
Rein Houben/Sebastian Mboma
Karonga Prevention Study
TB incidence over time

- South Africa
- Zimbabwe
- Botswana
- Kenya
- Malawi
- Tanzania
- Senegal
- Cameroon
- Benin

HIV

ART??
• Williams & Dye (Science – 2003): early start, high coverage and compliance necessary for ART to reduce TB burden in population

• Studies have suggested
  – Relative incidence of TB lower amongst patients receiving ART (in CD4 strata)
  – Late starters (CD4<100) remain at elevated risk of TB

• Limitations
  – Most studies are done in intensely supervised study settings – not representative of rural Africa
  – Few cases of TB
  – No HIV negative or positive comparison group
  – Effect of ART on TB incidence in wider population
Research Questions

• What is the relative incidence of TB by HIV/ART status?

• What is the effect of the ART roll-out on TB incidence trends in Karonga District?
Karonga Prevention Study

TB epidemiological studies since 1985

- All TB cases
  - Laboratory tests
  - Demographic information
  - HIV status (from 1988)

- ART since July 2005
  - Low level of clinical and laboratory support
Population denominators

Adult population size

HIV prevalence in population
• Mathematical model based on population data for HIV prevalence White R.G. et al (Epi Inf, 2007)

Uptake of ART in population
• ART clinic registers
• Person years on ART in Karonga
  – Recently started on ART --> 6 months or less
  – On ART for longer period --> more than 6 months
TB cases

• Main analysis
  – Only new SS+ pulmonary TB cases since Jan 1986 – Aug 2009
    (Lab confirmed - at least 1 positive culture or 2 separate
    smears positive for Mtb)

• Sensitivity analyses on different TB case populations

• HIV and ART status
  – From linked KPS database of previously recorded data
  – Missing HIV and/or ART status were imputed using MICE
    (Multiple imputation using Chained Equations)
Analysis

• Relative TB incidence (July 2005 – Aug 2009)
  – Rate ratios by HIV status
  – Rate ratios By HIV/ART status

• Incidence trends analysis
# Relative incidence (05 – 09)

<table>
<thead>
<tr>
<th>Period and group</th>
<th>Observed</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n py inc</td>
<td>Crude Adjusted*</td>
</tr>
<tr>
<td>Overall</td>
<td>462 633686 73</td>
<td>n.a. n.a.</td>
</tr>
<tr>
<td>HIV negative</td>
<td>174 567555 31</td>
<td>1</td>
</tr>
<tr>
<td>HIV positive</td>
<td>249 66130 377</td>
<td>12.28 (10.12–14.91) 10.89 (8.87–13.36)</td>
</tr>
<tr>
<td>HIV+ no ART</td>
<td>124 51602 240</td>
<td>1</td>
</tr>
<tr>
<td>HIV+ &lt;=6m ART</td>
<td>29 1635 1774</td>
<td>7.38 (4.93–11.06) 6.41 (4.25–9.67)</td>
</tr>
<tr>
<td>HIV+ &gt;6m ART</td>
<td>32 4624 692</td>
<td>2.88 (1.95–4.25) 2.46 (1.66–3.67)</td>
</tr>
</tbody>
</table>

*RR’s adjusted for age group (15-24, 25-34, 35-44, 45-54, >=55) and sex

**Note:** The imputed data show roughly the same results, which suggests that the imputation did not do anything strange or introduce more bias.
Overall

KARONGA PREVENTION STUDY

Incidence (n/100,000/year)

Year

86-87 88-90 91-93 94-96 97-99 00-02 03-05 06-09

0 20 40 60 80 100 120

All cases
All cases & HIV negative
Change in incidence trend

RR express linear annual change in TB incidence, baseline is first year of the period (1997 or 2005). Imputed datasets were used.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Annual change 1997 – 2005</th>
<th>Annual change 2005 - 2009</th>
<th>P values*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IRR (95% CI)</td>
<td>IRR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>0.93 (0.91 – 0.95)</td>
<td>1.01 (0.96 – 1.07)</td>
<td>0.03</td>
</tr>
<tr>
<td>HIV negative</td>
<td>0.91 (0.88 – 0.95)</td>
<td>1.09 (0.99 – 1.19)</td>
<td>0.005</td>
</tr>
<tr>
<td>HIV positive</td>
<td>0.96 (0.93 – 0.99)</td>
<td>0.99 (0.92 – 1.07)</td>
<td>0.58</td>
</tr>
</tbody>
</table>

*p-value for change in trend in 2005.
Summary of results

• Relative incidence
  – High incidence early after initiation ART
  – Decreases with time, but still elevated

• Incidence trend
  – Decrease until introduction ART, when it plateaus

• Imputation
  – Does not affect relative incidence estimates
  – Corrects bias in incidence trends
Limitations

• No CD4 counts
  – Low CD4 at start ART would explain high relative incidences

• Population estimates are always a bit uncertain

• HIV estimates
  – Not include effect ART, but fitted new data reasonably well.
Interpretation

• Well supported DOTS programme controlling TB incidence
  – Area with generalised HIV and moderate TB transmission

• Advent of ART coincided with plateau in TB incidence
  – Affects HIV positive and HIV negative population
  – Very high risk of TB in HIV patients starting ART (too) late

• Incidence trends
  – Extra TB cases following roll-out of ART
    • Direct effect on incidence in HIV positive population
    • Indirect effect in HIV negative population
  – Indirect effect difficult to quantify
Implications/Recommendations

• Start ART earlier

• Further collaboration/Integration of TB and ART programmes

• Intensified case finding in high risk population of patients receiving ART
Acknowledgements
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Funders
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THANK YOU