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Dual Diagnosis: Co-occurring Mental Illness and Substance Use Disorders

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Dual Disorders: A Definition

- Co-occurrence (comorbidity) of two conditions: substance use disorders and other psychiatric disorders
- Both conditions must have clinical significance --- associated with some impairment of functioning

Dual Disorders Significance

- Comorbidity is common
- Complicates diagnosis
- Complicates treatment
- **Worsens prognosis** [*adapted from: Manwani & Weiss (2003) Current Psychiatry 2(9):41-50*]
 - higher rates of
 - relapse
 - hospitalization
 - violence
 - incarceration
 - homelessness
 - infectious diseases: HIV, Hepatitis C, TB

Epidemiology of Dual Disorders

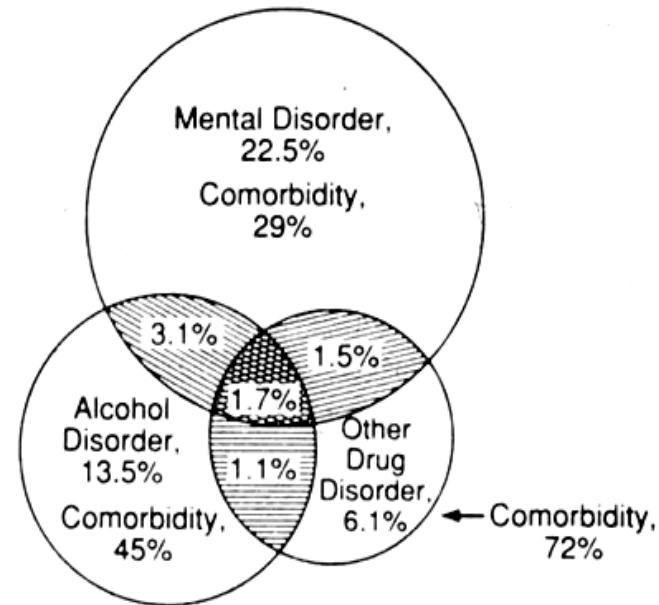
Dual Disorders Epidemiology: Major Studies

- Epidemiologic Catchment Area (ECA) Study: Regier et al 1990
- National Comorbidity Study: Kessler 1994, Kessler 1996; Kessler 1997
- National Comorbidity Study- Replication: Kessler 2004
- National Epidemiologic Survey on Alcohol and Related Conditions: Stinson 2005; Grant 2004 and 2006

Epidemiology of Comorbidity

(ECA Study: Regier et al, 1990 JAMA)

- The prevalence of comorbid alcohol, other drug, and mental disorders was determined
- In the US total community and institutional population
- 20,291 persons interviewed in the National Institute of Mental Health Epidemiologic Catchment Area (ECA) Program.



Lifetime prevalence of comorbid mental and addictive disorders in the United States, combined community and institutional five-site Epidemiologic Catchment Area data, standardized to the US population.

Mental Illness in SUDs

- Among those with an alcohol disorder, 37% had a comorbid mental disorder.
- Among those with non-alcohol drug disorders, more than half (53%) were found to have a mental disorder, with an odds ratio of 4.5

(Regier 1990 JAMA)

**Extent of Comorbidity Among Respondents with DSM-IV Alcohol
and Drug Use Disorders
in the General Population and Among Those
in Treatment for These Disorders During the Past 12 Months**

# of Other Psychiatric Disorders	Alcohol Use Disorder		Drug Use Disorder	
	General Population	Treatment	General Population	Treatment
0	40.9%	21.3%	14.5%	4.9%
1	26.8%	18.7%	21.7%	14.2%
2	14.2%	17.9%	22.2%	14.5%
3	7.2%	11.3%	12.2%	15.9%
4-5	6.7%	17.0%	16.6%	27.4%
6+	4.2%	13.7%	12.9%	23.1%

Specific 12-month DSM-IV Mood and Anxiety Disorders Among Respondents with 12-month Alcohol or Drug Use Disorders Who Sought Treatment in the Past 12 Months

	Alcohol Use Disorder	Drug Use Disorder
<u>Any Mood Disorder</u>	40.7%	60.3%
Major depression	32.7%	44.3%
Dysthymia	11.0%	25.9%
Mania	12.6%	20.4%
<u>Any Anxiety Disorder</u>	33.4%	42.6%
Panic disorder with agoraphobia	4.1%	5.9%
Panic disorder without agoraphobia	9.1%	8.6%
Social phobia	8.5%	12.1%
Specific phobia	17.2%	22.5%
Generalized anxiety	12.4%	22.1%
<u>Any Alcohol Use Disorder</u>	—	55.2%
<u>Any Drug Use Disorder</u>	33.1%	—

Suicide and Substance Abuse

30,000 Americans die by suicide/year

- Alcohol abuse is a major factor in 25% of all suicides.
- 40-60% of those who die by suicide are intoxicated at time of death.
- 1-6% of Alcohol dependent die by suicide.

(SAMHSA, 2002)

SUDS in Mental Illness

- Among those with a mental disorder, the odds ratio of an addictive disorder was 2.7, with a lifetime prevalence of about 29%
 - including an overlapping 22% with an alcohol,
 - and 15% with another drug disorder

(Regier 1990 JAMA)

Lifetime Prevalence of Substance Use Disorder in Mental Illness

(Regier et al, 1990)

	<u>SUD</u>	<u>AUD</u>	<u>DUD</u>
• Schizophrenia	47%	34%	28%
• Anxiety Disorder	24%	18%	12%
• Affective Disorder	32%	22%	19%
• Bipolar Disorder	56%	44%	34%

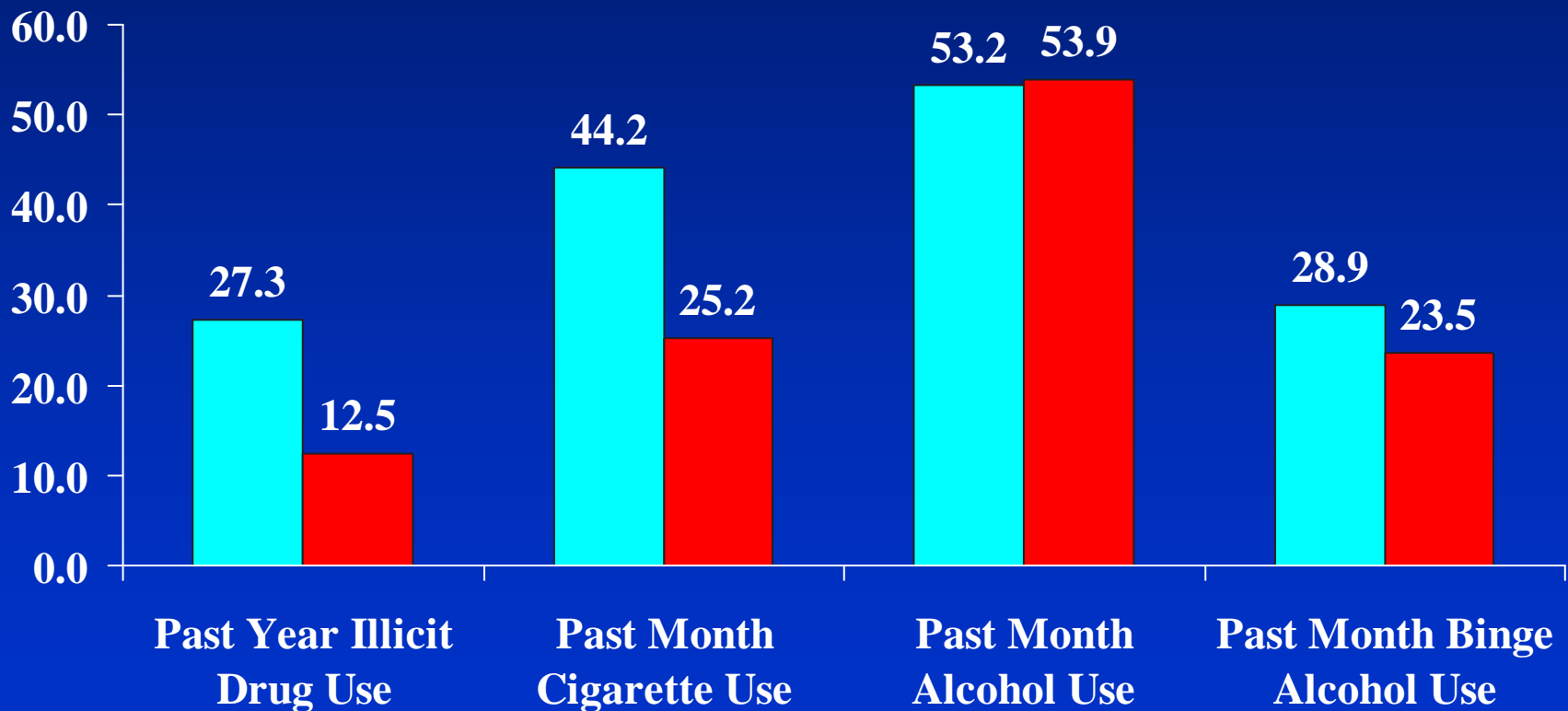
Associations of 12-month DSM-IV Alcohol & Any Drug Dependence & Mood & Anxiety Disorders

(Odds Ratios, Adjusted for Sociodemographic Characteristics)

Disorder	Alcohol Dependence	Any Drug Dependence
<u>Mood Disorders</u>		
Major depressive disorder	2.1*	3.8*
Bipolar I	4.0*	10.3*
Bipolar II	3.1*	2.6*
Dysthymia	2.2*	6.9*
<u>Anxiety Disorders</u>		
Panic disorder with agoraphobia	3.6*	9.2*
Social phobia	2.3*	4.5*
Generalized anxiety	3.2*	10.3*

Substance Use among Adults Aged 18 or Older, by SMI: 2003

Percent Using



(NSDUH 2003)

■ Had Past Year SMI

■ Did Not Have Past Year SMI

Patterns of Comorbidity

Dual Disorder Patients are Not Homogeneous

- A heterogeneous group
- Patients differ in
 - diagnoses (psychiatric and substance use)
 - severity
 - causality
 - motivation/readiness for treatment

[*adapted from:* Manwani & Weiss
(2003) Current Psychiatry 2(9):41-50]

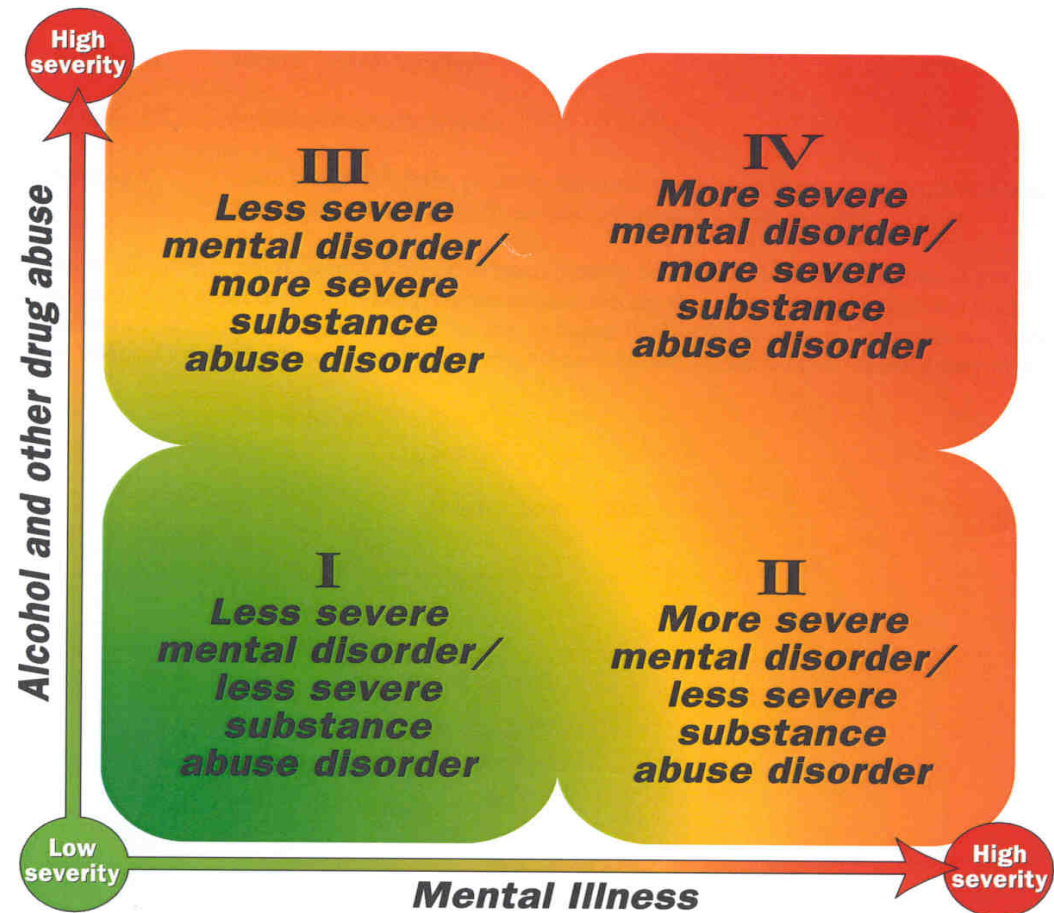
Patterns of Severity in Dual Disorders:

(NASMHPD/
NASADAD, 1998)

[After Ries RK.
(1993) J Addictive
Dis, 12:103-122]

Figure 2

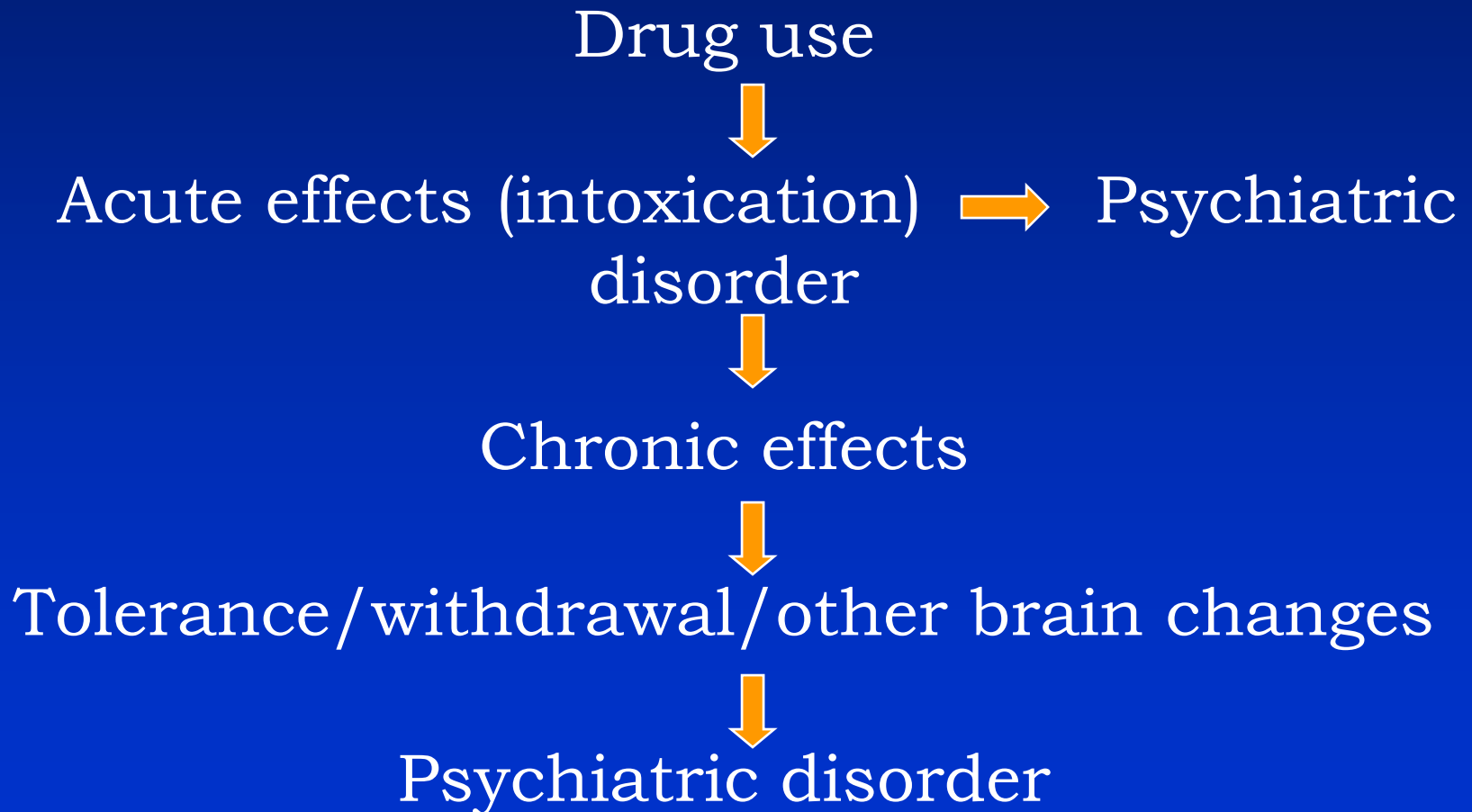
Co-occurring disorders by severity



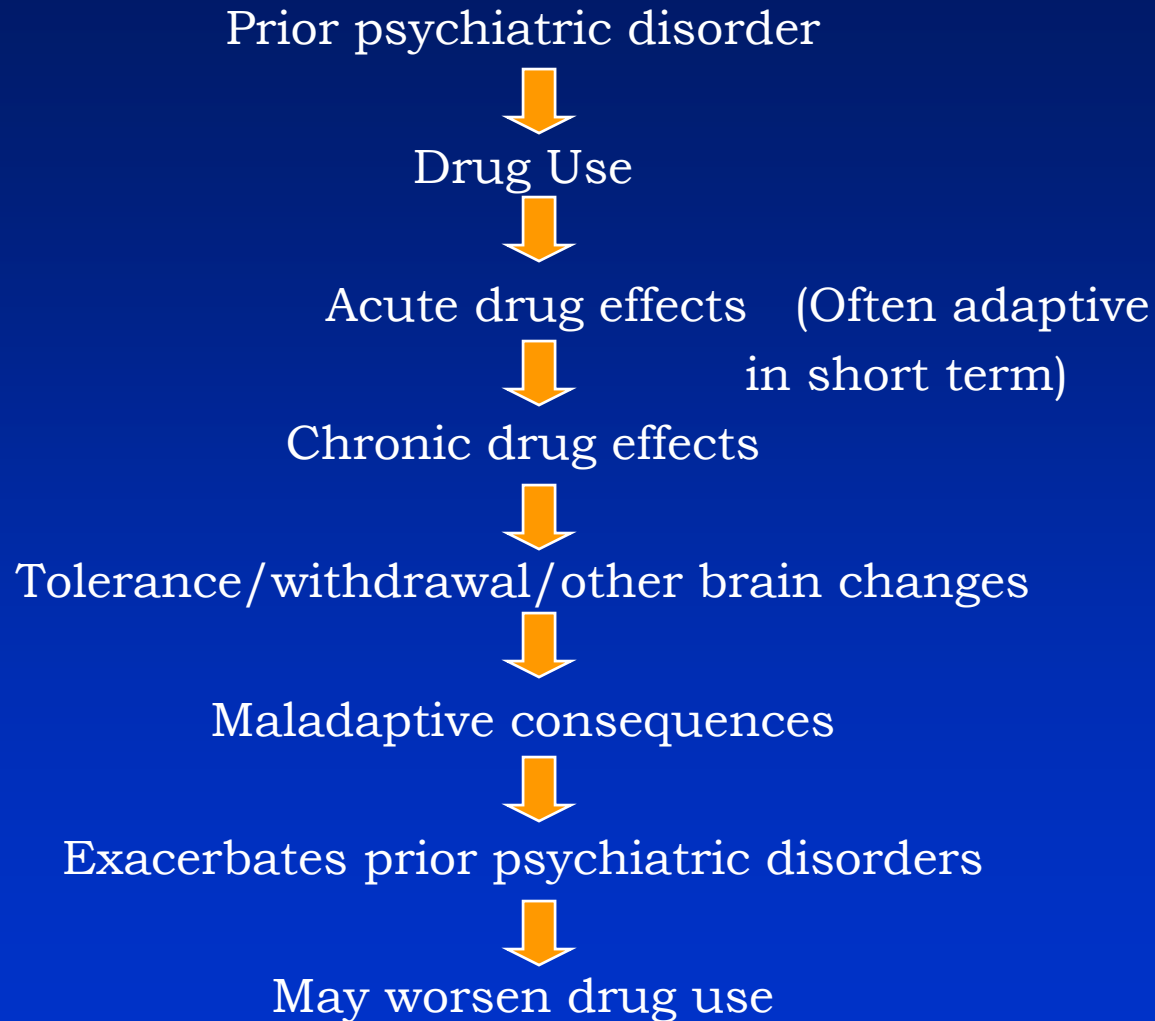
Dual Disorders Diagnostic Questions

1. Are symptoms due to psychiatric disorder, substance use, or both?
2. What came first, substance use or psychiatric disorder?
3. Is psychiatric disorder endogenous, secondary, or both?

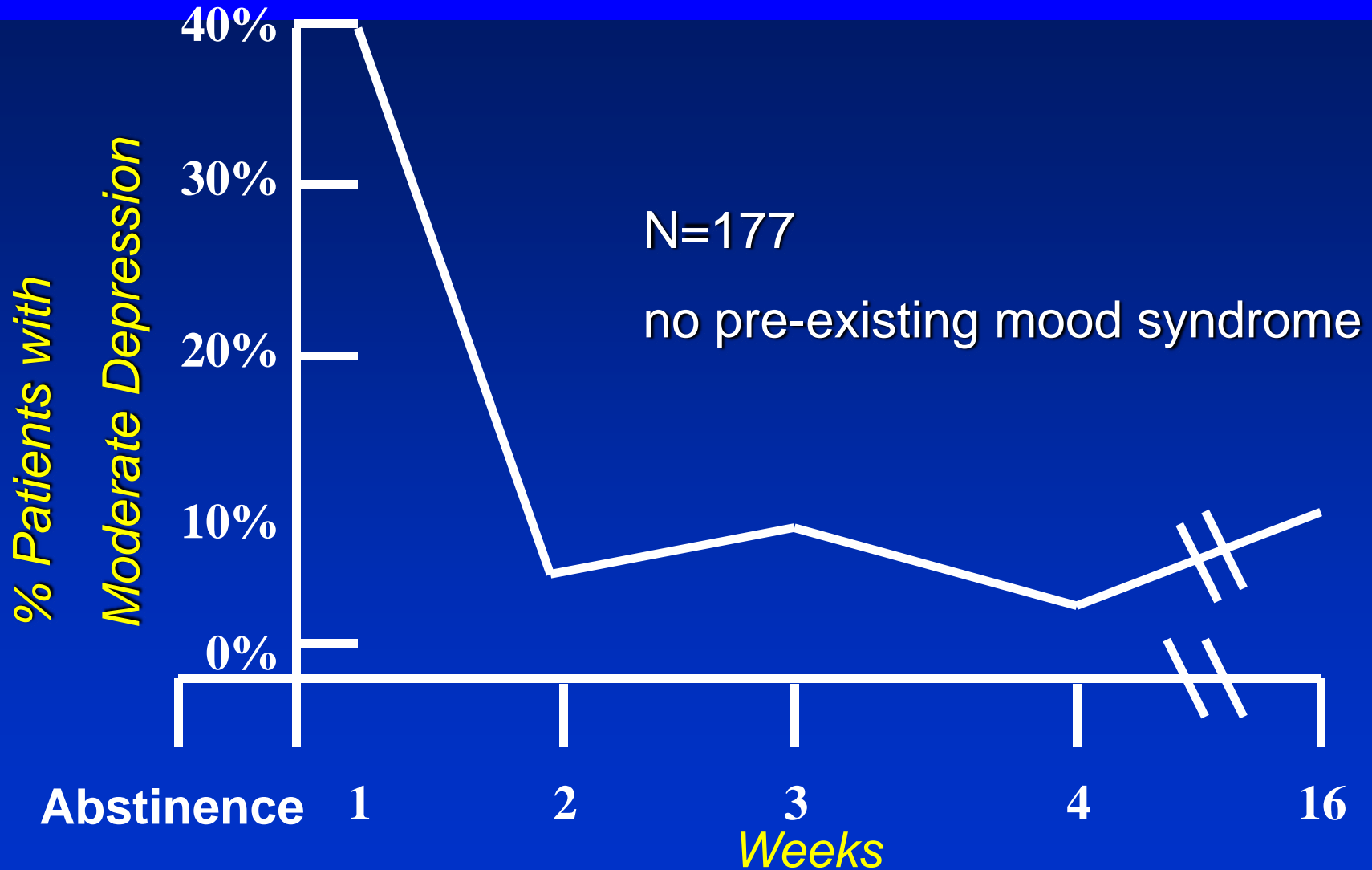
Patterns of Causality in Dual Disorders, 1: Drugs as Cause



Patterns of Causality in Dual Disorders, 2: Drugs as “Cure”

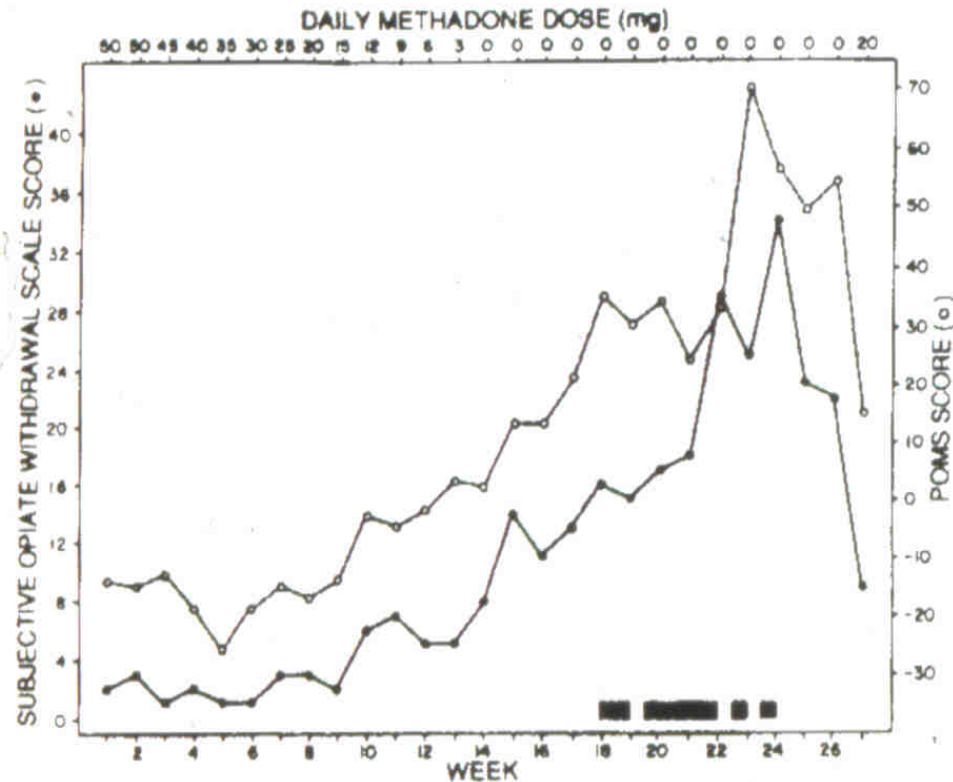


Remission of Depressive Symptoms with Alcohol Abstinence



Dysphoria of Opioid Withdrawal

FIGURE 1. Time Course of the Emergence of Symptoms of Dysphoria Measured by the POMS and the Emergence of Symptoms of Opiate Withdrawal Measured by the Subjective Opiate Withdrawal Scale in One Patient^a



^aThe patient was detoxified from 50 mg/day of methadone. The dark bars denote periods during which the urine toxicology reports showed a resumption of illicit heroin use.

Resolution of Cocaine-associated Depressive Symptoms (Weddington et al)

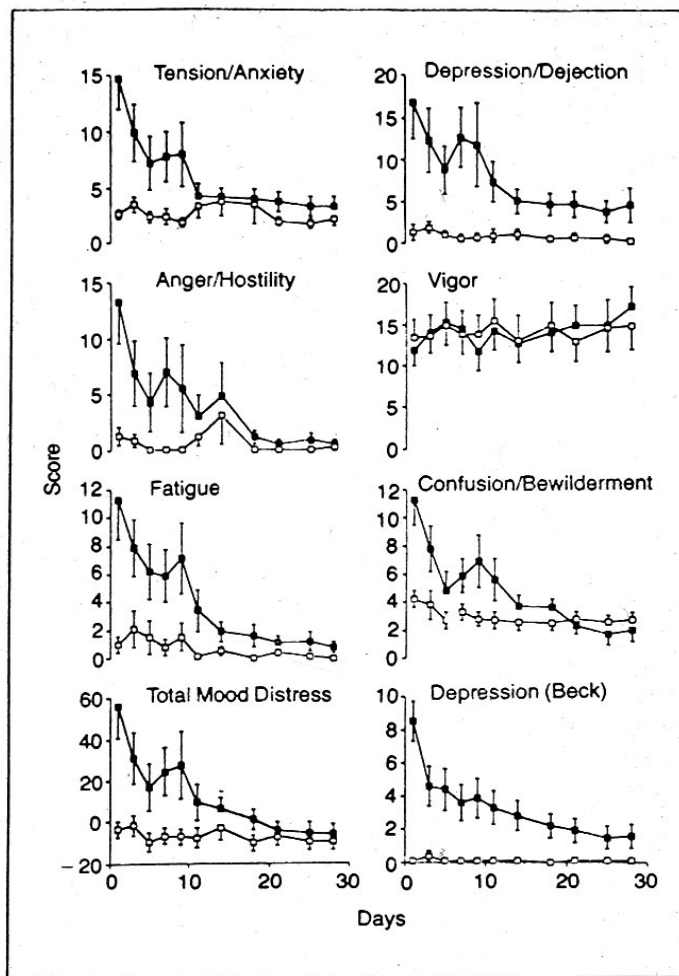


Fig 1.—Mean (\pm SEM) scores of mood over time using the Profile of Mood States and the Beck Depression Inventory. Day 1 is the day of admission. Solid squares represent cocaine-addicted subjects; open squares, control subjects. Addicted subjects demonstrated significantly elevated scores of mood disturbances and rates of mood change over time for all scores other than "Vigor" (see Table 2).

Temporary nature of substance-related anxiety or depression symptoms

- DSM-IV-TR
 - substance-related = within one month of substance use

Treatment Approaches for Dual Disorders

Essential Approaches to Dual Diagnosis Treatment

- Integrated treatment models
 - “One-stop shopping”
- Focus on adherence
- Cross training
- Flexibility of clinical philosophy

Different Treatment Models for Dual Diagnosis

- Sequential
 - Usually substance abuse treatment first, then psychiatric treatment
- Parallel
 - Concurrently but separated
- Integrated

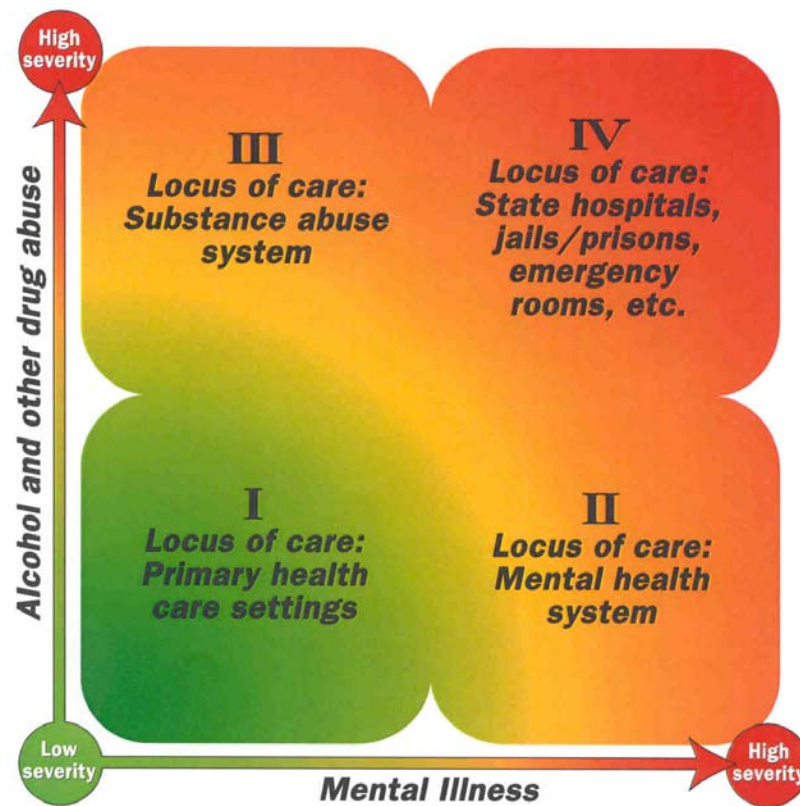
» (Mueser et al, 1998)

Psychosocial Aspects of Dual Disorders treatment

Where to Treat: Locus of Care

Figure 3

Primary locus of care by Severity



NYS Model

Stage-appropriate Treatment

- *Flexibility:*
 - *Abstinence vs Harm Reduction*
- Engagement
 - build an alliance; attract patient to treatment program
- Persuasion
 - persuade patient to accept longer, more intense, or sobriety-oriented treatment
- Active treatment
 - help patient develop attitudes/techniques to maintain sobriety
- Relapse prevention
 - maintain gains, deal with lapses/relapse

(adapted from Osher & Kofoed, 1989)

Integrated Treatment for Dual Diagnosis

- Assertive outreach/case management
- Comprehensiveness
- Shared decision making
- Long-term commitment
- Stage-wise treatment
- Pharmacotherapy

» (adapted from Mueser et al, 1998)

Why Use Psychiatric Medications in Patients with SUD Comorbidity?

1. To treat psychiatric disorders
2. To attempt to treat substance use disorders
 - directly or indirectly

Reluctance to Prescribe

- Lack of available prescribing providers
- Concerns about psychological issues: over-reliance on medications
- Concerns about “enabling”
- Concerns about medication safety and related issues

Concerns regarding the use of psychiatric medications in SUD

- Abuse potential
- Safety
 - Side effects
 - Overdose
 - Interactions w. substance
- Effectiveness
- Antianxiety agents
- Antidepressants
- ADHD medications
- Mood stabilizers
- Antipsychotics
- Sleep medications (sedative-hypnotics, etc.)

Abuse Liability

- Are psychiatric medications abusable/addictive?
- Two relevant questions:
 1. Are they rewarding?
 2. Do they cause physiological dependence?
- A related question:
 - Are they sedating?

Abuse Potential of Psychiatric Medications

LITTLE/NONE	SOME	SIGNIFICANT
Antipsychotics*	Tricyclic antidepressants	Benzodiazepines
Mood stabilizers	Anticholinergic antiparkinsonians	Barbiturates
Most anticonvulsants		Stimulants
Non-tricyclic antidepressants		
buspirone		
* little or none (however, sedating atypical APs may be overused, e.g. quetiapine)	?zolpidem ?zaleplon ?eszopiclone ?pregabalin ??modafinil	

Combining Drugs and Alcohol with Psychiatric Medications: Drug Interactions

- Medications
- Alcohol
- Drugs



Alcohol and Antipsychotics

- Haloperidol
 - “use of alcohol should be avoided due to possible additive effects and hypotension” (PDR 2004)
 - “may...(potentiate)...alcohol” (PDR 2004)
- Clozapine
 - likely increased psychomotor impairment and sedation with alcohol
- Olanzapine
 - olanzapine has no significant metabolic interaction with alcohol, but may increase sedation (Callaghan et al 1999)
 - “Patients should be advised to avoid alcohol while taking olanzapine” (PDR 2004)
- Risperidone
 - likely increased psychomotor impairment and sedation with alcohol
 - “Patients should be advised to avoid alcohol while taking ...”
- Ziprasidone
 - Less likely to have increased psychomotor impairment and sedation with alcohol
- Aripiprazole
 - no effect on alcohol effects on gross motor skills (PDR 2004)
 - yet PDR states: “Patients should be advised to avoid alcohol while taking (aripiprazole)”.

Alcohol & Atypical Antipsychotics: Oversedation

- May be a risk with
 - clozapine
 - olanzapine
 - quetiapine
 - risperidone
- Less likely to be a risk with
 - ziprasidone
- Unlikely to be a risk with
 - aripiprazole

Alcohol and Antidepressants

- additive impairment with sedating ADs,
 - tricyclics
 - mirtazapine (PDR)
 - fluvoxamine (PDR)
- no apparent additive impairment:
 - SSRIs (PDR)
 - paroxetine, sertraline, citalopram
 - venlafaxine (PDR)
 - nefazodone
 - bupropion

Alcohol: Interactions with Psych Meds/Substances

- Effects of alcohol depend on:
 - Amount
 - Rate of absorption
 - Tolerance
- Opioids, benzodiazepines:
 - increased CNS depression
- Cocaine: increased cardiac toxicity, rapid heart rate, high BP

Opioids: Interactions with Psych Meds/Substances

- Methadone:
 - Tricyclic antidepressants: raise methadone levels & vice versa
 - Fluvoxamine: raises methadone levels to dangerous/life-threatening levels (other SSRIs cause non-clinically significant elevations)
 - Carbamazepine: lowers methadone levels, as do (to a lesser degree) phenobarbital and phenytoin

Opioids: Interactions with Psych Meds/Substances, 2.

- All opioids:
 - benzodiazepines: increased CNS depression, respiratory depression, death
 - alcohol: increased CNS depression

Cocaine: Interactions with Psych Meds / Substances

- Epinephrine (and probably other sympathomimetic drugs):
 - cardiac arrhythmias
- MAO inhibitors: hypertensive crisis
- Alcohol: more toxicity, hypertension, tachycardia
- Antipsychotics: increased potential for seizures, rigidity, hyperthermia

Amphetamines: Interactions with Psych Meds/Substances

- MAO inhibitors: hypertensive crisis
- Antipsychotics: increased potential for seizures, rigidity, hyperthermia
- potential for serotonin syndrome in combination with serotonin-increasing medications

Effectiveness of Psych Meds in SUDs

Antidepressants in Co-occurring Depression and SUDs

Treatment of Depression in Patients With Alcohol or Other Drug Dependence (A Meta-analysis)

Nunes (2004 JAMA, April 21,, vol 291, 15, p1887-1896)

- 14 randomized, double-blind, placebo-controlled, meet diagnostic criteria for current unipolar depression and current substance dependence (N=848 patients)
- 8 studies (alcohol), 4 studies (methadone), 2 cocaine

Nunes (2004) - Results, 1

- Diagnosis of depression after one week of abstinence was associated with greater antidepressant effect
- A trend for medication effect to be larger in studies of alcohol than drug dependence
- High placebo-response rates (nonabstinent or no long-standing depression)

Nunes (2004) - Results, 2

- Antidepressant medication effective for treatment of depressive syndromes among patients with substance dependence
- Antidepressant medication can diminish quantity of substance use but not helpful in sustained abstinence
- Improvement in substance use correlated with improved depression regardless of medication response

Nunes (2004) - Conclusions

- If diagnosis of depression, then a period of abstinence is preferred but not required for antidepressant tx
- Current recommendations that alcohol and drug abuse not to be a barrier to treatment of depression
- Antidepressant treatment may have some impact on alcohol and drug use (reduced amount vs. abstinence)

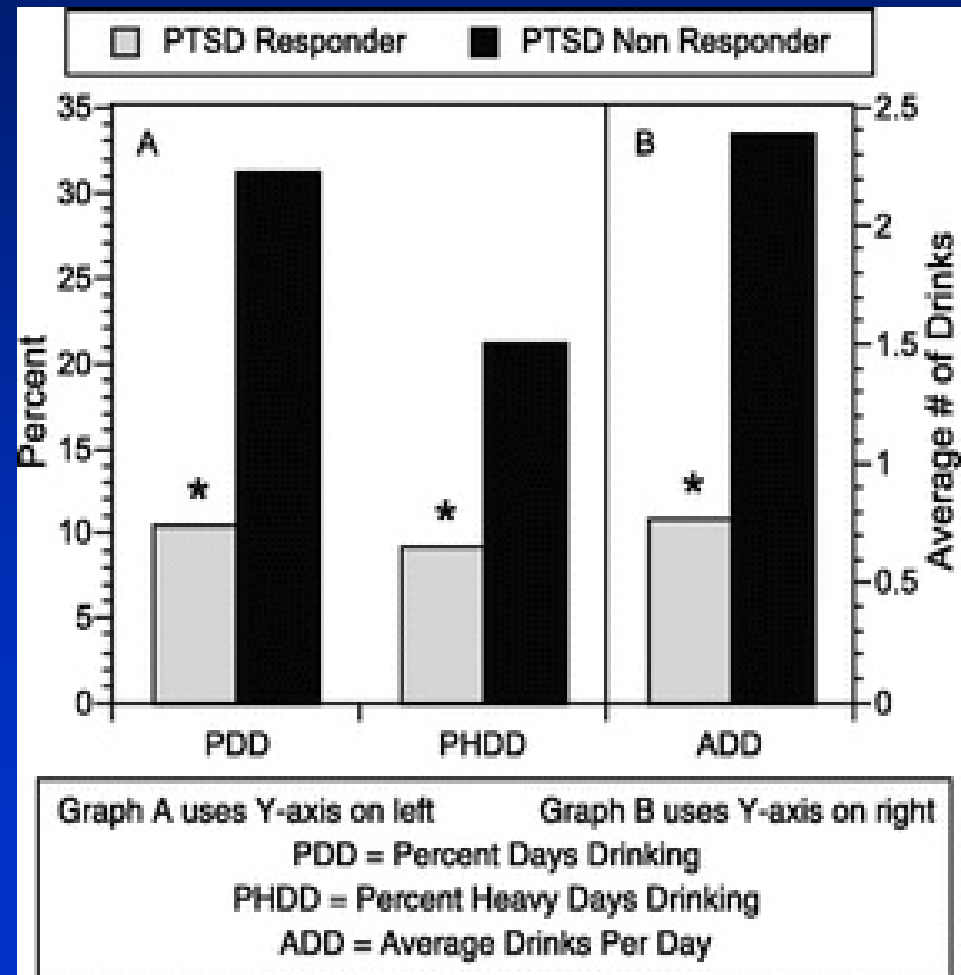
Medications for Comorbid Anxiety Disorders and SUDs: PTSD

- PTSD
 - Sertraline DB PC Trial, N = 94: Brady 2005
 - Significant decrease in alcohol use in both the sertraline and the placebo groups.
 - Cluster analysis revealed significant medication group by cluster interactions for alcohol-related outcomes.
 - Sertraline-treated participants with less severe alcohol dependence and early-onset PTSD
 - had significantly fewer drinks per drinking day ($p < 0.001$).
 - For participants with more severe alcohol dependence and later onset PTSD
 - the placebo group had significantly greater decreases in drinks per drinking day ($p < 0.01$) and drinks consumed per day ($p < 0.05$).
 - **Conclusions: There may be subtypes of alcohol-dependent individuals who respond differently to serotonin reuptake inhibitor treatment.**

Symptom Improvement in Co-occurring PTSD and Alcohol Dependence

(Back, Brady et al 2006)

- In a treatment study of alcohol-dependent pts with PTSD, nearly 50% of subjects had substantial improvement in both alcohol and PTSD sx
- Improvement in PTSD symptoms appeared to have a greater impact on alcohol treatment response than the reciprocal relationship.



Medications for Comorbid Anxiety Disorders and SUDs: Social Anxiety

Paroxetine DB PC Trial, N= 42: Randall 2008; Thomas 2008

- 16-week trial of paroxetine for social anxiety in patients with co-occurring alcohol problems.
- Paroxetine **improved social anxiety** more than placebo.
- Paroxetine reduced self-reported reliance on alcohol for self-medication purposes
 - **but was not different than placebo in changing quantity and frequency drinking** or the proportion of drinking days that were identified as coping-related.
 - for the placebo group, drinking during the trial was correlated with social anxiety severity,
 - whereas for the paroxetine-treated group, drinking was uncoupled from social anxiety severity.
 - **CONCLUSIONS: Successfully treating social anxiety symptoms with paroxetine does not reduce drinking in pts who are not seeking treatment for alcohol problems.**
 - Paroxetine does, however, reduce reliance on alcohol to engage in social situations, and may change the reasons why one drinks (such that drinking occurs for other reasons besides coping with anxiety).

Pharmacotherapy of Co-morbid Alcohol and Bipolar Disorder

Valproate:

- 59 patients with BP I disorder and alcohol dependence
- decreased heavy drinking days compared to placebo. *Salloum et al, 2005.*

Antipsychotic Medications in Comorbid Disorders

- Antipsychotics **are** effective in treating psychosis in patients with SUDs
 - Antipsychotics should not be withheld in psychotic or manic patients just because substance use is also present
- But are antipsychotics -- especially atypicals -- and especially CLOZAPINE -- effective in reducing substance use?

Clozapine in the Treatment of Substance Abuse in Schizophrenia

- Clozapine--> reduced alcohol use in schizophrenia (Drake et al., 2000)
 - n=151
 - prospective but post-hoc, non-randomized
 - ave 12.5 drinking days per 6 months on CLZ vs 54.1 off CLZ
- Clozapine associated with reduced alcohol and cannabis use compared to risperidone
 - Retrospective study (Green et al, 2003)
 - N= 8 CLZ; 33 RIS
 - Abstinence rates higher in CLZ group (54% vs. 13%, p=0.05)
- Clozapine: NO Data on Prospective Randomized Controlled Trials

Atypicals and Substance Use in “Real World” Clinical Practice

- Petrakis et al, 2006
 - N=249, VA sample
 - Patients maintained on typicals (n=55) vs those maintained (n=161) on, or switched to, atypical (n=33)
 - No greater improvement in substance-related outcomes in those treated with atypicals
 - Only 3 (1.2%) received clozapine

Use of Medications Specific for Alcohol Use Disorders in Schizophrenia

Pharmacological Treatment of Alcohol Dependence in Schizophrenia

Naltrexone

- Effective in schizophrenia and alcohol use disorders: more days abstinent and less craving
 - open trial: Batki et al, 2002 & 2007
 - controlled trials: Petrakis et al, 2004; Petrakis et al 2005; Batki et al, 2005 and ongoing)

Disulfiram

- Effective in SMI and alcohol, controlled trial (Petrakis et al., 2005)
 - More consecutive days abstinence, less craving
 - No major adverse effects
- Earlier caveats @ safety; concern about increased psychosis (Larson et al 1992); more recent studies did not show problems (Mueser et al 2003 & Petrakis)

Acamprosate

- No trials in schizophrenia to date

Effectiveness of Medications in Serious Mental Illness and SUDs: Summary

- **All antipsychotics are effective for psychotic states**, regardless of alcohol use comorbidity, although adherence may be worse
- **No clear evidence for atypicals in reducing alcohol use**
- **Case is strongest for clozapine having specific effects on substance use**, but even with CLZ, controlled trials are needed.
- Most **medications specific for alcohol dependence are probably effective** and should be used in patients with schizophrenia and other SMI
- Most **medications specific for nicotine dependence are probably effective** and should be used in patients with schizophrenia and other SMI
- Most **medications specific for opioid dependence may be effective** and should be used in patients with schizophrenia and other SMI

Pharmacologic Treatment of Dual Disorders

- Whom to treat
 - Anyone with severe enough symptoms
- When to treat
 - Psychosis and mania: immediately
 - Depression and anxiety
 - If dx is clear: immediately
 - If dx uncertain—wait 1-2 weeks