



**Elizabeth Glaser
Pediatric AIDS Foundation**
Fighting for an AIDS-free generation

RESEARCH



Above Photo: Eric Bond/EGPAF, 2020
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The Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) is a recognized global leader in the fight to end pediatric HIV/AIDS through research, advocacy, and delivery of comprehensive HIV services. Elizabeth Glaser was one of the first public figures to advocate for research focused on the prevention and treatment of HIV and AIDS in children. She co-founded EGPAF in 1988 to give hope to children and families by catalyzing support and resources for pediatric HIV research. Through its provision of critical funding for research, EGPAF has contributed to the most significant scientific breakthroughs in pediatric AIDS, including major advances in how HIV enters cells, research on the effects of early combination therapy in children, and discoveries that helped to dramatically reduce the rate of mother-to-child transmission of HIV around the world.

While remarkable scientific advances in HIV and AIDS have saved millions of lives globally, we have not yet reached our mission of eliminating pediatric AIDS. EGPAF remains committed to advocating for, conducting, and using research to improve the reach and quality of HIV services in low-resource settings. Currently, we directly lead a broad portfolio of over 30 clinical and implementation research studies in 14 African countries. Our research focuses on optimizing health

service delivery, building an evidence base for innovative strategies and novel technologies, and effectively scaling-up promising HIV and maternal, newborn, and child health (MNCH) interventions. Our Global Research Unit brings expertise in clinical, implementation, community, qualitative, and quantitative research as well as skills in biostatistics and regulatory compliance. These global research experts are committed to building local research capacity. They work closely with EGPAF's country-based staff, Ministries of Health (MOHs), and partner organizations to design and conduct rigorous research and evaluation activities across Africa.

As a leading implementing partner for the U.S. President's Emergency Plan for AIDS Relief and other donors, EGPAF provides programmatic support to over 5,000 sites in Africa. We work with and through national systems to improve local capacity to deliver high-quality health services. With our decades of program implementation experience and vast network of sites, we are uniquely placed to conduct research studies and evaluations within existing service delivery programs. We understand the critical problems facing health systems and can identify where research may have the greatest impact in solving them. With our deep medical and research expertise and on-the-ground

experience working with health facilities, communities, and patients, we are well-placed to design and evaluate interventions to improve service quality and health outcomes. As a trusted MOH partner at national, regional, and local levels, we also understand national priorities and where research can best inform national policies and strategies. In fact, findings from our research have influenced national and international HIV policies and guidelines for adults and children.

Key elements of EGPAF's research program include:

Commitment to building local research capacity:

EGPAF prioritizes building the research capacity of local EGPAF staff, MOH staff, and partner organizations. All of our studies and evaluations have an in-country Principal Investigator and many include MOH investigators. We also routinely engage MOH staff at national and decentralized levels, as well as other stakeholders throughout study activities from study design, implementation, and monitoring, to analysis and dissemination of results. EGPAF's global research experts also provide didactic training and hands-on mentoring in protocol development, regulatory compliance, study implementation, data analysis, and manuscript writing.

Using research to improve programs and inform policy:

With our strong capacity in both program implementation and research, EGPAF can rapidly translate study findings into actions to improve programs. Program improvement recommendations can be quickly disseminated across our global programs for greater impact. We also prioritize MOH engagement in studies, which ensures findings will meet evidence needs and inform policy, while building local ownership.

Continued advocacy for pediatric HIV research:

In its early years, EGPAF awarded basic science research grants to attract scientists to study pediatric HIV and organized pediatric HIV think tanks to bring leading scientists together. Since then, EGPAF has remained a leading advocate for ensuring children are prioritized in the global research agenda, including in cure and vaccine research. Our global experts also serve on prominent international committees including the World Health Organization Pediatric Antiretroviral Drug Optimization Working Group, the International AIDS Society Collaborative Initiative for Paediatric HIV Education and Research, the United States Public Health Service Perinatal and Pediatric Antiretroviral Drug Guidelines Panels, and the U.S. National Institutes of Health (NIH) Office of AIDS Research Advisory Committee, and the NIH Adolescent HIV Implementation Science Alliance, among others.

Research Awards

From 1989-2013, EGPAF granted more than 1,000 research awards totaling nearly \$79 million. This funding attracted a new cadre of researchers to the field of pediatric HIV and contributed to significant breakthroughs on HIV in children. EGPAF's priorities have now shifted to conducting clinical and implementation research, but our goal of ensuring children and families benefit from research and effective, evidence-based treatments and health services remains.

Conducting ethical research:

Research ethics and the protection of the rights and wellbeing of participants in studies are of utmost importance at EGPAF. All of our research studies involving human subjects are approved by an Institutional Review Board and local ethics committee. Study investigators complete certificates in the protection of human subject in research every two years. We also ensure compliance with international standards and applicable laws and regulations in countries where studies are conducted.

Partnering with leading research institutions:

EGPAF partners with global, U.S., and local academic institutions and research organizations. As part of the U.S. Agency for International Development (USAID)-funded Project SOAR, EGPAF collaborates with the Population Council, Johns Hopkins University, the University of North Carolina, Avenir Health, and Palladium. We also maintain the longstanding Partnership for Pediatric AIDS and Public Health with George Washington University's Milken Institute School of Public Health. We also collaborate with researchers at the U.S. Centers for Disease Control and Prevention, USAID, as well as local research institutions, such as the University of Kinshasa's School of Public Health and the National School of Statistics and Applied Economics of Abidjan.

Wide dissemination of study findings:

EGPAF understands that disseminating study results at local, national, and global levels is critical to creating impact. Our study findings are shared widely with local stakeholders, including community members and health facility staff, local organizations, the MOH and other government agencies, and donors. Study findings and the resulting program improvement recommendations are also shared across EGPAF's broad network of country programs. In addition to presentations at global technical forums and international conferences, study findings are published in leading peer-reviewed journals, such as AIDS, Journal of Acquired Immune Deficiency Syndromes (JAIDS), Journal of the International AIDS Society (JIAS), PLOS ONE, AIDS Behavior, AIDS Research and Treatment, and BioMed Central (BMC) Public Health.

EGPAF's Research Portfolio

To achieve our mission of ending pediatric AIDS, EGPAF conducts research studies and evaluations across a range of technical areas. We evaluate the effectiveness of HIV, MNCH, and tuberculosis (TB) programs under real-world conditions and assess ways to improve the delivery and quality of health services at facility and community levels. This includes developing effective and replicable comprehensive service delivery models that are well integrated within health systems with strong linkages to the communities that they serve. We also develop and evaluate innovative technologies, interventions, and strategies to increase the efficiency of health systems and health service delivery, improve the demand for services, and promote family- and patient-centered care. Our research priorities are described below by technical area.

Prevention of Mother-to-Child Transmission (PMTCT) and HIV-Free Survival

While enormous strides have been made in reducing mother-to-child transmission of HIV, too many babies are still becoming infected through pregnancy, labor and delivery, and breastfeeding. EGPAF's priorities are: to prevent mother-to-child transmission, to ensure all HIV-exposed infants are tested early, to initiate HIV-infected infants on HIV treatment as soon as possible, and to monitor HIV-exposed, but uninfected infants, who are at increased risk of early morbidity and mortality. Our research seeks to maximize the effectiveness of PMTCT service delivery models, build an evidence base for effective PMTCT interventions, and evaluate HIV-free survival and health outcomes among HIV-exposed children. For example, as lifelong antiretroviral treatment (ART) for all pregnant and breastfeeding women (also called Option B+) was being rolled out, EGPAF led studies in Cameroon, Lesotho, Malawi, Mozambique, Rwanda, and Zimbabwe to better understand acceptability, effectiveness, and barriers and facilitators to initiation, adherence, and retention in the PMTCT program. Previously, PMTCT programs used antiretroviral drugs only to prevent mother-to-child transmission and to treat those who were already sick. While reaching many more women, our studies showed that the switch to lifelong ART resulted in higher loss to follow-up in study countries, indicating a need for enhanced adherence and retention support for women and stronger patient tracking systems. Our qualitative studies filled critical gaps in understanding why newly diagnosed women struggled with immediate initiation of ART and how counseling could be improved to prevent these women from dropping out of HIV services. EGPAF's studies also found that additional support to prevent loss to follow-up was particularly needed for adolescents, and unmarried, apparently healthy women, and at the periods immediately following HIV diagnosis and around the time of breastfeeding cessation. EGPAF continues to lead additional PMTCT research focused on evaluating long-term health outcomes for mothers

and children and lifelong ART retention among pregnant adolescents. For example, EGPAF conducted large community-based, household surveys in Swaziland and Lesotho to determine population-based HIV-free survival among HIV-exposed infants and to explore factors associated with continued HIV infection and mortality among HIV-exposed infants.

The Kabehe Study

EGPAF's USAID-funded Kigali Antiretroviral and Breastfeeding Assessment for the Elimination of HIV (Kabehe) Study was one of the first studies to assess the implementation of lifelong ART for pregnant women as a national program and the resulting long-term PMTCT outcomes. The study enrolled a cohort of 608 HIV-positive pregnant or postpartum mothers and their children and followed them for two years after delivery. The study demonstrated that:

- It is possible to achieve low mother-to-child transmission rates and high HIV-free survival, similar to those in high-income, non-breastfeeding populations with 93.2% of children HIV-free and alive at two years of age.
- High ART adherence and positive treatment outcomes among both children and mothers can be achieved.
- The study also provided important insights about which subgroups of women may need more support and during which time periods as well as where health worker training can be strengthened to further improve program outcomes.

Pediatric and Adolescent Testing, Care, and Treatment

EGPAF remains committed to its mission of ending pediatric AIDS. We maintain a strong focus on ensuring HIV-positive children and adolescents are identified, initiated on lifesaving ART, and retained in care and treatment services. Improving health outcomes for children and adolescents requires a focus on their situational and age-specific needs. EGPAF conducts a wide range of studies from assessing how best to provide timely access to early infant diagnosis (EID) for HIV-exposed infants to evaluating interventions designed to improve pediatric retention in care, to exploring how to make health facilities “adolescent friendly” to encourage adolescents to access HIV-related services. Findings from recent EGPAF studies have identified key gaps in the early infant diagnosis and treatment cascade, including timely return of HIV test results to caregivers, and explored HIV resistance and the need for second- and third-line drugs among children and adolescents. We are currently leading a prospective cohort study that will assess different service delivery models for actively finding HIV-positive children in Kenya and Uganda. In Swaziland, we are evaluating the effect of implementing a family-centered model of care program on viral suppression and retention in children as compared with the standard model of care, where adults and children receive care in separate clinics. In Kenya, EGPAF designed and is evaluating the effect of the Red Carpet Program, which provides specific services and interventions for adolescents and young adults during the critical period right after diagnosis, on early linkage to and retention in HIV care.

The Very Early Infant HIV Diagnosis Study

A recent EGPAF study assessed the feasibility, acceptability, and costs associated with adding birth HIV testing to the routine testing algorithm for infants born to HIV-positive women in Lesotho and Rwanda. The study demonstrated that:

- Women and health care workers were in favor of introducing birth testing.
- Ensuring that infants of women who deliver outside of the facility are tested within two weeks of birth could be an important challenge.
- Although infants tested at birth did receive test results and initiate ART earlier, issues within the health system, such as the long turnaround time for test results, remained a significant issue. Further research is planned to see how point-of-care testing could reduce this problem.





Adult Testing, Care, and Treatment

To end pediatric AIDS, we must also address HIV in adults. Due to ART, people living with HIV (PLHIV) are living longer, healthier lives, yet many challenges remain in identifying adults with HIV and providing them with HIV care and treatment services. EGPAF's priorities include identifying successful approaches for improving retention and ART adherence, tracking patient viral load to optimize ART regimens, and HIV drug resistance monitoring. Our past studies have explored the knowledge, attitudes, and practices of both adult patients and health care workers toward provider-initiated testing and counseling and assessed the effect and cost-effectiveness of text message reminders on retention of adults in HIV services. We are leading a variety of new studies focused on adults. In Lesotho, we are evaluating a differentiated model of care to better serve PLHIV with advanced HIV disease. Another study will evaluate the effectiveness and cost-effectiveness of three models of ART provision for stable ART patients, including community-based, multi-month dispensing of ART. EGPAF is also leading cross-sectional surveys to estimate the prevalence of HIV drug resistance.

Community Approaches to Enhance HIV and MNCH Services

Community-based approaches, such as engaging community health workers or local religious or political leaders, or conducting community outreach activities, can increase demand for, uptake of, and retention in HIV and MNCH services. EGPAF assesses the effectiveness of community-based programs and interventions to build evidence so that successful community models can be replicated. Our past studies have evaluated the effect of community-based interventions on the uptake of MNCH services, and explored the barriers and facilitators to male involvement in antenatal care (ANC) and delivery services. We are currently leading studies to evaluate community-based ART programs, assess a community score card approach for improving retention across the PMTCT cascade, and evaluate new interventions designed to improve community-facilities linkages.

Innovative Technologies

New and innovative health technologies are changing the landscape of public health. EGPAF supports and evaluates the effectiveness, feasibility, acceptability, and scalability of novel health technologies that can increase access to health services and products, promote efficiencies, reduce costs, and/or improve the quality of care. In 2014, we introduced study results showing successful use of Gene Xpert machines, traditionally used for TB diagnosis, as a tool for EID. We are currently evaluating the implementation and effects of our Unitaid-funded Point-of-Care (POC) EID Project, which is rolling out POC EID platforms in nine African countries. Additional studies will evaluate the impact of POC EID versus conventional EID on key outcomes and the cost-effectiveness of POC EID. In Uganda, EGPAF is evaluating the effectiveness of the innovative Pratt Pouch as a tool for expanding access to infant nevirapine prophylaxis for HIV-exposed infants nationwide. The pouch, which is similar to a ketchup packet, offers a unique way for mothers to provide pre-measured, single doses of nevirapine to their infants immediately after birth to prevent mother-to-child transmission of HIV.

Project ACCLAIM

The Advancing Community Level Action for Improving MCH/PMTCT (ACCLAIM) Project was a community-based trial which evaluated the effects of three community-based interventions on the demand for, uptake of, and retention in MNCH services. This study demonstrated that:

- Community-level interventions can improve early attendance at antenatal clinics.
- Engaging community leaders shows great promise for increasing the demand for, uptake of, and retention in MNCH services.

Maternal, Newborn, and Child Health

MNCH services remain the most critical point for identifying, preventing, and treating HIV in mothers, children, and adolescents. EGPAF has led numerous studies to evaluate the effectiveness of interventions designed to increase access to and uptake of MNCH services, improve ANC attendance and retention, and improve overall maternal and child survival. In Tanzania, we are assessing the effectiveness of case management and quality improvement intervention models on retention in MNCH/PMTCT through a mixed methods study. Another study in Tanzania is evaluating a program which integrates early childhood development messages and practices into facility- and community-based services.

Other Areas

EGPAF also leads studies in a range of other technical related areas, including TB and sexual and gender-based violence. In Lesotho, we assessed a model for the progressive roll-out of active TB case finding and introduction of Isoniazid preventive therapy for HIV-positive pregnant women in whom active TB has been excluded. The study findings influenced the Lesotho MOH to roll-out the model nationwide. Upcoming studies will continue to look at HIV-TB co-infection as well as pediatric TB. In Zimbabwe, we led a national household survey to estimate the prevalence of violence among Zimbabwean youth ages 13-24 years and to characterize the relationship between violence and HIV. In Mozambique, we led a study which explored the sexual violence survivors care cascade and institutional barriers to accessing post-exposure HIV prophylaxis.

In summary, EGPAF works hand-in-hand with MOHs and partner organizations to conduct rigorous clinical and implementation research studies and evaluations that generate evidence that can improve health programs and inform policy. We remain committed to advocating for, conducting, and using research to fight the HIV epidemic until no child has AIDS.

For more information on EGPAF's current and completed studies, please see our website: www.pedaids.org.

The IMPROVE Study

With funding from USAID under Project SOAR, EGPAF is implementing and evaluating a novel, multidisciplinary management team intervention for improving maternal and child health, ART, and HIV service uptake and retention. The "Integrated Management Team to Improve Maternal-Child Outcomes (IMPROVE)" intervention was designed to achieve patient-focused and outcome-oriented MNCH services with coordination at the facility and community levels. Cohorts of HIV-positive and HIV-negative pregnant women will be enrolled and prospectively followed until their child reaches 24 months of age. A qualitative component has also been included in the study to evaluate the feasibility and acceptability of integrating this intervention into routine national systems.

