Mortality of HIV-infected Patients starting Antiretroviral Therapy: Comparison with the General Population in sub-Saharan Africa

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for the

ART in Lower Income Countries Collaboration (ART-LINC)
of the International epidemiological Databases to Evaluate AIDS (IeDEA)
Why compare mortality of patients on ART to background mortality?

- Background mortality as point of reference for ART effectiveness
- Standardization of mortality is required to account for variation in background mortality between countries
Patient mortality relative to mortality in the general population

- Standardized mortality ratio = \[
\frac{\text{Observed number of deaths}}{\text{Expected number of deaths}}
\]

- **Observed**: number of deaths in patients on ART
- **Expected**: based on age- and sex-specific HIV-unrelated mortality rate in general population
Source of patient data: ART-LINC of IeDEA

- A network of HIV treatment programs in Africa, Latin America and Asia
Patient data from five ART programmes in four sub-Saharan Africa countries

• Gugulethu township, Cape Town, RSA
• Khayelitsha township, Cape Town, RSA
• Newlands Clinic, Harare, Zimbabwe
• Centre de Prise en Charge de Recherche et de Formation (CEPREF), Abidjan, Côte d’Ivoire
• Lighthouse Clinic, Lilongwe, Malawi

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Inclusion criteria for analysis

• Treatment naïve at start of HAART

• Age 16 years or older
Patient Characteristics

- 13,249 patients; 14,695 person-years of follow-up and 1,177 deaths
- 67% women
- Median age: 34 years (IQR 29-41)
- Median baseline CD4: 107 (46-175)
- 85% advanced disease (WHO stage 3 & 4)
- Overall cumulative mortality at 2 years: 11.7% (95% CI: 11.1%-12.3%)
Data on mortality in general populations

- Data provided by WHO
- Death registries or life-table approach based on demographic survey data
All-cause mortality in general populations (women and men combined)

Source of data: World Health Organization

- Côte d’Ivoire
- South Africa
- Malawi
- Zimbabwe

HIV-related
HIV-unrelated

Mortality / 1000 population

5-year age group
Statistical Methods

- SMRs estimated by Poisson regression, adjusting for differences in prognostic factors
- Random-effect to account for between-cohort variation
- Multiple imputation: baseline CD4, clinical stage, outcome
- Separate estimates for months 1-3, 4-6, 7-12, and 13-24
- SMRs presented by baseline CD4 count and clinical stage
SMRs by baseline CD4 count and clinical stage

Mortality on ART = HIV-unrelated background mortality

PLoS Medicine, in press
Mortality on ART = HIV-unrelated background mortality

SMRs by baseline CD4 count and clinical stage

Months 13-24

<table>
<thead>
<tr>
<th>Baseline CD4</th>
<th>SMR</th>
</tr>
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<tbody>
<tr>
<td>&lt;25</td>
<td></td>
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<tr>
<td>25-49</td>
<td></td>
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<tr>
<td>50-99</td>
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<tr>
<td>100-199</td>
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<tr>
<td>≥200</td>
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</tbody>
</table>

- less advanced stage
- advanced stage
## Overall SMRs for months 1-24

<table>
<thead>
<tr>
<th>Baseline CD4 count</th>
<th>Baseline Clinical Stage</th>
<th>Less advanced</th>
<th>Advanced</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 25</td>
<td>15.8 (9.0-27.9)</td>
<td>47.1 (39.1-56.6)</td>
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<tr>
<td>25-49</td>
<td>10.6 (6.1-18.4)</td>
<td>31.4 (26.1-37.7)</td>
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<tr>
<td>50-99</td>
<td>6.6 (3.6-12.1)</td>
<td>19.6 (15.1-25.5)</td>
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<tr>
<td>100-199</td>
<td>4.6 (2.7-7.8)</td>
<td>13.6 (11.5-16.1)</td>
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<tr>
<td>≥ 200</td>
<td>3.4 (1.9-6.2)</td>
<td>10.2 (7.6-13.7)</td>
<td></td>
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</tbody>
</table>
Summary and Conclusions (1)

- SMRs are a useful metric to evaluate patient mortality across ART programmes in sub-Saharan Africa

- Two-year mortality in HIV-infected patients starting ART with very low CD4 counts and advanced clinical disease is 50 times higher than mortality in the general population
Summary and Conclusions (2)

• Patients starting ART with 200 cells or more and less advanced clinical disease have a more modest, 3- to 4-fold, increased mortality compared to the general population

• Earlier initiation of ART is key in improving patient outcomes in sub-Saharan Africa
Acknowledgements

• ART-LINC collaboration of IeDEA:

• WHO
  Y Souteyrand
Funding

- Office of AIDS Research, NIH, USA
- National Institute of Allergy and Infectious Disease (NIAID), USA
- Agence Nationale de Recherches sur le SIDA (ANRS), France