF-supported PMTCT and HIV care and treatment sites in Rwanda's Eastern Province since 2010 and is currently being evaluated as part of an EGPAF-led operations research study.

Research Protocol Design and Implementation

In 2011, EGPAF-Rwanda drafted a research protocol to evaluate the one-stop model at the five rural pilot sites (four public and one faith-based). The protocol was developed jointly by the MOH and EGPAF, with principal investigators representing both groups and RBC serving as co-investigator. The protocol received institutional review board (IRB) approval in April 2012. Research methodologies used included key informant interviews with policymakers and managers at the national, district, and health center levels; focus group discussions with health workers; and observations and structured interviews among beneficiaries of MCH services. For comparison, research was also conducted at five similar EGPAF-supported sites in the same districts that had not implemented the model.

Six research assistants and a data entry clerk were recruited and trained on the protocol, data collection instruments, and use of consent forms in May 2012. Data collection took place between June and September 2012. Transcripts from interviews, focus group discussions, and observations were translated from Kinyarwanda to English and entered into a qualitative analysis database (MAXqda). All data from interviews with beneficiaries have been entered into an SPSS database; coding and analysis of these data by EGPAF and the MOH is currently under way.

Achievements

With technical support from EGPAF's global research team and in close collaboration with MOH and RBC, EGPAF-Rwanda was able to design a research proposal that was approved by local and U.S.-based IRBs. The data collected, after rigorous analysis, will be used to guide the MOH and other stakeholders in decisions relating to scale-up of the model. Preliminary responses from those involved in the evaluation indicate that

Photo credit: James Pusey

the one-stop model has been implemented without major challenges and is acceptable to both health workers and beneficiaries.

Challenges

Staff time and workload was one particular challenge encountered. More than 300 pages of Kinyarwanda transcripts had to be collected and translated into English, and about 300 variables for 170 respondents had to be entered into SPSS, all of which required considerable staff time and expertise. EGPAF-Rwanda does not have a designated research unit, and at several stages of the evaluation, additional staff had to be hired to complete certain tasks.

Another challenge was length of time. Even before data collection took place, the design of the research and development of the research protocol took about five months. Training staff on complex data collection instruments also increased the length of time needed to conduct the research.

Conducting beneficiary interviews also proved difficult, as average enrollment of HIV-positive women in PMTCT programs at each site was very low, at an estimated 15 clients per year. Social workers from the facilities approached eligible clients, explained the purpose of the evaluation, and

» *continued on pg. 26*

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

2005

▶ Jake Glaser, an EGPAF spokesperson and healthy young adult, celebrates his 21st birthday.

LESOTHO:

Strengthening Program Implementation Through Operations Research

Appolinaire Tiam (atiam@pedaids.org), Majoalane Mokone, Ashley Thompson, Michelle Gill, and Anthony Isavwa

The Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) has been working in Lesotho since 2006 and to date has supported the delivery of prevention of mother-to-child HIV transmission (PMTCT) services to more than 105,000 pregnant women. Since the program's inception, EGPAF-supported HIV care and treatment sites in Lesotho have enrolled more than 96,000 people living with HIV on antiretroviral therapy (ART), including more than 4,600 children under the age of 15 years (as of October 2012).

Introduction

EGPAF began supporting Lesotho's national HIV/AIDS program in 2006 through a partnership with the Ministry of Health (MOH). EGPAF-Lesotho has since provided the MOH with technical assistance aimed at scaling up and strengthening HIV prevention, care, and treatment services in 184 public and 20 private health facilities. EGPAF supports HIV/AIDS program implementation in all 10 districts of Lesotho, work that is funded by the U.S. President's Emergency Program for AIDS Relief (PEPFAR) through the U.S. Agency for International Development (USAID).

As HIV services expanded in Lesotho, there was a growing need to identify promising practices in program implementation and to improve service quality while making optimal use of limited resources. In response, EGPAF-Lesotho introduced operations research (OR) as a key component of its support to the MOH; this support was formally articulated in EGPAF-Lesotho's 2010 strategic plan.

Building an OR Team

EGPAF-Lesotho began advancing its OR agenda by establishing a dedicated research team in 2010 with financial support from Johns Hopkins University. The team consisted of a research coordinator, a data officer, a data clerk, and eight technical advisors. Research staff were integrated into EGPAF-Lesotho's Programs Department to ensure that all research activities were well coordinated and beneficial to program activities.

The research team's primary aim was to generate evidence on the effectiveness of program interventions and to build the capacity of MOH and LENASO (a local partner) staff in OR. EGPAF-Lesotho coordinated the training of several MOH staff in key aspects of OR, such as how to generate research questions, ethics, and institutional review board (IRB) approval processes. While EGPAF staff were responsible for leading all OR activities, MOH staff served as co-investigators and were involved in generating research protocols. This training and active collaboration with the MOH proved useful in developing strong local OR mechanisms.

Developing a Local Research Agenda

Based on EGPAF-Lesotho's research program objectives, OR questions were defined by EGPAF and MOH technical staff to address issues perceived by both parties as critical to program improvement. OR protocols were developed locally with technical assistance from EGPAF-global research staff. Since 2010, EGPAF-Lesotho has conducted several OR studies to address key programmatic challenges.

Ongoing Studies and Early Findings

The Impact of HIV Test Results on Subsequent Antenatal Care Attendance by Women in Rural Hospitals in Lesotho: A Retrospective Cohort Study. This study, carried out between February and March 2011, found that women who know their HIV status before pregnancy attend ANC earlier and more frequently than women who are unaware of their status. HIV testing and counseling for women and couples prior to pregnancy can promote safe motherhood practices, including opportunities to provide PMTCT services for HIV-positive pregnant women. To build on these results, EGPAF-Lesotho is working to establish collaborative partnerships with home-based HIV counseling and testing implementing partners in Lesotho.

Towards Getting More HIV-Positive Infants on Lifesaving Treatment: A Review of the Early Infant Diagnosis (EID) System, Results, and Outcomes in Selected Sites in Lesotho. This one-year study—the first to be supported with funds raised by the dance marathon held annually at the University of California, Los Angeles (UCLA)—was launched in March 2012 and is working to characterize the current EID process, early perinatal

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

2006

- EGPAF receives funding from the Bill & Melinda Gates Foundation for enhancing PMTCT through implementation and operations research (OR).

infection rates, and the PMTCT services received by HIV-positive mothers and their infants who had an HIV test at six to eight weeks of age in Lesotho. The study will help EGPAF-Lesotho determine necessary steps to improve early initiation of HIV-positive infants in ART programs. Data analysis is ongoing, but the study has already revealed gaps in program documentation and the use of multiple registers to monitor programs.

Integration of Active Case-Finding for Tuberculosis (TB) for Isoniazid Preventive Therapy with Prevention of Mother-to-Child Transmission of HIV Services in Lesotho. Started in June 2011 and anticipated to end in March 2013, this study is evaluating the roll-out of active TB case-finding among HIV-positive and HIV-negative pregnant women and the roll-out of isoniazid preventive therapy among HIV-positive, TB-negative pregnant women. Preliminary study results were presented in November 2012 at the 43rd Union World Conference on Lung Health in Malaysia.

Pilot Test of HIV and Infant Feeding Indicators in Lesotho. Initiated in October 2012, this study is examining the feasibility of collecting national infant feeding indicators at primary health care facilities and looking at whether these indicators reflect actual feeding practices and ART uptake among HIV-exposed infants.

Assessing the Feasibility, Acceptability, and Health Services Utilization Outcomes of the Use of Mother-Baby Packs (MBPs) for Delivery of Antiretroviral Drugs to HIV-Infected Pregnant Women and Their Infants in Lesotho. Launched in November 2012, this study will assess the acceptability of implementing three MBPs (one for HIV-negative pregnant women, one for HIV-positive pregnant women on antiretroviral prophylaxis, and one for HIV-positive pregnant women eligible for ART) among women and health care workers (facility- and community-based); the feasibility of MBP implementation at individual, site, and program levels; and the uptake of key maternal and child health / PMTCT services among women receiving MBPs compared with those who do not receive MBPs.

PMTCT Program Effectiveness: Measuring HIV Transmission Among HIV-Exposed Infants in Lesotho. Launching in early 2013, this study will measure mother-to-child HIV transmission rates and HIV-free survival of infants born to HIV-positive mothers. The study will also measure adherence to key PMTCT services among HIV-positive pregnant women and their infants.

Challenges

When EGPAF first began OR in Lesotho, fundamental questions arose concerning the program's readiness to conduct OR, how to generate research questions, and how to include OR in staff work plans. As with any research effort, identifying funding sources was a challenge. In working through these issues, EGPAF-Lesotho realized that the review of program implementation results can serve as a good platform for OR idea generation and prioritization.

Country program teams may be somewhat research-shy, given that rigorous data collection adds to a team's workload. However, establishing a devoted research team and allowing all program team members to generate their own research questions can ease the workload and serve as an incentive for creative problem solving. Retrospective data review is a particular challenge for the EGPAF-Lesotho research team, and the program is working on establishing a small group of sentinel sites (i.e., pilot sites) where more rigorous supervision will be performed. EGPAF-Lesotho is also working to install a computerized data collection system in late 2012 to collect more detailed patient-level data.

The OR work in EGPAF's Lesotho program has been made possible by the Lesotho MOH, research participants, the dedicated EGPAF staff in Lesotho and in global offices, as well as donors including the United Nations Children's Fund (UNICEF), the World Health Organization (WHO), UCLA, Johns Hopkins University, and various private donors.

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

2007

- EGPAF launches its Pediatric HIV Vaccine Program with funding from the Bill & Melinda Gates Foundation.
- EGPAF funds its first OR project to enhance PMTCT, including a sub-grant to Cameroon partner organization Cameroon Baptist Convention Health Board (CBCHB) to participate in the PEARL study of PMTCT effectiveness.
- EGPAF launches its first intramural OR project in Swaziland to look at the impact of specific health care worker training on the performance of repeat HIV testing in labor and delivery and identifies a high rate of HIV seroconversion among pregnant women.

TANZANIA:

Conducting Operations Research in a Country Program Context

Gaspar Mbita (gmbita@pedaids.org), Marta Moroni, Michelle M. Gill, Nuru Kilimba, Tatu Mtambalike, and Roland van de Ven

Since 2003, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) has supported the Tanzania Ministry of Health and Social Welfare (MOHSW) to scale up PMTCT services in six regions (Arusha, Kilimanjaro, Mtwara, Shinyanga, Tabora, and Lindi) with support from the U.S. President's Emergency Plan for AIDS Relief through the U.S. Agency for International Development (USAID). Since 2004, EGPAF has also worked with the MOHSW to scale up care and treatment services through funding from the U.S. Centers for Disease Control and Prevention. EGPAF supports 1,354 reproductive and child health clinics to provide PMTCT services, which as of October 2012 have been accessed by more than 2.2 million pregnant women. In 2012, EGPAF entered into an agreement with USAID to support scale-up of comprehensive reproductive and child health and PMTCT services in supported regions.

Background

In partnership with the MOHSW, EGPAF-Tanzania focuses on expanding quality, comprehensive HIV-related and reproductive health services for women and families. Since 2007, EGPAF-Tanzania has pursued an operations research (OR) agenda to advance program implementation and national policy formulation. As part of this effort, EGPAF-Tanzania established a Public Health Evaluation unit in 2007 in order to conduct HIV program assessments using OR methodologies. This article provides an overview of a recent OR activity undertaken by the unit and the lessons learned stemming from this and similar OR activities to date.

OR on Integration of Family Planning into HIV Care and Treatment Services in Shinyanga Region, Tanzania

In 2011, the United Nations Population Fund provided funding to EGPAF-Tanzania to develop, implement, and evaluate a family planning / HIV integration model in Tanzania's Shinyanga Region. The model was based on a similar model implemented by Family Health International and the International Center for AIDS Care and Treatment Programs for which positive outcomes had been documented.[1] The model involved colocation of family planning (screening, counseling, and commodities) and HIV care and treatment services at HIV care and treatment centers in Shinyanga. The study, which was launched in August 2011, aimed to assess challenges arising during the model's implementation and gauge its acceptability among district health managers, service providers, and clients.

Implementation of the model included the training of care and treatment center health providers on family planning counseling and provision and documentation of family planning services, approaches to supporting district leadership to ensure overall coordination (including site supervision and supply management and distribution), and community involvement. The study used a variety of data collection methods, including structured interviews (at baseline), semistructured interviews (post-implementation), focus group discussions, pre- and post-tests of training participants, and key informant interviews with district leadership. Preliminary results indicate that both health care workers and clients were accepting of the model, although some health workers cited increased workloads as a challenge. The study is ongoing and dissemination of results is expected in June 2013.

Challenges Conducting OR in a Country Program Context

Ethical Clearance

Research activities that involve human subjects require ethical clearance from Tanzania's national research coordination body, the Medical Research Coordinating Committee (MRCC). The MRCC delegates registration, ethical review, approval, and monitoring of research to the National Health Research Ethics Review Sub-Committee. The MRCC's proposal review and approval process generally takes four to six weeks, but in the case of EGPAF-Tanzania's study on family planning integration, the process took roughly three months. Approval processes can be time consuming, but advance planning and perseverance can alleviate this issue.

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

2008

- EGPAF funds the first round of Pediatric HIV Vaccine Program basic research grants with a focus on pediatric immune responses to HIV and mechanisms of breast milk transmission.
- Dr. Laura Guay joins EGPAF as vice president of research.

Photo credit: James Pursey

Internal Capacity

Essential research skills are needed to perform the tasks that will move a study from conception to completion (e.g., writing of study protocols, securing funding, data collection and analysis, writing of manuscripts, dissemination of findings, etc.), but people who possess these skills are hard to come by in many country program settings. The EGPAF-Tanzania team has learned that research capacity building, if done well, can adequately prepare country research staff to design and complete OR studies.

Research Assistants

Skilled research assistants are needed at every stage of the process. In the case of the family planning integration acceptability study, many interviews had to be conducted and variables assessed, and it was difficult to assemble a team that could perform these activities. Using a qualitative approach (which involves interviews with key informants on a particular topic) requires specific expertise that is particularly difficult to source locally.

Logistics

Managing research timelines, from defining a research question to dissemination of findings, was another significant challenge. If a response to the national ethics committee is delayed, this will lead to delays in certification, research, and subsequent analysis. Good project management can help ensure the accountability of researchers for meeting deadlines and can strengthen collaboration and working relationships.

Community Involvement

Misperceptions about a study's intent can spread rapidly and negatively impact community participation. To ensure that studies are conducted ethically and that they are well understood by participating communities, community representatives should be involved in all aspects of a study's design and implementation.

Conclusion

Research can help program implementers assess the feasibility, acceptability, and effectiveness of service delivery strategies. Integrating research methodologies into program activities can help staff improve the effectiveness of their programs while generating evidence to influence national health policies and approaches.

Key Recommendations

- Local staff capacity should be built at every step of the OR process, from developing protocols to the dissemination of findings.
- Programs should identify donors that are interested in supporting research activities.
- It is important to build good relationships with the local institutional review board.
- Research and program staff must be well versed in the human subjects research code of ethics, and these principles must be closely followed in all research activities.

References

1 Mpangile G, Green M. Results of the operational research study on the integration of family planning and HIV/AIDS care and treatment services in Tanzania. Presented at: Results Dissemination Meeting; September 2010; Dar es Salaam, Tanzania.

2 Zachariah, R. The Sydney Declaration: good research drives good policy and programming—a call to scale up research. Paper presented at: Fifth International AIDS Society on Pathogenesis, Treatment and Prevention; July 19–22, 2009; Cape Town, South Africa.

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

2009

- EGPAF holds its first OR think tank in tandem with its first OR training in Kampala, Uganda. The think tank brings together EGPAF OR grant recipients, country research staff, and external advisors for a focused discussion on the current results of the ongoing EGPAF OR studies.
- Results of a large vaccine study in Thailand (RV144) show the first ever partial protection from HIV infection.

Statistical Humor

Content for this section has been adapted from the following sources: Internet gallery of statistics jokes (http://www.docstoc.com/docs/26538606/Jokes-in-Statistics) and Ramseyer's first Internet gallery of statistics jokes (http://my.ilstu.edu/~gcramsey/Gallery.html).

Sizing Up Samples

A statistics professor describing sampling theory to a class explains how a sample can be studied and used to generalize to a population. One of the students in the back of the room shook his head. "What's the matter?" asked the professor. "I don't believe it," said the student. "Why not study the whole population in the first place?" The professor continued explaining the ideas of random and representative samples. The student shook his head. The professor launched into the mechanics of proportional stratified samples, randomized cluster sampling, the standard error of the mean, and the central limit theorem. The student remained unconvinced. Attempting a more practical example, the professor explained scientific rigor and meticulous sample selection of the Nielsen television ratings, used to determine how multiple millions of advertising dollars are spent. The student remained unimpressed, saying, "You mean that just a sample of a few thousand can tell us exactly what over 250 million people are doing?" Finally, the professor, disgruntled with the skepticism, replied, "Well, the next time you go to the campus clinic and they want to do a blood test, tell them that's not good enough. Tell them to take it all!"

Lesson learned: Use a sample to draw inferences about a population.

What's in a Word

Checking some questionnaires that had just been filled in, a census clerk was amazed to note that one of them contained the figures 121 and 125 in the spaces for "Age of Mother, if Living" and "Age of Father, if Living." "Surely your parents can't be as old as this?" asked the incredulous clerk. "Well, no," was the answer, "but they would be if living!"

Lesson learned: Pay attention to the wording of questions on data collection forms.

A Matter of Principle

There was once a group of biostatisticians and a group of epidemiologists riding together on a train to joint meetings. All the epidemiologists had tickets, but the biostatisticians had only one ticket between them. Inquisitive by nature, the epidemiologists asked the biostatisticians how they were going to get away with having only one ticket when the conductor came through. One of the biostatisticians said, "Easy. We have methods for dealing with that." Later, when the conductor came to punch tickets, all the biostatisticians slipped quietly into the bathroom. When the conductor knocked on the door, they slipped their one ticket under the door, fooling the conductor. After the joint meetings, the biostatisticians and epidemiologists again found themselves on the same train. The epidemiologists had decided to purchase one ticket between them. The biostatisticians had purchased NO tickets for the trip home. Confused, one of the epidemiologists asked, "We understand how your methods worked when you had one ticket, but how can you possibly get away with no tickets?" A biostatistician responded, "We have different methods for dealing with that situation." When the conductor was in the next car, all the epidemiologists trotted off to the bathroom with their ticket and all the biostatisticians packed into the other bathroom. The

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

2010

- South African researchers announce results of a clinical trial (CAPRISA 004) showing that use of microbicide gel significantly reduces risk of HIV infection among sexually active women.

head biostatistician then crept over to the epidemiologists' bathroom and knocked authoritatively on the door. The epidemiologists slipped their one ticket under the door. The head biostatistician took it and returned triumphantly to the group. The epidemiologists were subsequently discovered and publicly humiliated.

Lesson learned: Do not use statistical methods unless you understand the principles behind them.

Regression

Two statisticians were traveling in an airplane from Los Angeles to New York. About an hour into the flight, the pilot announced that they had lost an engine. "But don't worry," he said. "There are three left." However, instead of five hours it would take seven hours to get to New York. A little later, he announced that a second engine failed; they still had two left, but it would take 10 hours to get to New York. Somewhat later, the pilot came on the intercom and announced that a third engine had died. The plane could fly on a single engine, but it would now take 18 hours to get to New York. At this point, one statistician turned to the other and said, "Gee, I hope we don't lose that last engine or we'll be up here forever!"

Lesson learned: Use caution when interpreting regression models.

Assumptions

A physicist, a circus weight lifter, and a statistician are marooned on a desert island. A box of canned food washes ashore, and the question is how to open the cans. The physicist suggests dropping them from the trees so that they break open. The strong man says that's too messy. Instead he will rip the cans open with his bare hands. The statistician says that's still too messy, but he knows how to open cans without making a mess. "First," he says, "assume we have a can opener."

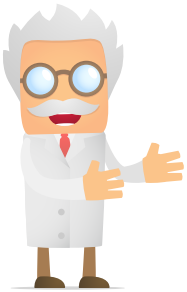
Lesson learned: Statistics always requires assumptions.

A Question of Power

One day there is a fire in a wastebasket in the dean's office, and in rush a physicist, a chemist, and a statistician. The physicist immediately starts to work on how much energy would have to be removed from the fire to stop the combustion. The chemist works on which reagent would have to be added to the fire to prevent oxidation. While they are doing this, the statistician sets fire to all other wastebaskets. "What are you doing?" they demand. The statistician replies, "To solve this, we need a large sample size!"

Lesson learned: An adequate sample size is needed to ensure study results have sufficient statistical power, but use common sense.

Communication Is Key



Three men are in a hot air balloon and find themselves lost in a canyon. One of the three men says, "I've got an idea. We can call for help in this canyon and the echo will carry our voices." He leans over the basket and yells out, "Hellllooooo! Where are we?" They hear the echo several times. Fifteen minutes pass. Then they hear an echoing voice: "Hellllooooo! You're lost!" One of the men says, "That must have been a statistician." Another of the men asks, "Why do you say that?" The reply: "For three reasons: (1) he took a long time to answer, (2) he was absolutely correct, and (3) his answer was absolutely useless."

Lesson learned: Open communication between principal investigators and statisticians is crucial.

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

2011

- Results of the Swaziland OR study Improved Detection of Incident HIV Infection and Uptake of PMTCT Services in Labor and Delivery in a High HIV Prevalence Setting are published.

continued from pg. 19

Key Lessons Learned from Country Teams on Conducting Research, Rwanda

asked them return to the health facility for an interview on a predetermined day.

Lessons Learned

- Conducting qualitative research has led to the increased capacity of EGPAF-Rwanda staff to design a research protocol, use data collection instruments, and conduct data analysis using several software packages, including MAXqda.
- Conducting qualitative and operations research requires a strong principal investigator and good teamwork. This study has been a team- and capacity-building opportunity for EGPAF staff.
- Evaluation of a new model of service delivery can be conducted effectively through operations research. Comparing certain indicators before and after an intervention (which requires good baseline data)—and performing qualitative research on inputs and processes or quantitative research on outputs—can strengthen analyses of health service delivery.
- It is helpful to think about research and evaluation methodologies before the introduction of a new service delivery model.
- Design and implementation of a research protocol is time consuming and should commence early in the project period to ensure that deadlines are respected and that there is adequate time for dissemination and formal publication.
- Projects with limited research capacity should take care not to be overambitious. If time allows, the protocol can be split into smaller pieces and the research conducted step-by-step.

Next Steps

Once the analysis is complete, results will be shared with the national MCH and PMTCT technical working groups and submitted to the MOH for approval. Results are expected to be formally disseminated nationwide in December 2013.

This research was conducted with funding from the U.S. Agency for International Development (USAID) through the President's Emergency Plan for AIDS Relief (PEPFAR) and with the participation of the MOH, district directors of health, district hospital directors, health centers, and beneficiaries of MCH services. The EGPAF-Rwanda and global teams, the consultants, the research assistants, and the translators were all instrumental to this evaluation.

HIV RESEARCH AND EGPAF HISTORICAL TIMELINE

2012

- A large multinational study of discordant, primarily heterosexual couples shows that early treatment of HIV-infected persons greatly reduces transmission to their HIV-negative partners (HPTN 052).
- EGPAF research activities continue to grow, with 25 studies currently under way (see pages 28–31 for a full list of EGPAF-led studies).

Q&A with…

Suzanne May

Suzanne May is a regulatory officer within EGPAF's Research Department. In this role she oversees the institutional review board (IRB) processes for all EGPAF-led research activities and provides ongoing technical assistance and support on issues related to human subjects protections. Prior to joining EGPAF, Suzanne worked in a similar capacity at the U.S. Centers for Disease Control and Prevention (CDC), as well as other organizations. She is a certified IRB professional.

Is an institutional review board (IRB) approval needed in cases where only existing program data are being used?

An IRB approval is needed whenever you are engaged in human subject research. The U.S. Department of Health and Human Services regulations define a human subject as a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual or (2) identifiable private information. The collection of existing identifiable private information about an individual may constitute human subject research. Staff should seek official determination from an IRB, ethics committee, or other regulatory authority before beginning a project that involves collecting data from individual records, even if it's information they have access to under routine program activities.

When is it necessary for a U.S. IRB to review proposals for non-U.S. research projects?

As a part of the terms of the Federalwide Assurance for the Protection of Human Subjects, any study that is funded by the U.S. Government (e.g., by the U.S. Agency for International Development [USAID] or the Centers for Disease Control and Prevention [CDC]) must be reviewed by a U.S. IRB. Projects funded by other donors may also require U.S. IRB review; if you are in doubt about which IRB approvals are required for your project, please contact your regulatory officer or other relevant research personnel.

How is the need for a non-research determination (NRD) rather than a full IRB review determined?

It is best to seek an NRD whenever you are unsure whether a project is considered research or if you are concerned that the project may appear to be research. If the project or program is CDC funded, then it's possible to work with the CDC to obtain an NRD. If it is funded by another source, then you can obtain an NRD from an IRB or ethics committee.

If we plan to present the results of our evaluation at a conference or poster session rather than in a journal, does the project still need IRB approval?

If you would like to share the results of a project with an external audience, either an NRD or IRB approval is required *before* data collection. Poster presentations, abstracts, and other forms of dissemination are considered to contribute to generalizable knowledge and therefore meet the U.S. Department of Health and Human Services definition of research.

If we complete a program assessment or evaluation and then find the data are interesting and wish to publish, can we request IRB review after the work is complete?

No, the regulations prohibit an IRB from approving or granting an NRD for work that has already been completed. Because of this, it is recommended that you seek an approval or NRD before beginning any work that you may want to be able to share outside your organization.

CURRENT RESEARCH PROJECTS AT EGPAF (as of December 2012)

Country	Title	Summary	Project Period	Principal Investigator(s) (EGPAF staff unless otherwise indicated)
Kenya	Mobile Phone Technology for Prevention of Mother-to-Child Transmission of HIV: Acceptability, Effectiveness, and Cost	This cluster randomized study being conducted in rural Kenya aims to determine the effect of mobile phone technology on key prevention of mother-to-child transmission (PMTCT) milestone completion from antenatal care (ANC) to six weeks postpartum.	May 2011–April 2014	John Ong'ech and Seble Kassaye
Lesotho	The Impact of HIV Test Results on Subsequent Antenatal Care Attendance by Women in Rural Hospitals in Lesotho	The aim of this study is to explore the impact of a positive or negative HIV test result received during a woman's first ANC visit on subsequent ANC attendance, an area in which existing research was limited.	January 2011–March 2013	Appolinaire Tiam
Lesotho	System Development and Mentoring for Integration of Active Case-Finding for TB (ACF) and Isoniazid Preventive Therapy (IPT) with Prevention of Mother-to-Child Transmission of HIV Services (PMTCT) in Lesotho	The focus of this systems development and mentoring project is to conduct operations research on ACF and IPT in the antenatal clinical context. The project will assess progressive roll-out of ACF among HIV-positive and HIV-negative pregnant women and measure the uptake of IPT among women in whom active TB has been excluded.	October 2010–March 2013	Richard Chaisson (Johns Hopkins University), Appolinaire Tiam, and Seble Kassaye
Lesotho	Towards Getting More HIV-Positive Infants on Lifesaving Treatment: Measuring HIV Test Turnaround Times and Early Effectiveness of HIV Mother-to-Child Prevention Programs Using Early Infant Diagnosis Records	The aim of this study is to describe the current early infant diagnosis process, early mother-to-child infection rates, and the PMTCT services received by HIV-positive mothers and their infants who underwent an HIV test at six to eight weeks in selected sites in Lesotho in order to determine necessary steps to improve early initiation of HIV-positive infants into antiretroviral (ARV) treatment programs.	March 2012–December 2012	Appolinaire Tiam and Michelle Gill
Lesotho	Pilot Test of HIV and Infant Feeding Indicators in Lesotho	The objective of this pilot test evaluation is to determine whether routine collection of the proposed indicators is feasible at primary health care facilities, and also whether the indicators reflect actual feeding practices of HIV-exposed infants.	August 2012–December 2012	Appolinaire Tiam and Emily Bobrow
Lesotho	Assessing the Feasibility, Acceptability, and Health Services Utilization Outcomes of the Use of Mother-Baby Packs (MBPs) for Delivery of Antiretroviral Drugs to HIV-Infected Pregnant Women and Their Infants in Lesotho	The introduction of the MBP aims to address some of the missed opportunities for women to receive appropriate HIV prevention, care, and treatment for themselves and their infants. The goal to virtually eliminate pediatric HIV will require higher coverage rates and a reduction in missed opportunities for ARV prophylaxis. Given the challenges of interruptions in ARV dosing due to drug stock-outs and the low rates of completion of the PMTCT cascade from ANC through the end of breastfeeding, it is important to assess the influence of this novel drug delivery system, the MBP, on PMTCT coverage and retention for both pregnant women and their newborns.	May 2011–June 2013	Laura Guay and Appolinaire Tiam

Country	Title	Summary	Project Period	Principal Investigator(s) (EGPAF staff unless otherwise indicated)
Malawi	Barriers and Facilitators of Early Infant Diagnosis and Treatment (EIDT) Services in Malawi	This is an exploratory study to better understand the key gaps and potential solutions in EIDT in Dedza, Ntcheu, and Lilongwe districts in order to strengthen EIDT services delivery.	November 2012–March 2013	Aida Yemane Berhan
Malawi	Acceptability of Lifelong Treatment (ART) Among HIV Positive Pregnant and Postpartum Women in Selected Sites in Malawi	The primary objective of this study is to understand the barriers and facilitators that encourage women to accept or reject lifelong therapy.	January 2013–June 2013	Aida Yemane Berhan and Leila Katirayi
Mozambique	Exploring Facilitators and Barriers to Participation of HIV-Exposed and HIV-Infected Children in Care and Treatment Services in Two Provinces in Mozambique	This qualitative study is aimed at identifying barriers to HIV testing, enrollment into care, and follow-up services for HIV-exposed children in Mozambique.	August 2011–February 2012	Laura Guay and Caroline De Schacht
Mozambique	Maternal HIV Seroconversion During Pregnancy and Postpartum Period: Incidence and Associated Risk Factors	This prospective cohort study is following two cohorts of HIV-uninfected women—one cohort from ANC to delivery and the other from delivery to 18 months postpartum—with serial HIV testing to identify HIV seroincidence in each cohort.	January 2008–December 2012	Cathrien Alons and Caroline De Schacht
Mozambique	Field Evaluation of Point-of-Care (POC) Technologies in Maternal and Child Health (MCH) Services and in the PMTCT Program	This study will evaluate the feasibility and acceptability of the introduction of three POC technologies for diagnosis of syphilis, hemoglobin, and CD4 T-lymphocyte enumeration within MCH services.	December 2011–December 2012	Caroline De Schacht (EGPAF) and Ilesh Jani (Mozambique Ministry of Health)
Rwanda	The Kabeho Study: Antiretroviral and Breastfeeding Assessment for the Elimination of HIV	This project seeks to determine the 18-month HIV-free survival in a cohort of children born to HIV-positive pregnant women receiving universal lifelong ART (PMTCT Option B-Plus), coupled with comprehensive infant feeding counseling and support, in selected high-volume antenatal clinic sites in Kigali, Rwanda.	July 2012–June 2015	Emily Bobrow (EGPAF) and Anita Asiimwe (Rwanda Ministry of Health)
Rwanda	Health-Seeking Behaviors of Pregnant Women in Rwanda: Contributing Factors Towards High Dropout of Pregnant Women Between First and Fourth ANC Visit	This exploratory study aims to document the reasons why pregnant women come late to ANC, why they come for fewer than four visits, and what proportion of pregnancies among known HIV-positive women are planned.	August 2012–December 2013	Paul Dielemans
Rwanda	Integration of HIV Services into Maternal and Child Health: A Post-Implementation Evaluation of a "One-Stop" Model in Rwanda	This study will assess how the implementation of the one-stop model was carried out in order to determine the perceptions of different stakeholders and to make recommendations regarding the potential scale-up of the model throughout Rwanda.	March 2012–December 2012	Paul Dielemans and Emily Bobrow

continued

Country	Title	Summary	Project Period	Principal Investigator(s) (EGPAF staff unless otherwise indicated)
Swaziland	Barriers to ART Initiation	The primary objective of this study is to determine the facilitating factors and barriers associated with ART initiation among HIV-positive women during pregnancy in Swaziland.	July 2011–March 2013	Mohammed Ali Mahdi
Swaziland	Knowledge, Attitudes, and Practices of Health Care Workers and Patients Towards HIV Testing and Counseling (HTC) in Selected Health Facilities in Swaziland	The primary aim of this study is to understand the knowledge, attitudes, and practices of health care workers and patients toward provider-initiated HIV testing and counseling.	January 2013–June 2013	Mohammed Ali Mahdi
Swaziland	An Exploratory Study of the Behaviors and Practices That May Increase HIV Risk Among Pregnant and Lactating Women in Communities in Swaziland	This is an exploratory study to better understand the sexual practices of pregnant women that may affect HIV seroconversion during pregnancy.	November 2012–March 2013	Mohammed Ali Mahdi and Mary Pat Kieffer
Tanzania	Enhancing Family Planning (FP) Counseling and Provision of Services Through Integration into HIV Care and Treatment Services in the Shinyanga Region of Tanzania	The overall study aim is to assess changes resulting from the integration of FP services into HIV services and to assess the acceptability of the integrated model among district health managers, health care providers, and clients.	June 2011–June 2013	Marta Moroni, Emily Bobrow, and Gaspar Mbita
Uganda	Promoting Constructive Male Engagement to Increase Use of PMTCT Services in Kabale District, Uganda	The primary objective of this study is to assess the effectiveness of the overall intervention aimed at constructively engaging men in the use of PMTCT services and FP decision making, measured in terms of dual-method use (condoms along with another contraceptive), by HIV care and treatment clients.	January 2013–September 2013	Theresa Hoke (FHI360)
Zambia	An Exploratory Study of Zambian Pregnant Women's Perceptions of the Use of Extended Infant Nevirapine to Prevent HIV Transmission During Breastfeeding	This study aims to improve our understanding of unforeseen challenges and possible solutions to implementing Option A of the World Health Organization (WHO) 2010 PMTCT guidelines. It will provide insight into possible solutions to overcome such challenges from the perspective of HIV-positive pregnant and lactating women.	May 2012–May 2013	Susan Strasser
Zambia	Identifying and Understanding Effective Interventions for Orphans and Vulnerable Children (OVCs) Affected by HIV	EGPAF is working with Johns Hopkins University on an NIH-funded OVC study to evaluate the effectiveness of a cognitive-behavioral intervention compared with an existing intervention in improving a wide range of OVC outcomes including reduction in HIV risk behaviors, improved well-being, mental health, functioning, education, and caregiver health and support.	April 2012–April 2017	Susan Strasser

Country	Title	Summary	Project Period	Principal Investigator(s) (EGPAF staff unless otherwise indicated)
Zimbabwe	A Community Randomized Study to Evaluate the Effect of a Community-Based Peer Facilitator Intervention on PMTCT Program Outcomes in Zimbabwe	The primary goal of this study is to test whether providing community-based, peer-facilitator-led support for pregnant and postpartum women improves MCH and PMTCT program uptake and adherence to health care recommendations, as compared with communities without the peer support intervention.	October 2011–September 2014	Auxilia Muchedzi and Godfrey Woelk
Multicountry	Maternal Events and Pregnancy Outcomes in a Cohort of HIV-Infected Women Receiving Antiretroviral Therapy in Sub-Saharan Africa	This multicountry study will evaluate maternal and infant outcomes in women receiving ART at the time of conception and during pregnancy as part of routine HIV service delivery.	October 2010–March 2013	Richard Marlink
Multicountry	Project ACCLAIM (Advancing Community-Level Action for Improving MCH/PMTCT) Increasing Demand, Access, and Retention in MCH/PMTCT Services at the Community Level	The goal of this project is to test the effect, individually and jointly, of the implementation of three community-based interventions on demand, uptake, and retention of MCH/PMTCT services. These interventions are (1) the engagement of community leaders to generate increased demand for MCH/PMTCT services through development of Community Action Plans; (2) the hosting of Community Days, a forum for community events for sensitization, information, education, and broad dialogue on MCH/PMTCT and general health issues; and (3) the establishment of peer support groups to promote greater involvement by men in MCH/PMTCT services and improve knowledge of and attitudes to utilizing MCH/PMTCT services by pregnant women.	April 2012–March 2016	Godfrey Woelk
Multicountry	HIVCORE (HIV Operations and Research and Evaluation)	Through a retrospective chart review, this project aims to assess retention across the PMTCT cascade in examples of countries implementing Option A, B, and B-Plus guidelines.	October 2011–September 2014	Godfrey Woelk

ELIZABETH GLASER
PEDIATRIC AIDS
FOUNDATION
www.pedaids.org

Office Locations

UNITED STATES (HEADQUARTERS)
1140 Connecticut Ave. NW, Suite 200
Washington, DC 20036
+1 202-296-9165

UNITED STATES (LOS ANGELES)
11150 Santa Monica Blvd., Suite 1050
Los Angeles, CA 90025
+1 310-314-1459

CÔTE D'IVOIRE
2 Plateaux les Vallons
Rue J 50
08 BP 2678 Abidjan 08
Côte d'Ivoire
+225 22 41 45 05

DEMOCRATIC REPUBLIC OF CONGO
Avenue Colonel Mondjiba N° 63
Kinshasa Gombe
Concession COTEX - Bâtiment N° 10 B1
République Démocratique du Congo
+243 82 382 42 48

GENEVA
WCC Center
150, Route de Ferney
1 Route des Morillons
P.O. Box 2100
Bureaux Rhône 168 et 169
CH-1211 Geneva 2, Switzerland
+41 22 791 6088/457

INDIA
EGPAF India Consortium Office
c/o SAATHII-Hyderabad
H # 1-4-880/2/36/1
New Bakaram, Gandhi Nagar
Hyderabad-500 080, India
+91 40-27654688

KENYA
Ariel House
Westlands Avenue
Off David Osieli Road
P.O. Box 13612 – 00800
Nairobi, Kenya
+254 20 44 54 081/2/3

LESOTHO
Sechaba House, 1st Floor
4 Bowker Road
P.O. Box 0166
Maseru West 105
Lesotho
+266 223 116 62

MALAWI
Green Heritage Building
P.O. Box 2543
Lilongwe, Malawi
+265 1772 052

MOZAMBIQUE
Av. Kwame Kruma N°417
Maputo, Mozambique
+258 21488904

RWANDA
Rue du lac Mpanga N°10
Avenue de Kiyovu
BP 2788 Kigali, Rwanda
+250 252 570583

SWAZILAND
P.O. Box A507
MTN Office Park
Karl Grant Street
Mbabane, Swaziland
+268 2404 8081

TANZANIA
P.O. Box 1628
Plot # 8 & 10, off Haile Selassie Road
Oysterbay
Dar es Salaam, Tanzania
+255 22 260 1692

UGANDA
EGPAF/Kampala
Plot 18A, Kyadondo Road
P.O. Box 21127
Kampala, Uganda
+256 312264380

STAR-SW Office
Plot 13, McAllister Road
P.O. Box 881
Mbarara, Uganda
+256 485420160

ZAMBIA
P.O. Box 39111
Reliance House
Thabo Mbeki Road
Lusaka, Zambia
+260 211 256 481

ZIMBABWE
107 King George Road
Avondale, Harare
Zimbabwe
+263 4 302 144

The work of the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) is made possible by the generous support of the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) through the U.S. Agency for International Development (USAID) and the U.S. Centers for Disease Control and Prevention (CDC), and through the generous support of Abbott Fund, the Bill & Melinda Gates Foundation, Boehringer Ingelheim, The Children's Investment Fund Foundation, Jewelers for Children, Johnson & Johnson, United Nations Children's Fund (UNICEF), and ViiV Healthcare. The contents are the sole responsibility of EGPAF and do not necessarily reflect the official views of USAID, CDC, the United States government, or other EGPAF donors and partners.

Haba Na Haba is a publication of the
Elizabeth Glaser Pediatric AIDS Foundation.
We welcome your feedback, comments, and questions at
techbulletin@pedaids.org.

Executive Editor: Christian Pitter
Managing Editor: Sara Teitelman
Associate Editor: Alex Ekblom
Contributing Editors: Laura Guay, Jeff Safrit, Chris Hudnall
Document Design: Susan Gillham
Production: Matt Mayerchak