Alcohol and Substance Abuse and Their Comorbidity with Mood Disorders

Ihsan M. Salloum, MD, MPH, DFAPA
Professor of Psychiatry
Chief, Division of Alcohol and Drug Abuse: Treatment and Research
Director, Addiction Psychiatry Fellowship Program
Department of Psychiatry
University of Miami Miller School of Medicine
Miami, FL
Ihsan M. Salloum, MD, MPH, DFAPA

Disclosures

- **Research Support:** The National Institute on Alcohol Abuse and Alcoholism (NIAAA); National Institute of Drug Abuse (NIDA)
- **Consultant:** Orexigen Therapeutics Inc.; Takeda Pharmaceuticals U.S.A., Inc.
Acknowledgment

Research Supported by
- The National Institute on Alcohol Abuse and Alcoholism (NIAAA)
- The National Institute of Drug Abuse (NIDA)
- The National Institute of Mental Health (NIMH)
- The Department of Veterans Administration
Learning Objectives

- Describe the relationship between mood disorders and substance use disorders.
- Implement evidence-based, best-practice options for treatment of mood disorders and comorbid alcohol and substance use disorders.
Audience Response

How confident are you in identifying clinical signs and symptoms of common mood disorders when treating alcohol and substance use disorder patients?

A. Extremely confident
B. Confident
C. Somewhat confident
D. Not at all confident
What percentage of people with alcohol dependence report having depressive symptoms?

A. 40%
B. 50%
C. 70%
D. 80%
Audience Response

Which of the following are common measures used in addiction for withdrawal symptoms?

A. CIWA, COWS
B. CIWA, OCDS
C. COWS, CAGE
D. OCDS, CAGE
Agenda

1. Significance of the problem
   - Prevalence & Consequences
2. Challenges
   - Diagnostic & Treatment Issues
3. Pharmacotherapy Trials
4. Summary
Mood disorders and substance use disorders are among the most frequent causes of disability worldwide.

Disease Burden DALY
USA, Canada, and West Europe, 2000

Disability Adjusted Life Year (DALY), 15 – 44 yr olds

Unipolar Depressive Disorders
Alcohol Use Disorders
Road Traffic Accidents
Drug Use Disorders
Self Inflicted Injuries
Bipolar Disorder
Migraine
Schizophrenia
Hearing Loss, adult onset
HIV/AIDS

Lifetime Rates of Alcoholism in Major Psychiatric Disorders

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Proportion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP I</td>
<td>46.2</td>
</tr>
<tr>
<td>BP II</td>
<td>39.2</td>
</tr>
<tr>
<td>Schiz</td>
<td>33.7</td>
</tr>
<tr>
<td>PD</td>
<td>28.7</td>
</tr>
<tr>
<td>OCD</td>
<td>24</td>
</tr>
<tr>
<td>Dysthymia</td>
<td>21</td>
</tr>
<tr>
<td>MDD</td>
<td>16.5</td>
</tr>
<tr>
<td>Gen Pop</td>
<td>13.5</td>
</tr>
</tbody>
</table>

BP = bipolar disorder; Schiz = schizophrenia; PD = Panic disorder, OCD = obsessive compulsive disorder; MDD = major depression
Mood Disorders and Substance Abuse

20 Yrs Follow-Up: The Zurich Cohort Study

Substance Use and Mood Disorders

12 Months Likelihood (ORs) of an Additional SUD in Mania and Hypomania

AL = Alcohol; Dr = Drugs; DP = Dependence, AB = Abuse; GP = General Population
N = 42,000 (NESARC) Odds Ratio

Depression is Very Common in Alcohol Dependence

Those with alcohol dependence:
● 80% report depressive symptoms
● 33% have MDD diagnosis
● Women > men

Alcohol Dependence with Comorbid Major Depression or Dysthymia

OR MDD = Men: 2.95; Women: 4 – OR DYS = Men: 3.8; Women: 8

Alcoholism in Bipolar Men and Women

- N = 267
  - 116 men, 151 women
- Rates of alcoholism:
  - BP men = 49%
  - BP women = 29%

*Odds ratio compared to ECA sample weighted by age, race, gender; BP men OR=2.8 (95% CI: 1.59-4.81); BP women OR= 7.35 (95% CI: 3.32-16.26)
† P < .0001
The Challenge of Mood Disorders–SUD comorbidity

- Complicated course (Rec/Relap/polysympt.)
- Suicidality and increased mortality
- Dysfunctions (family, social, emp/edu)
- Multiple morbidities (Medical & psychiatric)
- Unstable housing and homelessness
- Violence, legal problems, incarceration
- More service use (days in hospital, ER visits, use of SUD and MH services)

SUD = substance use disorder, MH = mental health
Reciprocal Negative Impact

MD ↔ SUD

- Diagnostic confusion
- Treatment compliance
- Treatment response
- Course and outcome of illness
Diagnostic Issues

- Drinking vs. alcoholism; sadness vs. depression; alcohol induced vs. primary
- Rating scales & structured interviews
- *DSM-5* guidelines
  - Prior or during abstinence from alcohol
  - Better accounted for by depression
  - Does not occur only during intoxication/withdrawal
- Prior episodes & family history
Diagnostic Accuracy & Medications in the Context of Alcoholism & SUD

- Diagnostic Accuracy
  - Duration of drug free observational period: 4 vs....... 1 week?
  - Advantage & disadvantage of initiating medication
  - Studies of depressed alcoholics
Limited Change in Depressive Symptoms on Placebo (HAMD-24)

# Alcohol & SUDs Impact on the Course of Mood Disorders

<table>
<thead>
<tr>
<th>Mood Disorders Course</th>
<th>Alcohol &amp; SUD Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response</td>
<td>Worsens respond to medication</td>
</tr>
<tr>
<td>Remission</td>
<td>Prolong sick state</td>
</tr>
<tr>
<td>Recovery</td>
<td>Maintain persistent symptom &amp; impair coping skills</td>
</tr>
<tr>
<td>Relapse</td>
<td>Increase risk for depression relapse</td>
</tr>
<tr>
<td>Recurrence</td>
<td>Maintain sub-syndromal state; Psychosocial stress</td>
</tr>
</tbody>
</table>

Mood Disorders as a Risk for Alcohol & SUDs Relapse

- Alcohol & substance use as “self-medicating” the symptoms of mood disorders?
- Mood disorders increases vulnerability to alcohol relapse by decreasing stress coping abilities
Depression as a Risk for Alcohol & SUDs Relapse

- Stressors that exceed the adaptation capacity of the individual lead to relapse
- Depression impacts multiple areas of adaptation abilities predictive of relapse
- Effect of stress on alcohol problem was found to be mediated by depression

Depression Impacts on Adaptation Capacity Which Predicts Relapse

● Impairment in coping skills
● Impairment in self-efficacy
● Influence availability of social support
● Cognitive distortion
● Irrational beliefs
Major Depression & Gender Predict Relapse

Untreated Depression Leads to Early Relapse

Untreated Depression Leads To Early Relapse

Fluoxetine in Depressed Alcoholics
One Year Follow-up

Bipolar SUDs Relationship

**SUD on Bipolar**
- **Course Modifier**
  - Earlier onset
  - Shorter cycle length
  - Persistent symptom
  - Delayed recovery
  - Rapid cycling?
- **Episode Modifier**
  - More symptoms
  - Worsens depression
  - Mixed episodes
  - Episode switch?

**Bipolar on SUD**
- **Bipolar as risk factor**
  - Bipolar predate SUD
  - Mood states (mania)
  - Impulsivity
  - Self-medication
  - Impaired coping skills
  - Neurobiological factors
- **Adolescent onset BPD**

Bipolar Multi-Symptoms Disorder

**MANIA**
- Euphoria/ Grandiosity
- Pressured speech
- Impulsivity
- Excessive libido
- Recklessness
- Social intrusiveness
- Decrease need for sleep
- Hyperactivity

**DEPRESSION**
- Depression
- Anxiety
- Irritability
- Hostility
- Violence or suicide

**PSYCHOSIS**
- Delusions
- Hallucinations

**COGNITION**
- Racing thoughts
- Distractibility
- Disorganization
- Inattentiveness

Long-term Natural History of the Weekly Symptomatic Status of Bipolar I Disorder

Percentage of Follow-up Weeks Spent at Specific Affective Symptom During Long-term Follow-up of 146 Patients With Bipolar I Disorder

- Asymptomatic: 52.7%
- Depression: 31.9%
- Mania: 9.3%
- Cycling/Mixed: 5.9%

Residual Symptoms Increase Future Episode Relapse Risk

Etiology: Pathophysiology

+Risk Factors: Genetic, Environmental, Stress

Reward Transmitters Implicated in the Motivational Effects of Drugs of Abuse

Positive Hedonic Effects
- ↑ Dopamine
- ↑ Opioid peptides
- ↑ Serotonin
- ↑ GABA

Negative Hedonic Effects of Withdrawal
- ↓ Dopamine ... “dysphoria”
- ↓ Opioid peptides ... pain
- ↓ Serotonin ... “dysphoria”
- ↓ GABA ... anxiety, panic attacks

Mania: Positive hedonic state
Depression: Negative hedonic state

Medical Burden in Patients with Severe Psychopathology

Chronic mental disorders are associated with physical disorders and excess mortality

- Major depression
- Bipolar disorder
- Schizophrenia
- Alcoholism and other substance use disorders
- Obesity
- Diabetes
- Cardiovascular
- Chronic resp.
- HIV / V.Hep /
- STD/ TB
- Trauma, Suicide

Mortality in Unipolar, Bipolar, and Schizophrenia for Females (SMR)

SMR = standardized mortality ratio (# of observed cases / # of expected)

Death by Injury

Adjusted Odds of Death by Injury in Medicaid Beneficiaries

Odds Ratio

- Psychosis: 3.55
- Psychosis + SUD: 8.11
- OMI: 2.84
- OMI + SUD: 6.09
- SUD only: 3.57

OMI = other mental illness; SUD = substance use disorders

Management of Mood Disorders with Comorbid SUD
Treatment Integration for Comorbid Bipolar & Addictive Disorders

- System Integration
  - From financing to access

- Provider Factors
  - Training and commitment

- Interventions
  - Medications and psychosocial interventions

- Consumer Factors
  - Recognition of interrelationship of the two diseases
Integrated RX at the Programmatic Level

Outcome of “FIRESIDE” program, Alcoholism + Mood (N = 228 adults) Abstinence rates: 60% @ 3m; 50% @ 6m

Slide Courtesy of Dr. Conor Farren
Common Measures Used in Addiction

- **Short screening & syndrome measures:**
  - CAGE, AUDIT, AUDIT-C, DUDIT, TLFB, DSM-5 checklist
- **Measures of craving:**
  - Penn Alcohol Craving Scale, OCDS
- **Measures of consequences/severity:**
  - SIP, ASI (alcohol, drug, social, family, medical, employment and legal)
- **Measures of withdrawal syndromes:**
  - CIWA, COWS

SAMHSA-HRSA. Clinical Practice Screening Tools. SAMHSA Website: http://www.integration.samhsa.gov/clinical-practice/screening-tools
Alcohol Use Disorder Identification Test-C (Score 0-12)

- How often did you have a drink containing alcohol in the past year?
  - 0: never, 1: 1 or less month, 2: 2-4 month, 3: 3x week, 4: 4-5/week, 4: 6 x week

- How many drinks did you have on typical day when you were drinking in the past year?
  - 0: 0 or 1-2 drinks, 1: 3-4, 2: 5-6, 3: 7-9, 4: 10 or more

- How often did you have 6 or more drinks on one occasion in the past year?
  - 0: never, 1: <1/month, 2: monthly, 3: weekly, 4: daily

Score of 3: Sensitivity: 90% active abuse/dep; 98% heavy drinkers; Specificity 60%;
Score of 4: 86% specificity heavy drinking; 72% for abuse/dependene

Stabilization of Bipolar Disorder and Substance Abuse

- Aggressive acute stabilization
  - Mania
  - Depression
  - Rapid cycling
  - Alcohol/SUD withdrawal

- Relapse Prevention
  - Maintenance mood stabilization
  - DBSupportAlliance
  - Alcohol relapse prevention
  - AA/DD support
Treatment of Alcohol Withdrawal in Psychiatric Patients

- **Goals**
  - Prevent complications
  - Alleviate withdrawal symptoms
  - Initiate process of recovery “window of opportunity”

- **Principles**
  - Medication half-life
  - Symptom-triggered therapy
  - Effective in preventing complications

WAS Symptom Triggered Diazepam Loading Dose

Diazepam loading dose/ CIWA-Ar (Seller, et al. 1983)
Paradigms of Medications Trials for Mood Disorders & SUD

Monotherapy Trials: 1 med. – 2 outcomes
● Medications Bipolar Dis.
  ● Mood Stabilizers (Lithium, Anticonvulsants)
  ● Valproic acid, carbamazepine (ER), lamotrigine
  ● Antipsychotics (Atypical)
    ● Quetiapine, aripiprazole risperidone, olanzapine, ziprasidone, clozapine
  ● Antidepressants SSRI, SNRIs, TCAs,

Combined meds: 2 meds. – 2 outcomes
● Medications for SUD
  ● Alcoholism
    ● Disulfiram*, Naltrexone* (PO, IM), Acamprosate*, Topiramate, Gabapentin
  ● Tobacco
    ● Varenicline, bupropion, NPT
  ● Cocaine
  ● Cannabis
  ● Opioid
    ● Methadone, suboxone, naltrexone

* FDA approved for SUD
## Placebo-Controlled Trials in Bipolar Disorder and Cocaine Use Disorder

<table>
<thead>
<tr>
<th>Study</th>
<th>Medication</th>
<th>N</th>
<th>Wks</th>
<th>Design</th>
<th>Cocaine outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brown et al, 2007</td>
<td>Citicoline</td>
<td>44</td>
<td>12</td>
<td>D-blind</td>
<td>Advantage over PBO</td>
</tr>
<tr>
<td>Brown et al., 2012</td>
<td>Citicoline</td>
<td>60</td>
<td>12</td>
<td>D-blind</td>
<td>Advantage* Methamphetamine Depression(BP&amp;MDD)</td>
</tr>
<tr>
<td>Brown et al., 2012</td>
<td>Lamotrigine</td>
<td>112</td>
<td>110</td>
<td>D-blind</td>
<td>Advantage on money spent on cocaine</td>
</tr>
<tr>
<td>Brown et al., 2015</td>
<td>Citicoline</td>
<td>130</td>
<td>12</td>
<td>D-blind</td>
<td>Advantage on + urine early in trial</td>
</tr>
</tbody>
</table>

### Placebo-Controlled Trials in Bipolar (I-II) Disorders and Alcoholism

<table>
<thead>
<tr>
<th>Study</th>
<th>Medication</th>
<th>N</th>
<th>Wks</th>
<th>Design</th>
<th>Alcohol outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salloum et al., 2005</td>
<td>Valproic acid</td>
<td>59</td>
<td>24</td>
<td>D-blind</td>
<td>Advantage over PBO</td>
</tr>
<tr>
<td>Brown et al., 2008</td>
<td>Quetiapine</td>
<td>115</td>
<td>12</td>
<td>D-blind</td>
<td>No advantage</td>
</tr>
<tr>
<td>Brown et al., 2009</td>
<td>Naltrexone</td>
<td>50</td>
<td>12</td>
<td>D-blind</td>
<td>Trend toward advantage</td>
</tr>
<tr>
<td>Stedman et al., 2010</td>
<td>Quetiapine</td>
<td>362</td>
<td>12</td>
<td>D-blind</td>
<td>No advantage</td>
</tr>
<tr>
<td>Tolliver et al., 2012</td>
<td>Acamprosate</td>
<td>33</td>
<td>12</td>
<td>D-blind</td>
<td>No advantage</td>
</tr>
<tr>
<td>Brown et al., 2014</td>
<td>Quetiapine*</td>
<td>90</td>
<td>12</td>
<td>D-blind</td>
<td>No Advantage</td>
</tr>
</tbody>
</table>


Divalproex Impact on Heavy Drinking Days

Divalproex Significantly Decreases % of Heavy Drinking Days

\[ p = .02 \]

Divalproex Efficacy in Alcohol Use Disorder

P = .02*; *Medication adherence as covariate in the Mixed Model

Divalproex Significantly Decreases # of Drinks per Heavy Drinking Days

- **PBO (n = 25)**
  - Number of Drinks per Heavy Drinking Days: 10.2

- **Valproate (n = 27)**
  - Number of Drinks per Heavy Drinking Days: 5.59
Relapse to Sustained Heavy Drinking

Figure 1

Kaplan-Meier log rank 3.90, \( p < .05 \)

Valproate: mean 93 days to relapse

Placebo: mean 62 days to relapse

Valproate vs. Placebo Effect on Glutamyl Transpeptidase (GTP)

\[ p = 0.045 \]

### SSRIs Studies in Comorbid MDD & Alcoholism

<table>
<thead>
<tr>
<th>Study</th>
<th>Medication</th>
<th>N</th>
<th>Wks</th>
<th>Design</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kranzler, 2006</td>
<td>Sertraline</td>
<td>328</td>
<td>12</td>
<td>D-blind</td>
<td>No advantage</td>
</tr>
<tr>
<td>Gual, 2003</td>
<td>Sertraline</td>
<td>83</td>
<td>24</td>
<td>D-blind</td>
<td>No advantage*</td>
</tr>
<tr>
<td>Moak, 2003</td>
<td>Sertraline</td>
<td>82</td>
<td>12</td>
<td>D-blind</td>
<td>No advantage**</td>
</tr>
<tr>
<td>Pettinati, 2001</td>
<td>Sertraline</td>
<td>100</td>
<td>14</td>
<td>D-blind</td>
<td>- if MDD hx ***</td>
</tr>
<tr>
<td>Roy, 1998</td>
<td>Sertraline</td>
<td>36</td>
<td>6</td>
<td>D-blind</td>
<td>↓ MDD</td>
</tr>
<tr>
<td>Cornelius, 1997</td>
<td>Fluoxetine</td>
<td>51</td>
<td>12</td>
<td>D-blind</td>
<td>↓ MDD, ↓ AL</td>
</tr>
<tr>
<td>Kranzler, 1995</td>
<td>Fluoxetine</td>
<td>101</td>
<td>12</td>
<td>D-blind</td>
<td>↓ MDD, ↓ AL***</td>
</tr>
<tr>
<td>Adamson, 2015</td>
<td>Nalt ± Citalopram</td>
<td>130</td>
<td>12</td>
<td>D-blind</td>
<td>No advantage</td>
</tr>
</tbody>
</table>

*+ on MDD for severe sub.; ** ↓ MDD in females, ↓ # D/DD ; *** Alcohol dep. sample
## Non-SSRI Studies in Comorbid MDD and Alcoholism

<table>
<thead>
<tr>
<th>Study</th>
<th>Medication</th>
<th>N</th>
<th>Wks</th>
<th>Design</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garcia-Portilla, 2005</td>
<td>Venlafaxine</td>
<td>90</td>
<td>24</td>
<td>Open Label</td>
<td>Improved MDD/AL</td>
</tr>
<tr>
<td>Hernandex-Avila, 2005</td>
<td>Nefazadone</td>
<td>40</td>
<td>10</td>
<td>D-blind</td>
<td>Improved AL</td>
</tr>
<tr>
<td>Roy-Byrne, 2000</td>
<td>Nefazadone</td>
<td>64</td>
<td>12</td>
<td>D-blind</td>
<td>Improved MD</td>
</tr>
<tr>
<td>McGrath, 1996</td>
<td>Imipramine</td>
<td>69</td>
<td>12</td>
<td>D-blind</td>
<td>Improved MD</td>
</tr>
<tr>
<td>Mason, 1996</td>
<td>Desipramine</td>
<td>71 (28)</td>
<td>24</td>
<td>D-blind</td>
<td>Improved MDD/AL</td>
</tr>
<tr>
<td>Nunes, 1993</td>
<td>Imipramine</td>
<td>60</td>
<td>12</td>
<td>D-blind</td>
<td>Improved MDD/AL</td>
</tr>
<tr>
<td>Altamura, 1990</td>
<td>Viloxazine</td>
<td>31</td>
<td>12</td>
<td>D-blind</td>
<td>Improved MDD/AL</td>
</tr>
</tbody>
</table>

## Comorbid MDD and Opioid

<table>
<thead>
<tr>
<th>Study</th>
<th>Medication</th>
<th>N</th>
<th>Wks</th>
<th>Design</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carpenter, Brooks, et al., 2004</td>
<td>Sertraline</td>
<td>95</td>
<td>12</td>
<td>D-blind</td>
<td>No advantage&lt;br&gt;Role of environment</td>
</tr>
<tr>
<td>Dean et al. 2002</td>
<td>Fluoxetine</td>
<td>49</td>
<td>12</td>
<td>D-blind</td>
<td>No advantage</td>
</tr>
<tr>
<td>Petrakis et al, 1998</td>
<td>Fluoxetine</td>
<td>44</td>
<td>12</td>
<td>D-blind</td>
<td>No advantage</td>
</tr>
<tr>
<td>Nunes, 1998</td>
<td>Imipramine</td>
<td>84</td>
<td>12</td>
<td>D-blind</td>
<td>Decreased depression&lt;br&gt;less so drug</td>
</tr>
<tr>
<td>Kleber et al, 1998</td>
<td>Imipramine</td>
<td>48</td>
<td>8</td>
<td>D-blind</td>
<td>No advantage</td>
</tr>
</tbody>
</table>

All in methadone maintenance population

## Comorbid MDD and Cocaine

<table>
<thead>
<tr>
<th>Study</th>
<th>Medication</th>
<th>N</th>
<th>Wks</th>
<th>Design</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schmitz et al., 2001</td>
<td>Fluoxetine</td>
<td>68</td>
<td>12</td>
<td>D-blind</td>
<td>No advantage</td>
</tr>
<tr>
<td>Ciraulo et al. 2005</td>
<td>Nefazadone</td>
<td>69</td>
<td>8</td>
<td>D-blind</td>
<td>Dec cocaine*</td>
</tr>
<tr>
<td>McDowell et al, 2005</td>
<td>Desipramine</td>
<td>111</td>
<td>12</td>
<td>D-blind</td>
<td>Dec depression but not cocaine</td>
</tr>
<tr>
<td>Nunes, 1995</td>
<td>Imipramine</td>
<td>113</td>
<td>12</td>
<td>D-blind</td>
<td>Dec depression but not cocaine</td>
</tr>
</tbody>
</table>

*Groups not balanced at baseline

Effect of Antidepressant Medication on Outcome of Depression (Hamilton Depression Scale)

<table>
<thead>
<tr>
<th>Source</th>
<th>Sample Size, No.</th>
<th>Effect Size (95% CI)</th>
<th>Favors Placebo</th>
<th>Favors Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo Response &lt;25%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Altamura et al.,17 1990</td>
<td>27</td>
<td>1.07 (0.23 to 1.92)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Roy,18 1998</td>
<td>36</td>
<td>1.08 (0.34 to 1.79)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mason et al.,19 1996</td>
<td>24</td>
<td>0.93 (0.04 to 1.82)</td>
<td></td>
<td></td>
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<tr>
<td>Nunes et al.,20 1998</td>
<td>137</td>
<td>0.68 (0.33 to 1.03)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nunes et al.,21 1995</td>
<td>63</td>
<td>0.62 (0.09 to 1.14)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cornelius et al.,22 1997</td>
<td>51</td>
<td>0.57 (−0.00 to 1.15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>McGrath et al.,24 1996</td>
<td>69</td>
<td>0.40 (−0.09 to 0.83)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pooled</td>
<td>407</td>
<td>0.68 (0.49 to 0.88)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo Response &gt;25%</td>
<td></td>
<td></td>
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<tr>
<td>Roy-Byrne et al.,23 2000</td>
<td>56</td>
<td>0.47 (−0.08 to 1.02)</td>
<td></td>
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</tr>
<tr>
<td>Moak et al.,25 2003</td>
<td>82</td>
<td>0.15 (−0.29 to 0.59)</td>
<td></td>
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<tr>
<td>Carpenter et al.,26 in press</td>
<td>95</td>
<td>0.07 (−0.34 to 0.48)</td>
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<tr>
<td>Schmitz et al.,28 2001</td>
<td>68</td>
<td>0.00 (−0.48 to 0.48)</td>
<td></td>
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<tr>
<td>Kleber et al.,27 1983</td>
<td>46</td>
<td>0.00 (−0.59 to 0.59)</td>
<td></td>
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<tr>
<td>Petrakis et al.,29 1998</td>
<td>44</td>
<td>−0.13 (−0.74 to 0.43)</td>
<td></td>
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<tr>
<td>Pettinati et al.,30 2001</td>
<td>29</td>
<td>−0.21 (−0.99 to 0.55)</td>
<td></td>
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<tr>
<td>Pooled</td>
<td>420</td>
<td>0.08 (−0.11 to 0.27)</td>
<td></td>
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<tr>
<td>Overall</td>
<td>827</td>
<td>0.38 (0.18 to 0.58)</td>
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</table>
Effect of Antidepressant Medication on Outcome of Substance Use

Combined Sertraline and Naltrexone in MDD + Alcoholism

Time to Relapse to Heavy Drinking (days)

Abstinence Rate  Not Depressed

N = 170, 14 wks, 4 grps (Sertraline (SER) 200 mg, Naltrexone (NTX) 100 mg, Placebo (PBO), SER + NTX)
Summary

- Bipolar disorder with comorbid alcoholism is still an area of treatment needs
- No clear medication of choice although published data so far favors anticonvulsants use
- Naltrexone may be a promising adjunctive medication
- Multisite trials are needed for this population
- Innovative technologies and methods may enhance identification of markers of treatment response
Summary

- Antidepressants in general decrease depression but are less effective for SUD in comorbid MDD+SUDs pts
- There are no clear antidepressants of choice for DD
- Lack of response is likely due to SUD-related behavior vs. true treatment resistance
- Maximizing MDD treatment helps prevent SUD relapse
- Clarifying the nature of depression still relies on historical information
  - structured clinical assessment is more helpful than self-report
- Psychotherapy for DD is important ingredient of clinical care

DD=Dual diagnosis
What percentage of people with alcohol dependence report having depressive symptoms?

A. 40%
B. 50%
C. 70%
D. 80%
Which of the following are common measures used in addiction for withdrawal symptoms?

A. CIWA, COWS
B. CIWA, OCDS
C. COWS, CAGE
D. OCDS, CAGE
Thank You