



SURVIVING AND THRIVING HIV-FREE:

REPORT OF THE 4TH HIV-EXPOSED UNINFECTED
CHILD AND ADOLESCENT WORKSHOP

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ABSTRACT

As access to maternal antiretroviral treatment during pregnancy and breastfeeding has increased in high HIV burden countries, up to 30% of children are born HIV-exposed but uninfected (HEU). Among children and adolescents who are HEU, a significant proportion experience psychosocial challenges without the benefit of multidisciplinary supportive services afforded to those living with HIV. During the 4th HEU Child and Adolescent Workshop, immediately preceding the 22nd International AIDS Conference in Amsterdam in 2018, nearly 150 researchers, community members, program implementers and policymakers met to review key research findings and consider policy implications for the rapidly growing population of children and adolescents who are HEU. Particular attention was paid to how the World Health Organization's Nurturing Care Framework might protect the psychosocial wellbeing of the current population of HEU infants and children as they mature into adolescents and adulthood.

INTRODUCTION

As the global HIV epidemic matures, an increasing proportion of pregnant and breastfeeding women living with HIV (WLHIV) have access to antiretroviral treatment (ART).

In turn, the population of children below 15 years of age who are HIV exposed and uninfected (HEU) has increased from an estimated 7 million in 2000 to 14.8 million in 2018, with sub Saharan Africa home to 90% of this population.(1) In particular, estimates indicate that six countries account for more than 50% of this population, specifically South Africa (21%), Mozambique (7%), United Republic of Tanzania (7%), Uganda (6%), Kenya (6%), and Zimbabwe (5%).(1) This population experiences higher rates of infectious morbidity, mortality, poorer growth outcomes, and developmental delays compared with children born to women without HIV.(2-12) While research is ongoing to identify specific biological, social and structural etiologies of these outcome disparities, it has been shown that growing up in an HIV-affected household contributes to a unique set of psychosocial stressors for HEU children. Collectively, the vulnerable population of children and adolescents who are HEU are not surviving and thriving as well as their HIV-unexposed peers. Since 2015, the Child and Adolescent HEU Workshop has been the only international forum where researchers, policymakers, program implementers, and affected persons have convened to review current science, practical challenges, and implications for health and education policies related to children and adolescents who are HEU.(13, 14) Herein, we report on the proceedings of the 4th Child and Adolescent HEU Workshop, held as a pre-conference at the 22nd International AIDS Conference in 2018, Amsterdam, the Netherlands. This workshop highlighted the psychosocial challenges experienced by many adolescents who are HEU and the importance of nurturing care for all young children.

It considered how the World Health Organization's Nurturing Care Framework could be employed to strengthen programming capable of fostering optimal early childhood development (ECD), and to improve developmental outcomes and resiliency among infants and children who are HEU. There was review of recent research findings on factors that affect the physical and mental health of adolescents who are HEU or living in an HIV-affected household. Finally, a continuum of care approach designed to position children and adolescents who are HEU to thrive was reviewed.



PSYCHOSOCIAL IMPLICATIONS FOR ADOLESCENTS WHO ARE HEU

Today's population of adolescents (aged 10-19 years) and youth (aged 15-24 years) (15) who are HEU have survived the HIV epidemic from its earliest period. In utero exposure to maternal HIV infection, and in some cases antiretroviral drugs (ARVs), coupled with the milieu of family, community, and social stressors, highlight the need for ongoing assessment of the psychosocial wellbeing of adolescents and youth who are HEU. This is particularly important as this group transitions to early adulthood, as poor mental health can adversely influence physical health and wellbeing.(16) Risk factors for mental health disorders among adolescents who are HEU are similar to those in adolescents and youth living with HIV (AYLHIV). Nonetheless, very few studies have been conducted with a primary focus on the mental health of adolescents who are HEU. The existing body of literature is concentrated in high income countries, where adolescents who are HEU have often only been included as comparison groups in studies designed to evaluate mental health among AYLHIV.(17-20) In these studies, depression, anxiety, trauma, difficulty in psychosocial adjustment with significant loss of self-esteem, as well as suicidal behaviors have been reported among adolescents and youth who are HEU.(21) Important drivers of increased mental health morbidity include negative life events such as living with a caregiver with mental health morbidity, parental loss and the bereavement cycle, stigma, economic challenges as well as household and community violence.(21-25)

Evidence from two United States (US)-based cohorts demonstrated that the prevalence of mental health morbidity is higher among adolescents who are HEU compared with those who are HIV-unexposed and similar to that of adolescents living with HIV. The Child and Adolescent Self Awareness and Health (CASAH) study, conducted in New York City, observed that adolescents who are HEU suffered from a range of mental health disorders similar to adolescents living with perinatally-acquired HIV (ALpHIV).(26) Likewise, in the multi-site US-based Pediatrics HIV/AIDS Cohort Study (PHACS) mental health disorders among adolescents who are HEU occurred at substantially higher rates than reported in the general US adolescent population and included depression, anxiety, behavioral and substance use disorders.(27) In fact, mental health problems were more prevalent in adolescents who are HEU than in ALpHIV (38% vs. 25%, $p < 0.01$), yet fewer adolescents who are HEU were accessing mental health treatment.(27, 28) Despite mental health and psychosocial risks, both ALpHIV and adolescents who are HEU in the CASAH study demonstrated resilience and achieved many milestones indicative of successful transition into adulthood. (17, 29)

However, one significant difference was that a higher proportion of youth living with perinatally-acquired HIV (YLpHIV) had resources to pay for housing while fewer youth who are HEU reported comparable resources. This difference is ascribed to housing and other subsidies received by YLpHIV in New York City, while youth who are HEU often living in the same challenging HIV-affected circumstances do not receive equivalent social support.(17) Despite these concerning findings, adolescents who are HEU remain invisible, with most healthcare systems essentially unaware of their HIV-exposure status. The multidisciplinary approach to the care and support of AYLHIV does not exist for adolescents who are HEU.

There is almost a complete absence of data on adolescents who are HEU in low and middle income countries (LMICS). To understand how family and social circumstances affect their risks in LMICs, data from work related to adolescents living in HIV-affected households or with parents/caregivers living with HIV can provide useful insight. Limited research from ongoing studies in South Africa has demonstrated that adolescents of parents/caregivers living with HIV have poorer school outcomes compared with those from HIV-unaffected households.(30) Similarly, a sub-group of "dual affected" adolescents (either death of both parents due to HIV, or loss of one parent due to HIV with the second parent debilitated by advanced HIV disease) experienced the highest rates of stigma (22), demonstrating the importance of considering adolescents in the context of parental health and social wellbeing. Furthermore, economic challenges compound risk behaviors in adolescents. In a South African study, 57% of adolescent girls living with a parent with advanced HIV, who did not have enough to eat and were physically or emotionally abused, were engaging in transactional sex compared with only 7% of girls living with a parent with advanced HIV but who were not hungry or abused.(31) Supportive parenting can protect adolescents to a certain extent, but combining it with economic empowerment has shown compelling cognitive outcome gains among HIV-affected children and adolescents. (32) Furthermore, psychosocial support for bereaved adolescents has been shown to reduce mental health distress. (25) Community-based organizations providing services to HIV-affected households reported a significant reduction in adolescent-related risk of depression, stigma and behavioral problems.(33)



Another key population includes adolescent mothers living with HIV. Adolescent girls and young women aged 15 to 24 years have one of the highest rates of new HIV infections despite their relatively smaller numbers.(1) Adolescent mothers living with HIV are particularly vulnerable, experiencing significant challenges, especially with ART adherence during pregnancy, increasing the risk of perinatal HIV transmission. Until recently, these mothers have been overlooked in programmes and research although their children comprise another important HEU group.

Longitudinal evaluation of dynamic mental health outcomes will aid in understanding the needs of adolescent HEU populations as they transition into adulthood. A wide range of mental health screening tools, validated in LMICs and useful for obtaining repeated measures, are available to identify at-risk adolescents to provide efficacious interventions (34) that result in tangible mental health and psychosocial improvements. Having strong family and community support systems with access to health facilities can ensure that mothers living with HIV are equipped to cope with their own health and empowered to provide appropriate care and support to their children and adolescents who are HEU. Furthermore, transparent disclosure of parental HIV status may contribute to a reciprocally supportive relationship.

A lifespan perspective is needed for children, adolescents, and youth who are HEU, with an approach that provides applicable screening, referral for requisite services, and outcome tracking. The lack of mental health screening and management for the vulnerable population of adolescents who are HEU highlights the need for additional training of healthcare workers. Also urgently needed is a multidisciplinary approach, including the involvement of psychologists and social workers, support from healthcare workers, and non-governmental organizations with appropriate expertise, coupled with appropriate social protection for marginalized adolescents who are HEU. While mental health infrastructure should be adapted to support this population, working with families who currently have infants and children who are HEU may significantly improve mental health and resiliency of this group as they age into adolescence and adulthood.

The well-established ECD science highlights the combined contributions of the genetic blueprint, or nature, and the early care environment, or nurture, on positioning young children to achieve their developmental potential. All children need nurturing care that encompasses provision of good health practices, adequate nutrition, love, safety and security, and opportunities for early learning, all accompanied by responsive caregiving. In addition to a nurturing and stimulating environment in infancy and early childhood provided by the caregiver, optimization of ECD requires foundational elements well ahead of the birth of a child, including parental preconception health and maternal health in pregnancy.⁽³⁵⁾ Children who are conceived and grow in stable, nurturing environments are better prepared to become healthy and productive adolescents, optimizing their educational attainment, physical and mental health. The WHO's Nurturing Care Framework presents an evidence-informed approach to transforming health and human potential to exceed a goal of mere child survival, maximizing a child's ability to thrive. With a focus on the period from pregnancy to age 3 years, it proposes a roadmap of actions to create the enabling environments of policies, services, and information that are needed for every child to thrive.⁽³⁶⁾ Grounded in a multisectoral approach, the framework promotes the role of the health sector and extends responsibility to social welfare programming (e.g. cash transfer programmes), child protection services, the education sector (e.g. day care centers), and involves community stakeholders (e.g. women's groups). It recognizes the vulnerabilities of children living in HIV-affected households and promotes targeted support for children who are HEU and are not thriving through provision of home visits, cash transfers, and other social support services.

Many countries with the highest numbers of children at risk of suboptimal neurodevelopment are also those with large populations of children who are HEU, most situated in sub-Saharan Africa.⁽³⁷⁾ It is important to recognize that many HIV-affected families are vulnerable to additional challenges that prevent an environment conducive to optimal early childhood development (see Box 1). For example, poor physical and mental health of parents living with HIV may compromise responsive caregiving and opportunities for early learning of their children. Furthermore, poor parental health may result in loss of household income contributing to food insecurity and suboptimal nutrition for the child who is HEU. As infancy is a key period of brain development, suboptimal nutrition, poor health, and reduced caregiver-infant interactions can contribute to preventable developmental delays.

In a number of HIV high-burden countries, more than 1 in 10 children are HEU, with that number exceeding 30% in some countries.⁽¹⁾ Empowering both caregivers of children who are HEU and families affected by HIV to provide the nurturing care that optimizes the development of their children is a valuable investment in human capital. Targeted interventions must not be confined to children with HIV, but should be adapted and applied to the growing number of children who are HEU. There is an opportunity to use the Nurturing Care Framework to strengthen existing services providing care to infants who are HEU, such as the HIV programme's Early Infant Diagnosis (EID) visits or well-child health sector encounters for immunizations and/or growth assessments. These services can be strengthened and augmented with attention to maternal mental health issues, as well as children with poor growth and development. Health sector personnel are well-positioned to identify at risk infants and educate caregivers on age appropriate stimulation, communication, and play to improve caregiver-child interactions. Additionally, health sector personnel can serve as facilitators, ensuring that parent-infant dyads receive the support and interventions needed to optimize developmental outcomes. Examples of infants who are HEU at highest risk of developmental disparities include those born preterm or small-for-gestational age, those experiencing nutritional deficits, as evidenced by stunting, wasting or being underweight-for-age, or those cared for by women experiencing mental health challenges.

A pilot study has been conducted in selected Malawian public sector outpatient clinics to assess the feasibility and acceptability of incorporating ECD activities, including the Nurturing Care Framework, into existing programs that provide lifelong ART to any pregnant or breastfeeding WLHIV, termed "Option B+" by WHO guidelines. Mother-infant pairs participating in Malawi's national Option B+ program during pregnancy and attending EID clinics in the postpartum period were eligible for inclusion in the pilot study. For women or caregivers queueing for routine clinic appointments, long waiting times provided opportunities to offer training in responsive caregiving practices, a foundational element of ECD. This training was offered monthly to enrolled women over nine consecutive months. Healthcare providers and trained expert clients conducted Responsive Caregiving sessions with components of WHO's Nurturing Care Framework incorporated into group teaching sessions, focusing on appropriate caregiver-infant play, infant stimulation, and communication. The promoted activities were simple, could occur in any setting including the home, and did not require additional resources or money (e.g. homemade toys, storytelling, and singing). Women perceived

a decrease in waiting time for EID and ART services, appreciated the opportunity to access multiple services during a single visit, and demonstrated high retention of HIV care three months after the final session. Having been found feasible and acceptable to both healthcare workers and participants, it is being further adapted to include a community component staffed by community health workers. This pilot established that existing health encounters with infants and children who are HEU can be used provide a viable venue to model nurturing care and educate caregivers.

CONCLUSION

The 4th HEU Child and Adolescent Workshop explored psychosocial exposures and mental health outcomes of adolescents who are HEU and considered practical opportunities to protect today's infants and children who are HEU against these exposures through the WHO's Nurturing Care Framework. In a nurturing environment, the psychosocial challenges of growing up in an HIV-affected household can foster resilience, equipping adolescents and youth to successfully transition through adult milestones. However, inadequate nurturing in early childhood and psychosocial stressors during adolescence contribute to physical and mental vulnerability among children and adolescents. Awareness is required that children and adolescents who are HEU are more likely than their HIV-unexposed counterparts to experience psychosocial stressors. Mental health screening and intervention services must be prioritized for adolescents and youth who are HEU, especially in LMICs (see Box 2). Equally important are interventions that support nurturing care earlier in the lives of children who are HEU. The Nurturing Care Framework provides necessary structure and promotes multisectoral involvement for optimizing the development of all children, but is particularly applicable to the development of the vulnerable population of children who are HEU. Integrating the Framework into established health infrastructure, including existing HIV and child health programs, represents a logical next step and is aligned with the United Nations' Sustainable Developmental Goals. Advocacy for greater investment in neurodevelopmental support for this vulnerable population should not be neglected, particularly in countries where over 10% of children and adolescents have been exposed in utero to HIV and ARVs, and are living in HIV-affected households. Proactive multidisciplinary support for this group will benefit the overall prosperity and stability of nations in the decades to come.

A PROFILE OF CHALLENGES WITHIN AN HIV-AFFECTED HOUSEHOLD

Imagine learning of your new HIV diagnosis when you are pregnant with your first child, a girl. You are initially so sick from HIV shortly after delivery that you cannot hold your child or provide the nurturing care needed to optimize her development. Over the first year after delivery, your health is improving as you have accessed antiretroviral treatment (ART). At the same time, your firstborn child, after experiencing multiple illnesses, is diagnosed with HIV. In one of your daughter's many hospitalizations, you have the first real opportunity to bond with her and provide nurturing care. At the time, your daughter's HIV disease state does not qualify her for ART under prevailing national guidelines. However, as she approaches the age of 4 years, her HIV disease state worsens. At the same time, you learn you are pregnant with your second child. By the time you give birth to your second child, you are so focused on the declining health of your first child that you do not have sufficient opportunity or energy to bond with your second child. Fortunately, your first child gains access to ART and is returning to better health as your second child reaches his first year of life. However, you notice that your second child has been experiencing repeated infections and is slow to speak. Concerned, you repeatedly have him tested for HIV until he is 4 years of age. Finally, you are admonished by a health care worker to stop subjecting your child to needle sticks. After all, the health worker impatiently explains, he is HIV-uninfected. This is the story of Clara Banyu, a Community Advisory Board member for the Coalition for Children Affected by AIDS and a vocal advocate for women living with HIV and their family members. During a panel discussion, Clara provided a detailed depiction of the challenges experienced in households affected by HIV. Clara's experience, including her encounters with the health system, clearly identify gaps in supporting parents living with HIV and their children. While this is Clara's personal story, many other households have similar experiences that are contributing to health and development outcome disparities among children who are HEU.

Finally, advocates have been successful in introducing person first language to refer to individuals living with HIV and this has had traction in the global community of researchers, care providers and government sectors. A similar challenge is needed for the pediatric population exposed to HIV who are uninfected. We have opted to use person first language in this publication, but it will be important to engage with community members globally to identify the person first terminology that is least stigmatizing while allowing for identification of this important population, some of whom will need additional support to thrive.

ACTION PLAN TO OPTIMIZE OUTCOMES ACROSS THE LIFE-COURSE FOR CHILDREN AND ADOLESCENTS WHO ARE HIV-EXPOSED UNINFECTED

Action plan to optimize outcomes across the life-course for children and adolescents who are HIV-exposed uninfected

1. RESEARCH INVESTMENTS:

- A.** Identify biological and social-structural mechanisms for observed developmental disparities in children and adolescents who are HEU, particularly in low and middle-income countries, to inform the design of feasible interventions
- B.** Develop contextually-appropriate adolescent-informed interventions to support mental health and psychosocial wellbeing of adolescents who are HEU
- C.** Qualitative research with families affected by HIV to understand their thoughts, feelings and concerns regarding long-term monitoring and identification of children and adolescents HEU

2. HEALTH SERVICE INTEGRATION AND STRENGTHENING:

- A.** Incorporate the existing WHO Nurturing Care Framework into programs currently providing care to HEU infants, such as Early Infant Diagnosis Programs or well-child health sector encounters
- B.** Integrate support of children who are HEU into comprehensive maternal-child health services to address HIV-specific and general vulnerabilities common to all maternal-child pairs, particularly in low and middle-income countries, without stigmatizing HIV-affected families
- C.** Within emerging adolescent health services, promote the utilization of existing screening tools to identify adolescents who are HEU in need of additional psychosocial support

3. NATIONAL MONITORING STRATEGIES:

- A.** Develop standardized national program monitoring, disaggregating child and adolescent HEU data from that of those living with and those without HIV exposure, such that monitoring tools inform local and global policy and programming
- B.** Design and test strategies to identify and track children who are HEU beyond infancy into adolescence, so that longer-term care and support can be provided as needed

CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

AUTHOR CONTRIBUTIONS

GE, WJ, AS and KP drafted the initial manuscript and they all worked to edit it. Co-authors suggested changes which were taken into consideration. SL, BD, AS, UF, EU, CB, SE, LS, SM, AG, AB, CM, LC, DB and MV all critically reviewed the manuscript and provided important edits. The final draft of the manuscript was prepared by GE.

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