



UW PACC

Psychiatry and Addictions Case Conference

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ANTICONVULSANTS IN ALCOHOL WITHDRAWAL TREATMENT: A BETTER WAY?

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GENERAL DISCLOSURES

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SPEAKER DISCLOSURES

- ✓ No conflicts of interest

OBJECTIVES

1. Review Alcohol Withdrawal Symptoms and Course
2. Review Pros and Cons of Treatment with Benzodiazepines
3. Review Alcohol Withdrawal Treatment utilizing Anti-Convulsants and Comparison with Benzodiazepines

CASE-

- Meg is a 35 yo w female in your practice the last few years, with a good health and work history, but arrives to clinic looking red and bloated.
- She reports heavy drinking over the last 6 weeks, had been sober going to AA for 5 years, never told you of her alcohol Hx
- She says both stresses at work and relationships may have pushed her back to drinking and now she cannot stop.
- She want to get sober and back to AA and her previous good health. Can you help?

TYPICAL ALCOHOL WITHDRAWAL INPATIENT PROTOCOL *EXAMPLE*

- Chlordiazepoxide
- Give 50 mg PRN CIWA-Ar 10 or Greater
 - **continue hourly until CIWA-Ar score < 10**
 - **hold if signs of alcohol or benzodiazepine intoxication**
- Measure CIWA-Ar 1 Hour After Each Dose
 - **and at least Q shift until acute withdrawal resolved**
- *Modify if Needed* for Individual Patients
- Diazepam 10mg, Lorazepam 2mg

- **However ALL Benzodiazepines cause tolerance and withdrawal themselves- thus may create their own WD syndromes- which show up after discharge from “detox” or inpt care-**

- **See rebound Alcohol/BZP WD symptoms in slide 8**

Altered Sleep Physiology in Chronic Alcoholics: reversal with abstinence.

[Williams HL](#) [Rundell OH Jr](#)

Abstract

Somnograms obtained from recently abstinent chronic alcoholics reveal gross disruption succinctly described as "fractured" sleep. **Sleep onset is delayed and the rhythmic properties of the sleep pattern are markedly disturbed with numerous brief arousals and changes of sleep stage.**

Excessive stage 1 and stage rapid eye movement sleep are present while the high voltage slow wave sleep is markedly reduced or absent.

With continued sobriety (9 mo or more) the sleep stage percentages tend to return to normal levels,

but the disruption of the sleep pattern persists after as much as 21 mo of abstinence.

ANTICONVULSANTS FOR ALCOHOL WITHDRAWAL

- Anti-kindling
- GABA Enhancement
- Glutamate Inhibition
- Used More Extensively in Europe
- Recent RCT's in USA may outperform BZP's
- May hold special advantages for Out-pt Detox.

ANTICONVULSANTS AS ALCOHOL DETOXIFICATION AGENTS

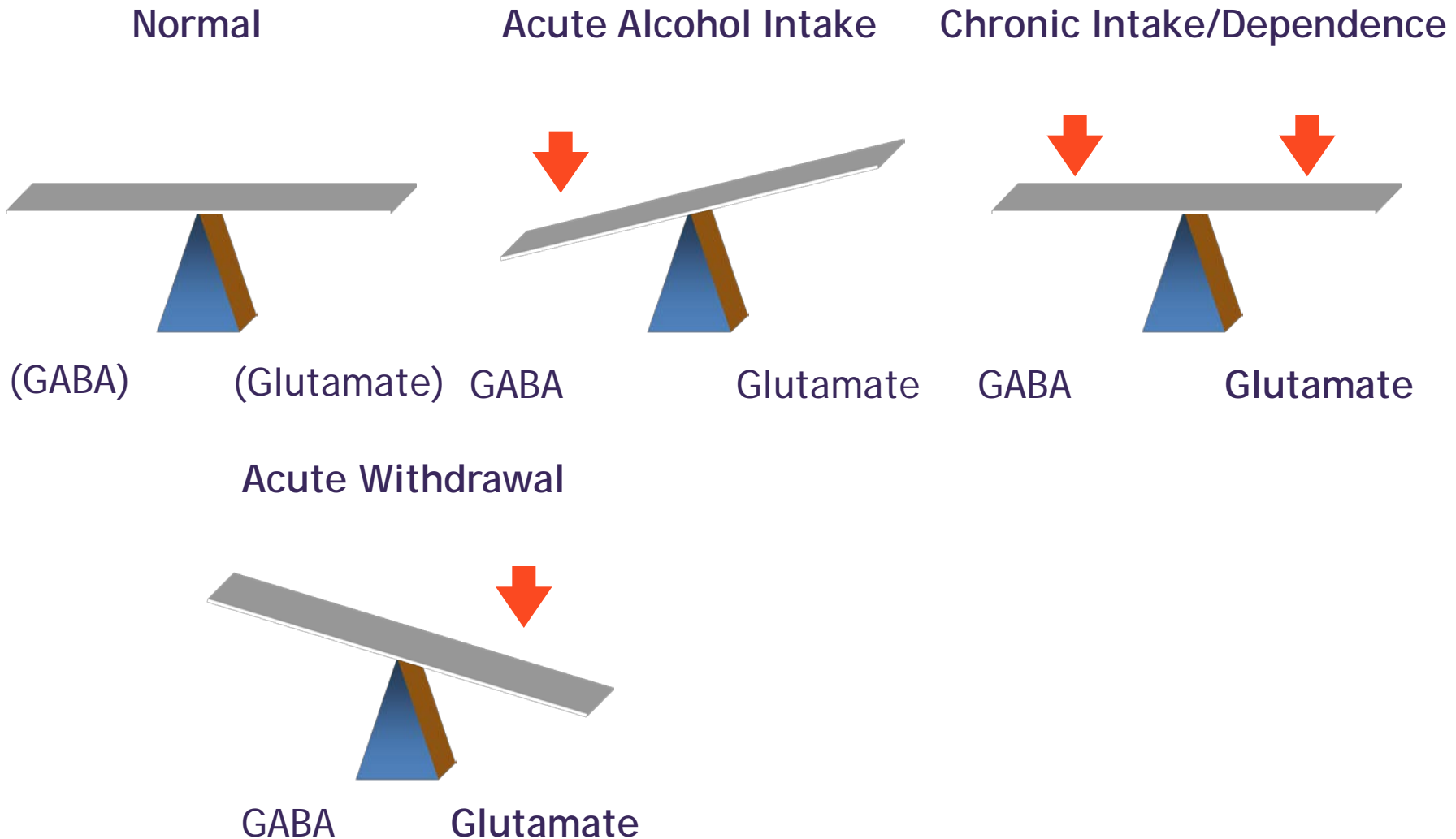
Advantages

- No abuse liability
- Seizure medication
- Neuroprotective
- Cognition
- Extended time Rx

Disadvantages

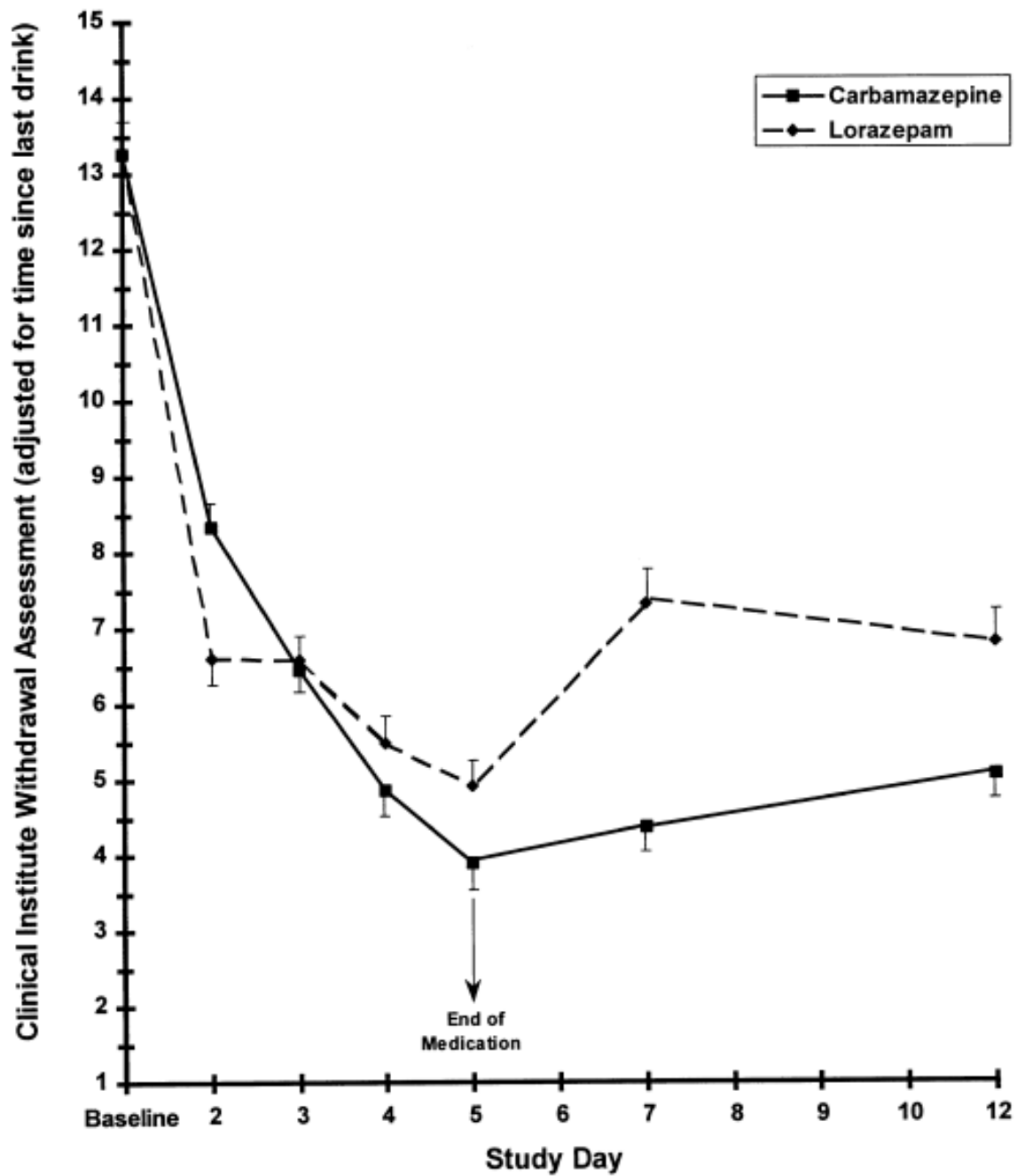
- Limited clinical experience
- Heme side effects
- Liver toxicity (not gabap)
- Confusion (topiramate)
- ? DT role/Acute Sz role ?

EFFECTS OF ALCOHOL ON NEUROCHEMICAL BALANCE



CARBAMAZEPINE

- Carbamazepine
 - 600-800mg/d tapered over 5 days
 - vs. lorazepam 6-8mg/d tapered over 5 d
- Equal Reduction in CIWA-Ar Scores
- Better Sleep, Greater Reduction in Anxiety
 - *(Malcolm et. al, Am J Add, 11:141-50, 2002)*
- Less Rebound, Reduced Alcohol Use
 - *(Malcolm et. al, J Gen Int Med, 17:349-55, 2002)*

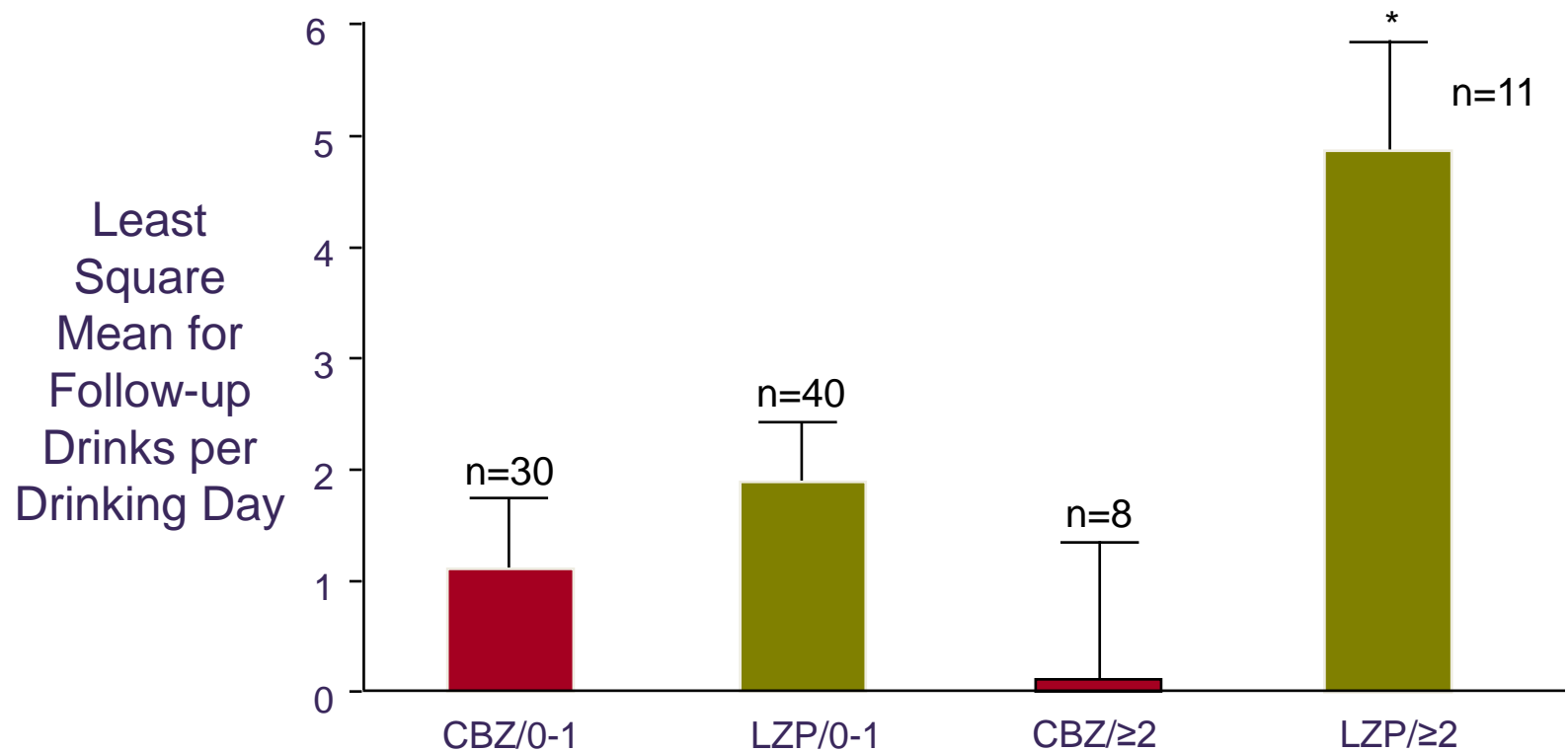


*p=0.007

CARBAMAZEPINE VS. LORAZEPAM IN ALCOHOL WITHDRAWAL

- Double-blind, outpatient trial (n=136)
- CIWA-AR ≥ 10 for inclusion
- 5 day tapering dose
 - CBZ = 600-800 mg/d tapered to 200mg by day 5
 - LZ = 6-8 mg/d tapered to 2 mg by day 5
- Compared single (0-1) vs. multiple (≥ 2) medicated detoxifications

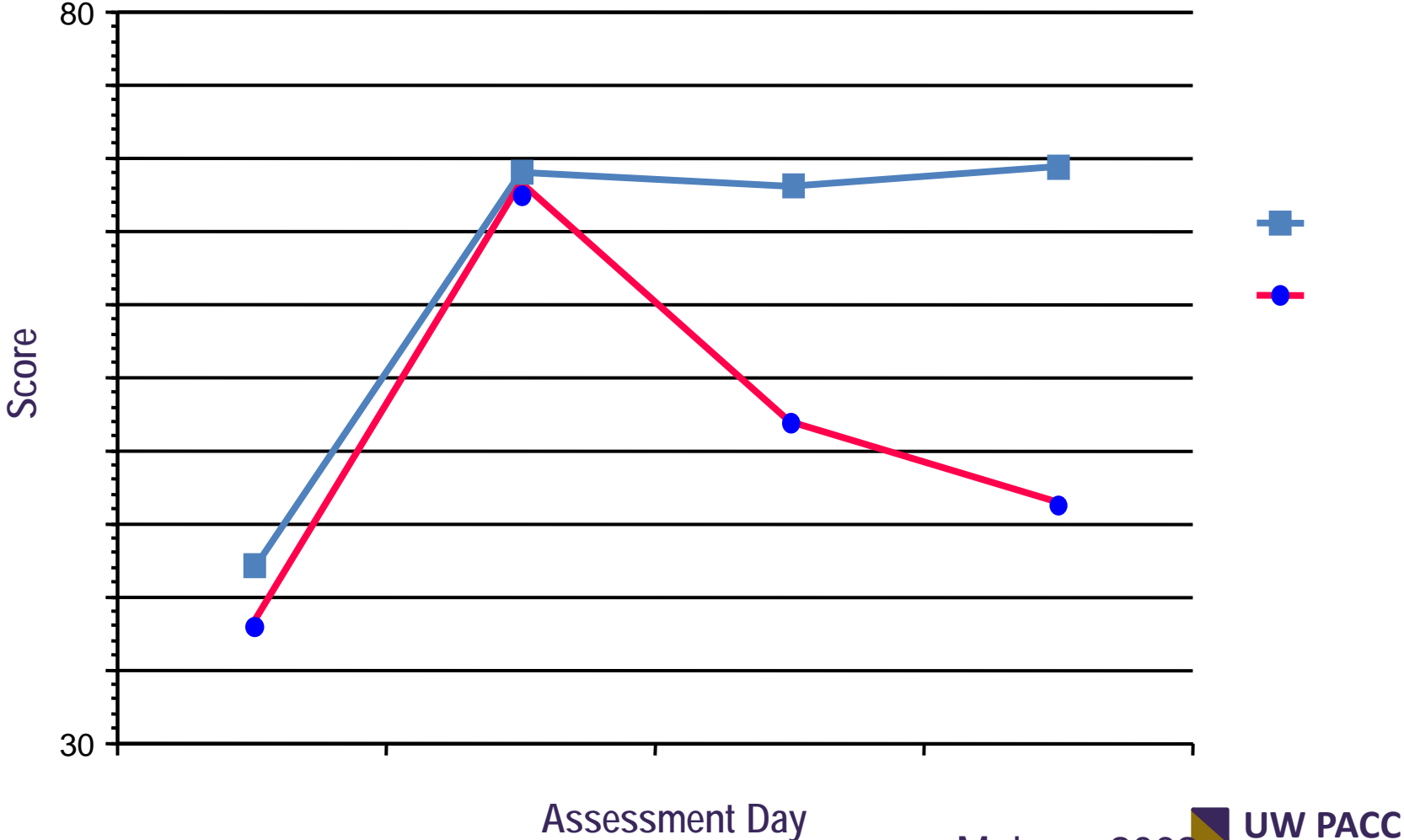
DRINKS PER DRINKING DAY: DAY 6 TO DAY 12 COMPARING DETOX HISTORIES



* Drug main effect, $P=.0032$; Drug x Detox Hx, $P=.0333$.

Malcolm R et al. *J Gen Intern Med.* 2002;17:349-355.

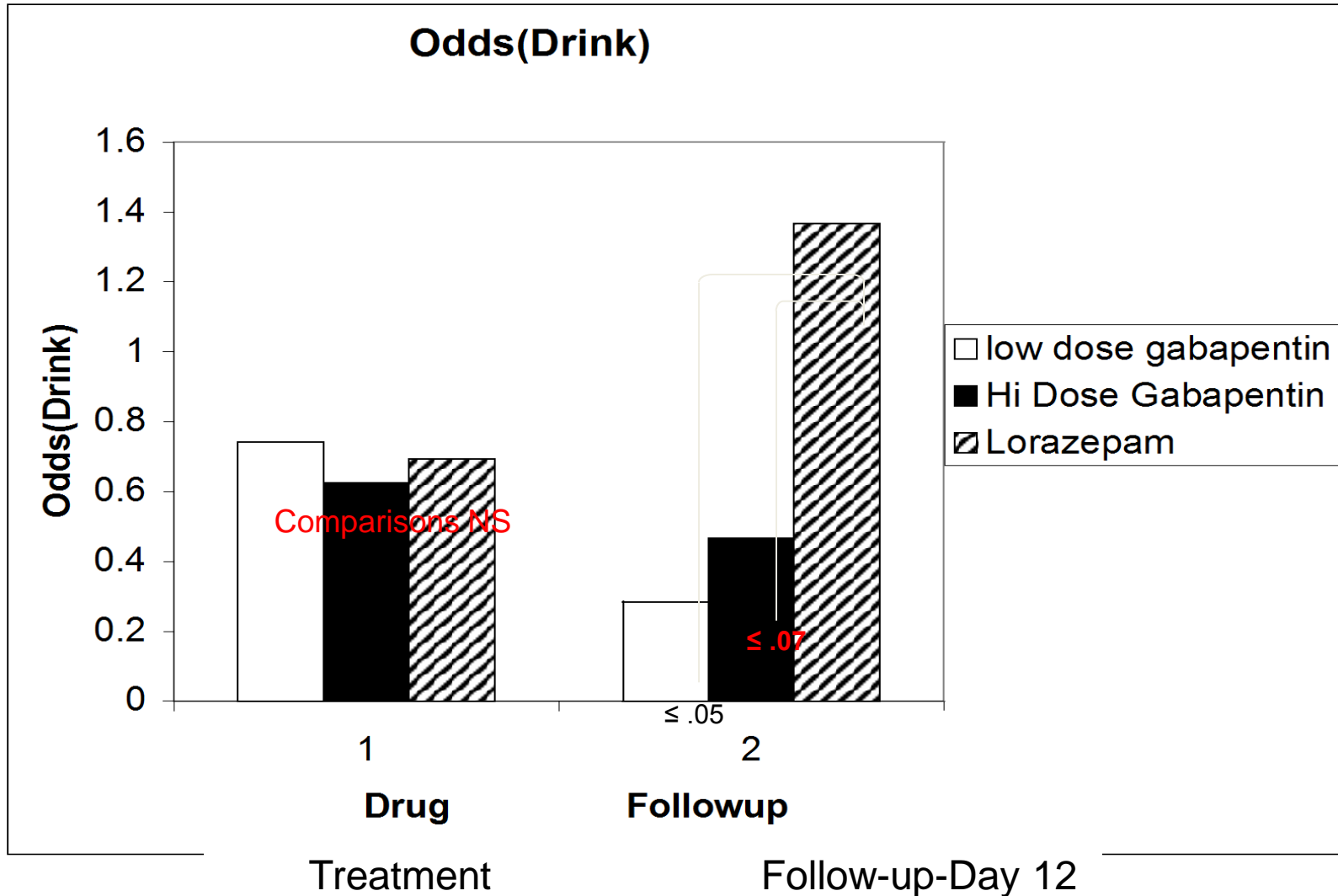
IMPROVEMENT IN SLEEP



GABAPENTIN VS. LORAZEPAM IN ALCOHOL WITHDRAWAL

- Double-blind, outpatient trial (n=101)
- CIWA-AR ≥ 10 for inclusion
- Tapering dose
 - GBP = 900-1200 mg/d tapered over 4 days
 - LZ = 6 mg/d tapered over 4 days
- Acoustic Startle assessed on Days 0, 4, and 7
- Follow-up at Day 7 and 12

DRINKING ODDS



[Am J Psychiatry](#). 2011 Jul;168(7):709-17. Epub 2011 Mar 31.

Gabapentin Combined with Naltrexone for the Treatment of Alcohol Dependence.

[Anton RF](#) [Myrick H](#) [Wright TM](#) [Latham PK](#) [Baros AM](#) [Waid LR](#) [Randall PK](#)

METHOD:

A total of 150 alcohol-dependent individuals were randomly assigned to a 16-week course of naltrexone alone (50 mg/day [N=50]), naltrexone (50 mg/day) with gabapentin (up to 1,200 mg/day [N=50]) added for the first 6 weeks, or double placebo (N=50). All participants received medical management.

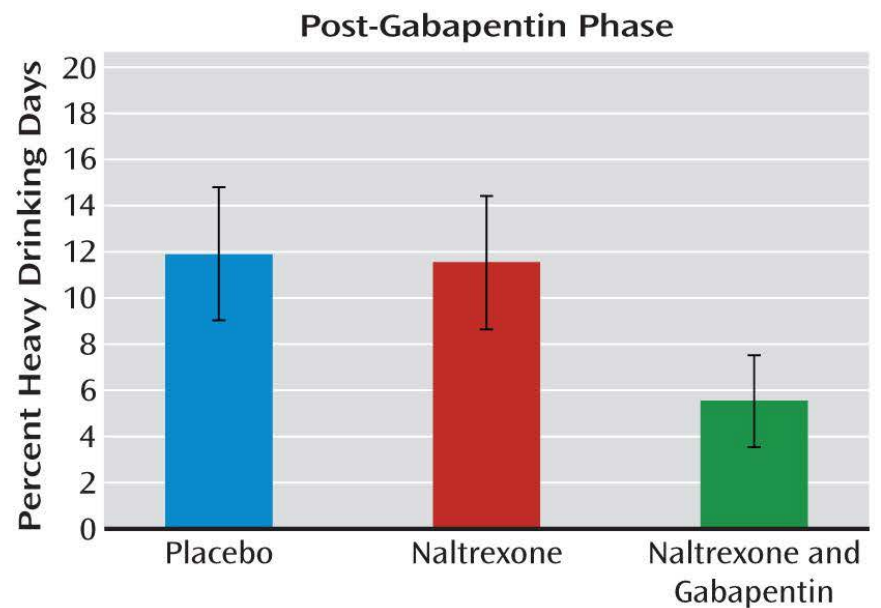
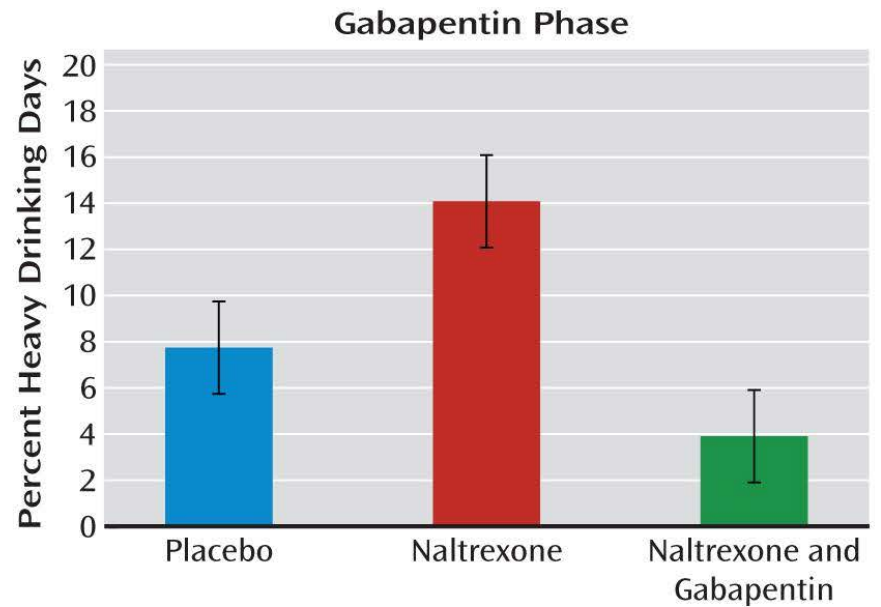
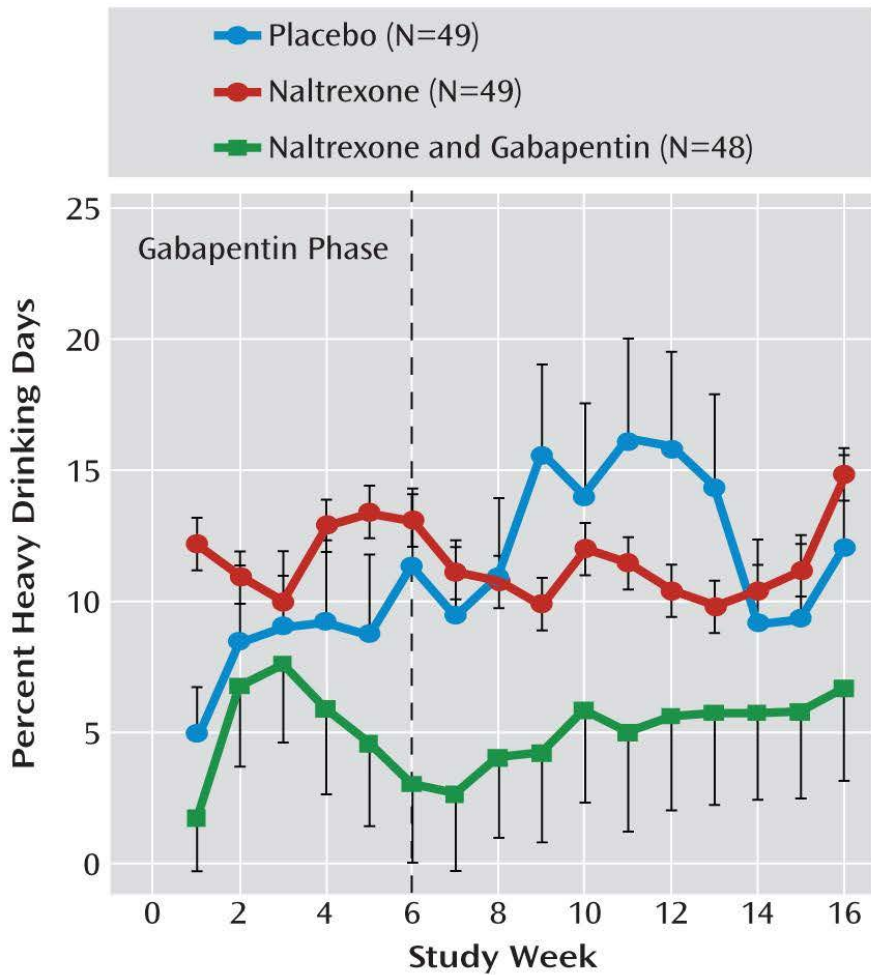
RESULTS:

During the first 6 weeks, the naltrexone-gabapentin group had a longer interval to heavy drinking than the naltrexone-alone group, which had an interval similar to that of the placebo group;

Poor sleep was associated with more drinking in the naltrexone-alone group but not in the naltrexone-gabapentin group, while

a history of alcohol withdrawal was associated with better response in the naltrexone-gabapentin group.

Anton- 2011



Efficacy of Extended-Release Naltrexone in Alcohol-Dependent Patients Who Are Abstinent Before Treatment.

O'malley SS, Garbutt JC, Gastfriend DR, Dong Q, Kranzler HR. *Department of Psychiatry, Yale University

In these patients, all of whom received counseling, the rate of abstinence was severalfold higher for XR-NTX 380 mg compared with placebo:

-time to first drink41 days versus 12 days(P = 0.02)

-continuous abstinence32% versus 11% (P = 0.02).

-time first heavy drinking >180 days vs 20 days; P = 0.04)

-decr days drink/mo..> 90% diff (0.7 vs 7.2; P = 0.005)

ANTICONVULSANTS- “POST ACUTE WITHDRAWAL”

- Alcohol withdrawal physiological symptoms may be abnormal for weeks or months in many individuals
 1. Dexamethasone suppression tests
 2. Abnormal sleep and Sleep EEG's
- Anticonvulsants may be used for weeks or months for ongoing alcohol withdrawal Rx without causing tolerance and dependence
- How to identify which pts need this? (likely repeat WD's and extended detox sx in past (not researched)

Gabapentin Treatment for Alcohol Dependence: A Randomized Clinical Trial.

[Mason BJ](#) [Quello S](#) [Goodell V](#) [Shadan F](#) [Kyle M](#) [Begovic A](#)

Design

12-week, double-blind, placebo-controlled, randomized dose-ranging trial of 150 men and women.

INTERVENTIONS Oral gabapentin (dosages of 0 [placebo], 900 mg, or 1800 mg/d) and concomitant manual-guided counseling.

RESULTS Gabapentin significantly improved the rates of abstinence and no heavy drinking.

Abstinence Rate-

4.1% (95% CI, 1.1%-13.7%) placebo

11.1% (95% CI, 5.2%-22.2%) 900-mg

17.0% (95% CI, 8.9%-30.1%) 1800-mg (P = .04)

[NNT] = 8 for 1800 mg).

[JAMA Intern Med.](#) 2013 Nov 4. doi: 10.1001/jamainternmed.2013.11950 2

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The no heavy drinking rate

22.5% (95% CI, 13.6%-37.2%) placebo group,

29.6% (95% CI, 19.1%-42.8%) 900-mg group,

44.7% (95% CI, 31.4%-58.8%) 1800-mg group (P = .02 NNT = 5).

Similar linear dose related effects for:

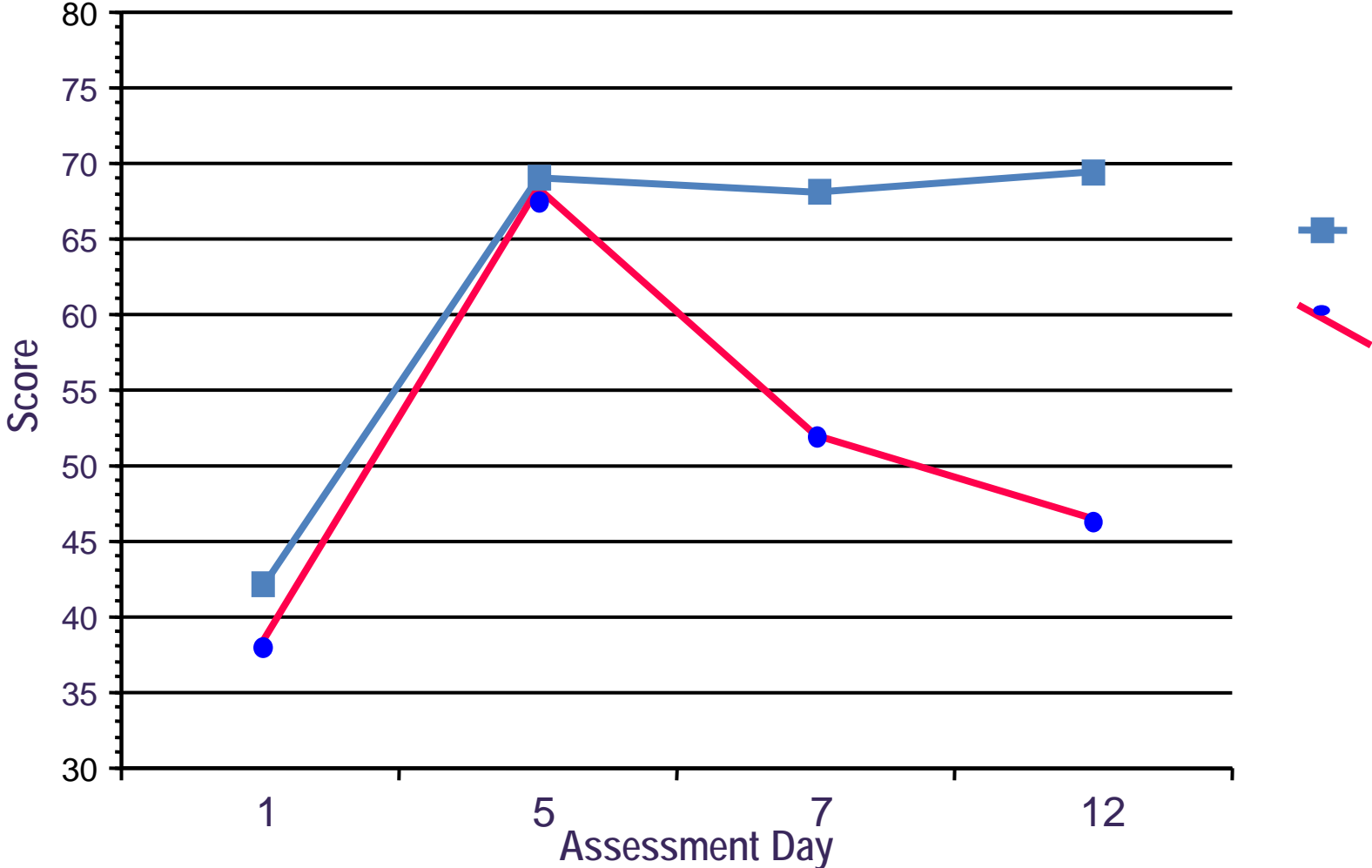
mood (F2 = 7.37; P = .001),

sleep (F2 = 136; P < .001),

craving (F2 = 3.56; P = .03).

No group differences in serious side effects or completion rate (85 of 150 participants)

IMPROVEMENT IN SLEEP



Malcom 2002

MEG--

- Was started on a combination of gabapentin 600 tid, and naltrexone 50 mg a day. Told to call clinic in 2 days to check in
- Had been able to stop drinking and was sleep was better, went to an AA meeting last night
- Told to check in again in 2 days and a clinic apt in a week-
- A week later was sober, felt pretty normal, and vitals and labs were normal. Told the doc she was back to work and had stopped the mid day gabapentin dose due to sedation.

SUMMARY ANTICONVULSANTS IN ALCOHOL WITHDRAWAL

- Mildly Sedative
- Non-Addictive, can be used for weeks/months
- Relatively friendly to REM architecture
- Direct Rx of WD and Post Acute WD for Alc and BZP's
- Certain Pain syndromes (neurogenic pain-Gabapentin/
Cluster headaches
- CBZ, Gabapentin, Depakote, Topiramate
- Enhance Sobriety/Decrease drinking, improve sleep in alcohol recovery-
- May use along with Naltrexone, Antabuse etc.