Inequality in outcomes for adolescents living with perinatally-acquired HIV in sub-Saharan Africa:

a Collaborative Initiative for Paediatric HIV Education and Research (CIPHER) cohort collaboration analysis

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for the CIPHER Cohort Collaboration Adolescent Project Team

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Disclosures

The authors have no conflicts to declare
Global analysis of 38,187 adolescents living with perinatally-acquired HIV (APH)

30,296 (79%) sub-Saharan Africa

2-4 x greater mortality hazard
• Home to 80% of the 1.8 million adolescents living with HIV
• 14/15 countries with the highest burden of adolescent HIV
• Progress in diagnostic and treatment interventions not uniform across the continent
• Younger adolescent AIDS-related deaths starting to decline in some countries, but continue to rise in others
Primary Objective

Compare characteristics and outcomes (mortality, transfer out, loss to follow-up) of APH by country income group (CIG) in sub-Saharan Africa

Definitions

• APH – entered care before age 10 years, with no known non-vertical route of HIV-infection and were followed beyond age 10 years (survived beyond age 10 years)

• Lost to follow-up (LTFU) – last contact >365 days prior to database closure; censored 365 days after last visit
Methods

• CIPHER Global Cohort Collaboration
  – Pooled individual retrospective data from 12 cohort networks

• This sub-Saharan Africa analysis: 25 countries represented by 7 networks
  Baylor International Pediatric AIDS Initiative (BIPAI)
  International Epidemiology Databases to Evaluate AIDS (IeDEA)
    IeDEA - Central Africa
    IeDEA - East Africa
    IeDEA - Southern Africa
    IeDEA - West Africa
  Médecins Sans Frontières (MSF) Pediatric Cohorts
  Identifying Optimal Models for Care in Africa (Optimal Models ICAP)
Methods

• Characteristics compared by Country Income Group (CIG)
  – at first visit, ART start, age 10 years and last visit
• World Bank CIG designation for median year of first visit
  – low, lower-middle, upper-middle income
• Cumulative incidence for outcomes calculated by competing risks analysis (mortality, transfer out, loss to follow-up)
• Mortality hazard ratios - Cox proportional hazards models
APH in sub-Saharan Africa by Country Income Group

Total APH
N=30,296

Low Income
N=22,925 (75.7%)
20/25 countries

Lower-Middle Income
N=1,386 (4.6%)
3/25 countries

Upper-Middle Income
N=5,985 (19.8%)
2/25 countries

78,619 person-years of adolescent follow-up
Birth Cohort

All APH
64% born ≥2000
Range 1990-2005

Low Income
65% born ≥2000
Range 1991-2004

Lower-Middle Income
65% born ≥2000
Range 1996-2004

Upper-Middle Income
57% born ≥2000
Range 1990-2005
Age in Years
Median (IQR)

<table>
<thead>
<tr>
<th></th>
<th>First Visit</th>
<th>ART Start</th>
<th>Last Visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>L</td>
<td>7.3 (5.5; 8.7)</td>
<td>8.1 (6.3; 9.5)</td>
<td>12.0 (10.9; 13.7)</td>
</tr>
<tr>
<td>LM</td>
<td>7.2 (5.7; 8.6)</td>
<td>7.8 (6.2; 9.3)</td>
<td>12.1 (10.9; 13.8)</td>
</tr>
<tr>
<td>UM</td>
<td>6.6 (4.3; 8.4)</td>
<td>7.3 (5.2; 8.9)</td>
<td>12.4 (11.0; 14.3)</td>
</tr>
</tbody>
</table>
CD4 Count in cells/µl
Median (IQR)

Mean (95% CI) CD4 change ART Start – Last Visit:
- Low: 295 (286; 303) cells/µl
- Lower Middle: 463 (440; 486) cells/µl
- Upper Middle: 353 (338; 367) cells/µl

<table>
<thead>
<tr>
<th></th>
<th>First Visit</th>
<th>ART Start</th>
<th>Age 10</th>
<th>Last Visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>418 (211; 721)</td>
<td>310 (165; 520)</td>
<td>652 (414; 947)</td>
<td>668 (434; 945)</td>
</tr>
<tr>
<td>LM Low</td>
<td>391 (221; 616)</td>
<td>292 (174; 417)</td>
<td>707 (479; 972)</td>
<td>735 (532; 985)</td>
</tr>
<tr>
<td>UM Low</td>
<td>361 (172; 662)</td>
<td>318 (162; 558)</td>
<td>719 (475; 1006)</td>
<td>729 (523; 971)</td>
</tr>
</tbody>
</table>
WHO Height-for-Age Z-score

Median (IQR)

Mean (95% CI) HAZ change ART Start – Last Visit:
- Low: 0.16 (0.14; 0.18)
- Lower Middle: 0.04 (-0.10; 0.02)
- Upper Middle: 0.44 (0.40; 0.49)
Outcomes
Cumulative Incidence (95% CI)
By Country Income Group

<table>
<thead>
<tr>
<th></th>
<th>Low Income</th>
<th>Lower Middle Income</th>
<th>Upper Middle Income</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality (%)</td>
<td>3.5 (3.1; 3.8)</td>
<td>3.9 (2.7; 5.4)</td>
<td>1.1 (0.8; 1.4)</td>
</tr>
<tr>
<td>Transfer out (%)</td>
<td>17.5 (16.8; 18.3)</td>
<td>27.5 (24.2; 31.0)</td>
<td>23.7 (22.4; 25.1)</td>
</tr>
<tr>
<td>LTFU (%)</td>
<td>13.1 (12.4; 13.8)</td>
<td>8.3 (6.3; 10.6)</td>
<td>14.1 (12.9; 15.3)</td>
</tr>
</tbody>
</table>
## Survival Analysis

### Hazard Ratio (95% CI)

<table>
<thead>
<tr>
<th></th>
<th>Low Income</th>
<th>Lower Middle Income</th>
<th>Upper Middle Income</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Unadjusted HR</td>
<td>3.05 (2.27; 4.09)</td>
<td>3.57 (2.30; 5.54)</td>
<td>Reference</td>
</tr>
<tr>
<td>2. Adjusted* HR</td>
<td>3.75 (2.02; 6.95)</td>
<td>3.74 (1.80; 7.78)</td>
<td>Reference</td>
</tr>
<tr>
<td>3. Adjusted* HR</td>
<td>2.50 (1.85; 3.37)</td>
<td>2.96 (1.90; 4.61)</td>
<td>Reference</td>
</tr>
<tr>
<td>4. Adjusted HR#</td>
<td>2.67 (1.94; 3.67)</td>
<td>3.07 (1.91; 4.95)</td>
<td>Reference</td>
</tr>
</tbody>
</table>

* Adjusted for baseline characteristics – gender; age, CD4 count-, WAZ-, HAZ- at first visit; birth cohort; on ART ever

# Adjusted for baseline characteristics – gender; age, CD4 count-, WAZ-, HAZ- at first visit; birth cohort
Conclusions

- The current generation of APH in SSA largely experienced improvement in immune status and growth despite starting ART at an advanced age.
- Even when receiving ART, inferior growth improvement and higher mortality was seen in Low & Lower Middle Income compared to Upper Middle Income Countries.
- Limitation: differences in outcomes by CIG may represent differential mortality ascertainment and the type of cohorts in each CIG (routine care vs. centres of excellence) rather than inequality according to CIG.
Next Steps

→ Detailed growth analysis planned

→ A better understanding of outcomes in APH that are not retained in care is needed to appropriately compare and interpret estimates of mortality

→ Value in ongoing cohorts of APH to understand the changing population of adolescents living with perinatally-acquired HIV
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