

**Learning Seminar: HIV Exposed Children and Early Childhood Development**  
UCLA Luskin Conference Center  
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**Opening Remarks and introductions**

**Thomas J. Coates, UCLA David Geffen School of Medicine**

Despite the success of peri- and post-natal HIV transmission programs in sub-Saharan Africa, the population growth in this region means more mothers living with HIV, with more infants exposed to HIV. With the growth in the region ECD becomes even more important for the future.

**Lisa Bohmer, Hilton Foundation**

This seminar highlights the importance of a multidisciplinary discussion, gathering experts from different disciplines. Both HIV and ECD are strategic interests of the Hilton Foundation and the Foundation welcomes the opportunity to support this seminar.

**The Nurturing Care Framework and the Conrad N. Hilton Foundation Initiative for Young Children Affected by HIV and AIDS**

**Lisa Bohmer**

Background on Conrad N. Hilton Foundation (the Foundation) and the Young Children Affected

by HIV and AIDS Initiative The Foundation's support for this strategic area began in 2012 to support a "thrive" agenda in recognition of the multiple threats to healthy growth and development that HIV and AIDS poses. The Foundation's focus countries are Kenya, Malawi, Mozambique, Tanzania and Zambia. They are currently supporting efforts to field test approaches to improve caregiving and child development outcomes as part of health systems and within local communities, with focus on areas with high HIV prevalence.

The initiative has responded to recent developments in both brain science and HIV and AIDS, bringing in early childhood programming earlier than traditional pre-school efforts to address the first thousand days when development is most rapid. Importantly, the Foundation collaborated on the Lancet 2016 Special Edition on *Advancing Early Childhood Development: from Science to Scale* (<https://www.thelancet.com/series/ECD2016>) in an effort to encourage the health sector to do more to foster the healthy growth and development of young children.





Nurturing Care Framework (NCF) see *summary document included in folder*. Launched in 2018 by the World Health Organization and partners, the NCF emphasizes that ECD efforts must begin in the earliest years- from pregnancy to age 3- and how nurturing care is critical for enabling children to reach their full potential. Nurturing care includes health, nutrition, early learning, responsive caregiving and safety. Within the NCF the Foundation’s programming largely focuses on the least understood elements of responsive care giving and early learning, and addressing the needs of children *and* care givers. Next steps in the NCF include developing operational guidance and policy briefs, including HIV. The Foundation will be also be involved in developing recommendations for priority implementation research questions.

Discussion: The NCF approach recognizes the importance of multi-sectoral approaches towards broadening HIV treatment services to include the new elements of early learning and responsive caregiving. The Coalition of Children Affected by AIDS advocates for a holistic approach, within the context of people’s lived experiences. Meeting participants recognized the complexities of reaching HIV affected people who remain un-reached for a variety of reasons, noting that people living with HIV have multiple vulnerabilities and challenges – including poverty and stigma. Mental health issues impact caregiving as well: these need to be better understood and tackled. Specific cultural contexts and norms have an important effect on engaging those affected by HIV. Substance abuse and HIV share many similarities, including stigma and impact on children. One of the benefits noted of integrating approaches (ECD and HIV) is that by combining services there are often bi-directional benefits. For example, by adding parenting support to HIV treatment programs, children benefit and caregivers may find the health services more user-friendly, leading to better retention in care. Increased involvement of men has also occurred when ECD is integrated into HIV/ ART programming. It was noted that integrated programming, while effective for many reasons, including cost effectiveness, can be a challenge when trying to conform to inflexible funding streams. Perhaps with an enhanced focus on data and impact, funders would be more open to supporting integrated approaches.

**The Evolving Epidemiology of HIV Exposed Uninfected Children** (*see presentation*)

**Kathleen Powis, Harvard Medical School and Amy Slogrove, Stellenbosch University**

1. HEU children in global context: 2018 UNAIDS estimates: 14.8m HEU children globally (0-14 years of age) in 2017, 90% in sub Saharan Africa; 5 countries where 50% of HEU children live. Increase in HEU children from 2000-2017, often exceeding background population growth.<sup>1</sup>



2. HEU child risk factors: Universal: household pathogens (for example TB), prematurity (ART increases risk of premature birth); sub optimal breastfeeding practices; maternal health; poverty. Unique: exposure to HIV, exposure to ART, mother’s immune system compromised translating to compromised immune system of infant. Note that there are many variations in HIV and ARV exposure among HEU children. Dolutegravir related neutral tube defects brought attention to ART safety in pregnancy.<sup>2</sup> In high HIV burden countries (Botswana, Eswatini, South Africa) at least one in five children are exposed to HIV *in utero* and an increasing proportion are also exposed to antiretroviral drugs.



3. HEU child outcomes- current evidence: Three meta analyses demonstrate elevated mortality in HEU children in first 2 years of life which does not decline over time despite expanding ART, improved maternal health and safer breastfeeding.<sup>3-5</sup> Using HEU infant mortality data from research studies in Botswana and South Africa in 2013 prior to the availability of ART for all women living with HIV, modeling demonstrated  $\geq 15\%$  of mortality in the population of all HIV-uninfected infants, both those exposed to HIV *in utero* and those born to HIV-uninfected women, is associated with the excess mortality experienced by HEU infants.<sup>6</sup> For women on Efavirenz based ART impacts include low birth weight, preterm birth and subsequent impact on infant development. There is a 40% increased risk of preterm birth when conceiving on ART compared to initiating ART during pregnancy, even now that women are starting ART in a healthier state and using safer ART regimens.<sup>7</sup> While maternal ART use is imperative as one strategy in efforts to eliminate infant HIV acquisition, work is needed to identify ART regimens with the highest efficacy in blocking transmission and the lowest adverse effect profile in the short and long term for the mother, pregnancy and child. Furthermore, we are approaching a new potential safety issue with the promotion of pre-exposure prophylaxis (PrEP). Since pregnant women are eligible for PrEP, we need to monitor the effects of exposure to ARVs on infants born to women taking PrEP in pregnancy. HEU Child Anthropometrics (growth)- In a South African cohort of breastfed infants where all women living with HIV received antiretroviral treatment in pregnancy, HUU infants born with a birth weight < the 10<sup>th</sup> percentile for gestational age, also known as small for gestational age (SGA), were noted to have a weight that was appropriate for age by the first year of life.<sup>8</sup> In the same cohort, HEU infants born SGA did not achieve catch up growth by one year of life, suggesting a fetal insult to growth with long term implications.<sup>8,9</sup> Stunting is a strong marker for poor later life outcomes. We need to take a closer look at who the HEU children are at risk of these adverse outcomes.

SHINE study initial outcomes: Water, Sanitation and Handwashing (WASH) and nutrition interventions were employed in a community clustered randomized trial. In the SHINE study, *combined* nutrition and WASH normalized HEU neurodevelopment.<sup>10</sup> At 18 months of age less than 50% of HEU children were alive, HIV free and non-stunted (alive and thriving).<sup>11</sup> Significant differences in gross and fine motor and language skills but not social or behavioral performance at 24 months were noted in HEU compared to HUU infants, even after adjusting for social factors such as marital status, age or substance abuse.<sup>9</sup> There is some data to indicate less protective effect of breast milk among women living with HIV compared to women without HIV.<sup>12,13</sup> However, further research is underway in the SHINE study, evaluating breast milk quality by maternal HIV status. Additionally, the SHINE study team is investigating child gut microbiome and how it might affect immune system phenotype or function. A Belgian study demonstrated that initiation of ART before pregnancy may reduce infectious morbidity risk in HEU infants; ART *in utero* exposure at a period after conception in this study of formula fed infants was found to be associated with a higher risk of hospitalization in the first year of life among HEU infants.<sup>13</sup> whereas rates of hospitalization among HEU infants exposed to ARVs from conception and HUU infants did not differ.

A high priority is the need to address preterm birth risk: we need to understand *in utero* mechanisms of this risk to find the safest ART regimen.

4. The long-term view: Most sub Saharan countries have developed sound programming in recognition of the concept and importance of “the first 1000 days of life”. However, the long term outcomes of *in utero* antiretroviral exposure are not being systematically tracked. For example, we have no idea of the impact of exposure to antiretrovirals on the reproductive system of the female fetus. Potential generational effects as those seen with diethylstilbestrol (DES) use in



pregnancy would be devastating at an individual and population level. There is an urgent need to track generational impact through a life span approach, including social factors. Of note is that the fetus is potentially impacted by many detrimental exposures *in utero*: maternal smoking, alcohol, obesity, TB/ TB treatment, ARVs, HIV, nutrition, and maternal mental health. We need to help Ministries of Health, researchers and implementers to recognize these important factors and create urgency for monitoring and measuring longer term outcomes to tease out the relative impact of these exposures.

In conclusion, the evidence we have to date underscores the need to ensure that HEU children are not left behind or overlooked as HIV programming advances.

### Parent-Child Interactions and Child Development

#### Catherine Sandhofer, UCLA Department of Psychology

There are three main developmental areas in parent or care giver/ child interaction: social emotional health, cognition, and language. Language: early studies indicated a 30 million word gap between children from “welfare” families and “professional class” families- noting some study difficulties with cultural and socio-economic issues. Implementers need to be aware of cultural preferences in language: there can be more number talk to boys than girls, or whether adults directly address a child.



Emphasizing age appropriate talk is important, as is role modeling for mothers, health care workers, and care givers. Explaining how communication is part of the child’s overall health is critical, making use of relevant cultural practices. These skills are competing within a higher level priority of survival so implementers should strive to make these skills relevant to the future of the child. There is a need to not only focus on the absence of speech but to address *harmful* speech, which is often overlooked. Retention is key: it is important to

note recollection of what the child hears, not just hearing overall. Pay attention to timing- vary efforts from all at once to spaced across time, and expanding; be aware of contextual variability: input from different people, in different places, and various activities around the child.

### UCLA's Integration of Early Childhood Development into ART Delivery in Malawi

#### Kate Dovel and Laurie Bruns, UCLA David Geffen School of Medicine

The average time spent seeking one ART service appointment in Malawi is 5 hours – this presented an opportunity to engage Option B+ HIV positive women in ECD while they wait for routine HIV care. In the pilot phase of the Option B+ / ECD program, 197 mother-infant pairs were enrolled. Participants were provided with monthly group ECD sessions at health facilities while waiting for ART services over a 9-month period. Initial outcomes: mothers felt supported through group work, and felt clinics treated them better - “as a human”.

Phase II of the program is currently being implemented in health facilities through existing community ART support workers (Expert Clients) who provide ECD / maternal ART services for HIV positive mothers during routine HIV care visits. We aim to enroll 500 mother-infant pairs.





Several challenges have been identified during the implementation of Phase II: (1) ECs tend to tell mothers what to do, but we want to help them start encourage mothers in nurturing behaviors; (2) Expert Clients prioritize routine ART activities over ECD; (3) and there are unique challenges with an evolving ART program and differentiated ART delivery models (e.g., longer refill periods, community based distribution). One of the innovations of this ECD program is the collection of bidirectional data: looking for improved ART retention and adherence in relation to the understood benefit of ECD on infant development and long term outcomes.

### Discussion points from participants

- *Is ECD trauma informed?* Work has been done on *in utero* exposure to drought, famine, and other insults in relation to later life impacts (test scores, wages, employment). These factors need to be considered when evaluating overall impacts on HEU children.
- *How much should we focus on provider behavior change versus caregiver behavior change?* Need to invest in both. Bidirectional- can be mutually reinforcing but in resource limited settings, service providers themselves have their own life challenges so we can expect that behaviors will vary widely. Caregivers listen to what nurse tells them to do so very important to target health care provider.
- *Implementation and technology:* Need to recognize that mobile phones can be a resource to integrate care delivery into a patient experience and interaction. Prompt and guide service delivery mobile services already exist, generating monitoring data, and potential to guide screening priorities. The ultimate aim is to ensure continuous quality improvement and to task shift using technology, using data to inform priorities at service delivery level (provider/patient level). Used appropriately technology can provide immediate *actionable data* available to the health care provider to trigger improvements. The goal would be not to replace human interaction but to enhance it.
- *Challenges presented by funders to meet targets:* smaller learning projects have more flexibility and may lead to standard of care outcomes. We need to document how the program is affecting people: what are their stories?
- *How do ART medications affect children's dental health?* 70% of children have early childhood caries. There is a need to advocate for awareness and research in this area.
- *Depression in perinatal context impacts early childhood development:* there are limited human resources in sub-Saharan Africa to address depression. A Rand Corporation study will train peer mothers to implement structured problem solving therapy with HIV positive mothers. The study will look at impact on mothers and infants in Uganda.
- *Stigma* affects self esteem which in turn affects parenting. There is a Rand program in Uganda to empower people living with HIV to discuss HIV in the community. There are also studies on internalized stigma and disclosure aiming for community level change. Multiple stigmas – including substance abuse, intersectionalities, require a layered approach.

### Closing Remarks

#### Thomas J. Coates and Lisa Bohmer

Aside from viral suppression and ART retention data, we must reorient our programs to acknowledge that we are working with human beings navigating stressful environments- with a human centered approach.

In years from birth 0-2, we are dealing with multiple generational effects. We need to program with an awareness of population growth and an understanding of access to technology. As we



modify an initial focus on preventing vertical HIV transmission and helping mothers live longer we recognize that there are numerous, complex factors that affect long term outcomes and strive to better support both caregivers and young children – including the growing population of children that are born HIV exposed but uninfected. We must also recognize that our work is within health systems struggling to cope and that are not patient centered and that strengthening these systems is a critical piece of the puzzle.

Despite the challenges, important new data is emerging and must inform our implementation and research efforts going forward. We need to think more holistically, using scientific data and recommendations, such as those contained in the Nurturing Care Framework, to test more human centered service delivery models in real world settings. This learning session has brought together a number of the critical dimensions we need to keep in mind as part of these efforts.

#### Endnotes from Powis/ Slogrove presentation:

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