

Medication Treatment Approaches for Co- Occurring Disorders

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National Comorbidity Survey (1990-1992)

- 48% of people 15-54 have a lifetime psychiatric illness or SUD
- 27% had a lifetime SUD
 - 14% with lifetime Alcohol Dependence
 - 8% with lifetime Drug Dependence
- Co-occurring disorders: Of those with a lifetime history of a mental disorder, 51% with a history of a SUD (OR 2.4) and conversely those with a lifetime SUD, 51% meet criteria for a lifetime mental disorder

NESCARC 2001-2002

- Individuals with lifetime mood or anxiety disorder
 - Approximately 20% with SUD
- Individuals with lifetime SUD
 - 41% with mood disorder
 - 30% with anxiety disorder
- Comorbidity stronger in women with SUDs despite lower rates of SUDs than men

Prevalence of Co-occurring Disorders

Study Populations	Findings
General Population	3-4% in the community
Mental Health Treatment Programs	40-60%
Substance Abuse Treatment Programs	50-60%

Hendrickson EL: Designing, Implementing, and Managing Treatment Services for Individuals with Co-Occurring Mental Health and Substance Use Disorders: Blueprints for Action. Binghamton, New York, The Haworth Press Inc., 2006, pp 5-40

Comorbidity Prevalence

- 56% of Bipolar patients, and 46% of Schizophrenia patients have SUD- compared to 15% of the general population
- 60+% of psychiatric inpatients have a current or previous substance use problem.
- Estimated that up to 50% of patients with substance use disorder may have a treatable psychiatric illness.

-SAMHSA, 2007

Challenges for Dually Diagnosed

- Patients with CODs are more likely to have:
 - Increased severity of mental illness
 - Medication noncompliance
 - Worse treatment prognosis (more severe course, etc.)
 - Lower income and resources.
 - Worse physical health
 - Increased risk of incarceration.

Buckley 2006, J Clin Psychiatry; SAMHSA 2007

Treatment Challenges w/ COD

- Due to complexities in the patient populations, there is little consensus for the best type of treatment
- Ex.: antidepressants have had mixed results on substance use in users with depression in clinical trials.

-Torrens et al 2005, Drug Alcohol Depen

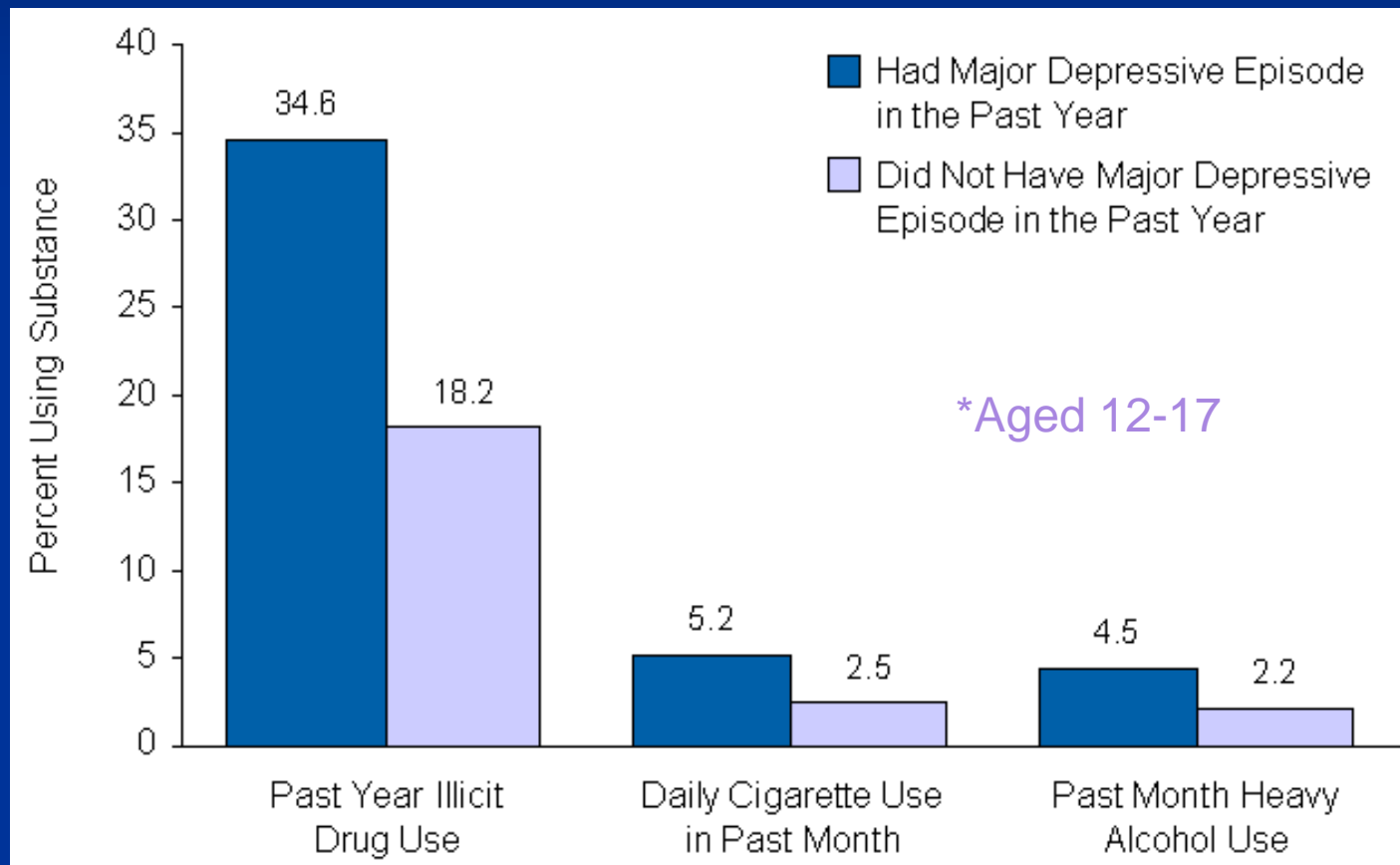
Comorbidity in Youth

- Epidemiological studies consistently report high rates of mental health comorbidity among adolescents with SUD (e.g., Kandel et al., 1999)
 - (MECA): 32% of adolescents with a current SUD had a co-occurring mood disorder (Kandel et al., 1999).
 - NCS: co-occurrence of SUD with mental health disorders was highest among those aged 15–24 years. (Kessler et al., 1996).
- Association between frequency of alcohol, tobacco, and drug use and likelihood of psychiatric d/o, especially conduct d/o
- Onset of psychiatric d/o more often precedes SUD, especially conduct and anxiety d/o (Burke et al., 1994; Kessler et al., 1996).

Adolescents with Substance Use Disorders...

- Are largely **undiagnosed**
- Are distributed across diverse health and social service systems
- Are more likely to be **involved in the juvenile justice** system;
- Have higher rates of **child abuse** (neglect, physical and sexual abuse);
- Have high **co-morbidity** with psychiatric conditions.

Substance Use among Youth*, by MDE in Past Year (2006)



Bipolar Spectrum and Substance Use Disorders

Bipolar D/O and SUDs

- High rates of comorbidity:
 - >50% of individuals with Bipolar meet criteria for comorbid SUD/Alcoholism.
- Mixed or rapid cycling diagnosis and alcohol disorders
 - Slower recovery
 - Poorer prognosis
- Bipolar patients with comorbid substance abuse
 - more severe course of affective illness (earlier onset of mood disorder, PTSD, Panic disorder)

Keller, AJP, 1986, Sonne, JNMD, 1994, Brady, ASAM-PAM, 2003

Evidence for Combined Treatment 1

- Salloum et al, 2005, Arch Gen Psych.
- 59 patients with Bipolar disorder and Alcohol Dependence, on therapeutic dosages of Lithium (+/- perphenazine), receiving psychosocial therapy for EtOH.
 - Double blind, placebo controlled.
 - Depakote added on to half at therapeutic levels.
 - Results: No effect on mood symptoms, but decreased drinking in +VPA add-on group.

Evidence for Combined Treatment 2

-Salloum et al, 2007 *Addict Behav*

- 15 patients, open label study
- Cocaine dependent patients with bipolar illness
 - reduced cocaine use with therapeutic dosages of VPA/Depakote.

Evidence for Combined Treatment 3

-Geller et al 1999, *J Amer Acad Child Adol Psych*

- 21 adolescents with bipolar and SUD, double blind, placebo controlled.
- Adolescents with mood symptoms and substance abuse: therapeutic levels of lithium reduced substance use and bipolar symptoms.

Post Traumatic Stress Disorder and SUD

Post-Traumatic Stress Disorder

- PTSD- nightmares, flashbacks, emotional detachment, insomnia, avoidance, hypervigilance at least 1 month after severe, life-threatening trauma.
- Often Co-morbid with depression, substance use (particularly EtOH).
- 75% of Vietnam Vets with PTSD also met Alcohol Dependence criteria.
- Civilian PTSD- 20-40% rate of lifetime SUD.

-SAMHSA 2007

PTSD 2

- Research demonstrates that PTSD is effectively treated by trauma-focused psychotherapy (CBT).

-Bisson et al 2007, Br J Psychiatry

- PTSD and Alcohol dependence- exposure therapy works for PTSD and reduced Alcohol cravings.

-Coffey et al 2006, Psychol Addict Behavior

- PTSD and Cocaine dependence- exposure therapy worked for both PTSD and decreased Cocaine use.

-Back et al 2006, Addict Beh

PTSD 3

- Study of 94 patients with PTSD + EtOH dependence: -
-double blind, placebo controlled trial of 150mg of Sertraline for 12 weeks.
- PTSD +EtOH users treated with Sertraline (Zoloft)-
younger onset PTSD, lighter drinkers: *less drinking* than controls.
- Older onset PTSD, heavier drinkers: *more drinking* than controls with Sertraline.

-Brady et al 2005, Alcohol Clin Exp Res

- Individualized treatment- Depakote for irritability, hostility, heavy SUDs in PTSD sufferers?

Attention Deficit Disorders

Attention Deficit Disorders

- ADD/ADHD- by definition, must be present by age 7 in order to qualify.
- Symptoms- must be manifested in 2/3 of home, school, or extra-scholastic activities.
- Inattention/hyperactivity, forgetfulness, impulsivity, distractibility.
- 60% of children with ADHD continue to have symptoms as adults.
- About 5% of children may have symptoms.

ADHD 2

- ADHD highly comorbid with SUDs (50% lifetime, 20% in last year).
- Childhood medication treatment for ADHD does NOT cause increased adult SUD.
- 20-35% of adult Cocaine users had childhood ADHD- 15-19% met adult ADHD criteria.
- Treatment seekers with ADHD were less likely to finish program than those without.

-Willens and Upadhyaya 2007, J Clin Psychiatry

ADHD 3

- Definitive studies are not available, but preliminary evidence suggests that medications used to treat ADHD also mildly decrease comorbid cocaine/methamphetamine use.
 - -Wilens et al 2005, *J Child Adolesc Psychopharmacol*
- Problem: Stimulants (Ritalin/Adderall) have abuse potential (but not at therapeutic doses?).
 - -Volkow et al 1995, *Arch Gen Psychiatry*
- More promise with other treatments for ADHD in SUD populations?

C-II

SHIRE US INC.



5 mg



7.5 mg



10 mg



12.5 mg



15 mg



20 mg



30 mg

Adderall®

(dextroamphetamine saccharate/
dextroamphetamine sulfate/amphetamine
aspartate/amphetamine sulfate)

C-II

NOVARTIS PHARMACEUTICALS



7* 5 mg



3* 10 mg



34* 20 mg

Ritalin® hydrochloride
(methylphenidate HCl tablets, USP)



Prescription Stimulants

- Methylphenidate (Ritalin/Concerta)
- Methylphenidate patch (Daytrana)
- Dextroamphetamine (Dexedrine)
- Amphetamine/dextroamphetamine (Adderall)
- Lisdexamfetamine (Vyvanse)

Medication Management in ADHD and Substance Use

- If stimulant necessary:
 - Long-acting formulations (e.g., Concerta), Daytrana patch
- For patients with ADHD and SUD, consider:
 - Atomoxetine (Strattera)
 - Bupropion SR or XL (Wellbutrin)
 - Clonidine
 - Modafinil (Provigil)

Psychotic Disorders and SUD

Psychotic symptoms and abstinence

- 165 chronic psychotic patients with cocaine abuse or dependence
- 6 weeks of abstinence needed for diagnosis of schizophrenia
- 81% could not make a definitive diagnosis
 - 78% insufficient abstinence, 24% poor memory
 - After 18 months, 75% still diagnostic uncertain

-Shaner, Psych Ser, 1996

Theoretical Advantages of Atypical Agents

- Multiple receptors
- Side-effects
- Improved negative symptoms
- Improved mood
- Decrease craving (??)
- Increase working memory
- Diminish suicidality (clozapine)
- Decrease aggression and impulsivity

Schizophrenia and SUDs

- Clozapine showed the most robust results in reducing smoking and drinking among patients with schizophrenia
- All other atypical agents showed mild to modest results

-Drake, SB, 2000, Buckley, JCP, 1998, Zimmet, JCPsychophar, 2000, Tsuang, JCPsychphar, 2002, Newton, PR, 2001, Grabowski, JCPsychphar, 2000, Green, SchRes,2003, Tsuang, JCP, 2002, Long, JCP, 2002, Noordsy, PsySer, 2001, Brown, JCPsychophar, 2003, Akerele, Am J Add, 2007

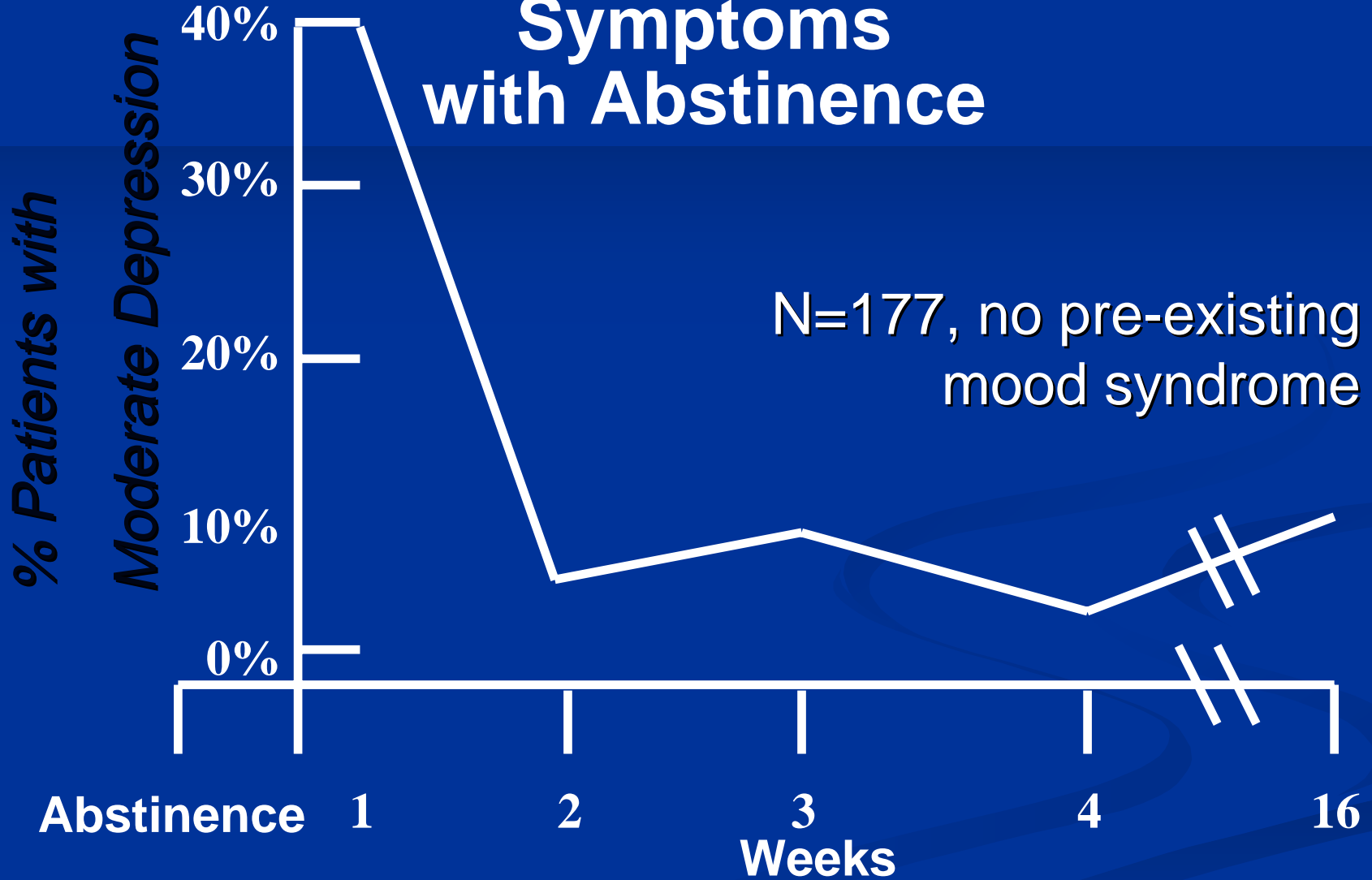
Naltrexone for alcoholic patients with schizophrenia

- 19 schizophrenia spectrum disorder and alcohol use disorders
- 8 weeks, prospective, open pilot study
- Naltrexone 100-150mg, direct administered
- Results: sig reduction number of drinks per week, drinks per drinking days, days of drinking to intoxication, and alcohol craving. Also improved ASI, PANSS

-Batki, S. *American Journal on Addiction*, 16:253-259, 2007

Depression and SUDs

Remission of Depressive Symptoms with Abstinence



Treatment of Depression in Patients With SUDs (A Meta-analysis)

- Antidepressant medication effective for treatment of depressive syndromes among patients with substance dependence
- Improvement in substance use correlated with improved depression
 - Studies with greater depression effect sizes showed reduced substance abuse
 - Studies with lower depression effect sizes showed no reduced substance abuse
- Diagnosis of depression after one week of abstinence was associated with greater antidepressant effect

Depression and SUDs

- Current recommendations that alcohol and drug abuse not be a barrier to treatment of depression
- Care is needed in diagnosis of depression: a period of abstinence is preferred but not required
- Antidepressant treatment may have limited impact on alcohol and drug use (reduced amount vs. abstinence)
- Specific psychosocial or pharmacological interventions for addictive disorders will be necessary

Caveats for depression/SUD

- In a retrospective chart review, SUD was a strong predictor of Antidepressant-induced Mania (OR 5.06, $p < 0.5$).

-Manwani et al, 2006, J Clin Psych.

- SUDs + mood symptoms- really atypical variants of bipolar spectrum disorders?

-Maremanni et al 2006, J Affect Disorders

-Altamura 2007, J Affect Disorders

- Bipolar III?- some investigators question whether a “substance-impulsivity” variety of bipolar exists.

-Camacho and Akiskal 2005, J Affect Disor

Approach to CODs

- Perform comprehensive psychiatric evaluation including SUD screening
- Obtain info from multiple sources
- Have a high index of suspicion for SUD co-morbidity when patient not responding to tx
- Individualize and integrate treatment for CODs whenever possible – contact with PMDs, etc.
- Family meetings/involvement
- Consider random drug testing
- Consider need for higher level of care
- Consult addiction medicine specialist if necessary

Medication Management in COD

- Ambivalence is common re: use of meds in patients with SUDs.
- Q: When to initiate pharmacotherapy when diagnosis is unclear?
 - With psychosis, moderate to severe depression, or mania, treat sooner
- Strategies include:
 - Verbalize clear expectations re: medication outcomes
 - Assume potential for misuse and drug interactions
 - Schedule frequent follow-ups

Evidence for Integrated Care

- Research has shown that the following are helpful but not sufficient:
 - Screening for mental disorders
 - Provider training and treatment guidelines
 - Referrals to specialty mental health providers
 - Strongest evidence: for *integrated care*.
 - Less than 50% of patients in need of care receive it
- (Unützer J et al., 2006)

The Case for Integrated Treatment

- Mental health in primary care:
 - Primary care is where the patients are.
 - PC is the 'de facto' health care system for common mental disorders.
- Medical care in mental health care settings:
 - Patients with severe mental disorders (SMI) receive poor medical care and die on average 25 years earlier than those without SMI.

Concluding Thoughts

- Importance of good psychiatric history and interview for clinical symptoms, medication history.
- Bipolar, ADHD, PTSD evidence is strongest:
 - treatment of the underlying psychiatric illness will improve the SUD, even if active.
- Psychosocial treatments/adjuvant medications to target SUD are critical in Dually Diagnosed

Thank you!

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