Attrition and Treatment Outcomes among Perinatally and Behaviourally HIV-infected Adolescents and Youths in Thai National AIDS program

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No conflicts of interest
Background: Thai National AIDS program (NAP)

National Access to ARV Treatment for PLHIV (NAPHA)
(Pilot program)

Universal Coverage
National AIDS program (NAP)
managed by National Health Security Office (NHSO)

PMTCT National Program

Start ART at CD4<200

Start ART at CD4<350

Start ART at any CD4
Background: Thai HIV-infected adolescents and youths starting ART

These groups consists of children who were acquired HIV by
- perinatally transmission (PIY age 10-14 years)
- behaviourally transmission (BIY1 age 15-19 years, BIY2 age 20-24 years)

Source: NHSO database 2014
Objectives

To describe attrition and treatment outcomes among behaviourally HIV-infected youths (BIY1, BIY2) and perinatally HIV-infected young adolescents (PIY) who initiated antiretroviral treatment (ART) through the National AIDS Program (NAP)
Methods: Study population

- NHSO database of whom linkage to the National Death Registry
- Patients initiated ART at age 10-24 years from 2008-2013
- ART defined as at least 3 drugs, including NNRTI or PI, and 2-3 NRTIs
- Baseline was defined at the date of ART initiation

*Ethics approval was obtained from the Institute for Development of Human Research Protection, Ministry of Public Health, Thailand*
Methods: Study Outcomes

- **Mortality** – confirmed death linkages with the National Death Registry

- **Loss to follow-up (LTFU)** - not having of 2 consecutive CD4 tests during follow-up, irrespective of whether or not patients later returned to NAP

- **Treatment failure at the 1st year of ART is a composite endpoint**
  - For patients who had VL tested
    1) Virological failure (VF) was defined as a VL ≥ 1,000 copies/mL
  - And patients who did not have VL tested
    2) LTFU / death during the first year of treatment
    3) Switching major regimen from NNRTI to PI or vice versa
Methods: Statistical analysis

- Cox regression model were used to assess predictors of mortality
  - Covariates including gender, baseline age, baseline CD4 counts, First regimen, year of ART initiation, regions and loss to follow-up (LTFU)

- Logistic regression model were used to assess predictors of treatment failure at the 1st years of ART initiation
  - Covariates including gender, baseline age, baseline CD4 counts, First regimen, year and regions
# Results: Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristics (N=11,954)</th>
<th>PIY 10-14 years n = 2,045</th>
<th>BIY1 15-19 years n = 3,118</th>
<th>BIY2 20-24 years n = 6,791</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (IQR) Age, yrs</td>
<td>12 (11-14)</td>
<td>18 (17-19)</td>
<td>22 (21-23)</td>
</tr>
<tr>
<td>Female</td>
<td>1,194 (58%)</td>
<td>2,159 (69%)</td>
<td>3,155 (46%)</td>
</tr>
<tr>
<td>Regimens</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NNRTI based ART</td>
<td>1,908 (93%)</td>
<td>1,850 (59%)</td>
<td>5,282 (78%)</td>
</tr>
<tr>
<td>PIs based ART</td>
<td>137 (7%)</td>
<td>1,268 (41%)</td>
<td>1,509 (22%)</td>
</tr>
<tr>
<td>Median (IQR) CD4 count, cells/mm³</td>
<td>154 (39 - 307)</td>
<td>241 (74 - 412)</td>
<td>172 (45 - 303)</td>
</tr>
<tr>
<td></td>
<td>n = 1,417 (69%)</td>
<td>n = 2,088 (67%)</td>
<td>n = 4,222 (62%)</td>
</tr>
<tr>
<td>Median (IQR) duration on ART, yrs</td>
<td>4 (2 - 6)</td>
<td>2 (1 - 3)</td>
<td>2 (1 - 4)</td>
</tr>
</tbody>
</table>
## Results: Study outcomes

<table>
<thead>
<tr>
<th>Characteristics (N=11,954)</th>
<th>PIY 10-14 years n = 2,045</th>
<th>BIY1 15-19 years n = 3,118</th>
<th>BIY2 20-24 years n = 6,791</th>
</tr>
</thead>
<tbody>
<tr>
<td>Person – years</td>
<td>8,096</td>
<td>7,140</td>
<td>17,345</td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N (%) of death</td>
<td>206 (10%)</td>
<td>223 (7%)</td>
<td>504 (7%)</td>
</tr>
<tr>
<td>Mortality rate per 100 PY, (95% CI)</td>
<td>2.5 (2.2 - 2.9)</td>
<td>3.1 (2.7 - 3.6)</td>
<td>2.9 (2.7 - 3.2)</td>
</tr>
<tr>
<td>Median (IQR) CD4 count at death</td>
<td>31 (12 - 119)</td>
<td>41 (18 -129)</td>
<td>43 (12 - 141)</td>
</tr>
<tr>
<td>LTFU</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N (%) of LTFU</td>
<td>224 (11%)</td>
<td>871 (28%)</td>
<td>1,459 (21%)</td>
</tr>
<tr>
<td>LTFU rate per 100 PY, (95% CI)</td>
<td>2.9 (2.4 - 3.3)</td>
<td>13.9 (12.9 -14.8)</td>
<td>9.5 (9.0 - 9.9)</td>
</tr>
</tbody>
</table>
Figure 1 probability of LTFU after ART initiation by baseline age groups

- BIY1, 28% (26-30)%
- BIY2, 21% (20-22)%
- PIY, 6% (5-7)%

Number at risk
- PIY 10-14 yrs: 2045
- BIY1 15-19 yrs: 3118
- BIY2 20-24 yrs: 6791

Probability of loss to follow-up
### Results: Factors associated with Mortality

<table>
<thead>
<tr>
<th>Characteristics (N=11,954)</th>
<th>N of death n = 933</th>
<th>Multivariate</th>
<th>aHR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Year of ART initiation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td>218</td>
<td>ref</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td>187</td>
<td>0.88 (0.72 - 1.07)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td>193</td>
<td>0.98 (0.80 - 1.21)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td>156</td>
<td>0.89 (0.72 - 1.12)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td>107</td>
<td>0.72 (0.56 - 0.92)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td>72</td>
<td>0.67 (0.51 - 0.90)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td><strong>First regimen</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NNRTI based ART</td>
<td>872</td>
<td>ref</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>PI based ART</td>
<td>61</td>
<td>0.53 (0.40 - 0.70)</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td><strong>Baseline CD4 counts, cells/mm3</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 200</td>
<td>517</td>
<td>ref</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>200 - 350</td>
<td>66</td>
<td>0.36 (0.28 - 0.47)</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>≥ 350</td>
<td>16</td>
<td>0.11 (0.07 - 0.19)</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>unknown</td>
<td>334</td>
<td>0.68 (0.59 - 0.79)</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td><strong>Loss to follow-up</strong></td>
<td>154</td>
<td>3.17 (2.32 - 4.34)</td>
<td>&lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>
## Results: Factors associated with LTFU

<table>
<thead>
<tr>
<th>Characteristics (N=11,954)</th>
<th>N of LTFU n = 2,554</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>aHR (95% CI)</td>
</tr>
<tr>
<td>Female</td>
<td>1,851</td>
<td>1.47 (1.32 - 1.62)</td>
</tr>
<tr>
<td>Age at ART initiation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PIY age 10 - 14 years</td>
<td>224</td>
<td>ref</td>
</tr>
<tr>
<td>BIY1 age 15 - 19 years</td>
<td>871</td>
<td>2.95 (2.52 - 3.45)</td>
</tr>
<tr>
<td>BIY2 age 20 - 24 years</td>
<td>1,459</td>
<td>2.72 (2.35 - 3.16)</td>
</tr>
<tr>
<td>First regimen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NNRTI based ART</td>
<td>1,433</td>
<td>ref</td>
</tr>
<tr>
<td>PI based ART</td>
<td>1,121</td>
<td>2.42 (2.17 - 2.70)</td>
</tr>
<tr>
<td>Baseline CD4 counts,cells/mm^3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 200</td>
<td>531</td>
<td>ref</td>
</tr>
<tr>
<td>200-350</td>
<td>374</td>
<td>1.39 (1.22 - 1.60)</td>
</tr>
<tr>
<td>≥ 350</td>
<td>611</td>
<td>1.99 (1.74 - 2.27)</td>
</tr>
<tr>
<td>unknown</td>
<td>1,038</td>
<td>1.49 (1.33 - 1.66)</td>
</tr>
</tbody>
</table>
Figure 2 Proportion of composite endpoint by baseline age groups

Proportion of VF, only if VL tested, n = 7,160

PIY - 22% vs BIY1 - 18% vs BIY2 - 12%
## Results: Factors associated with Treatment failure**

**Composite endpoint – VF, LTFU /death / switching major ART regimen**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Failure n = 3,616</th>
<th>Multivariate</th>
<th>aOR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=11,954</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>2370</td>
<td></td>
<td>1.34 (1.22 - 1.48)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Age at ART initiation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PIY age 10 - 14 years</td>
<td>532</td>
<td>ref</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>BIY1 age 15 - 19 years</td>
<td>1130</td>
<td>1.45 (1.26 - 1.66)</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>BIY2 age 20 - 24 years</td>
<td>1954</td>
<td>1.22 (1.08 - 1.38)</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>First regimen</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NNRTI based ART</td>
<td>2316</td>
<td>ref</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>PI based ART</td>
<td>1300</td>
<td>2.28 (2.02 - 2.58)</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Baseline CD4 counts</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 200</td>
<td>1161</td>
<td>1.42 (1.25 - 1.63)</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>200 - 350</td>
<td>470</td>
<td>ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 350</td>
<td>640</td>
<td>1.21 (1.03 - 1.41)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>unknown</td>
<td>1345</td>
<td>1.31 (1.15 - 1.49)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Discussion (1)**

Mortality rate in BIY 15–24 years was **2.8 vs** (range: 0.8 – 13.5) per 100 PY

LTFU rate in BIY 15–24 years was **8.7 vs** (range: 7.0 – 30.1) per 100 PY (Nigeria, Uganda, Côte d’Ivoire, Swaziland, Mozambique, Zambia, and *Tanzania*)

- The rate of LTFU among BIY 15–24-year-olds was more than double than that found among PIY 10–14-year-olds after ART initiation, whereas mortality was similar among all age groups

<table>
<thead>
<tr>
<th></th>
<th>PIY 10-14 years</th>
<th>BIY1 15-19 years</th>
<th>BIY2 20-24 years</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality rate /100 PY</td>
<td>2.5 vs 3.6 / 4.1</td>
<td>3.1 vs 5.4 / 4.4</td>
<td>2.9 vs 6.6 / 5.4</td>
<td><em>Zimbabwe</em>² / <em>South Africa</em>³</td>
</tr>
<tr>
<td>LTFU rate /100 PY</td>
<td>2.9 vs 4.2 / 6.1</td>
<td>13.9 vs 10.9 / 23.3</td>
<td>9.5 vs 16.8 / 17.6</td>
<td><em>Zimbabwe</em>² / <em>South Africa</em>³</td>
</tr>
<tr>
<td>LTFU at 2 yrs</td>
<td>6% vs 18.5%</td>
<td>28% vs 30%</td>
<td>21% vs 38%</td>
<td><em>Kenya</em>⁴</td>
</tr>
</tbody>
</table>

Discussion (2)

- **Strengths**
  - Evaluating outcomes based on a practical healthcare setting
  - Linkage to National death registry enabled us to accurately estimate mortality and LTFU rates

- **Limitations**
  - Information of pregnant females through PMTCT program are limited
  - Missing VL or CD4 results might affect the results of the treatment outcomes
  - No information on information behavioural factors available
Conclusions

• No difference in mortality rates between PIY, BIY1 and BIY2 (range: 2.5 – 3.1 per 100 PY)

• **BIY1 aged 15-19 years** had the highest risk of LTFU
  • This influenced the composite endpoint of treatment failure

• There is still a need for health policies to specifically address the needs of HIV-infected youths, such as providing access to adolescent-friendly clinics
Acknowledgments

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• Ministry of Public Health (MOPH), Thailand

• The HIV Netherlands Australia Thailand Research Collaboration (HIV-NAT), The Thai Red Cross AIDS Research Centre (TRCRC)