Couple-Level Support Improves HIV Medication Adherence: Results from a Randomized Controlled Trial and The Challenges of Achieving Optimal Adherence
SMART means:

S haring
M edical
A dherence
R esponsibilities
T ogether
Funded by the National Institute of Mental Health (NIMH R01 MH61173)

Supported by CR-CFAR
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Estimated Number of AIDS Cases and Deaths among Adults and Adolescents with AIDS, 1985–2003—United States

No. of cases and deaths (in thousands)

Year of diagnosis or death

Note. Adjusted for reporting delays.
Antiretroviral Adherence is Essential to Antiretroviral Success

- Levels of medication adherence are correlated with durable viral load suppression (<50 copies/mL)

- Inadequate adherence can lead to virologic failure and the development of resistant virus

- Public health concern: Increased rates of transmission of drug resistant HIV
What Degree of Adherence is Needed?

Adherence to a PI-containing regimen correlates with HIV RNA response at 3 months.

Newer, potent ART regimens effectively suppress viral replication at adherence levels as low as 60%.

Each class of medications has a unique adherenceresistance relationship; not necessarily linear$^2$

- Single protease: mod-high levels of adherence
- Ritonavir-boosted: middle ranges of adherence
- NNRTI: low-moderate levels of adherence

Are there Effective Adherence Interventions?

- 21 published studies*
  - Utilized four intervention strategies: cognitive-behavioral, behavioral, directly observed therapy, and affective
  - Most were pilot or feasibility studies
  - 10 included control or comparison groups, but only seven included random assignment; of these, only 4 incorporated follow-up assessments


SMART Couples Project
Adherence Interventions (con’t)

◆ The most comprehensive (behavioral, educational, social support) had non-significant findings ¹

◆ The other three studies had encouraging findings but also had numerous methodological problems ²-⁴
  
  ✔ small sample sizes
  
  ✔ reliance on self-report
  
  ✔ absence of intent-to-treat analysis

**Bottom line:** there is a paucity of tested interventions shown to be effective in improving adherence to ART

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Adherence Interventions (con’t)

- Literature dominated by reports of factors that are associated with adherence
- Among adherence interventions, multifaceted strategies appear to be the most promising
- However, there remain few controlled studies substantiating their effectiveness and mechanisms by which they promote adherence are not well understood

*Bottom line:* more well powered, rigorously evaluated ART intervention trials are urgently needed (39 currently in the field)

Rationale for SMART Couples Study

- Adherence to antiretroviral therapy (ART) is challenging
- The healthcare field is in need of effective interventions to improve adherence to ART
- Many factors are associated with adherence (e.g., mood, substance use, treatment beliefs and attitudes, doctor-patient communication, cognitive functioning)
- An important factor, consistent across many studies and patient populations, is social support for adherence
Rationale for SMART Couples Study (continued)

- Interventions have not directly tried to enhance social network support for adherence to ART.
- To date, adherence interventions have targeted “the individual;” none have had a dyadic focus.
- Family and other “systems” oriented approaches have been shown to be effective in other diseases (e.g., mental illness, drug abuse, diabetes, cancer).
- HIV serodiscordant couples have the added challenge of the potential for transmission of HIV.
Primary Aim

To determine whether a brief (4-session), clinic-based and theory-driven counseling intervention with both members of the couple is effective in improving medication adherence among HIV+individuals who are having adherence problems (over that which is observed in “usual” clinic care).
Secondary Aims

- Explore:
  - Impact of partner-related psychosocial variables on adherence
  - Effects of behavior change on biomedical outcomes
  - Relationship between treatment attitudes and sexual risk behavior
  - Relationship between medical adherence and adherence to safer sex
  - Potential differences by gender/sexual orientation
Eligibility Criteria

- HIV serodiscordant couples
  - Relationship length of 6 mos. or more
  - HIV+ partner:
    - In primary care
    - Taking antiretroviral medication
    - Demonstrated poor adherence:
      - < 80% of prescribed doses taken at regular intervals over 2 weeks (MEMS)
Participant Recruitment

- St. Luke’s-Roosevelt Hospital HIV/AIDS outpatient treatment clinics
- Additionally:
  - Other HIV/AIDS treatment clinics
  - Private medical practices mailings
  - HIV/AIDS service organizations
  - Community groups/events
  - Provider and participant referrals
  - Ads/articles in community publications
  - Mailings to magazine subscription lists
  - Internet postings
Participant Screening

- **Pre-screening**
  - With individual via telephone or in-person
  - Assess basic eligibility criteria

- **Main screening**
  - With both partners present
  - Confirm antiretroviral regimen
  - Assess validity as a (serodiscordant) couple

- **Final screening**
  - With couple after 2 weeks of MEMS use
  - Determine adherence level of HIV+ partner
  - Baseline completed prior to randomization

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STUDY DESIGN

SMART Couples Project
Assessment Domains

- Medication adherence
- Moderators/mediators of adherence
- Blood samples for clinical assays
- Chart data for appointment attendance
MEMS caps
(Medication Event Monitoring System)
MEMS results

SMART Couples Project
MEMS Results

Chronology

SMART Couples Project
MEMS Results
Medication Adherence

- **Measures**
  - MEMS cap (two weeks)
  - Self-report of MEMS errors (two weeks)
  - Self-report of adherence (three days)

- **Primary outcomes**
  - % prescribed doses taken at regular intervals (MEMS)
  - % prescribed doses taken (MEMS adjusted by self-report)
Modulators/Mediators

- Audio-Computer Assisted Self-Interview (ACASI)
- HIV+ partner at all four time-points
- HIV- partner at first two time-points

Measures included:

- Demographics
- Therapeutic burden
- Side effects
- Cognitive functioning
- Depression
- Substance Use
- HIV knowledge
- Adherence self-efficacy
- Relationship dynamics
- Adherence support
Biological Markers

- Blood samples collected from HIV+ partner at baseline and post-intervention
- Assays conducted through CFAR lab:
  - Viral load (copies/ml)
  - CD4+ (abs)
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Theoretical Approaches to Behavior Change

- Health Belief Model (Beck, 1974)

- Theory of Reasoned Action (Fishbein & Azjen, 1980)

- Self-Efficacy Model (Bandura, 1986)

- Common elements:
  - *understanding* of costs and benefits
  - *confidence* in carrying out the behavior
  - perceived *norms* and *social support*
Ewart’s Social Action Theory (Ewart, 1991)

- With a strong emphasis on *context*, explains health protection behavior as an interaction between three domains:
  - *Self-regulation* capabilities of the individual
  - Larger *environmental context*
  - Responses to *internal affective states*, that also influence the self regulation process
Ewart’s Social Action Theory

- Self-regulation of health behavior is influenced by:
  - *Skills* (e.g., adherence monitoring)
  - *Attitudes* (e.g., outcome expectancies, treatment beliefs)
  - *Norms* (e.g., community norms re: treatment, family beliefs)
Ewart’s Social Action Theory

- **Environmental context** of health behaviors include:
  - *Health-care system* (e.g., doctor-patient communication)
  - *Relationship* functioning (e.g., communication, support for adherence)
  - *Disclosure* of serostatus (e.g., family, friends, workplace)
Ewart’s Social Action Theory

- **Internal affective states include:**
  - *Motivational* states (e.g., concerns about resistance development)
  - *Mood* (e.g., depression, anxiety)
  - *Self-identity* (e.g., “HIV” identity, self-esteem)
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POTENTIAL MODERATORS
- Demographics
- Living circumstances
- Medical characteristics
- Neuropsychiatric characteristics
  - Depression
  - Substance use
  - Cognitive functioning

MEDIATORS ADDRESSED IN INTERVENTION
- Knowledge and Understanding
  - HIV (general)
  - Treatment-specific
- Adherence Motivation, Commitment, and Couple Communication
- Social Support for Adherence
- Adherence Self-Efficacy
- Problem-solving to Overcome Barriers to Adherence/Beh Skills

OUTCOMES
- Medication Adherence
- Clinic Attendance
- Clinical Outcomes
Intervention Goals

- Primary focus: Medical care adherence
- Secondary focus: Sexual risk taking
- Overall approach:
  - Cognitive-behavioral framework
  - Foster couple communication and mutual care-giving
  - Promote problem-solving skills
  - Reinforce motivation for health promotion
Intervention Description

- **Individual couple focus**
  - 4 sessions, delivered a week apart, with two weeks between sessions 3 & 4
  - Facilitators: Nurse practitioners from the clinics

- **Activities across all sessions**
  - “Check-in” and ongoing support
  - Adherence monitoring (MEMS as a personal tool)
  - Between sessions tasks
  - Provide referrals, as needed
Session #1

“What are our goals?”

- Clarify information about HIV disease and treatment, biomarkers, medical and medication regimen
- Discuss commitment/motivation for health maintenance in general and medication adherence, specifically

**Key theoretical components:** knowledge of treatment regimen, general knowledge of HIV and consequences of nonadherence, commitment/motivation to adhere
Session #2

“How can we improve?”

- Identify barriers to adherence
- Increase problem solving skills and apply to specific barriers
- Increase skills around couple communication and support

- **Key theoretical components**: adherence self-efficacy, identification of adherence barriers, communication and problem solving skills around adherence, regimen specific support, couple-level monitoring of adherence, commitment and motivation
Session #3

“How do we work together?”

- Continue with joint problem solving
- Increase relationship coping skills
- Explore risk perception and sexual risk behaviors
- Explore what it means to care for and support each other

**Key theoretical components:** adherence self-efficacy, communication and problem solving skills around adherence, attitudes towards combination therapy in relation to sexual behaviors, regimen specific support, self-monitoring of adherence, commitment/motivation to adhere
“How well are we doing?”

- Increase self monitoring skills (adherence and sexual risk)
- Reinforce problem solving skills
- Reinforce commitment to health and protective behaviors
- Increase self-efficacy

**Key theoretical components:** adherence self-efficacy, communication and problem solving skills around adherence, regimen specific support, self-monitoring of adherence, commitment/motivation for adherence
Study Enrollment

- 215 HIV serodiscordant couples
  - 81 HIV+ female with HIV- male
  - 78 HIV+ male with HIV- female
  - 38 HIV+ male with HIV- male
  - 18 HIV+ female with HIV- female
  - Median relationship length = 3 years
Screening Results

Recruitment

1014 Pre-screens Done

378 Ineligible (37%)

636 Eligible (67%)

377 Main-Screens Done

26 Ineligible (7%)

351 Eligible (93%)

302 Final-Screens Done

81 Ineligible (27%)

221 Eligible (73%)

215 Baselines Done

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Demographics of HIV+ Partners at Baseline

- Mean age = 42
- Race/ethnicity
  - 62% African American
  - 24% Latino
  - 10% White
  - 2% Other/multiracial
  - 1% Asian/Pac. Islander
  - 1% Native American
- 72% H.S./GED degree or less
- 76% not employed
- 82% yearly income < $20,000
- Median CD4 count = 375
- Median viral load = 172
- Provider type
  - 26% SLRHC
  - 43% Hospital HIV clinic
  - 27% Non-HIV clinic
  - 3% Private doctor
Retention

- **Did not vary by study arm**
  - 91% post-intervention
  - 85% three month follow-up
  - 75% six month follow-up

- **Intervention attendance**
  - 86% attended at least 3 of 4 sessions
  - 71% attended all 4 sessions
Outcome:
Prescribed doses taken at regular intervals (MEMS)
Outcome: Prescribed Doses Taken (MEMS-adjusted)

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Baseline (n.s.)  Post-intervent (p=.02)  3 mo followup (n.s.)  6 mo followup (n.s.)

- Intervention
- Control

75%  76%  73%  66%
72%  60%  66%  66%
Significant differences in high adherence rates at post-intervention

% Prescribed doses taken (MEMS-adjusted)

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Significant differences in high adherence rates at post-intervention

% Prescribed doses taken at regular intervals (MEMS)

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Percent taking > 90% of prescribed doses at three time-points

(MEMS-adjusted)

SMART Couples Project
Percent taking > 90% of prescribed doses at regular intervals at three time-points

(MEMS)

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Clinical Outcomes: 
Median CD4+ Count (abs)

Baseline (n.s.) Post-intervention (n.s.)

381 361
375 345

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Clinical Outcomes: Undetectable Viral Load (copies/ml)

- Baseline (n.s.): 40% Intervention, 42% Control
- Post-intervention (n.s.): 43% Intervention, 41% Control

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What level of adherence is necessary for clinical success?

- Mean adherence (measured w/ MEMS) generally range from 50-80%
- Increasing evidence that failure to reach 95% adherence and full viral suppression does not preclude clinical benefit
  - Any 10% increase in mean adherence is associated with a halving of viral load and a 20-30% decreased risk of progression to AIDS
  - Newer, potent ART regimens effectively suppress viral replication at adherence levels as low as 60%

SMART Couples Project
Most participants reported high levels of satisfaction with intervention content overall (means of 1.3 on scales of 1 to 5, with 1=very satisfied and 5=very dissatisfied).

The percent of HIV+ partners who felt the intervention was very helpful with their adherence ranged from 84% to 93% across each of the four sessions.

The corresponding ratings by HIV− partners ranged from 95% to 97%.
Process Evaluation (continued)

- Participants expressed support for adding sessions to the brief intervention.
  - One-third of the HIV- partners and 40% of the HIV+ partners stated that the intervention had too few sessions, whereas only one HIV- partner and no HIV+ partners felt that the invention contained too many sessions.
Process Evaluation (continued)

- What participants liked best:
  - Spending time with medical provider
  - Learning all about the treatment
  - Helping with communication in our relationship
  - Seeing the MEMS feedback
What facilitators thought was most effective:

- Treatment instruction ("HIV 101")
- Fostering concrete support from partner
- Problem-solving training
- MEMS feedback
Results

- The intervention was well-received by patients (and their partners) and by clinic staff.
- The intervention is feasible in HIV medical clinic settings.
- The intervention demonstrated significant improvements in medication adherence above and beyond usual clinic care.
Results (continued)

- Improvements were seen in both:
  - doses taken
  - doses taken within appropriate time intervals
- There is still room for improvement; many remained sub-optimal
- In the absence of booster sessions, improvements in adherence diminished over time.
- We were unable to demonstrate improved clinical outcomes with biological markers measured.
Research Implications

- Identify mediators/moderators of changes in adherence
- Develop stronger interventions and ways of sustaining effects
- Identify new biological markers that would be useful in behavioral trials
- Develop new models of adherence that are less “individualistic”
Clinical Implications

- Include “significant others” in clinical care for HIV+ patients
- Increase social support for achieving and sustaining high adherence levels
- Consider use of adherence feedback tools
- Devote time and effort for improving and sustaining good adherence