Addressing Mental Health, Substance Abuse, and HIV Treatment Adherence

Steven A. Safren, Ph.D.
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

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

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

MMWR (60), 2011
• 95 independent samples
• Depression significantly associated with non-adherence ($p < .00001$; $r = 0.19$: 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

<table>
<thead>
<tr>
<th></th>
<th>1 problem</th>
<th>2 problems</th>
<th>3 and 4 problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk sex</td>
<td>1.6</td>
<td>2.4</td>
<td>3.5</td>
</tr>
<tr>
<td>(P &lt; .01)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV prevalence</td>
<td>1.8</td>
<td>2.7</td>
<td>3.6</td>
</tr>
<tr>
<td>(P &lt; .001)</td>
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</table>

Example frequent Synderm:

Mental ill-health
Instability → Homelessness
Substance Use
Mental Health / Substance Use Can Interfere with Adherence Intervention Models

Information → Behavioral Skills → Adherence

Motivation → Behavioral Skills

Depression / Anxiety, substance use dx

Mental Health / Substance Use Can Interfere with Adherence Intervention Models

Example Mental Health Disorder: Depression

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

- 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

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

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

F(1,42) = 9.68, p < .01, Cohen d = .91
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

- 2 arm study (ETAU or CBT-AD) NIDA R01
- Participants (N=89) recruited from methadone clinics and community in Massachusetts and Rhode Island
- 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 ($\gamma$slope= 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
Evidence suggesting that antidepressant treatment can increase adherence

Observational studies (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

Marginal structural modeling (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.
Strategies to Link Antidepressant and Antiretroviral Management at Duke, UAB, and UNC

- 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)
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

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