Infants, young children and adolescents:

Missing voices in the HIV epidemic

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Global Plan

Towards Elimination of new HIV infections among children and keeping their mothers alive

Number of new infections among children:
By May 2012: 292,500 New infections (-25%)
By 2015: 39,000 New infections (-90%)
Towards elimination of new HIV infections among children

- Infants born with HIV, children & adolescents growing up with HIV
- HIV- and ARV- exposed uninfected children
## HIV infection in women and children -2010

<table>
<thead>
<tr>
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<th>Global</th>
<th>Sub-Saharan Africa</th>
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<tbody>
<tr>
<td>Number of women living with HIV</td>
<td>16.8 million</td>
<td>13.8 million (82%)</td>
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<tr>
<td>Number of pregnant women living with HIV</td>
<td>1.48 million</td>
<td>1.37 million (93%)</td>
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<tr>
<td>Number of children living with HIV</td>
<td>3.4 million</td>
<td>3.1 million (91%)</td>
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<tr>
<td>Number of children newly infected with HIV</td>
<td>390,000</td>
<td>350,000 (90%)</td>
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<tr>
<td>Number of children dying from HIV</td>
<td>250,000</td>
<td>230,000 (92%)</td>
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Percentage of children living with HIV receiving antiretroviral therapy in low- and – middle income countries 2005, 2009, and 2010

Key challenges in the cascade of testing to treatment

1. Identify and test exposed infant
2. Provide results & guide through test algorithm
3. Enroll positives in ART Clinic
4. Retain alive in care/treatment

Exposed infants never tested
Exposed infants tested
Positive infants never received results
Positive infants receiving results were never enrolled into care
Positive infants in care & treatment were lost
Positives alive
Potential causes of loss

- Weak health system
- Limited human resource capacity
- Poor referral system (between PMTCT, EID, ART programmes)
- Lack of opportunities to capture infants outside formal health facilities
- Poor documentation and tracking systems
- Lack of point of care diagnostics
  - Few laboratories with PCR capacity
  - Lack of trained staff
  - Long turnaround times
- Poverty
- Distance to health facility
- Stigma & Discrimination

Modified slide from Charles Kiyaga
Infant testing in the first 2 months of life (2008)

Less than one half of infants ever tested via EID across these four countries were tested in their first two months of life. Coverage of the optimal service (early testing) is consequently even lower.

Portion of HIV Exposed Infants in Need Receiving EID Service in First Two Months of Life

Lost opportunities: PMTCT follow up appointments, vaccination schedule

Courtesy of Chewa Luo, UNICEF
Fragmented pediatric ARV market

*risky and difficult to sustain*

- The pediatric market is relatively small (~450,000 patients)
- Further fragmented into sub-groups by age and weight bands
- Slow transition to new products further fragments volumes

- Lack of Production
- Lack of registration
- Reluctance to invest in research

Source: CHAI, adopted from Joanna Sickler’s slide
Clinical Management Concerns When Treating HIV-Infected Children

<table>
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<tr>
<th>Area</th>
<th>Management Issues Requiring Research</th>
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<td>Neurocognitive development</td>
<td>Children with HIV accelerate their neurologic development after starting HAART, but they do not catch up with other children. Neurocognitive development in HIV-exposed but uninfected children is also below normal and needs further study. The socioeconomic and medical reasons for residual developmental delay in HAART-treated children remains to be delineated.</td>
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<tr>
<td>Bone growth</td>
<td>HAART in general, as well as specific antiretroviral agents, has been associated with subnormal bone mineral content. Children may be especially vulnerable to these effects. A major confounding factor is the worldwide deficiencies in calcium and vitamin D.</td>
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<td>Metabolic abnormalities</td>
<td>HAART initiation is associated with decreases in inflammatory cytokines. Children on HAART nevertheless experience high rates of fat wasting, insulin resistance, dyslipidaemia and hyperlactataemia. High cholesterol levels may lead to cardiovascular disease, but aggressive lipid management is lacking in children.</td>
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<tr>
<td>HIV/TB coinfection</td>
<td>Concurrent HAART improves the response to TB therapy, but TB therapy can have negative effects on HAART effectiveness and toxicity. Drug-drug interactions and overlapping toxicities pose challenges to concurrent treatment of HIV and TB. Pharmacokinetic data on the drug-drug interactions are sparse in children. Data on management of TB and malnutrition, extrapulmonary disease, drug resistance and IRIS in children are very limited.</td>
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<td>HIV/Malaria coinfection</td>
<td>HIV’s effect on childhood malaria is unclear. There is only limited paediatric data on PK and toxicity interactions between antiretroviral and antimalarial agents. Some HAART components may be active against malaria, but this requires further study.</td>
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<td>Malnutrition</td>
<td>Malnutrition may interfere with absorption of HAART drugs. Malnourished children have relatively poor outcomes after initiating HAART, but there are no long-term data in this area. Researchers have not developed optimal antiretroviral/nutritional strategies for malnourished children.</td>
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HIV- and ARV- Exposed Uninfected children

Every year, approximately 1.5 million babies are born to HIV-positive mothers around the world.

In Southern Africa, an estimated 300,000 HIV-Exposed but Uninfected (HEU) infants are born annually.

Source: Global Health Magazine
TABLE 2. Summary of Potential Adverse Effects of In Utero Antiretroviral Exposure in HIV-Exposed but Uninfected Children

**Birth Defects**
Sample size to date can only rule out very large increase in risk of neural tube defects with first-trimester EFV exposure.
Larger numbers with first-trimester exposure are needed to rule out for rare outcomes such as neural tube defects.
Available data for other commonly used antiretroviral drugs suggest lower defect rates similar to a background rate of 2%-3%.

**Premature Delivery, Low Birth-Weight**
Mixed results regarding association with in utero antiretroviral exposure possibly due to a large number of confounding factors that are uniformly measured, including the timing of antiretroviral drug initiation.
Some data suggest elevated prematurity risk with antepartum combination antiretroviral regimens, particularly if protease inhibitor based.
Fewer data suggest association of combination regimens with lower weight.

**Mitochondrial Toxicity**
Severe, clinically evident mitochondrial diseases secondary to in utero antiretroviral exposure are likely to be rare.
Further studies are needed that account for confounding factors, in particular maternal disease severity.

**Hematologic Abnormalities**
Transient anemia is frequent and more severe with in utero exposure to combination-drug regimens but generally resolves by the age of 3–6 months.
Small but persistent abnormalities in neutrophil and/or lymphocyte cell count with in utero antiretroviral exposure have been observed in studies from multiple geographic locations and seem to be more severe with in utero exposure to multiple drugs.
Clinical relevance of abnormalities is unclear but may be providing biomarker suggesting potential long-term effect of antiretroviral drug exposure.

**Growth and Development**
Mixed data on effect of in utero exposure to combination drug regimens on growth; effect, if exists, seems transient.
Very limited studies on neurodevelopment suggest that more advanced maternal disease may be an additional important confounder.

**Malignancies**
Limited data are reassuring regarding the risk of malignancy in the short term (to age <5–10 years).
No reports with follow-up into adolescence or young adulthood, when the effect on promotion of malignancies may be more likely to be observed.
Adolescence is tough
(irrespective of HIV)

A complex set of psychosocial, cognitive, physical, behavioral changes during adolescence

- Higher rate of virological failure in HIV+ adolescents (cmp young adults) in SA (Nglazi et al 2012)
- Differences in perinatally and sexually infected adolescents (Nglazi et al 2012)
- Limited knowledge about HIV, ARVs and hormonal changes during puberty (SEX/GENDER DIFF)
Community = ”Unit of Solution”
(Hawe 1994)

”The idea of community intervention is propelled by the concern to reach as many people as possible and make the best use of scarce resources”

Communities have the potential and the competence to deliver programmes that are relevant, appropriate, and culturally sensitive to safeguard sustainability and diffusion.
The Role of Community

• **Advocacy**
  – Investment in research and development
  – Routine monitoring of psychological and physical development of HIV+ and HEU children and adolescents

• **Community-Based Programmes**
  – Integration of prevention, treatment and care support in existing services
  – Family-centered and family-based approaches to improve recruitment, adherence and retention
  – Task-shifting and task-sharing (**Role of men**)

• **Community-Based Research**
  – Community to be more engaged in research to improve prevention, treatment and care
Acknowledgement

- Yannis Mameletzis
- Chewe Luo
- Charles Kiyaga
- Joanna Sickler