

Adherence

**The Achilles heel of antiretroviral
therapy**

Adherence to Antiretroviral Therapy

- Definition of adherence
- Importance of adherence
- Measurement of adherence
- Components and determinants of adherence
- Interventions and strategies to improve adherence
- South African context

Definitions

- **Compliance**
- **Adherence**
- **Therapeutic alliance**
- **Classic definition of *adherence*: the extent to which a person's behavior corresponds with medical advice.**
 - **The ability to take medication as prescribed**
 - **not at all**
 - **too little**
 - **intermittently**
 - **too much**

Adherence to ARV therapy (HAART)

Importance

- Major determinant of biologic, clinical and public health outcomes of HAART
 - Poor adherence is a major cause of ARV failure
 - Poor adherence is a major cause of ARV resistance and, with continuing risk behavior, transmission of resistant organisms
- Long since known with other diseases-TB

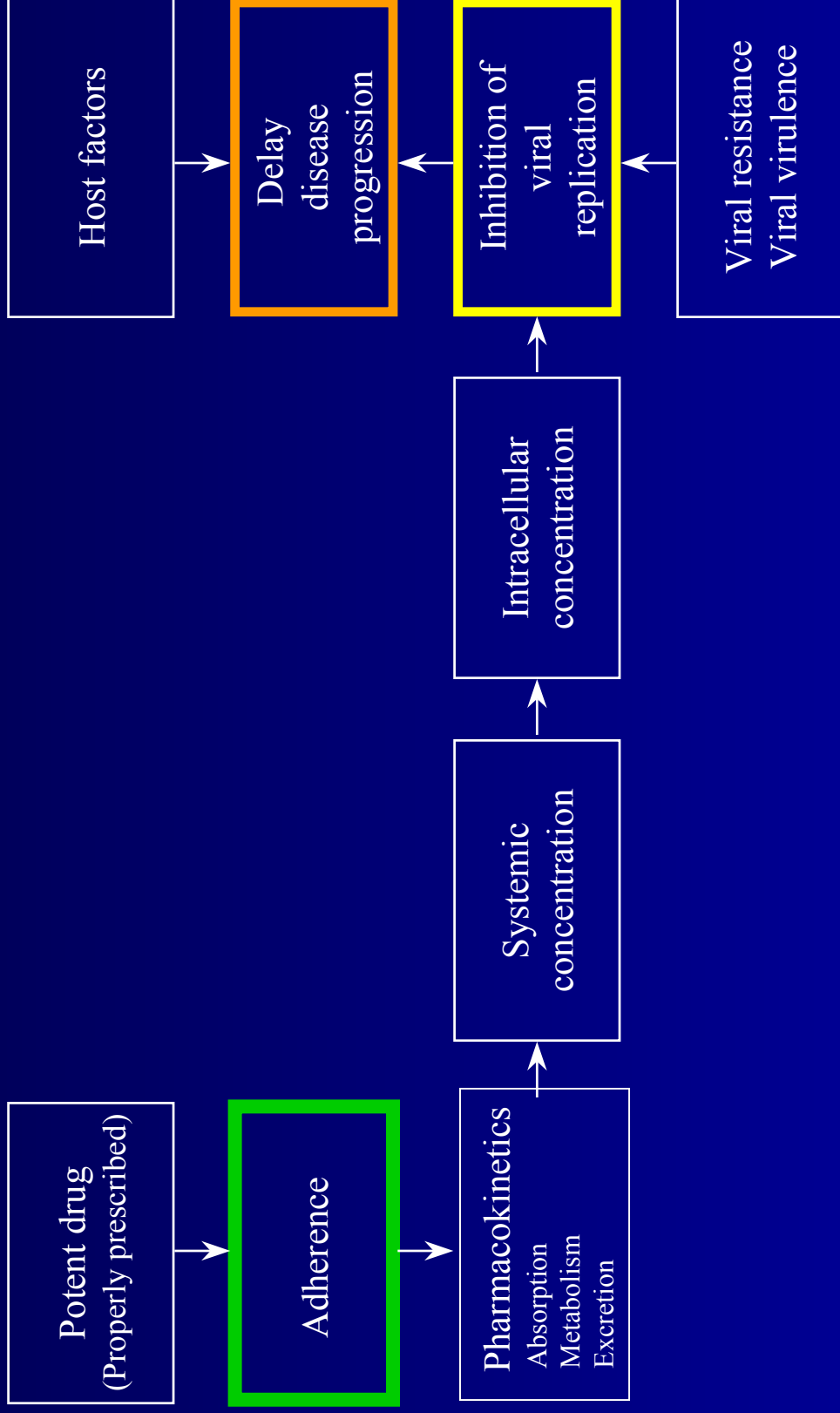
Adherence to HAART

Importance

- No other infectious disease requires such difficult life-long therapy
- Without expertise and resources to evaluate and support adherence, antiretroviral therapy can be ineffective, wasteful and dangerous
- Adherence has not been carefully studied or documented in the developing world context

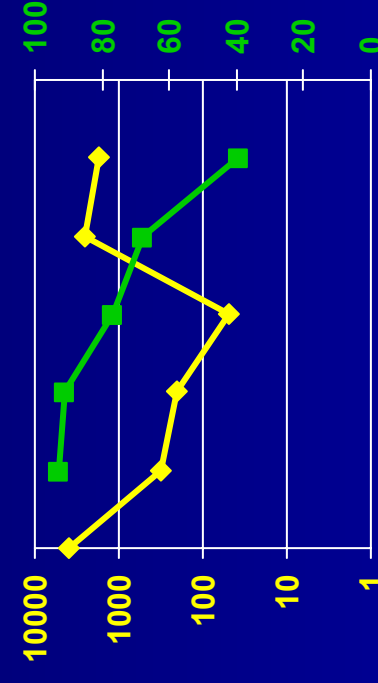
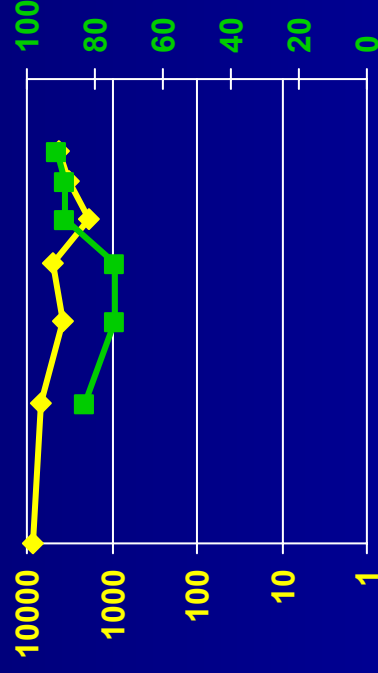
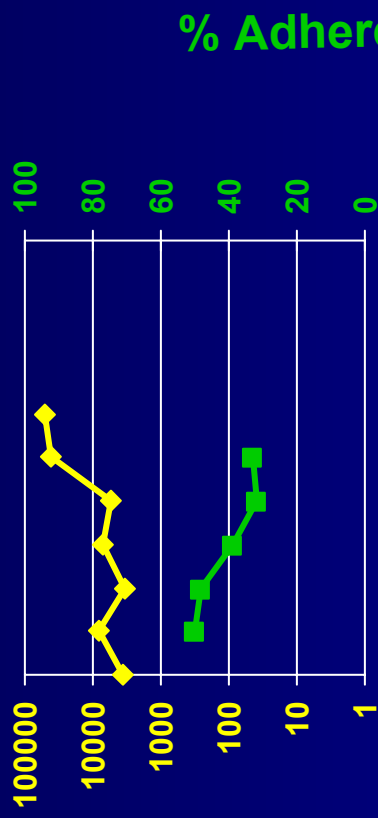
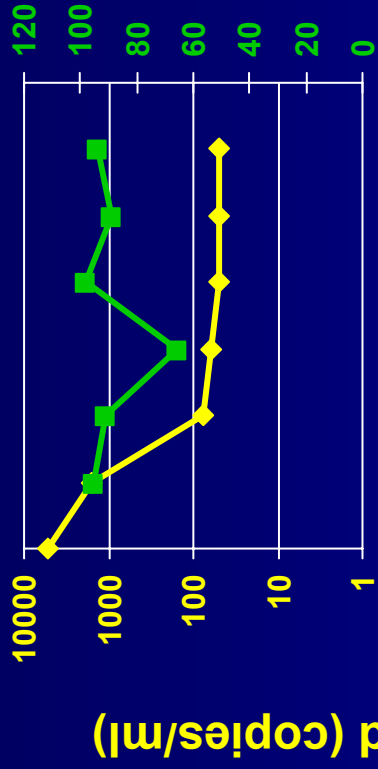
HIV Therapeutics

Drug Efficacy



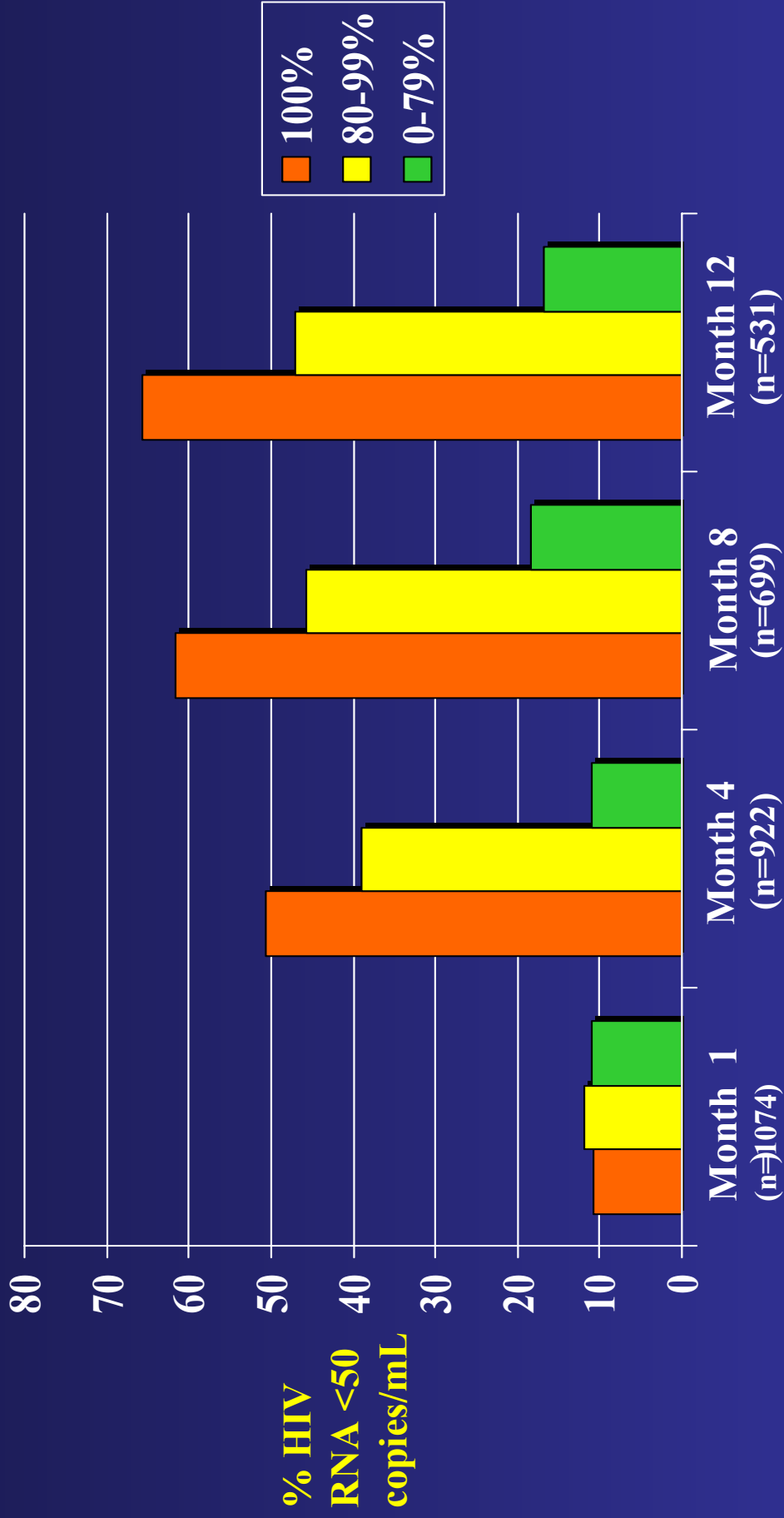
Viral Load and Adherence in Four Selected Patients at Six Monthly Timepoints

Measured by MEMS caps
Arnsten et al, Durban 2000



Virologic Outcomes by Adherence Level

% HIV RNA <50 copies/ml



P<.005 at months 4,8,12

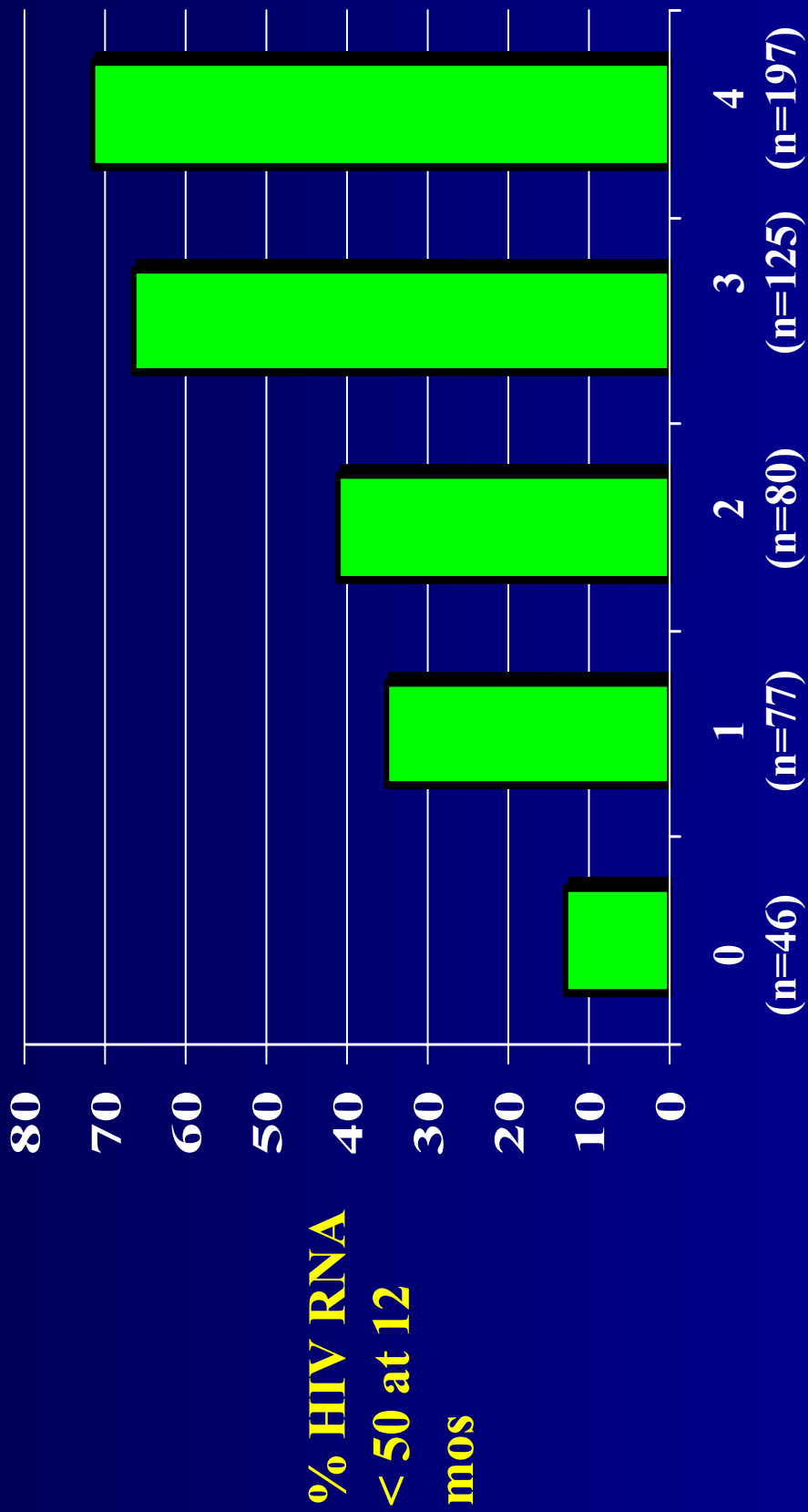
Importance of Adherence Clinical Outcomes

- **Hospitalization**
- **New Opportunistic Infections**
- **Death**
- **Transmission**

Adherence to Antiretroviral Therapy

- How much?
- How long?
 - What is the durability of adherence over the course of lifelong therapy?
- Pill fatigue
- Change in life circumstances
- Long term toxicities

Consistency of 100% adherence and virologic outcomes among patients with 12 mos follow-up (n=540)



Number of follow-up visits in which participants reported 100% adherence, $p < .001$

Measurement of Adherence

- clinician estimate
- pill count
 - announced or unannounced
- MEMS Caps-
- pharmacy refills
- blood levels
- *self report
 - social desirability, provides reasons
- biologic and clinical outcome

3-DAY HIV MEDICATION SELF-REPORT

Attach PID Label Below

PID:									
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Form Date: day month year

 200

SECTION C

TO BE COMPLETED BY STUDY PARTICIPANT. If you did not miss any doses in the last three days do not complete this section.

1. Below are some reasons why people miss taking their antiretroviral medicine. Check "Yes" or "No" to indicate whether or not each of the following reasons describes why you usually **MISSED** taking your anti-HIV medicine **during the last 3 days**:

- a. 1 Yes 2 No I feel worse when I take the pills
- b. 1 Yes 2 No There are too many pills to take
- c. 1 Yes 2 No I forget to take the pills
- d. 1 Yes 2 No I ran out of pills
- e. 1 Yes 2 No I don't think I need the pills
- f. 1 Yes 2 No I was away from home
- g. 1 Yes 2 No I did not want others to notice
- h. 1 Yes 2 No I am too busy
- i. 1 Yes 2 No I had problems taking pills at specified times
- j. 1 Yes 2 No I was confused or uncertain about how to take the pills
- k. 1 Yes 2 No I slept through a dose
- l. 1 Yes 2 No I had a change in my routine
- m. 1 Yes 2 No I did not want to mix medicine with drugs or alcohol
- n. 1 Yes 2 No I was too depressed
- o. 1 Yes 2 No I miss doses on weekends
- p. 1 Yes 2 No I was not able to follow the special diet instructions for the medicine (with meals, on empty stomach, etc.)
- q. Other, please explain: _____

Determinants of Adherence

- Characteristics of:
 - Patient-
 - Demography (age, sex, race/tribe/language, SES)
 - Information(knowledge, cognition)
 - Motivation(beliefs,depression, substance use)
 - Behavior skills(pill taking, scheduling)
 - Provider-expertise, trust
 - Regimen-simplicity, toxicity, disruption of activities
 - Disease-stage
 - Clinical setting-

Acceptance of and Adherence to ART

Importance of Trust

Altice, Mostashari, Thompson, Friedland

Acceptance

	A O R	p value
TRUST in Physician Scale	0 .08	<0.0001
MISTRUST Medications	0.30	<0.001

** There is an 8% increase in adherence for each unit increase in the 11-55 item Trust in Physician Scale (Anderson and Dietrick)*

Acceptance of and Adherence to ART

Altice, Mostashari, Thompson, Friedland

Adherence

OR p value

SIDE EFFECTS

Has side effects and stop meds

0.09

0.0001

SOCIAL ISOLATION

0.08

0.0001

COMPLEXITY

Antiretroviral Regimen:

(mono vs. nuc comb vs. prot com)

0.33

0.01

Reasons for Missing Doses of Antiretroviral Therapy (N=75/51)

Chesney et al. AIDS Care 2000

Simply Forgot	66
Away From Home	57
Change in Routine	51
Busy with Other Things	53
Slept Through the Dose	40
Too Sick	28
Depressed	18

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Improvement of Adherence *Interventions*

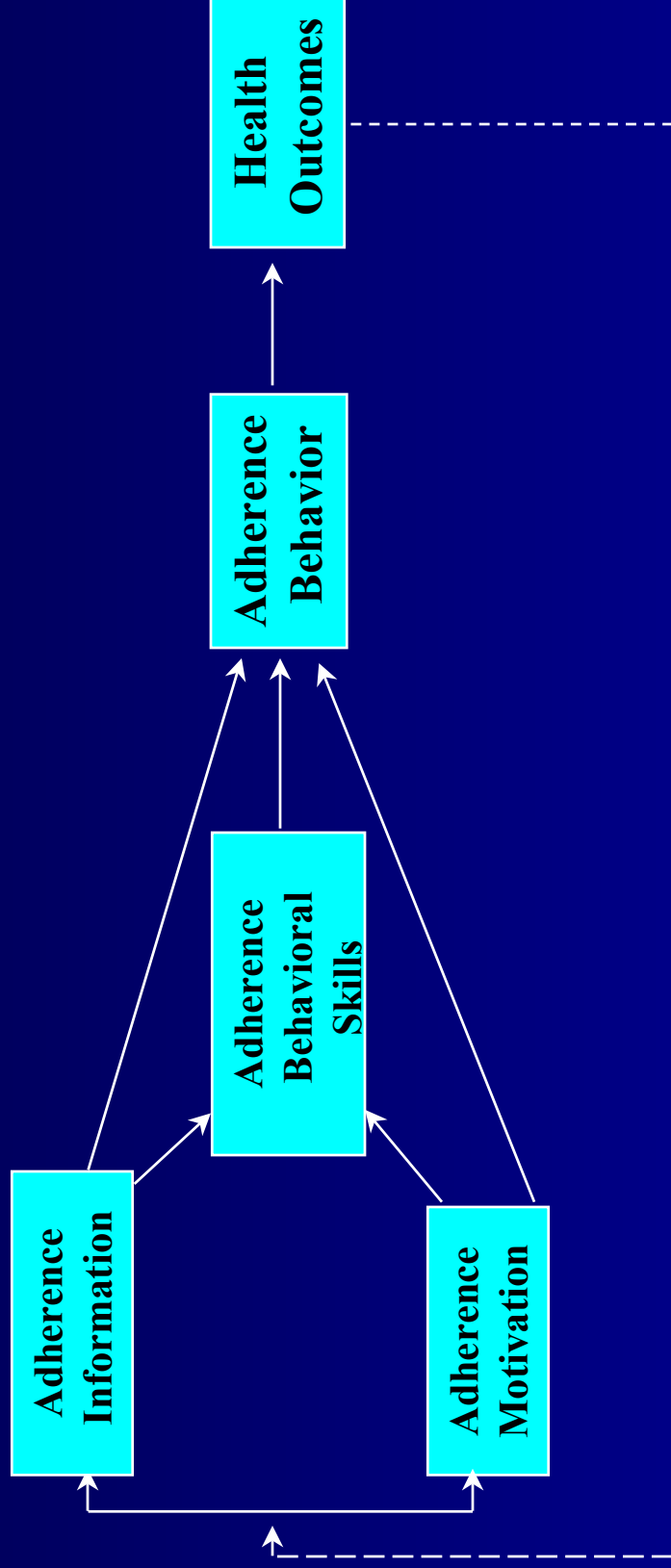
- Few rigorous studies with HIV/AIDS yet reported, many underway
- Can significantly improve adherence (Effect size small)
- Many strategies work (Provider-based, patient involvement, rewards)
- Combined approaches work best (Combination intervention-dose response)
- Durability of effect requires continuing intervention
- Theoretically based

Interventions to Improve Adherence

Behavioral models inform interventions

- Transtheoretical Model of Change (Prochaska)
 - pre-contemplation,
 - contemplation,
 - preparation,
 - action,
 - maintenance (and relapse)

The Information-Motivation-Behavioral Skills Model of Adherence



Simplify the Regimen

- Reduce dosing frequency
 - TD to BD
 - Once daily regimens
 - ddl, 3TC, nevirapine, efavirenz,
new proteases
- Fewer pills
- Fewer side effects
- Food neutral

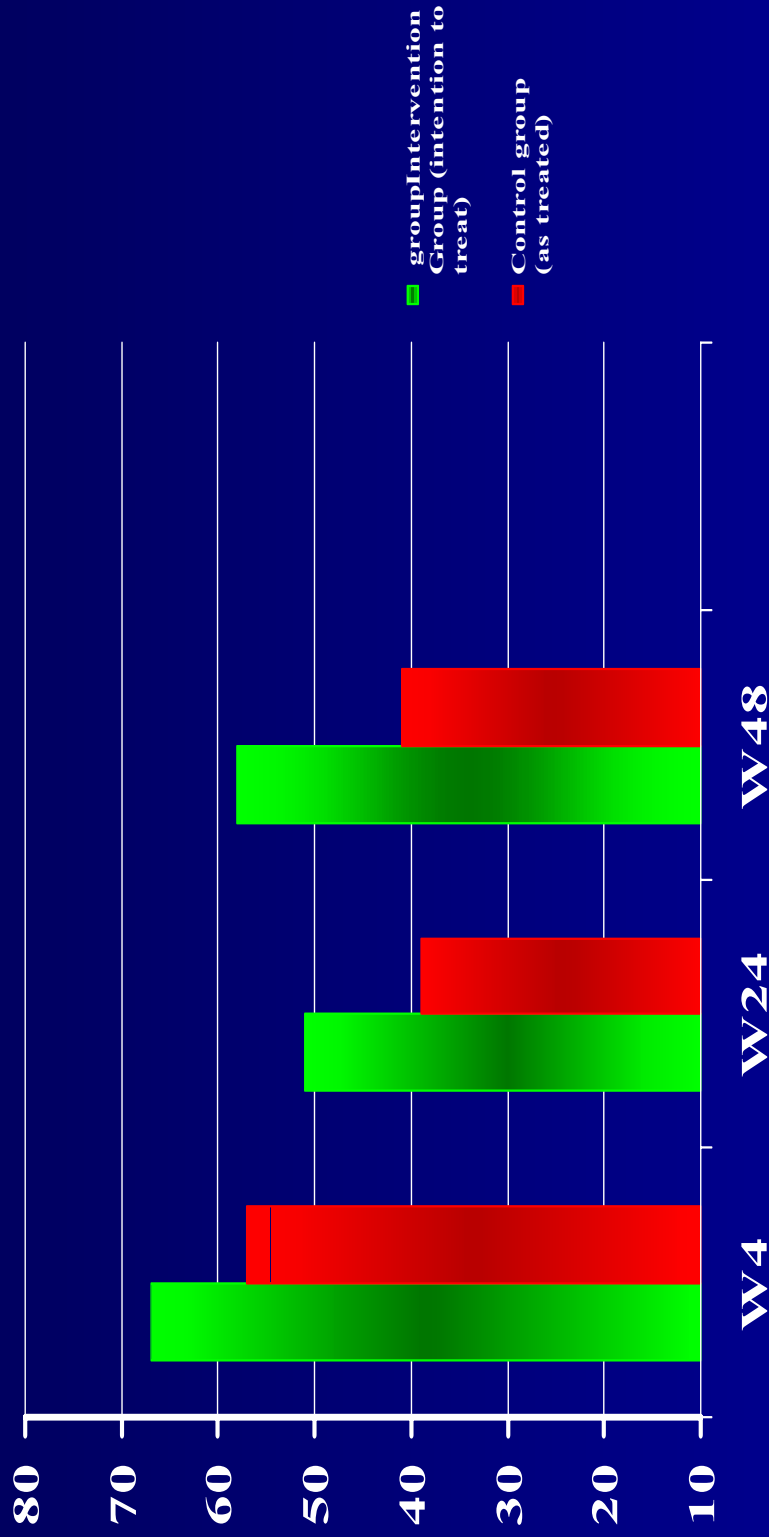
Improvement of Adherence

Interventions Under Study

- **Medication manager**
- **Peer support**
- **Electronic reminders**
- **Home visiting**
- **Modified DOT**
 - **prisons**
 - **drug treatment**
 - **other**

Efficacy of Intervention to Improve Long-Term HAART Adherence

Tuldra, JAIDS, 2000



Percentage of patients with adherence $\geq 95\%$ at weeks 4, 24, and 48.

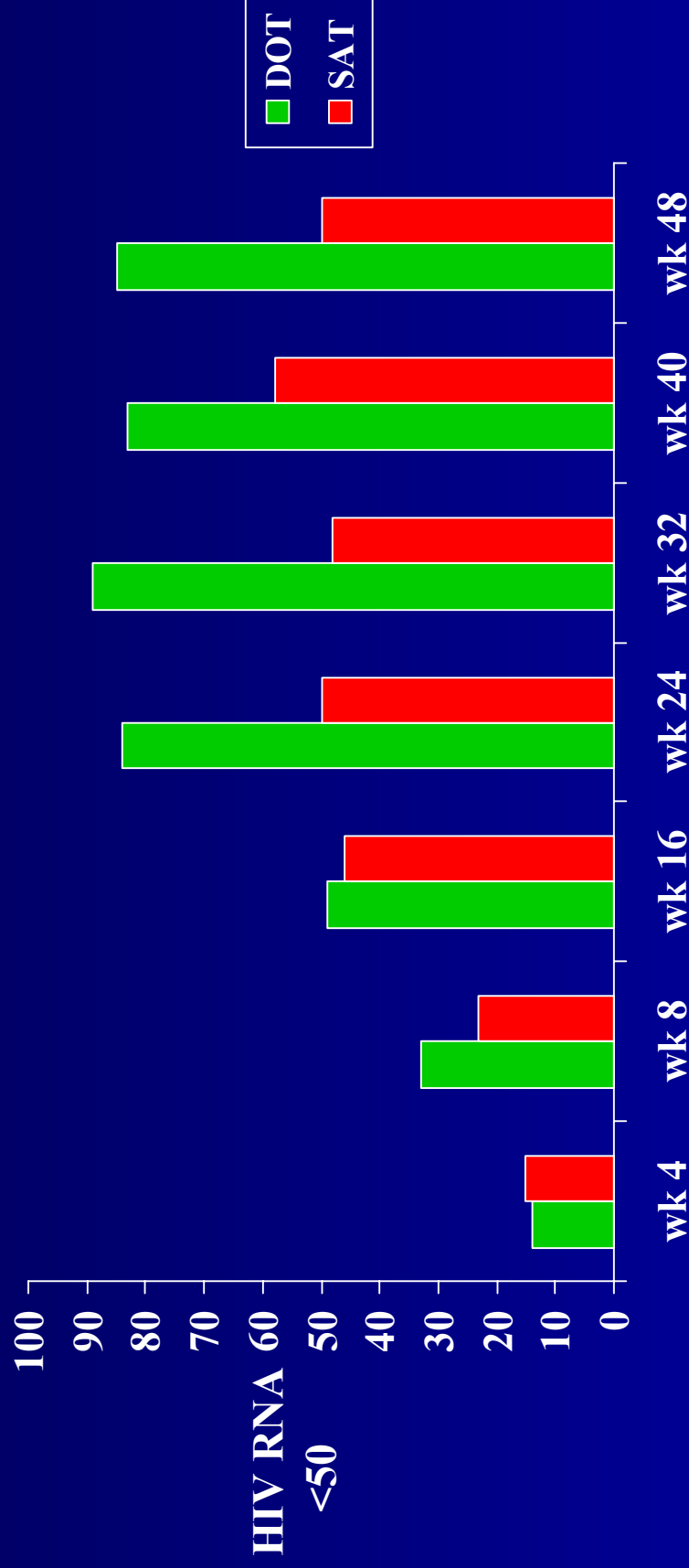
Adherence Protocol (CPCRA 062)

**Adherence Strategies Using a
Medication Manager and an
Electronic Medication Reminder
System for HIV-Infected Patients
Receiving HAART**

Directly Observed Therapy and RNA Decline

Fischl et al 7th CROI 2000

- Prisoners in 4 clinical trials by DOT or self administration (SAT)
- Proportion declines in HIV RNA ($p < 0.01$)



Adherence to Antiretroviral Therapy

Strategies

Readiness

- Patients and providers are partners in the process of HIV therapeutics
- There are few antiretroviral emergencies
- Do not prescribe ART until the patient is ready
- Assess stage and degree of readiness
 - How do you know when the patient is ready?

Adherence to Antiretroviral Therapy

Information

- Provide information about HIV, treatment, measures of efficacy, adherence using clear, explicit and patient appropriate language
 - Assess comprehension of information given-ask patient to explain dosing
 - Use visual aids such as pictures of pills and simplified viral life cycle
 - Provide written information

Adherence to Antiretroviral Therapy

Motivation

- Identify cultural and health beliefs
- Identify perceptions of treatment, including fears of side effects
- Provide treatment for substance abuse and depression or refer
- Assess patient's belief in their ability to adhere to treatment
- Assess the home environment, when possible

Adherence to Antiretroviral Therapy

Motivation (continued..)

- Identify support systems, involve loved ones in the treatment and adherence process
- Link adherence to treatment goals (viral load, CD4)

Adherence to Antiretroviral Therapy

Behavioral Skills

- Provide medication aids
- Provide pilltaking skills
- Teach identification and management of side effects
- Tailor treatment to daily activities, not activities to treatment regimen (tailoring)
 - Identify vulnerable times for non-adherent behavior
 -

Tailoring Examples

- **Patient Karim, 36 y.o. salesman**
 - **Morning: before shaving**
 - **Afternoon: use timer or at break**
 - **Evening: at 11 o'clock news**
 - **plan for weekends**
- **Patient Philani, 28 y.o. single mother**
 - **Morning: at drug treatment program**
 - **Afternoon: before picking up daughter at school**
 - **Evening: after putting daughter to bed**
 - **plan for weekends**

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Adherence to ARV in South Africa

Research questions

- **What is the background level and characteristics of information, motivation and behavioral skills?**
 - **HIV/AIDS, medication in general, ARVs**
 - **How do cultural, psychological behavioral and contextual circumstances influence this?**
- **What is the best way(s) to measure adherence?**
- **How does adherence influence therapeutic outcome?**
 - **efficacy, resistance**
- **What appropriate and effective interventions to improve adherence are available and/or can be designed and tested?**

Study Design

