Addressing Mental Health, Substance Abuse, and HIV Treatment Adherence

Steven A. Safren, Ph.D.

FENWAY HEALTH

MASSACHUSETTS GENERAL HOSPITAL

HARVARD MEDICAL SCHOOL

Initial Trials that General Do Not Address Mental Health or Substance Use Comorbidity

- Minimal interventions – MGH/Fenway work
  - "Life-Steps" – single session adherence intervention; significant effects but comparison group "caught up" over time (Safren et al., 2001)
  - Pager study – significant but modest effects (Safren et al., 2003)
- Meta analyses of adherence interventions: significant but modest effects
 - Simoni (2006): 19 RCTs
  - Amico (2006): 25 studies

Safren et al., 2001, Behaviour Research and Therapy; Safren et al., 2003; AIDS Care; Amico et al., 2006. JAIDS; Simoni et al., 2006. JAIDS
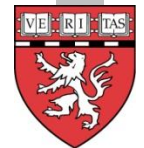
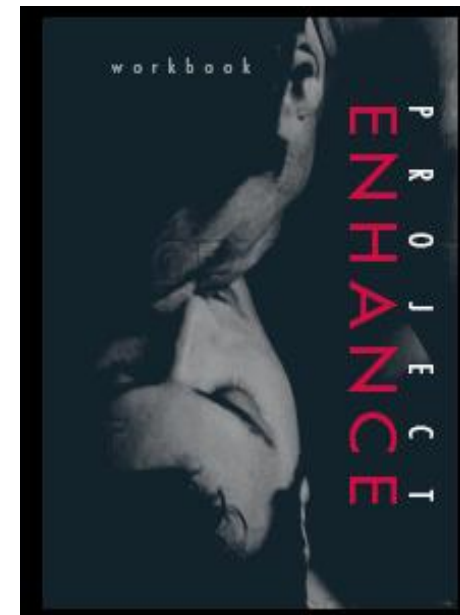# High mental health and substance use comorbidity in HIV

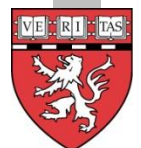| Condition	% Screening Positive (95% CI)*	
	HCSUS (N=2864) HIV-infected	NHSDA (N=22181)
Major Depression	**36.0** (33.6-38.3)	7.6
Dysthymia	**26.5** (23.5-29.5)	---
Generalized Anxiety Disorder	**15.8** (14.0-17.7)	2.1
Panic Attack	**10.5** (8.0-13.0)	2.5
Any psychiatric disorder	**47.9**	
No drug use	**49.9** (46.0-53.71)	89.7
Marijuana use only/ no dependence	**12.1** (10.2-14.8)	---
Other drug use/ no dependence	**25.6** (22.1-29.1)	---
Drug dependence	**12.5** (10.2-14.8)	---

Bing et al., 2001; Archives of General Psychiatry
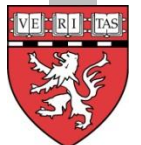
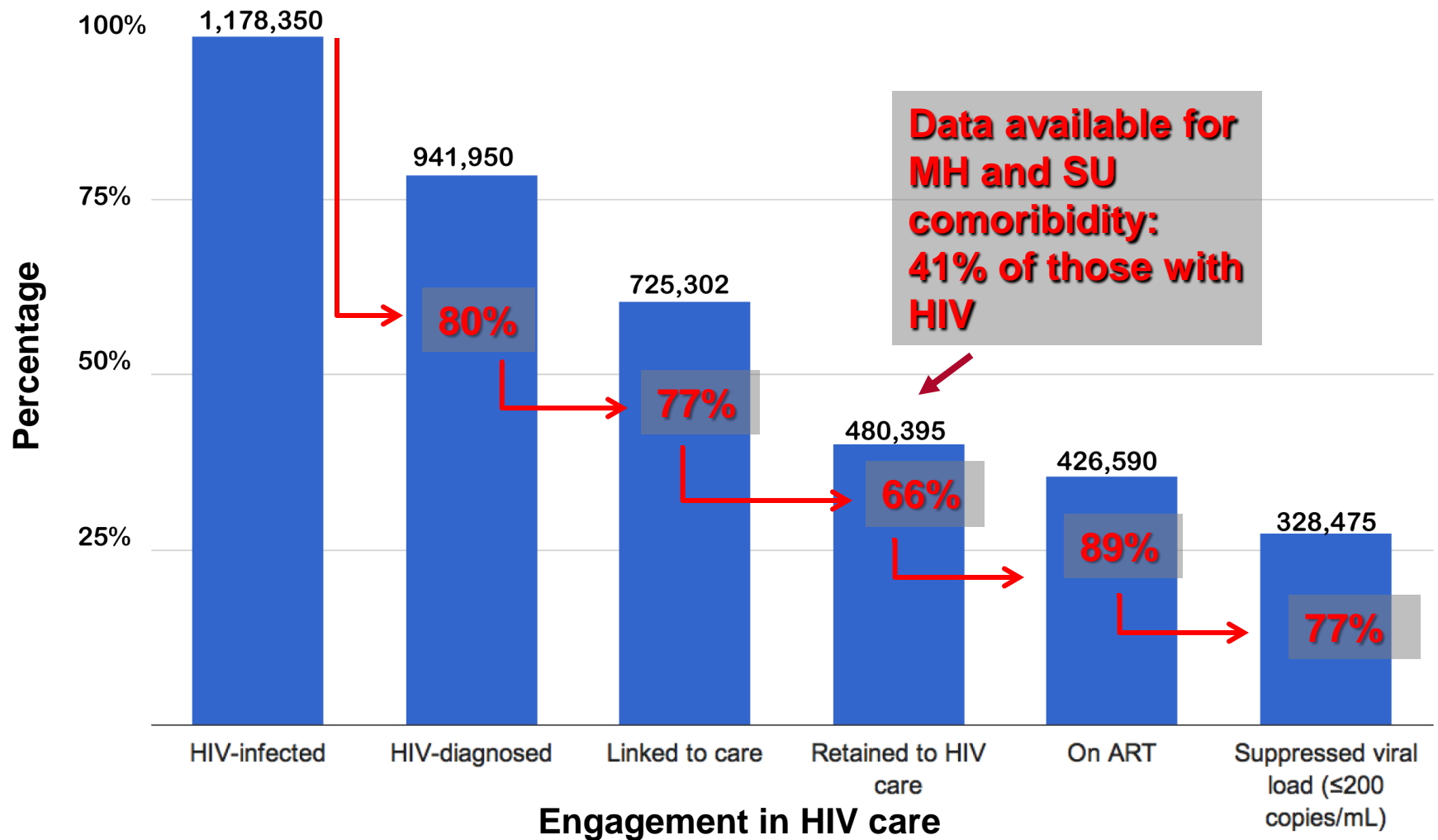# Fenway Data: Mental Health Comorbidity in HIV-infected MSM (N = 503)

- Major Depression:13.01%
- Other Depression: 10.0%

- Any illicit drug use: 39%
- 5 Drinks in one sitting once a week or more: 20.0%
- Any crystal meth use: 20.8%

- PTSD: 34.8%
- Social Anxiety Disorder: 22.9%
- Panic: 9.5%
- Other Anxiety Syndrome (GAD): 7.9%

- Somatoform Disorder: 12.3%
- ADHD: 10.6%

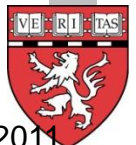- History of childhood sexual abuse: 46%

O'Cleirigh et al., under revision

The Continuum of HIV Care--US

Data available for MH and SU comoribidity: 41% of those with HIV

Chart: Percentage vs Engagement in HIV care

- HIV-infected: 1,178,350 (100%)
- HIV-diagnosed: 941,950 — 80%
- Linked to care: 725,302 — 77%
- Retained to HIV care: 480,395 — 66%
- On ART: 426,590 — 89%
- Suppressed viral load (≤200 copies/mL): 328,475 — 77%

Mental Health and Substance Use comorbidity may be even higher in individuals not in care

MMWR (60), 2011

Depression and HIV/AIDS Treatment Nonadherence: A Review and Meta-analysis

Jeffrey S. Gonzalez, PhD,*†‡ Abigail W. Batchelder, MPH, MA,* Christina Psaros, PhD,‡§ and Steven A. Safren, PhD‡§

- 95 independent samples
- Depression significantly associated with non-adherence (p < .0.00001; r = 0.19: CI: .14 - .25)
- Adherence via interview versus self-report higher association
- Continuous measures versus dichotomies higher
- Not limited to those with clinical depression
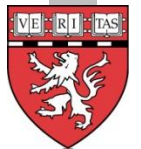
Adherence to Antiretroviral Therapy Among HIV-Infected Drug Users: A Meta-Analysis

Monica Malta · Monica M. F. Magnanini ·
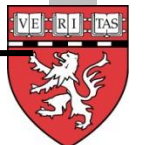Steffanie A. Strathdee · Francisco I. Bastos

- **Systematic Review**
  - **Active drug use = worse HAART outcomes (former DU, OST or support = better outcomes)**
- **Meta analysis:**
  - **38 studies; 14,960 patients**
  - **Drug users mean adherence 60%**
  - **Comparable to meta analysis of PLWH in N. America, reporting 55% (overlapping CIs; Mills et al., 2006)**

The Effects of "Syndemics" on HIV Risk in MSM

- Cross sectional household telephone survey of MSM in Chicago, LA, New York ,and SF (N = 2881)

- High occurrence and interconnectedness of depression, poly drug use, childhood sexual abuse, and partner violence

- Additive effects: Odds ratios increased as did number of these psychosocial health problems

	1 problem	2 problems	3 and 4 problems
High risk sex ($P<.01$)	1.6	2.4	3.5
HIV prevalence ($P<.001$)	1.8	2.7	3.6

Stall R et al (2003). *American Journal of Public Health*. 93:939-942.
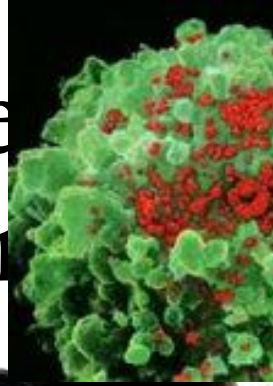
Example from Synder
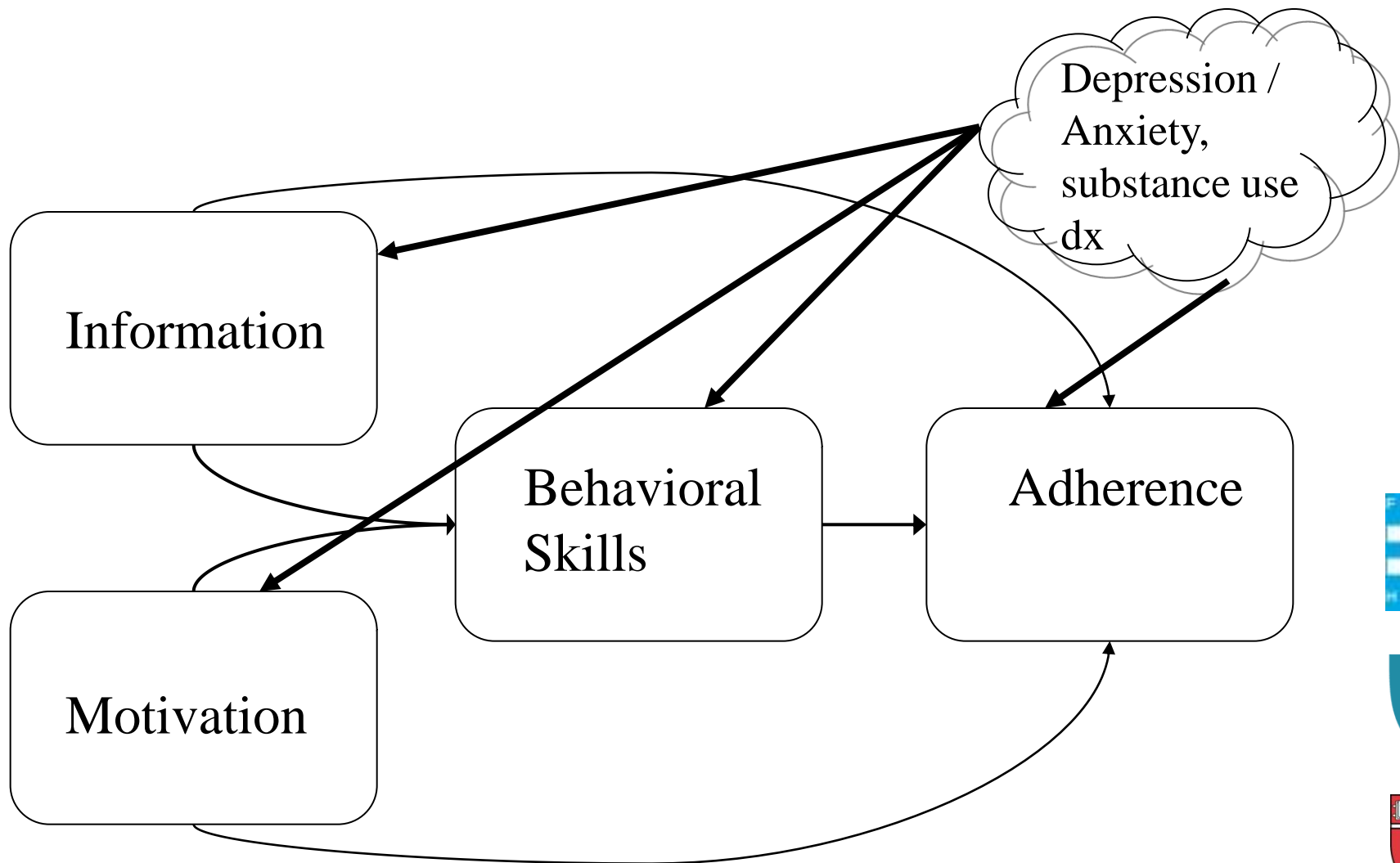
Mental ill-health

Instability → Homelessness

Substance Use

Mental Health / Substance Use Can Interfere with Adherence Intervention Models

Depression / Anxiety, substance use dx

Information

Behavioral Skills

Adherence

Motivation
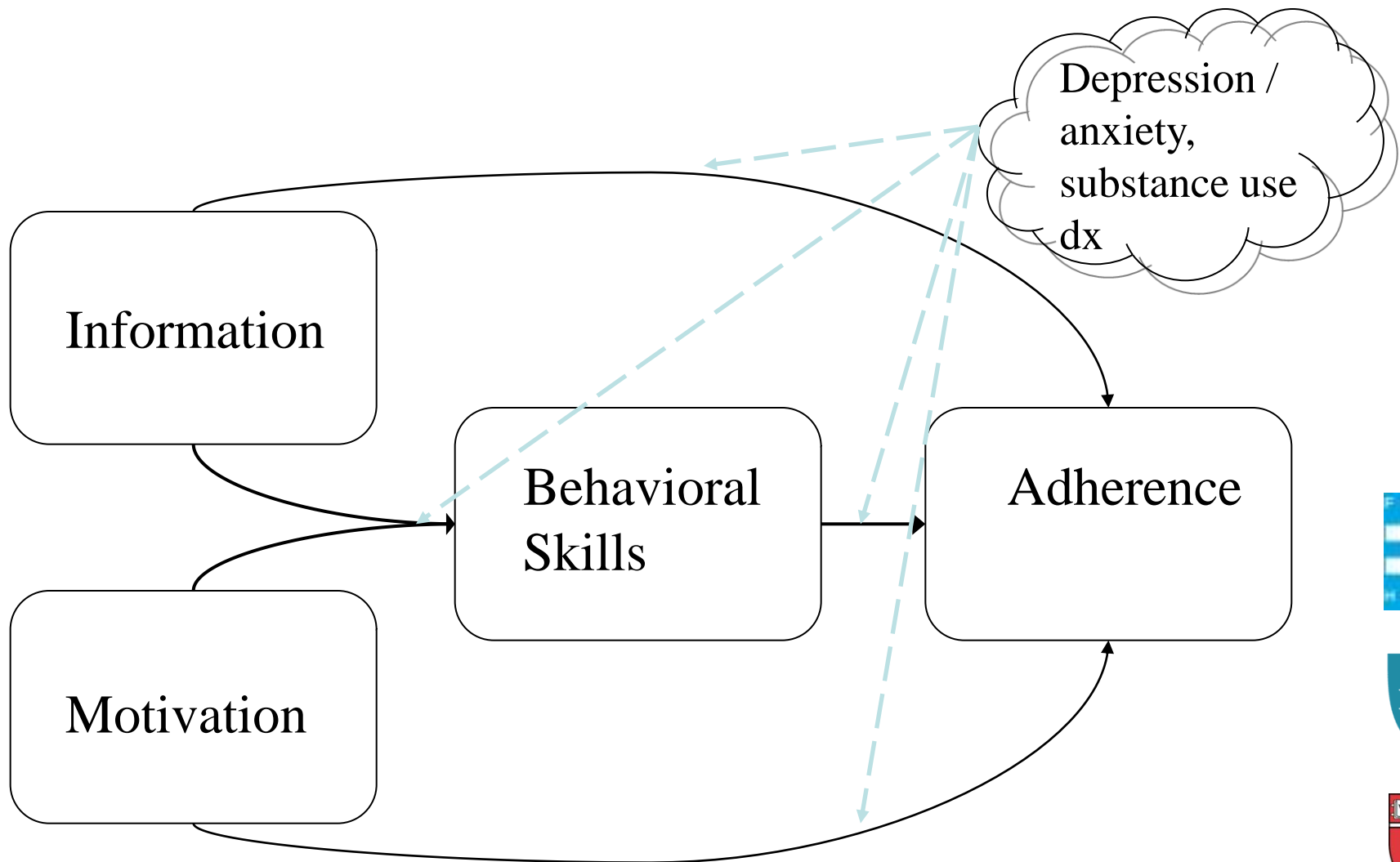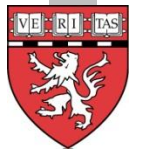
IMB model from Fisher et al, Health Psychology, 2006.

Mental Health / Substance Use Can Interfere with Adherence Intervention Models


IMB model from Fisher et al, Health Psychology, 2006.

Example Mental Health Disorder: Depression

- Sadness or depressed most of the time (most of the day, more days than not)
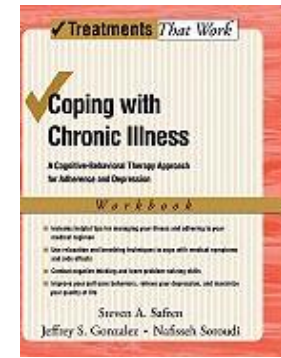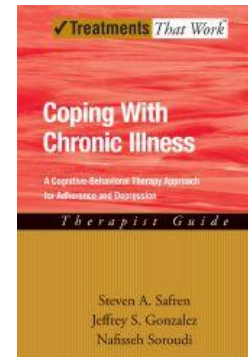
or

- Persistent loss of interest

With
- Sleep problems
- Guilt/worthlessness feeling
- Loss of energy
- Concentration problems
- Change of appetite (weight loss or gain)
- Psychomotor retardation or agitation
- Suicidality/hopelessness
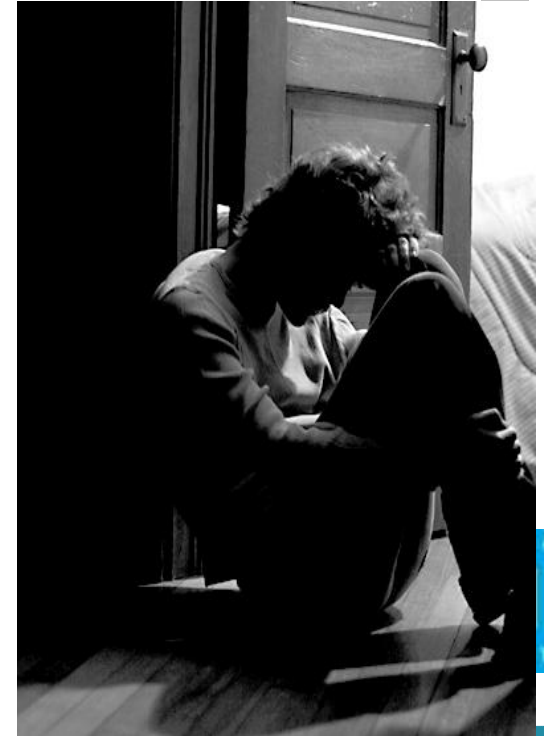
Need first two, and 5 total symptoms
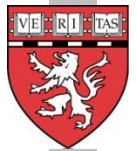
CBT-AD Overview

Modules: 12 sessions, each 50 minutes long

Each CBT module for depression integrates adherence counseling

1. Psychoeducation and Motivation………... 1 session

2. Adherence Training / Life-Steps…………. 1 session

3. Behavioral Activation …………………… 2 sessions

4. Adaptive thinking (cognitive restructuring).4 sessions

5. Problem Solving………………………… 2 sessions

6. Relaxation Training………………………. 1 session

7. Maintenance & Relapse Prevention…….. 1 session

Initial outcome study of CBT-AD

2 arm cross-over design – NIMH R21

Participants:

>300 phone screens, 118 baseline evaluations

45 patients randomized (3 dropped post-randomization)

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%)	ADHD 2 (5%)
Social Anxiety Disorder 9 (21%)	OCD 2 (5%)
Panic disorder 11 (26%)	GAD 2 (5%)

Safren et al., 2009 – Health Psychology

Initial Outcome of CBT-AD

MEMS outcomes, ITT

88%

62%

54%   54%

BASELINE   T2

CBT   ETAU
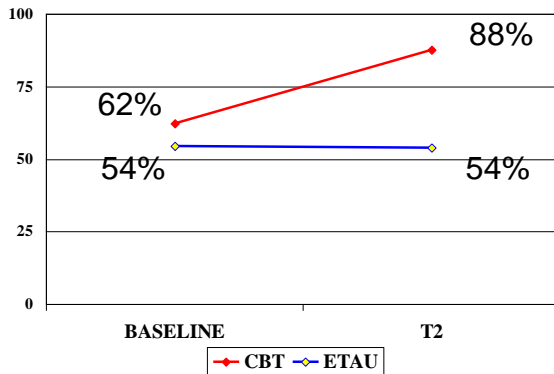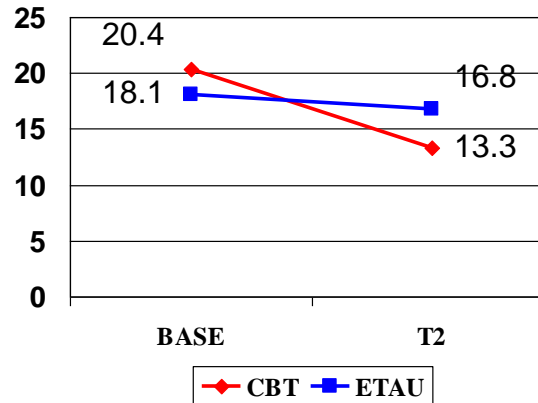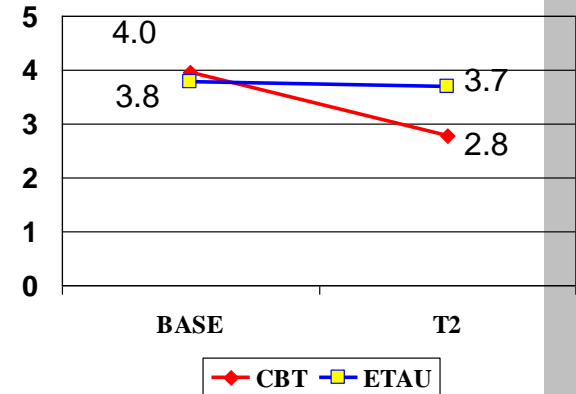
F(1,42) = 21.94, p< .0001, Cohen d = 1.0

HAM-D outcomes, ITT

20.4

18.1   16.8

                                         13.3

BASE   T2

CBT   ETAU

F(1,42) = 6.32, p < .02, Cohen d = .82

CGI outcomes, ITT

4.0

3.8   3.7

                                         2.8

BASE   T2

CBT   ETAU

F(1,42) = 9.68, p < .01, 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

*Note: effect size conventions .5 = medium, .8 = large, calculated with change scores*

Safren et al., 2009 – Health Psychology

Cultural Adaptation of CBT-AD to U.S. Mexico Border
Simoni, Weibe et al., NIMH R34)

- Goal to determine feasibility and effect size estimate adapting CBT-AD to HIV-infected Latinos at Mexico-U.S. border
- 2 Arm (N=40) RCT comparing intervention to TAU
- Longitudinal effects:
  - Adherence EDM and VAS
  - Depression (BDI), but not MADRS
  - Viral load not significant
  - Initial effect on CD4 but not at follow up
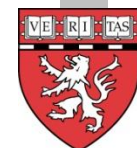
CBT for Medication Adherence and Depression in HIV+ IDU

o 2 arm study (ETAU or CBT-AD) NIDA R01
o Participants (N=89) recruited from methadone clinics and community in Massachusetts and Rhode Island
o History (or current) IDU but in SU treatment

- 62% at least one additional DSM-IV diagnosis
- 42% two or more additional DSM-IV diagnoses
  – Panic d/o 30%
  – GAD 18%
  – Social anxiety d/o 14%
  – PTSD 10%

Safren et al., 2012 – JCCP

CBT for adherence and depression in HIV-infected IDU (N=89): Acute outcomes
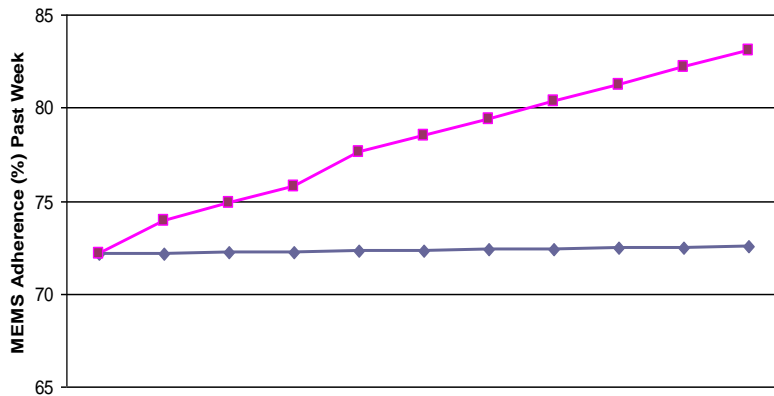


MEMs based adherence – above: HLM analysis of MEMs Weeks 0-10 = greater improvement in treatment versus control condition (slope = 0.887, t(86)= 2.38, p = .02)
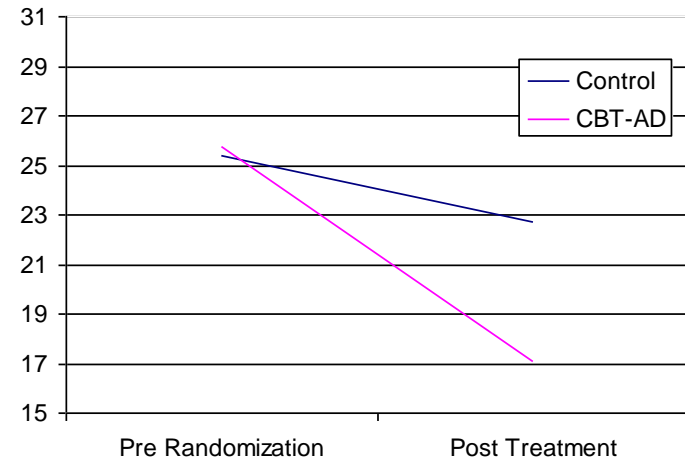
Depression: Pre-Post Treatment: Significantly greater improvements in depression in treatment versus control condition [MADRS (F(1,79)=6.52, p<.01)] (replicated with clinical global impression [(F(1,79)=14.77, p<.001)])

Safren et al., 2012– JCCP

Outcomes after intervention discontinuation (6 and 12 month)

- **Depression:** gains were maintained

- **MEMs based adherence**: gains not maintained
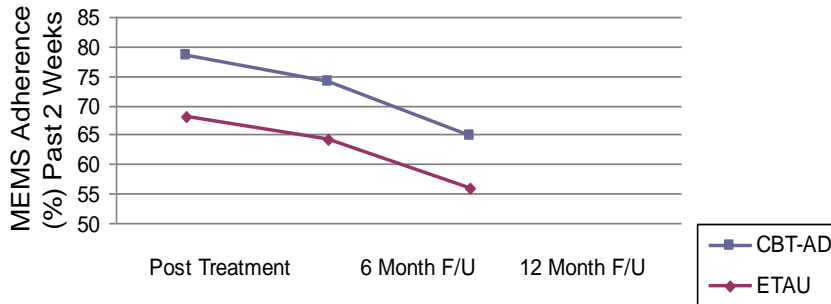
- **Viral load:** No differences across conditions
- **CD4:** the CBT-AD condition had significant improvements in CD4 cell counts over time compared to ETAU (γslope= 2.09, t (76) = 2.20, p = .03)
  - 61.2 CD4 cell increase intervention condition
  - 22.4 CD4 cell decrease control condition

Safren et al., 2012 – JCCP

Systematic Review of Adherence Interventions with Persons who Use Drugs

- **Short term gains plentiful**: Medication assisted, psychosocial/behavioral (including DAART and contingency management), integrated medication-assisted therapy and behavioral, integrated medication-assisted and HIV care) DAART, contingency management, Motivational Interviewing, CBT, nurse-delivered multi-component interventions, social support / peer interventions

- **Long term gains lacking:** Lack of interventions with post-treatment long-term maintenance of adherence gains (e.g. CM, DAART, CBT – etc taper off when intervention ends)

Camp, Kahana, and Altice, submitting
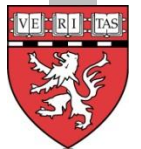
Project PLUS:
IMB/CBT for Heavy Alcohol Use and Adherence

- 143 HIV-positive individuals on ART and met criteria for hazardous drinking
- RCT of 8-session intervention that integrated alcohol use reduction with adherence improvement compared to time and content matched control
- Acute (3 month) effects for adherence, viral load, and Cd4
- Effects diminished when intervention ended (6 month follow up)
- Both groups showed reductions in alcohol use
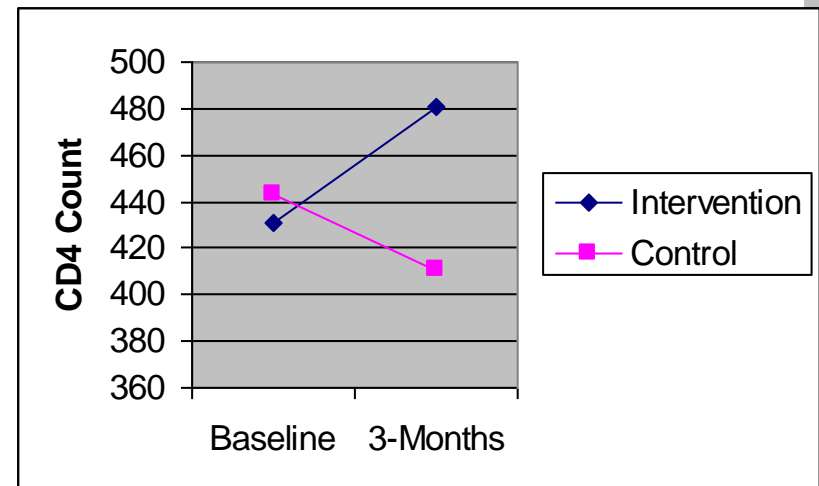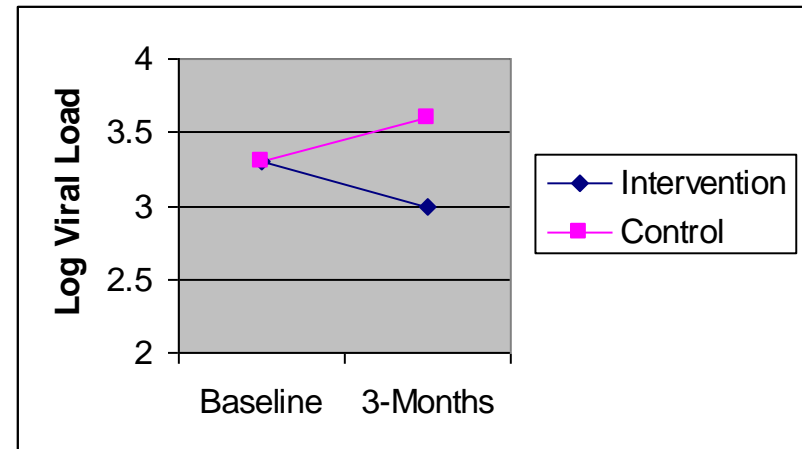

Parsons et al., 2009, JAIDS
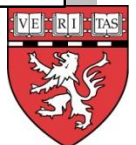
Evidence suggesting that antidepressant treatment can increase adherence

<u>Observational studies</u> (Horberg et al., 2008; Yun et al., 2005; Walkup et al. 2008)

- Medical record and refill claims
- Those with depression but treated with antidepressants generally have better HIV adherence

<u>Marginal structural modeling</u> (Tsai et al.)

- 158 homeless / marginally housed individuals with HIV and depression
- Those who started antidepressant more likely to attain viral suppression, start ART, and have better adherence
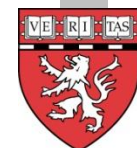
Implementation of collaborative care based treatment of depression in HIV clinic

- Retrospective chart review N=124
- Patients referred to in-HIV-clinic psychiatry consultation service based on BDI-II screen-in criteria
- BDI II reduced (23 to 15.7, p<.001)
- HIV RNA reduced (14.1K to 4K copies/ML p = .003)
- CD4 increases (518 to 592 cells /ul, p = .001)
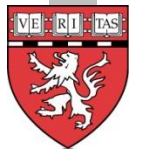
Coleman et al., 2012. Psychosomatics

Antidepressant RCT effects on depression but not ART adherence

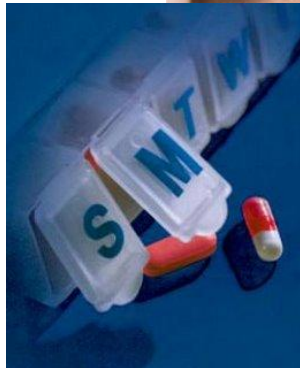**Bangsberg (2009, IAPAC presentation; Tsai et al., in press AJPH):**
DOT weekly fluoxetine in pts with HIV and depression

Results: treated depression but no increases in adherence

Author conclusion: need to address both depression and adherence in adherence interventions with pts with depression
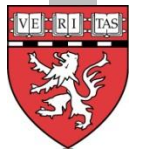
Ongoing work

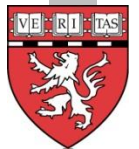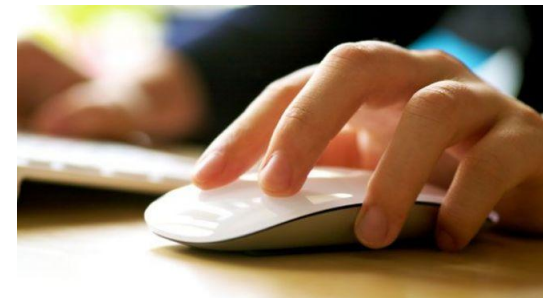The MEMS monitor is composed of a microswitch, a clock and a memory.

SLAM DUNC
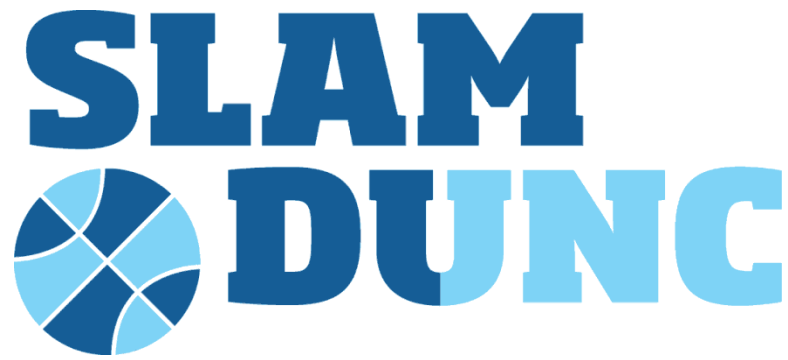
Strategies to **L**ink **A**ntidepressant and Antiretroviral **M**anagement at **D**uke, **U**AB, and U**NC**

- Randomized clinical effectiveness trial funded by NIMH (Brian Pence, Bradley Gaynes)
- Does Measurement Based Care (MBC) for depression affect ARV adherence
- PLWHA with depression (n=390) randomized to enhanced usual care or a depression treatment model called Measurement-Based Care (MBC).
- MBC = clinically supervised Depression Care Manager (DCM) to guide evidence-based antidepressant treatment recommendations to a non-psychiatric prescribing provider
- MBC includes adherence counseling

Pence et al., 2012. Contemporary Clinical Trials

Project "TRIAD"

- NIMH funded efficacy trial (PI: Safren)
- 3 arm study (2:2:1 randomization)
  - Life-Steps plus provider letter
  - CBT-AD
  - Information/supportive psychotherapy

- 3 site study (MGH, Brown, Fenway)
- Wide inclusion criteria
- Large N (80 randomized per site)

Pre-consent Screen → Screen out/ Drop out

Baseline Assessment → Screen out/ Drop out

Life-Steps (Weekly Visit One)

Treatment as Usual → 5 Non-Treatment Visits

CBT-AD → 11 Treatment Visits

ISP-AD → 11 Treatment Visits

4 month

8 month

12 month
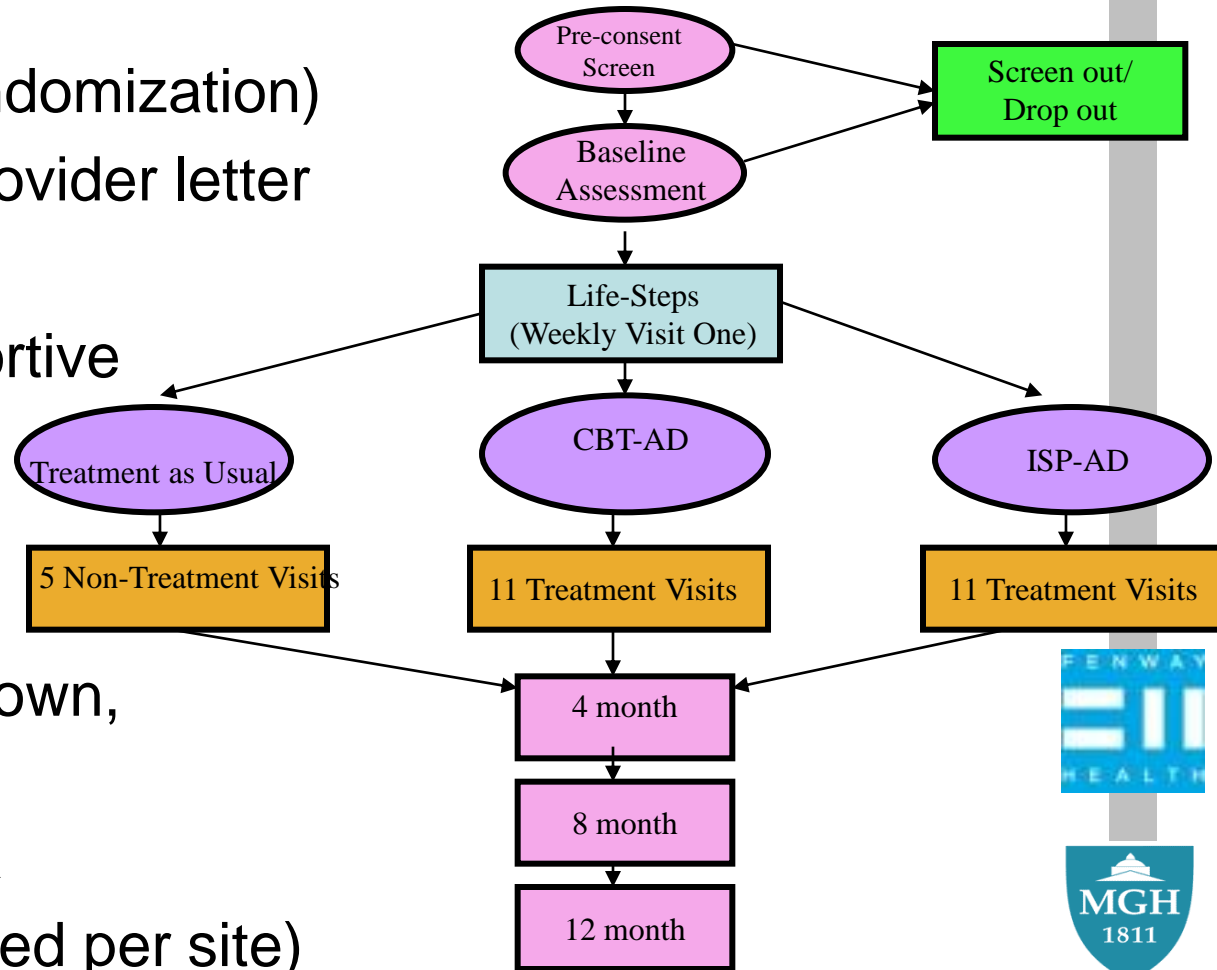
So, what should we do?

- **HIV treatment providers – proactively screen and triage for mental health and substance use; refer to evidenced based treatments**

- **Continue adherence counseling even after successful SU or mental health treatment**

- **For those patients with mental health or substance use comorbidity, do not expect big changes from brief interventions**
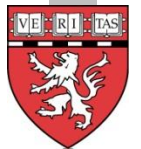
What next?

- **Syndemics / comorbidity (K24)**
- **Dissemination**
  - **Implementation and Adaptation** evidenced based interventions for available interventionists (Global and Domestic Settings).
    - Ziphamandla – Lena Andersen: who are best interventionists in resource poor settings
  - **Telemedicine** intervention (Mirjam Kempf, R34) for adherence and depression in Rural South (Timothy Heckman's)
  - **Web based** application: integration of mood and stress management with adherence [Life-Steps/CBT-AD] (Royer Cook SBIR)
- **PrEP**

Thank you

Major collaborators/contributors

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