The global epidemiology of perinatally HIV-infected adolescents:
a Collaborative Initiative for Paediatric HIV Education & Research (CIPHER) Global Cohort Collaboration analysis

Amy Slogrove, Ali Judd, Valeriane Leroy for the CIPHER Global Cohort Collaboration Adolescent Project Team

AIDS 2016, Durban, South Africa
Background

- Global access to antiretroviral therapy (ART) is expanding
- Emerging population of perinatally HIV-infected adolescents (PHA) across all regions
- HIV-infected adolescents face barriers compared to adults
  - Access to ART
  - Remaining in care
Objective & Definitions

Primary Objective
Describe the global epidemiology and geographic trends of characteristics and outcomes (mortality, transfer out, loss to follow-up) of PHA surviving beyond age 10 years

Definitions

- PHA – entered care before age 10 years, with no known non-vertical route of HIV-infection and were followed beyond age 10 years
- Lost to follow-up (LTFU) – last visit >365 days prior to database closure; censored 365 days after last visit
Methods

- CIPHER Global Cohort Collaboration
- Individual retrospective data from 12 cohort networks were pooled, representing 50 countries
  - South America & Caribbean: CCASAnet
  - North America: IMPAACT & PHACS
  - Europe & Central Asia: EPPICC
  - South & Southeast Asia: EPPICC, IeDEA - Asia-Pacific, MSF
Methods

- Characteristics at first visit, ART start, age 10 years and last visit
- Cumulative incidence for outcomes calculated by competing risks analysis (mortality, transfer out, loss to follow-up)
- Mortality hazard ratios - Cox proportional hazards regression
  - Unadjusted
  - Adjusted
    - Complete cases only
    - Multiple imputation for missing CD4 and height measurements
Perinatally HIV-infected Adolescents

North America
1 032 (3%)
Female 50.1%

Europe & Central Asia
3 054 (8%)
Female 51.7%

South America & Caribbean
903 (2%)
Female 53.8%

South & SE Asia
2 902 (8%)
Female 50.1%

Sub-Saharan Africa
30 296 (79%)
Female 50.5%

Total
N = 38 187
Female 50.6%
Median (IQR) year of birth

**North America**
Year 1994 (1992; 1996)

**Europe & Central Asia**
Year 1995 (1991; 1999)

**South America & Caribbean**
Year 1998 (1995; 2000)

**Sub-Saharan Africa**

**South & SE Asia**
Year 2001 (1999; 2002)

**Total**
Age: Median (IQR)

**Age in Years**

- **First Visit**
  - Median: 6.7 (4.4; 8.4)

- **ART Start**
  - Median: 7.5 (5.2; 9.2)

- **Last Visit**
  - Median: 12.4 (11.1; 14.4)
CD4 Percent: Median (IQR)

First Visit  
- Median: 16% (IQR: 9; 25)

ART Start  
- Median: 14% (IQR: 8; 20)

Age 10 Years  
- Median: 28% (IQR: 20; 34)

Last Visit  
- Median: 28% (IQR: 21; 35)
CD4 Percent: Median (IQR)

<table>
<thead>
<tr>
<th></th>
<th>First Visit</th>
<th>ART Start</th>
<th>Age 10 Years</th>
<th>Last Visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 percent (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>On ART</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>29% (21; 35)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not on ART</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>25% (19; 32)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Proportion on ART

88% (33 514)
Ever received ART

<table>
<thead>
<tr>
<th>Region</th>
<th>First Visit</th>
<th>Age 10 Years</th>
<th>Last Visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>8% (3 091)</td>
<td>67% (26 953)</td>
<td>80% (30 072)</td>
</tr>
<tr>
<td>North America</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Europe</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>South America</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S&amp;SE Asia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Africa</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

www.iasociety.org
Virologic Suppression

HIV viral load available in 39% of adolescents on ART

75% (6,627/8,825)
72% (9,388/13,114)

Age 10 Years

Last Visit

% Suppressed
WHO Height-for-Age Z-score (HAZ)

First Visit: Median (IQR) HAZ = -1.92 (-2.91; -0.97)
ART Start: Median (IQR) HAZ = -1.95 (-2.91; -1.02)
Age 10 years: Median (IQR) HAZ = -1.53 (-2.35; -0.72)
Last Visit: Median (IQR) HAZ = -1.59 (-2.45; -0.72)
Outcomes: Total Cohort

- Transferred out: 15.6% (95% CI 15.1; 16.0)
- LTFU: 11.3% (95% CI 10.9; 11.8)
- Mortality: 2.6% (95% CI 2.4; 2.8%)
Outcomes: by Region

Cumulative Incidence Function

- All PHA
- South America & Caribbean
- North America
- Europe
- South & Southeast Asia
- Sub-Saharan Africa

Time in years from age 10
# Mortality Hazard Ratios

<table>
<thead>
<tr>
<th>Region</th>
<th>Unadjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total N</strong></td>
<td><strong>38 187</strong></td>
</tr>
<tr>
<td>Europe &amp; Central Asia</td>
<td>1.00</td>
</tr>
<tr>
<td>North America</td>
<td>1.70 (0.87; 3.31)</td>
</tr>
<tr>
<td>South &amp; Southeast Asia</td>
<td>3.21 (2.03; 5.07)</td>
</tr>
<tr>
<td>South America &amp; Caribbean</td>
<td>6.07 (3.88; 9.50)</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>4.35 (3.02; 6.28)</td>
</tr>
</tbody>
</table>
### Mortality Hazard Ratios

*Adjusted for gender, calendar period of birth, age at first visit, CD4% at first visit, HAZ at first visit*

<table>
<thead>
<tr>
<th>Region</th>
<th>Unadjusted HR (95% CI)</th>
<th>Adjusted HR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total N</strong></td>
<td>38 187</td>
<td>38 187</td>
</tr>
<tr>
<td>Europe &amp; Central Asia</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>North America</td>
<td>1.70 (0.87; 3.31)</td>
<td>2.18 (1.11; 4.31)</td>
</tr>
<tr>
<td>South &amp; Southeast Asia</td>
<td>3.21 (2.03; 5.07)</td>
<td>1.75 (1.06; 2.89)</td>
</tr>
<tr>
<td>South America &amp; Caribbean</td>
<td>6.07 (3.88; 9.50)</td>
<td>4.52 (2.85; 7.18)</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>4.35 (3.02; 6.28)</td>
<td>2.53 (1.65; 3.88)</td>
</tr>
</tbody>
</table>
Discussion

- Survivor cohort that beat the odds
- Limited to PHA that presented before 10 years of age
- At first visit and ART start, age & CD4% differed substantially by region
- By 10 years and at last visit, CD4%, proportion on ART and proportion virologically suppressed were similar across regions
- Height growth remained severely impaired in most regions even in those receiving ART
- Observed mortality < 3% during adolescence in PHA surviving to 10 years of age should be considered as a conservative estimate
- Mortality during adolescence is substantially elevated for perinatally HIV-infected adolescents in South America & Africa relative to Europe
Adolescent Project Team

Co-chairs: Ali Judd (EPPICC) and Valeriane Leroy (IeDEA-West-Africa)
Data center: Mary-Ann Davies, Michael Schomaker, Amy Slogrove
Data managers: Sebastian Wanless, Charlotte Duff

Members:
1. BIPAI (Baylor): Nancy Calles
2. CCASA.net: Jorge Pinto
3. EPPICC: Josiane Warszawski
4. IeDEA Asia-Pacific: Kulkanya Chokephaibulkit
5. IeDEA Central Africa: Marcel Yotebieng
6. IeDEA East Africa: Kara Wools-Kaloustian
7. IeDEA Southern Africa: Nicky Maxwell
8. IeDEA West-Africa: François Eboua
9. IMPAACT: Paige Williams
10. MSF: Jihane Ben-Farhat
11. Optimal Models (ICAP): Chloe Teasdale
12. PHACS: George Seage
Acknowledgements

• International AIDS Society
• CIPHER Steering Committee
• CIPHER Global Cohort Collaboration Oversight Group
• Marissa Vicari – Manager, CIPHER
• UCT CIDER Data Centre
  – Mary-Ann Davies, Michael Schomaker, Dolphina Cogill, Nicky Maxwell
• Networks
LTFU-Mortality Scenarios

Reference = Europe

A: Original HR estimate

B: 100% of all LTFU is mortality

C: 50% of all LTFU is mortality

D: 20% of all LTFU is mortality
LTFU-Mortality Scenarios

Reference = Europe

- **A**: Original HR estimate
- **B**: 50% of LTFU in Africa & 5% of LTFU rest
- **C**: 20% of LTFU in Africa & 5% of LTFU rest
- **D**: 5% of LTFU in Africa & 20% of LTFU rest
### Mortality Hazard Ratios

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted HR (95% CI)</th>
<th>Complete Cases Only Adjusted HR* (95% CI)</th>
<th>Multiple Imputation Adjusted HR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total N</strong></td>
<td><strong>38,187</strong></td>
<td><strong>10,302</strong></td>
<td><strong>38,187</strong></td>
</tr>
<tr>
<td>Europe &amp; Central Asia</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>North America</td>
<td>1.70 (0.87; 3.31)</td>
<td>2.63 (0.67; 10.41)</td>
<td>2.18 (1.11; 4.31)</td>
</tr>
<tr>
<td>S&amp;SE Asia</td>
<td>3.21 (2.03; 5.07)</td>
<td>1.77 (0.57; 5.47)</td>
<td>1.75 (1.06; 2.89)</td>
</tr>
<tr>
<td>South America &amp; Carib</td>
<td>6.07 (3.88; 9.50)</td>
<td>3.75 (1.14; 12.36)</td>
<td>4.52 (2.85; 7.18)</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>4.35 (3.02; 6.28)</td>
<td>4.10 (1.51; 11.13)</td>
<td>2.53 (1.65; 3.88)</td>
</tr>
</tbody>
</table>

* Adjusted for gender, calendar period of birth, age at first visit, CD4% at first visit, HAZ at first visit
## Mortality Hazard Ratios

<table>
<thead>
<tr>
<th>Region</th>
<th>Unadjusted HR (95% CI)</th>
<th>Complete Cases Only Adjusted HR* (95% CI)</th>
<th>Multiple Imputation Adjusted HR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total N</td>
<td>38 187</td>
<td>10 302</td>
<td>38 187</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Europe &amp; Central Asia</td>
<td>0.23 (0.16; 0.33)</td>
<td>0.24 (0.09; 0.66)</td>
<td>0.40 (0.26; 0.61)</td>
</tr>
<tr>
<td>North America</td>
<td>0.39 (0.22; 0.69)</td>
<td>0.64 (0.18; 2.33)</td>
<td>0.86 (0.44; 1.68)</td>
</tr>
<tr>
<td>S&amp;SE Asia</td>
<td>0.74 (0.55; 1.00)</td>
<td>0.43 (0.23; 0.81)</td>
<td>0.69 (0.51; 0.94)</td>
</tr>
<tr>
<td>South America &amp; Carib</td>
<td>1.39 (1.03; 1.88)</td>
<td>0.92 (0.36; 2.34)</td>
<td>1.79 (1.28; 2.50)</td>
</tr>
</tbody>
</table>

* Adjusted for gender, calendar period of birth, age at first visit, CD4% at first visit, HAZ at first visit