

# The Importance of ARV Adherence

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*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  
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*February 2007*



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*Strengthening pharmaceutical management for better health worldwide*

## 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

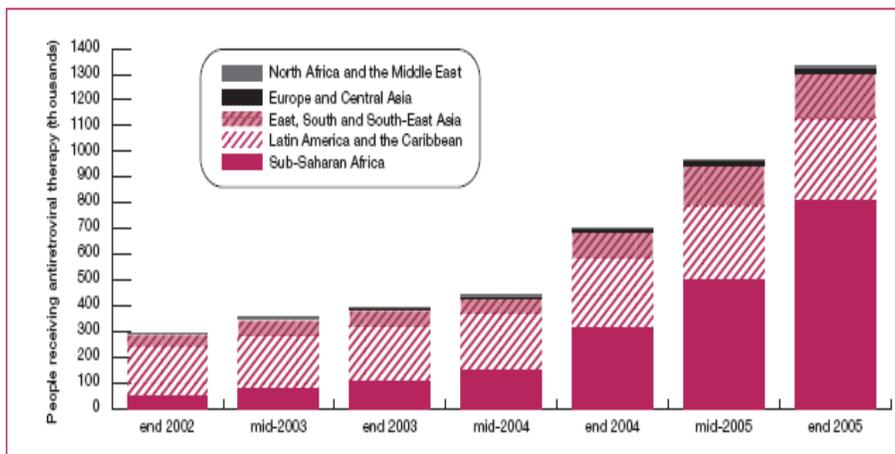
Abiola Johnson, Program Associate, RPM Plus Program



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## Number of People Receiving ARVs in Low- and Middle-Income Countries, 2002–2005



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## 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

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## Overview of Methods for Measuring Medication Adherence

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

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## 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%)

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## 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

	Ethiopia	Kenya	Rwanda	Tanzania	Uganda
Systems of care	7	6	1	5	5
Earliest program, yr	2003	2001	1999	2004	1991
Health facilities	102	248	84	177	52
Facilities in survey*	10	14	5	10	9
ART patients on treatment:					
adults	22,000	70,035	17,615	38,757	51,332
children	2,000	4,500	1,443	3,783	6,106
Patients represented:					
adults	9,720	22,933	5,375	19,779	22,332
children	331	1,618	697	1,667	2,560

\* 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)

	Ss,%	Fs,%		Ss,%	Fs,%
Non-attendance			After missed appt		
6 months	10	4	2 days	—	4
4 months	—	4	3 days	—	4
3 months	21	13	7 days	2	8
2 months	4	4	2 weeks		8
1 month	15	8	One week without drugs	2	—
No. of missed appts			Never classified	2	—
1	13	—	Not defined or not clear	17	29
2		4			
3	15	8			

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## Potential Availability of Data for Adherence Monitoring and Validation

48 Facilities Reporting Availability of Data by Type, %

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

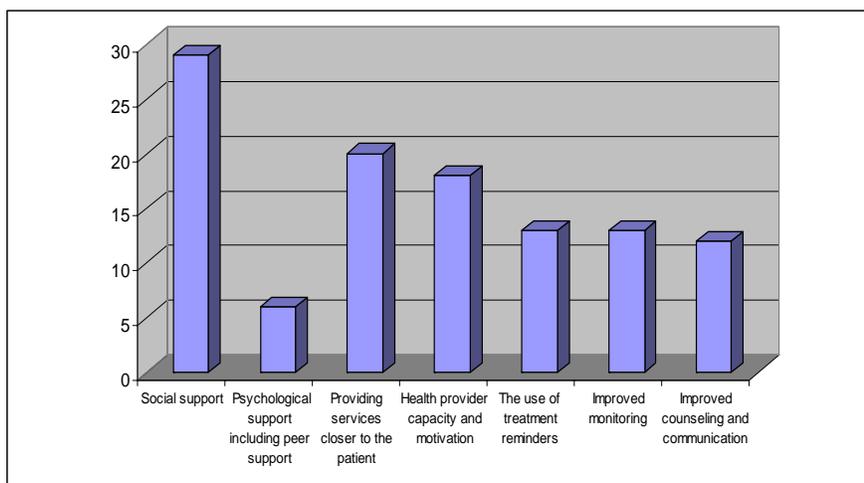
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## Current Interventions for Adherence

	% of Facilities		% Systems of Care	
	Use	Plan to	Use	Plan to
Patient counseling before starting ARVs	100	-	100	-
Repeated counseling after ARVs	98	2	100	-
Support person/care partner	77	6	79	5
Systematic monitoring at clinic	67	19	63	0
Social support	44	19	63	11
Use of a device	38	19	21	21
Community-based health workers	30	35	47	42
Fast track service at health facility	27	6	26	16
Other interventions	23	2	5	0
Reminder phone calls	21	13	16	5
Reimbursement of travel	15	6	16	11
Additional financial incentives	10	2	5	5

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## Recommendations for Interventions



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## 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

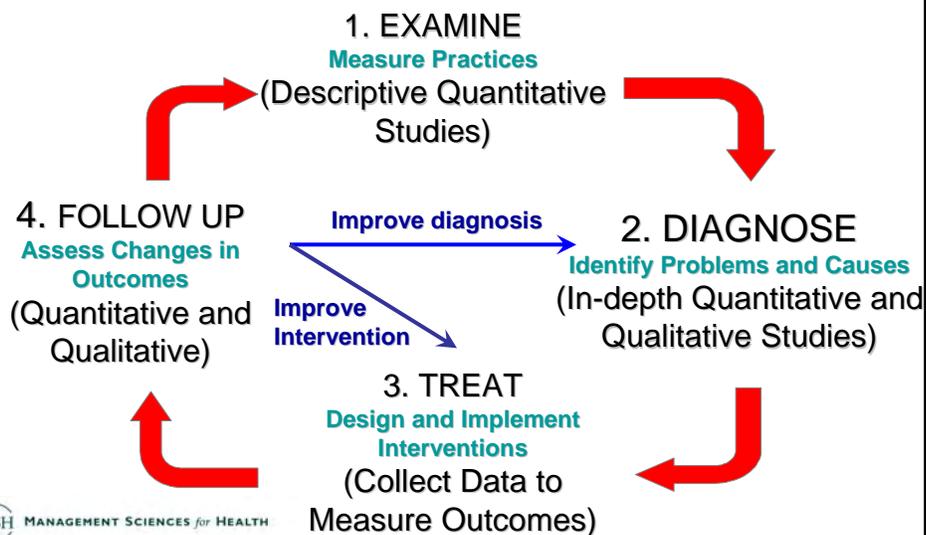
## INRUD Initiative on ARV Adherence

- 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



## 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

	Rwanda			Kenya		
	Total	Average	Lowest	Total	Average	Lowest
Exit Interviews (30 per facility wanted)	285	15.8	<ul style="list-style-type: none"> <li>▪2 with none</li> <li>▪2 with 3</li> <li>▪2 with 5</li> </ul>	373	19.6	<ul style="list-style-type: none"> <li>▪1 with none</li> <li>▪3 with 3</li> </ul>
Recent Retrospective (100 per facility wanted)	1,601	80.1	Lowest 50	1,263	63.2	<ul style="list-style-type: none"> <li>▪1 with none</li> <li>▪Lowest 24</li> </ul>
Long Retrospective (100 per facility wanted)	1,532	76.6	Lowest 45	986	49.3	Lowest 6
Self-Report from Recent Retrospective	160	10%	<ul style="list-style-type: none"> <li>▪10 with none</li> <li>▪1 with 3; 5; 7</li> </ul>	608	48%	<ul style="list-style-type: none"> <li>▪7 with none</li> <li>▪1 with 5</li> </ul>
Pill Count from Recent Retrospective	709	44%	8 with none	150	12%	<ul style="list-style-type: none"> <li>▪8 with none</li> <li>▪1 with 3; 8</li> </ul>
Pill count from Long Retrospective	754	49.2%	8 with none	116	11.8%	<ul style="list-style-type: none"> <li>▪12 with none</li> <li>▪1 with 1</li> <li>▪2 with 6</li> <li>▪1 with 9</li> </ul>
Dispensing over time from Long Retrospective	16 of 20 facilities			20 of 20 facilities		

## Comparison of Facility-Level Adherence Measures in Pilot Studies

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

Facility Average	Self-Report (exit interviews)		Self-Report (last 3 months recorded)		Pill Count (last 3 months recorded)		Dispensing (still in treatment)	
	Ken. N=19	Rwan. N=19	Ken. N=13	Rwan. N=7	Ken. N=6	Rwan. N=12	Ken. N=20	Rwan. N=17
Highest	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
75%ile	100.0	100.0	100.0	100.0	99.0	98.4	98.0	98.0
<b>Median</b>	<b>98.3</b>	<b>100.0</b>	<b>99.3</b>	<b>100.0</b>	<b>97.8</b>	<b>96.7</b>	<b>95.1</b>	<b>96.9</b>
25%ile	95.1	91.1	98.1	100.0	96.8	93.8	84.5	95.4
Lowest	67.8	65.3	87.5	97.9	86.7	73.6	53.3	88.7

## Patient Retention, Defaulting, Treatment Discontinuation

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

Facility Average	Three -month retrospective cohort				Long-term retrospective cohort *			
	Missed next appointment		Among missed, not re-attend**		Gap in treatment >30 days		No drugs within last month	
	Ken. n=18	Rwan. n=19	Ken. n=18	Rwan. n=17	Ken. n=20	Rwan. n=17	Ken. n=19	Rwan. n=17
Highest	54.3	86.0	100.0	66.7	78.8	25.7	30.8	43.0
75%ile	26.9	20.4	22.6	50.0	32.1	7.6	14.5	12.8
<b>Median</b>	<b>19.3</b>	<b>7.6</b>	<b>10.2</b>	<b>11.1</b>	<b>16.3</b>	<b>4.7</b>	<b>6.7</b>	<b>4.0</b>
25%ile	10.5	4.2	0.0	0.0	8.0	1.0	4.7	0.0
Lowest	4.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0

\* 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

	Rwanda			Kenya		
	Average	Max	Min	Average	Max	Min
Pt load/week	<b>188</b>	750	30	<b>313</b>	1525	48
Pts/hour/clinician	<b>2.6</b>	7.6	0.4	<b>3.2</b>	19.6	0.6
Pts per week per support staff	<b>35.4</b>	94	10	<b>32.6</b>	89.5	8
Average travel time to clinic (mins)	<b>108</b>	266	14	<b>167</b>	496	42
Average time in clinic (mins)	<b>70</b>	128	15	<b>80</b>	187	41

## 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  $\mu$ l
  - (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