

A Double-Blind, Placebo-Controlled Pilot Trial of Quetiapine for the Treatment of Type A & B Alcoholism

Helen M. Pettinati, PhD

Professor & Treatment Division Director

University of Pennsylvania School of Medicine

Philadelphia, Pennsylvania

USA

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Disclosure of financial relationships with drug companies in past 3 yrs

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- **Consultant:**

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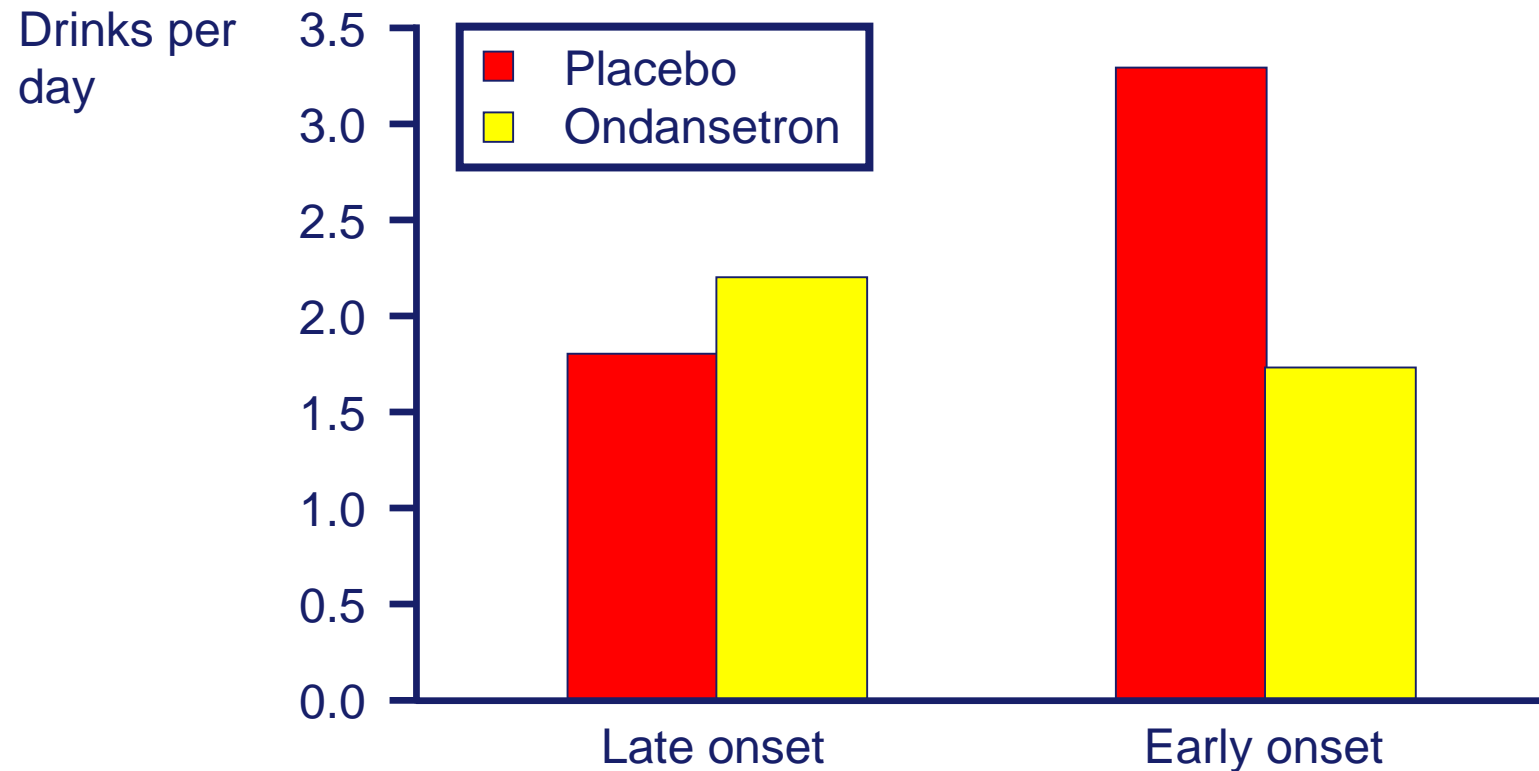
NOTE: Primary support is from NIH funding

Quetiapine for treating alcoholism?

- Preliminary data from comorbid studies have suggested that some of the newer antipsychotic medications may be effective in reducing alcohol craving and excessive drinking
- Quetiapine, one of the atypical antipsychotics, has a unique action that includes a balance of D-2 and 5-HT antagonism, as well as other actions, which may have a positive effect on reducing excessive drinking
- That is...
 - D-2 antagonism has been shown to reduce alcohol craving and reward
 - 5-HT antagonism has been shown to reduce alcohol drinking in harder-to-treat alcoholic subgroups

Ondansetron (5-HT₃ antagonist) for alcohol dependence

Ondansetron reduces drinking in early onset alcoholics^a

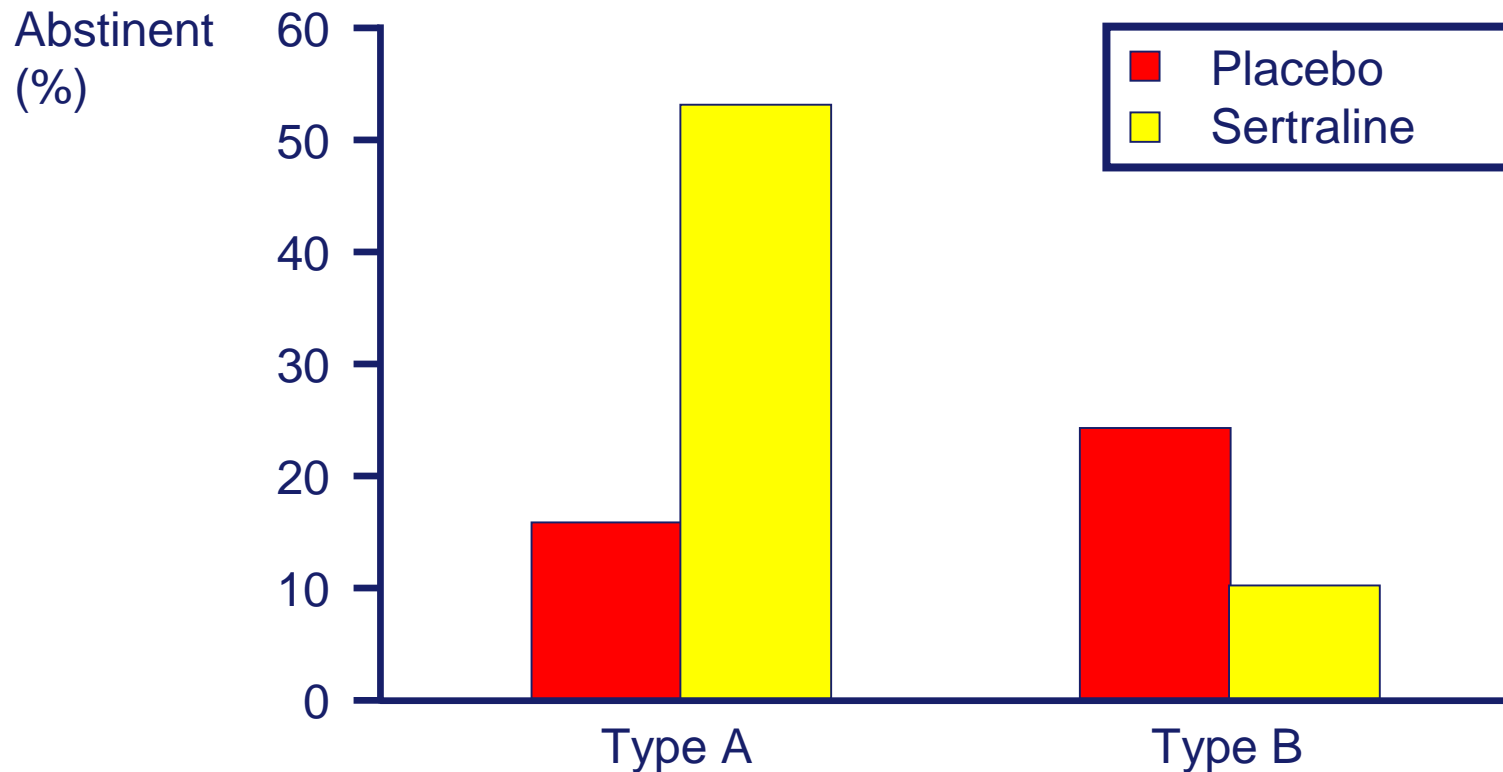


^aProblem drinking earlier than 25 years old

Johnson et al 2000

Sertraline (5-HT reuptake inhibitor) for alcoholism

Sertraline promotes abstinence in type A alcoholics



Type A vs Type B alcohol dependence

TYPE A

Late onset

Few childhood risk factors

Less alcohol-related problems

Less likely sociopathic

Less psychopathology

Less severe dependence

Better outcome

TYPE B

Early onset

Many childhood risk factors

More alcohol-related problems

More likely sociopathic

More psychopathology

More severe dependence

Worse outcome

Quetiapine for treating alcoholism?

University of Pennsylvania's quetiapine pilot study prediction:

order-to-treat alcoholic patients (eg, Type B alcohol-dependent patients) will be successfully treated for alcohol dependence with quetiapine.

this pilot study was published in part in the Journal of Clinical Psychopharmacology, vol. 27 (4), August 2007, pp. 344-351.

Pilot trial: Subject inclusion / exclusion

- **Inclusion**

- Alcohol dependent (SCID)
- Current drinking
- 48 drinks / 30 days in past 90 (40% days drinking) plus two or more days of heavy drinking

- **Exclusion**

- Other drug dependence
- 4.5x normal elevated AST or ALT liver function tests (LFTs)
- Current hepatitis
- Unstable medical or psychiatric illness
- Seizure or head trauma unrelated to alcohol
- Taking other psychotropic medications
- Pregnancy

Distinguishing Type B alcoholics

- **Type B**
 - 12 or more drinks per drinking day for men
 - 10 or more drinks per drinking day for women
- **Plus at least one of the following**
 1. Onset of alcohol dependence before age 25
 2. HAM-D >14 at Week 1
 3. ≥ 3 childhood criteria for ASPD or
Antisocial Personality Disorder

Pilot trial: Study design

Pilot trial for evaluating quetiapine for the treatment of alcohol dependence



Medication groups

- 1. Quetiapine 400 mg at bedtime (N=29)**
- 2. Matching placebo (N=32)**

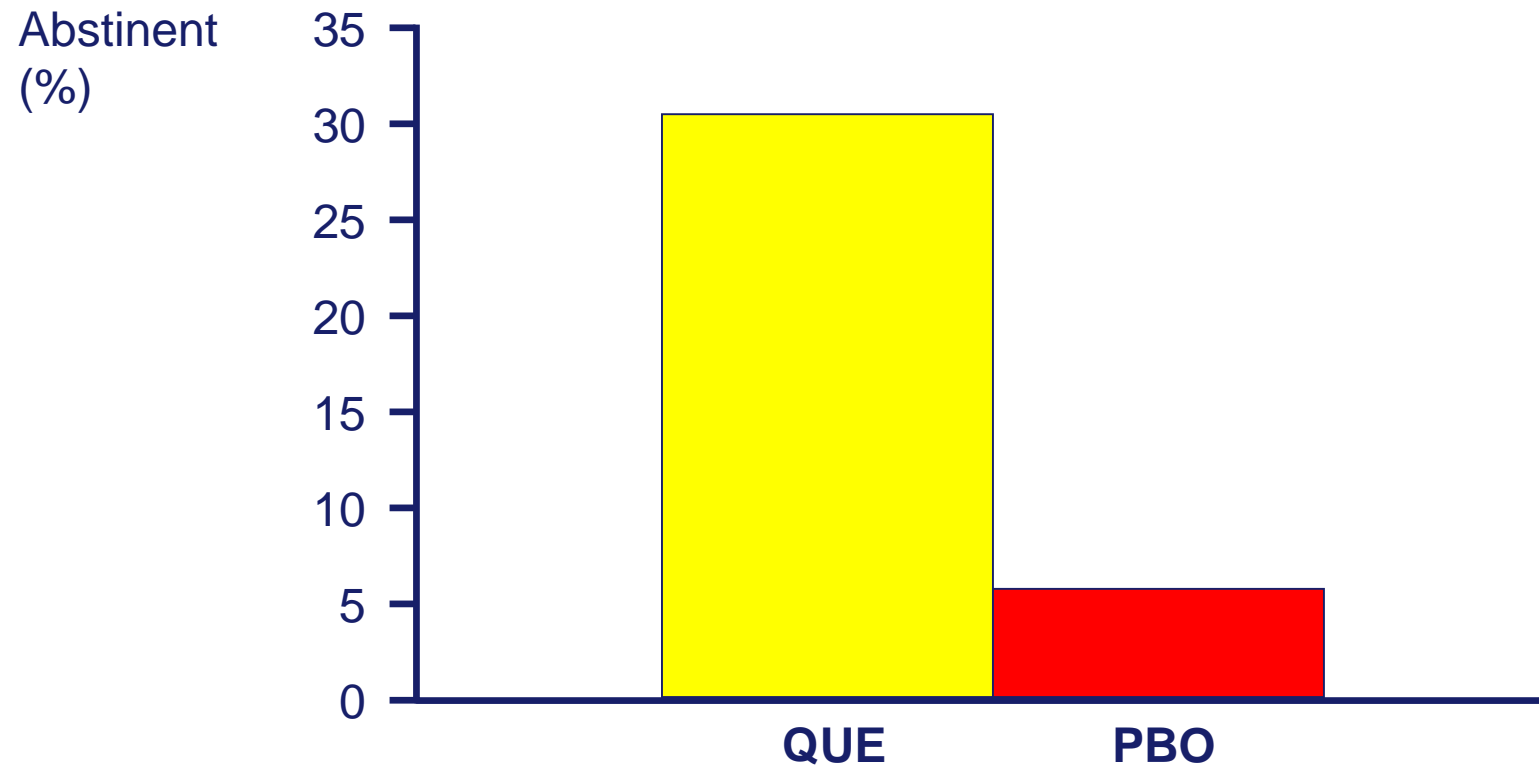
Weekly counseling by medical practitioners

Pilot trial: Outcome measures

- **Efficacy** (timeline follow-back method)
 - Complete abstinence
 - % days of drinking
 - % days of heavy drinking
- **Secondary**
 - Craving (PACS - Penn Alcohol Craving Scale)
 - Depression and anxiety (HAM-A and -D)
- **Safety**
 - Adverse events
 - LFTs

Complete abstinence for two study groups

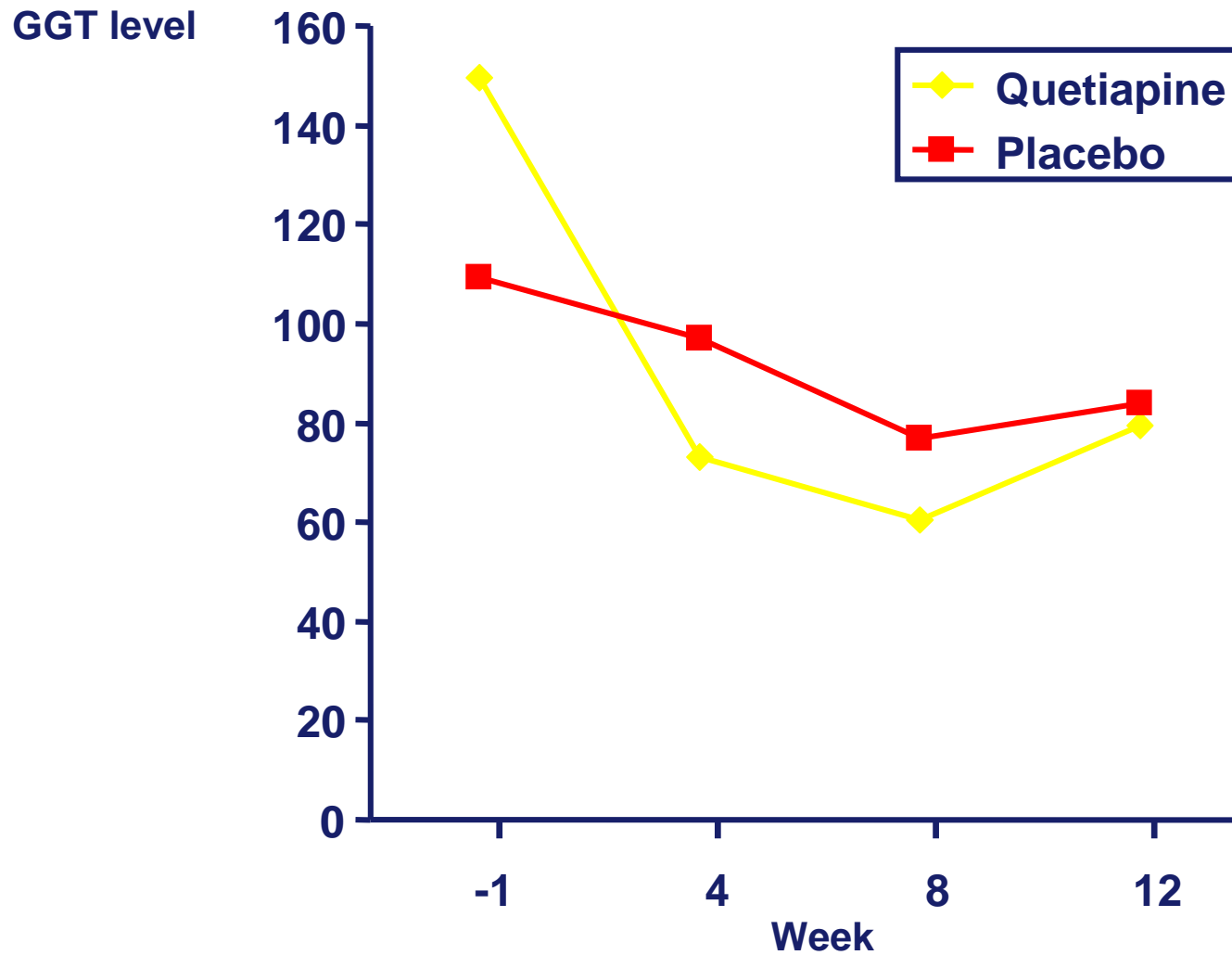
Percent of patients completely abstinent



Adverse events for two study groups

Variable	Quetiapine	Placebo
Aches and pains	45%	56%
Sedation (p<0.01)	52%	19%
GI complaints	41%	37%
Upper respiratory infection	38%	31%
Headache	28%	28%
Dysphoria	31%	22%
Dry mouth (p=0.001)	31%	0%
Light-headedness	17%	12.5%
Insomnia	3.4%	19%
Skin rash	10.3%	3.1%

GGT (gamma-glutamyl transferase levels)



Demographics for four study groups

Variable	Quetiapine A	Placebo A	Quetiapine B	Placebo B
Patients (n)	16	17	13	15
Mean age, years	47	52	46	43
Male (%)	62%	76%	85%	87%
Race (% Caucasian)	38%	59%	46%	73%
Years of education, mean	13.9	14.6	12.8	13.7
Employed (%)	81%	88%	100%	93%

Note: the mean is shown for continuous variables

Pre-tx alcohol & psychiatric severity

Variable	Quetiapine A	Placebo A	Quetiapine B	Placebo B
Days of drinking in past 30 days (%)	76%	84%	77%	70%
Days of heavy drinking in past 30 days (%)	69%	76%	75%	70%
Drinks / drinking day in past 30 days, mean	13	10	22	19
ASI alcohol, mean	0.61	0.63	0.67	0.67
HAM-A, mean	3	4	5	8
HAM-D, mean	4	7	7	10

Note: the mean is shown for continuous variables

ASI alcohol = mean composite score for the alcohol subscale of the Addiction Severity Index

Treatment retention for four study groups

Mean number of counseling visits attended (of 12)

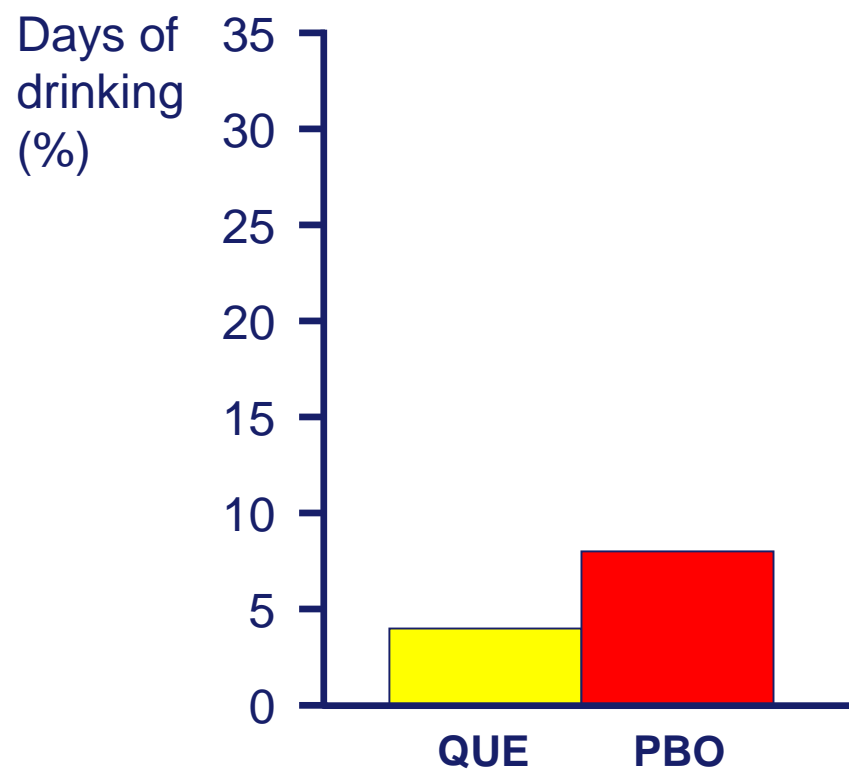
Quetiapine A	Placebo A	Quetiapine B	Placebo B
10 visits	10 visits	9 visits	6 visits

There was no significant interaction in patient attendance at counseling visits for medication group by alcohol subtype

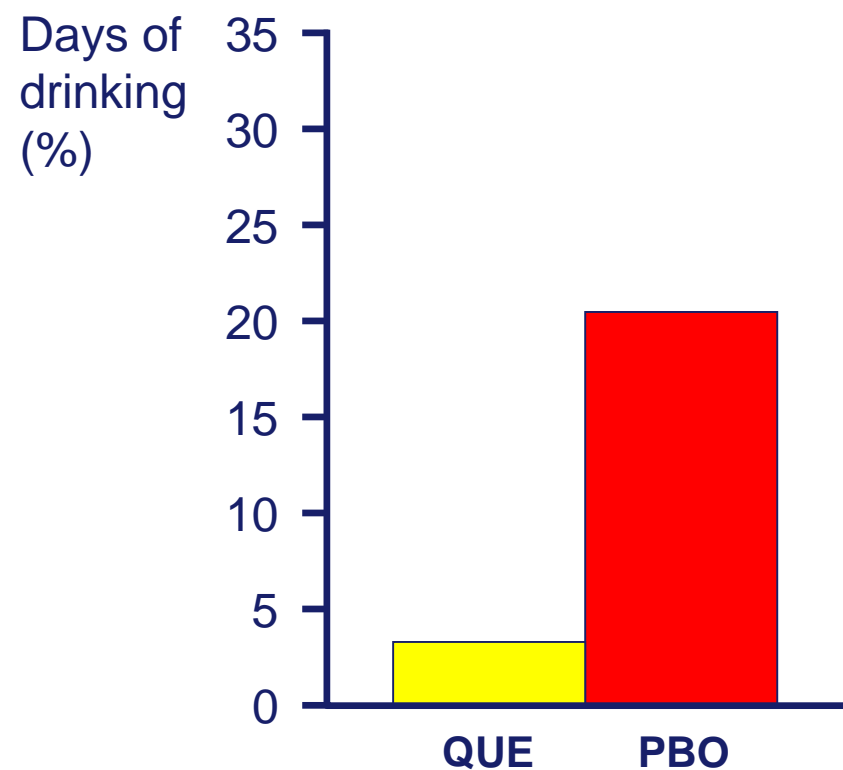
Days of drinking while in treatment

Percent days of any drinking

Type A patients

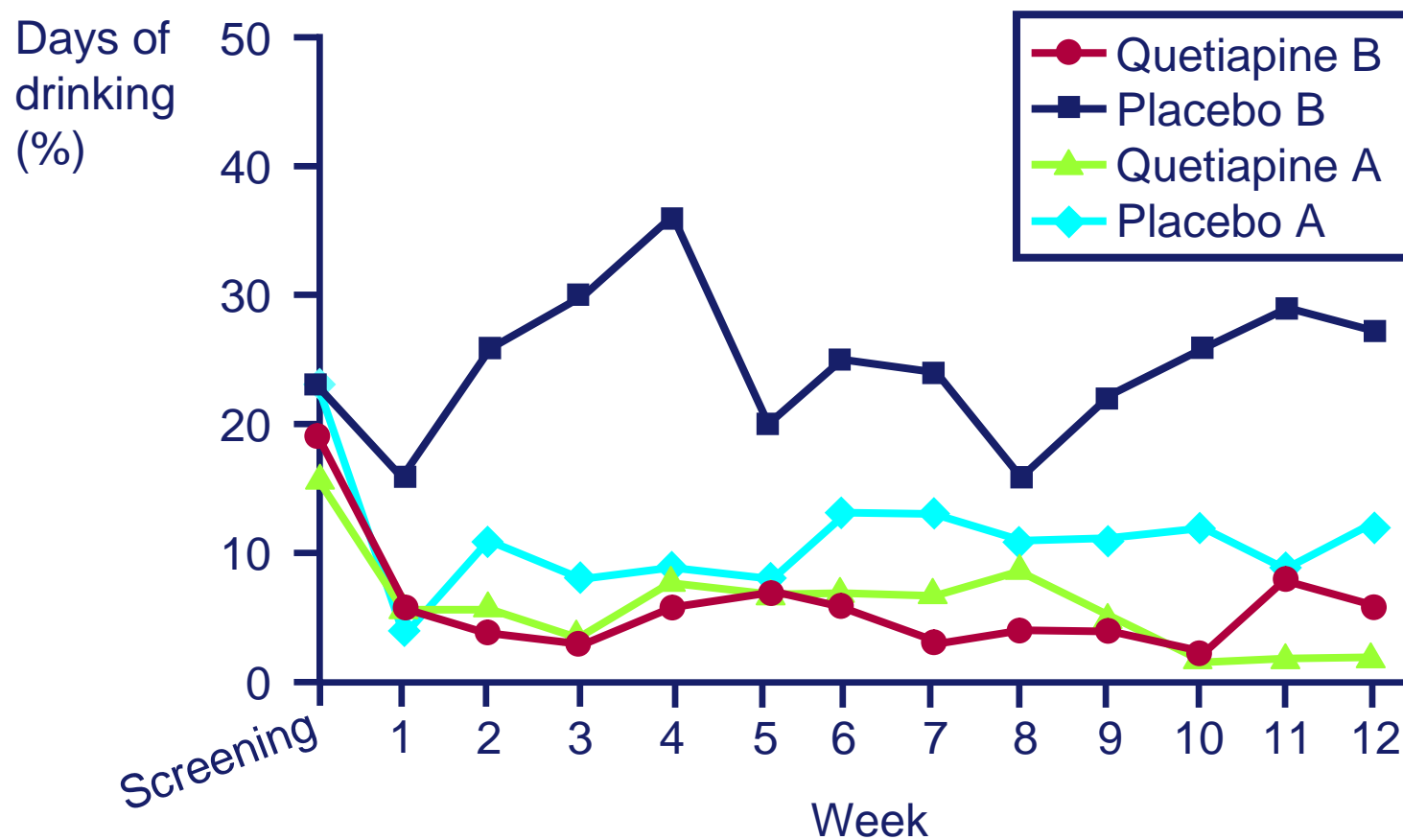


Type B patients



Days of drinking while in treatment

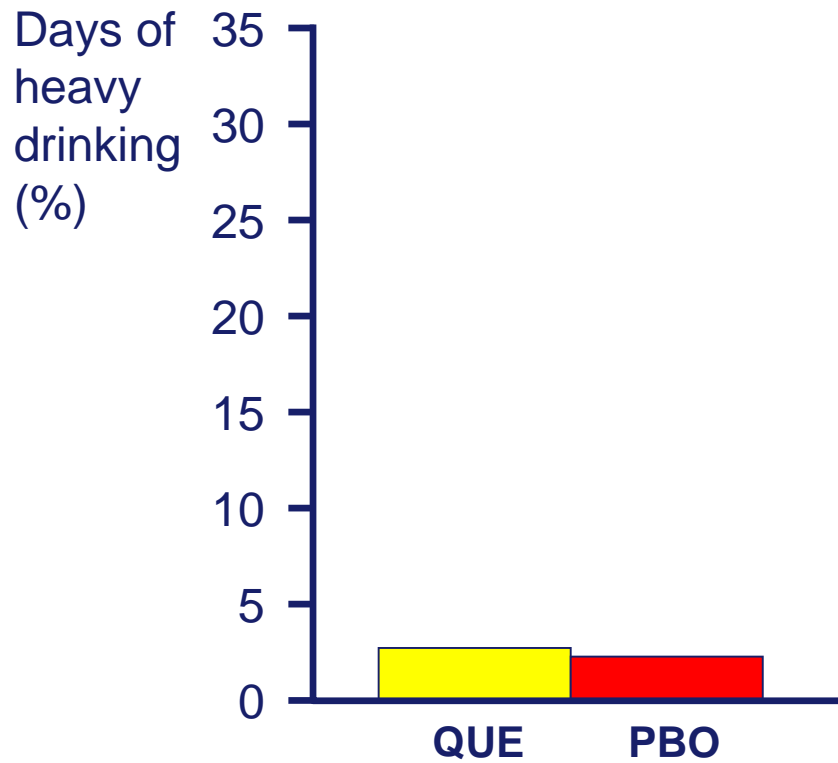
Percent days of drinking by week



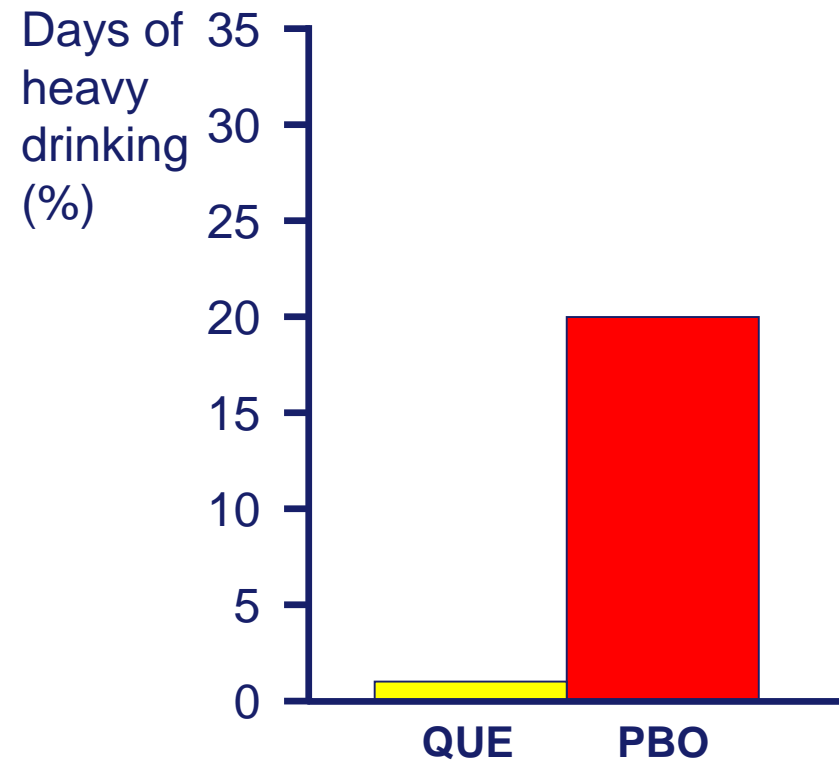
Days of heavy drinking while in treatment

Percent days of heavy drinking

Type A patients

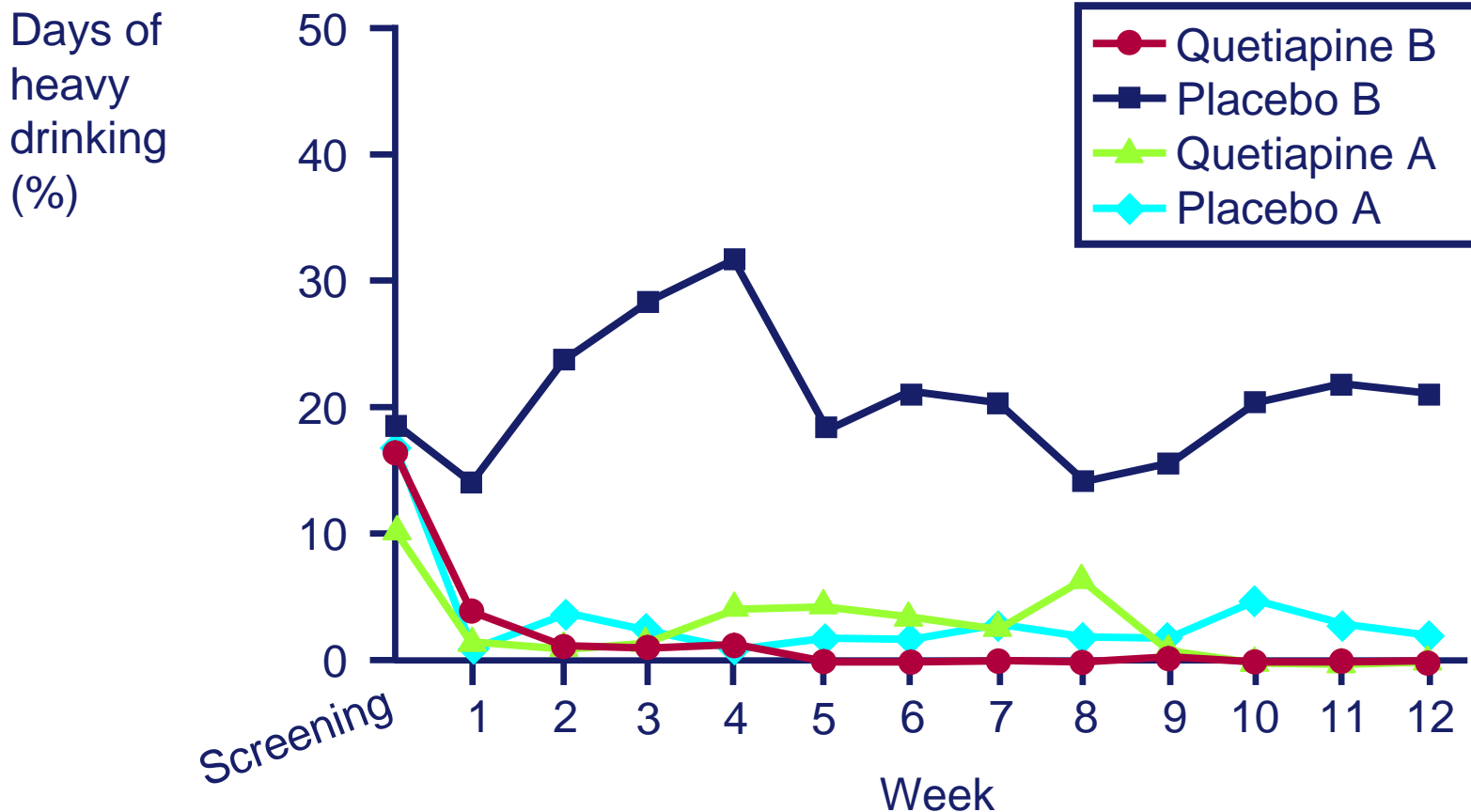


Type B patients



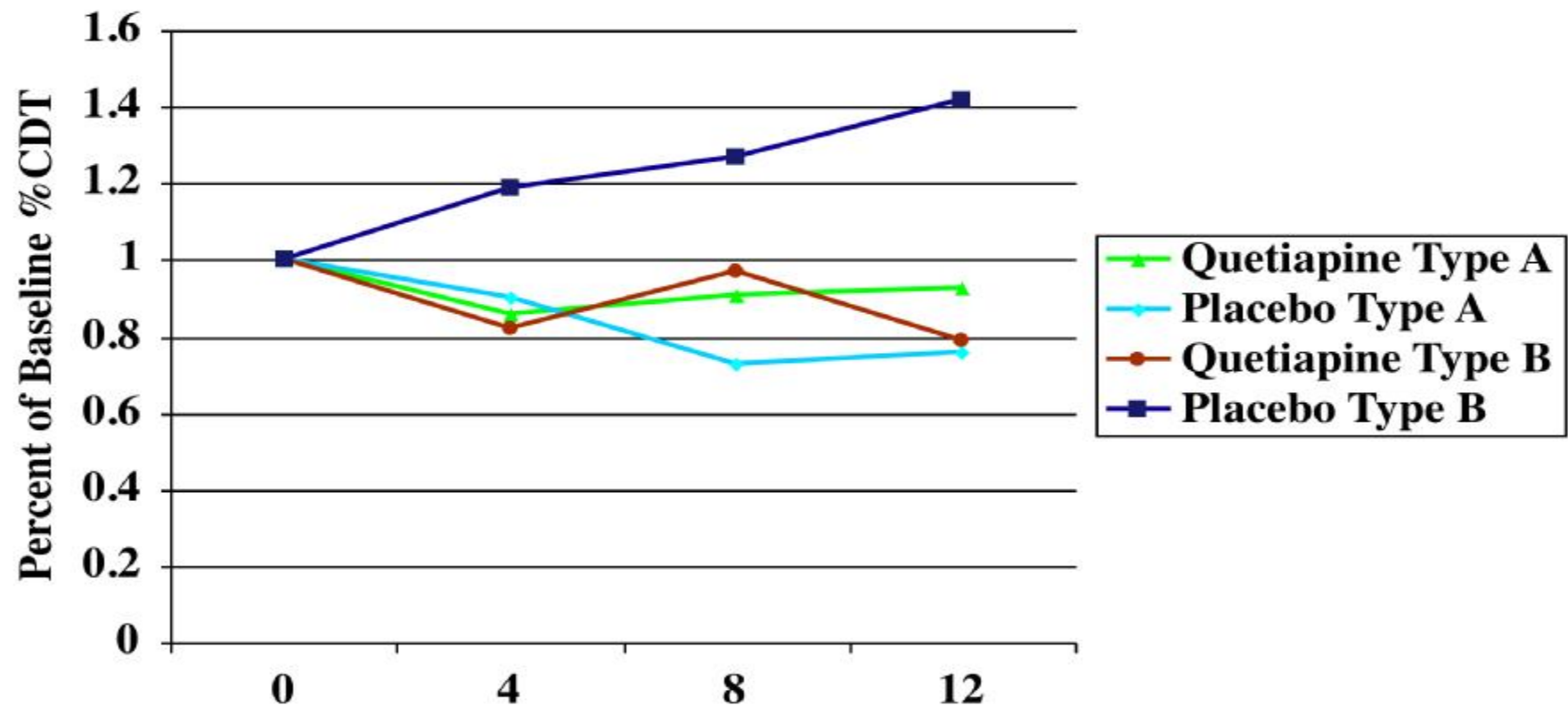
Days of heavy drinking while in treatment

Percent days of heavy drinking by week



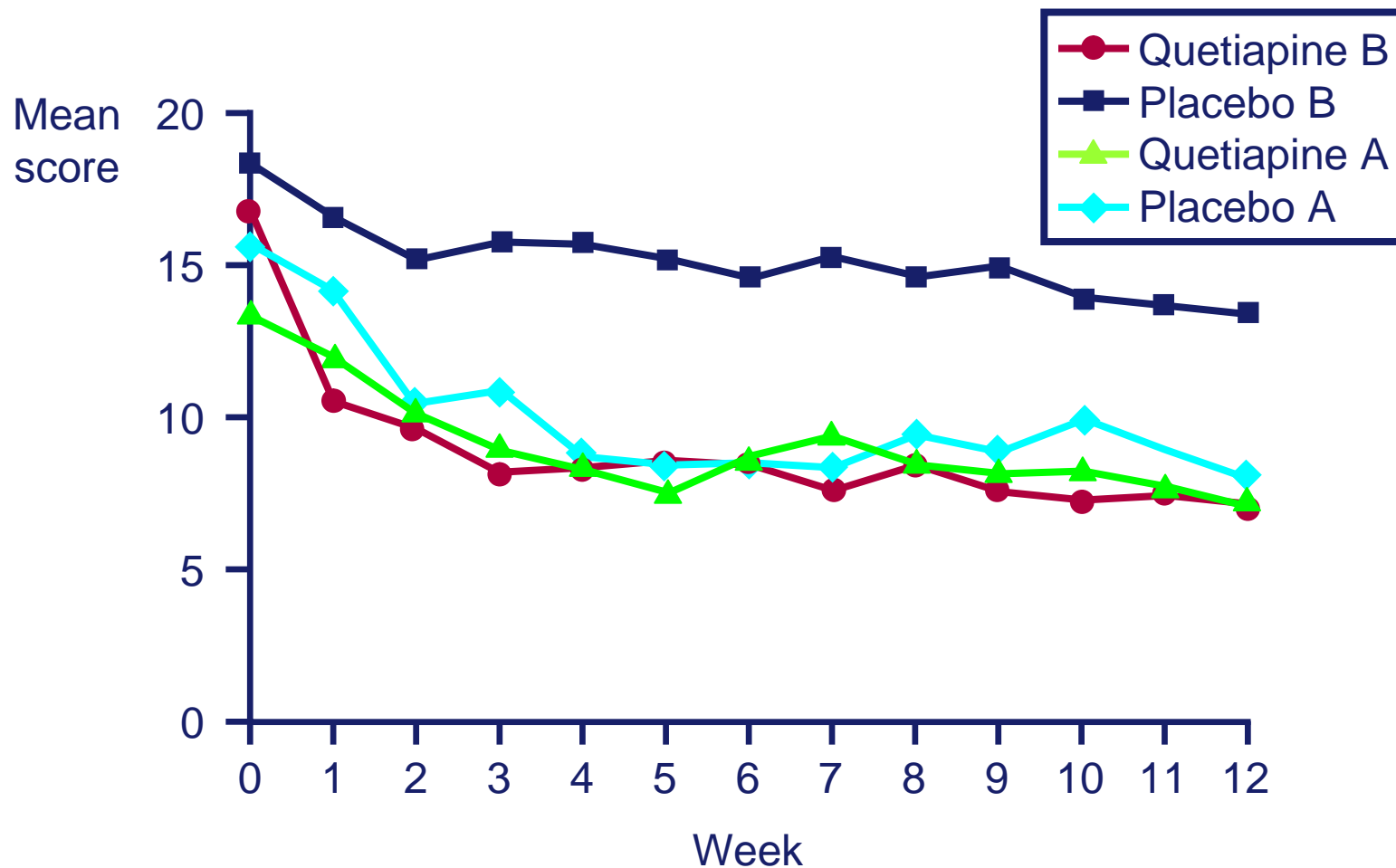
CDT--Carbohydrate-Deficient Transferrin

% CDT change from pre-treatment



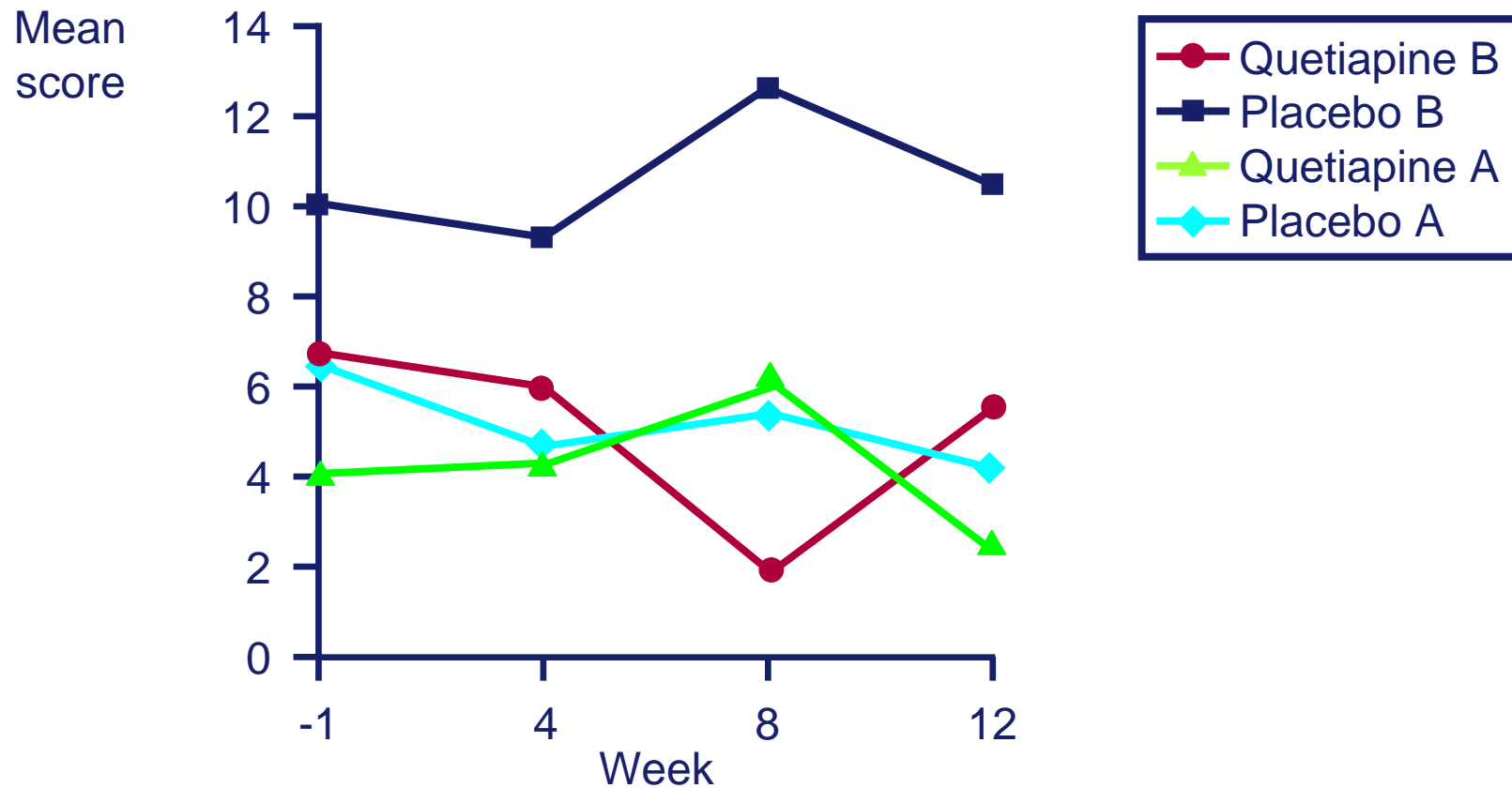
Craving for alcohol while in treatment

Mean craving score from PACS



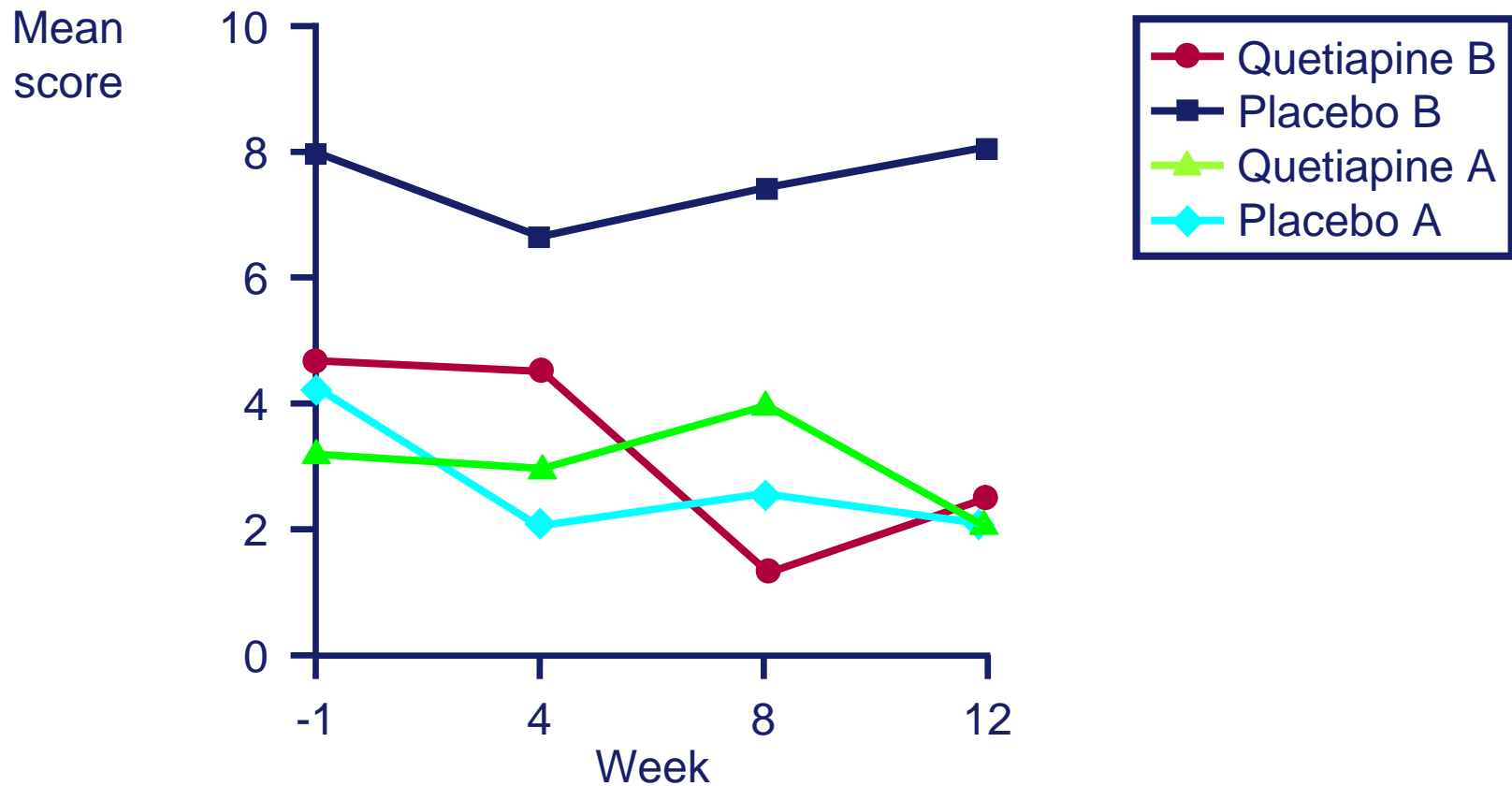
Depression symptoms while in treatment

HAM-D scores



Anxiety symptoms while in treatment

HAM-A scores



Preliminary findings

- ***Quetiapine:***
 - promoted abstinence
 - reduced heavy drinking
 - reduced alcohol craving
 - reduced depression and anxiety symptoms
 - most effective in harder-to-treat Type B alcoholics



Future directions

- **Pilot findings are being replicated by a larger (5 sites) NIH/NIAAA-sponsored double-blind, placebo-controlled trial**
- **Predicting more specifically which patients with alcohol dependence will benefit from quetiapine**

Penn Faculty Study Team

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