Linkage to HIV care

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The Problem

- Only ~40% of HIV-infected who need antiretroviral therapy (ART) in South Africa are receiving it
- How much of this gap is due to failure to link to care after a new HIV diagnosis?
- What can be done to improve linkage?

WHO, 2010
HIV care continuum

- HIV Test
- On ART
Linkage: HIV care continuum

The problem: Pre-ART loss to follow up
Road Map

- Why worry about the pre-ART period?
- What is the magnitude of the problem of pre-ART loss from care?
- What are the risk factors?
- What are possible solutions?
Why worry about pre-ART?

- Early ART initiation
  - Improves survival
  - Reduces morbidity
  - Decreases transmission
- Treatment is more widely available
- CD4 counts at ART initiation remain low—most cohorts still report CD4 <<<200
- Increased CD4 thresholds, “Test and Treat”
- Need strategies to improve entry into care
Why pre-ART is hard to study

- HIV testing and subsequent care often at different locations
- No system with unique identifier allows tracing of transfers or deaths, who may be deemed “lost”
- Clinical and M+E focus has been on patients on ART

Rosen, 2010; Bassett, 2009; Mwanaga, 2008; Tweya, 2010;
Who Starts ART in Durban, South Africa? …Not Everyone Who Should

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2006-2010
Objectives

- To evaluate rates of ART initiation within 12 months of a positive HIV test in Durban, South Africa
- To identify baseline factors that predict failure to be on ART at 1 year
Methods: Observational study

- Enrolled adults prior to HIV testing
- 2 study sites in Durban
- Asked questionnaires at baseline, 6, 12 mo
- Reviewed medical record
- Two outcomes:
  - CD4 within 90 days
  - ART initiation within 12 months if eligible
Results
How many start ART?

- HIV+*: 1,467
- CD4/results: 605
- Eligible for ART: 368
- Start ART: 154

*Screened 11/06-10/08, enrolled in study and have known HIV status

Failure to obtain CD4
Failure to start ART when eligible

Bassett, 2010
Results: Long delay from HIV diagnosis to ART start

- Males: 40% started ART by 6 months
- Females: 55% started ART by 6 months

Bassett, 2010
Results: High rate of mortality

- 15% of HIV-infected cohort (216 deaths/1,467)
- 21% of ART-eligible cohort (76 deaths/368)

Bassett, 2010
High rate of mortality pre-ART

Most patients died pre-ART or with unknown ART status

P<0.001

CD4 (/µl) strata

Bassett, 2010
Study conclusions

- Substantial loss between diagnosis and ART
- Men less likely to initiate ART
- Severe immune suppression at diagnosis
- Long delays to ART initiation
- High rates of pre-ART mortality

How does this compare with other studies?
Obtaining CD4 count to assess eligibility

<table>
<thead>
<tr>
<th>Location</th>
<th>Time interval allowed for CD4 count</th>
<th>% obtained CD4 count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Durban, SA&lt;sup&gt;1&lt;/sup&gt;</td>
<td>8 weeks</td>
<td>55%</td>
</tr>
<tr>
<td>Cape Town, SA&lt;sup&gt;2&lt;/sup&gt;</td>
<td>6 months</td>
<td>63%</td>
</tr>
<tr>
<td>Johannesburg, SA&lt;sup&gt;3&lt;/sup&gt;</td>
<td>12 weeks</td>
<td>35%</td>
</tr>
<tr>
<td>Beira &amp; Chimoio, Mozambique&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Enrolled ≤ 60d</td>
<td>44%</td>
</tr>
</tbody>
</table>

<sup>1</sup>Losina, 2010; <sup>2</sup>Kranzer, 2010; <sup>3</sup>Larson, 2010; <sup>4</sup>Micek, 2009
From CD4 to ART initiation: pre-ART loss for ART-eligible

<table>
<thead>
<tr>
<th>Location</th>
<th>Time interval allowed for ART initiation</th>
<th>% Retained and started ART</th>
<th>% eligible died pre-ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Durban, SA&lt;sup&gt;1&lt;/sup&gt;</td>
<td>12 months</td>
<td>42%</td>
<td>21%</td>
</tr>
<tr>
<td>Free State, SA&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Up to 3.5 yrs</td>
<td>58%</td>
<td>23%</td>
</tr>
<tr>
<td>Cape Town, SA&lt;sup&gt;3&lt;/sup&gt;</td>
<td>6 months</td>
<td>67%</td>
<td></td>
</tr>
<tr>
<td>Beira &amp; Chimoio, Mozambique&lt;sup&gt;4&lt;/sup&gt;</td>
<td>≤90d of eligibility</td>
<td>31%</td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup>Bassett, 2010; <sup>2</sup>Ingle, 2010; <sup>3</sup>Kranzer, 2010; <sup>4</sup>Micek, 2009
## ART-ineligible patients

<table>
<thead>
<tr>
<th>Location</th>
<th>Outcome</th>
<th>Retention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hlabisa, SA&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Repeat CD4 within 13 months</td>
<td>Overall: 45%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>201-350: 52%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>351-500: 43%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;500: 35%</td>
</tr>
<tr>
<td>Johannesburg, SA&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Repeat CD4 within 12 mo</td>
<td>251-350: 41%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;350: 26%</td>
</tr>
<tr>
<td>Cape Town, SA&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Repeat CD4 count during study period</td>
<td>&gt;200: 46%</td>
</tr>
<tr>
<td>Thyolo District, Malawi&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Repeat CD4</td>
<td>3 mo: 11%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 mo: 4%</td>
</tr>
</tbody>
</table>

<sup>1</sup>Lessels, 2011; <sup>2</sup>Larson, 2010; <sup>3</sup>Krazner, 2010; <sup>4</sup>Tayler-Smith, 2010
Risk factors for pre-ART loss

- Male gender\textsuperscript{1,2,3,4}
- Younger age\textsuperscript{2}
- Unemployed\textsuperscript{5,6}
- Low CD4 counts\textsuperscript{3,4,6}
- ART-ineligible\textsuperscript{5,7}
- Rural clinics\textsuperscript{3}
- Longer distance from ART initiation site\textsuperscript{3}
- Low staffing levels\textsuperscript{3}
- Not having an HIV-infected family/friend\textsuperscript{1}

\textsuperscript{1}Bassett, 2010; \textsuperscript{2}Lessels, 2011; \textsuperscript{3}Ingle, 2010; \textsuperscript{4}Amuron, 2009; \textsuperscript{5}Larson 2010; \textsuperscript{6}Bassett 2009; \textsuperscript{7}Tayler-Smith, 2010;
Why failing to link in Malawi? Cross-sectional study

- Rural Malawi (MSF)
- Defaulters missed appointment by >1 mo
- 874 adults pre-ART traced, 71% found:
  - 51% dead
  - Reasons for defaulting: stigma, dissatisfaction with care/staff, perceived improved health, transport costs

McGuire, 2010
ART refusal in Soweto

- 20% ART-eligible clients refused to initiate upon learning CD4 count
- 92% continued to refuse post 2 mo counseling
- Most common reasons: feeling healthy, unable to disclose, side effects, unable to adhere, cultural beliefs, stigma

Katz, 2011
### sub-Saharan Africa systematic review (Jan 2011)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Outcome</th>
<th>Median [range]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testing to staging</td>
<td>Received CD4 result</td>
<td>55% [35-88%]</td>
</tr>
<tr>
<td>Retention in pre-ART care</td>
<td>Remained in pre-ART care until repeat CD4 count, ART initiation or censoring</td>
<td>46 [42-95%]</td>
</tr>
<tr>
<td>Eligibility to initiation</td>
<td>Initiated ART</td>
<td>66% [14-85%]</td>
</tr>
</tbody>
</table>

- $55\% \times 46\% \times 66\% = 17\%$ (assuming no re-entry)
- Most complete study of all stages suggests 33% retention
- Rosen: ~1/3 of HIV-diagnosed in sub-Saharan Africa remain continuously in pre-ART care from test to ART start

Rosen, CROI, 2011; Krazner, 2010
Implications

- Promote early HIV diagnosis and care
- Improve access to care for men, minimize delays in care system
- Examine reasons for failure to link
- Interventions to improve linkage to care during early stages following diagnosis
Interventions

- Few interventions have been evaluated
- Need to change patients preferences for pre-ART care – lack of incentive to return
- Make pre-ART care more appealing
  - Easier, less expensive, less intimidating
  - More or better services, improve patients understandings of pre-ART care benefits

Rosen, 2011; Lessells, 2011
Possible strategies: Easier, less expensive, less intimidating

- Co-locate multiple services
- Transport assistance
- Lessen waiting times
- Reduce number of steps and lag time
- Use point-of-care (POC) diagnostic tools

Geng, 2008; Ochieng, 2007; Tweya, 2010; Faal, 2011; Rosen, 2010; Etienne, 2010; Forster, 2008
Evidence for POC CD4 count: 2 studies published in 2011

<table>
<thead>
<tr>
<th>Location and type</th>
<th>Outcome</th>
<th>Standard CD4</th>
<th>POC CD4</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Johannesburg, SA(^1) Randomized Trial Urban PHC</td>
<td>Report for further care (pre-ART or ART care)</td>
<td>34%</td>
<td>48%</td>
<td>Immediate group 2.6x more likely to attend ART initiation*</td>
</tr>
<tr>
<td>Maputo and Sofala provinces, Mozambique Peri-urban and rural PHCs X 4</td>
<td>Assessed for eligibility by 90d Start ART within 60d of staging</td>
<td>21%</td>
<td>57%</td>
<td>Only 21% had POC CD4 and staging consult same day</td>
</tr>
</tbody>
</table>

*No effect of POC CD4 on ART-INELIGIBLE enrolling in pre-ART care

\(^1\)Faal, 2011; \(^2\)Jani, 2011
Possible strategies: Services and patient understanding

- Improve counseling and education regarding pre-ART care
- Proactive support, including phone calls, home visits, community collaborations
- Conditional incentives
- Provide more services at each visit
  - Pre-ART wellness package, quality measures

Scott, 2011; Ochieng, 2007; Tweya, 2010; Rosen, 2011; Rosen, 2010; Etienne, 2010; Forster, 2008
More services at each visit: ART-ineligible patients

- Kenya, before and after free cotrimoxazole
- Before: follow-up every 6 months
- After: every 1-2 mo for pharmacy visit
- Outcome: 12 mo retention in care
- 63% before vs 84% after (p<0.001)

Kohler, 2011
More services: Health System Navigator

- **Idea:** Provide time-limited, in-person, telephone and SMS contact to improve uptake of early steps in care pathway

- **Why:**
  - Pre-ART loss rates very high in early pathway
  - US-based RCT efficacious
  - Mobile phones common in South Africa
  - SMS being used for health topics in Africa

Gardner, 2005
Sizanani Trial

- Assess clinical impact and cost-effectiveness of a health system navigator assigned in the outpatient setting
- Navigator in-person, SMS, phone contacts
- 3 study sites: urban OPD, rural OPD, primary health clinic
- Evaluate linkage to HIV care and TB treatment completion
- Currently enrolling through 2012
Conclusions

- Pre-ART losses from care are high at each point along care pathway.
- Best estimate is that <1/3 of people who test positive for HIV remain continuously in pre-ART care to ART start.
Conclusions

- Promoting HIV testing alone is not enough, need to ensure linkage to care to ensure maximum benefits of ART
- Need innovative approaches to improve access to care for men, minimize delays
- Need better ways to monitor pre-ART losses, mortality, and transfers
- Examine reasons for why people fail to link or decline care
Future directions for interventions

- Rigorous evidence largely lacking for linkage interventions
- Interventions are needed that:
  - Expedite care, consolidate steps, co-locate services, provide point of care diagnostics
  - Emphasize value of being in care, offer psychosocial support, reminders, a well-defined and worthwhile pre-ART care package
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- Buyi Mkhize
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