

# Adherence to Medical Therapy

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# Learning Objectives

Upon completion of this presentation, learners should be better able to:

- Screen for sub-optimal adherence to anti-retroviral therapy
- Recommend to your patients some support tools to improve adherence

# Outline

- The spectrum of HIV care
- Adherence to ART: Prevalence and impact
- Screening for sub-optimal adherence
- Interventions and recommendations
- Conclusions

# Audience Response: Who are you?

1. An HIV primary care physician, NP, or PA
2. An HIV Specialist (I leave the primary care to others)
3. An HIV nurse
4. A social worker or case manager
5. A pharmacist
6. Other clinical
7. I don't see patients

# The Spectrum of HIV Care

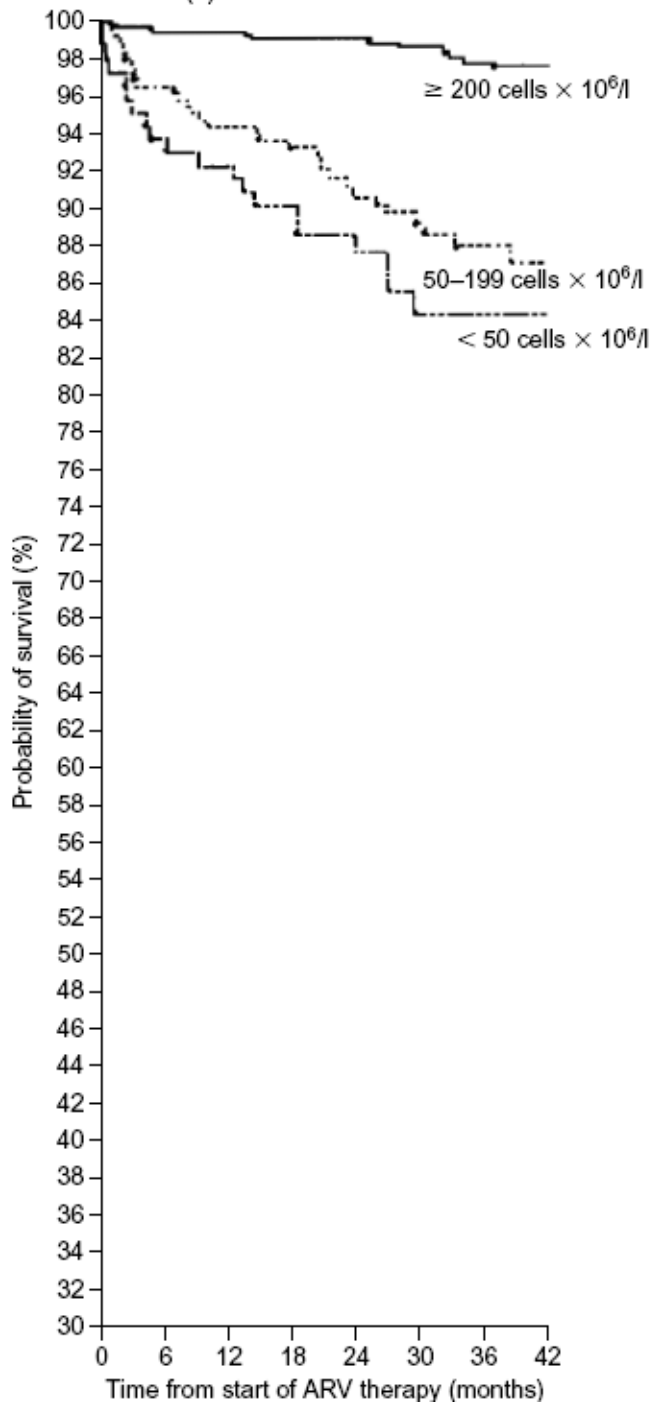
- Link to care after HIV diagnosis
  - Generally, attend one visit with a provider who can prescribe highly active antiretroviral therapy
- Be retained in care, or stay in care chronically
  - Attend required provider visits for primary HIV care
- Adhere to medications



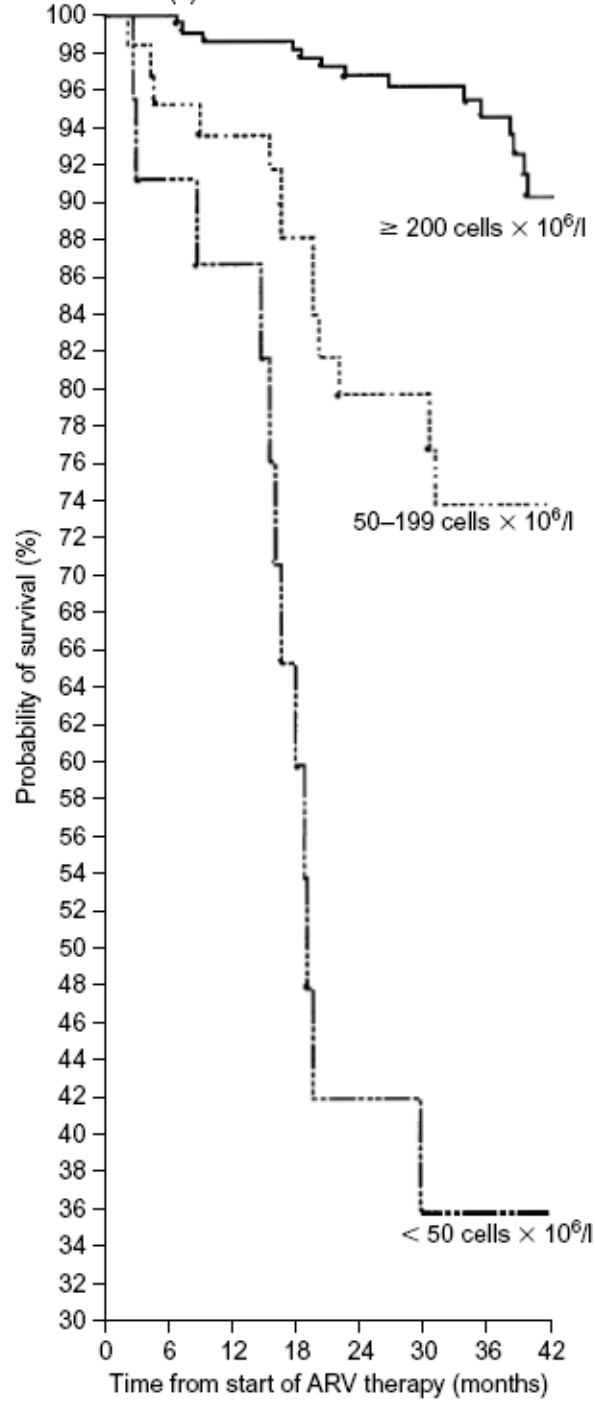
# Magnitude of the Problem

- Meta-analysis for adherence to ART:
  - 55% in North America achieved adequate levels of adherence
- Meta-analysis for retention in care:
  - 59% “had multiple HIV medical care visits averaged across assessment intervals of 6 months to 3-5 years.”

(a)  $\geq 75\%$  adherent



(b)  $< 75\%$  adherent



# Adherence-Survival Relationship

Wood AIDS 2003; 17:711



# Predictors of Adherence

- Poorer adherence predicted by:
  - Substance use
  - Depression and psychiatric disease
  - Cognitive dysfunction
  - Social and economic instability
  - More complex dosing schedules
  - Pill burden
  - Side effects
  - Idiosyncratic reasons



# Barriers and Facilitators

- Co-pays
- Ease / difficulty of getting refills
- Support in pill taking
- Pill boxes and reminders
- Trust / relationship with provider
- Belief / fear in medications
- Forgetting
- Depression and substance use

Audience Response: When prescribing a new regimen for a patient, I can usually predict who is going to have adherence problems and who is not

1. All or nearly all of the time
2. Most of the time
3. About half of the time
4. Some of the time
5. Hardly ever or never
6. N/A: I don't prescribe

# Why We Need to *Measure* Adherence

- 40 patients, switching to new regimen
  - Adherence measured with MEMS for 4 months
  - Providers predict adherence at switch
  - Providers estimate adherence at end

**Table 1.** Accuracy of provider assessments and correlation with measured outcome [Caption for P11881]

Variable	Statistical association (95% confidence interval)
Prediction of adherence	Spearman's $\rho = +0.003$ ( $-0.31$ – $+0.31$ )
Prediction of undetectable viral load by 4 months	Accuracy rate 53%, kappa $-0.04$ ( $-0.24$ – $+0.16$ )
Estimation of adherence	Spearman's $\rho = +0.69$ ( $+0.46$ – $+0.84$ )

# Measuring Adherence to ART

- “Objective”
  - Electronic medication caps
  - Drug levels
  - Pharmacy refill dates
  - Directly observed therapy
  - Pill count
- “Subjective”
  - Patient self-report
    - AACTG: 3 or 4 day report of missed doses
    - CPCRA: Likert scale of doses taken
    - VAS: linear scale of doses taken
    - Qualitative: “excellent” to “poor”
  - Provider assessment



Audience Response: For those of you prescribed to take a medicine at least daily for the last month or more:

Have you missed taking any of your medicines in the last month?

1. Yes
2. No

# Audience Response: For the same group:

I know it is hard to take pills every day. Most people miss doses of their medicines at times for lots of different reasons. It wouldn't surprise me if you missed a lot of doses. How many doses of your medicines did you take in the last 4 weeks?

1. None or hardly any
2. Some but less than half
3. About half
4. Most but not all
5. All

# Audience Response: For the same group:

Which version of the adherence assessment made you more comfortable, trusting, and willing to disclose more honestly?

1. First version
2. Second version

# AIDS Clinical Trials Group

- After listing medication doses and frequency with the study nurse:

**PATIENT ONLY continue here.**

The next section of the questionnaire asks about your HIV study medications that you took over the last four days.

Most people with HIV have many pills to take at different times during the day. Many people find it hard to always remember their pills:

- Some people get busy and forget to carry their pills with them.
- Some people find it hard to take their pills according to all the instructions, such as “with meals,” or “on an empty stomach,” “every 8 hours,” “with plenty of fluids.”
- Some people decide to skip doses to avoid side effects or to just not be taking pills that day.

We need to understand how people with HIV are really doing with their pills. Please tell us what you are **actually** doing. Don't worry about telling us that you don't take all your pills. We need to know what is really happening, not what you think we “want to hear.”

# ACTG 4-day Recall

1. The next section of the questionnaire asks about the study medications that you may have missed taking over the last four days. Please complete the following table by filling in the boxes below.

IF YOU TOOK ONLY A PORTION OF A DOSE ON ONE OR MORE OF THESE DAYS, PLEASE REPORT THE DOSE(S) AS BEING MISSED.

Step 1 Names of your anti-HIV study drugs	HOW MANY DOSES DID YOU <u>MISS</u> . . .			
	Step 2 Yesterday	Step 3 Day before yesterday (2 days ago)	Step 4 3 days ago	Step 5 4 days ago
	<input type="text"/> doses	<input type="text"/> doses	<input type="text"/> doses	<input type="text"/> doses
	<input type="text"/> doses	<input type="text"/> doses	<input type="text"/> doses	<input type="text"/> doses
	<input type="text"/> doses	<input type="text"/> doses	<input type="text"/> doses	<input type="text"/> doses

# ACTG

- During the past 4 days, on how many days have you missed taking all your doses?
- Most anti-HIV medications need to be taken on a schedule, such as “2 times a day” or “3 times a day” or “every 8 hours.” How closely did you follow your specific schedule over the last four days?
- Do any of your anti-HIV medications have special instructions, such as “take with food” or “on an empty stomach” or “with plenty of fluids?”
  - If Yes, how often did you follow those special instructions over the last four days?
- Some people find that they forget to take their pills on the weekend days. Did you miss any of your anti-HIV medications last weekend—last Saturday or Sunday?
- When was the last time you missed any of your medications?
  - Within the past week, 1-2 weeks ago, 2-4 weeks ago, 1-3 months ago, More than 3 months ago, Never skip medications

**G. People may miss taking their medications for various reasons. Here is a list of possible reasons why you may miss taking your medications. How often have you missed taking your medications because you: (Circle one response for each question.)**

	<u>Never</u>	<u>Rarely</u>	<u>Sometimes</u>	<u>Often</u>
1. Were away from home?	0	1	2	3
2. Were busy with other things?	0	1	2	3
3. Simply forgot?	0	1	2	3
4. Had too many pills to take?	0	1	2	3
5. Wanted to avoid side effects?	0	1	2	3
6. Did not want others to notice you taking medication?	0	1	2	3
7. Had a change in daily routine?	0	1	2	3
8. Felt like the drug was toxic/harmful?	0	1	2	3
9. Fell asleep/slept through dose time?	0	1	2	3
10. Felt sick or ill?	0	1	2	3
11. Felt depressed/overwhelmed?	0	1	2	3
12. Had problems taking pills at specified times (with meals, on empty stomach, etc.)?	0	1	2	3
13. Ran out of pills?	0	1	2	3
14. Felt good?	0	1	2	3

# CPCRA 7-day Recall

## **SECTION B**

### **TO BE COMPLETED BY STUDY PARTICIPANT**

Many people have trouble taking all their pills all of the time. For each drug listed in Section A, indicate how many of your pills you took **during the last 7 days** (check only one answer for each drug listed). Please answer all of the questions as honestly and carefully as possible. How you answer these questions will not affect your care or participation in this study. If you are unsure about a question, please give the best answer you can.

**During the last 7 days, I took:**

<b><u>Drug Name</u></b>	<b><u>ALL</u> my pills <u>every day</u></b>	<b><u>MOST</u> of my pills</b>	<b><u>About</u> <u>ONE-HALF</u> of my pills</b>	<b><u>VERY FEW</u> of my pills</b>	<b><u>NONE</u> of my pills</b>
1. _____	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>
2. _____	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>

# Visual Analogue Scale

Most people with HIV have many pills to take at different times during the day. Many people find it hard to always remember their pills.

For example:

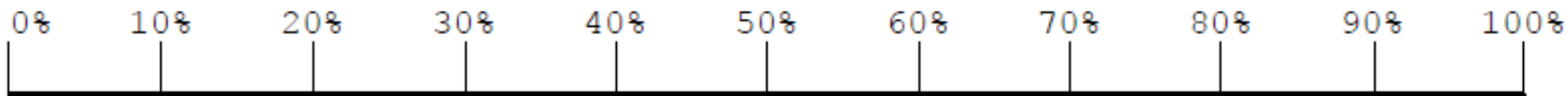
- . Some people get busy and forget to carry their pills with them.
- . Some people find it hard to take their pills according to all the instructions, such as "with food" or "on an empty stomach."
- . Some people decide to skip pills to avoid side effects or to just not take pills that day.

We need to understand what you are really doing with your pills. Don't worry about telling us you don't take all your pills. We need to know what is really happening, not what you think we "want to hear."

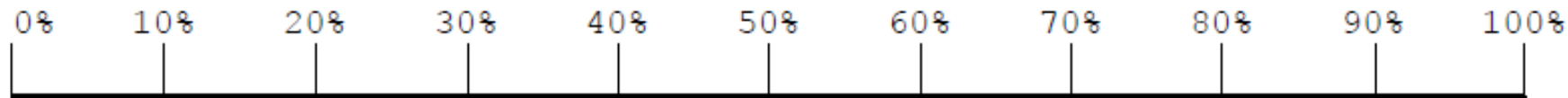
Now I am going to ask you some questions about these drugs. Please put an "X" on the line below at the point showing your best guess about how much **(DRUGS A-D)** you have taken in the last three to four weeks. We would be surprised if this was 100% for most people.

**HAND INSTRUMENT AND PEN TO RESPONDENT**

- e.g. 0% means you have **taken no (DRUG A)**  
50% means you have **taken half your (DRUG A)**  
100% means you have **taken every single dose of (DRUG A)**



**B1.** How about **(DRUG B)**?



Walsh AIDS 2002; 16:269;  
Giordano HIV Clin Trials 2004; 5:74



# Qualitative Measure

Thinking about the past 4 weeks, on average how would you rate your ability to take all of your HIV pills as your doctor prescribed?

Very Poor

Poor

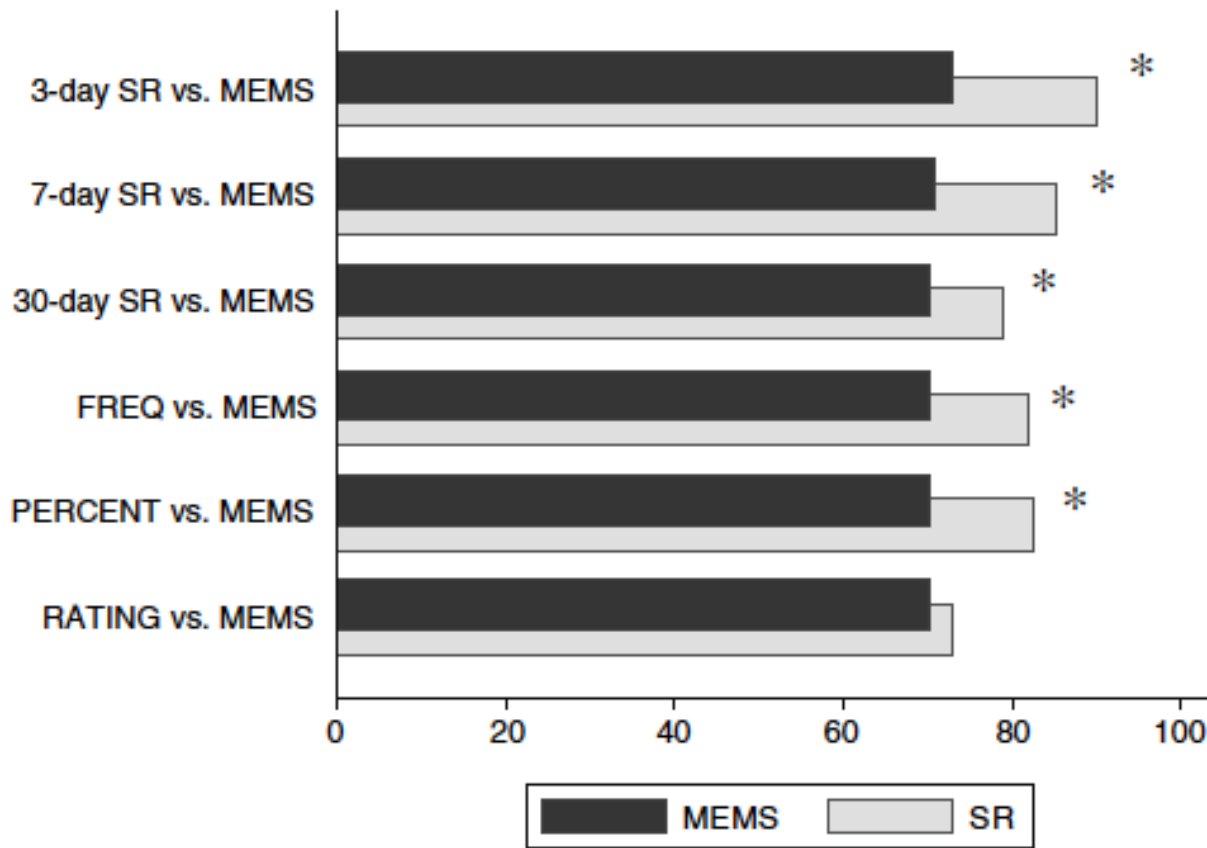
Fair

Good

Very Good

Excellent

# Is 30-day Recall Best?



\* Mean difference is significantly larger than zero, P<0.001

**Fig. 1** Mean difference between self-report (SR) and MEMS adherence

(taken; not ACTG)

(taken; not CPCRA)

(combined 30-day)

(30d: 'none' to 'all')

(30d: 0, 10, 20 ...100%)

(30d: 'very poor' to 'excellent')

156 participants, 643 visits  
(1 to 6 per pt)

Correlation to last VL  
similar in all

# Pharmacy Refill

- Medication possession ratio:
  - Pills dispensed over observation period divided by number of days in observation period
  - Need at least 3 months of data, preferably longer

# Pill Count

- Days from last refill divided by (days supply dispensed minus days supply remaining in bottle)
- Could use for more than a month if accurate refill dates available
- Announced or unannounced or telephone

# Strengths and Weaknesses of Different Approaches in Routine Care

(My expert opinion)

Tool	Time frame	Validity	Respondent ease of use	Reviewer ease of use	Use in diverse populations
ACTG	4 d	++	+	+	+++
CPCRA	7 d	++	+++	+++	++
VAS	30 d	++	++	+++	++
Qualitative	30 d	++	+++	++	+
Refills	≥ 3 m	+++	+++	+	+++
Pill Count	≥ 3 m	+++	+	+	++

# Audience Response: How do you regularly assess adherence in your patients or clinic?

1. ACTG
2. CPCRA
3. VAS
4. Qualitative rating measure
5. Pharmacy refill data calculations
6. Pill count
7. Another self-report instrument
8. Through discussion with the patient without a formal tool or calculation

# Assessing Adherence in Routine Care

- No standard, but some essential components
  - Non-judgmental
  - Non-confrontational
  - Permission to admit less than perfect adherence
  - Collaborative
  - Time frame to improve recall
  - Stories, specifics, and patience
  - Advocate and problem solver
- Any admission of poor adherence is likely true; a report of 100% adherence *may* be true

Audience Response: You missed your last dental cleaning and it has been a year. At the dentist office now, I tell you, “You really need to get your teeth cleaned every 6 months. Bad things could happen to your teeth if you don’t. They might even fall out.”

This statement makes you most feel:

1. More knowledgeable
2. More motivated
3. Guilty and imperfect
4. Mad, like you are being treated like a child

# Interventions to Improve Adherence

- Area of scientific study for over a decade
- General success: higher odds of suppression with interventions, depending on control
- All approaches have been multi-modal
- Intervention strategies: Skill building and behavior modification
  - Modified directly observed therapy (mDOT)
  - Contingency management (ie, pay for adherence or suppression)
  - Social support (individual, peer, group)
  - Cognitive therapy, motivational interviewing, problem-solving
  - Technology



# Given Accurate Adherence Data, How Do Physicians Talk To Their Patients?

**TABLE 2.** Comparison [Median (25th, 75th Percentile)] Between the Total (Patient Plus Provider) Number of Utterances in Control and Intervention Visits by Topic Code

Topic Codes	Intervention (n = 58)	Control (n = 58)	<i>P</i> *
Physical health	120.5 (68, 210)	97 (55, 167)	0.14
Psychosocial	24 (0, 53)	6 (0, 59)	0.77
Logistics	43.5 (18, 78)	40.5 (14, 72)	0.35
Physical exam	5 (0, 11)	5 (0, 12)	0.83
Studies/trials	4 (0, 15)	0 (0, 5)	0.001
Socializing	11 (5, 21)	9 (5, 22)	0.27
ART related	76 (52, 127)	49.5 (28, 113)	0.07
Adherence, current regimen	51.5 (37, 77)	32.5 (17, 52)	0.0002
ART side effects	0 (0, 11)	0 (0, 8)	0.96
ART prescribing	0 (0, 15)	0 (0, 17)	1.00
ART problem solving	0 (0, 12)	0 (0, 2)	0.05
Pharmacological, non-ART	13.5 (6, 59)	23.5 (9, 58)	0.71
Nonallopathic	0 (0, 0)	0 (0, 0)	0.50
Nonpharmaceutical	0 (0, 2)	0 (0, 4)	0.46
Total utterances	360 (258, 531)	311.5 (239, 492)	0.03

- Adherence dialogue increased
- Little problem solving
- Most was “directive”
- Adherence no different

# So Where Are We?

- We can measure adherence fairly well
- No measures have gained widespread use in routine care
- We can improve adherence
- No interventions are packaged for dissemination
- We often talk to patients about adherence
- We probably aren't doing it in the most effective way most of the time

# “Interventions” for Routine Care

(Level C evidence)

1. **Establish readiness** (C: recent review: Grimes Curr HIV/AIDS Rep. 2010 Nov;7(4):245-52)
2. **Tailor the regimen frequency and timing** (B: observational QD>BID>>TID; Bangsberg AIDS 2010; 24:2835)
3. **Prepare the patient, including addressing cultural beliefs**
4. **Anticipate and manage side effects**
5. **Assess adherence regularly; adherence declines with time and everyone is at risk**
6. **Promote retention in care and appointment adherence**



# “Interventions” for Routine Care

7. Promote the patient’s trust in the provider (B: observational, Saha AIDS Patient Care STDS. 2010; 24:415)
8. Assess and address barriers
  - Problem solve collaboratively with practical, specific solutions; multi-disciplinary approach
  - Admonishments or encouragements alone will not work (Wilson JAIDS 2010; 53:338)
9. Use multi-modal, on-going interventions
  - Support (group, individual, peer), education, technology (pill boxes and patient-selected reminders), pharmacy (A/B/C: recent review, Simoni Curr HIV/AIDS Rep Jan 2010)

# Conclusions

- Screen for less than optimal adherence to medications
- Intervene in a customized and collaborative way
- Stay tuned to the literature