The Importance of ARV Adherence

The Sida-funded Initiative in East Africa Technical Overview and Update, February 21, 2007

Management Sciences for Health
is a nonprofit organization
strengthening health programs worldwide.

John Chalker
Abiola Johnson

February 2007
The Importance of ARV Adherence –

*The Sida-funded Initiative in East Africa*

Technical Overview and Update, February 21, 2007

John Chalker, INRUD-IAA Project and INRUD Coordinator
Abiola Johnson, Program Associate, RPM Plus Program
Number of People Receiving ARVs in Low- and Middle-Income Countries, 2002–2005

Importance of Adherence

- Correlation with important clinical outcomes
  - Better weight gain and functioning
  - Better recovery in CD4 count
  - Lower viral load
- Development of resistance
  - Related, but not in linear fashion
- Appropriate adherence target is unclear
  - Early PI treatment achieved 95 percent but few studies of modern triple combination therapy exist
- Achieving rates over 80 percent for any chronic disease over the last 50 years has been shown to be problematic
Overview of Methods for Measuring Medication Adherence

<table>
<thead>
<tr>
<th>Method</th>
<th>Benefits</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOTS</td>
<td>Accurate</td>
<td>Impractical except unusual situations (TB, prison)</td>
</tr>
<tr>
<td>Blood levels of medicine, metabolite</td>
<td>Objective</td>
<td>Expensive, only practical in clinical trials</td>
</tr>
<tr>
<td>Clinical response (CD4, viral load)</td>
<td>Available in clinical records?</td>
<td>Bias in ascertainment</td>
</tr>
<tr>
<td>Electronic medication monitors (MEMS)</td>
<td>Precise, quantifiable, can measure timing</td>
<td>Expensive, obtrusive, open bottle does not equal consumption</td>
</tr>
<tr>
<td>Dispensing-based coverage</td>
<td>Routine data, somewhat more objective, longer time period</td>
<td>Pills not necessarily taken, data recording errors</td>
</tr>
<tr>
<td>Pill counts</td>
<td>Somewhat more objective</td>
<td>Additional process during care, pill dumping</td>
</tr>
<tr>
<td>Self-report</td>
<td>Simple, inexpensive, feasible in clinical setting</td>
<td>Recall error, selection bias, differences in recall period</td>
</tr>
</tbody>
</table>

Reported Reasons for Non-adherence in Low Resource Settings

- Malawi government clinic (van Oosterhout 2005)
  - Drugs not available in clinic (43%)
  - Personal financial problems (32%)
  - Forgetting (27%)
- Malawi scaled-up program (Ferradini 2006)
  - Away from home (34%)
  - Forgetting (30%)
  - Feeling sick or side effects (12%)
  - Run out of pills (9%)
- Children in Côte d’Ivoire (Arrivé 2005)
  - Drug out of stock (48.7%)
  - Forgetting (40.5%)
  - Child refuses to take (8.1%)
  - Delay in getting new prescription (2.7%)
Center for Pharmaceutical Management’s Adherence-Related Work

- Initiating a standardized method and record-keeping system to monitor adherence in health facilities
  - Gavin Steel and Mohan Joshi, South Africa (RPM Plus–Antimicrobial Resistance [AMR] budget)
- Develop a participatory tool to look at barriers to adherence and help facilities plan appropriate interventions to improve adherence
  - Hella Witt and Abiola Johnson (RPM Plus–HIV budget)
- International Network for Rational Use of Drugs (INRUD) Initiative on ARV Adherence (IAA)
  - Funded by Sida with initial funding from RPM Plus AMR

Documenting Current Practices

- East African Survey
  - What information is recorded regularly so that data can be easily retrieved?
  - What indicators are currently being collected?
    - What are their precise definitions?
    - What are their values?
- Teams from INRUD and the National AIDs Control organizations recruited from five East African countries February-March 2006
Survey of Current Practices in East Africa Treatment Programs

<table>
<thead>
<tr>
<th>Systems of care</th>
<th>Ethiopia</th>
<th>Kenya</th>
<th>Rwanda</th>
<th>Tanzania</th>
<th>Uganda</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health facilities</td>
<td>102</td>
<td>248</td>
<td>84</td>
<td>177</td>
<td>52</td>
</tr>
<tr>
<td>Facilities in survey*</td>
<td>10</td>
<td>14</td>
<td>5</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>ART patients on treatment:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>adults</td>
<td>22,000</td>
<td>70,035</td>
<td>17,615</td>
<td>38,757</td>
<td>51,332</td>
</tr>
<tr>
<td>children</td>
<td>2,000</td>
<td>4,500</td>
<td>1,443</td>
<td>3,783</td>
<td>6,106</td>
</tr>
<tr>
<td>Patients represented:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>adults</td>
<td>9,720</td>
<td>22,933</td>
<td>5,375</td>
<td>19,779</td>
<td>22,332</td>
</tr>
<tr>
<td>children</td>
<td>331</td>
<td>1,618</td>
<td>697</td>
<td>1,667</td>
<td>2,560</td>
</tr>
</tbody>
</table>

* 36 hospitals (13 referral, 12 provincial/district, 4 mission, 3 military/police, 4 private), 4 mission clinics, 5 NGO clinics, 2 health centers, 1 community-based organization

Current Adherence Measurement and Achievement in 48 Facilities

- Routine adherence measurement
  - Only 20 facilities calculate patient adherence
    - 2 by 3-day recall
    - 6 by pill count
    - 12 method unclear
  - Only 12 calculate clinic population adherence
- Reported adherence rates (11 facilities)
  - 9 facilities—median 95 percent (75–97 percent)
  - 2 facilities report rates > 85 percent
- Reported patient drop-out (19 facilities)
  - Median 3.9 percent (0.0–6.0 percent)
### 14 Definitions of Defaulters—
% of 24 Systems of Care (Ss) and 48 Facilities (Fs)

<table>
<thead>
<tr>
<th>No. of missed appts</th>
<th>Ss,%</th>
<th>Fs,%</th>
<th>Ss,%</th>
<th>Fs,%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>4</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>4</td>
<td>3 days</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>21</td>
<td>13</td>
<td>7 days</td>
<td>2</td>
</tr>
<tr>
<td>1 month</td>
<td>15</td>
<td>8</td>
<td>2 weeks</td>
<td>8</td>
</tr>
<tr>
<td>After missed appt</td>
<td></td>
<td></td>
<td>2 days</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 days</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>7 days</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 weeks</td>
<td>8</td>
</tr>
<tr>
<td>No. defined or not clear</td>
<td>17</td>
<td>29</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Potential Availability of Data for Adherence Monitoring and Validation

48 Facilities Reporting Availability of Data by Type, %

<table>
<thead>
<tr>
<th>Type of Data</th>
<th>Usually</th>
<th>Sometimes</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient self-reported adherence</td>
<td>63</td>
<td>27</td>
<td>10</td>
</tr>
<tr>
<td>Pill count</td>
<td>38</td>
<td>48</td>
<td>15</td>
</tr>
<tr>
<td>Reported reasons for non-adherence</td>
<td>44</td>
<td>44</td>
<td>13</td>
</tr>
<tr>
<td>Prescribed ARV dose</td>
<td>96</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Number of pills dispensed</td>
<td>98</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Date of next scheduled visit</td>
<td>98</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Date of actual vs. scheduled visit</td>
<td>29</td>
<td>10</td>
<td>60</td>
</tr>
<tr>
<td>CD4 count</td>
<td>0</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Viral load</td>
<td>0</td>
<td>31</td>
<td>69</td>
</tr>
</tbody>
</table>
Current Interventions for Adherence

<table>
<thead>
<tr>
<th>Intervention</th>
<th>% of Facilities</th>
<th>% of Systems of Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient counseling before starting ARVs</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Repeated counseling after ARVs</td>
<td>98</td>
<td>100</td>
</tr>
<tr>
<td>Support person/care partner</td>
<td>77</td>
<td>79</td>
</tr>
<tr>
<td>Systematic monitoring at clinic</td>
<td>67</td>
<td>63</td>
</tr>
<tr>
<td>Social support</td>
<td>44</td>
<td>63</td>
</tr>
<tr>
<td>Use of a device</td>
<td>38</td>
<td>21</td>
</tr>
<tr>
<td>Community-based health workers</td>
<td>30</td>
<td>47</td>
</tr>
<tr>
<td>Fast track service at health facility</td>
<td>27</td>
<td>26</td>
</tr>
<tr>
<td>Other interventions</td>
<td>23</td>
<td>5</td>
</tr>
<tr>
<td>Reminder phone calls</td>
<td>21</td>
<td>16</td>
</tr>
<tr>
<td>Reimbursement of travel</td>
<td>15</td>
<td>16</td>
</tr>
<tr>
<td>Additional financial incentives</td>
<td>10</td>
<td>5</td>
</tr>
</tbody>
</table>

Recommendations for Interventions

- Social support
- Psychological support including peer support
- Providing services closer to the patient
- Health provider capacity and motivation
- The use of treatment reminders
- Improved monitoring
- Improved counseling and communication
Conclusion—East African Survey

- Definitions of adherence, defaulters, or dropouts are variable
- Measurement at individual or facility level is haphazard with various data sources and various methods of calculation
- There is much data recorded at both the clinic and pharmacy, but it is unclear how frequently it is recorded (e.g., pill counts)
- A number of interventions are being used and planned, not all of which are being evaluated
- Recommendations indicate need to improve food security for patients and training for health personnel

INRUD Initiative on ARV Adherence

- Five-year project funded by Swedish International Development Cooperation Agency (Sida) (Sept. 1, 2006)
- Objectives
  - Develop and validate adherence indicators and methodology in low-resource settings
  - Investigate adherence rates and determinants of adherence for different programs and different types of individuals
  - Pilot model adherence interventions at individual and program levels
  - Work with national programs to scale up successful interventions as national policy
Collaborators for INRUD-IAA

- INRUD
  - Global INRUD network with coordinating center at Management Sciences for Health (John Chalker)
  - Country teams
- National AIDS Programs of Ethiopia, Kenya, Rwanda, Tanzania, Uganda
- Harvard Medical School Drug Policy Research Group
- Karolinska Institute Division of International Health Care Research (IHCAR)
- WHO Department of Medicine Policy and Standards

An Overview of the INRUD Process for Changing Use of Medicine

1. EXAMINE
   Measure Practices
   (Descriptive Quantitative Studies)

2. DIAGNOSE
   Identify Problems and Causes
   (In-depth Quantitative and Qualitative Studies)

3. TREAT
   Design and Implement Interventions
   (Collect Data to Measure Outcomes)

4. FOLLOW UP
   Assess Changes in Outcomes
   (Quantitative and Qualitative)
Characteristics of an Effective Adherence Measurement Methodology

- Relevant for management
  - Patient care
  - Facility quality improvement
- Feasible
  - Applicable in any setting
  - Limited human and financial resources
  - Rapid access to results
  - If possible, data from routine records
- Reliable—consistent results over time and with different observers
- Valid—correlated with actual practice and clinical outcomes

INRUD-IAA—Measurement Stage (1)

1. Stakeholder meeting to review East African survey results and propose indicators
2. Design data collection, entry, and consolidation instruments
3. Test feasibility and reliability of collecting these indicators in a random sample of facilities in two countries (with RPM Plus/USAID support)
   - Kenya
   - Rwanda
INRUD-IAA—Measurement Stage (2)

4. Test validity of proven possible indicators
5. Finalize data collecting instruments and instructions as to use
6. Test method again with less hands-on help
7. WHO to publish as working draft as standard method for assessing adherence

Timeline—
- Steps 1–6 complete by October 2007
- Step 7: During 2008

INRUD-IAA—Diagnostic Stage: Identify Determinants of Adherence

- Use indicator data collection method for finding facilities and individuals with good and bad adherence
- Build on what is known from other work
- Conduct in-depth studies of facilities and individuals with good and bad adherence to find reasons for adherence; this will inform design of interventions
- Use a modified version of discussion tool Abiola and Hella are developing to find what stakeholders believe are possible interventions

Timeline—By end of October 2007
INRUD-IAA – Intervention Stage

1. Pilot model adherence interventions at individual and programmatic levels in two target countries and measure effects
   Timeline—November 2007–October 2008 (Year 2)

2. Establish activities/processes required for national programs and scale-up successful interventions as national policy in the two target countries
   Timeline—November 2008–October 2009 (Year 3)

3. Disseminate successful approaches for developing national programs to the other three regional project countries and facilitate implementation
   Timeline—November 2009–August 2011 (Years 4-5)

Draft Core Indicators of Adherence and Treatment Defaulting

- Medication adherence
  - Self-report adherence, “In last 3 days, how many of your ARV doses did you miss completely or not take at the time you were supposed to take them?”
  - One-year (6 month) pharmacy-based adherence
  - Pill counts (if available)

- Clinical outcomes (CD4 count, viral load)

- Defaulting
  - Missed visits
  - Recapture within 60 days after missed visit
Other Draft Core Measures

- Facility-level determinants
  - Staffing and patient load
  - Open at convenient hours
  - Private space for counseling
  - Quality of record keeping
  - Availability and regularity of lab testing
  - Reliability of medication supply
  - Consistent dispensing and labeling

- Patient-level determinants
  - Travel and waiting time
  - Ability to function normally
  - Occurrence of opportunistic infections and side effects
  - Knowledge about regimen

Pilot National Adherence Survey Sampling Strategy

- Facilities (N = 20)
  - Major programs, types, geographic areas
  - Systems, staff load, ARV availability

- Patient exit interviews (N = 30 per facility)
  - Self-report, knowledge, dispensing, time

- Retrospective patients
  - Recent—3 months, N = 100 per facility
    - Self-report, pill count, defaulting
  - Long-term—12 months (preferable) or 6 months, N = 100 per facility
    - Pharmacy-based adherence, defaulting
Reliability

For each retrospective sample and the exit interviews, a proportion should be performed by two different people to compare and test for reliability.

Availability of Records and Patients

<table>
<thead>
<tr>
<th></th>
<th>Rwanda</th>
<th>Kenya</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Average</td>
</tr>
<tr>
<td>Exit Interviews (30 per facility wanted)</td>
<td>285</td>
<td>15.8</td>
</tr>
<tr>
<td></td>
<td>1,601</td>
<td>80.1</td>
</tr>
<tr>
<td></td>
<td>1,532</td>
<td>76.6</td>
</tr>
<tr>
<td>Recent Retrospective (100 per facility wanted)</td>
<td>160</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td>709</td>
<td>44%</td>
</tr>
<tr>
<td>Self-Report from Recent Retrospective</td>
<td>754</td>
<td>49.2%</td>
</tr>
<tr>
<td></td>
<td>16 of 20 facilities</td>
<td>20 of 20 facilities</td>
</tr>
</tbody>
</table>
Comparison of Facility-Level Adherence Measures in Pilot Studies

Average Percentage ARV Adherence
Summary of Facility-Level Averages Across Facilities

<table>
<thead>
<tr>
<th>Facility Average</th>
<th>Self-Report (exit interviews)</th>
<th>Self-Report (last 3 months recorded)</th>
<th>Pill Count (last 3 months recorded)</th>
<th>Dispensing (still in treatment)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highest</td>
<td>100.0 100.0</td>
<td>100.0 100.0</td>
<td>100.0 100.0</td>
<td>100.0 100.0</td>
</tr>
<tr>
<td>75%ile</td>
<td>100.0 100.0</td>
<td>100.0 100.0</td>
<td>99.0 98.4</td>
<td>98.0 98.0</td>
</tr>
<tr>
<td>Median</td>
<td>98.3 100.0</td>
<td>99.3 100.0</td>
<td>97.8 96.7</td>
<td>95.1 96.9</td>
</tr>
<tr>
<td>25%ile</td>
<td>95.1 91.1</td>
<td>98.1 100.0</td>
<td>96.8 93.8</td>
<td>84.5 95.4</td>
</tr>
<tr>
<td>Lowest</td>
<td>67.8 65.3</td>
<td>87.5 97.9</td>
<td>86.7 73.6</td>
<td>53.3 88.7</td>
</tr>
</tbody>
</table>

Patient Retention, Defaulting, Treatment Discontinuation

Average Percentage Defaulting and Discontinuing Treatment
Summary of Facility-Level Averages Across Facilities

<table>
<thead>
<tr>
<th>Facility Average</th>
<th>Three -month retrospective cohort</th>
<th>Long-term retrospective cohort *</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Missed next appointment Among missed, not re-attend** Gap in treatment &gt;30 days No drugs within last month</td>
<td></td>
</tr>
<tr>
<td>Highest</td>
<td>54.3 86.0 100.0 66.7 78.8 25.7 30.8 43.0</td>
<td></td>
</tr>
<tr>
<td>75%ile</td>
<td>26.9 20.4 22.6 50.0 32.1 7.6 14.5 12.8</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>19.3 7.6 10.2 11.1 16.3 4.7 6.7 4.0</td>
<td></td>
</tr>
<tr>
<td>25%ile</td>
<td>10.5 4.2 0.0 0.0 8.0 1.0 4.7 0.0</td>
<td></td>
</tr>
<tr>
<td>Lowest</td>
<td>4.3 0.0 0.0 0.0 0.0 0.0 0.0 0.0</td>
<td></td>
</tr>
</tbody>
</table>

* Kenya 12 months, Rwanda 6 months
** Kenya: within 60 days last appt; Rwanda, within 30 days of missed appt.
Patient Load and other Key Performance Indicators

<table>
<thead>
<tr>
<th></th>
<th>Rwanda</th>
<th></th>
<th>Kenya</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Average</td>
<td>Max</td>
<td>Min</td>
<td>Average</td>
</tr>
<tr>
<td>Pt load/week</td>
<td>188</td>
<td>750</td>
<td>30</td>
<td>313</td>
</tr>
<tr>
<td>Pts/hour/clinician</td>
<td>2.6</td>
<td>7.6</td>
<td>0.4</td>
<td>3.2</td>
</tr>
<tr>
<td>Pts per week per support staff</td>
<td>35.4</td>
<td>94</td>
<td>10</td>
<td>32.6</td>
</tr>
<tr>
<td>Average travel time to clinic (mins)</td>
<td>108</td>
<td>266</td>
<td>14</td>
<td>167</td>
</tr>
<tr>
<td>Average time in clinic (mins)</td>
<td>70</td>
<td>128</td>
<td>15</td>
<td>80</td>
</tr>
</tbody>
</table>

Discussion Point 1—Recommendations on Simplifying Sampling From Feasibility Surveys

- Take only one retrospective sample from six months ago (120 pts who attended 6 to 7 months ago or who were on treatment by the end of that month).
- Look at and record—
  - Dispensing over 6 months and gaps
  - Missed appointments and re-attendance for same patient followed forward 3 months
  - ID number; index visit date; months on ARVs at index visit; age; gender; latest CD4 count in last six months; if CD4 count is more than 300 cells per µl
  - (1 side of landscape-oriented paper, 25 patients per side—100 patients could be back-to-back on two pieces of paper)
Discussion Point 2—How to Grade Facilities?

- As yet an unanswered question—We know that the measures show gradation but how to classify?
- Suggested Methods
  - Take main measures and grade 1-3 on set standards. Then take average mark as final score (Need to define parameters and what to do with no measure)
  - Other?

Discussion Point 3—Adherence Promotion Planning Tool

- Hella Witt and Abiola Johnson are developing an Adherence Promotion Planning Tool—a workshop guide for planning interventions to improve adherence to ART in health facilities

- This is a discussion tool based on the one developed for TB to be carried out nationally
Discussion Point 4

**MSH / CPM Adherence Work**

- How to maximize collaboration and sharing of all our work on adherence between different Centers and Programs