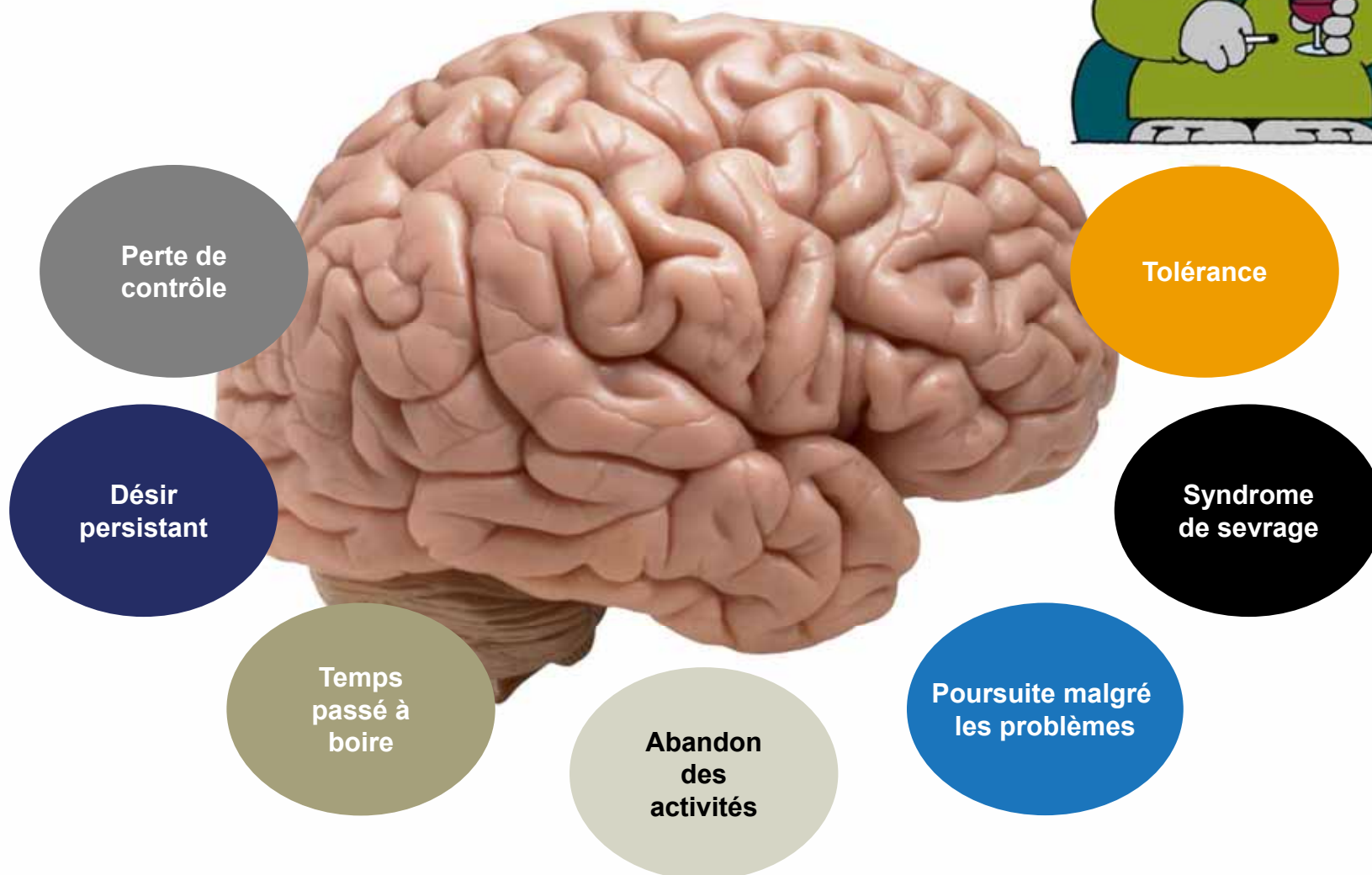

Dépendance à l'alcool : Evolution des stratégies thérapeutiques



Henri-Jean Aubin
Hôpital Paul Brousse
Université Paris-Sud 11

Le syndrome de dépendance



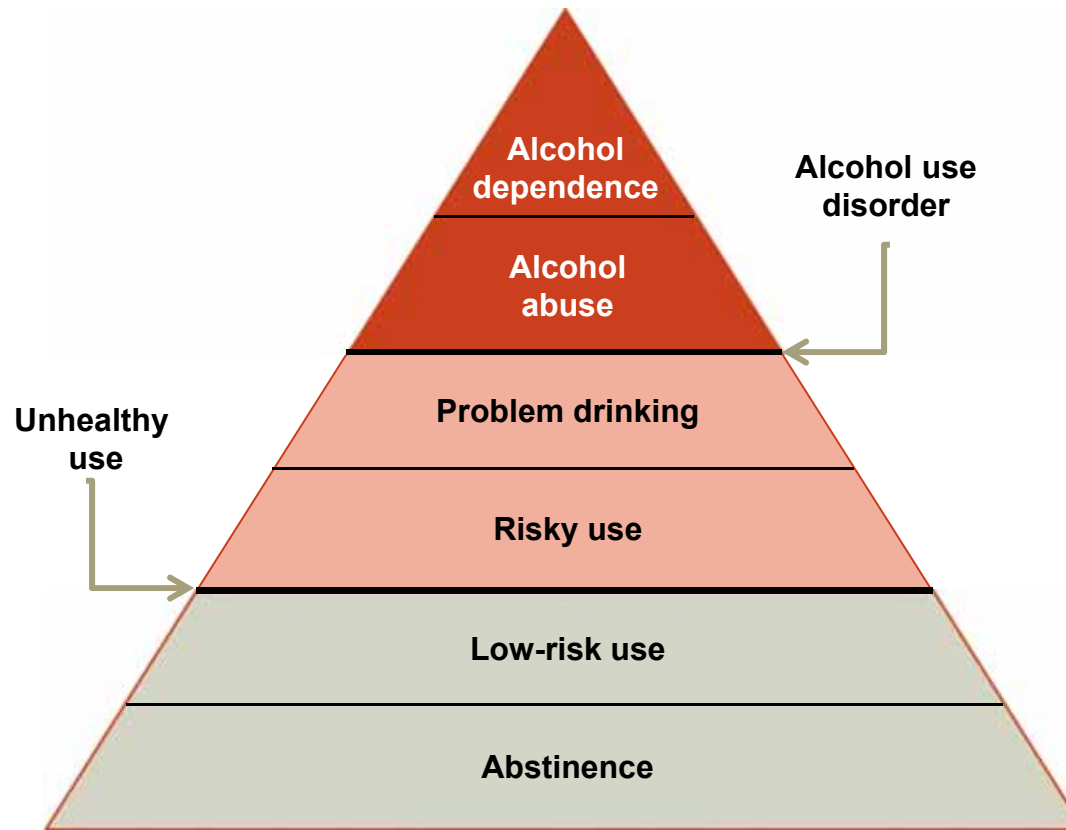
Les troubles liés à l'alcool : un continuum

Consumption

Heavy



None



Consequences

Severe



None

Risk levels of alcohol consumption (WHO)

Risk levels	Total consumption (g/day)	
	Men	Women
Low risk	1 to 40	1 to 20
Medium risk	>40 to 60	>20 to 40
High risk	>60 to 100	>40 to 60
Very high risk	>100	>60

Traitement de l'alcoolodépendance

Les questions à se poser

Objectif de consommation ?

- Réduction
- Abstinence

Syndrome de sevrage ?

- Risque d'accident de sevrage
- Traitement pharmacologique

Le patient est en danger ?

- Urgences
- Programme résidentiel

Quelle prévention de la rechute ?

- Pharmacologique
- Psychothérapie individuelle
- Psychothérapie de groupe
- Groupe d'entraide

Traitement de l'alcoolodépendance

Les questions à se poser

Objectif de consommation ?

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Le patient est en danger ?

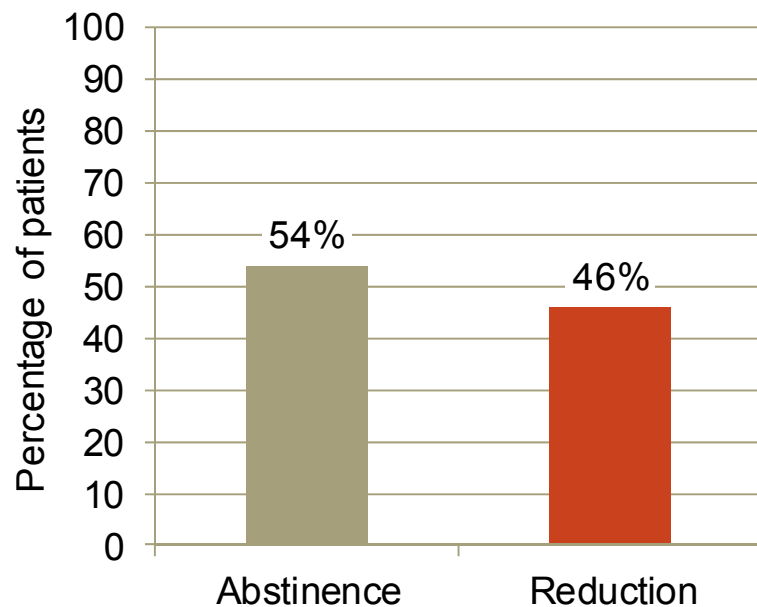
- Urgences
- Programme résidentiel

Quelle prévention de la rechute ?

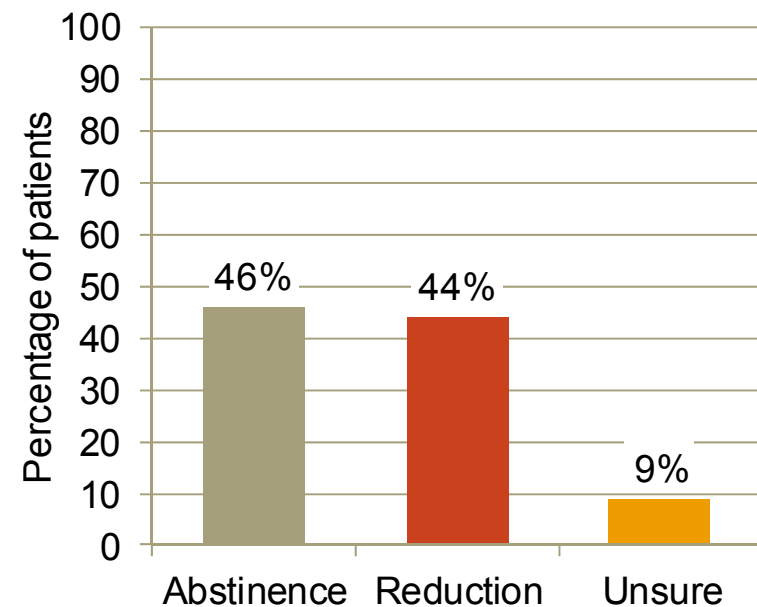
- Pharmacologique
- Psychothérapie individuelle
- Psychothérapie de groupe
- Groupe d'entraide

Treatment goal preference among patients

UK survey of patients with alcohol problems (n=742)¹



Canadian study of patients with chronic alcoholism (n=106)²



Approximately 50% of patients would choose reduction as a treatment goal

Treatment programmes for problem drinkers



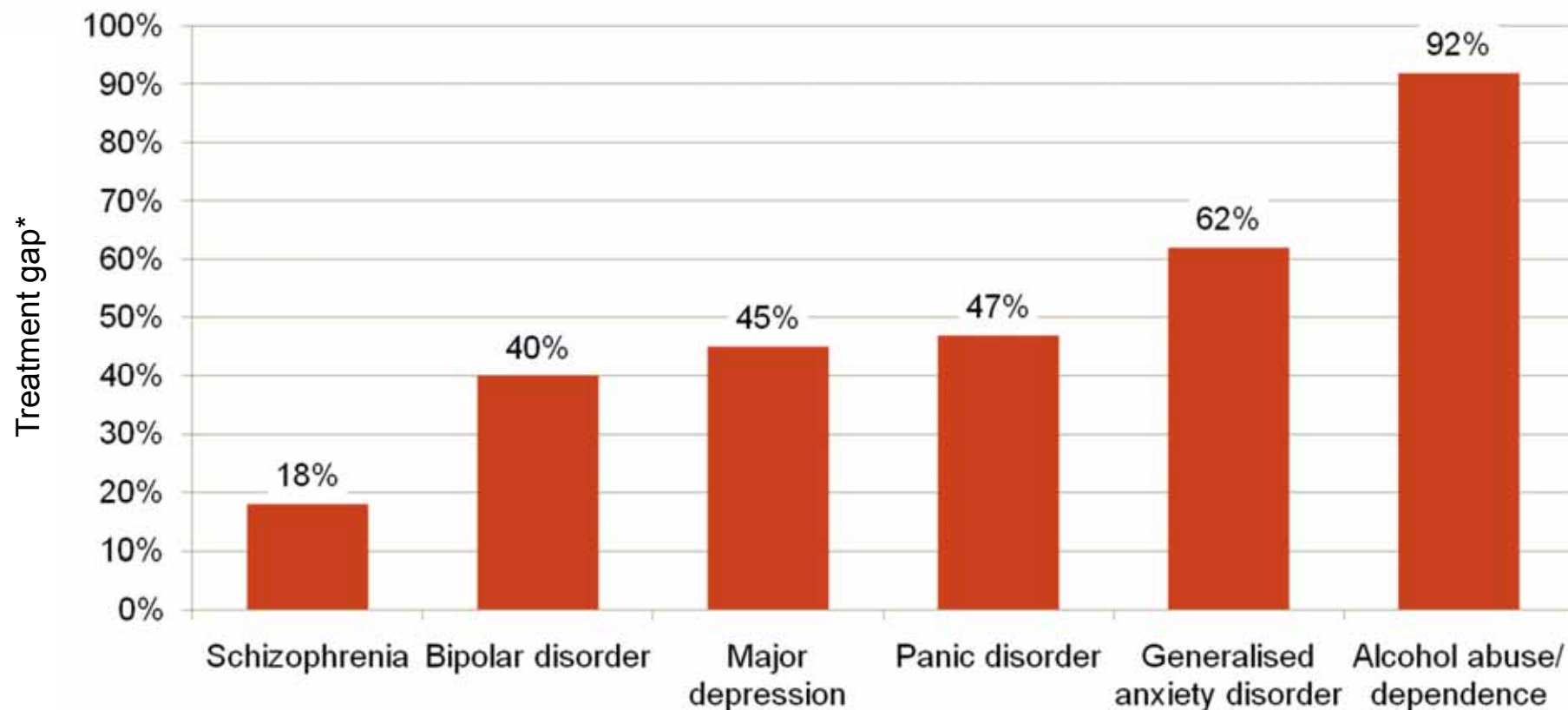
Treatment programmes for problem drinkers



Treatment programmes for problem drinkers



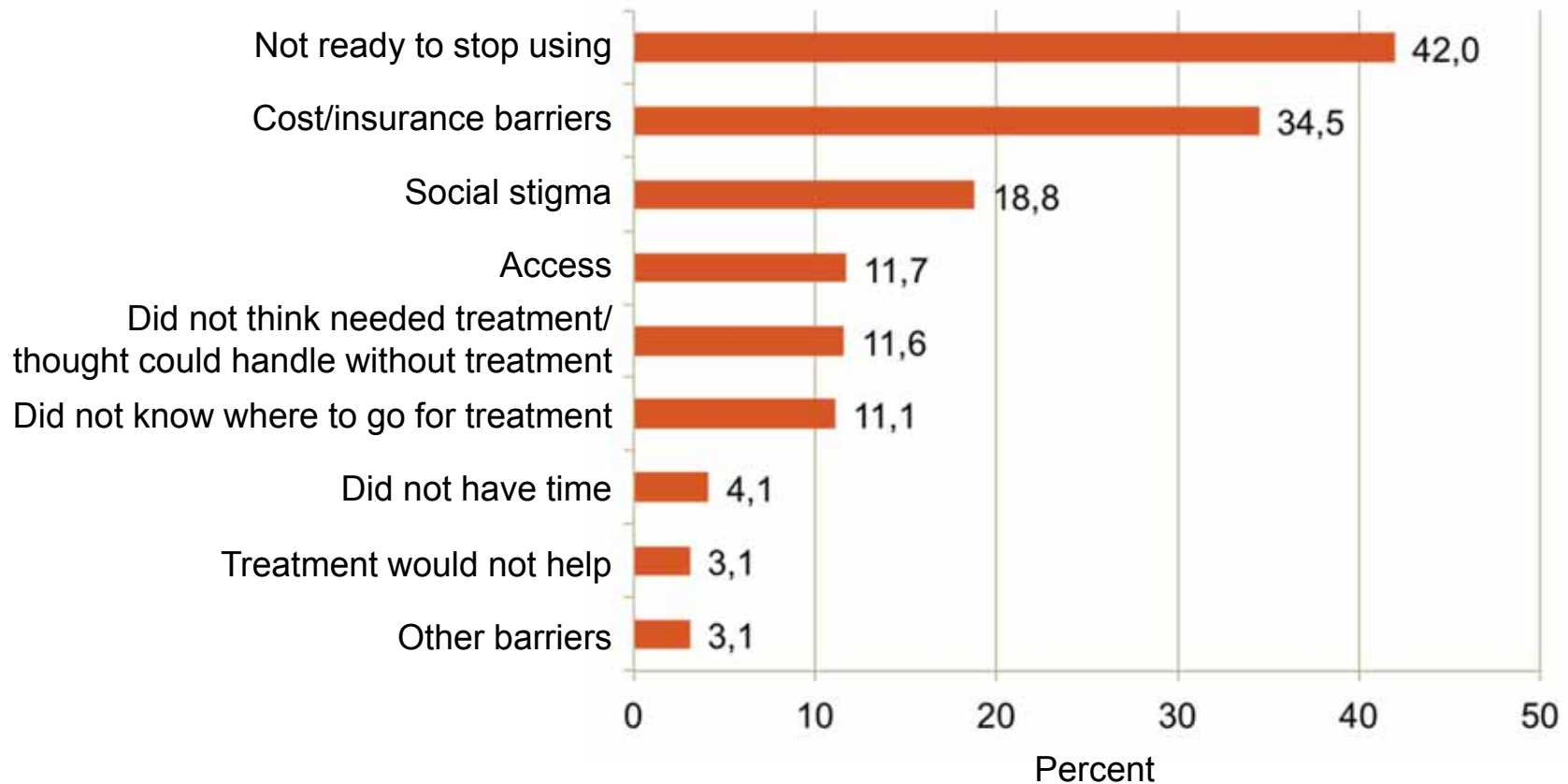
Treatment gap in alcohol dependence



Alcohol abuse and dependence have the widest treatment gap among all mental disorders
Less than 10% of patients with alcohol abuse and dependence are treated

*Treatment gap=difference between number of people needing treatment for mental illness and number of people receiving treatment

Reasons given for not receiving alcohol treatment in the past year by persons aged ≥ 12 who needed treatment and who perceived a need for it: 2004 to 2007



Treatment programmes for problem drinkers



OR



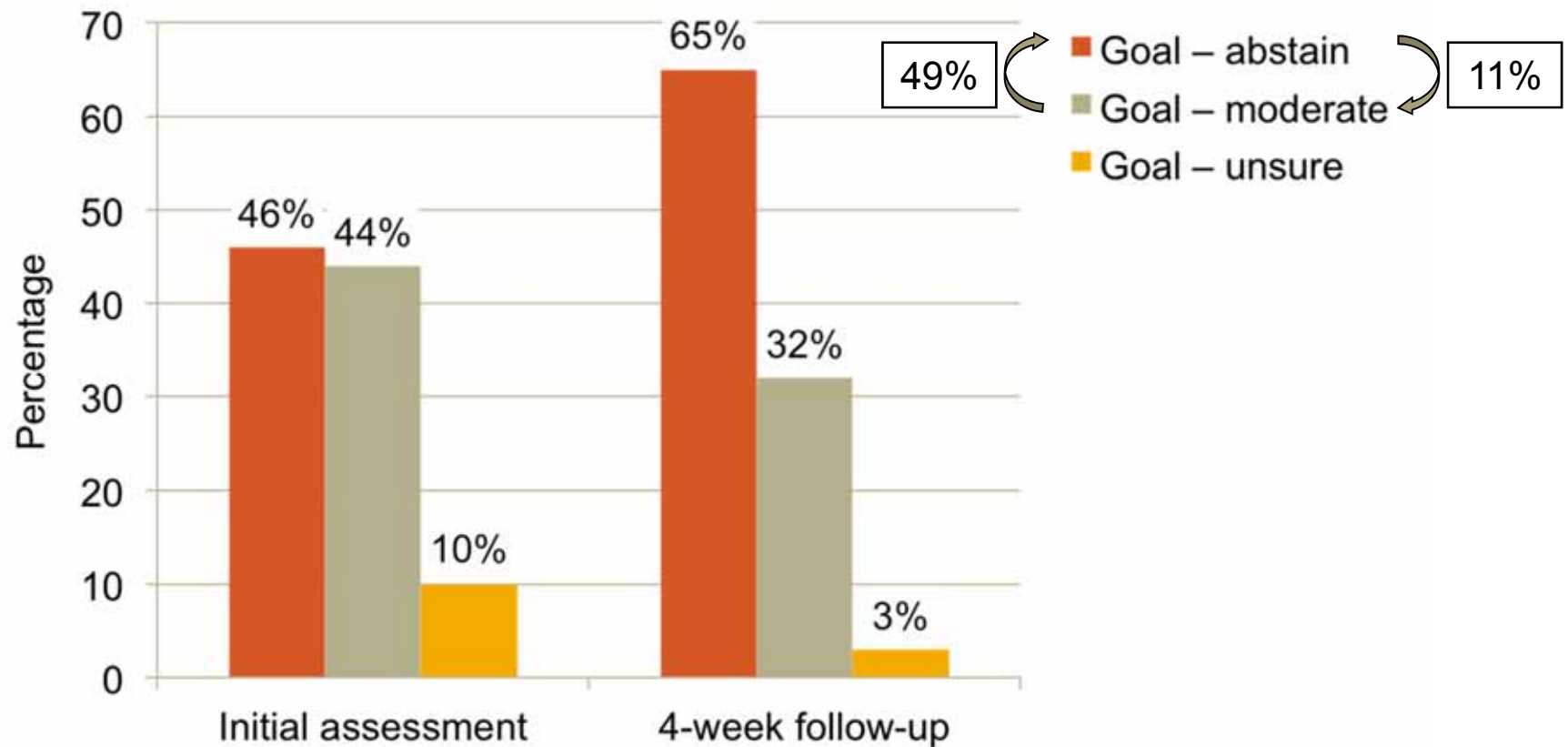
Treatment programmes for problem drinkers



OR

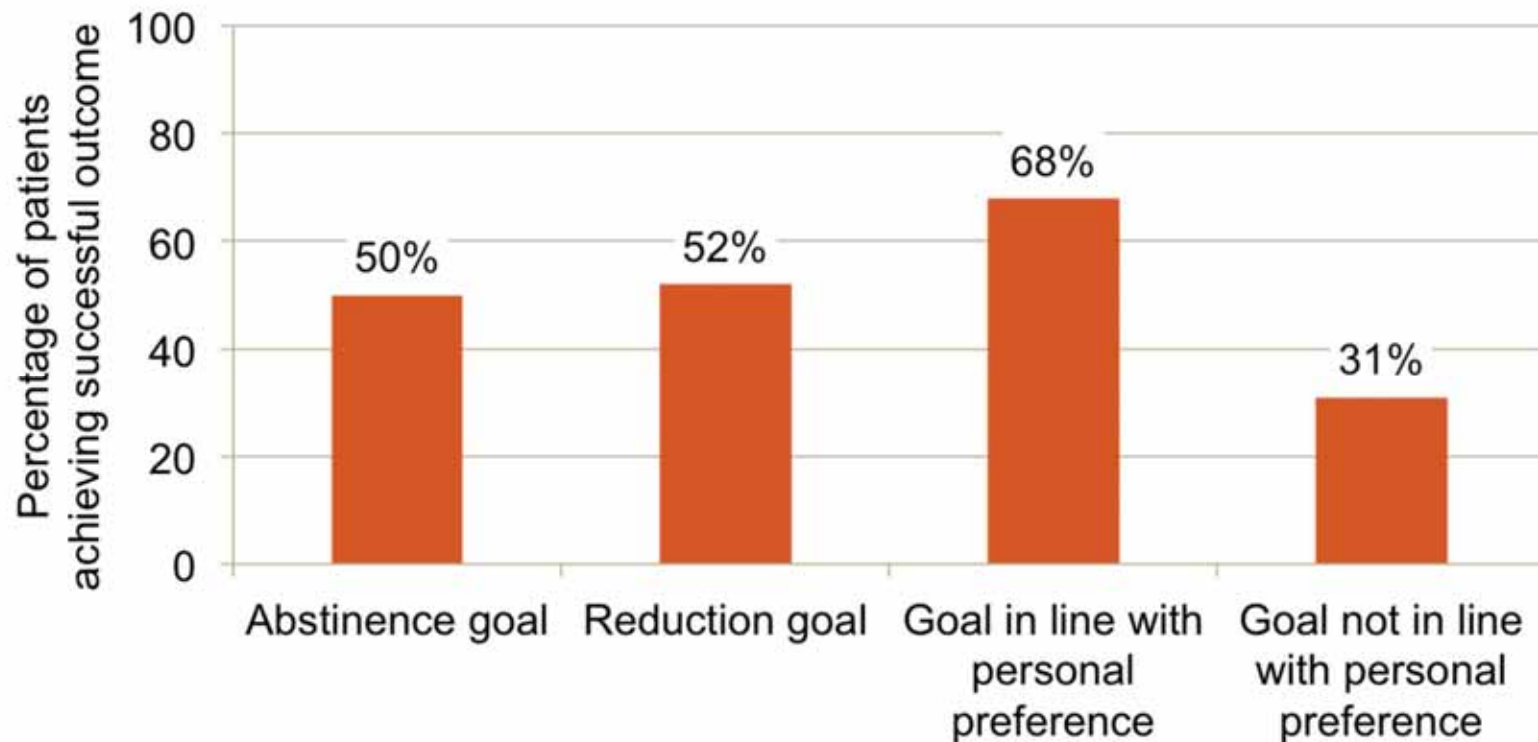


Treatment goal stability in severe chronic alcoholics



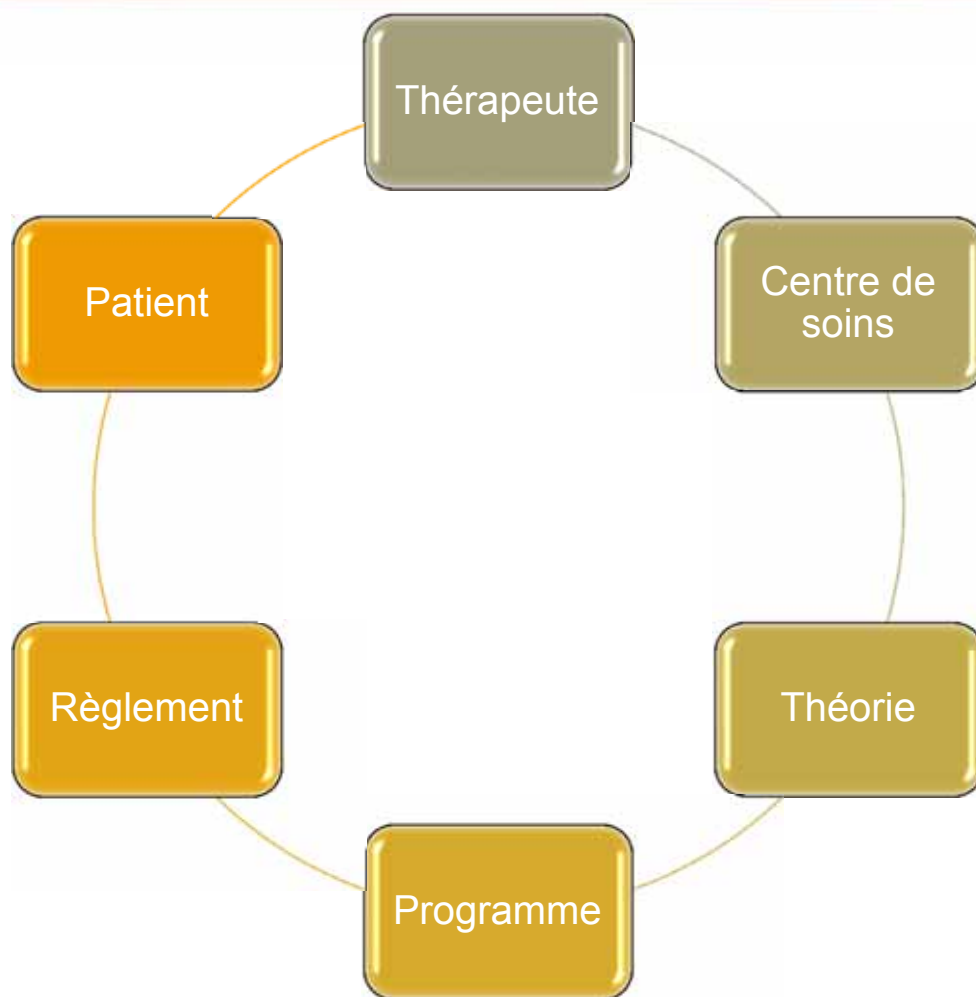
Patient involvement in treatment goals

12-month follow-up status by actual treatment received



Allowing patients to set their own treatment goals is more likely to result in a successful outcome

Qui est au centre ?



Traitement de l'alcoolodépendance

Les questions à se poser

Objectif de consommation ?

- Réduction
- Abstinence

Syndrome de sevrage ?

- Risque d'accident de sevrage
- Traitement pharmacologique

Le patient est en danger ?

- Urgences
- Programme résidentiel

Quelle prévention de la rechute ?

- Pharmacologique
- Psychothérapie individuelle
- Psychothérapie de groupe
- Groupe d'entraide

Benzodiazépines

- Quelle benzodiazépine ?
- Durée ?
- Voie ?
- Risques ?
- Alternatives ?



Vitamine B1

- Dose ?
- Durée ?



Traitement de l'alcoolodépendance

Les questions à se poser

Objectif de consommation ?

- Réduction
- Abstinence

Syndrome de sevrage ?

- Risque d'accident de sevrage
- Traitement pharmacologique

Le patient est en danger ?

- Urgences
- Programme résidentiel

Quelle prévention de la rechute ?

- Pharmacologique
- Psychothérapie individuelle
- Psychothérapie de groupe
- Groupe d'entraide

Traitement résidentiel

Antécédent d'accident de sevrage

- Crise grand mal
- Delirium tremens

Détérioration cognitive

Environnement social toxique

Traitement de l'alcoolodépendance

Les questions à se poser

Objectif de consommation ?

- Réduction
- Abstinence

Syndrome de sevrage ?

- Risque d'accident de sevrage
- Traitement pharmacologique

Le patient est en danger ?

- Urgences
- Programme résidentiel

Quelle prévention de la rechute ?

- Pharmacologique
- Psychothérapie individuelle
- Psychothérapie de groupe
- Groupe d'entraide

Traitement pharmacologique



Disulfirame

- Dissuasion
- Risque de réaction éthanol-disulfirame
- Abstinence continue d'un patient sevré



Acamprosate

- Excellente tolérance
- Abstinence continue d'un patient sevré

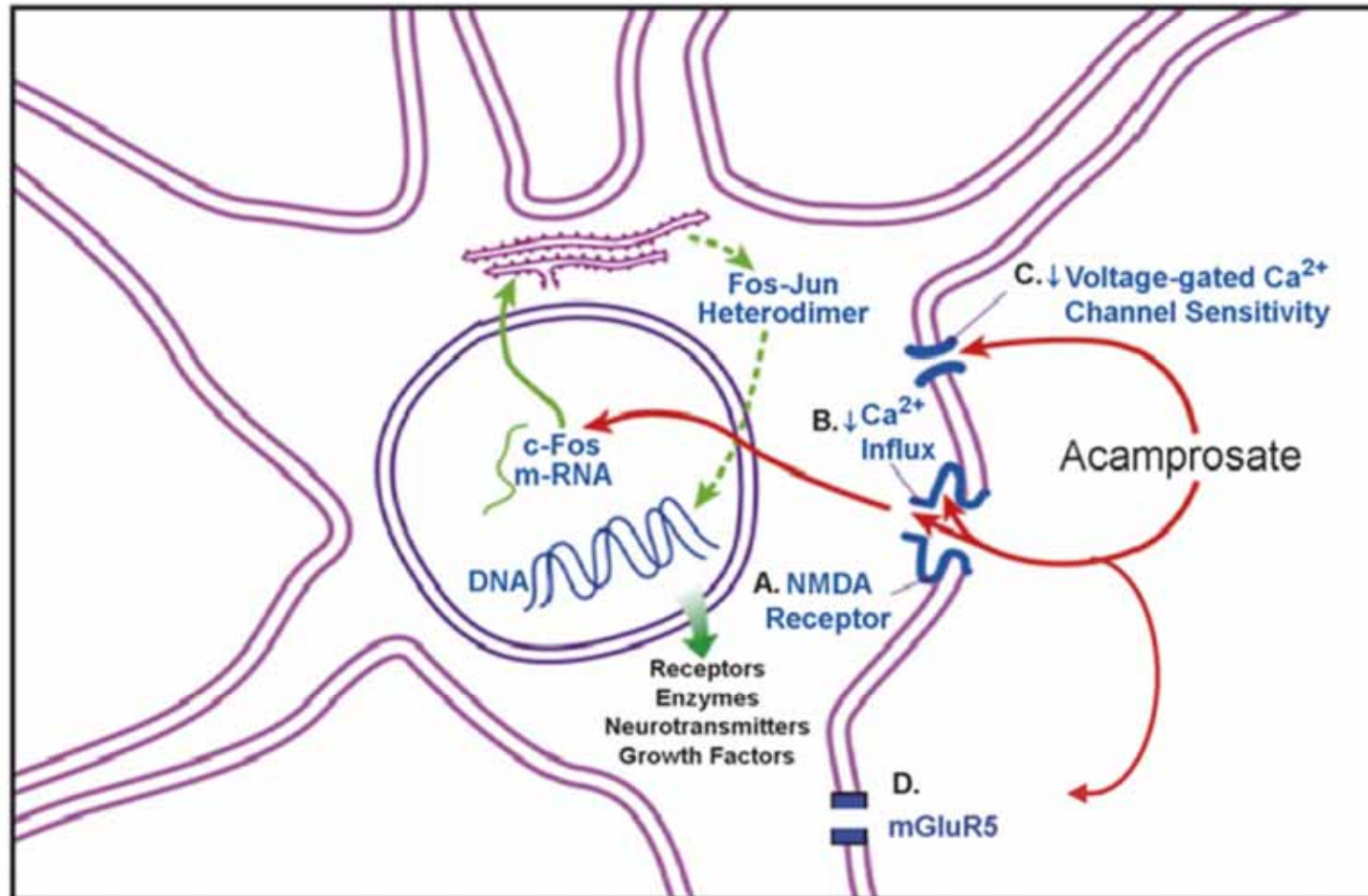


naltrexone

- Antagoniste opiacés
- Prévention du dérapage après la prise d'un premier verre

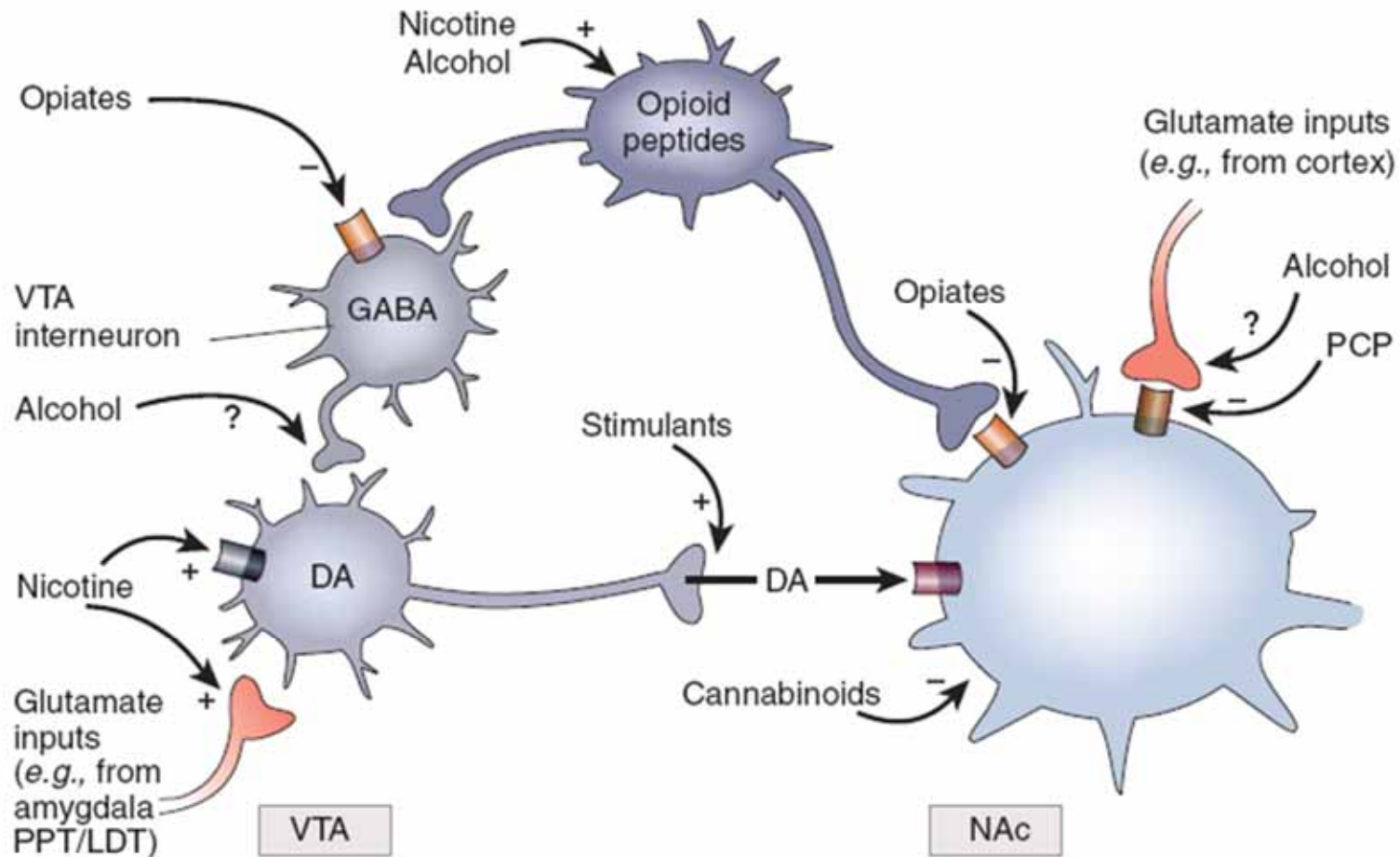
Campral

Maintien de l'abstinence



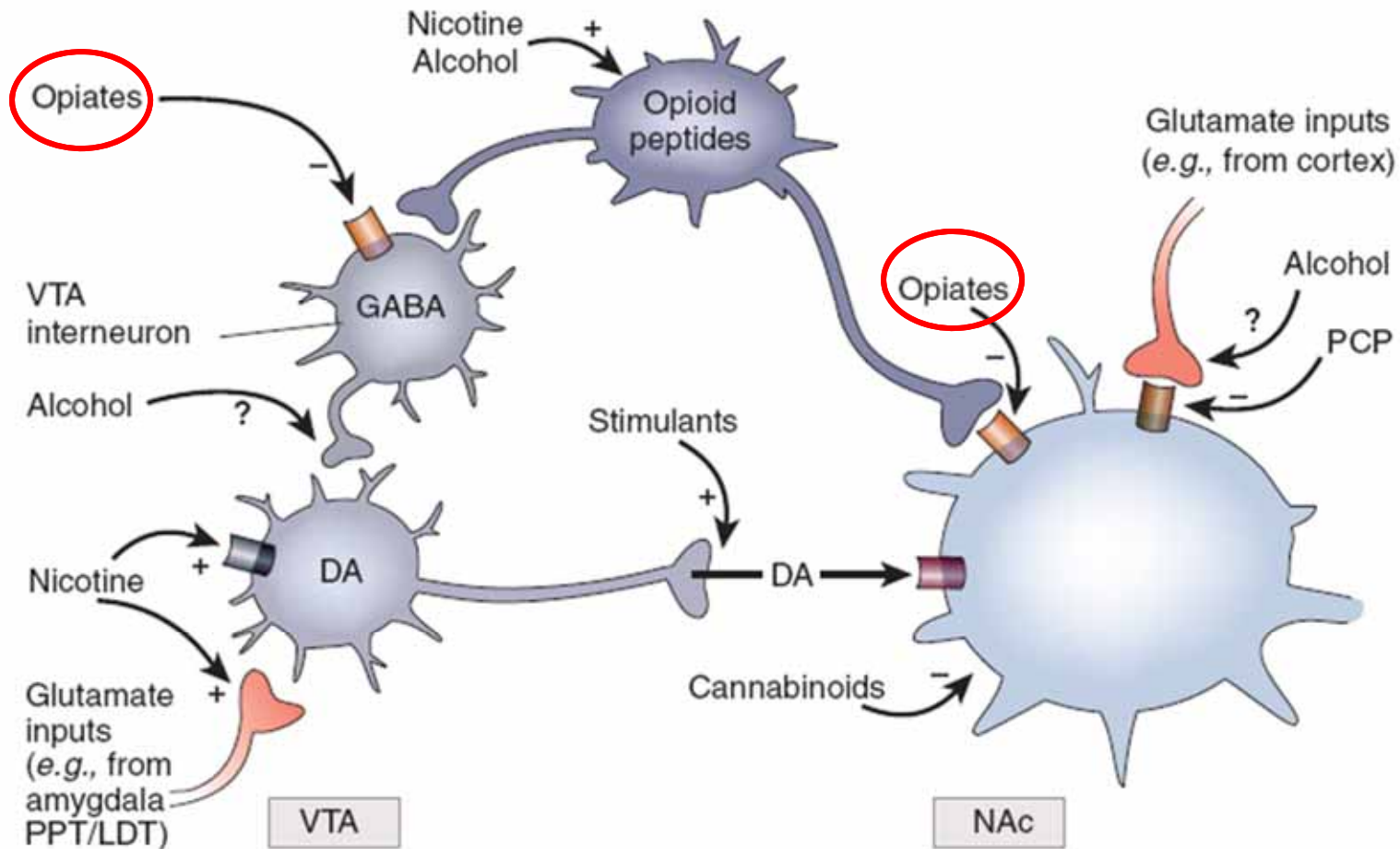
Naltrexone

Prévention de la rechute



Naltrexone

Prévention de la rechute



Acamprosate for alcohol dependence (Review)

Rösner S, Hackl-Herrwerth A, Leucht S, Leherer P, Vecchi S, Soyka M



This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2011, Issue 2

<http://www.thecochranelibrary.com>

Opioid antagonists for alcohol dependence (Review)

Srisurapanont M, Jaruraisin N



This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2008, Issue 3

<http://www.thecochranelibrary.com>

Rosner et al. Opioid antagonists for alcohol dependence. *Cochrane Database Syst Rev* 2010:CD001867.

Rosner et al. Acamprosate for alcohol dependence. *Cochrane Database Syst Rev* 2010:CD004332

Acamprosate supports abstinence, Naltrexone prevents excessive drinking: evidence from a meta- analysis with unreported outcomes

Susanne Rösner *IFT, Institut für Therapieforschung, Munich, Germany and Psychiatric Hospital, University of Munich, Munich, Germany.*

Stefan Leucht *Department of Psychiatry and Psychotherapy, Technical University of Munich, Munich, Germany.*

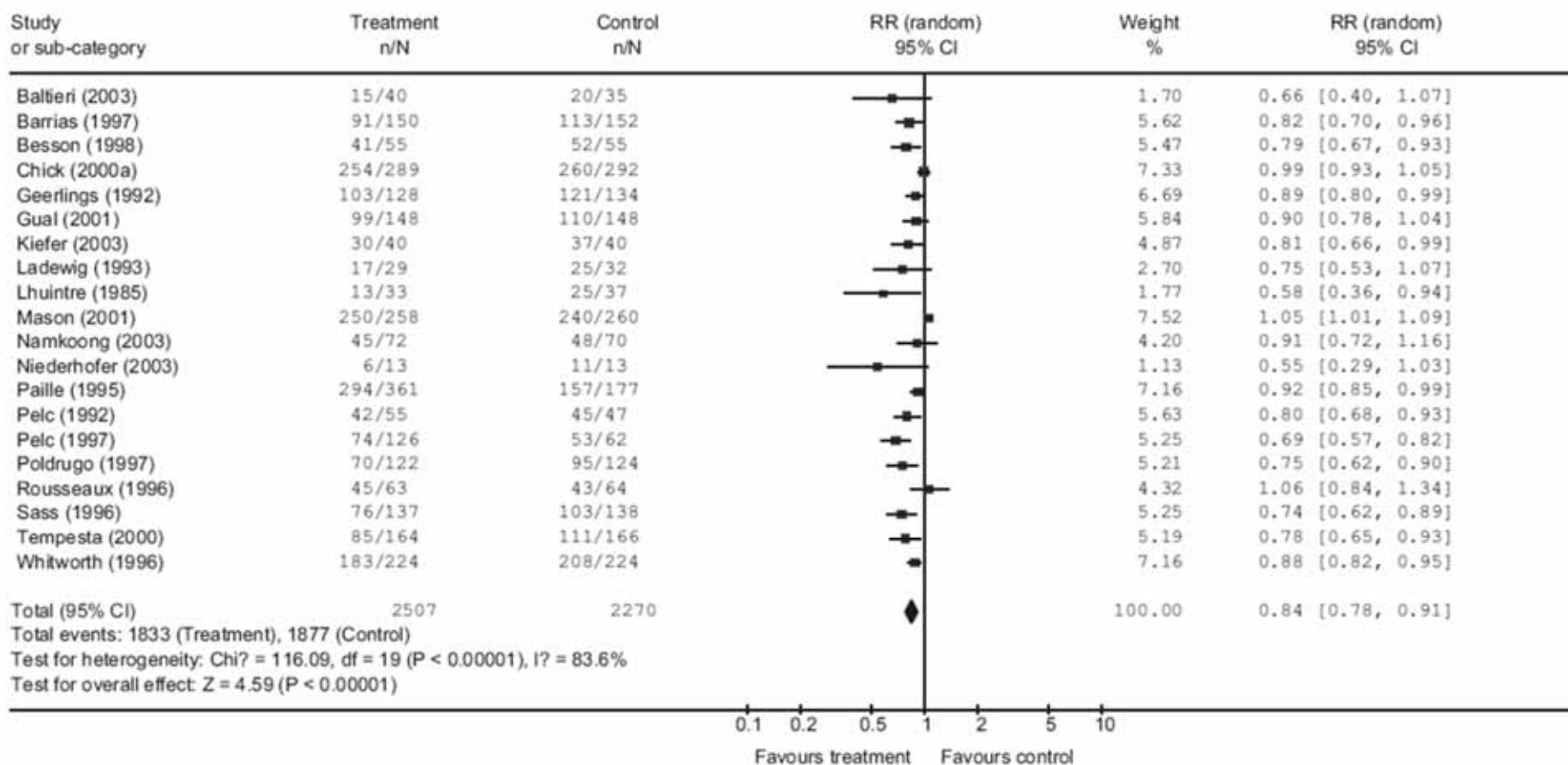
Philippe Lehert *Department of Statistics, University of Mons, Mons, Belgium.*

Michael Soyka *Psychiatric Hospital, University of Munich, Munich, Germany and Private Hospital Meiringen, Meiringen, Switzerland.*

Acamprosate

Premier verre

Review: Relapse prevention with acamprosate
 Comparison: 01 acamprosate vs placebo
 Outcome: 01 First drink

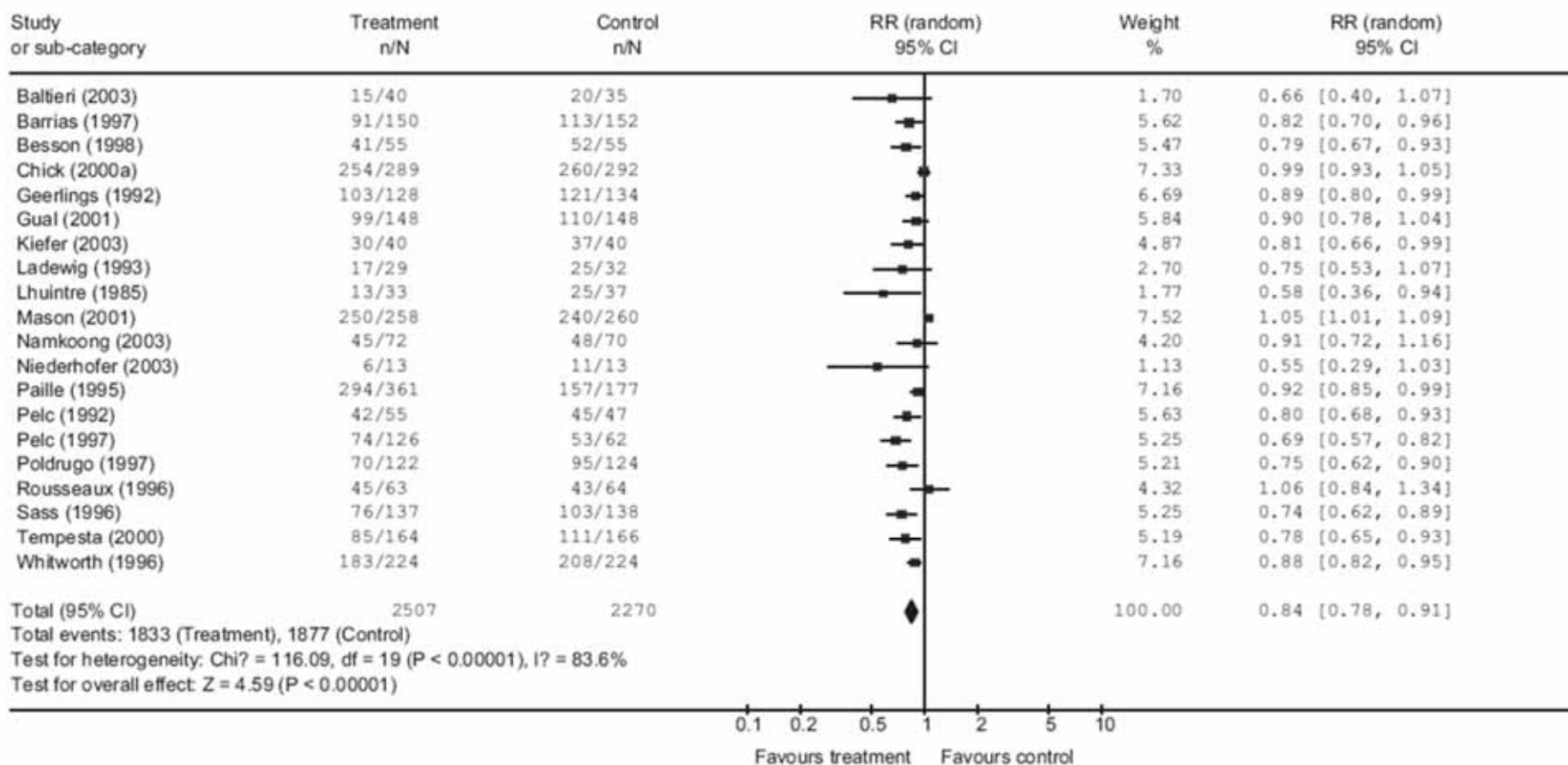


Acamprosate

Premier verre

- 16%

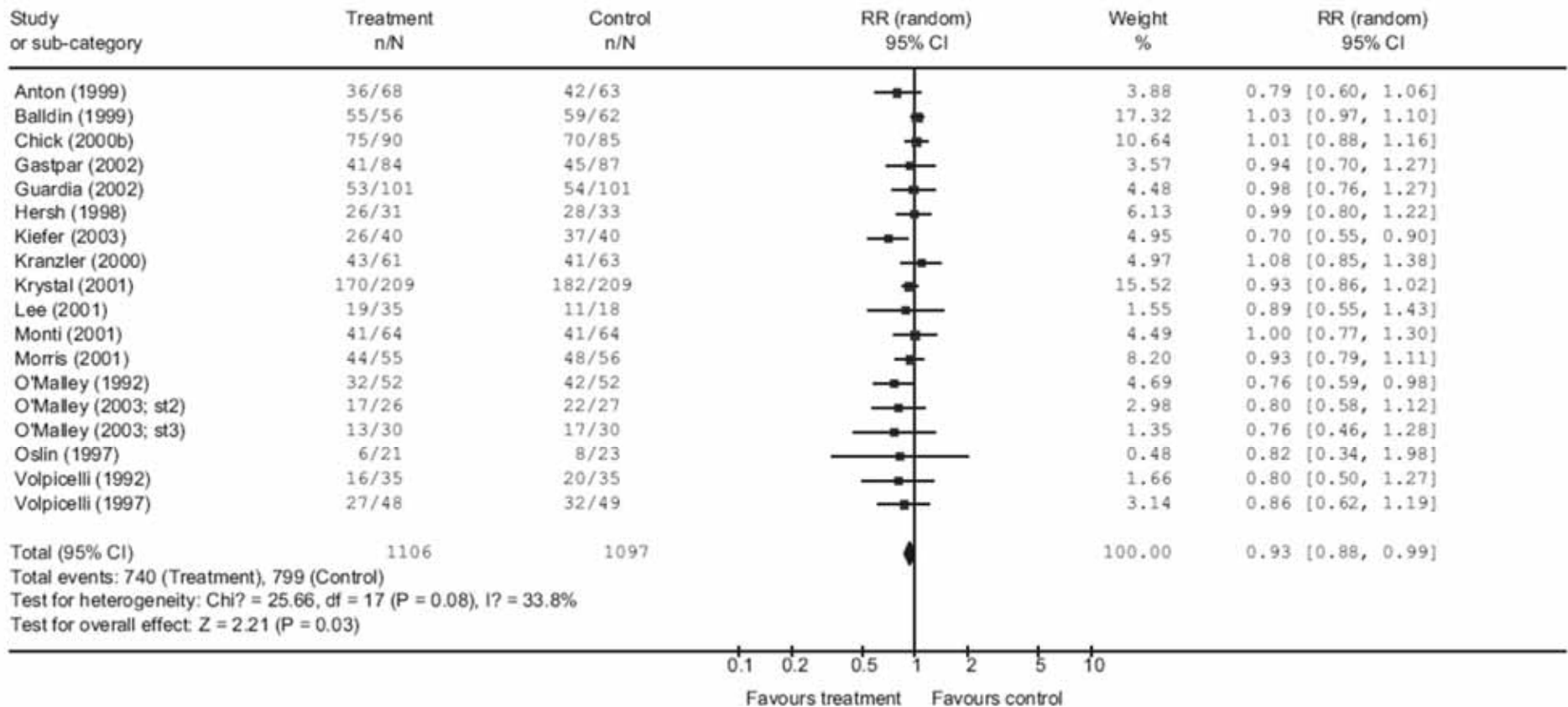
Review: Relapse prevention with acamprosate
 Comparison: 01 acamprosate vs placebo
 Outcome: 01 First drink



Naltrexone

Premier verre

Review: Relapse prevention with naltrexone
 Comparison: 01 naltrexone vs. placebo
 Outcome: 01 First drink

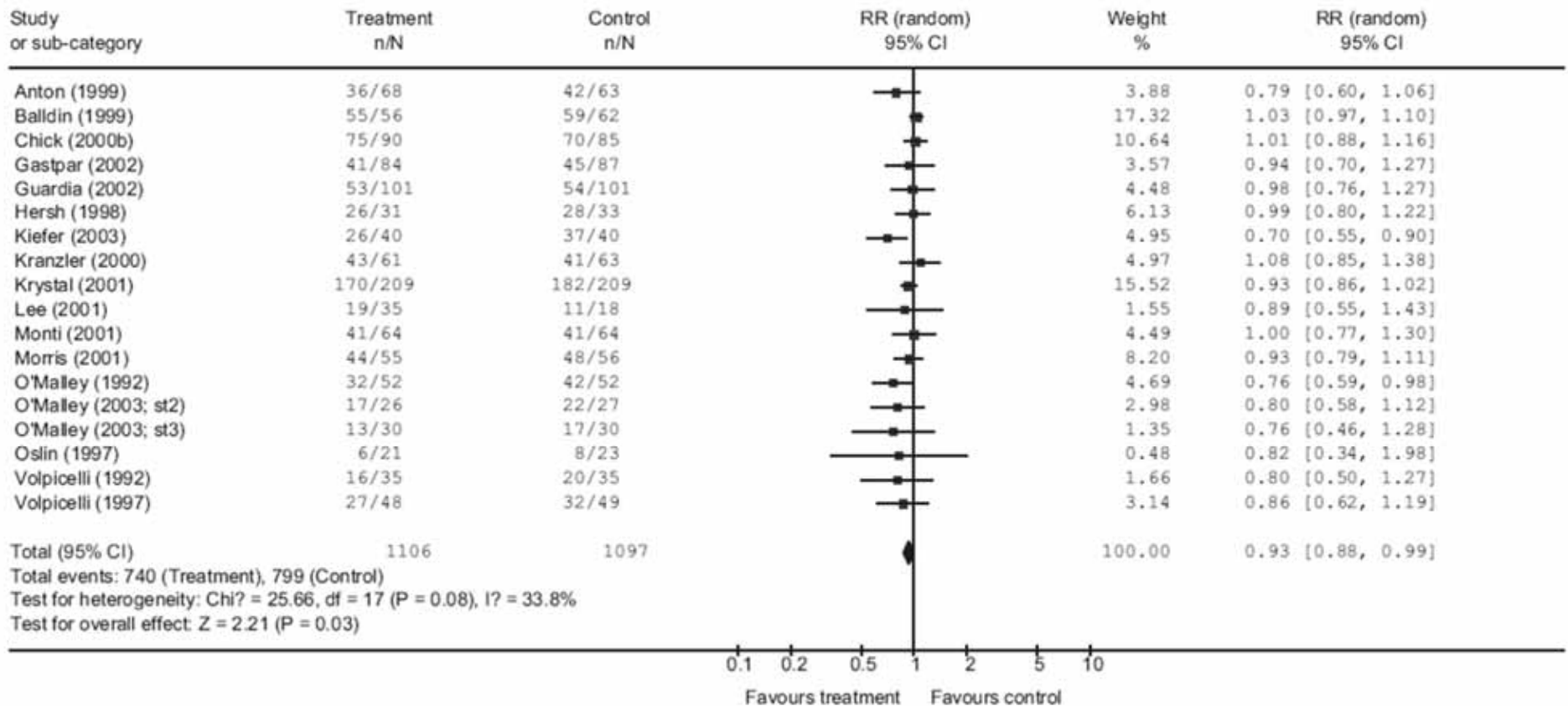


Naltrexone

Premier verre

- 7%

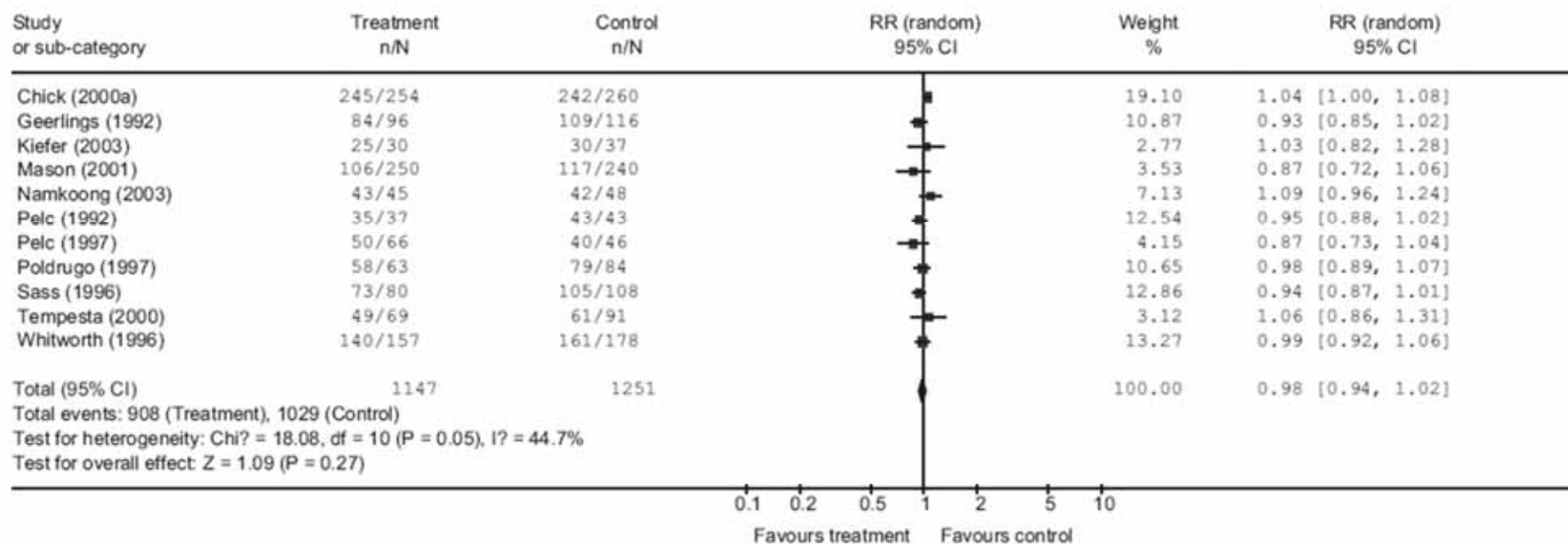
Review: Relapse prevention with naltrexone
 Comparison: 01 naltrexone vs. placebo
 Outcome: 01 First drink



Acamprosate

Rechute après le premier verre

Review: Relapse prevention with acamprosate
Comparison: 01 acamprosate vs placebo
Outcome: 03 Relapse/ First drink (intervall)

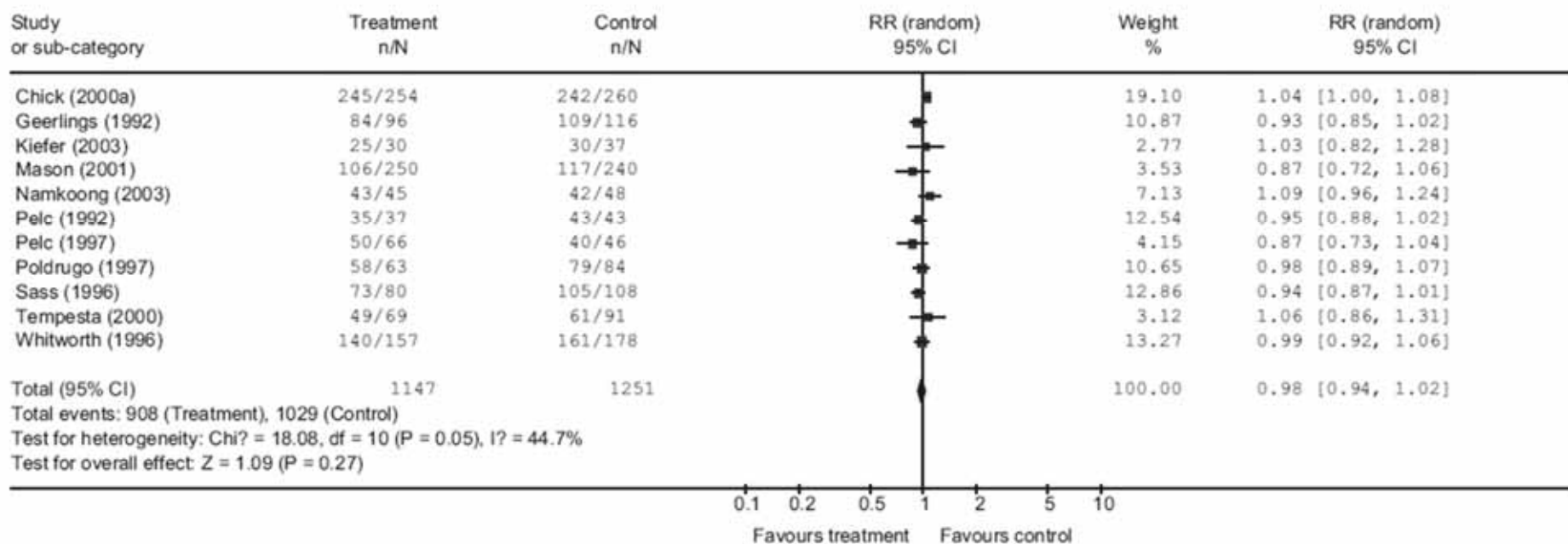


Acamprosate

Rechute après le premier verre

- 2%

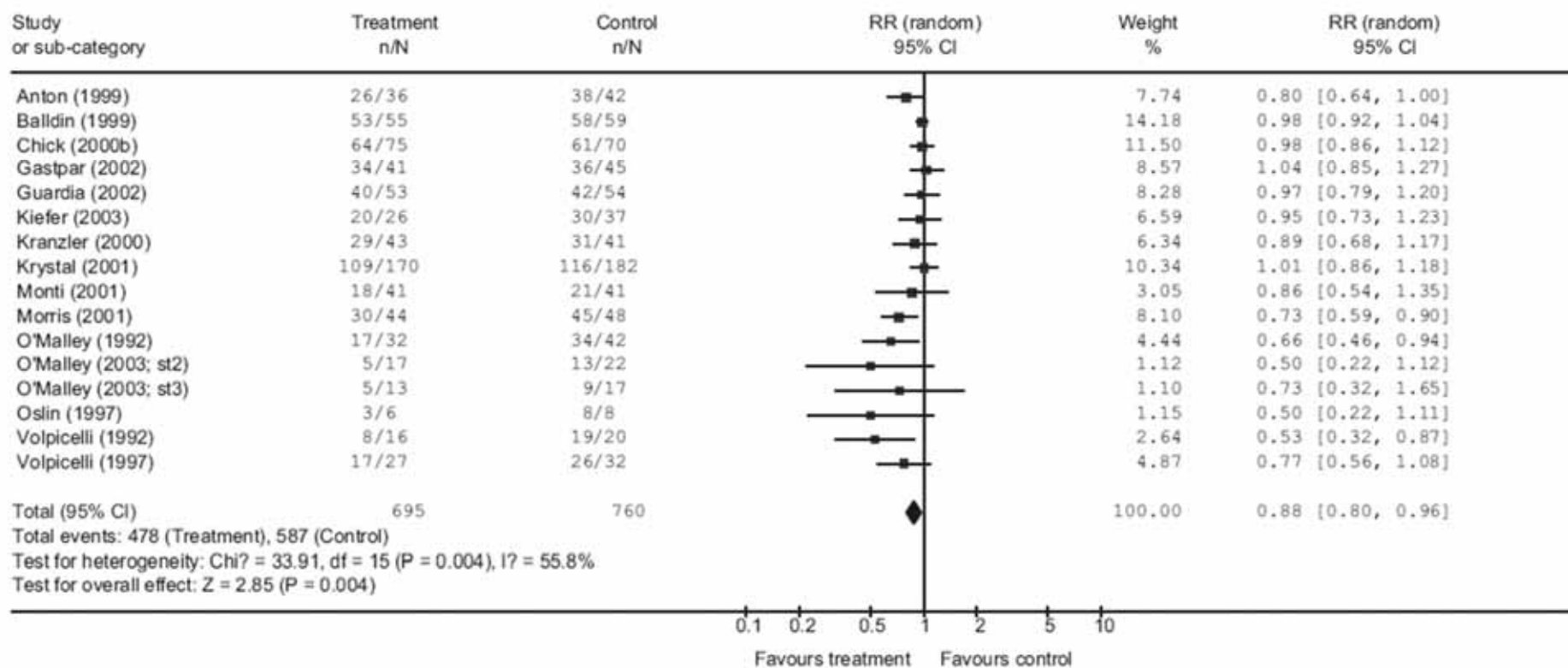
Review: Relapse prevention with acamprosate
Comparison: 01 acamprosate vs placebo
Outcome: 03 Relapse/ First drink (intervall)



Naltrexone

Rechute après le premier verre

Review: Relapse prevention with naltrexone
 Comparison: 01 naltrexone vs. placebo
 Outcome: 03 Relapse/ First Drink

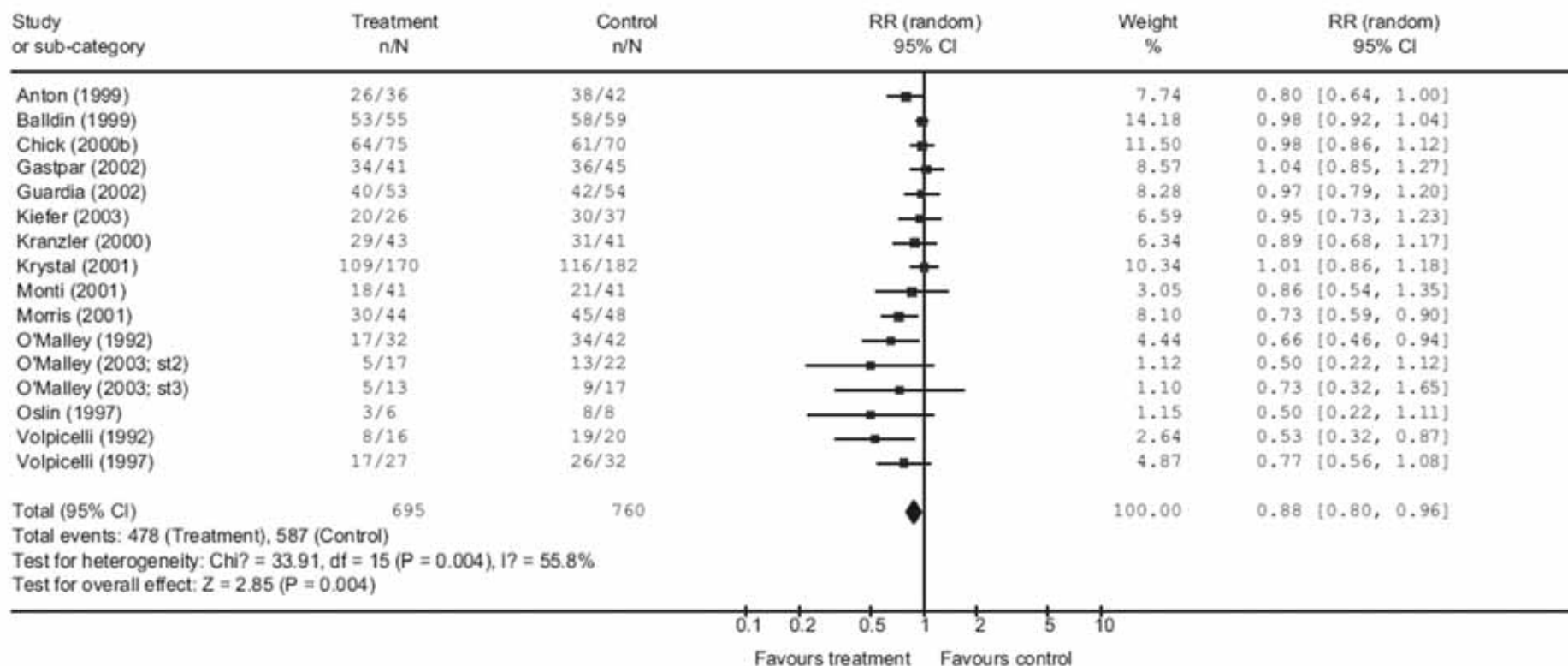


Naltrexone

Rechute après le premier verre

- 12%

Review: Relapse prevention with naltrexone
 Comparison: 01 naltrexone vs. placebo
 Outcome: 03 Relapse/ First Drink



Acamprosate

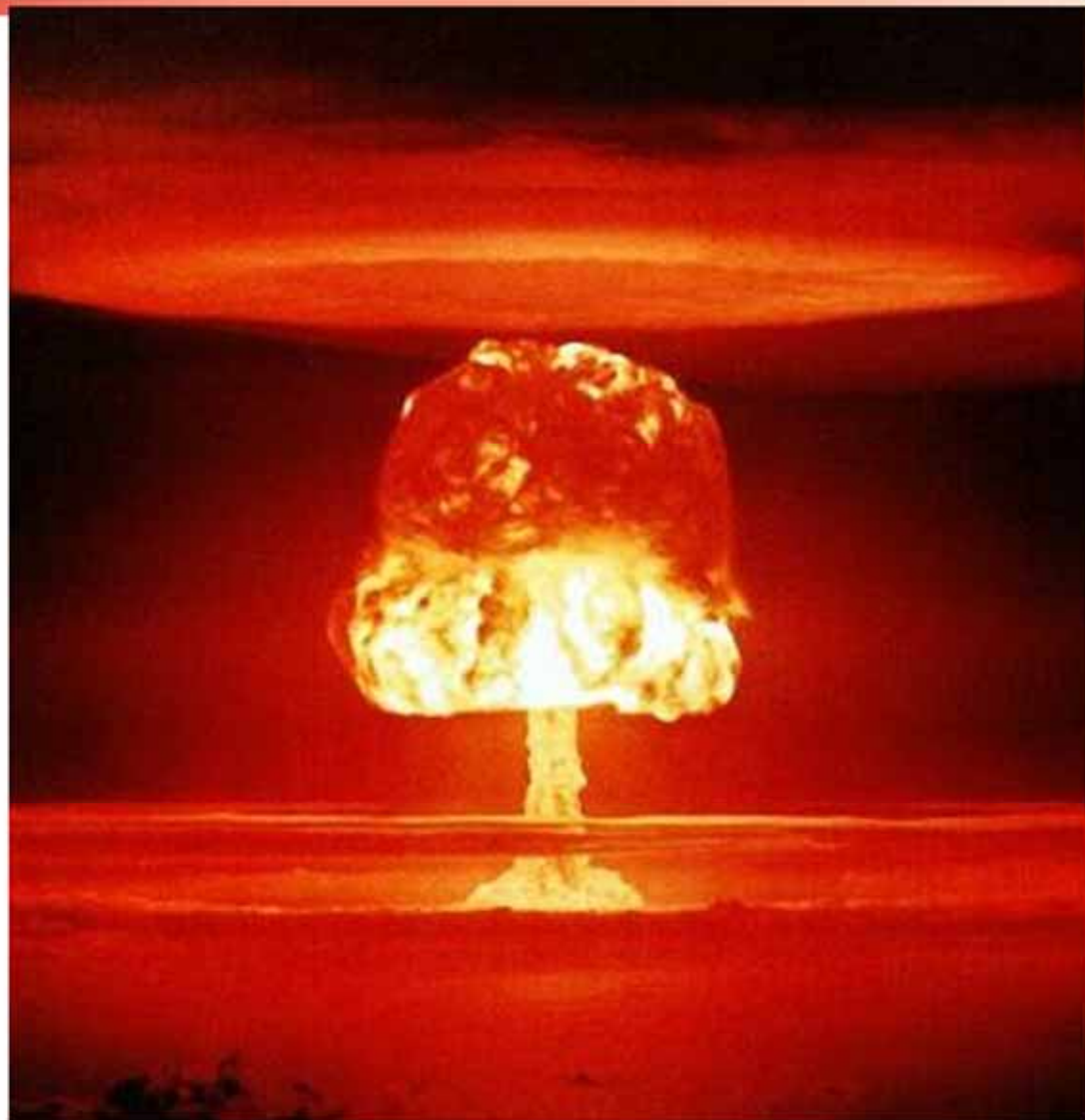
- Prescription
 - Aotal 6 cp / j (4 cp/j si < 60 kg)
 - Durée : 1 an
- Effets secondaires
 - Diarrhée
- Contre-indication
 - Insuffisance rénale

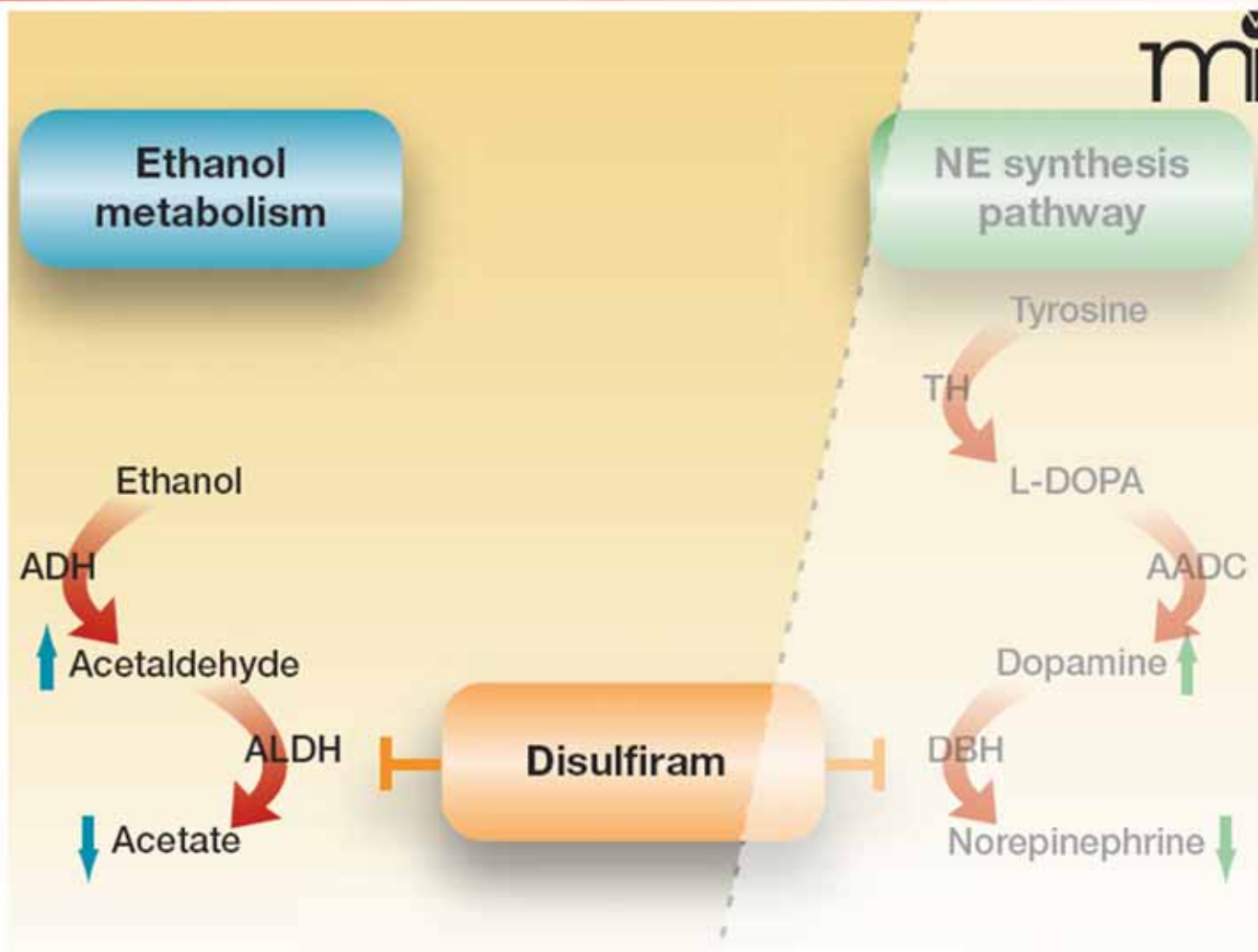
Naltrexone

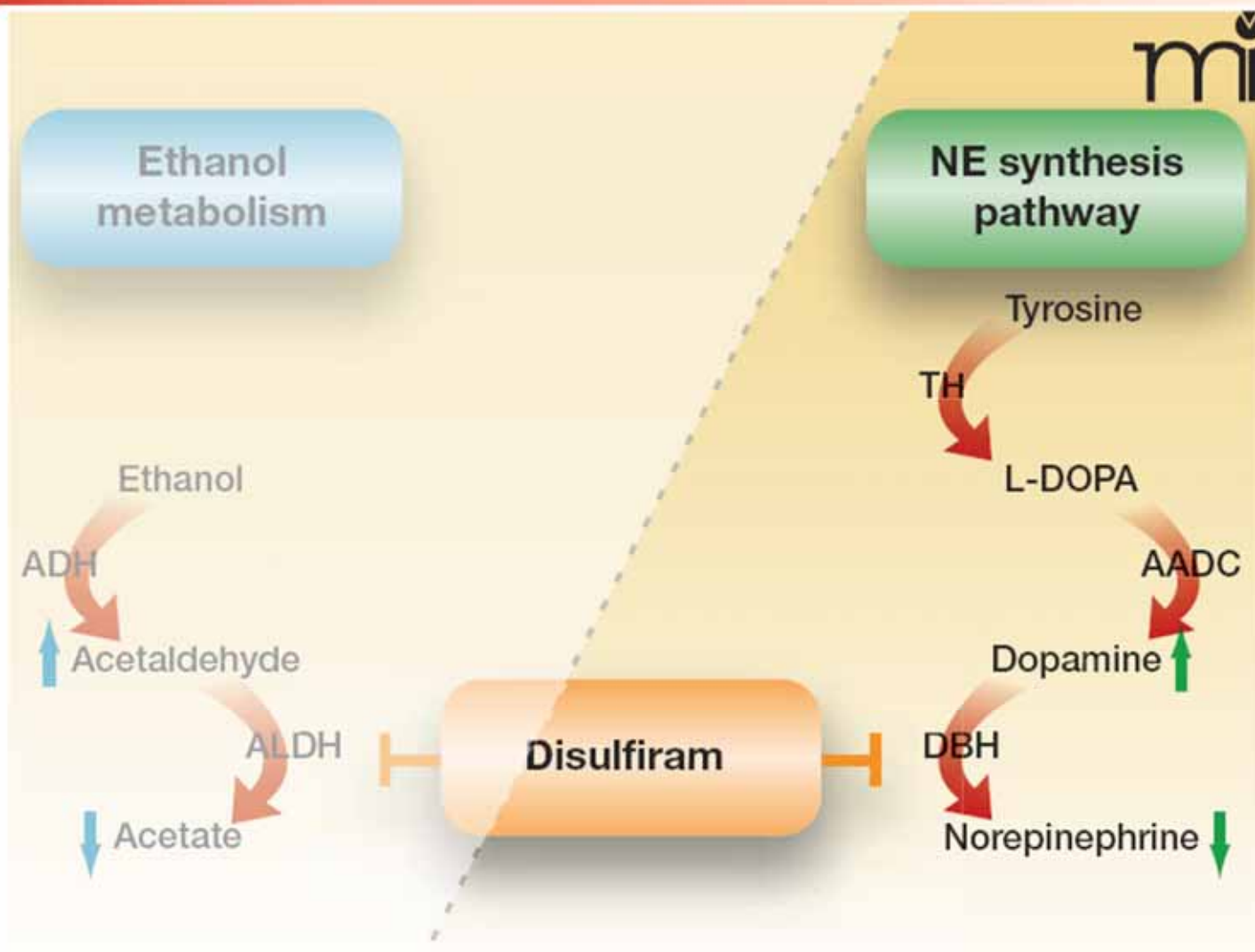
- Prescription
 - ReVia 1 cp / j le matin (1/2 à 2 cp / j)
 - Durée : 3 mois
- Effets secondaires
 - Nausées / vomissements, céphalées, insomnie, anxiété, nervosité, douleurs abdominales, douleurs articulaires / musculaires
- Contre-indications
 - Insuffisance hépatique sévère, prise d'opiacés

Espéral

Dissuasion de la reprise d'un verre







Gaval-Cruz & Weinshenker *Mol Interv* 2009

Réaction Ethanol-disulfirame

- Bouffées congestives du visage
- Nausées / vomissements
- Sensation de malaise
- Tachycardie
- Hypotension
- Exceptionnellement :
 - Collapsus, mort subite, TDR, angor, IDM, dépression respiratoire, accidents neurologiques

disulfirame

Efficacité

- Problèmes méthodologiques +++
- Etudes anciennes = pauvreté méthodologique
- Résultats équivoques
- Supériorité de la supervision dans le cadre d'une prise en charge globale

difficultés méthodologiques

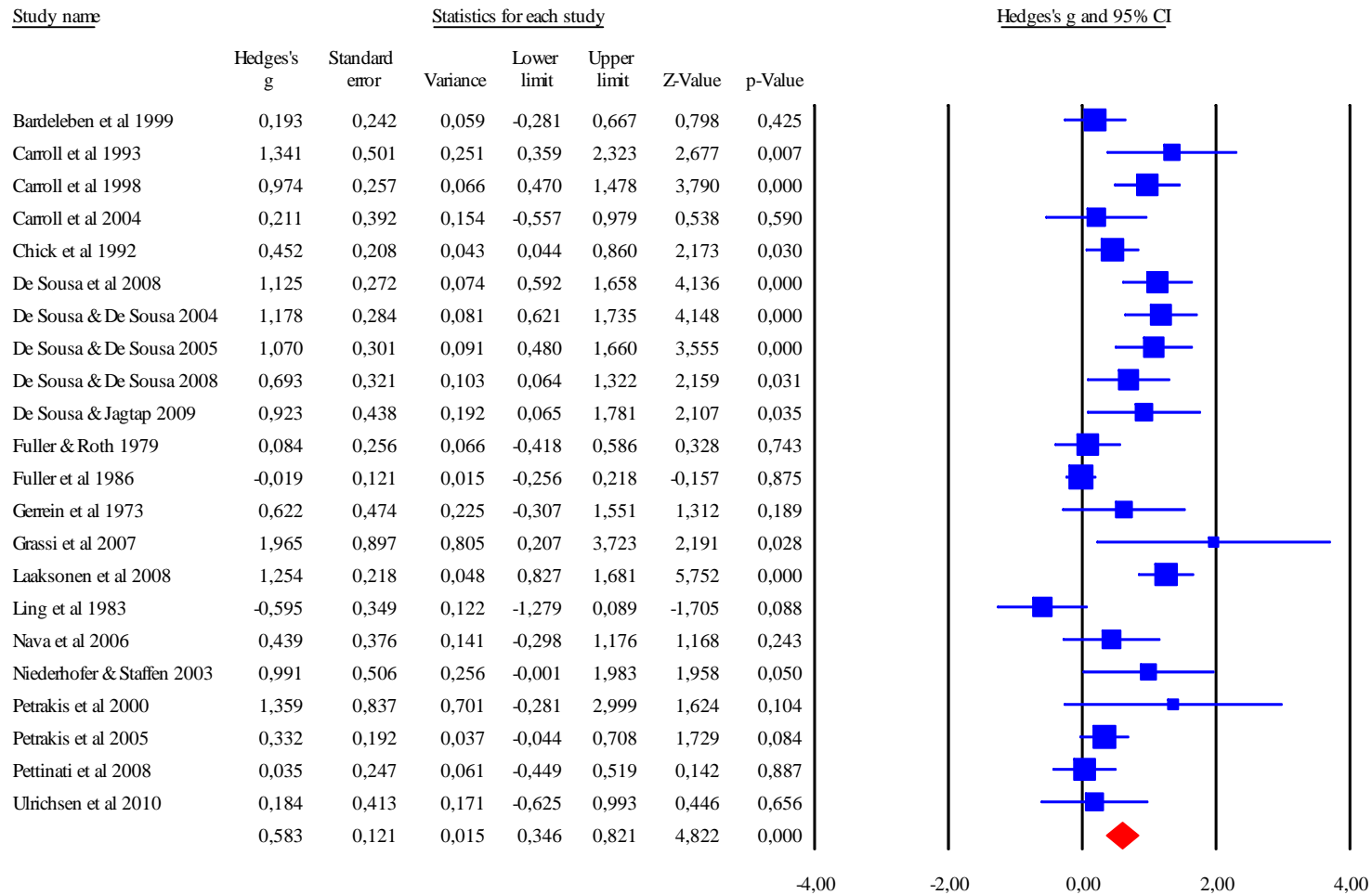


Effet thérapeutique = menace de la réaction aversive

Avant premier verre : menace identique dans les deux groupes

Après premier verre : rupture de l'aveugle

Meta-analysis of Hedges' g effect-size of all RCTs comparing the efficacy of disulfiram and controls

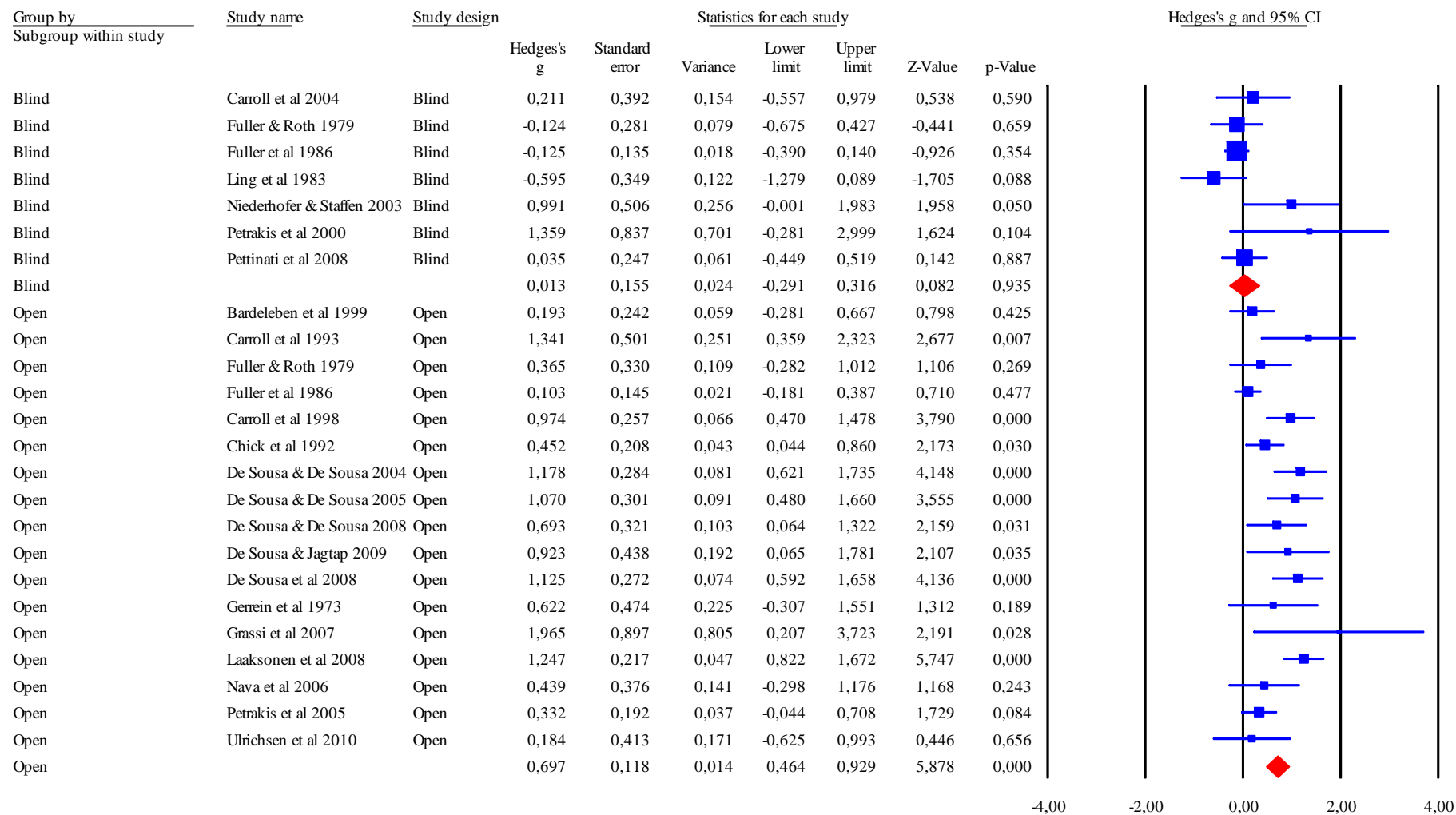


Controls

Disulfiram

Aubin et al.

Meta-analysis of Hedges' g effect-size comparing the efficacy of disulfiram and controls in blinded versus open-label RCTs

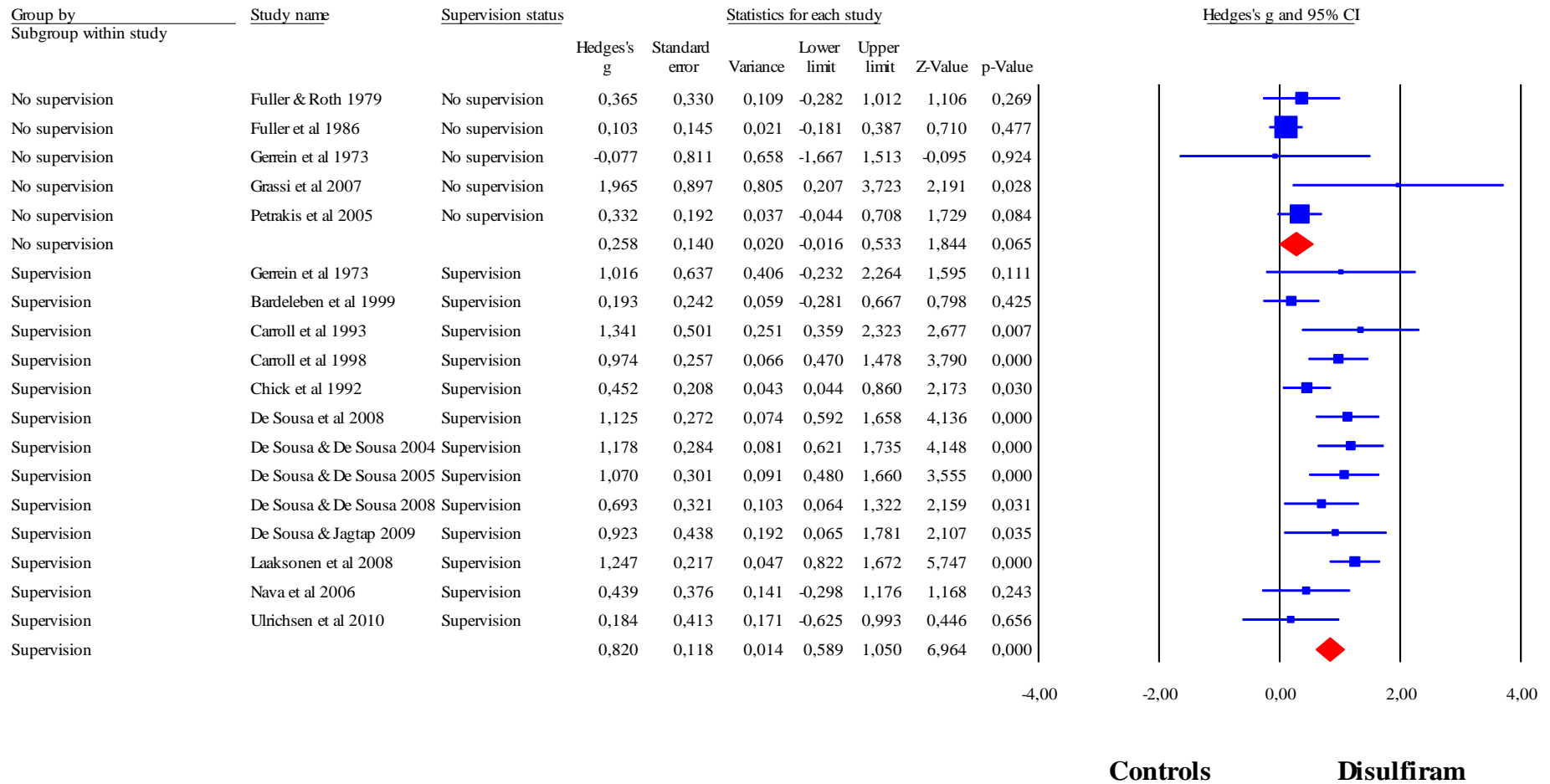


Aubin et al.

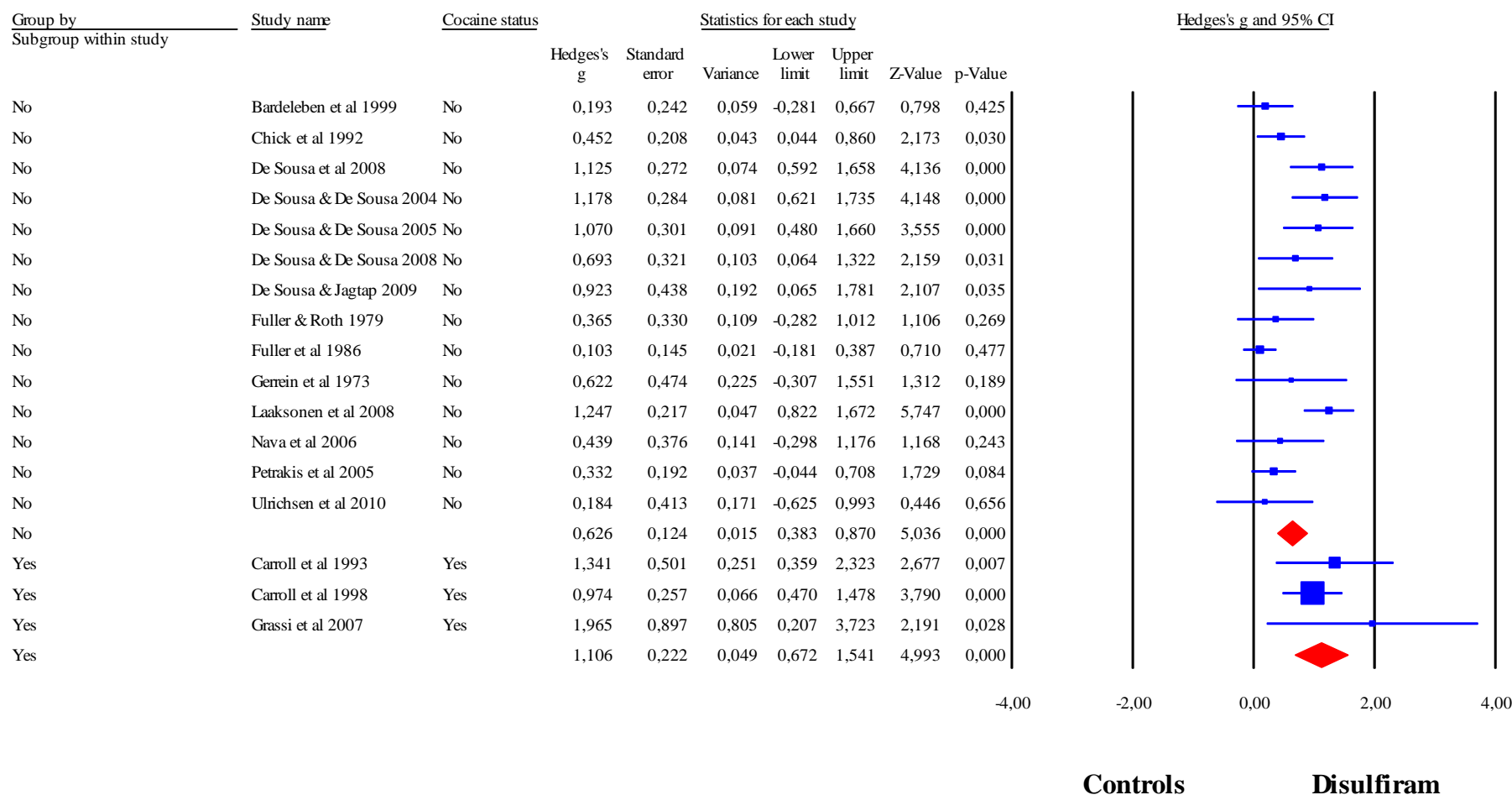
Controls

Disulfiram

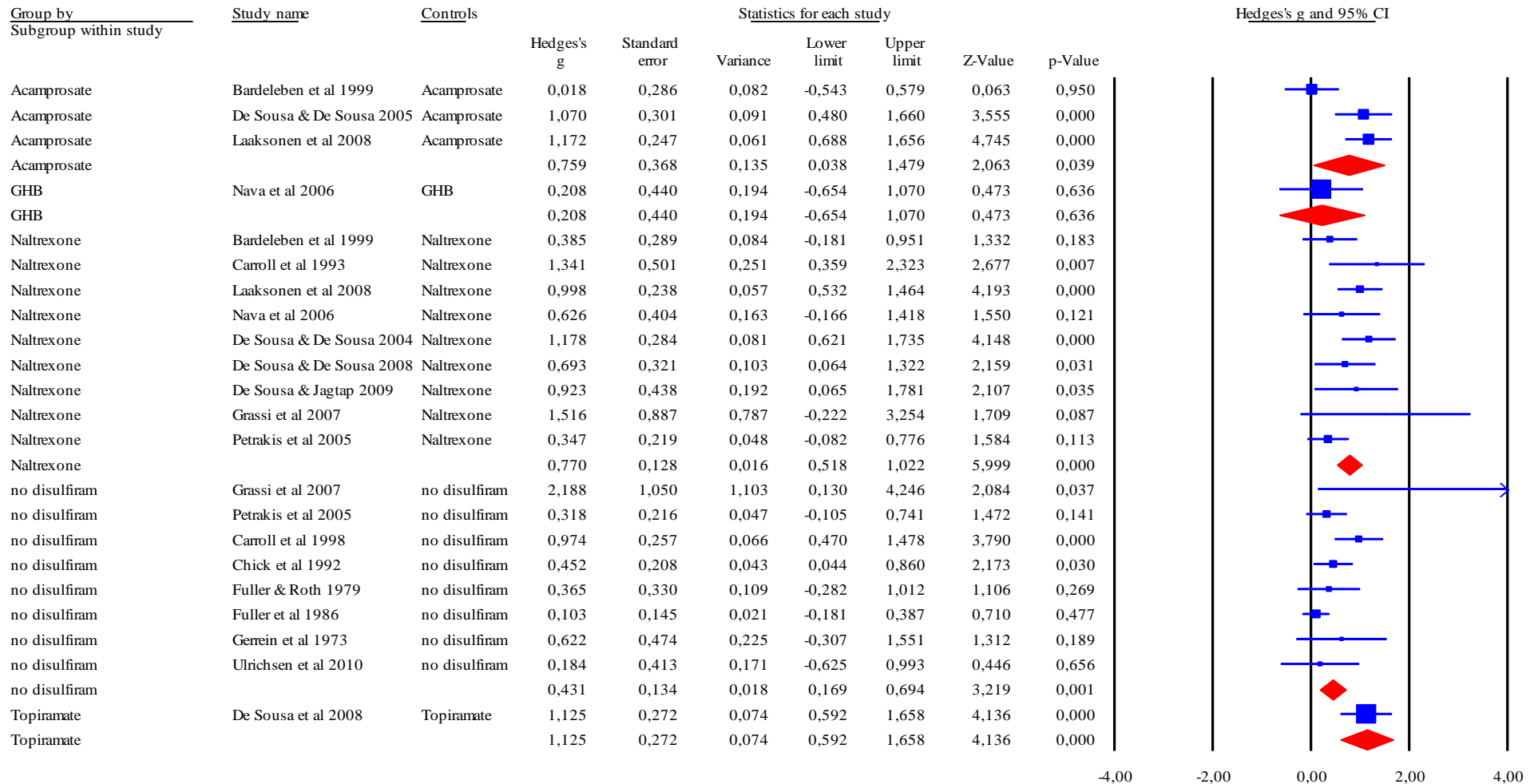
Meta-analysis of Hedges' g effect-size comparing the efficacy of disulfiram and controls in RCTs with supervision versus no supervision



Meta-analysis of Hedges' g effect-size comparing the efficacy of disulfiram and controls in RCTs that included alcohol dependent cocaine subjects versus those that did not include cocaine subjects



Subgroup analysis of Hedges' g effect-size comparing the efficacy of disulfiram and controls by control types



Aubin et al.

Controls

Disulfiram

Nalmefene (Selincro)



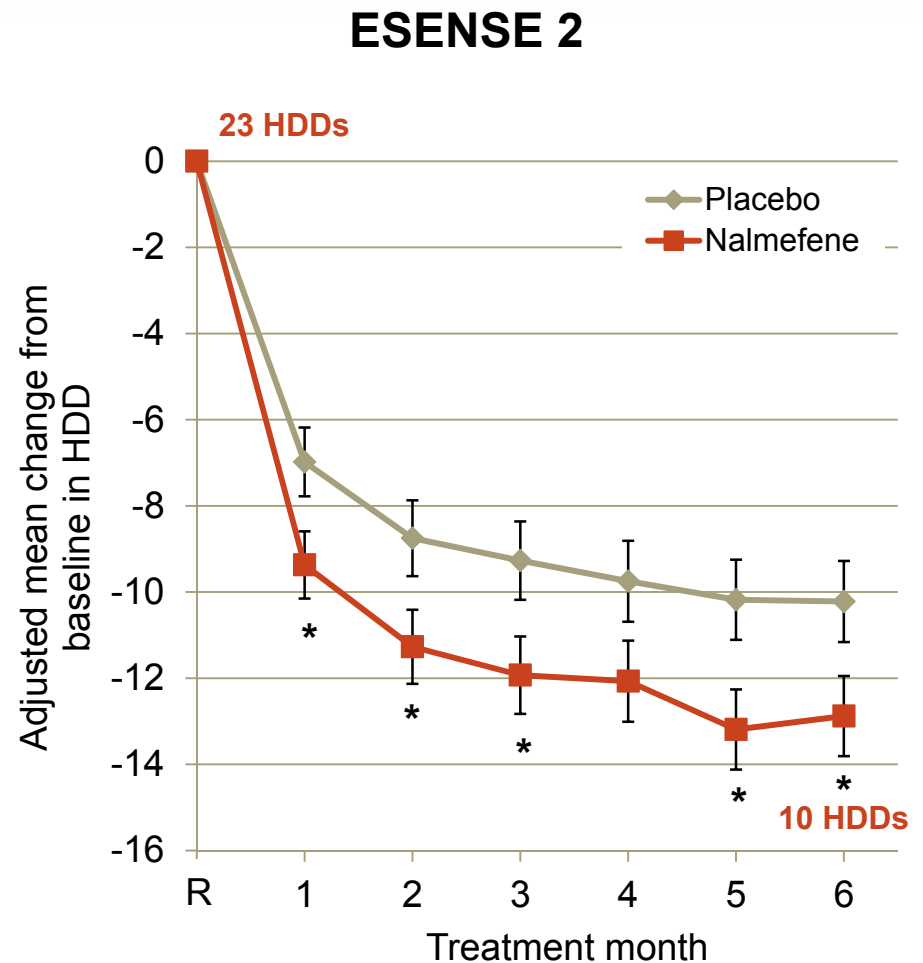
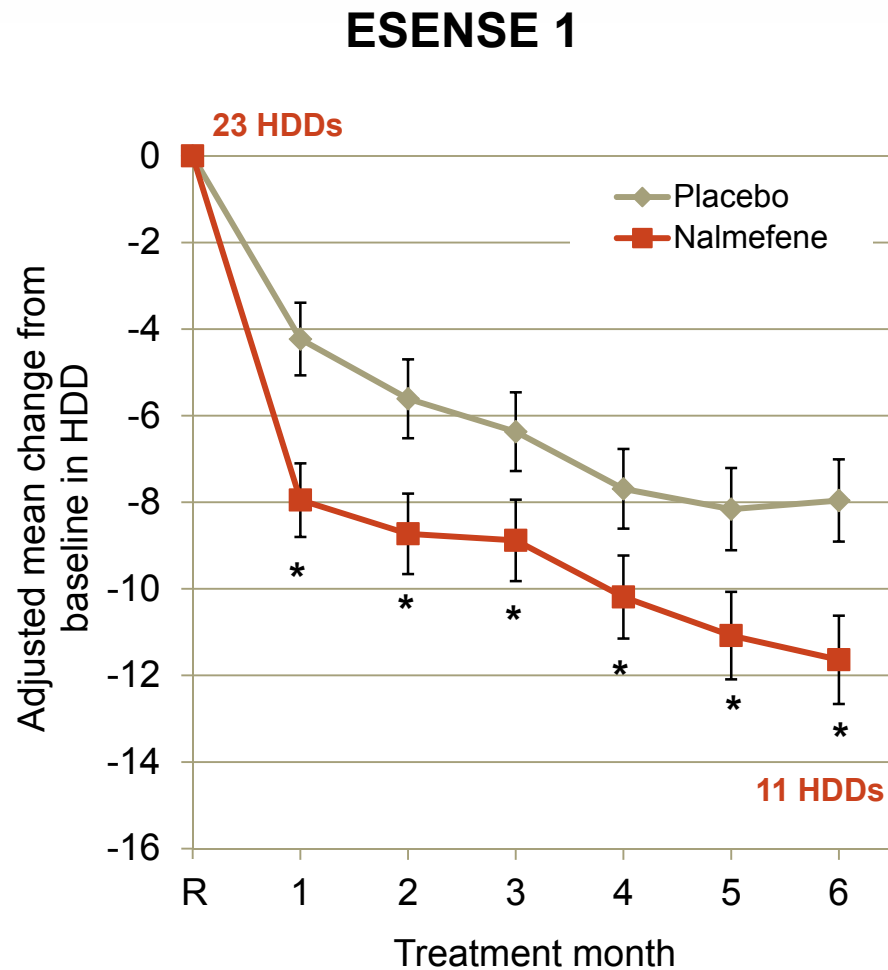
Nalmefene is an opioid system modulator with a distinct μ , δ , and κ profile

In vitro receptor profile

Antagonist at μ opioid receptors
Antagonist at δ opioid receptors
Partial agonist at κ opioid receptors

- Equal high potency on μ and κ opioid receptors
- Lower potency on δ opioid receptors

HDD – change from baseline in the 6-month studies 51

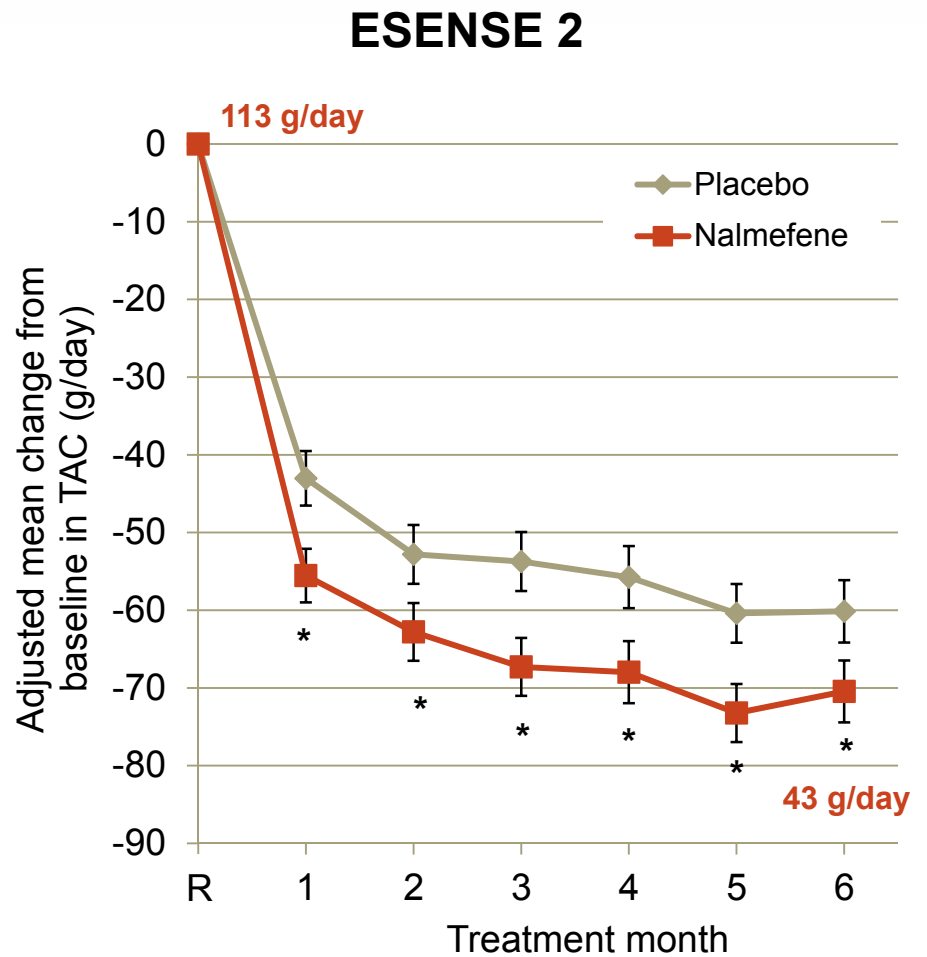
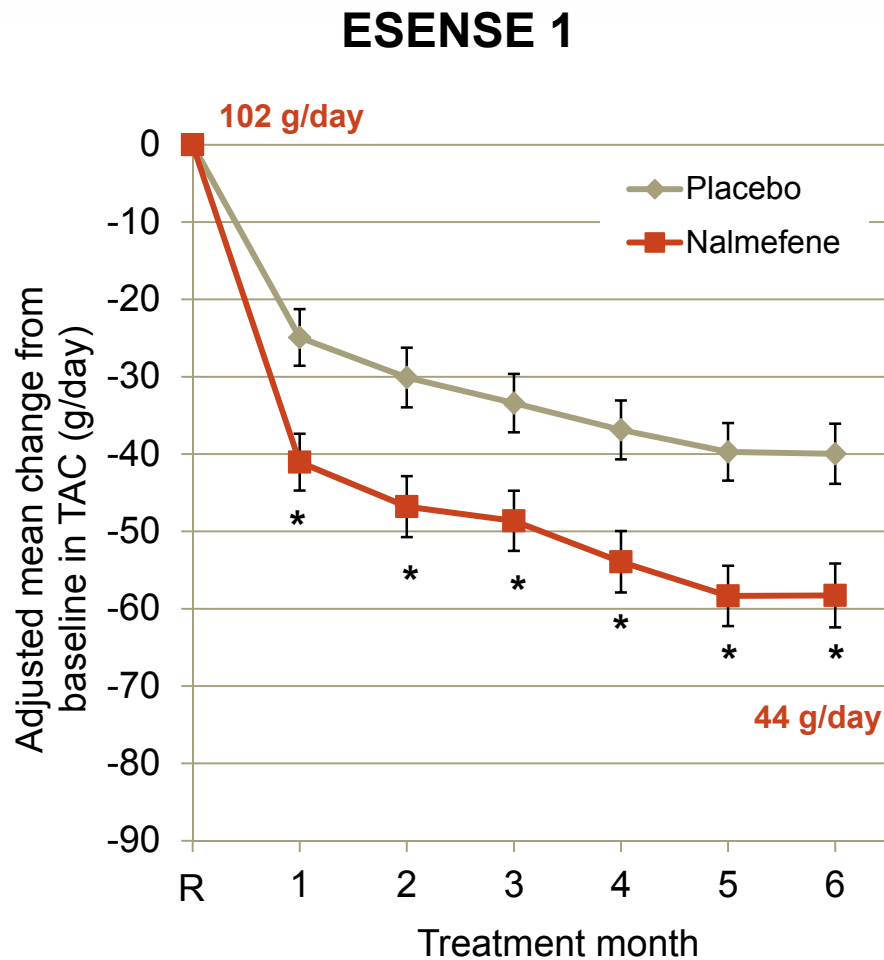


51

If possible, I'd prefer showing the pooled data

506620, 3/18/2013

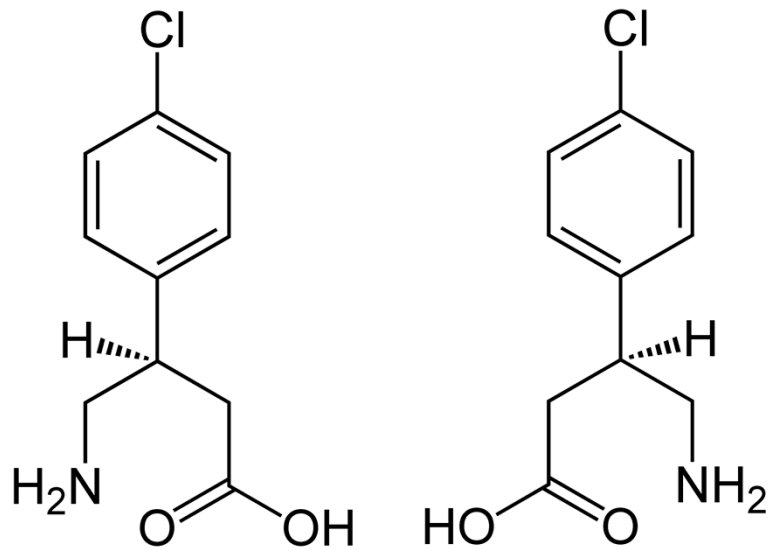
TAC – change from baseline in the 6-month studies 52



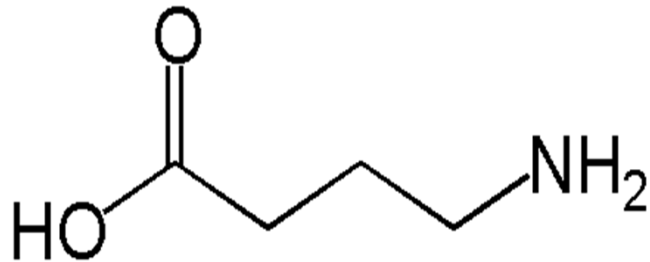
If possible, I'd prefer showing the pooled data

506620, 3/18/2013

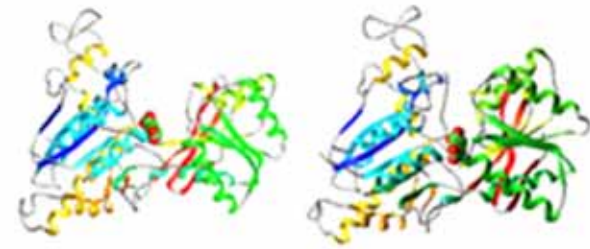
Baclofène



Baclofen



GABA-B



GABA-B
receptor



Baclofène 30 mg/j

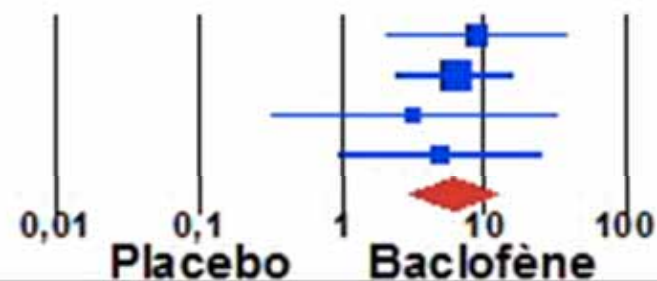
Efficacité sur l'abstinence

Study name

Statistics for each study

Odds ratio and 95% CI

	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Addolorato 2002	8,750	2,032	37,671	2,912	0,004
Addolorato 2007	6,250	2,425	16,108	3,794	0,000
Garbutt 2010	3,162	0,315	31,775	0,978	0,328
Addolorato 2011	4,889	0,931	25,670	1,876	0,061
	6,079	3,067	12,049	5,170	0,000



Dr Olivier Ameisen

LE DERNIER VERRE

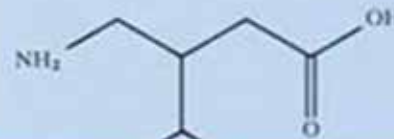
«Alors que j'avais sombré dans l'alcool, un médicament m'a libéré de l'envie compulsive de boire... Ce livre raconte ma maladie et ma guérison.»

DENOËL



Olivier Ameisen was a renowned cardiologist until alcoholism took over his life.

This is the story of how he cured himself.



THE END OF MY ADDICTION

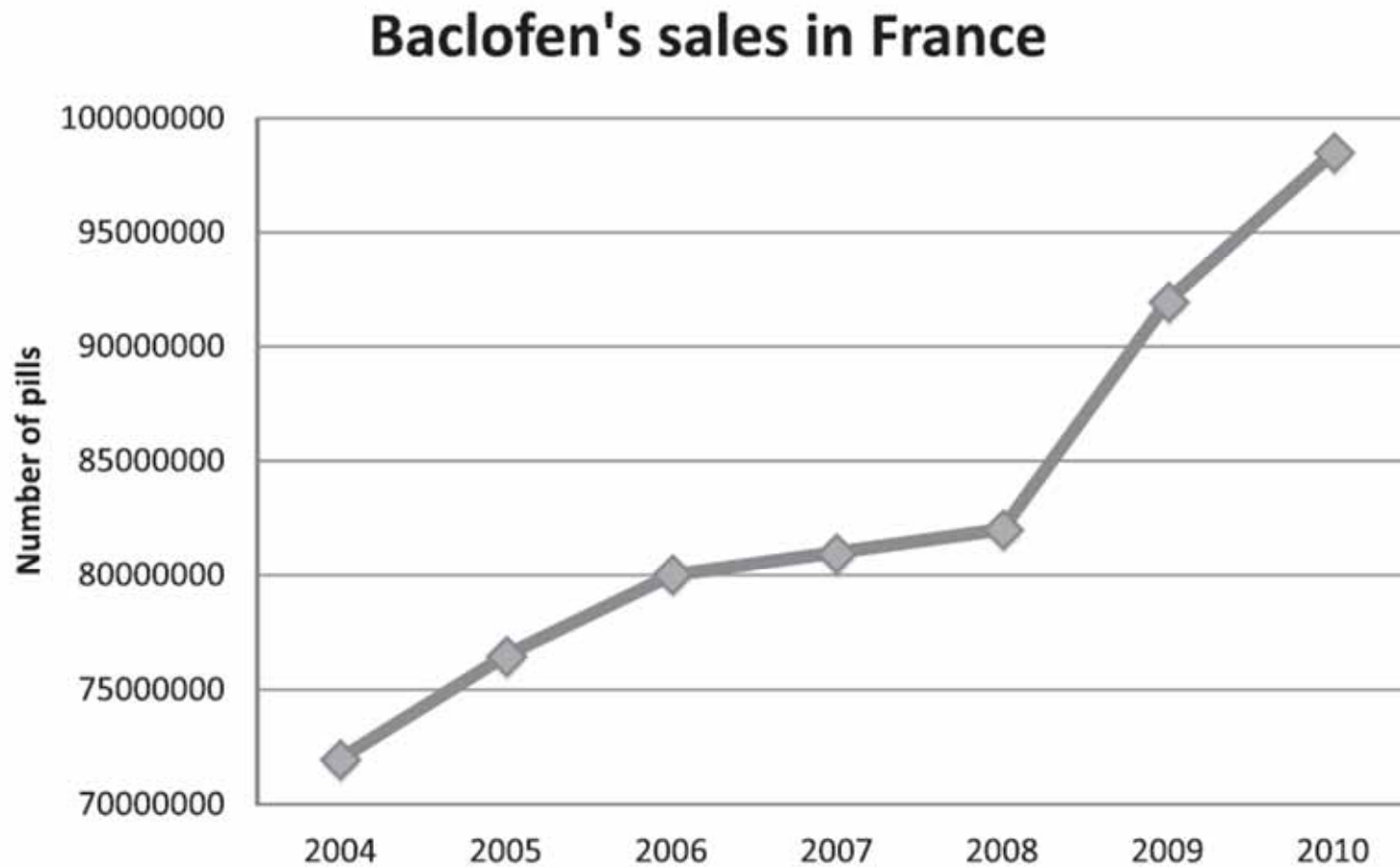


OLIVIER AMEISEN, M.D.

Foreword by **JEFFREY S. BORER, M.D.**

Gladys and Roland Harriman
Professor of Cardiovascular Medicine,
Weill Cornell Medical College

Alcohol-Dependence: The Current French Craze for Baclofen



Quelles doses ?

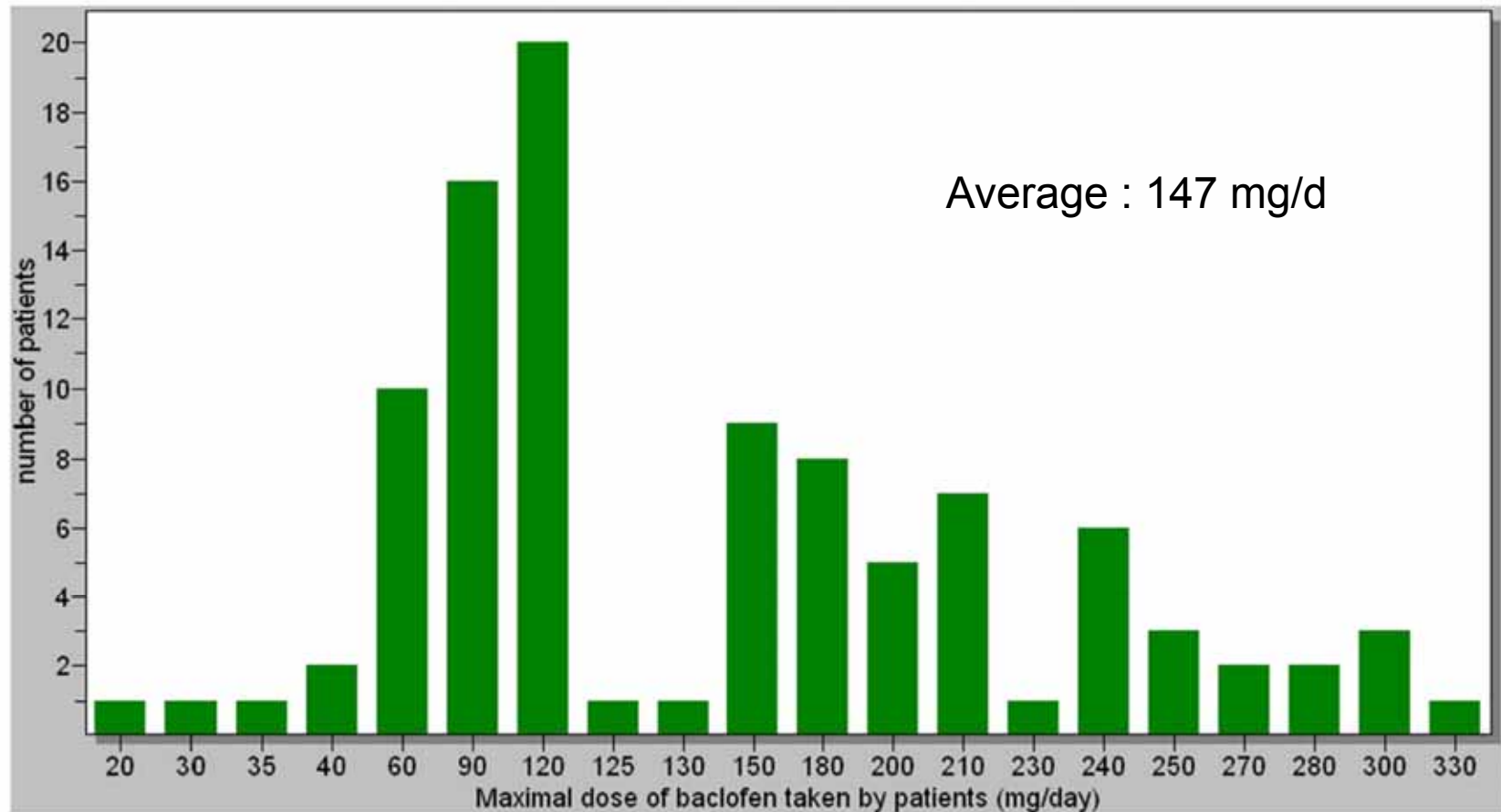


FIGURE 1 | Maximal dose taken by patients, with the number of patients for each maximal dose.

Psychothérapie



Psychothérapie



Associations d'entraide



®



