Defining and Studying Retention in pre-ART Care for HIV Infected Adults in sub-Saharan Africa

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Motivation

• Substantial published data on post-ART retention in but little published data on pre-ART period
  – May be because emergency response focused on ART (eligibility and treatment guidelines clear)
  – Management guidelines in pre-ART period less developed
  – Also likely because the stages of pre-ART care and measures of pre-ART retention have not been well defined

• Overview:
  – Review the current literature on pre-ART retention
  – Discuss why difficulties in defining terms arises
  – Make working suggestions for definitions of pre-ART retention
Part 1: Defining the Problem
Why Focus on Pre-ART Period?

- **Current ART guidelines call for higher thresholds:**
  - Reduce morbidity and mortality before and after initiation
  - Try to reduce overall care and treatment costs
  - Suppress viral load to diminish transmission risk

- **Little progress in achieving earlier initiation in SSA:**
  - Large scale HIV testing campaigns implemented, treatment is widely available
  - Little increase in starting CD4 counts
    - Most have a median CD4 count at ART initiation <200
    - Suggests we are not focused enough on pre-ART care
Some Terms and Definitions

• **Pre-ART care:**
  – All services provided between testing positive for HIV and dispensing of first dose of ARVs

• **Staging:**
  – Determination of whether newly-diagnosed patient should be referred to pre-ART care or to ART initiation

• **Enrollment in care:**
  – Active (intentional) registration by patient for pre-ART care

• **Retention in care:**
  – Patient generally maintaining expected schedule for visits, lab tests, etc. until initiation of ART, without long interruptions (remains in care continuously)

• **Loss to care:**
  – Patient discontinues care for any reason (death, loss, unreported transfer)
How would an ideal HIV care and treatment program function?

Disease Progression

Not ART eligible

ART eligible

Ideal Program Progression

Testing & Referral

Completion of referral

Staging

Determine ART eligibility

ART initiation

Monitoring

Long term ART

Actual Program Progression

Testing & Referral

Completion of referral

Staging

Determine ART eligibility

ART initiation

Monitoring

Long term ART
How would an ideal HIV care and treatment program function?

**Disease Progression**

- Not ART eligible
- ART eligible

**Ideal Program Progression**

- Testing & Referral
  - Completion of referral
  - Staging (eligible)
  - Determine ART eligibility
  - ART initiation
  - Long term ART

**Actual Program Progression**

- Testing & Referral
  - Completion of referral
  - Staging (eligible)
  - ART initiation
  - Long term ART
From Testing to Treatment Initiation

Stage 1
Testing to staging

- HIV+ diagnosed population
- Sample for CD4 count provided
- CD4 count sample not provided
- CD4 results obtained (staged)
- CD4 results not obtained (not staged)

Stage 2
Staging to ART eligibility

- ART eligible
- Pre-treatment steps completed
- Lost before completing pre-treatment steps
- Enrolled in pre-ART care
- Lost before enrolling in pre-ART care
- Pre-ART care until ART eligible
- Lost before ART eligible

Stage 3
ART eligibility to ART initiation

- Initiate ART
- Lost before ART initiation

HIV+ diagnosed population
Part 2: What Do We Know about Retention in Pre-ART care in sub-Saharan Africa?
Review of the Evidence

- Systematic literature review March 2011
- Identified 28 studies with quantitative data on at least one stage in the pre-ART period (38 observations)
- Only 7 countries represented; 1/2 conducted in South Africa
- Almost all published or presented in 2009 or later

<table>
<thead>
<tr>
<th>Stage</th>
<th>Outcome</th>
<th>Number of observations</th>
<th>Median [range]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1—HIV testing to staging</td>
<td>Received CD4 count results</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 2— Staging to enrollment in pre-ART care</td>
<td>Remained in pre-ART care until repeat CD4 count, ART initiation, or data censoring</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 3—ART eligibility to ART initiation</td>
<td>Initiated ART</td>
<td></td>
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</tbody>
</table>

### Median % Completing Stage (Range)

- **Stage 1**: 59%
- **Stage 2**: 46%
- **Stage 3**: 68%
- **Medians Multiplied**: 18%

### Summary of evidence

- 18% continuously in care if no “recycling”
- 33% in most complete study (South Africa)^2
  - Are only 1/5 to 1/3 of those who test HIV+ retained in care *continuously*?
- Data inconsistently measured and reported

Part 3: The Challenges to a Better Understanding of the Problem
Conceptual Problems in Defining Pre-ART Retention and Loss

- Should we focus on estimating retention across the entire period testing to treatment (all three stages)?
  - Requires large cohorts/person time, good info systems
  - Do estimates from single stages represent a consistent population?
- What is a successful outcome for each stage?
  - Is completion sufficient, or does it have to be timely?
    - For eligibility is it sufficient to be eligible, or eligible without illness/low CD4?
    - What is appropriate interval for success?
- For stage 1, how to track patients from testing to staging?
  - Patients at testing sites often have several options for referral to treatment sites that may be run by different providers
    - Must follow all positive patients to all initiation sites; or
    - Pair of 1 testing and 1 treatment site and limit retention denominator to patients who indicate a desire to go to that treatment site
Part 4: Suggestions for Defining Retention in pre-ART Care
Approach

• Define a set of explicit and consistent terms, time intervals, endpoints for pre-ART care
  – Ideal measure of pre-ART retention would cover entire time from testing to ART initiation, but not yet possible with routinely collected data
  – Focus on complete stages, not components of stage (e.g. HIV test to returning for CD4 result, not just a blood draw)
  – Avoid reporting to date of data censoring

• For each stage, determine:
  – What measures have been reported in the literature
  – Appropriate start points, outcomes, time frames to report
  – Who should be excluded from measures reported
# Stage 1: HIV Testing to Staging

<table>
<thead>
<tr>
<th>Study</th>
<th>Outcome Used</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>SA 1</td>
<td>≤ 6 months of HIV test</td>
<td>183</td>
</tr>
<tr>
<td>SA 6</td>
<td>≤ 6 months of HIV test</td>
<td>183</td>
</tr>
<tr>
<td>SA 6</td>
<td>Ever</td>
<td></td>
</tr>
<tr>
<td>SA 13</td>
<td>≤ 1 weeks of providing sample</td>
<td>7</td>
</tr>
<tr>
<td>Malawi 2</td>
<td>≤ 1 month of registering for care</td>
<td>31</td>
</tr>
<tr>
<td>SA 7</td>
<td>≤ 12 weeks of HIV test</td>
<td>84</td>
</tr>
<tr>
<td>SA 14</td>
<td>Ever</td>
<td></td>
</tr>
<tr>
<td>Uganda 1</td>
<td>Ever</td>
<td></td>
</tr>
<tr>
<td>Mozam 1</td>
<td>≤ 30 days of enrollment</td>
<td>30</td>
</tr>
<tr>
<td>Mozam 1</td>
<td>≤ 60 days of HIV test</td>
<td>60</td>
</tr>
<tr>
<td>SA 3</td>
<td>≤ 90 days of HIV test</td>
<td>90</td>
</tr>
<tr>
<td>SA 11</td>
<td>Ever</td>
<td></td>
</tr>
</tbody>
</table>

**Starting points:**
- HIV test
- Providing sample for CD4
- Registering for care
- Enrollment

**Outcomes:**
- Providing sample for CD4 test
- Returning for CD4 count results

**Range:**
- 1 week – Ever

**Median:**
- 4.5 months

*Citations in Rosen 2011 in press*
Stage 1: Working Proposal

- **Starting point:** Testing HIV-positive
- **Successful outcome:** Completing staging
  - Determination of whether patient should be referred for pre-ART care or ART (CD4 count and medical exam)
- **Negative outcomes:** Death, not completing staging
- **Reporting time:** 3 months and 1 year after HIV test
- **Exclusions:**
  - Patients previously enrolled in a later phase
  - When possible, exclude those who indicate a wish to use a different referral site from where outcome is measured
## Stage 2: Staging to Eligibility

<table>
<thead>
<tr>
<th>Study*</th>
<th>Outcome Used</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kenya 2</td>
<td>Attended HIV care 2-4 months after HIV test</td>
<td>122</td>
</tr>
<tr>
<td>Tanzania 1</td>
<td>Registering at HIV clinic ≤6 mo of referral from test</td>
<td>183</td>
</tr>
<tr>
<td>Uganda 2</td>
<td>Attendance at HIV clinic ≤6 months of HIV test</td>
<td>183</td>
</tr>
<tr>
<td>SA 8</td>
<td>Attended 1&lt;sup&gt;st&lt;/sup&gt; pre-ART medical appt 1 yr of staging</td>
<td>365</td>
</tr>
<tr>
<td>SA 12</td>
<td>Visited referral site after HIV test</td>
<td>?</td>
</tr>
<tr>
<td>SA 14</td>
<td>Access of HIV care</td>
<td>?</td>
</tr>
<tr>
<td>Ethiopia 1</td>
<td>“Immediate” linkage to HIV care after HIV test</td>
<td>?</td>
</tr>
<tr>
<td>Ethiopia 2</td>
<td>Visited referral site after HIV test</td>
<td>?</td>
</tr>
<tr>
<td>Malawi 2</td>
<td>Initiating /still in care at 7 months of follow-up</td>
<td>214</td>
</tr>
<tr>
<td>Kenya 3</td>
<td>In care 13 months after pre-ART enrollment</td>
<td>397</td>
</tr>
<tr>
<td>SA 10</td>
<td>Repeat CD4 ≤13 months of first CD4</td>
<td>397</td>
</tr>
<tr>
<td>SA 4</td>
<td>Initiating /still in care up to 3.5 years of follow-up</td>
<td>1278</td>
</tr>
<tr>
<td>SA 6</td>
<td>Repeat CD4 by up to 5 years of follow-up</td>
<td>1826</td>
</tr>
<tr>
<td>Ethiopia 3</td>
<td>Initiating or still in care at censoring</td>
<td>?</td>
</tr>
</tbody>
</table>

**Starting points:**
- Staging
- Referral from HIV test
- HIV test

**Outcomes:**

- **One time events:**
  - Visiting referral site
  - Registering
  - 1<sup>st</sup> pre-ART visit
  - Linkage to care
  - Accessing care

- **Repeat events:**
  - Attending care
  - In care
  - Repeat CD4

**Range:**
- 4 months – 5 years

**Median:**
- 1 year

*Citations in Rosen 2011 in press*
Stage 2: Working Proposal

- Challenging stage as success would be remaining actively in care and getting to ART eligibility before illness or low CD4
- Start point: Completion of staging w/referral to pre-ART care
- Successful outcomes (tentatively):
  - < 3 months late for learning eligibility status (last scheduled visit where patient gets results)?
  - Determination of eligibility prior to illness?
- Negative outcomes:
  - Death, no visit w/in 3 months of last eligibility status visit, illness prior to eligibility?
- Reporting time: 6 months, 1 year, yearly thereafter
- Exclusions: Transfers
### Stage 3: ART Eligibility to Initiation

<table>
<thead>
<tr>
<th>Study*</th>
<th>Outcome Used</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mozam 1</td>
<td>≤90 days of eligibility</td>
<td>90</td>
</tr>
<tr>
<td>SA 2</td>
<td>≤3 months after last pre-ART visit</td>
<td>92</td>
</tr>
<tr>
<td>SA 6</td>
<td>≤6 mo of HIV test if ART eligibility confirmed</td>
<td>183</td>
</tr>
<tr>
<td>SA 1</td>
<td>≤6 months of eligibility</td>
<td>183</td>
</tr>
<tr>
<td>Malawi 3</td>
<td>≥8 weeks after starting TB treatment</td>
<td>244</td>
</tr>
<tr>
<td>Uganda 3</td>
<td>≤1 year of enrollment in care if ART-eligible</td>
<td>365</td>
</tr>
<tr>
<td>SA 9</td>
<td>Date of data censoring up to 3 years</td>
<td>1096</td>
</tr>
<tr>
<td>SA 3</td>
<td>Date of data censoring</td>
<td></td>
</tr>
<tr>
<td>SA 4</td>
<td>Date of data censoring</td>
<td></td>
</tr>
<tr>
<td>Kenya 1</td>
<td>Date of data censoring</td>
<td></td>
</tr>
<tr>
<td>Malawi 2</td>
<td>Date of data censoring</td>
<td></td>
</tr>
<tr>
<td>Malawi 1</td>
<td>Not stated</td>
<td></td>
</tr>
<tr>
<td>Uganda 1</td>
<td>Unclear</td>
<td></td>
</tr>
<tr>
<td>SA 5</td>
<td>Unclear</td>
<td></td>
</tr>
</tbody>
</table>

**Start time:**
- ART Eligibility
- Last pre-ART visit
- HIV test
- Enrollment in care

**End time:**
- Data censoring
- Amount of time since start point

**Range:**
- 90 days-3 years

**Median:**
- 6 months

*References: Citations in Rosen 2011 in press*
**Stage 3: Working Proposal**

- **Start point:** Patient knows ART eligibility
- **Successful outcome:** ART initiation within 3 months of first determining eligibility
  - Initiation defined by ART being dispensed
- **Negative outcomes:**
  - In care but not initiated, death, lost from care
- **Reporting times:** 3 months and 3 monthly intervals
  - 3 months gives time for completion of ART preparation
- **Exclusions:**
  - Patients known to have transferred, initiated at other clinic
Conclusions

- Retention in pre-ART care has been under-researched to date
  - Review suggests that between 18-33% of patients who test-positive are retained in pre-ART care
  - Attention to pre-ART care sub-optimal
  - Current data lack consistent time periods and outcomes making it difficult to summarize
  - Proposals for standard outcomes and time frames can help give a better picture of the magnitude of the problem
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