



Novel Treatments for Cocaine and Opioid Use Disorder

Kyle M. Kampman M.D.

Department of Psychiatry

Perelman School of Medicine

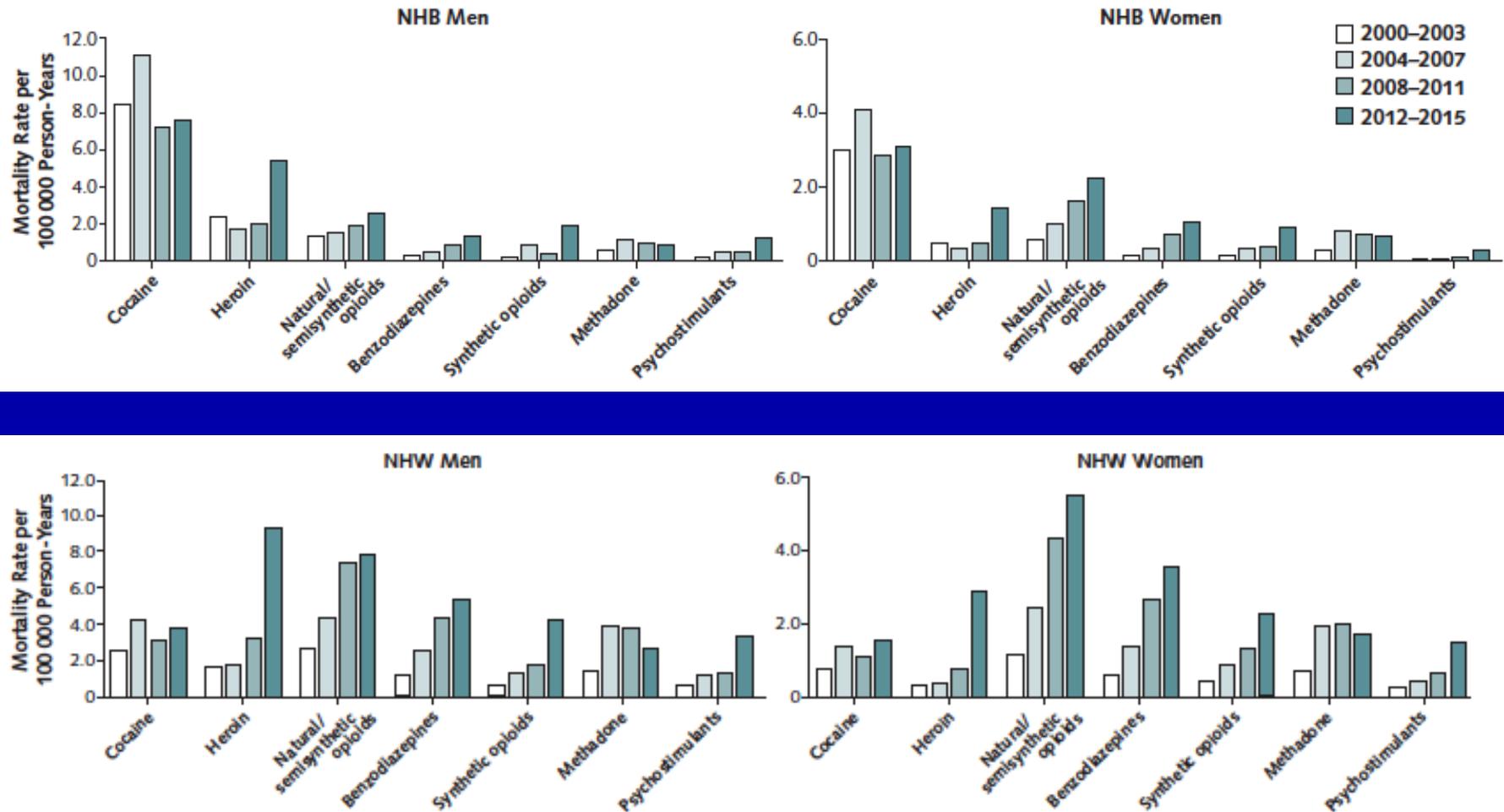
University of Pennsylvania

kampman@pennmedicine.upenn.edu

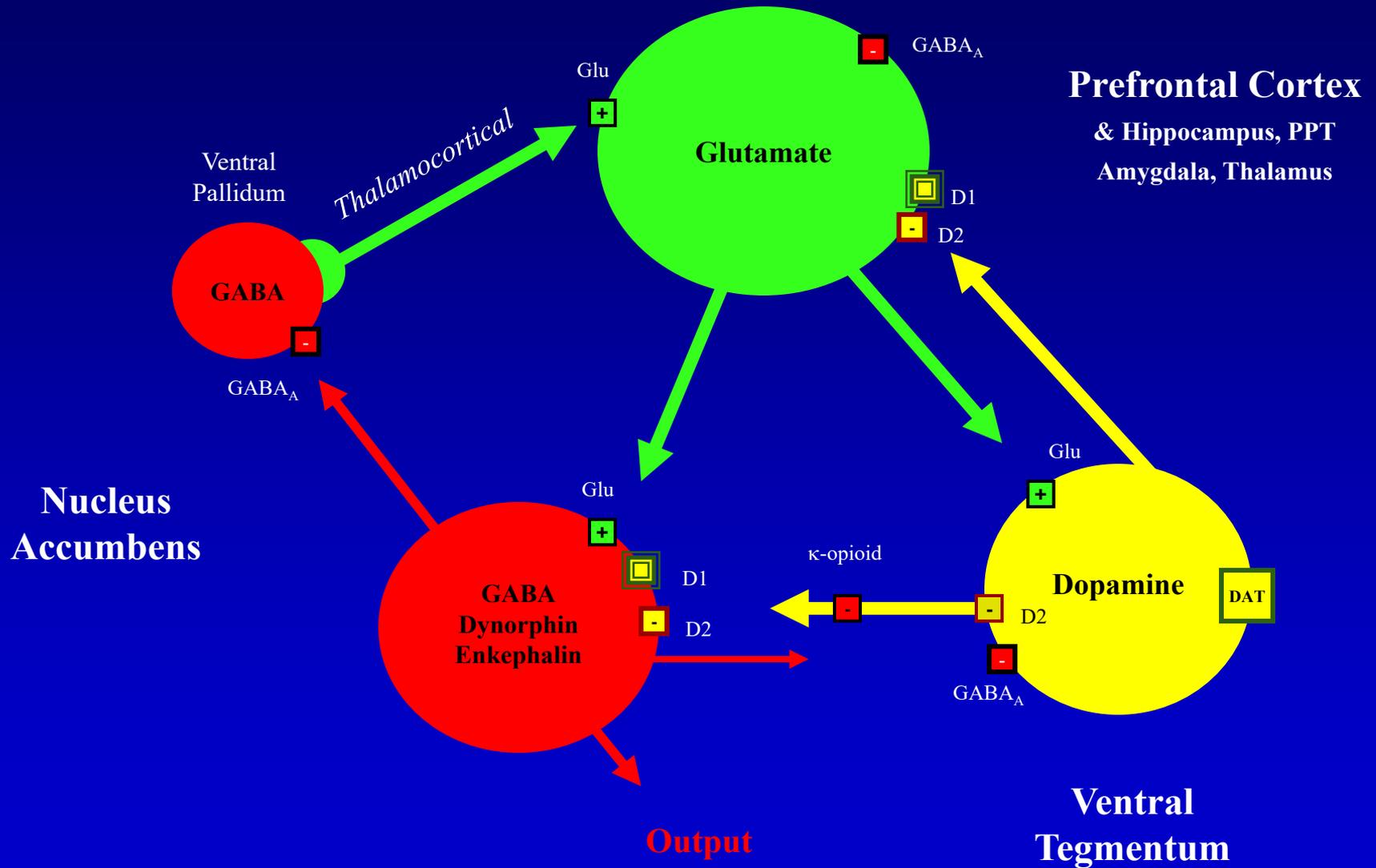
“How about cocaine?”

- Medications for Cocaine Use Disorder
 - A lot of pilot trials / a lot of failure
 - Topiramate +/- amphetamine for CUD
 - Cocaine biomarkers
 - Metyrapone and oxazepam for CUD
- Medications for Opioid Use Disorder
 - Injectables / Implantables
 - Rapid detoxification protocols

Cocaine overdose deaths are common in AAs

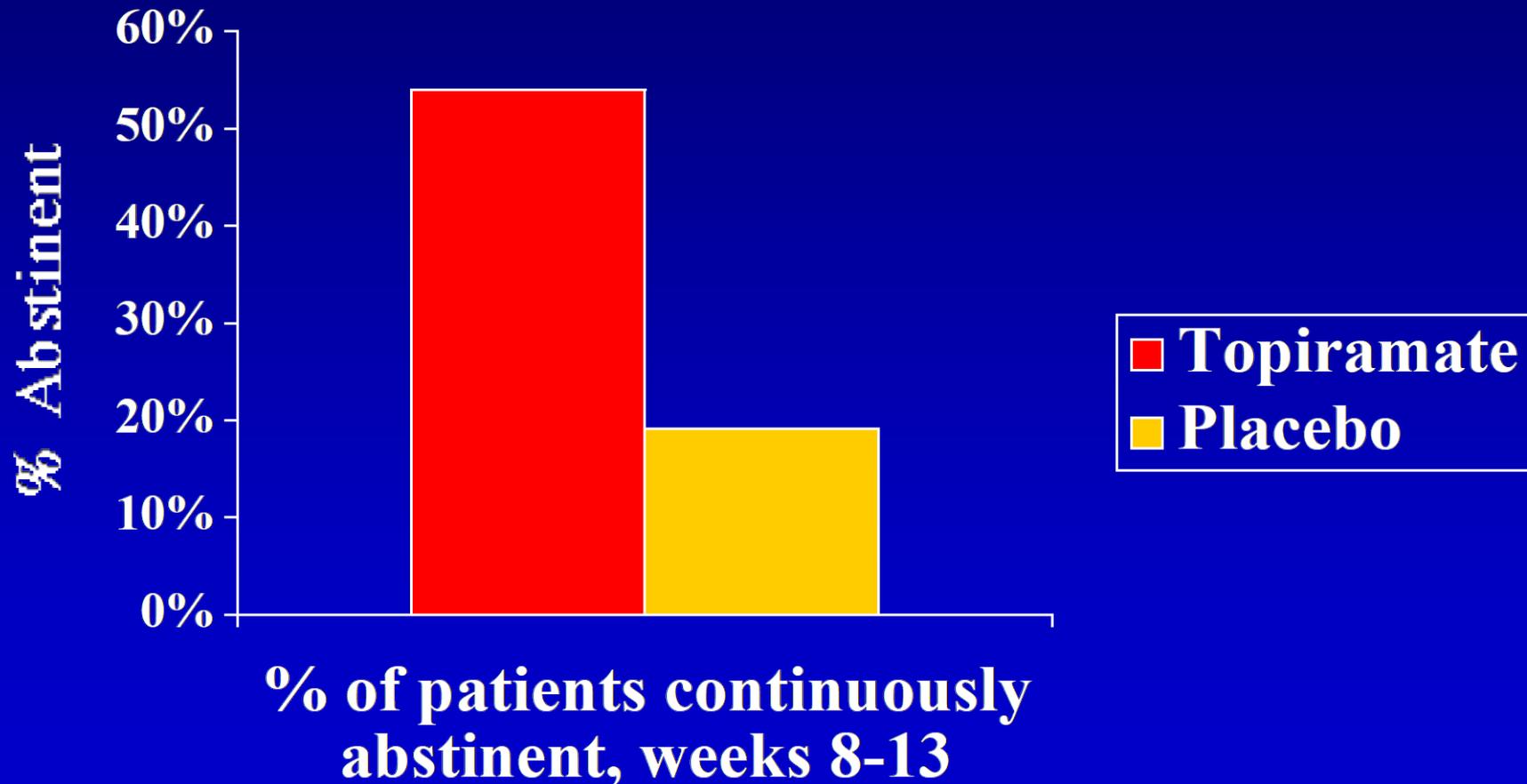


Targets for cocaine meds



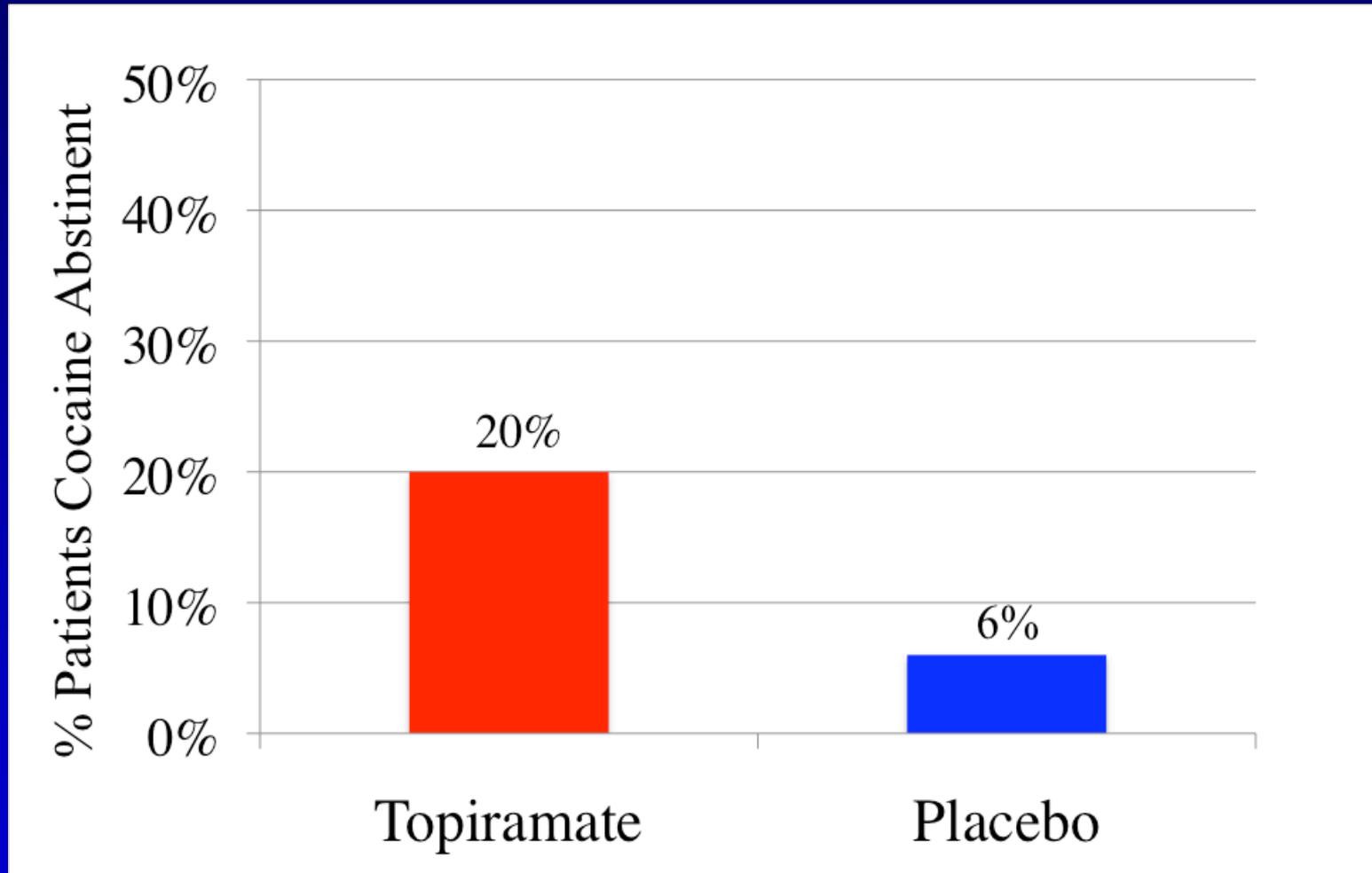
Treatment of cocaine dependence - topiramate

Topiramate is Associated with Cocaine Abstinence

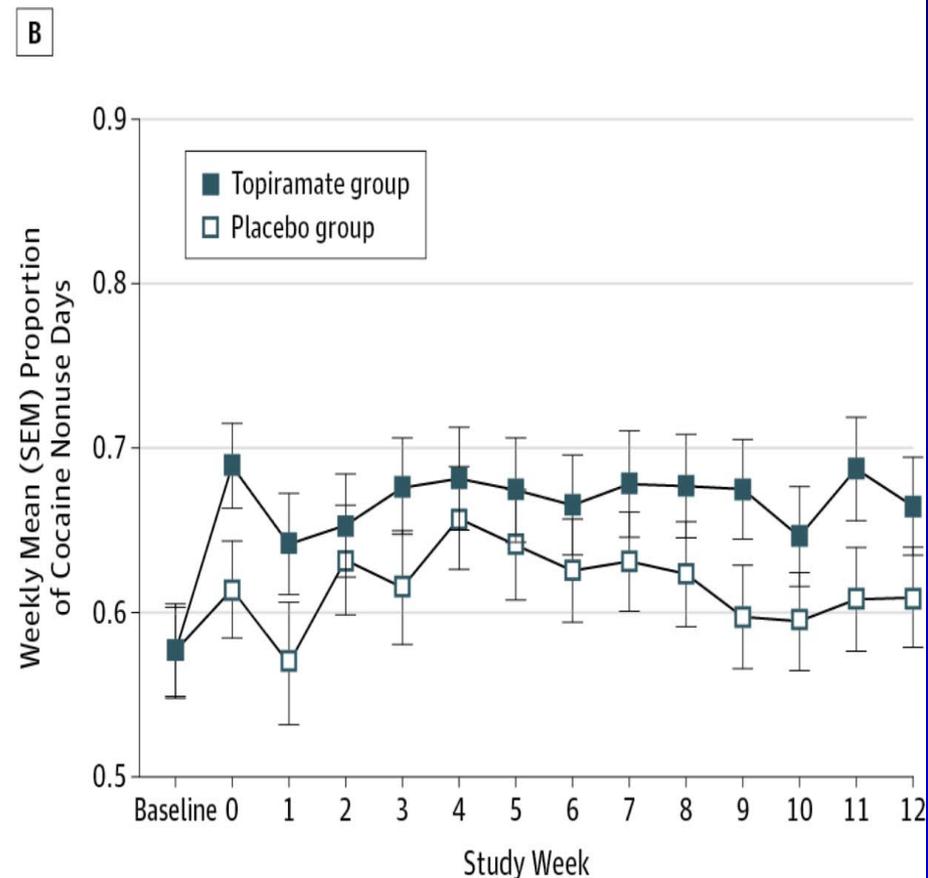
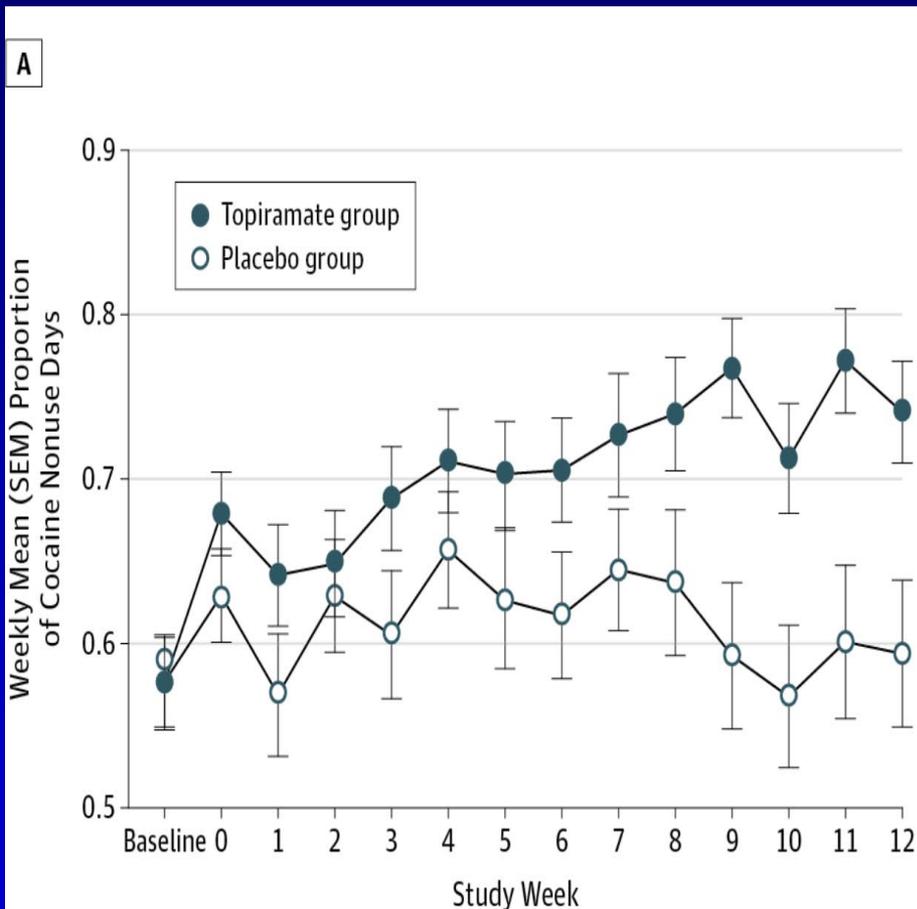


Topiramate for cocaine dependence

Topiramate Associated with Greater End of Trial Abstinence

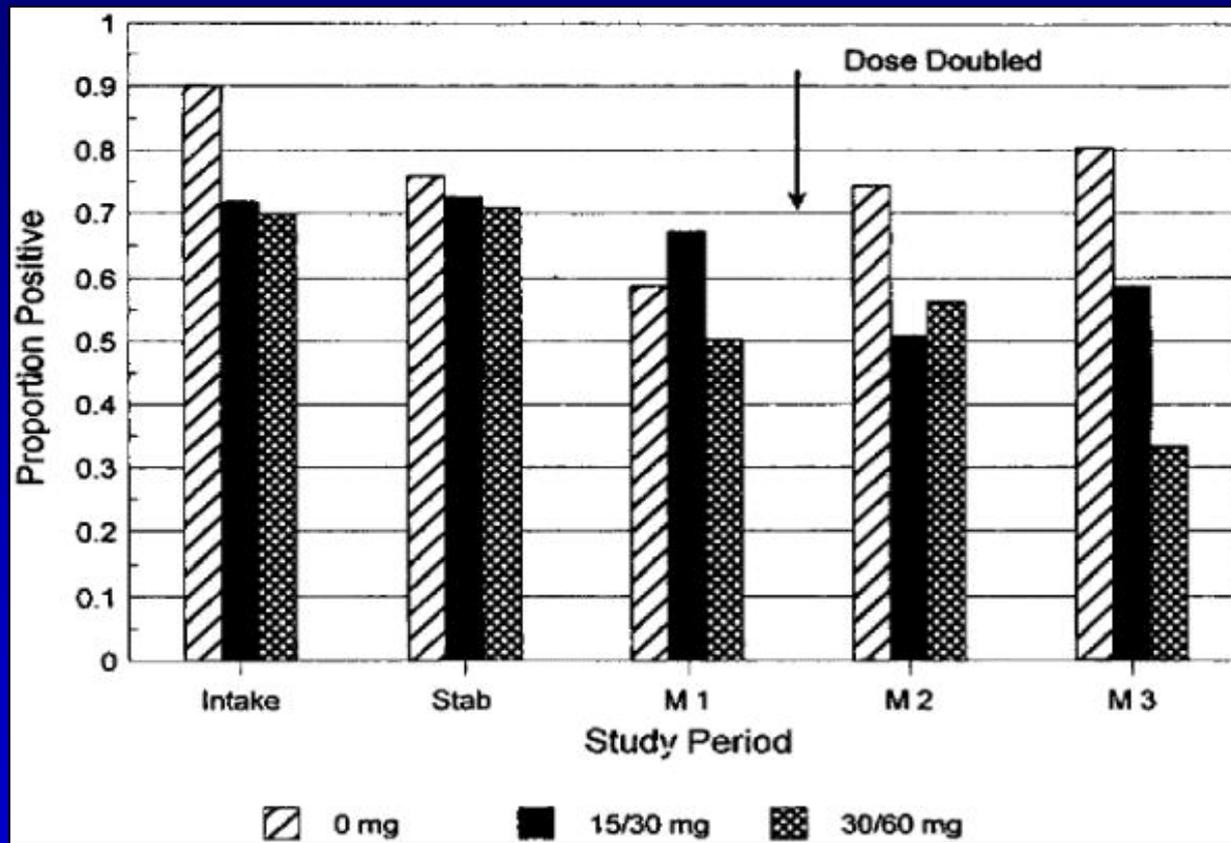


Topiramate Reduced Cocaine Use



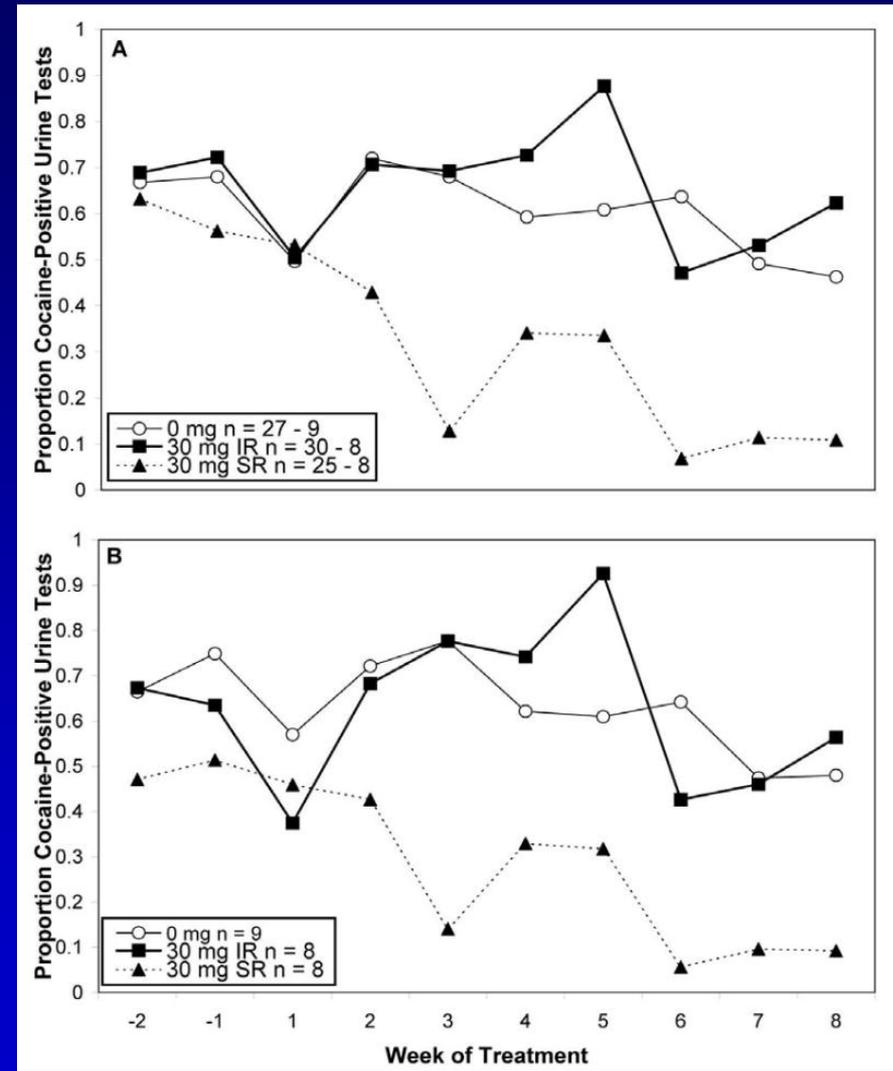
Dopaminergic Medications: Dextroamphetamine

Long-Acting Dextroamphetamine Reduced Cocaine Use



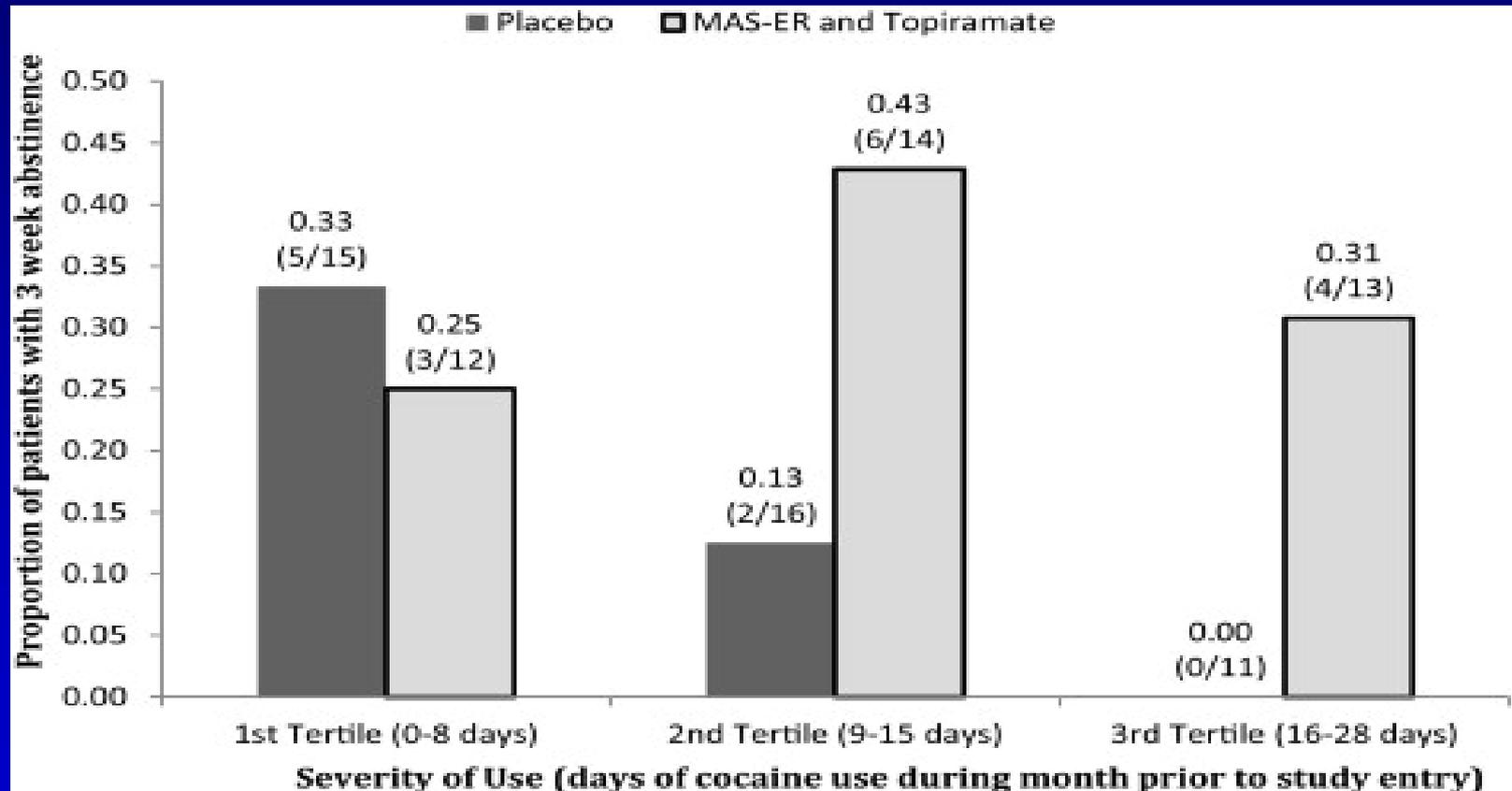
Dopaminergic Medications: Methamphetamine

Long-Acting Methamphetamine
Reduced Cocaine Use



Glutamatergic / Dopaminergic Combinations: MAS + Topiramate

The Combination of MAS and Topiramate Promoted Cocaine Abstinence



Topiramate plus MAS replication

The Combination of MAS and Topiramate Promoted Cocaine Abstinence

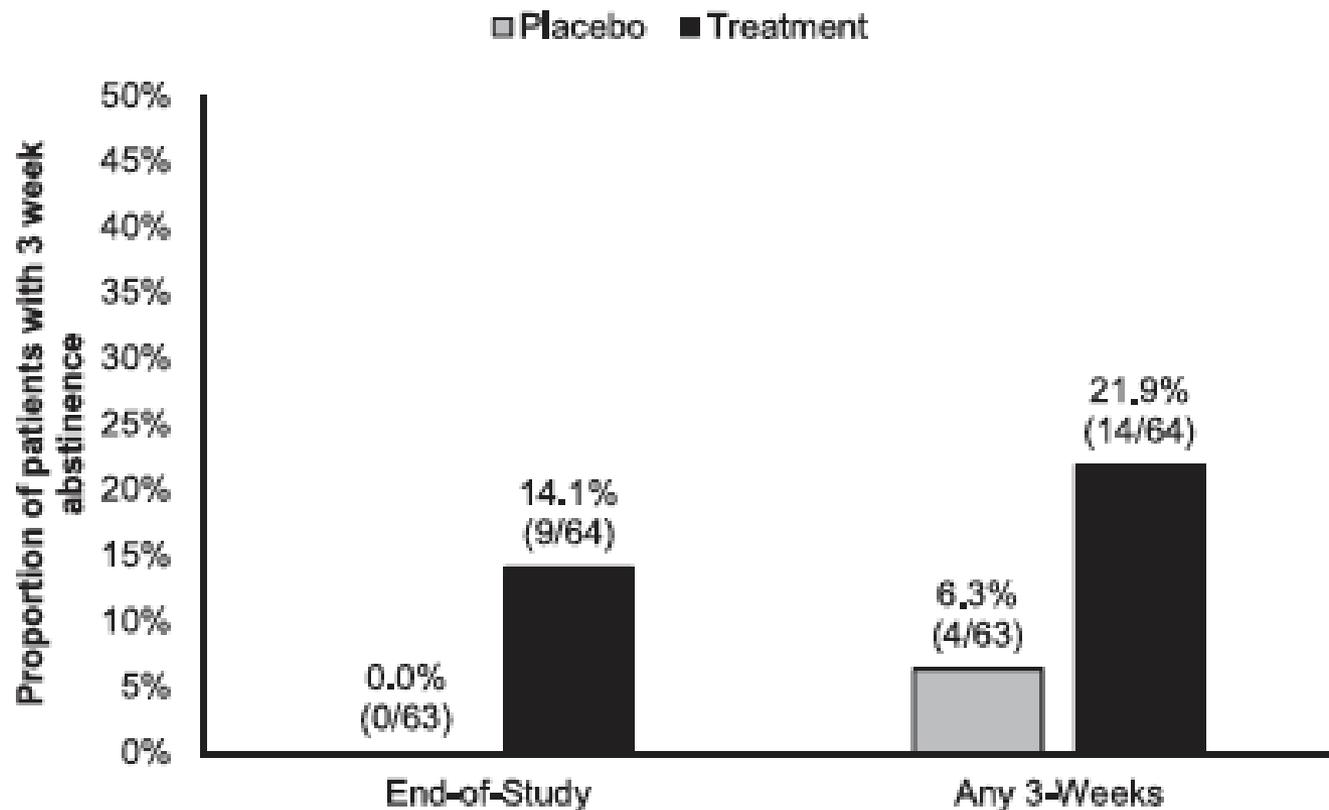


Fig. 2. Proportion of patients achieving 3 weeks of abstinence at end-of-study (primary outcome) and throughout the trial (secondary outcome).

Cocaine Selective Severity Assessment

- It is a measure of cocaine withdrawal
- 18 Item each measured on a 0-7 scale
- Signs and symptoms measured include:

appetite changes

sleep changes

cocaine craving

depressed mood

anxiety

irritability

lethargy

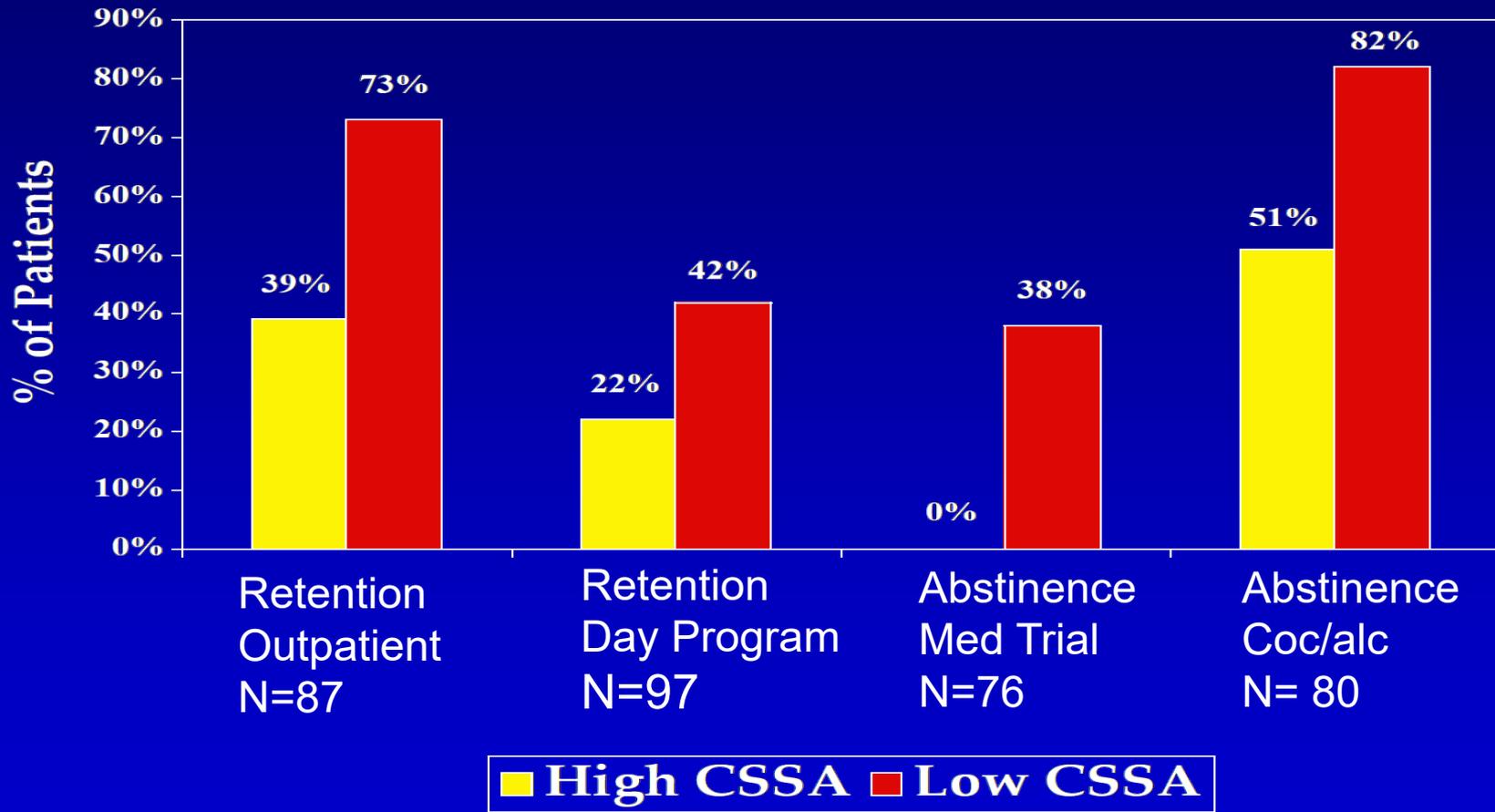
inattention

paranoia

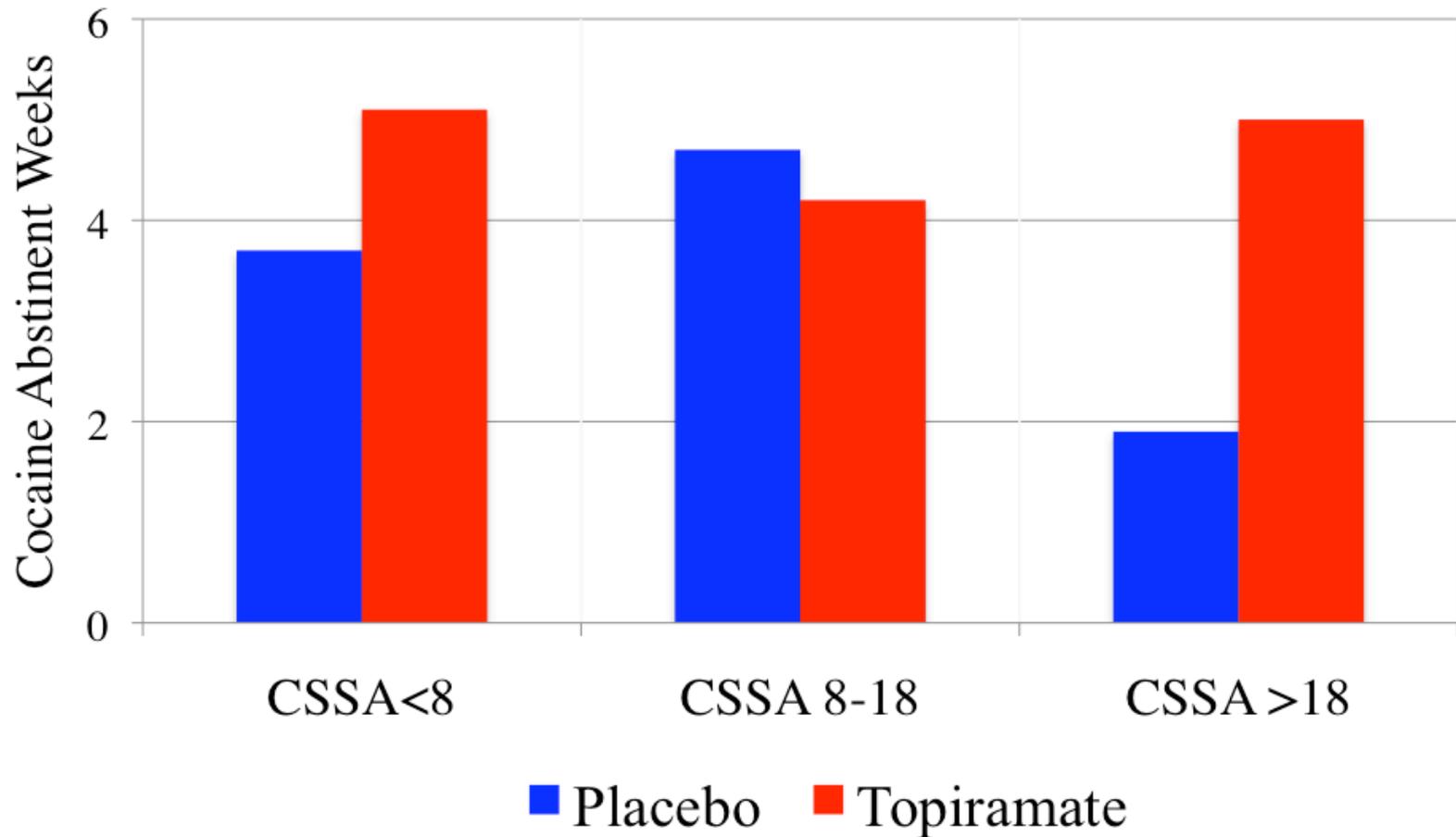
heart rate changes

Cocaine Biomarkers

High CSSA Scores Predict Poor Outcome



CSSA and medication response; topiramate



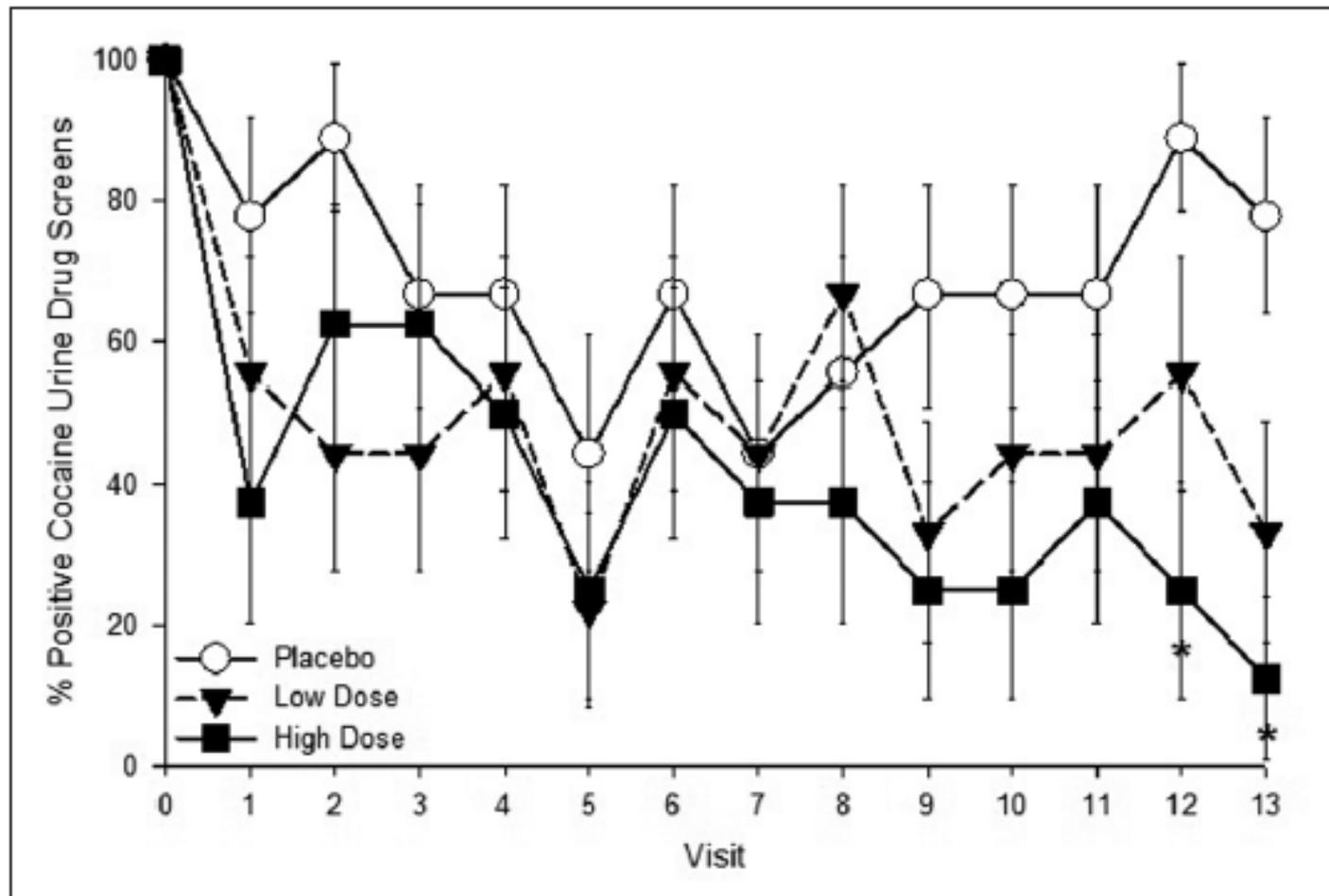


Metyrapone and oxazepam for CUD

Stress relief reduces cocaine self-administration

- Cortisol blocking agents reduce self-administration
- Benzodiazepines reduce self-administration
- Combining meds could allow for lower doses of benzos
- Metyrapone and oxazepam in a single capsule

Metyrapone and oxazepam reduced cocaine use





Metyrapone and oxazepam for CUD

- Multicenter double blind placebo controlled trial
- 80 subjects 4 sites
- 14 week trial
- Metyrapone (720 mg) plus oxazepam (24 mg) in a single capsule
- Twice daily dosing vs. placebo for 12 weeks
- Primary outcome is cocaine abstinence during the last 3 weeks

Pregabalin and lofexidine for opiate withdrawal

XRNT is effective for OUD

- A big problem is getting patients detoxified
- Tapering agonists / partial agonists delays starting XRNT
- Nonnarcotic detoxification meds can speed up the process

Lofexidine is a selective Alpha 2 agonist

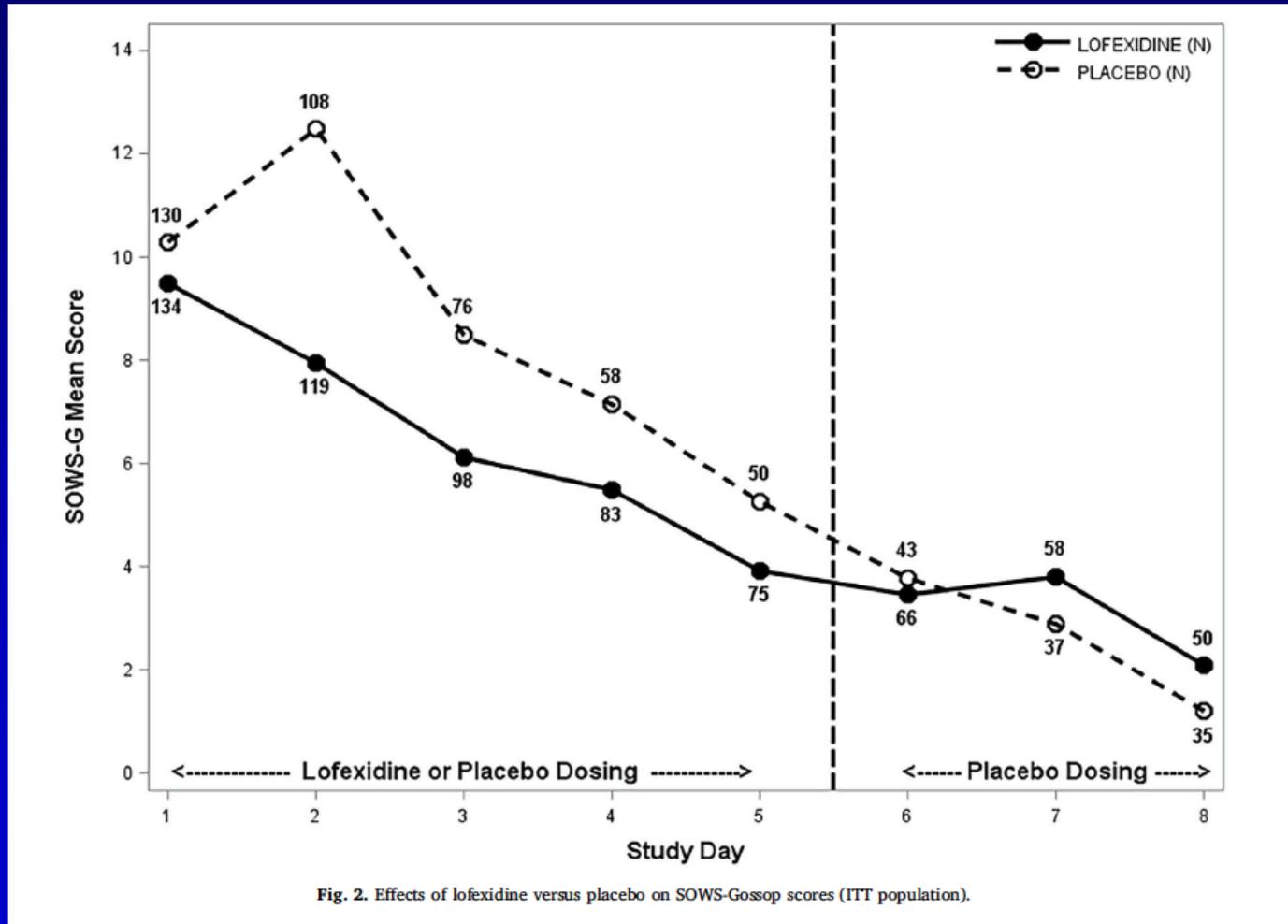
- Reduces withdrawal symptoms less hypotension
- Not as effective for pain and anxiety

Pregabalin

- Pregabalin blocks some calcium channels
- Pregabalin is effective for anxiety and pain

Lofexidine is effective for opiate withdrawal management

Effects of Lofexidine on SOWS –G Scores



Pregabalin was more effective than clonidine for opiate detox

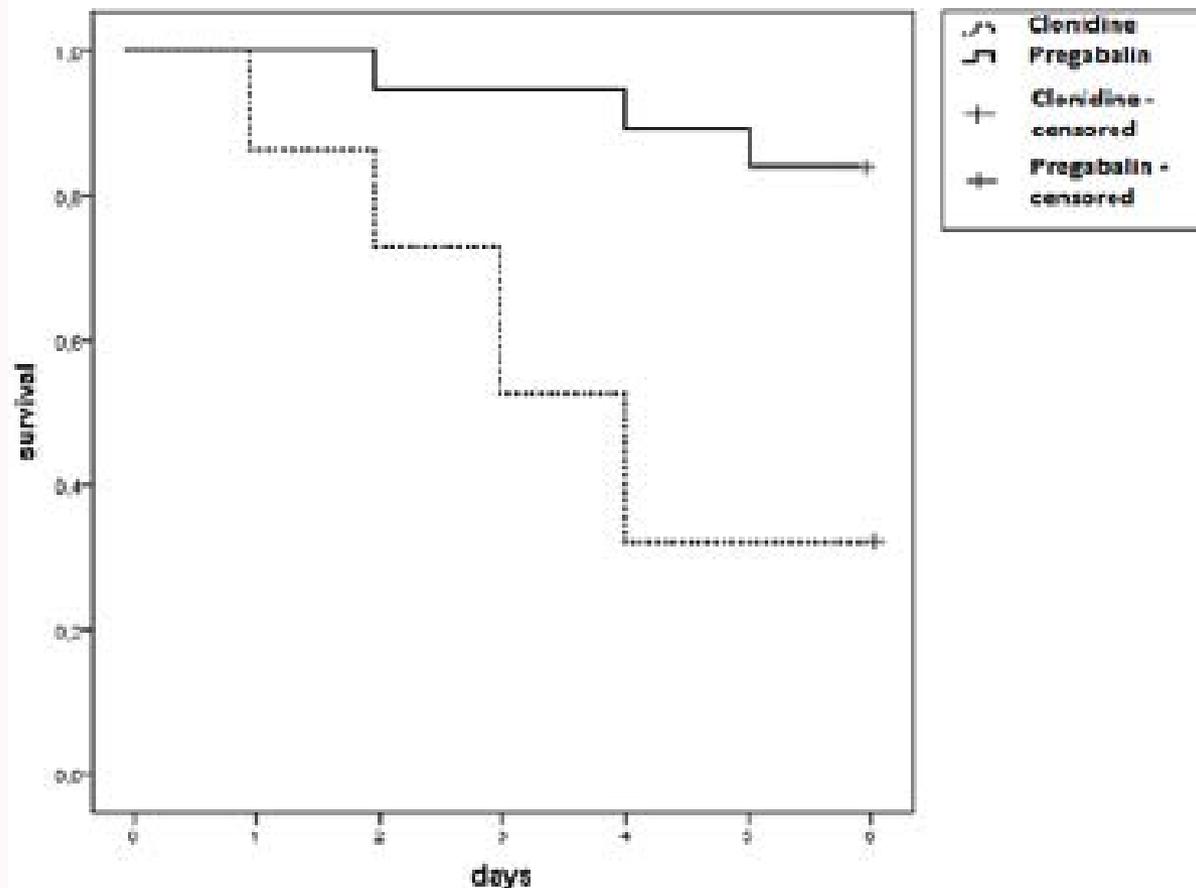


Figure 1: Kaplan-Meier survival analysis. Statistical significance of differences between groups: $p = 0.001$; Log Rank (Mantel-Cox) criterion.

Pregabalin + lofexidine for Opioid Withdrawal

- Inpatient multicenter double blind randomized trial
 - Penn, Columbia, Mountain Manor
 - 90 subjects
- 7 day withdrawal management
 - Pregabalin + lofexidine
 - Placebo pregabalin + lofexidine
- Primary outcome successful detoxification
- Secondary outcome – starting XRNTX



Discussion

- Cocaine is still a significant problem
- Cocaine pharmacotherapy research continues
- Biomarkers may help target appropriate patients
- XRNT efficacy limited by withdrawal management
- Lofexidine and pregabalin may offer a solution