Outcomes of Antiretroviral Treatment in Resource Limited and Industrialized Countries

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International epidemiological Databases to Evaluate AIDS (IeDEA) ART Cohort Collaboration (ART-CC) Swiss HIV Cohort Study (SHCS)

Universities of Bern and Cape Town Switzerland and South Africa
Overview of talk

• Sources of information
• When do patients start ART?
• What regimens are used?
• What are the outcomes?
  – Loss to program
  – Virologic response
  – Opportunistic illnesses
  – All cause mortality
• Conclusions
Sources of information

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Antiretroviral Therapy (ART) Cohort Collaboration

- **France**
  - French Hospital Database on HIV (FHDH)
  - Aquitaine Cohort
- **Germany**
  - Frankfurt HIV Cohort
  - Köln / Bonn Cohort
- **Italy**
  - Italian Cohort of Antiretroviral-Naive Patients (ICONA)
- **Switzerland**
  - Swiss HIV Cohort Study
- **Netherlands**
  - AIDS Therapy Evaluation project Netherlands (ATHENA)
- **Spain**
  - PISCIS, Catalonia and Balearic islands
- **United Kingdom**
  - Royal Free Hospital Cohort, London
- **The Multicenter Study Group on EuroSIDA**
  - 29 European countries
- **Canada**
  - British Columbia Centre for Excellence in HIV (BCCfE-HIV)
  - South Alberta Clinic
- **USA**
  - Collaborations in HIV Outcomes Research US (CHORUS)
  - 1917 Clinic Cohort, University of Alabama, Birmingham
  - University of Washington HIV Cohort, Seattle
  - Veterans Aging Cohort Study (VACS), West Haven

www.art-cohort-collaboration.org
International epidemiological Databases to Evaluate AIDS

• 7 regional networks
  • North America
  • South America / Caribbean
  • West Africa
  • Central Africa
  • East Africa
  • Southern Africa
  • Australia / Asia

• Resource limited countries networks
  • ART-LINC Collaboration
  • Kids-ART-LINC Collaboration
  • Treat Asia HIV Observational Database (TAHOD)

www.iedea-hiv.org
www.art-linc.org
www.anecca.org
www.amfar.org
Large, public scale up programs in Sub-Saharan Africa

- Gugulethu township, Cape Town, RSA
- Khayelitsha township, Cape Town, RSA
- Centre de Prise en Charge de Recherche et de Formation (CEPREF), Abidjan, Côte d’Ivoire
- Lighthouse Clinic, Lilongwe, Malawi
When do patients start antiretroviral treatment?
CD4 count at start of ART, 2003-2005
42 countries, 176 sites
CD4 count at start of ART, 2003-2005
33,008 treatment-naive patients
CD4 count at start of ART, 2003-2005
42 countries, 176 sites, 33,008 patients

Numbers are median CD4 counts
Median CD4 counts at start of ART
Trends over time

Europe & North America

Sub-Saharan Africa

CD4 cell count at start of ART

Year


MSM
HET
IDU
What treatment regimens are used?
First line regimens, 2003-2005
3 most common regimens by region

North America
- 3TC AZT EFV
- EFV ETC TNV
- 3TC AZT LPV/r

South America
- 3TC AZT EFV
- 3TC AZT NVP
- 3TC D4T EFV

West, Central & East Africa
- 3TC D4T NVP
- 3TC AZT EFV
- 3TC D4T EFV

Western Europe
- 3TC AZT LPV/r
- 3TC AZT EFV
- 3TC EFV TNV

Asia
- 3TC D4T NVP
- 3TC D4T EFV
- 3TC AZT NVP

Southern Africa
- 3TC D4T NVP
- 3TC D4T EFV
- 3TC AZT EFV

CROI 2007 – regimens – 13
**First line regimens, 2003-2005**

No. of regimens used to treat 90% of patients

<table>
<thead>
<tr>
<th>Region</th>
<th>North America</th>
<th>South America</th>
<th>West, Central &amp; East Africa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Western Europe</td>
<td>59</td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>Asia</td>
<td>47</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Southern Africa</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Loss to program
Loss to program

- 16 treatment programs in Africa, Asia and Latin America
  - 12 with active tracing of patients (home visits, telephone, reminder letters)
  - 4 with no tracing
- 5,575 adult patients starting ART
  - Median age 35 years, 46% women
  - Median baseline CD4 cell count 105 cells/µL
Loss to program

• No follow up after initial visit
  – 4% (0% to 9%)

• Loss to follow up during first 6 months
  – 17% (0% to 57%)
## Loss to program

<table>
<thead>
<tr>
<th>Calendar period</th>
<th>No follow up</th>
<th>Loss to follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio (95% CI)</td>
<td>Hazard ratio (95% CI)</td>
</tr>
<tr>
<td>≤ 2000</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2001-2002</td>
<td>4.46 (1.26-15.7)</td>
<td>2.77 (1.69-4.55)</td>
</tr>
<tr>
<td>2003-2004</td>
<td>5.01 (1.27-19.8)</td>
<td>7.86 (4.71-13.1)</td>
</tr>
</tbody>
</table>
## Loss to program

<table>
<thead>
<tr>
<th>CD4 cell count (cells/μl)</th>
<th>No follow up</th>
<th>Loss to follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio (95% CI)</td>
<td>Hazard ratio (95% CI)</td>
</tr>
<tr>
<td>≥ 50</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>25-49</td>
<td>2.76 (1.69-4.52)</td>
<td>1.04 (0.82-1.31)</td>
</tr>
<tr>
<td>&lt; 25</td>
<td>2.50 (1.43-4.37)</td>
<td>1.47 (1.23-1.75)</td>
</tr>
</tbody>
</table>
Tracing of patients and mortality

Months after starting ART

Cumulative mortality (%)

Active tracing of patients

No tracing

Lancet 2006; 367: 817–24
Virologic response

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Study population

- 1856 patients from Gugulethu and Khayelitsha, Cape Town
  - Median CD4 count 81 cells/µL, median age 33 years, 70% women
- 967 patients from Swiss HIV Cohort
  - Median CD4 count 212 cells/µL, median age 38 years, 33% women
Frequency of viral load measurements

South Africa

Switzerland

Months after starting ART

Standardized measurement frequency

CROI 2007 – response – 23
Initial virologic response
(<500 copies/ml)
Viral rebound (≥500 copies/ml)

% with viral rebound

South Africa
Switzerland

Months after first viral load <500 copies/ml
Treatment change
(any change, including switching, substitution)

% with treatment change

0 6 12 18 24

Months after starting ART

Switzerland

South Africa

CROI 2007 – response – 26
Opportunistic illnesses
Most common OIs in first 3 months

Europe & North America
- TB (pulmonary / extrap.)
- Herpes simplex disease
- Cryptococcal meningitis
- Pneumocystis pneumonia
- Oesophageal candidiasis
- Kaposi's sarcoma
- Toxoplasmosis of the brain
- Bacterial pneumonia, recurrent

Sub-Saharan Africa
- TB (pulmonary / extrap.)
- Herpes simplex disease
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- Kaposi's sarcoma
- Toxoplasmosis of the brain
- Bacterial pneumonia, recurrent

Incidence rate (cases / 1000 pyrs)

Arch Intern Med. 2005;165:416-423

CROI 2007 – OIs – 28
Study population

• Scale up programs in Sub-Saharan Africa
  – 11,231 patients
  – 777 deaths
  – 15,350 person years of follow up
  – Loss to follow up 13% over 2 years

• ART Cohort Collaboration
  – 38,050 patients
  – 2,026 deaths
  – 144,994 person years of follow up
  – Loss to follow up 6% over 2 years
Mortality over four years

Cumulative mortality (%)

0 5 10 15

Sub-Saharan Africa

Europe & North America

Months after start of ART

CROI 2007 – mortality - 31
Mortality by baseline CD4 cell count

Sub-Saharan Africa

Europe & North America

Cumulative mortality (%)

Months after starting ART

CROI 2007 – mortality - 32
Relative mortality over time
Sub-Saharan Africa vs. industrialized countries

Adjusted for:
- Age, sex, CD4 count,
- clinical stage at baseline

Reference (industrialized countries)

Lancet 2006; 367: 817–24
Mortality by cohort (unadjusted results)

Mortality in first year after ART initiation (%)

Europe & North America

Sub-Saharan Africa

CROI 2007 – mortality - 34
Mortality by cohort (adjusted for age, sex, CD4 count, year, stage)

Mortality in first year after ART initiation (%)

Europe & North America

Sub-Saharan Africa

ART Cohort Collaboration
Conclusions
Most patients in resource-limited and many patients in industrialized countries start ART late or very late.

In industrialized settings many different first-line regimens are used and changes are frequent.

Few regimens are used in resource limited settings and changes are less frequent.

Virologic and immunologic responses are very similar.
• In some resource-limited settings substantial proportions of patients are lost to the program early on

• TB is the most frequent complication in patients starting ART

• Mortality is substantially higher in resource-limited settings, particularly in the first months of ART

• Taking into account differences in prognostic factors, mortality in programs in sub-Saharan Africa is comparable to that observed in industrialized settings
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• ART Cohort Collaboration

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