

Pharmacotherapy for Comorbid Anxiety and Substance Use Disorders

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Overview

- Prevalence
- Relationship between anxiety and substance use disorders
- Treatment

12-Month Odds of SUDs and Independent Anxiety Disorder

	Any SUD	Alcohol Dependence	Drug Dependence
Any anxiety disorder	1.9	2.6	6.2
Panic disorder			
with agoraphobia	3.1	3.6	10.5
without agoraphobia	2.1	3.4	7.6
Social phobia	1.9	2.5	5.4
GAD	2.3	3.1	10.4

GAD=generalized anxiety disorder.

12-Month Prevalence of Anxiety Disorder in SUD Treatment Seekers

ALCOHOL TREATMENT

• Any anxiety	33.4
• Panic with agoraphobia	4.1
• Panic without agoraphobia	9.1
• Social phobia	8.5
• GAD	12.4

DRUG TREATMENT

• Any anxiety	42.6
• Panic with agoraphobia	5.9
• Panic without agoraphobia	8.6
• Social phobia	12.1
• GAD	22.1

Grant BF, et al. *Arch Gen Psychiatry*. 2004;61:807-816.

Comorbidity of PTSD and SUDs in National Comorbidity Survey

MEN	%	Odds Ratio
Alcohol abuse/dependence	51.9	2.06
Drug abuse/dependence	34.5	2.97

WOMEN	%	Odds Ratio
Alcohol abuse/dependence	27.9	2.48
Drug abuse/dependence	26.9	4.46

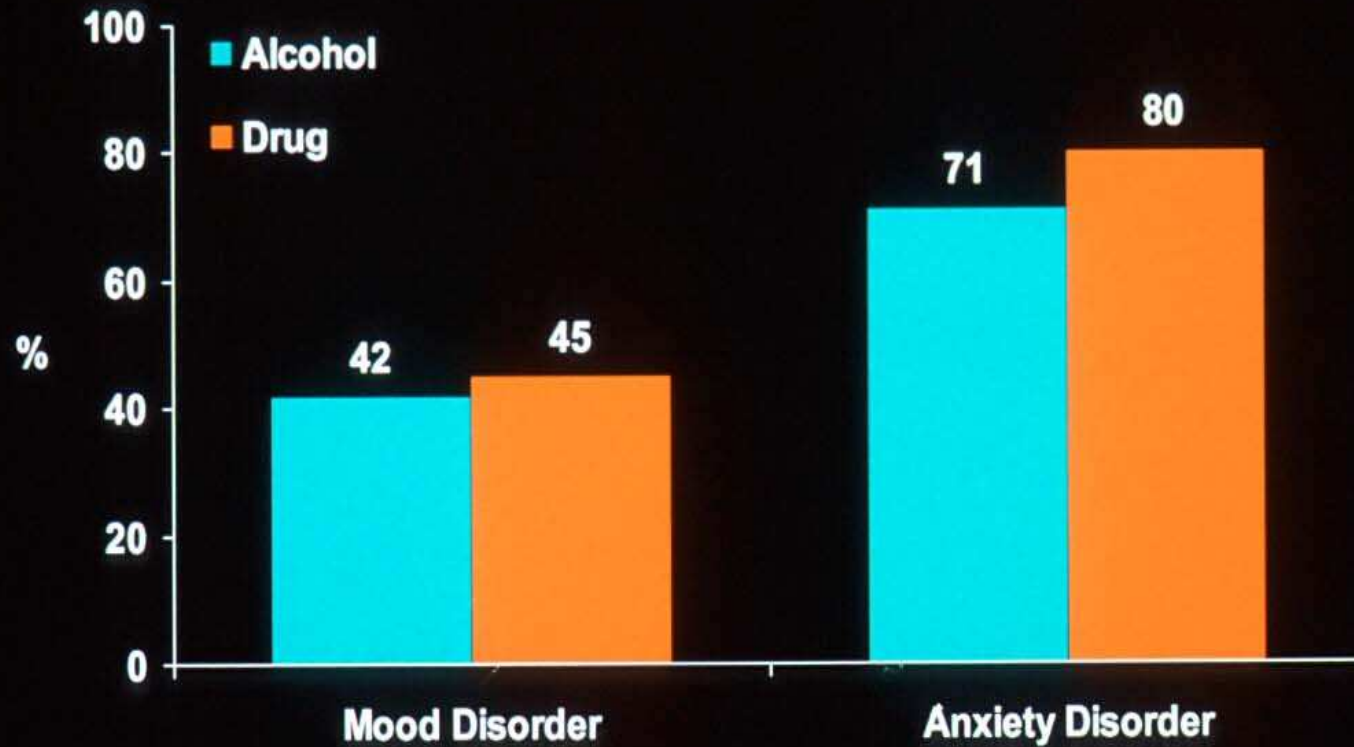
PTSD=postraumatic stress disorder.

Kessler RC, et al. *Arch Gen Psychiatry*. 1995;52:1048-1060.

Substance Dependence/Anxiety Interface

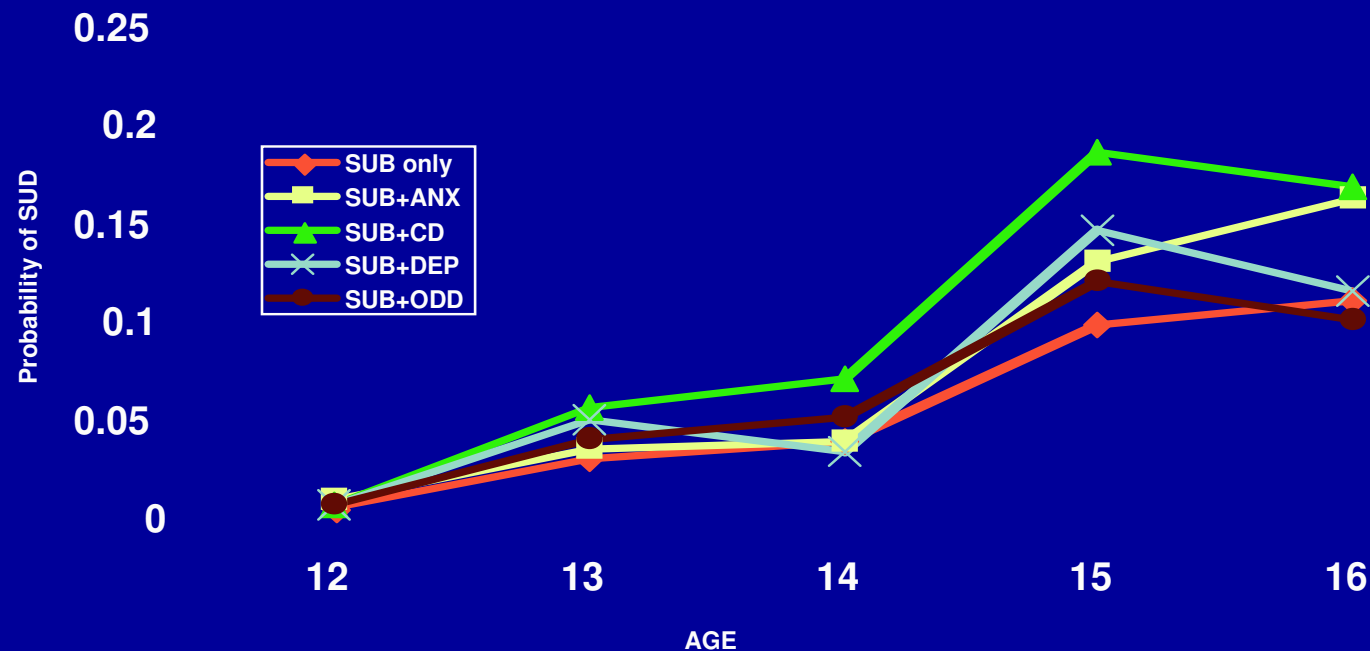
- Substance-induced anxiety
- Self-medication
- Common etiology
 - Common risk factors
 - Common neurobiology

Order Of Onset - Mood/Anxiety Disorder Prior To Dependence



Merikangas et al. *Psychologic Med.* 1998;28:773.

Age of First Substance Use and Psychiatric Comorbidity



- Age of first use and psychiatric comorbidity on SUD development. For girls, anxiety disorder interacts with early use to increase risk for dependence

Childhood Sexual Abuse and Psychiatric Disorders

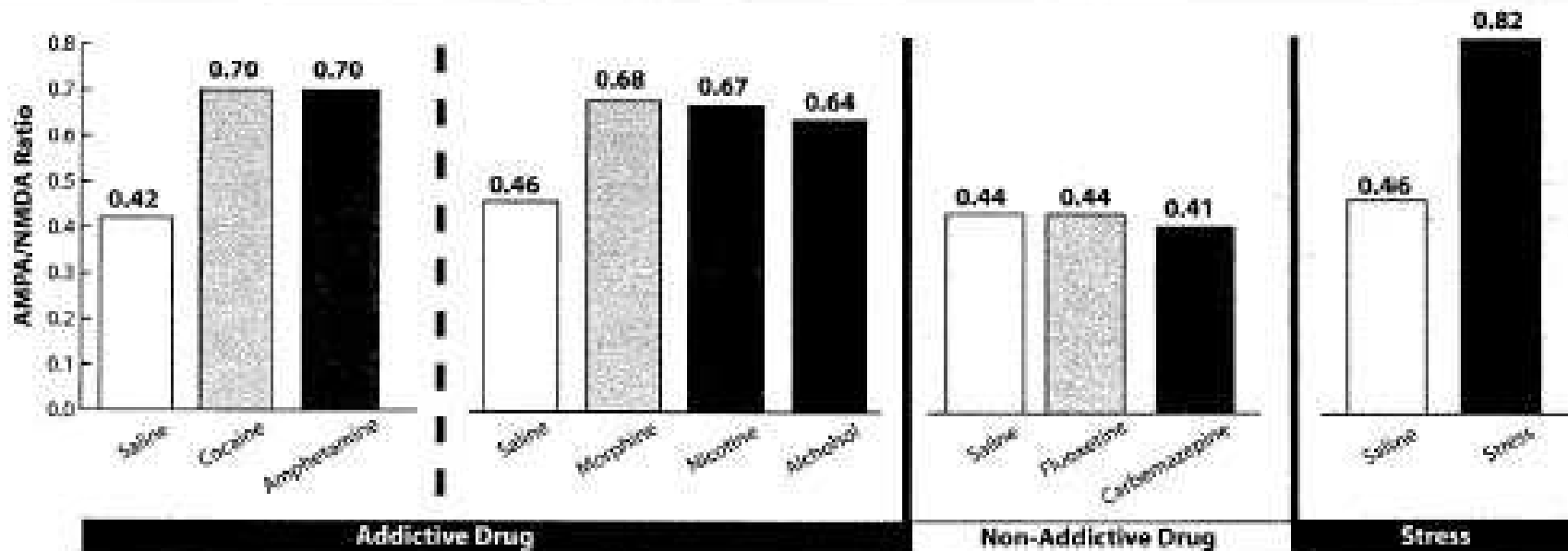
- Abuse positively associated with a number of disorders
- Strongest relationship with alcohol/drug use
- More severe abuse increases risk
- Not explained by background/familial factors

Enhanced Cocaine Self-Administration in Adult Rats After Neonatal Stress

- Neonatal isolation days 2-9
- Adult acquisition of cocaine self-administration lower doses, less training
- No difference in acquisition of other tasks
- Lower cortisol levels in isolated group

Kosten et al., 2000

Addictive Drugs and Stress Increase Sensitivity of Dopamine Cells in Mice



Saal et al., Neuron, 2003

General Principles in Treatment of Comorbidity

- Φ Address both problems simultaneously
- Φ Use medication with least abuse potential and least toxicity should relapse occur
- Φ Maximize the use of non-pharmacologic treatment
- Φ When possible, use medications which treat both disorders

Psychotherapy

- Important to maximize nonpharmacologic strategies
 - Enhance self-efficacy
 - Decrease helplessness/dependency
 - Enhance coping strategies
- CBTs effective in both SUDs and anxiety disorders

CBTs=cognitive-behavioral therapies.

Child Anxiety Disorder Treatment: Outcomes in Adolescence

- Evaluated clinical status of 84 individuals who received 16-week CBT 7.4 years earlier
- Less successfully treated adolescents:
 - More drinking days/month (8.3 vs 2.5; $P < .05$)
 - More marijuana use ($P < .01$)
 - Social/interpersonal consequences from drug use ($P < .005$)
 - Unsuccessful attempts to control drug use ($P < .05$)

Ideal Pharmacologic Treatment

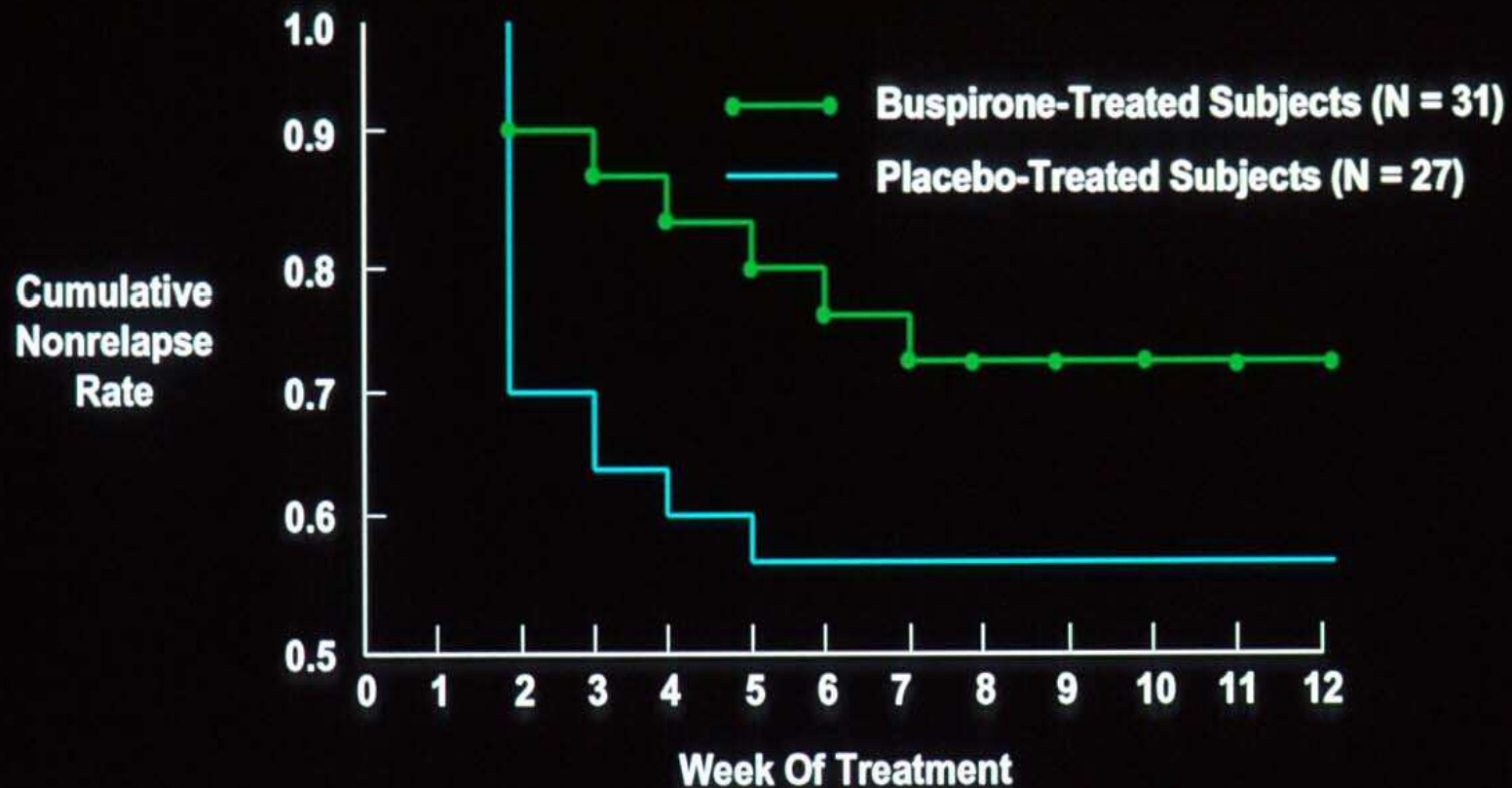
- Low abuse potential
- Safety
- Agents that treat both disorders

Buspirone In Anxious Alcoholics

- Randomized 12-week placebo-controlled trial of buspirone in 61 anxious (HAM-A ≥ 15) alcoholics, all of whom also received weekly relapse prevention psychotherapy
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Kranzler et al. *Arch Gen Psychiatry*. 1994;51:720.

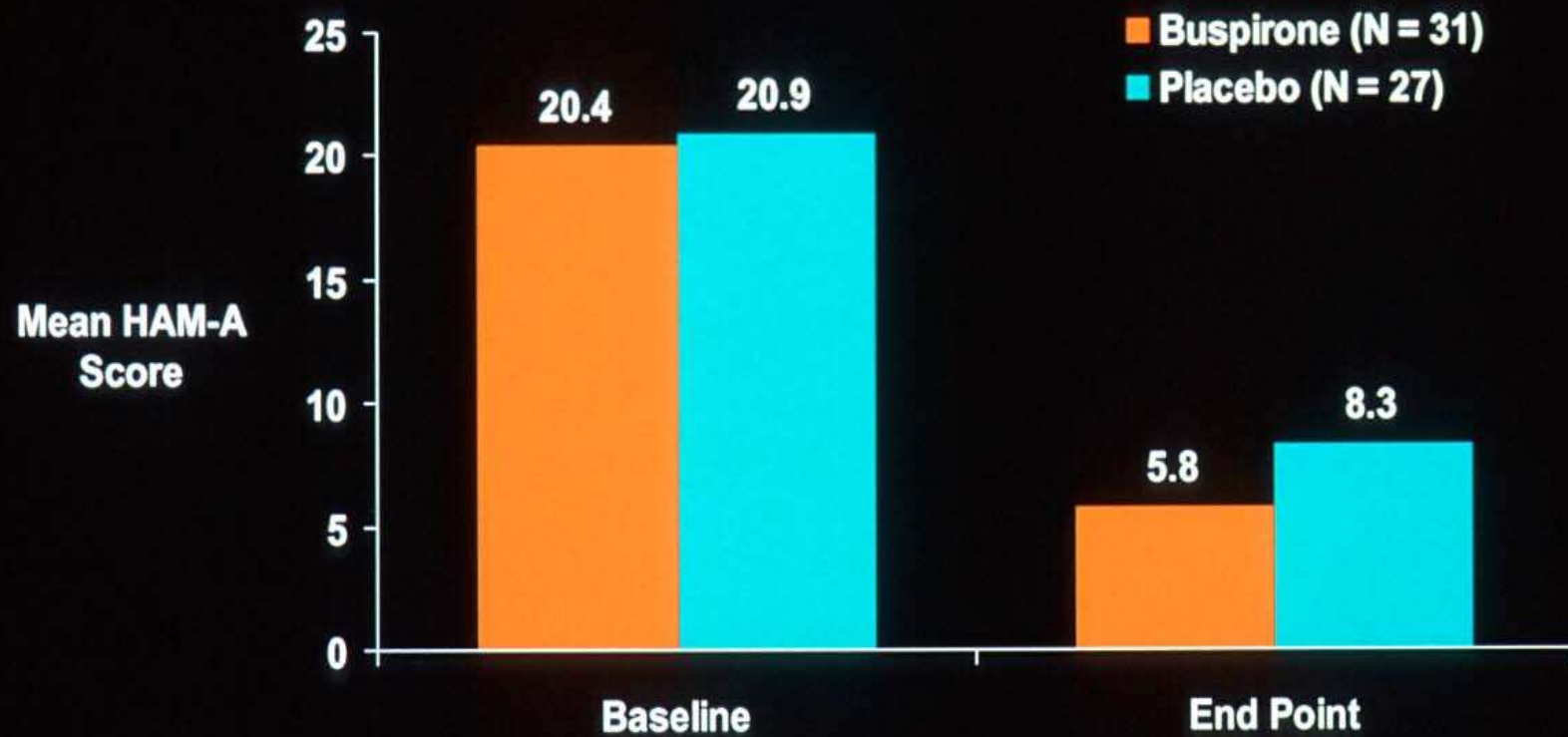
Rate Of Relapse To Heavy Drinking In Study Of Buspirone Treatment Of Anxious Adults



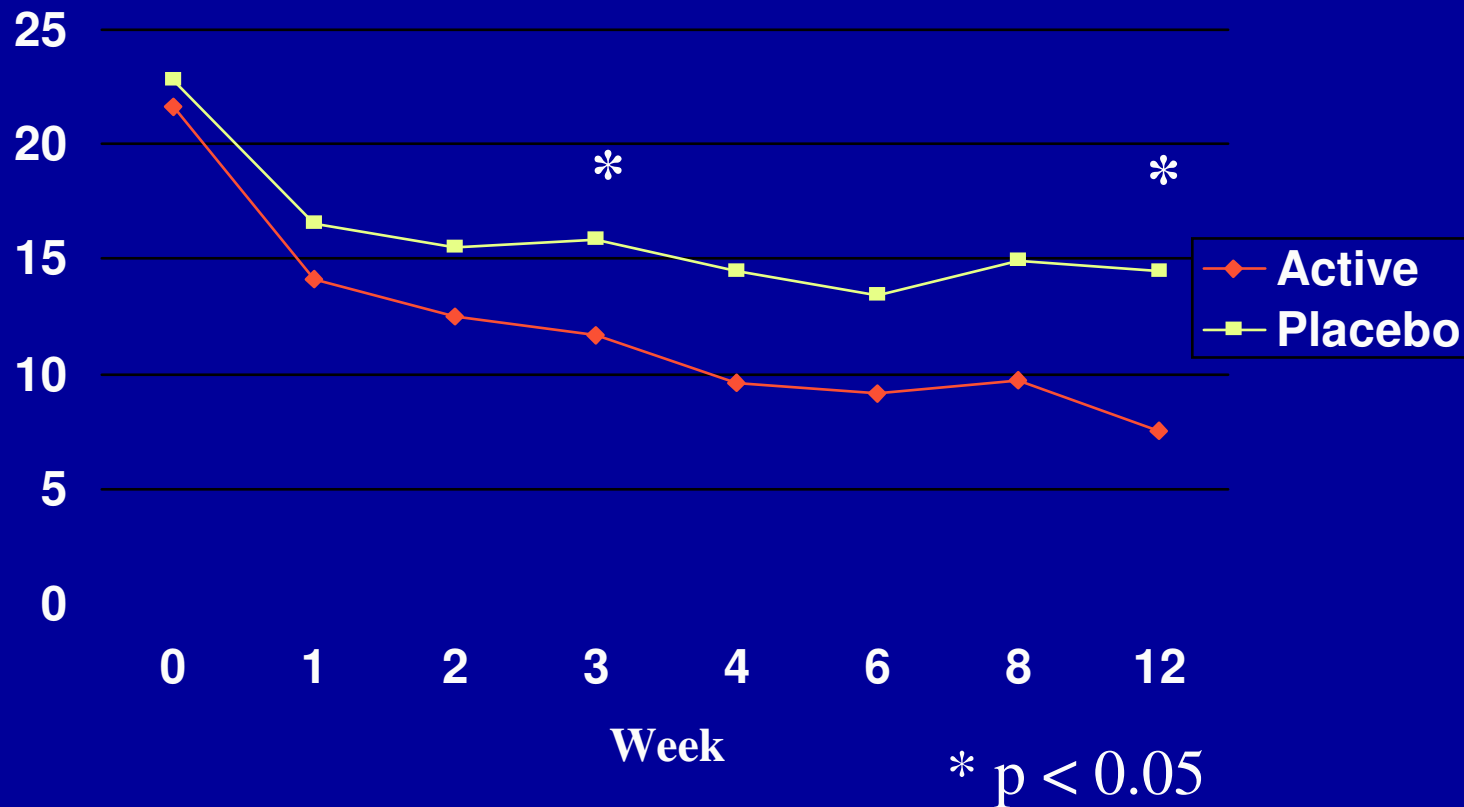
Heavy drinking = >5 drinks per occasion.
Kranzler et al. *Arch Gen Psychiatry*. 1994;51:720.

Hamilton Anxiety Rating Scale Scores

Buspirone Vs Placebo



Buspirone in Anxious Methadone Patients: Change in HAM-A Score



UDS Results

	Active	Placebo	Test statistic
% positive UDS	29.0%	52.3%	p<.001

Serotonin Reuptake Inhibitors

Efficacious in treatment of PTSD

Data in alcohol use inconsistent

- Overall studies predominantly negative or show only modest improvement
- Subtyping by age of onset of alcohol dependence and psychiatric comorbidity shows promise

PTSD and Alcoholism: Treatment With Sertraline

- 12-week study
- Double-blind, placebo-controlled trial
- Weekly CBT targeting alcoholism
- Measure alcohol and PTSD outcomes
- 94 subjects with both PTSD and alcoholism
 - 43 women; 51 men

Cluster Analysis Sertraline

Three distinct clusters

- Cluster one: Early onset PTSD; later onset, less severe alcoholism (N=14)
- Cluster two: Onset PTSD/alcohol relatively close; less severe alcohol dependence (N=53)
- Cluster three: Early onset, severe alcoholism; later onset PTSD (N=27)

Adjusted Mean Drinks per Drinking Day Over Treatment Period



Cluster x group $p=0.001$

Conclusions: Sertraline PTSD/Alcohol Trial

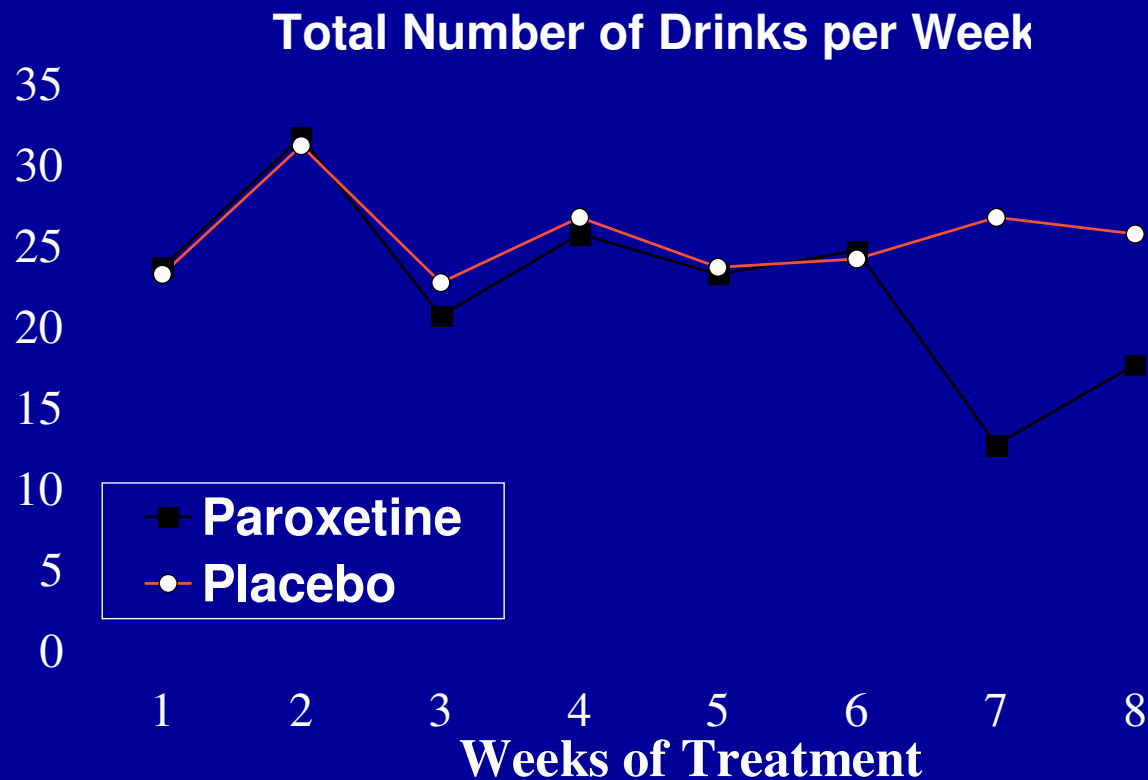
- Sertraline efficacious in treating PTSD in alcohol-dependent individuals
- In the sub-group of patients with early onset PTSD, sertraline significantly improved alcohol-related outcomes

Paroxetine in Comorbid Social Phobia and Alcoholism

- 15 men and women with social phobia and alcohol dependence or abuse
- Double-blind, placebo-controlled
- Paroxetine – flexible dosing up to 60 mg/d
- Brief motivational therapy for alcoholism

Paroxetine in Comorbid Social Phobia and Alcoholism

Adjusted Group Means



Randall CL, et al. *Depress Anxiety*. 2001;14:255-262.

Substance Use and Anxiety: the Future

- Exploration of agents that act on common neural pathways
- GABA-ergic/glutamatergic
 - Topiramate
 - Acamprosate
 - Gabapentin