

Toronto I-II 8:30 pm

# A depression intervention to improve adherence



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**Moderator: Trevor A. Hart**

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# Addressing Depression in Interventions with HIV-Infected Populations

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Assistant Professor, Harvard Medical School  
Associate Director, Behavioral Medicine, MGH

# “Minimal” Interventions for HIV Medication Adherence (Interventions that did not address Depression) Conducted at MGH and Fenway Health



# *Life-Steps*



1. Psychoeducation, Motivation for Adherence
2. Getting to Appointments
3. Communication with Treatment Provider
4. Side Effects
5. Obtaining Medications
6. Schedule
7. Storage of Medications
8. Cue Control Strategies
9. Guided Imagery (Rehearsal)
10. Slips
11. Review and Phone Follow-Up

*(Safren et al., 1999; Cognitive and Behavioral Practice)*

# Life-Steps: Self reported adherence



Analysis of those with baseline adherence problems

	<u>Week 0</u>	<u>Week 2</u>	<u>Week 12</u>
Medication Monitoring	84%	90% (n=26)	93% (n=25)
Life-Steps	74%	95% (n=30)	94% (n=28)

Week 2: Significant Interaction ( $F(1,54) = 4.41, p < .05$ ) favoring improvement for the Life-Steps Condition ( $\eta^2 = .075$ ).

Week 12: Significant Improvement in Both Groups with time ( $F(1,54) = 10.64, p < .01$ ); interaction not significant

# Correlations with self-reported adherence



<b>Predictor (N=84)</b>	<b>R, p's &lt;.01</b>
Depression (M=14.10, SD 8.77)	-.39
Satisfaction with Social Support (M=4.4, SD 1.5)	.38,
Punishment Beliefs About HIV Infection	-.34
Adherence Self-Efficacy	.34

- Regression analysis: Depression the only unique significant predictor ( $p < .001$ ).
- 75% had BDI scores greater than 10, 40% had scores over 20
- Depression associated with intervention outcome

## Amico et al: Meta-analysis of adherence intervention trials from 1996 to 2004 (25 studies)



- Small effect  $d=.35$ , but varied considerably across studies
- Effect sizes did not vary by sample design, sample demographics, articulation of a theory, intensity of intervention, duration of intervention exposure, or measurement strategy
- Effect sizes varied by baseline adherence: Those with known or anticipated adherence problems had medium effects ( $d=0.62$ ); Those that did not target participants with adherence problems had smaller effects ( $d = 0.19$ )
- Improvements did not decay across time

# Simoni et al: Meta-analysis – 19 RCTs

*2006 presentation of results – added 5 RCTs from Amico*



- Focus exclusively on RCTs
- Those who got interventions were 1.5 times more likely to attain 95% adherence than controls
- Those who got interventions were 1.25 times more likely to attain undetectable viral loads than controls
- Not due to any one study (sensitivity analyses)
- None of the stratification variables were significant (i.e. short versus long, group vs individual, trained professionals versus clinic staff, multiple component versus single session, use of external reminder or not)



# Consideration of Depression and Self-Care in HIV



## Estimates of depression

General Population	HIV-Infected Individuals
7% <sup>1</sup>	36% <sup>3</sup>

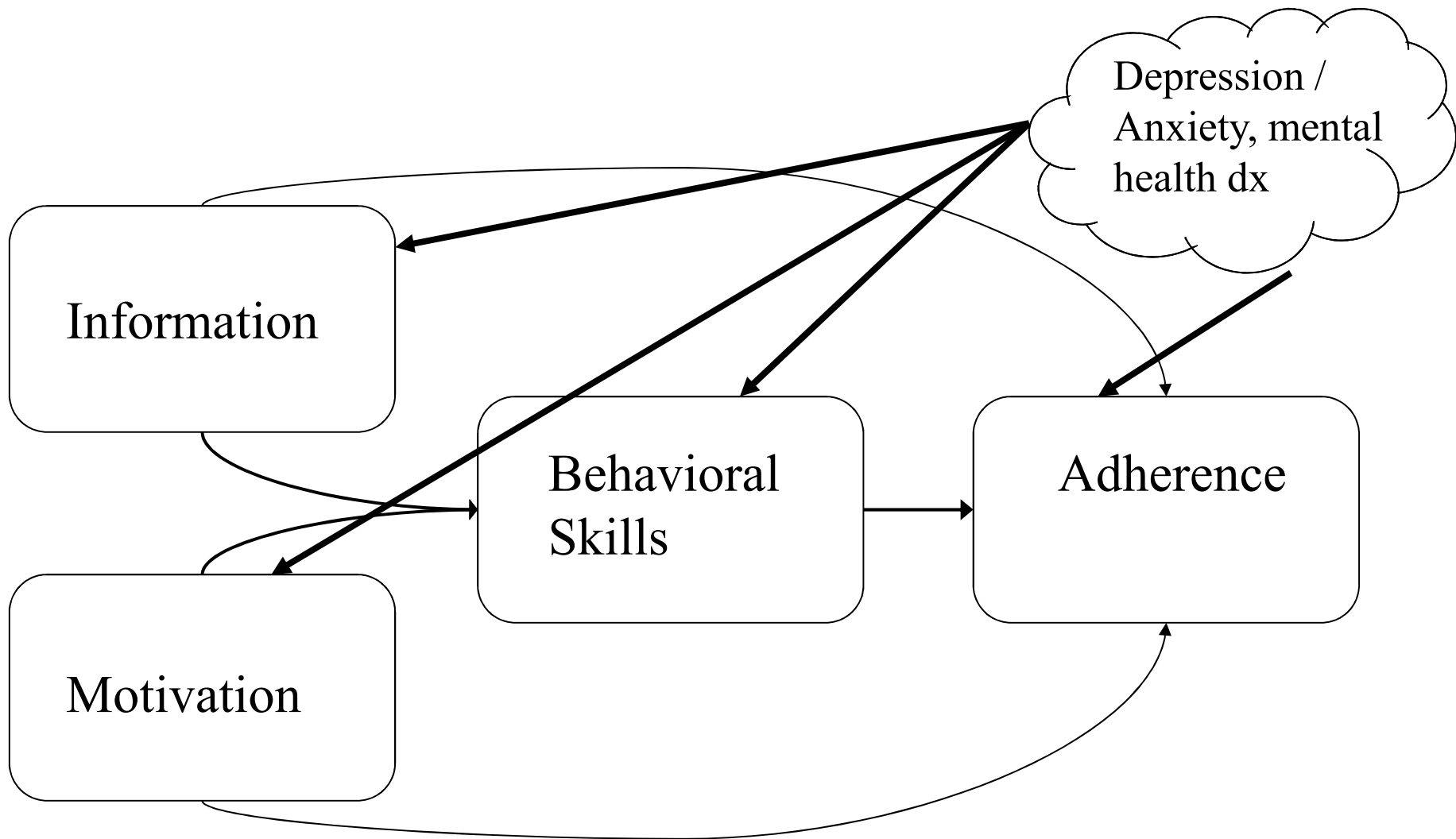
1. Kessler et al., 2005; *Archives of General Psychiatry*
2. Geffken et al., 1998; *Psychiatric Clinics of North America*
3. Krishnan et al., 2002; *Biological Psychiatry*, Bing et al., 2005



- Depression is associated with worse adherence in medical illness in HIV (Gonzalez et al., meta analysis submitted)
- 85-95% adherence to ART is required to maximize suppression of HIV viral load
- Depressed mood may be associated with difficulties in reducing HIV transmission risk behavior

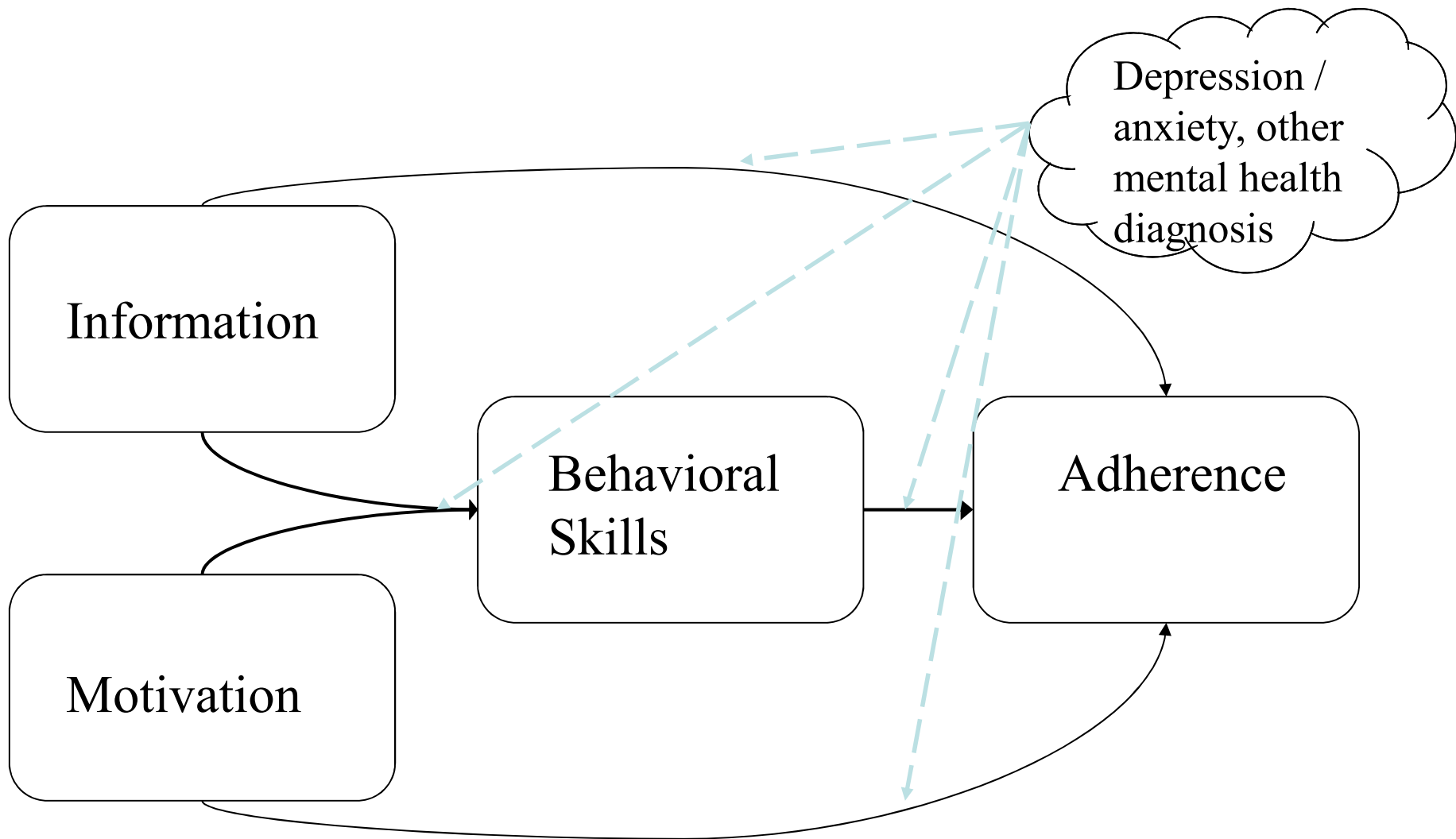


# Information-motivation-behavioral skills model



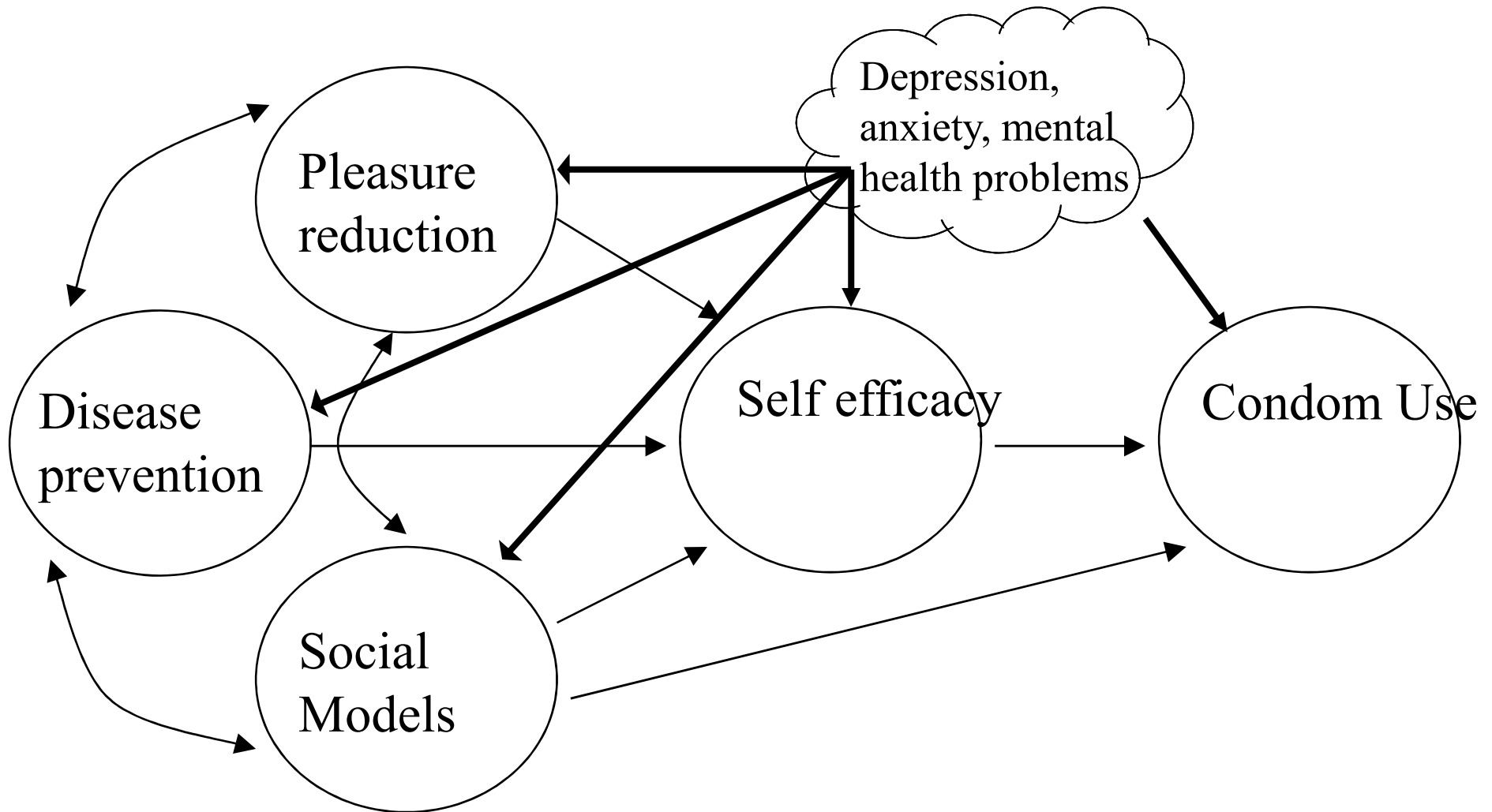
Fisher et al, Health Psychology, 2006.

# Information-motivation-behavioral skills model



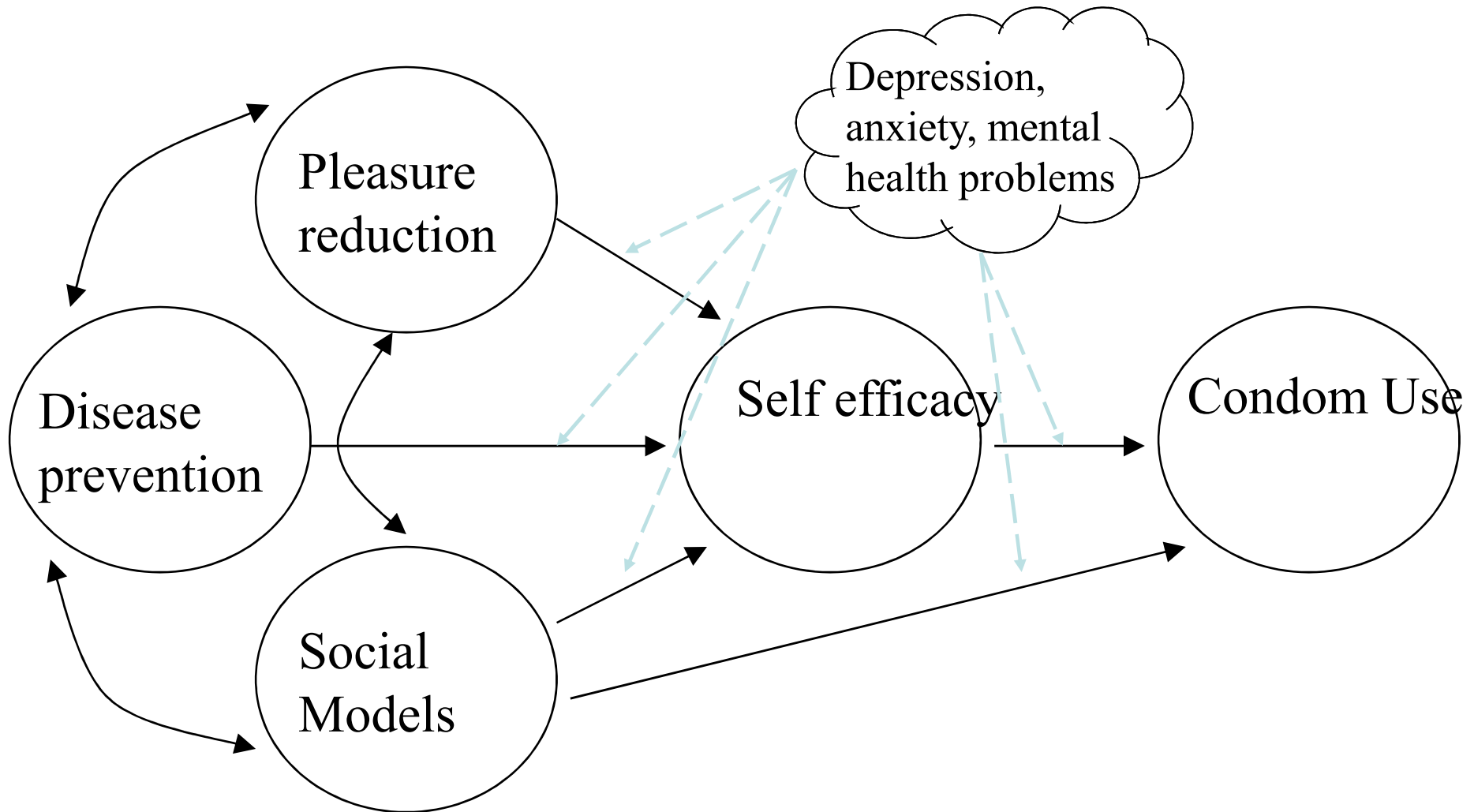
Fisher et al, Health Psychology, 2006.

# Example Model of Health Behavior Change: Self-efficacy Model for Condom Use



*Wulfert, Safren, et al., 1999; Journal of Applied Social Psychology*

# Social Cognitive Model

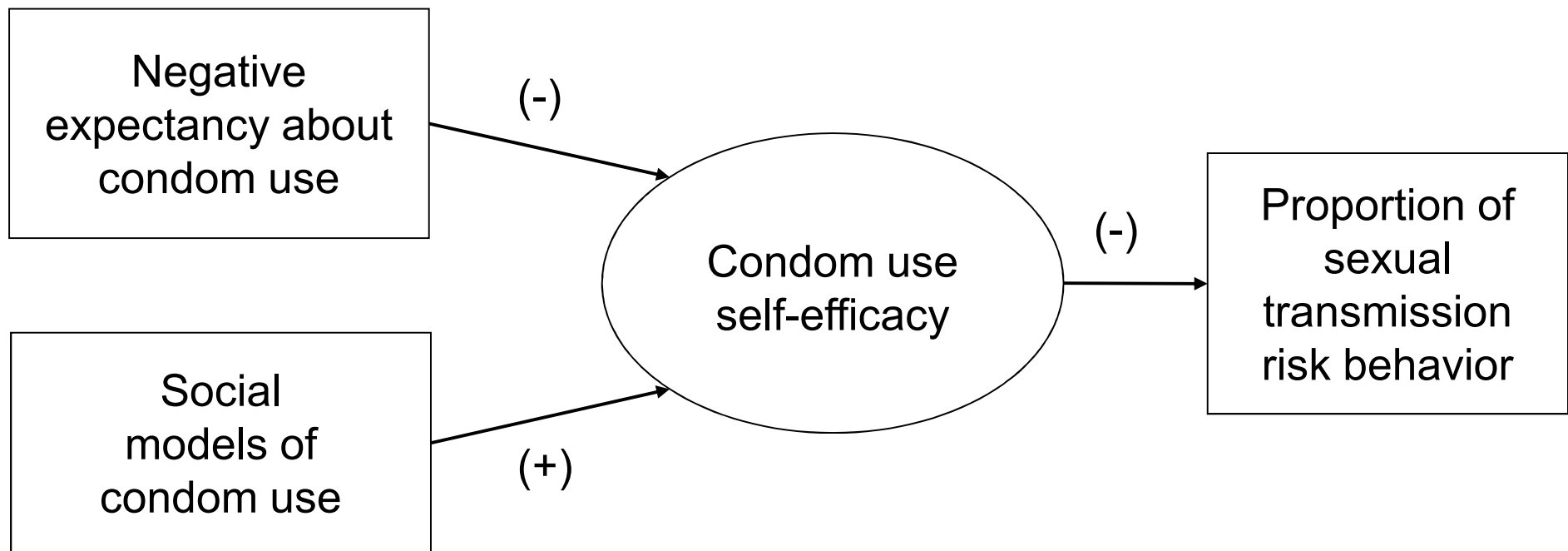


*Wulfert, Safren, et al., 1999; Journal of Applied Social Psychology*

# Proposed Model



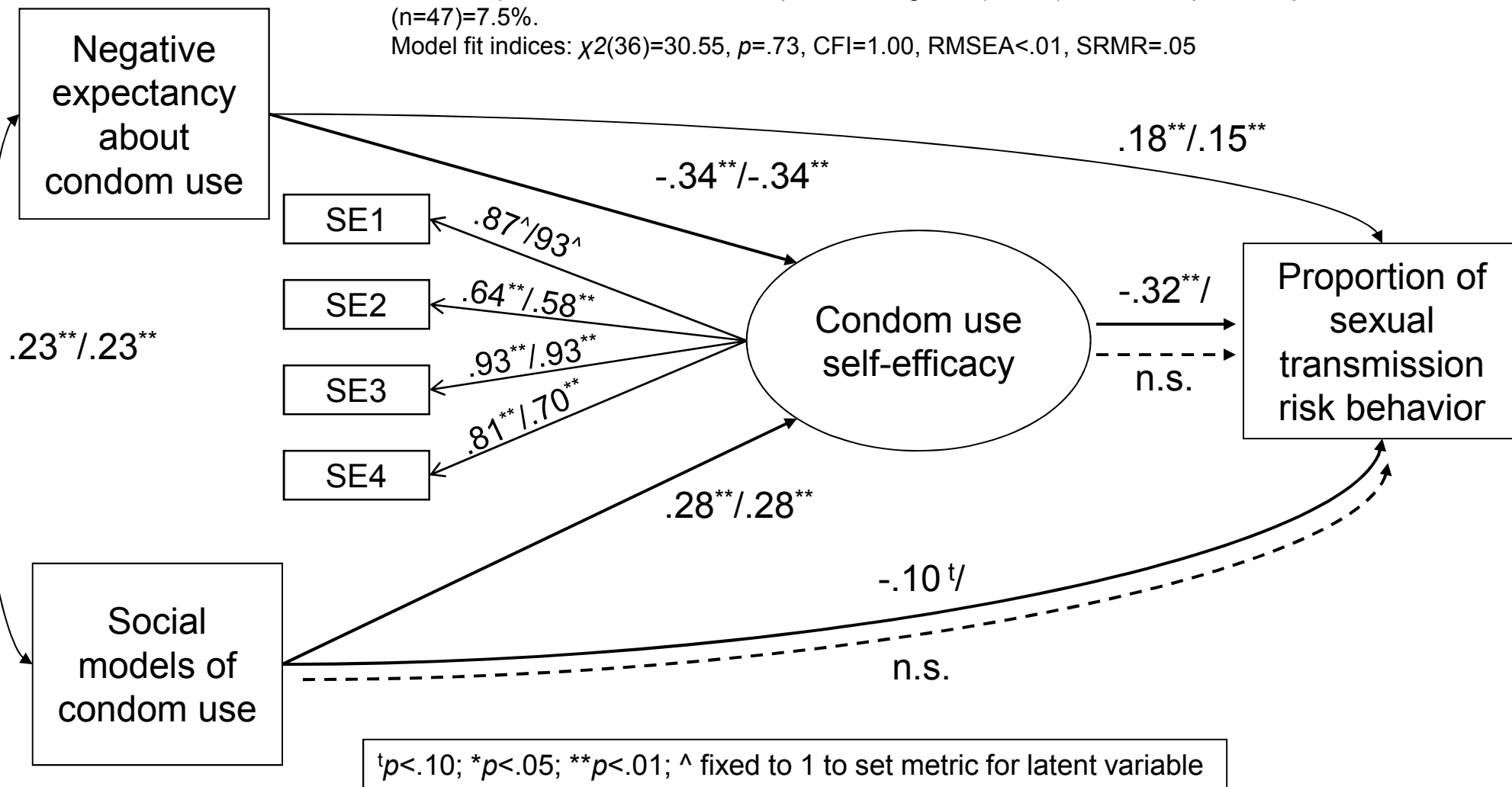
- 403 (of 503 total) sexually active MSM in care at Fenway Community Health
- Screening for one of two secondary prevention trials (NIMH, HRSA) between 2004-2007



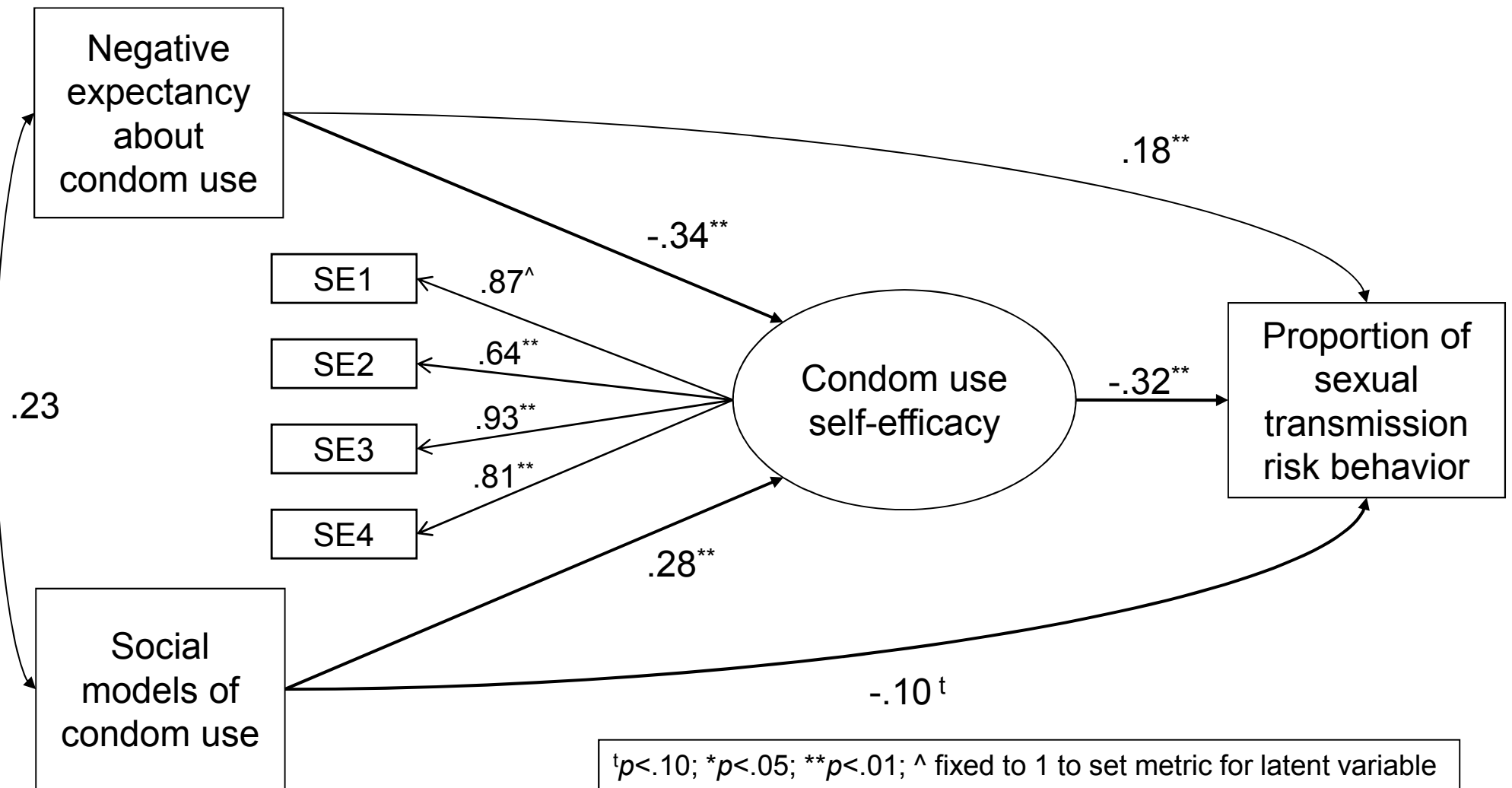
# Predicting TRB in Depressed and Not Depressed HIV-Infected MSM



$R^2$  for Proportion of Sexual TRB: Depression-negative ( $n=356$ )=20.3%, Depression-positive ( $n=47$ )=7.5%.  
 Model fit indices:  $\chi^2(36)=30.55$ ,  $p=.73$ , CFI=1.00, RMSEA<.01, SRMR=.05



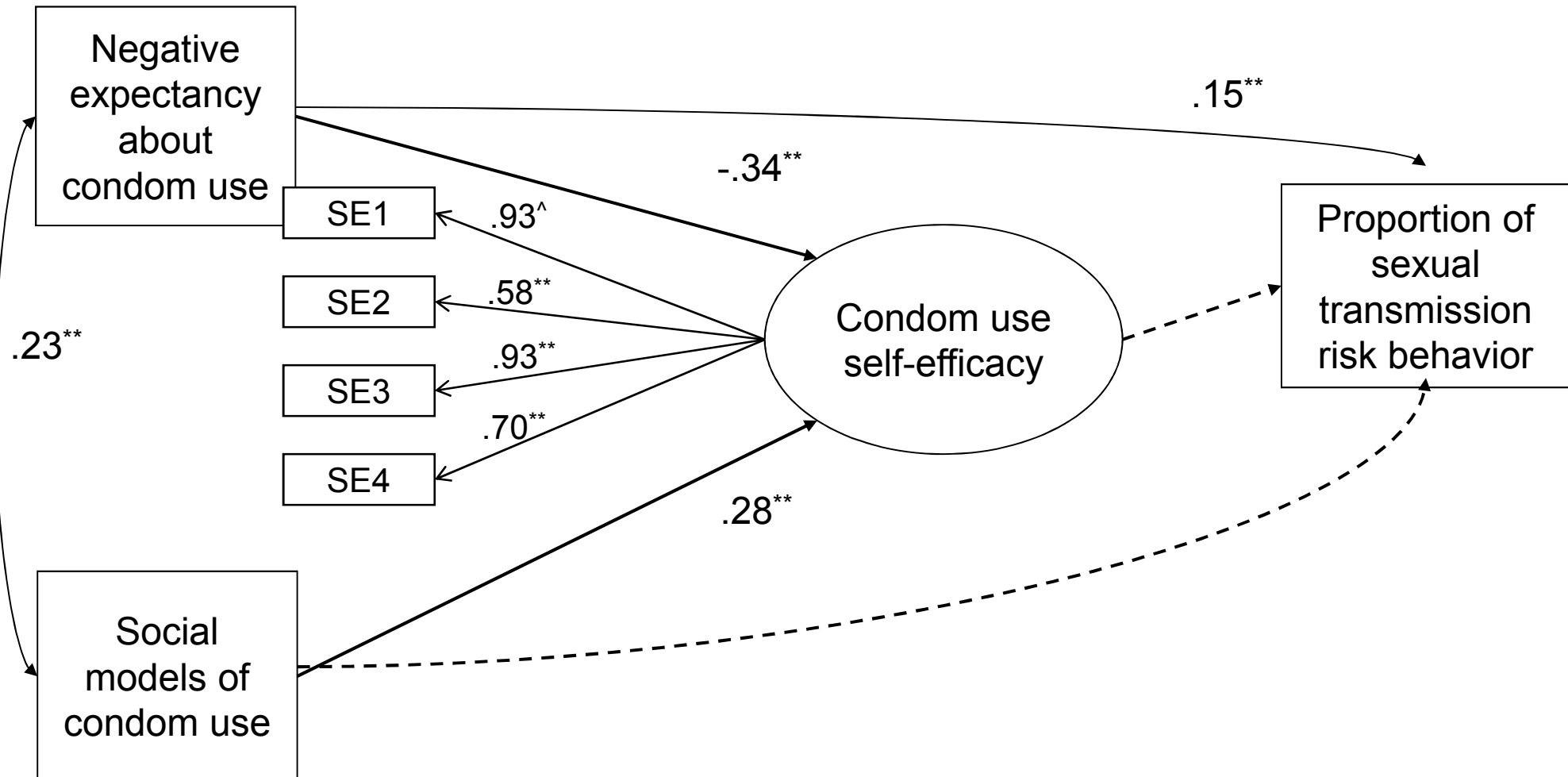
# Path model for those who did not screen in for major depressive disorder



$R^2$  for Proportion of Sexual TRB (n=356)=20.3%



# Participants who met screen-in criteria for MDD



\* $p < .05$ ; \*\* $p < .01$ ;  $\wedge$  fixed to 1 to set metric for latent variable

$R^2$  for Proportion of Sexual TRB ( $n=47$ )=7.5%.

# Major Depressive Episode (SIG-E-CAPS)

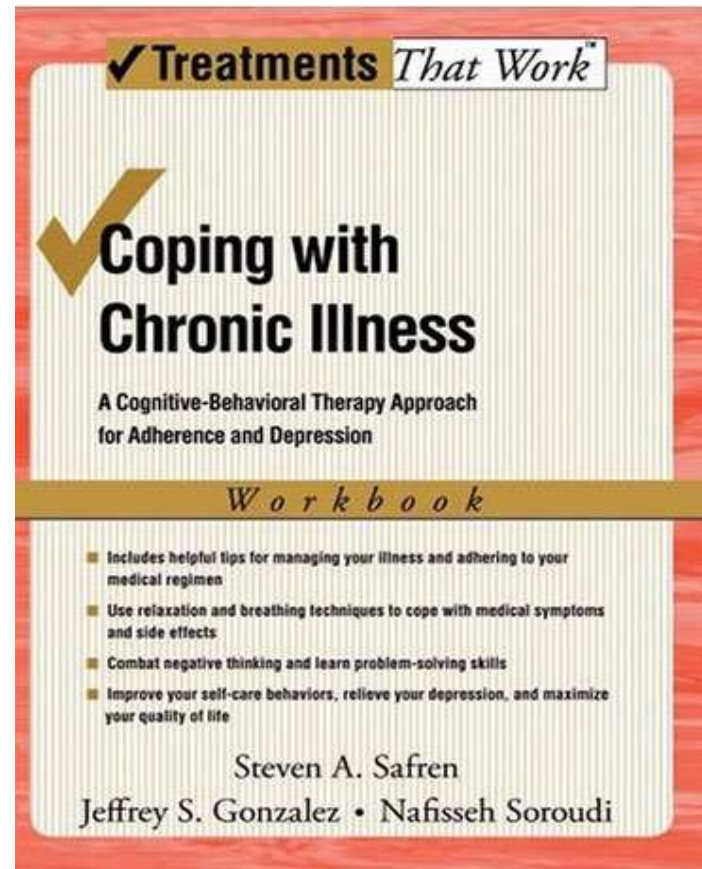
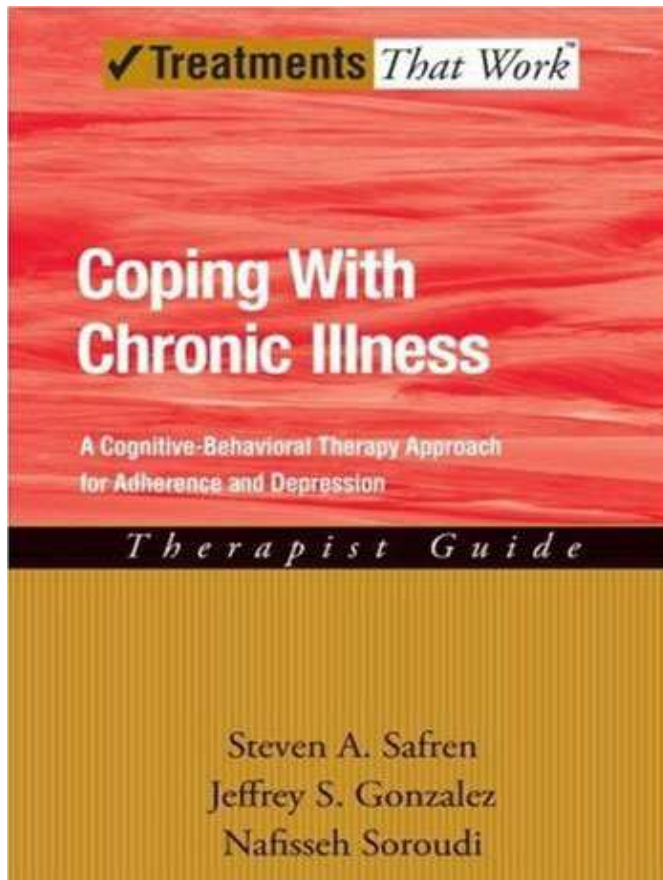


In addition to persistent sadness more days than not

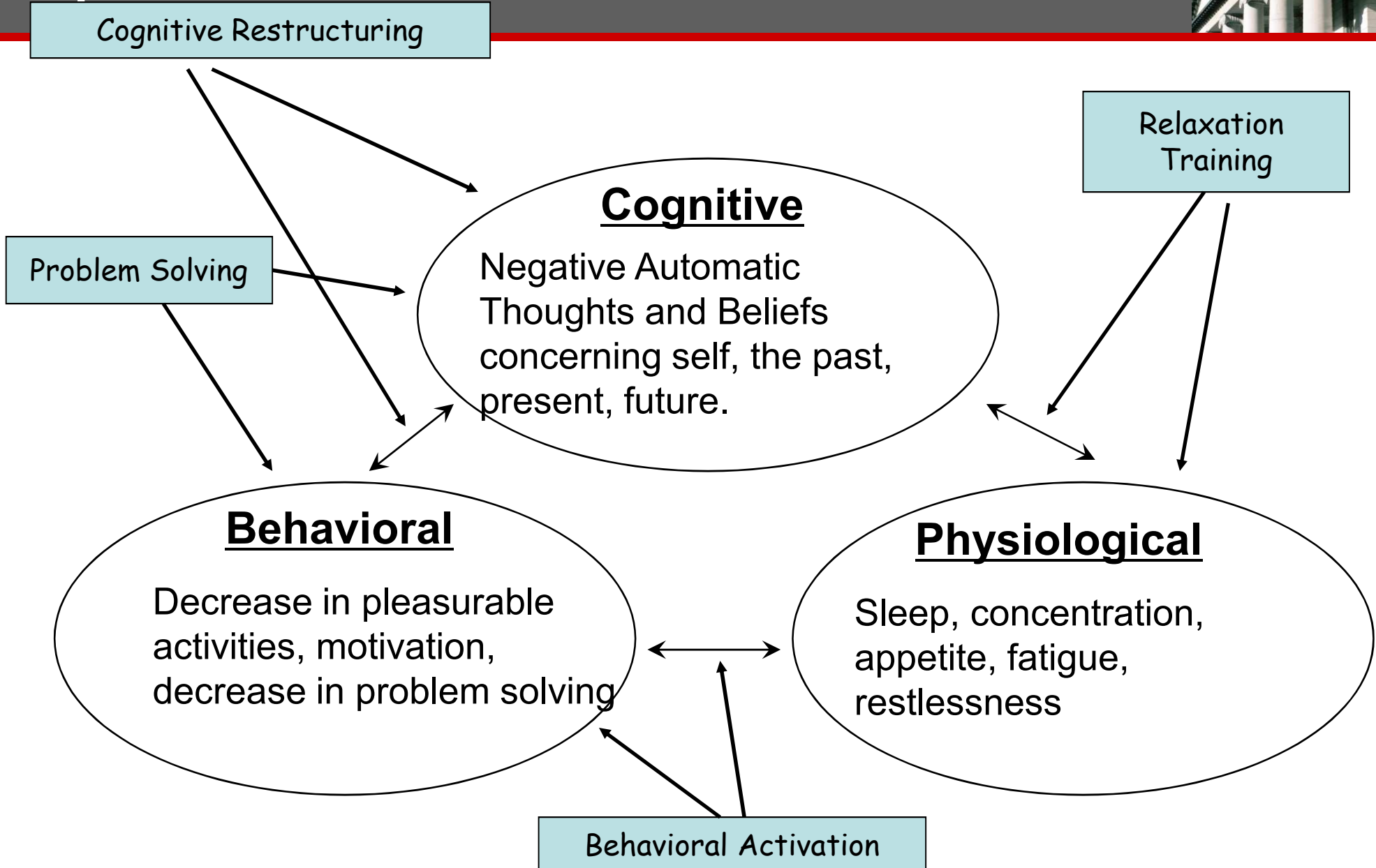
- Sleep
- Interest – loss of (can substitute sadness as a required symptom)
- Guilt/worthlessness
- Energy
- Concentration
- Appetite
- Psychemotor retardation
- Suicidality

\*\*need 5 symptoms, one must be sadness or loss of interest

# CBT-AD



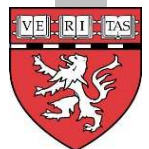
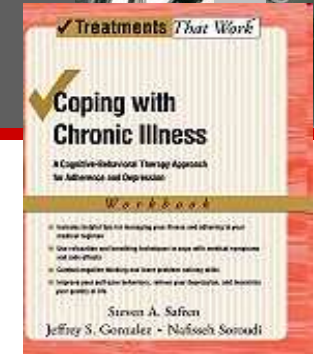
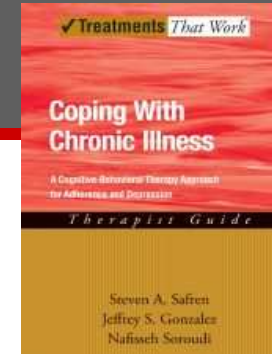
# Psychoeducation: CBT Conceptualization of Depression



# CBT-AD Overview

Modules: 12 sessions, each 50 minutes long

1. Psychoeducation and Motivation..... 1 session
2. Adherence Training / Life-Steps..... 1 session
3. Activity Scheduling..... 2 sessions
4. Cognitive Restructuring..... 4 sessions
5. Problem Solving..... 2 sessions
6. Relaxation Training..... 1 session
7. Maintenance & Relapse Prevention..... 1 session



# First Randomized Controlled Trial (NIMH R21 06660)



1. Estimation of effect size
2. Is actively treating depression necessary to increase adherence: Comparison of full intervention to minimal intervention
3. Continue acceptability and feasibility testing
4. Circumscribed inclusion criteria – maximize potential for effect and for internal validity

# Design



1. Two arm RCT (full CBT versus LifeSteps and provider letter)
2. Cross over: those who still met initial inclusion criteria could cross over from comparison group after post
3. Outcome: Adherence (MEMs), Depression (Independent assessor, self-report)

# Participants



>300 phone screens, 118 baseline evaluations

45 patients randomized (3 dropped post-randomization)

42 participants (29% AA, 15% Latino/Hispanic, 7% other; mean age = 44) completed baseline and T2

27 (64%) had at least one additional DSM-IV diagnosis

16 (38%) had two additional DSM-IV diagnoses

Most frequent comorbid diagnoses (includes participants with >1 comorbid diagnoses):

PTSD 13 (31%)

Social Phobia 9 (21%)

Panic disorder 11 (26%)

ADHD 2 (5%)

OCD 2 (5%)

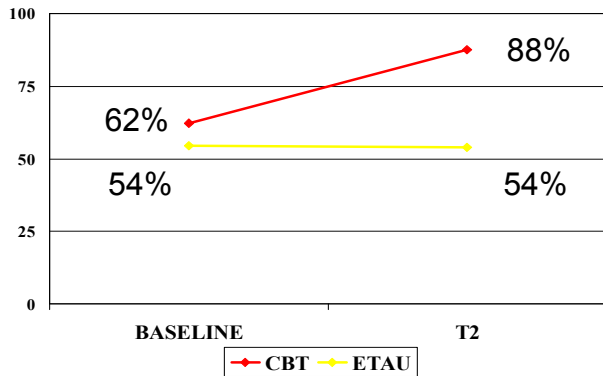
GAD 2 (5%)



# Outcome of CBT-AD

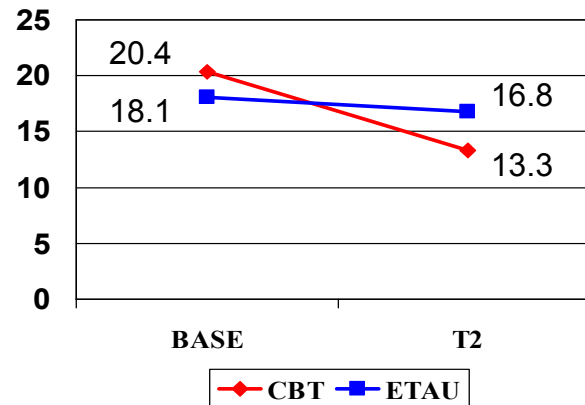


**MEMS outcomes, ITT**



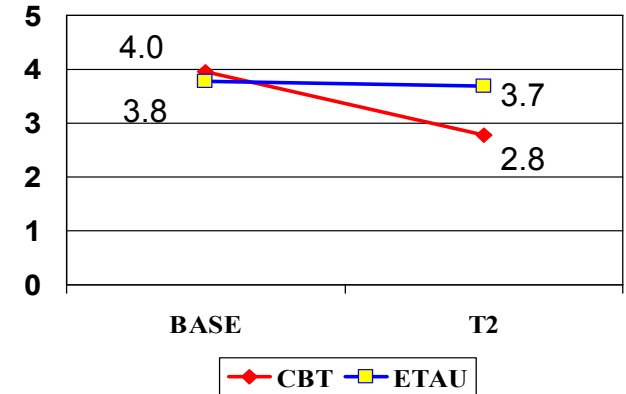
$F(1,42) = 21.94, p < .0001, \text{Cohen } d = 1.0$

**HAM-D outcomes, ITT**



$F(1,42) = 6.32, p < .02, \text{Cohen } d = .82$

**CGI outcomes, ITT**

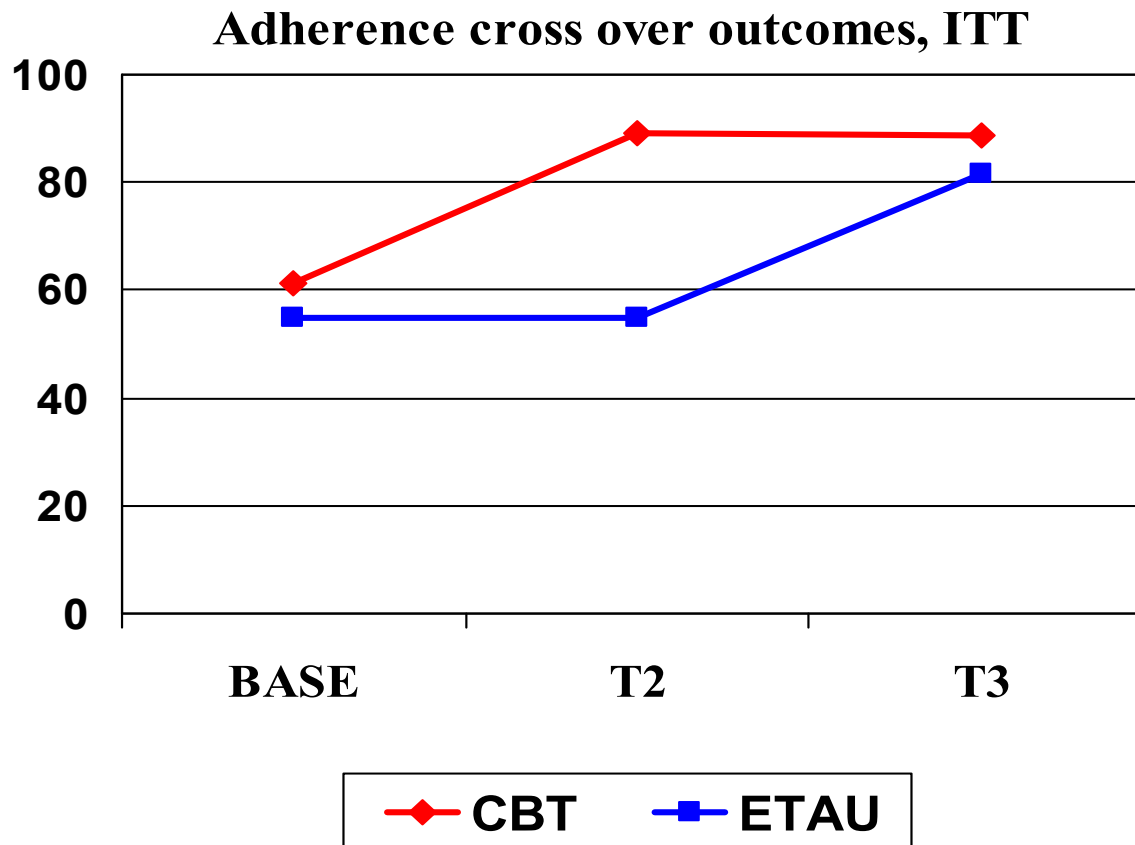


$F(1,42) = 9.68, p < .01, \text{Cohen } d = .91$

- Significant acute improvement in adherence (MEMS) and depression in intent-to-treat analyses
- Similar pattern of results for completer analyses
- Those who “crossed-over” caught up
- Intervention-associated improvements were generally maintained at 6 and 12 months

*Safren, O’Cleirigh et al., 2009 – Health Psychology*

# Those who crossed over “caught up” MEMs



2X3 ANOVA: significant interaction  $F(2,31) = 11.512, p < .0001$

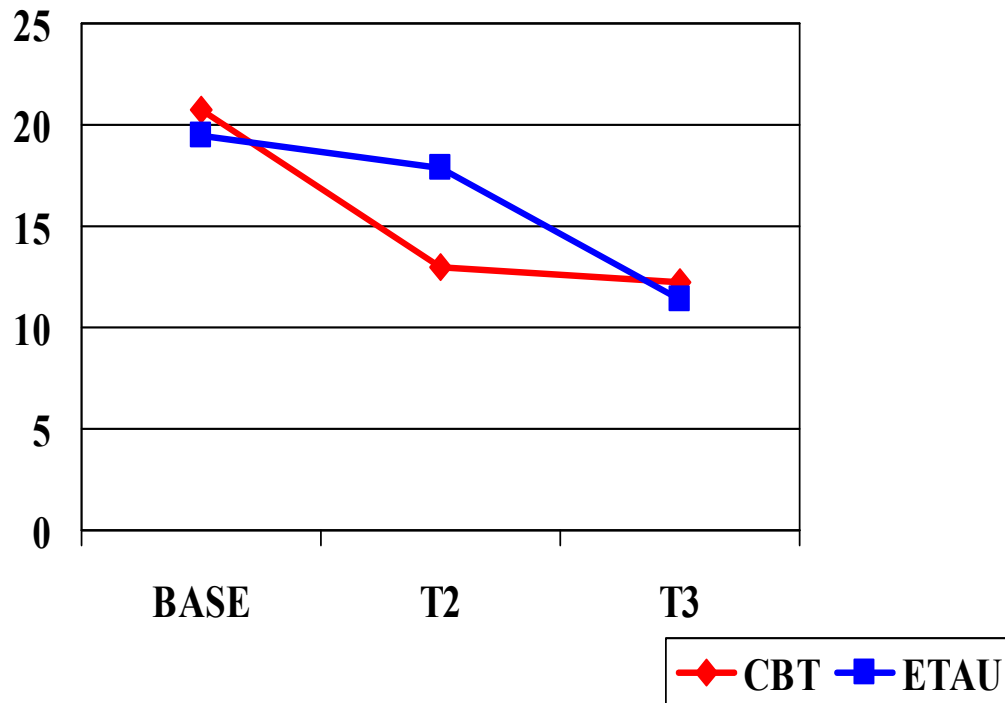
T2 to T3 2x2 ANOVA significant interaction:  $(F(1,32) = 23.461, p < .0001)$

T1 to T3 ANOVA: Main effects for time  $(F(1,32) = 43.206, p < .0001)$ .

# Those who crossed over “caught up” with improved depression

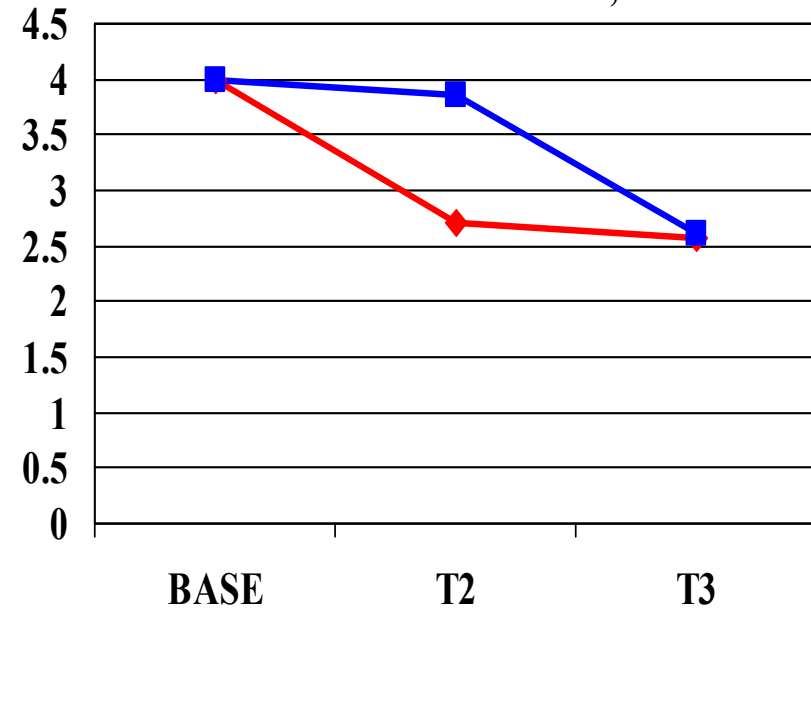


### HAM-D cross-over outcomes, ITT



2X3 ANOVA: significant interaction  $F(2,31) = 8.361, p < .01$   
T2 to T3 2x2 ANOVA significant interaction:  $(F(1,32) = 9.237, p < .01)$   
T1 to T3 ANOVA: Main effects for time  $F(1,32) = 28.637, p < .0001$

### CGI cross-over outcomes, ITT



2X3 ANOVA: significant interaction  $F(2,31) = 7.299, p < .01$   
T2 to T3 2x2 ANOVA significant interaction:  $F(1,32) = 9.848, p < .01$   
T1 to T3 ANOVA: Main effects for time  $F(1,32) = 33.767, p < .0001$

# Flexibility in delivering the intervention (delivered by doctoral or internship level psychologists)



Therapist adherence – to general principals of CBT and the manual versus every session following the outline

- Flexibility of adapting the modules
- Flexibility in sequence of modules
- Flexibility in time spent on modules
- Bring current problems back to CBT skills for adherence and depression

# CBT for Medication Adherence and Depression in HIV+ Methadone Patients



- o Participants (N=89) recruited from methadone clinics and community in Massachusetts and Rhode Island
- o Randomized to either ETAU or CBT-AD
- o Stratified by sex, depression severity (current MDD or residual symptoms only), and adherence (baseline MEMS adherence above or below 80%)

**MASSACHUSETTS GENERAL HOSPITAL**

**Living with HIV?  
On methadone maintenance?  
Feeling down or depressed?**

You may be eligible to take part in Project Target, a behavioral treatment research study being conducted at Massachusetts General Hospital

Study participants receive:  
Travel Reimbursement  
No Cost Assessments & Feedback  
Up to \$475 in Participant Payments

**Interested?  
1-877-33-TARGET**

Know someone else who might be interested in this study? Please pass this information on.

PROJECT **Target**

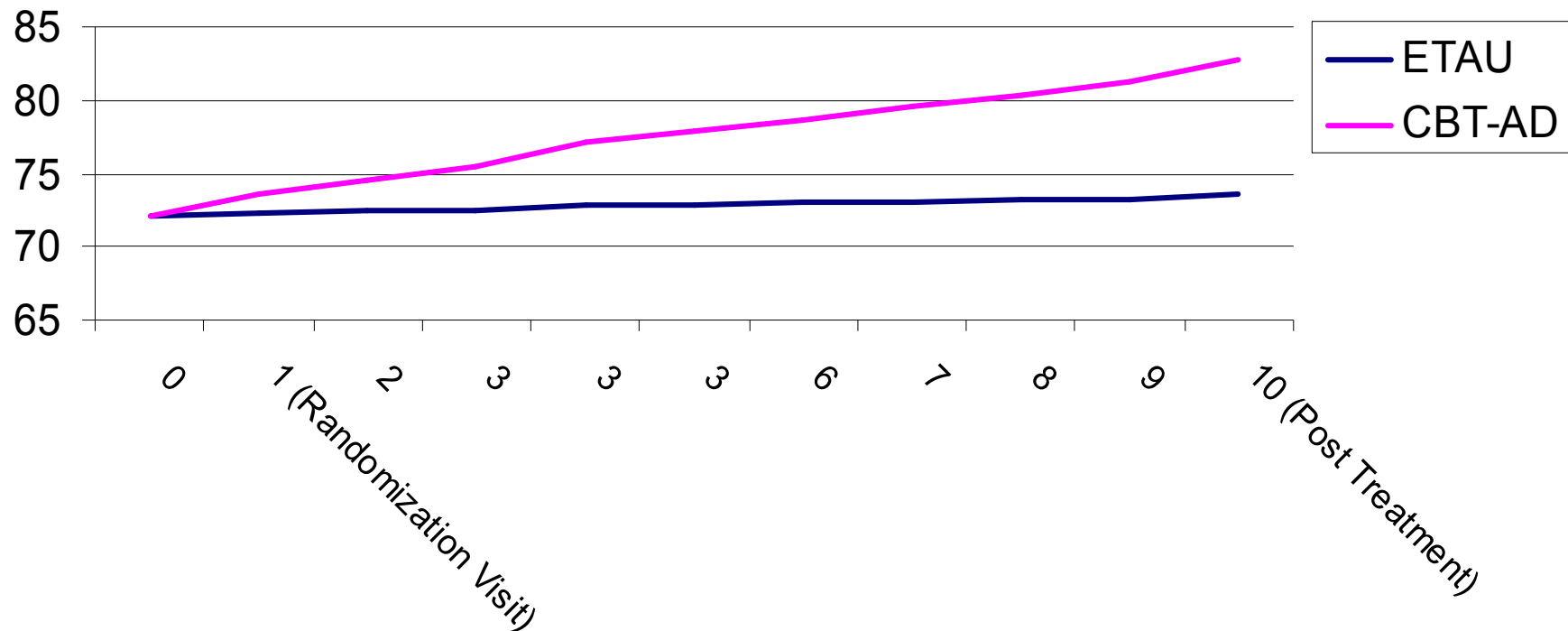
## • Inclusion Criteria:

- o HIV-positive
- o Prescribed antiretroviral therapy
- o History of injection drug use and enrollment in a drug abuse treatment program for at least one month
- o Current or subsyndromal depression
- o Between the ages of 18 and 65

# CBT-AD had greater acute adherence outcomes: Longitudinal (HLM) Analysis of MEMS



Acute MEMS Adherence Outcomes



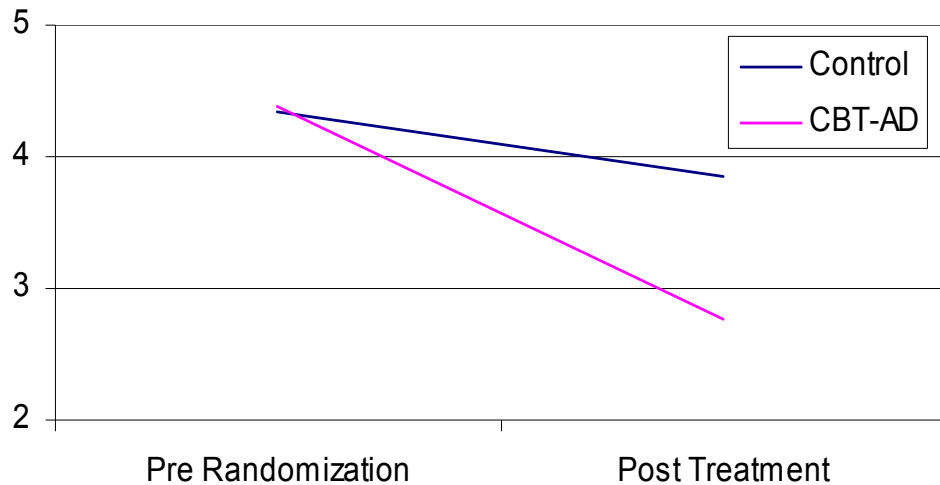
Improvement in the CBT-AD condition was greater than in the ETAU condition ( $\gamma_{slope} = 0.717$ ,  $t(87) = 2.01$ ,  $p < .05$ ).

*Safren, O'Cleirigh et al., 2012 – JCCP*

# CBT Had Better Clinician-Assessed Depression Outcomes. Analysis of CGI & MADRS

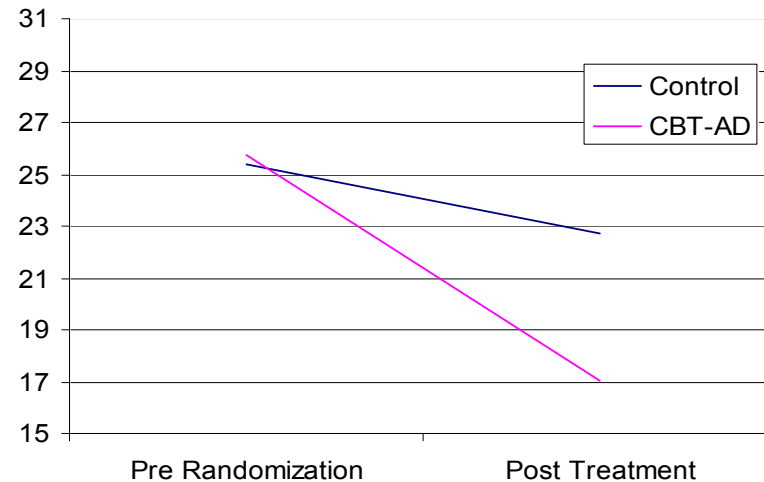


### Post Treatment CGI Outcomes



$F = 14.77, df = (1,79), p < .001$

### Post Treatment MADRS Outcomes



$F = 6.52, df (1,79), p < .01$

*Safren, O’Cleirigh et al., 2012 – JCCP*

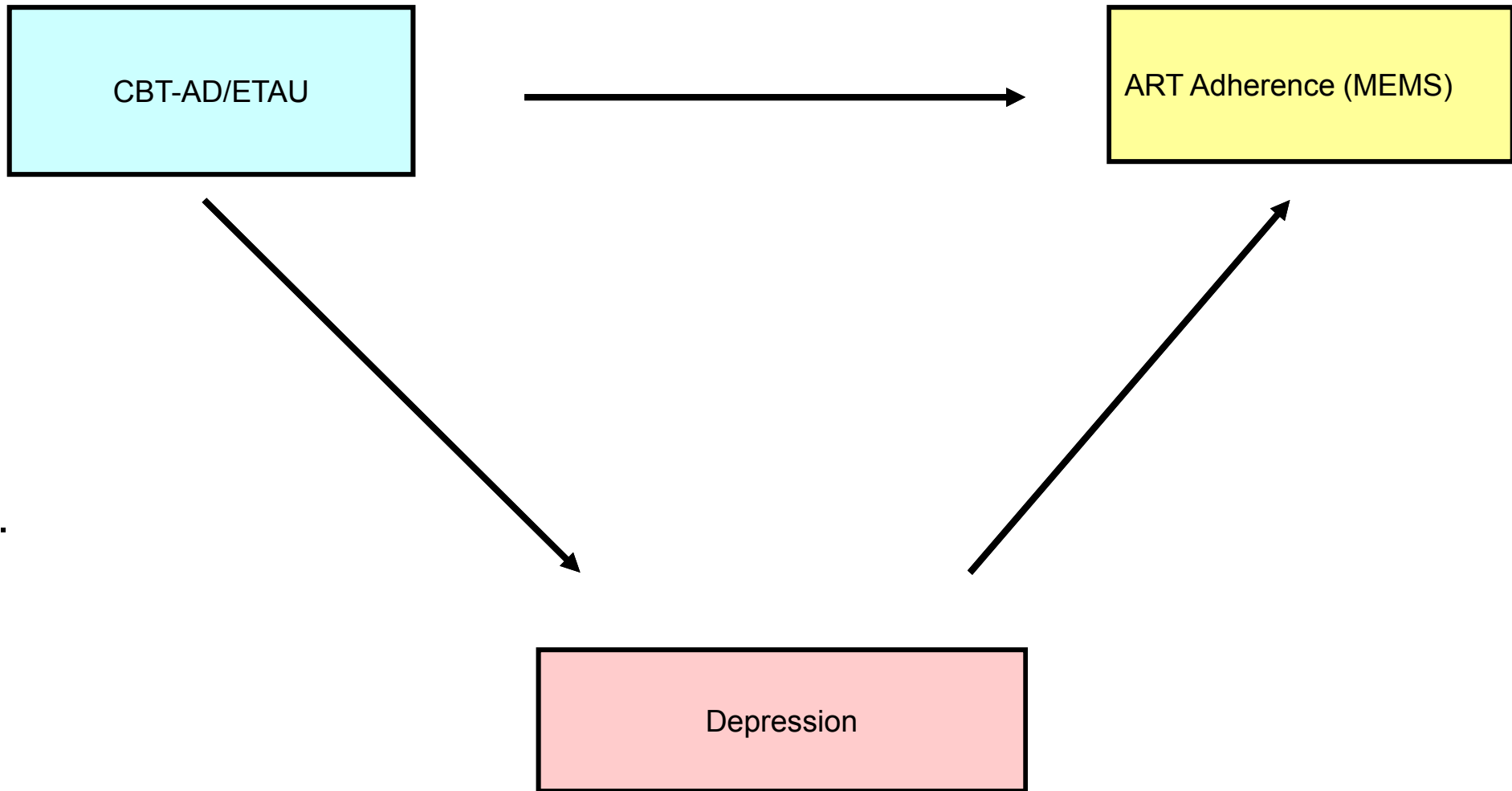
## Follow-up



- **Adherence**: Gains were not maintained – no difference between intervention and control over the 3 and 9 month follow-up
- **HIV Viral load**: no difference across conditions
- **Depression**: Gains were maintained across all indicators of depression
- **CD4**: Significant differences between conditions ( $\gamma$ slope = 2.09,  $t(76) = 2.20$ ,  $p = .03$ ) over the course of the study.
  - Intervention group: 61.2 CD4 cell increase
  - Comparison group: 22.4 CD4 cell decrease

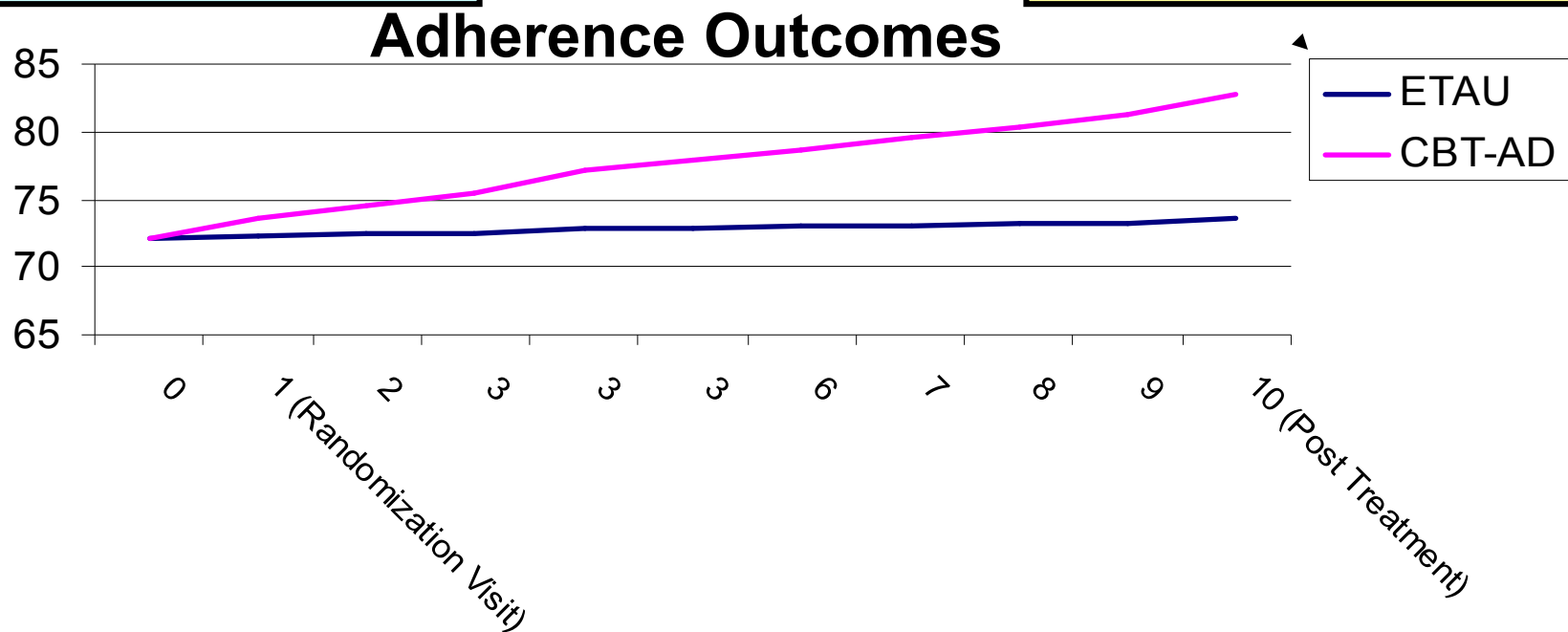
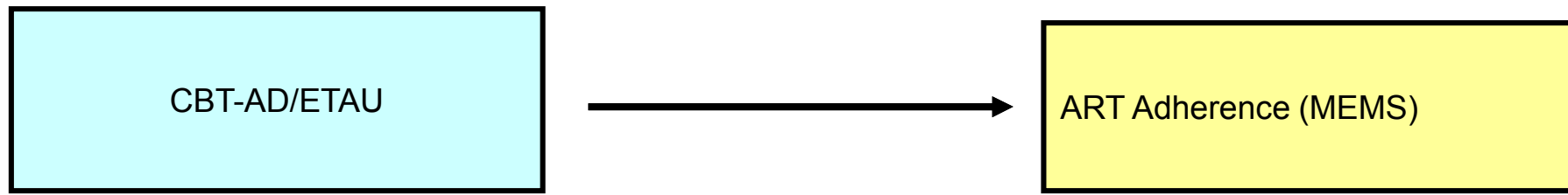


# Do Reductions in Depression Mediate Treatment Related Reductions in Adherence



# CBT-AD

## Integrated Treatment for Depression and Adherence



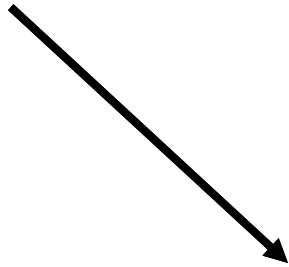
Improvement in the CBT-AD condition was significantly greater than in the ETAU condition (slope = 0.717,  $t(87) = 2.01$ ,  $p < .05$ ).

# CBT-AD

## Integrated Treatment for Depression and Adherence

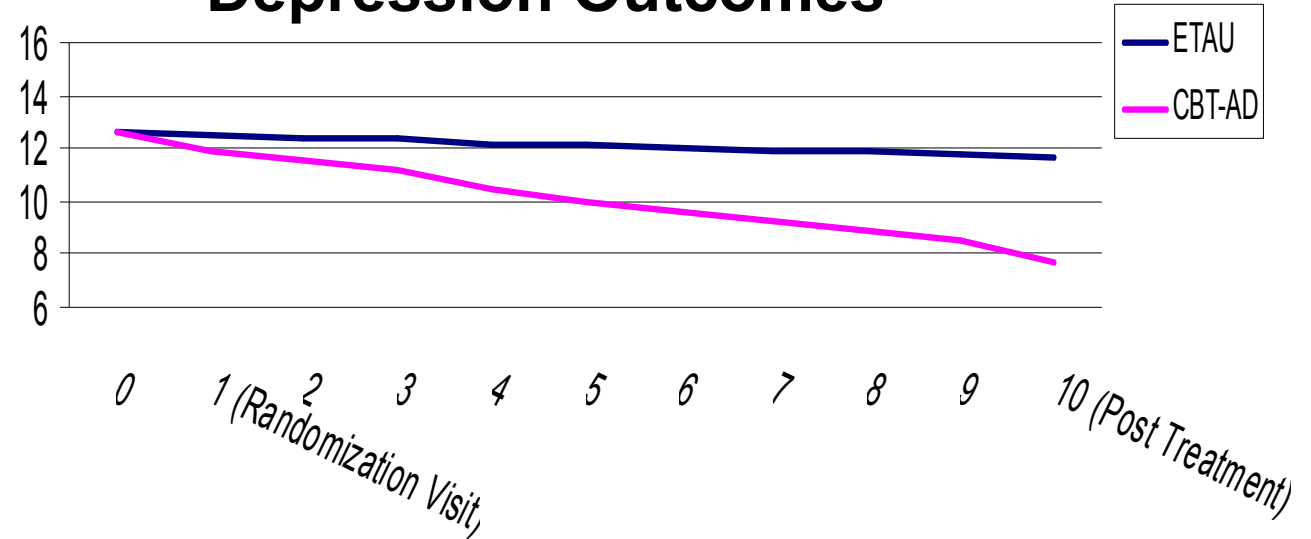


CBT-AD/ETAU



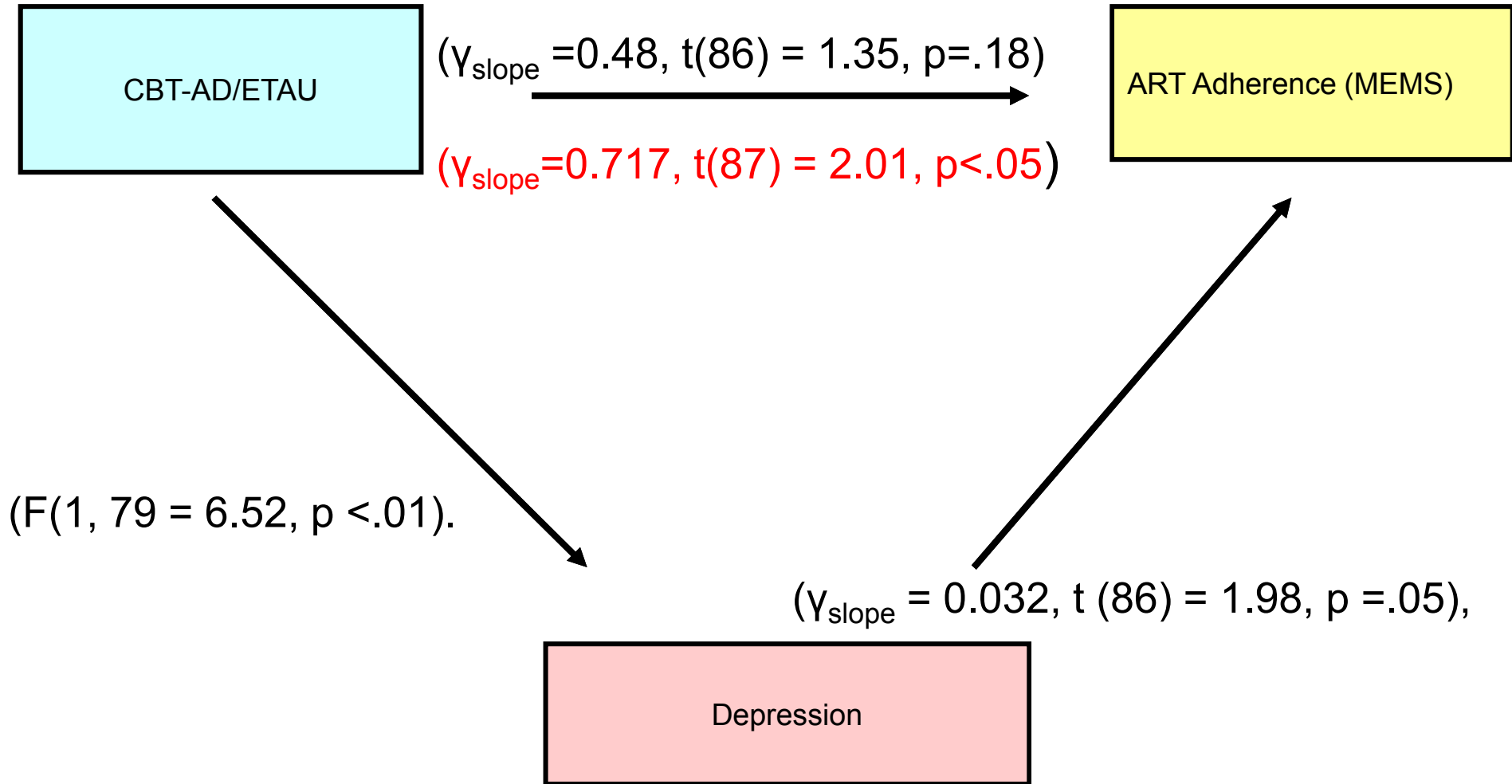
Depression

### Depression Outcomes



Trajectory of improvement in self-reported depression was greater for the CBT-AD condition than the ETAU condition ( $\gamma_{slope} = -0.30$ ,  $t(87) = -2.60$ ,  $p = .01$ ).

# Support for Integrated Treatment Model



# Current work - Project “TRIAD”

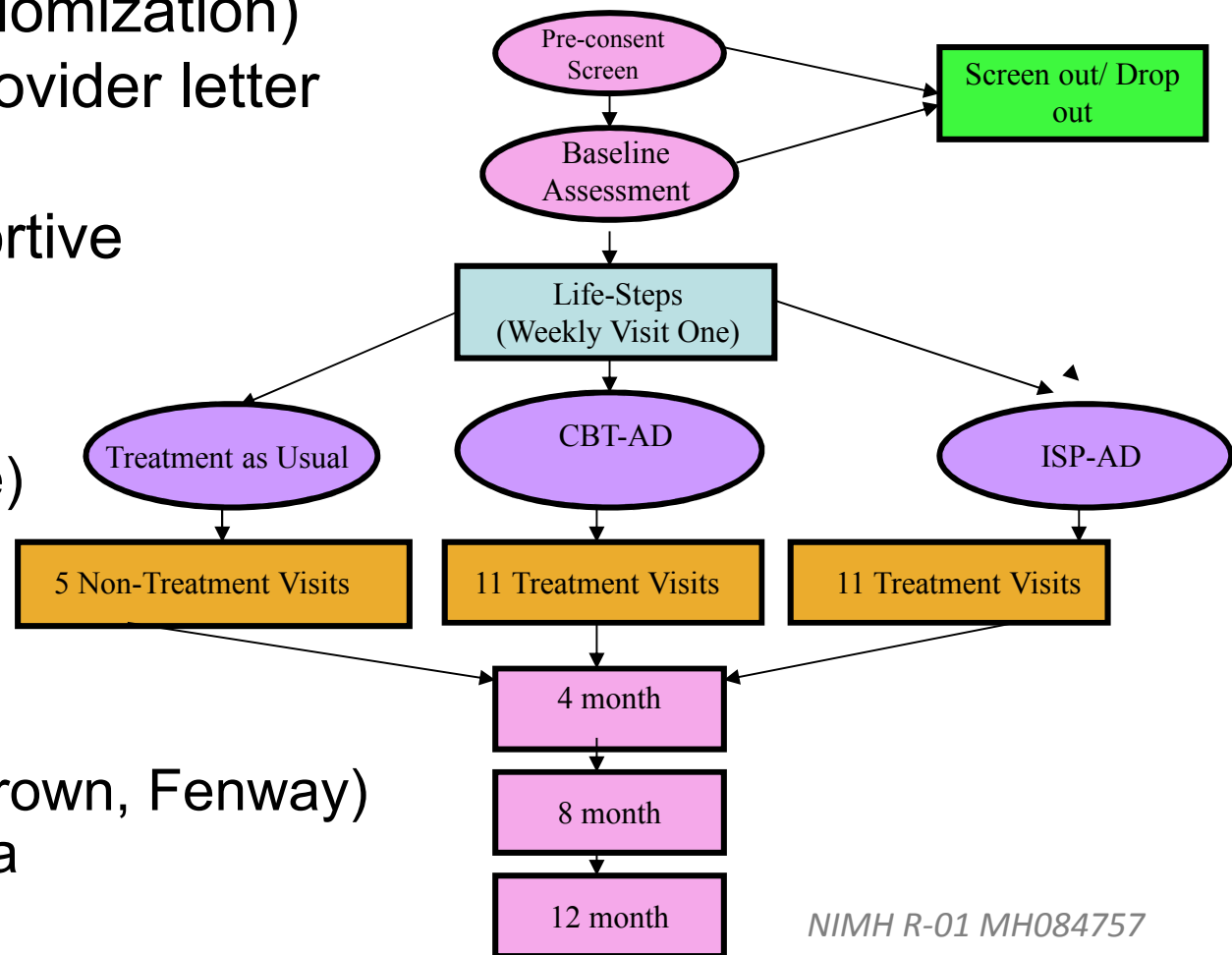


NIMH funded efficacy trial (PI: Safren)

R01MH084757-05

3 arm study (2:2:1 randomization)

- Life-Steps plus provider letter
- CBT-AD
- Information/supportive psychotherapy
- Large N (240; 80 randomized per site)
- 217 (90%) completers



- 3 site study (MGH, Brown, Fenway)
- Wide inclusion criteria

NIMH R-01 MH084757

# Lessons Learned from Integrating Treatment of Medical (Self-Care) and Psychiatric Problems



- ▶ Change is hard
- ▶ Exit interviews: high patient acceptance / appreciation
- ▶ But can use CBT techniques to improve adherence, even in the context of mental health comorbidity
- ▶ Which can improve medical outcomes (e.g. HIV outcomes)

- Need to analyze cost and cost-effectiveness
- Implications for “population based medicine” and integrated care



# What's next?

**10:00 a.m**    **Special Session**  
Mindfulness Workshop  
(Johnson)

**10:00 a.m**    **Guided Poster Tour**  
Care in Focus  
(Foyer)

