Entry Into and Retention in Care and Antiretroviral Adherence: Considerations for Resource-Limited Countries

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Washington, DC
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CONTEXT: IAPAC GUIDELINES

• IAPAC recommendations on entry into care, retention in care and adherence provide broad framework which addresses many issues common in both resource-rich and resource limited settings (RLS)

• Identified recommendations for future research, including key areas relevant for RLS

• Evolving data on innovative approaches from RLS may also inform resource-rich settings – e.g. innovative community approaches
CONTEXT: PARTICULAR CHALLENGES FOR RESOURCE-LIMITED COUNTRIES

• Though increasing data available on entry into care, retention, and adherence in RLS, still significant gaps in data (e.g. specific populations; long-term retention)
• More data becoming available on interventions in RLS, though relatively few intervention studies
• Particular gaps re interventions for
  – Pre-ART care
  – Specific populations – pregnant women; infants; children and adolescents; key populations
  – Limited data on long-term retention (>2-3 yrs)
CONTEXT: PARTICULAR CHALLENGES FOR RESOURCE-LIMITED COUNTRIES

- Evolving recommendations re earlier initiation of ART will have implications for retention and adherence:
  - Growing trend towards use of Option B+ for PMTCT - test/treat
  - WHO recommendations for serodiscordant couples, with early initiation of ART
  - Potential use of treatment as prevention in other contexts would also lead to early initiation of ART

- As patients start ART earlier, often when asymptomatic, this may pose additional challenges to maintaining them on lifelong treatment
DATA ON RETENTION IN SUB-SAHARAN AFRICA

- Rosen, Fox, Gill, 2007 – Retention on ART
  - 32 studies (74,192 patients); weighted mean retention rate at two years - 62%
- Fox and Rosen, 2010 – Retention on ART
  - Meta-analysis of 33 studies (226,307 patients); retention on ART at 3 years - 72%
- Rosen and Fox, 2011 – Retention in pre-ART care; 28 studies

<table>
<thead>
<tr>
<th>Stage</th>
<th>Retention -median</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: HIV testing to receipt of CD4 count results/clinical staging</td>
<td>59% (35%-88%)</td>
</tr>
<tr>
<td>2: Staging to ART eligibility</td>
<td>46% (31%-95%)</td>
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<tr>
<td>3: ART eligibility to ART initiation</td>
<td>68% (14%-84%)</td>
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</tbody>
</table>

EMERGING ISSUE: RETENTION IN PREGNANT WOMEN
CHALLENGES IN MEASURING RETENTION IN RLS

- Reported data on retention may not distinguish between patients who are alive but no longer in care, those who have transferred to another site, and those who have died.
- Geng et al tracked a representative sample of lost patients in Uganda, determined outcomes, and used this data to “correct” estimates of retention for entire clinic population.
- Accounting for “silent transfers” substantially increased estimates of patient retention and connection to care.

DATA ON ADHERENCE IN SUB-SAHARAN AFRICA

• Retention is necessary but not sufficient to attain adherence

• Adherence rates in *behavioral, cognitive, biological, structural, and combination* intervention studies:

<table>
<thead>
<tr>
<th>Measure</th>
<th>Adherence Rate without Intervention</th>
<th>Adherence Rate with Intervention</th>
<th>Types of Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pill Counts</td>
<td>58%-89%</td>
<td>69%-95%</td>
<td>Education and Counseling, Social Support, Home-based Care, Treatment Supporters</td>
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<tr>
<td>Self Report</td>
<td>43%-88%</td>
<td>80%-93%</td>
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</table>


FACTORS AFFECTING RETENTION & ADHERENCE IN RESOURCE LIMITED SETTINGS

<table>
<thead>
<tr>
<th>Personal Characteristics</th>
<th>Socioeconomic</th>
<th>Health Care System</th>
<th>Social</th>
<th>Psychosocial</th>
<th>Clinical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Distance</td>
<td>Quality of care</td>
<td>Family and social support</td>
<td>Denial</td>
<td>Stage of disease/CD4</td>
</tr>
<tr>
<td>Gender</td>
<td>Transportation</td>
<td>Wait time</td>
<td>Cultural</td>
<td>Stigma</td>
<td>Presence or absence of symptoms</td>
</tr>
<tr>
<td>Pregnant or post-partum</td>
<td>Family/job commitments</td>
<td>Drug shortages</td>
<td>Homeless</td>
<td>Fear of disclosure</td>
<td>Dosing – frequency, complexity</td>
</tr>
<tr>
<td>Marginalized/ key populations</td>
<td>Competing expenses (food, lodging, etc)</td>
<td>Referral vs integrated services</td>
<td>Incarcerated</td>
<td>Mental health conditions</td>
<td>Substance abuse</td>
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<tr>
<td></td>
<td></td>
<td>Perceived value of services</td>
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<td></td>
<td></td>
<td>Data systems that facilitate monitoring</td>
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</tbody>
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This table outlines various factors affecting retention and adherence in resource-limited settings, categorized into personal characteristics, socioeconomic factors, health care system, social, psychosocial, and clinical aspects.
**Some Key Recommendations**

- **Systematic monitoring of entry into and retention in HIV care**
- **Pharmacy refill data are recommended when medication refills are not automatically sent to patients**
- **Among regimens of equal efficacy and safety, fixed-dose combinations are recommended**
- **Labor ward-based PMTCT adherence services for women not receiving ART before labor**
- **Interventions providing case management services and resources to address food insecurity, housing, and transportation needs**
- **Reminder devices and use of communication technologies with an interactive component**
- **Education and Counseling Interventions**
Approaches to Improving Retention in Resource-Limited Settings

- Health systems
  - Decentralization
  - Addressing HR shortages; task-shifting
  - Improved linkages and/or integrated services
- Quality improvement
  - Reduce clinic wait time
  - Address structural barriers to care (limited hours, fees, etc)
  - Address drug shortages
  - Improve access to key lab tests/results – e.g. CD4, VL, EID
    - POC testing if available
    - Improved lab services – quality, accessibility
    - Improved access to results – e.g. SMS messaging
  - Improve data systems for patient monitoring
Approaches to Improving Retention in Resource-Limited Settings

• Community interventions
  • Community support groups
  • Community/home-based care
• Patient tracing (physical +/- phone)
• Mobile phone interventions
• Provide key commodities/services which may increase uptake of care – e.g. “basic care package” including cotrimoxazole, safe water/hygiene commodities, insecticide-treated nets; nutritional support
• Important to determine barriers and facilitators for different settings and patient populations in order to develop a package of interventions to address specific needs
Distribution of Antiretroviral Treatment Through Self-Forming Groups of Patients in Tete Province, Mozambique

Tom Decroo, MD,* Barbara Telfer, MPH,* Marc Biot, MD, MSc,* Jacob Maïkérê, MD, MSc, PhD,† Sergio Dezembro,* Luisa Isabel Cumba, MD,‡ Carla das Dores, MD,‡ Kathryn Chu, MD, MSc,§‖ and Nathan Ford, MPH, PhD§¶

*Acquir Immune Defic Syndr • Volume 56, Number 2, February 1, 2011
A Different Approach

• Community ART Group (CAG) – designed with patient input
  – Self-forming patient groups with up to 6 members
  – Stable non-pregnant adults on ART
  – One representative from the group visits the health facility every month on a rotating basis and does the following:
    • Undergoes clinical assessment and CD4 count
    • Provides feedback to the health facility about the five other members of the group (including pill counts to measure adherence)
    • Obtains lab results for other members
    • Collects one month’s worth of ARVs for each group member
Results from MSF – Tête Study

Cohort of 1384 ART patients in 12 health facilities in Tête Province
- 291 groups formed
- 12-month retention: 97.5%
- Mortality: 2%
- LTFU: 0.2%
- Median follow-up time: 12.9 months
- 92% adherence (based on pill counts)
- Clinicians reported about 4-fold reduction in consultations among patients in CAGs

Community ART Groups - Impact

• Impact on patient
  • Decreased number of clinic visits
  • Improved psychosocial support
  • Stigma reduction
  • Early warning system for illness
  • Improved monitoring and resources to address adherence
  • Social safety net

• Impact at health facility
  • Decreased congestion at clinic; decreased burden on clinic staff
  • Allows staff to focus on sick or complex patients
  • Increased capacity to enroll new patients
  • Improved reporting of patient outcomes

Outcomes/Next Steps

• Government of Mozambique, with PEPFAR support, piloting the model in all 11 provinces
• 12-month pilot, with national scale-up pending the results of retrospective evaluation
• Approach well-accepted by patients – initially developed together with patients in response to patient-reported barriers
• Considering whether approach could be adapted to address other populations – e.g. pregnant women, pre-ART patients, key populations
Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomised trial


Lancet 2010; 376: 1838–45
### FINDINGS FROM WELTEL KENYA

#### Table 2: Primary and secondary outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>SMS group (number [%])</th>
<th>Control group (number [%])</th>
<th>RR (95% CI)*</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome</strong></td>
<td></td>
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<td></td>
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<tr>
<td>Intention-to-treat analysis†</td>
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</tr>
<tr>
<td>Self-reported adherence (&gt;95%)</td>
<td>168 (62%)</td>
<td>132 (50%)</td>
<td>0.81 (0.69-0.94)</td>
<td>0.006</td>
</tr>
<tr>
<td>Viral suppression (&lt;400 copies per mL)</td>
<td>156 (57%)</td>
<td>128 (48%)</td>
<td>0.85 (0.72-0.99)</td>
<td>0.04</td>
</tr>
<tr>
<td>Complete-case analysis‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-reported adherence§</td>
<td>168 (91%)</td>
<td>132 (91%)</td>
<td>1.00 (0.94-1.07)</td>
<td>0.94</td>
</tr>
<tr>
<td>Viral suppression¶</td>
<td>156 (75%)</td>
<td>128 (66%)</td>
<td>0.88 (0.77-1.00)</td>
<td>0.047</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Total attrition (missing)</td>
<td>53 (19%)</td>
<td>61 (23%)</td>
<td>1.24 (0.82-1.89)</td>
<td>0.31</td>
</tr>
<tr>
<td>Loss to follow-up</td>
<td>17 (6%)</td>
<td>27 (10%)</td>
<td>1.69 (0.91-3.23)</td>
<td>0.094</td>
</tr>
<tr>
<td>Mortality</td>
<td>25 (9%)</td>
<td>30 (11%)</td>
<td>1.27 (0.72-2.22)</td>
<td>0.42</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>7 (3%)</td>
<td>3 (1%)</td>
<td>2.26 (0.59-8.67)</td>
<td>0.34</td>
</tr>
<tr>
<td>Transfer out</td>
<td>4 (1%)</td>
<td>1 (0%)</td>
<td>0.25 (0.19-2.17)</td>
<td>0.38</td>
</tr>
</tbody>
</table>

Percentages do not add up to 100% in some cases because of rounding. * For non-adherence or virologic failure. †273 patients in the SMS group and 265 in the control group. ‡Because the Intention-to-treat analysis classed all patients with missing data as non-adherent or having viral failure, the number of adherent patients and number of patients with viral suppression are the same here as in the Intention-to-treat analysis. §185 patients in the SMS group and 145 patients in the control group. ¶208 patients in the SMS group and 194 patients in the control group. ||Fisher's exact test.

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Further data on mobile phone interventions

- Another RCT from Kenya (Pop-Eleches, 2011) also showed that weekly SMS reminders improved adherence, measured using MEMS.

- Cochrane review (Horvath, 2012):
  - “There is high-quality evidence from two RCTs that mobile phone text-messaging at weekly intervals is efficacious in enhancing adherence to ART, compared to standard care. Policy-makers should consider funding programs proposing to provide weekly mobile phone text-messaging as a means for promoting adherence to antiretroviral therapy.”
Future Directions

• Encourage implementation of IAPAC recommendations
• Address Future Research Recommendations in the Guidelines
  • Particular gaps for pre-ART patients and specific populations (pregnant women, infants, children and adolescents, key populations)
  • Limited data on cost-effectiveness of interventions
• Promote quality improvement programs to address site-level barriers to entry, retention, and adherence
• Support ongoing WHO work addressing entry into and retention in care, in preparation for WHO Treatment 2.0 Guidelines
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Thank you