Nuevos abordajes terapéuticos de la dependencia alcohólica

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Índice

- Nuevos conceptos
- Las nuevas formas de expresión clínica
- Nuevos paradigmas de tratamiento y nuevos fármacos
- El abordaje psicosocial en el siglo XXI
- Conclusiones

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Nuevos conceptos

- La adicción como enfermedad del cerebro
- El DSM V
- Consumo Excesivo Reiterado (Heavy Use Over Time)
- La enfermedad no tan oculta

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- La enfermedad oculta

La adicción como enfermedad del cerebro

Moral model

Social model

Learning model

Symptomatic model

Drug model

Disease model

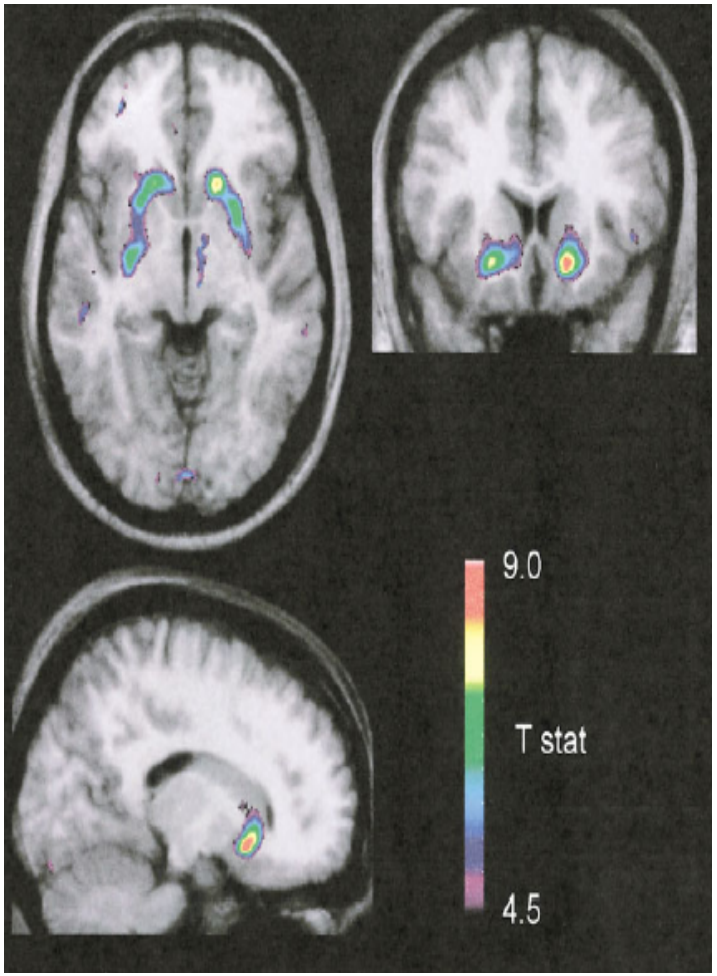
1976: Edwards & Gross

Biopsychosocial model

Alcohol dependence syndrome

Ideology → Evidence base

Alcohol promotes dopamine release in the human nucleus accumbens



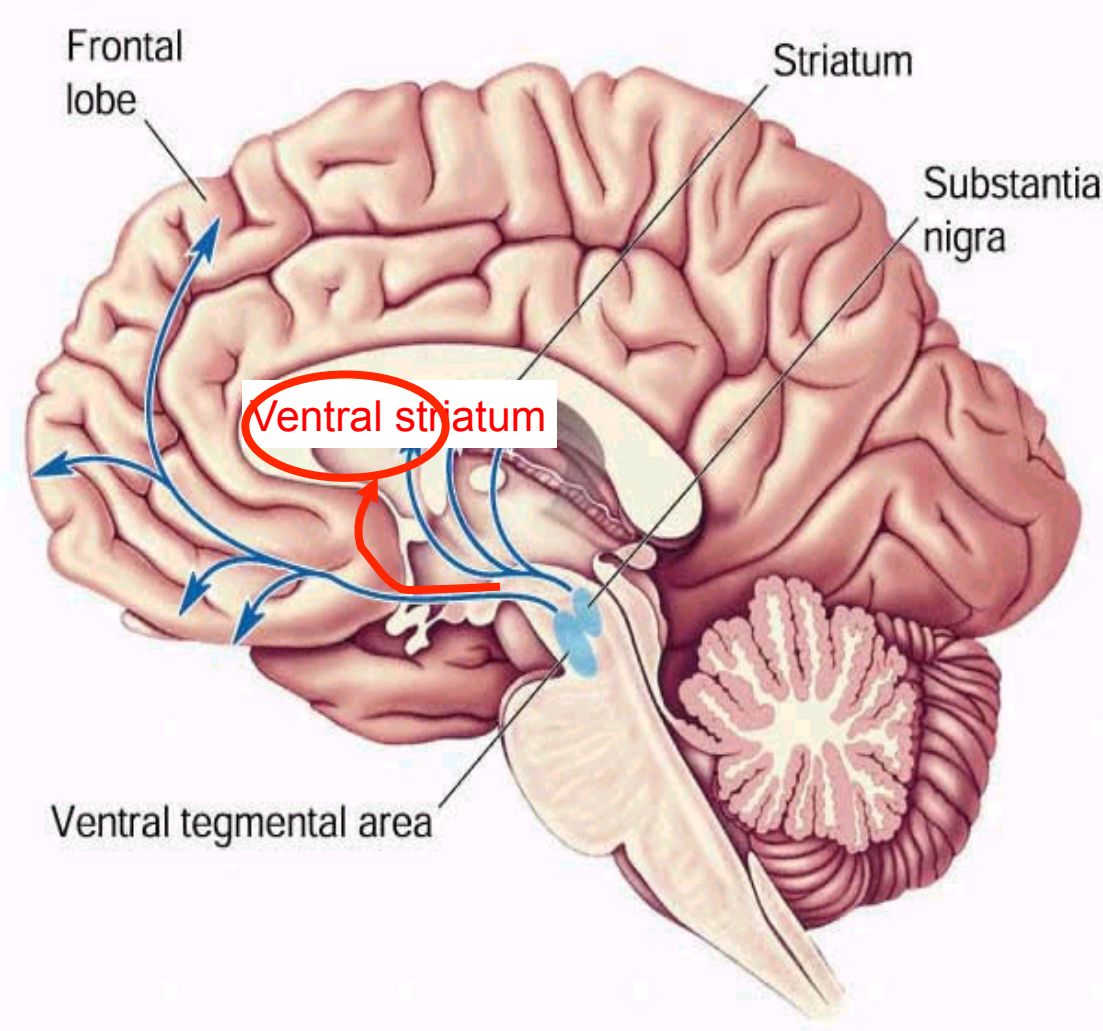
- In non-dependent alcohol drinkers, alcohol increases dopamine levels in nucleus accumbens / ventral striatum

Statistical t-map of the change in [^{11}C]-raclopride BP induced by an acute oral dose of alcohol (1 mg/kg) in healthy volunteers (n=6)

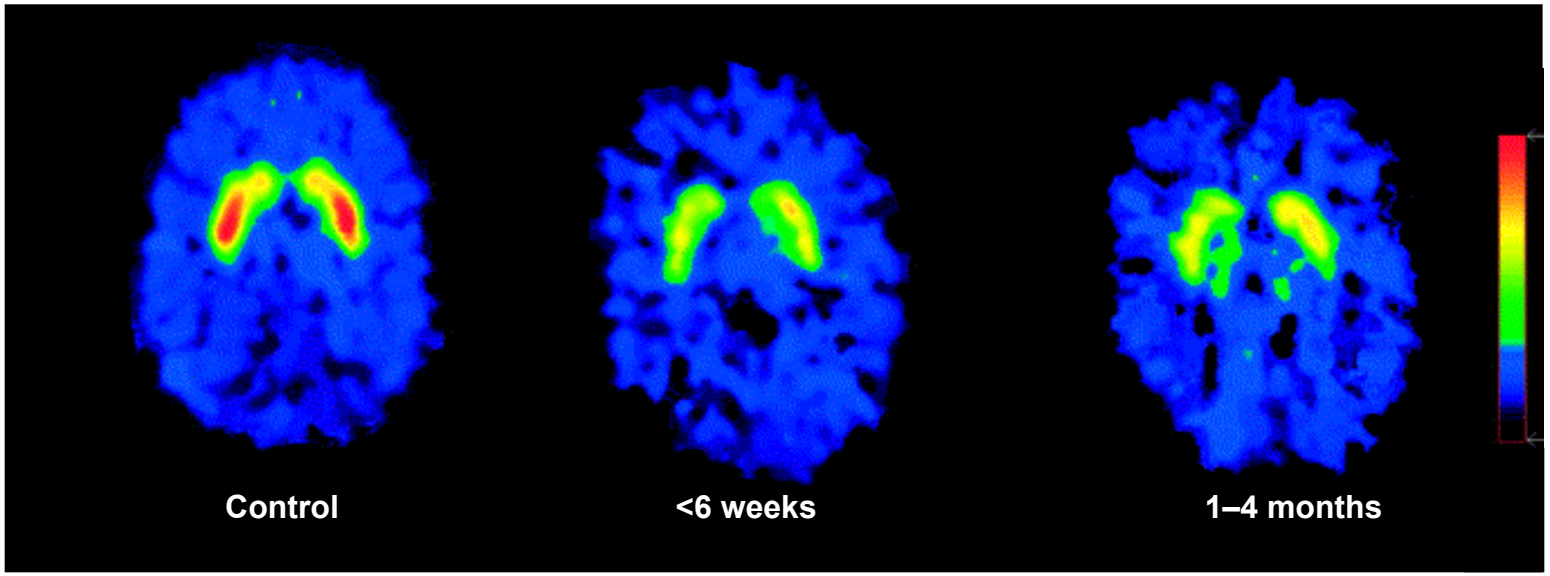
Boileau et al. Synapse 2003;49(4):226–231;
Ramchandani et al. Mol Psychiatry 2011;16(8):809–817

Los circuitos naturales de recompensa son mediados por la liberación de dopamina en el cerebro límbico

- Demostrado en recompensa biológica (comida, sexo)
- Amplificado en el consumo de alcohol y otras drogas
- ‘alcohol cheats the brain’



Los pacientes dependientes de alcohol presentan niveles mas bajos de receptores dopaminérgicos que cambian poco con la abstinencia.

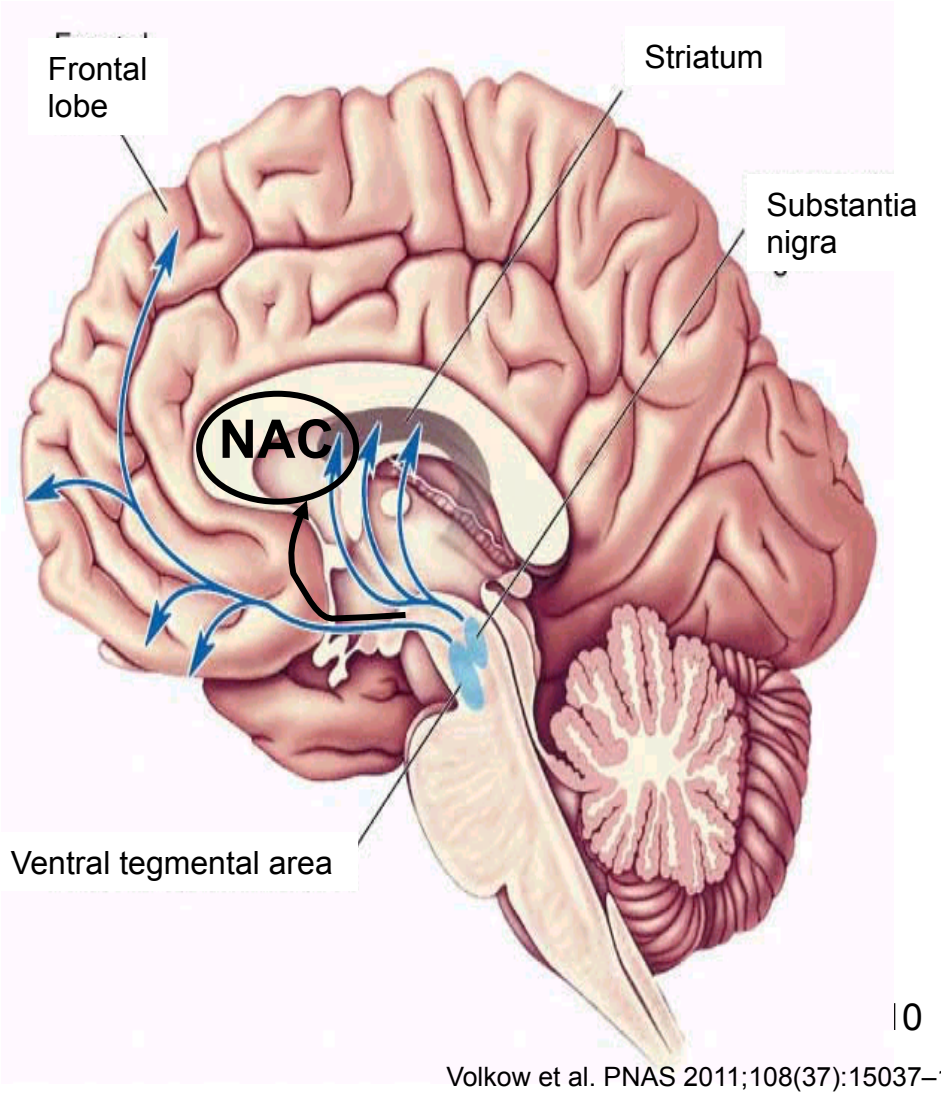


Niveles de captación de dopamina en los circuitos cerebrales de recompensa (Nucleus accumbens, ATV)

Volkow et al. PNAS 2011; 108(37):15037–15042

The dopaminergic reward and motivational dopamine system is modulated by other neurotransmitter systems

- Dopamine system is modulated by other neurotransmitters:
  - Glutamate
  - GABA
  - Opioids
  - 5-HT
  - Cannabinoid



Volkow et al. PNAS 2011;108(37):15037–15042

Nuevos conceptos

- La adicción como enfermedad del cerebro
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Basic diagnostic classifications

WHO – ICD 10

- Hazardous drinking
- Harmful drinking
- Alcohol dependence

ICD 11 (?)

APA – DSM-IVR

- Alcohol abuse
- Alcohol dependence

DSM V

Alcohol Use Disorder

ALCOHOL USE DISORDER

(DSM V)

Given the empirical evidence, the DSM-V Substance Use Disorders Workgroup recommends:

- To combine abuse and dependence into a single disorder
- With graded clinical severity
- Two criteria required to make a diagnosis

Alcohol Use Disorder (AUD)

1. Recurrent use resulting in a failure to fulfill major role obligations
2. Recurrent use in situations in which it is physically hazardous
3. Continued use despite persistent or recurrent problems caused or exacerbated by the effects of alcohol
4. Tolerance,
5. Withdrawal,
6. Alcohol is taken in larger amounts or over longer periods than intended
7. Persistent desire or unsuccessful efforts to cut down or control drinking
8. A great deal of time spent in alcohol-related activities
9. Important social, occupational, or recreational activities are given up or reduced because of drinking
10. Alcohol use is continued despite knowledge of having a problem probably caused or exacerbated by alcohol.
11. Craving or a strong desire or urge to drink alcohol.

Alcohol use disorder (AUD)

Severity specifiers:

- Mild: 2-3 criteria positive
- Moderate: 4-5 criteria
- Severe: 6 or more criteria

Specify Physiological Dependence:

- tolerance and/or withdrawal

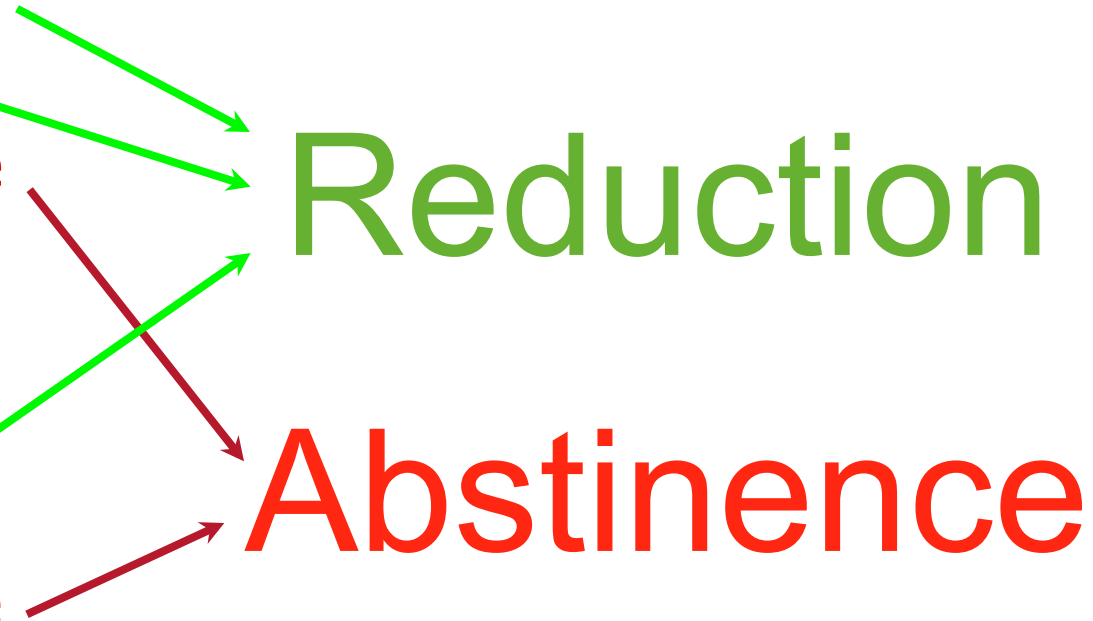
Basic therapeutic Goals classifications

WHO – ICD 10

- Hazardous drinking
- Harmful drinking
- Alcohol dependence

APA – DSM-IV TR

- Alcohol abuse
- Alcohol dependence



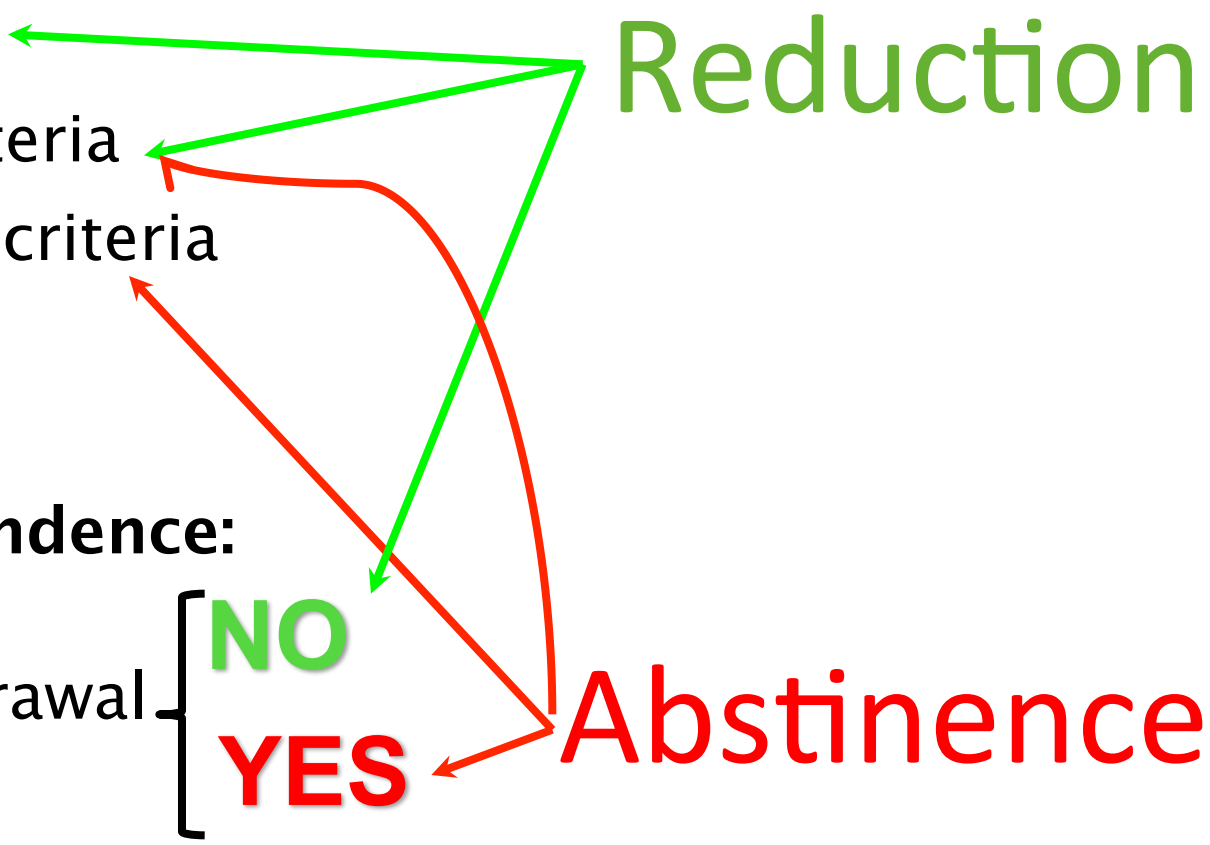
DSM 5: Alcohol use disorder (AUD)

Severity specifiers:

- Mild: 2-3 criteria
- Moderate: 4-5 criteria
- Severe: 6 or more criteria

Physiological Dependence:

- Tolerance / withdrawal



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Consumo Excesivo Reiterado (CER)
Heavy Use Over Time (HUOT)

Alcohol and Alcoholism Advance Access published August 7, 2013

Alcohol and Alcoholism pp. 1–8, 2013 doi: 10.1093/alcalc/agt127

Defining Substance Use Disorders: Do We Really Need More Than Heavy Use?

J. Rehm[1,2,3,4,5,*], S. Marmet[6], P. Anderson[7,8], A. Gual[9], L. Kraus[10,11], D.J. Nutt[12], R. Room[11,13,14], A.V. Samokhvalov[2,5], E. Scafato[15], M. Trapencieris[16], R.W. Wiers[17] and G. Gmel[2,6,18,19]

Alcohol and Alcoholism Advance Access published November 12, 2013

Alcohol and Alcoholism pp. 1–4, 2013 doi: 10.1093/alcalc/agt171

LETTER TO THE EDITOR

The Tangible Common Denominator of Substance Use Disorders: A Reply to Commentaries to Rehm *et al.* (2013a)

J. Rehm[1,2,3,4,5,*], P. Anderson[6,7], A. Gual[8], L. Kraus[9,10], S. Marmet[11], D.J. Nutt[12], R. Room[10,13,14], A.V. Samok
E. Scafato[15], K.D. Shield[2,3], M. Trapencieris[16], R.W. Wiers[17] and G. Gmel[2,11,18,19]

ADDICTIONS AND LIFESTYLES IN CONTEMPORARY EUROPE
Alice Rap
- REFRAMING ADDICTIONS PROJECT -

Why use HUOT ?

- HUOT is responsible for the changes in the brain and other physiological characteristics of SUD
- HUOT is responsible for intoxication and for the withdrawal and tolerance phenomena regarded as central to current definitions of addiction or dependence
- HUOT is responsible for the main social consequences of SUD, such as problems in fulfilling social roles
- HUOT is responsible for the majority of the substance-attributable burden of disease and mortality
- HUOT as a definition better fits the empirical data and may diminish stigmatization and avoids pointing attention away from highest-risk categories

Table 1. Average alcohol intake in grams per day by number of DSM-IV criteria fulfilled for alcohol dependence (last year), by whether treated in lifetime: from data of the US National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)

	Number of criteria of DSM-IV for alcohol dependence							
Gender	0	1	2	3	4	5	6	7
For people who have never been in treatment								
Men	9.1	27.1	35.9	56.5	73.6	88.0	107.4	189.0
Women	4.1	13.6	19.8	23.6	48.5	56.7	108.8	114.5
Total	6.6	21.6	29.5	45.4	64.7	77.5	107.8	170.3
For people who have been in treatment in their lifetime								
Men	20.6	35.2	98.2	75.2	109.1	124.2	119.8	214.1
Women	10.1	20.3	23.5	19.8	37.9	55.5	275.1	230.4
Total	17.5	31.7	77.9	61.5	91.2	104.7	165.1	218.3

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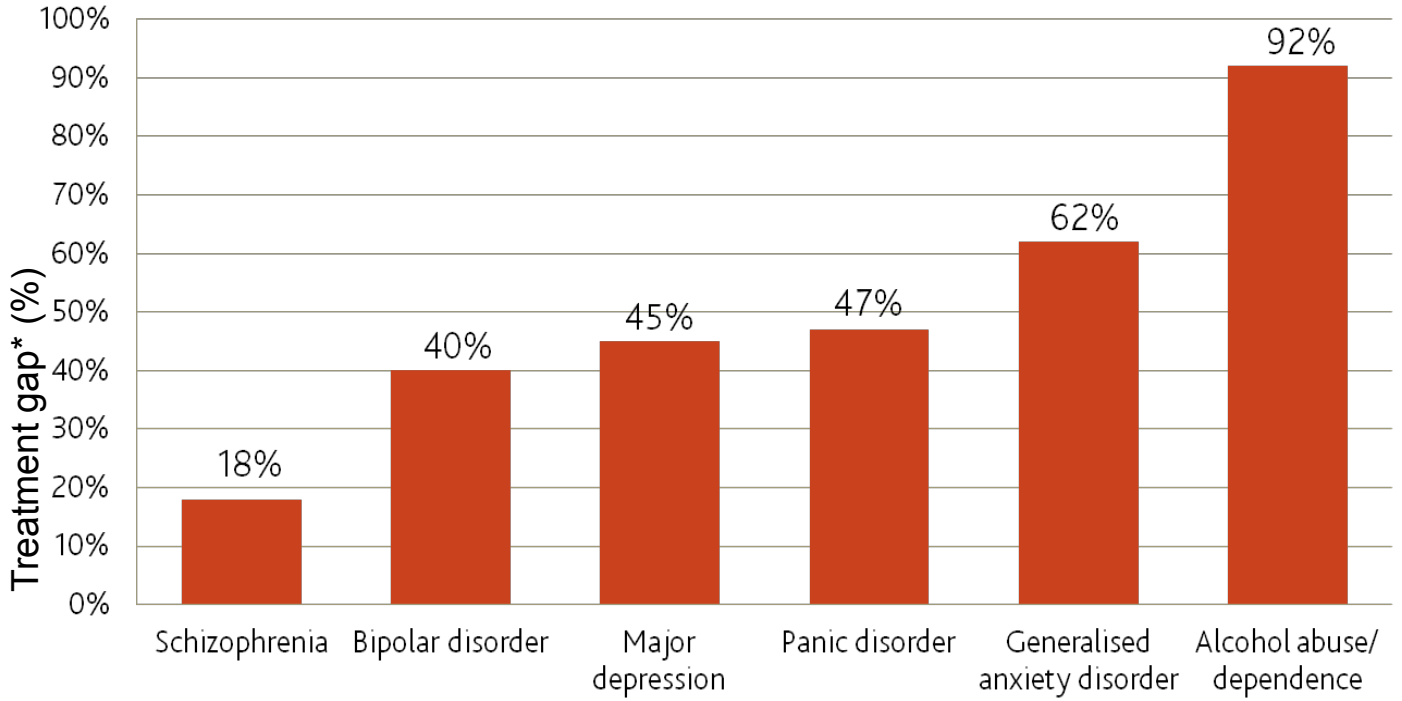
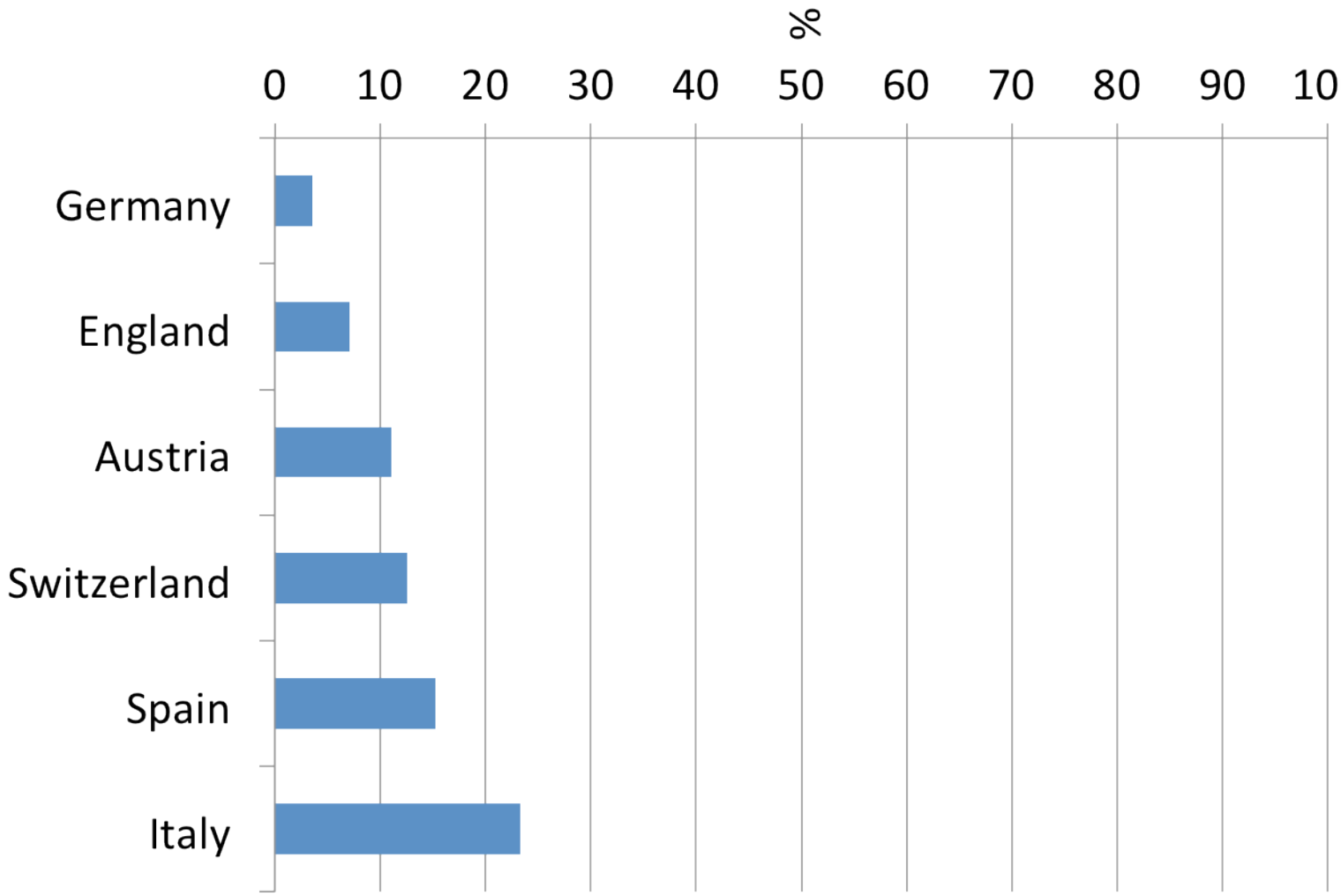
There is a huge unmet need in the treatment of alcohol dependency



- Widest treatment gap among all mental disorders: Less than 10% of patients with alcohol abuse and dependence are treated
- High prevalence and low treatment rates indicate a huge unmet medical need

Kohn et al. Bull World Health Organ 2004;82:858–866



Per cent of adults who would benefit from treatment for sustained heavy alcohol use who actually receive treatment

Wolstenhome, Drummond et al, 2012

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Nuevos patrones de consumo

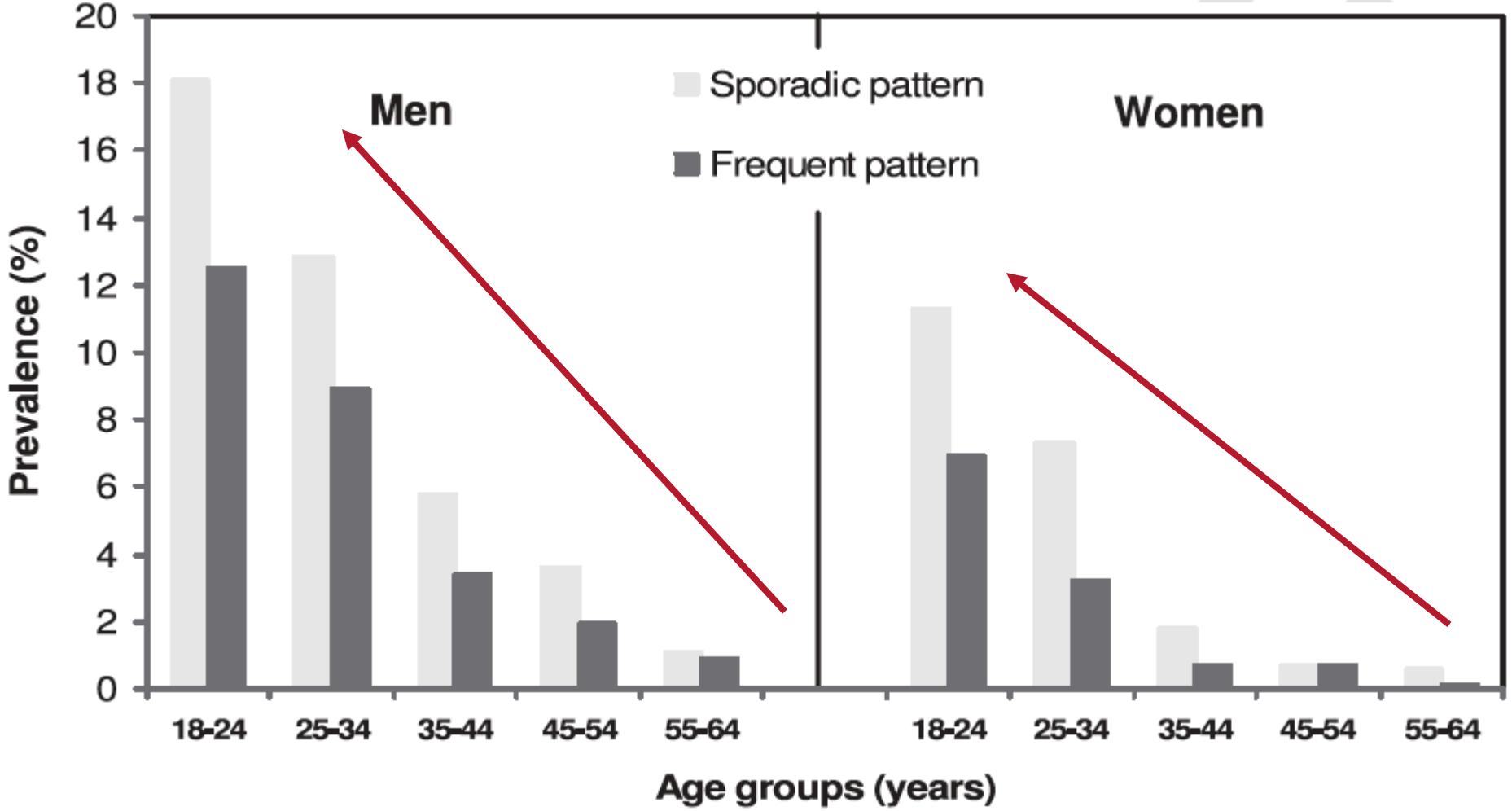
Alcoholism: Clinical and Experimental Research
Vol. 31, No. 10
October 2007

Binge drinking in Madrid, Spain

José Lorenzo Valencia-Martín, Iñaki Galán, and Fernando Rodríguez-Artalejo

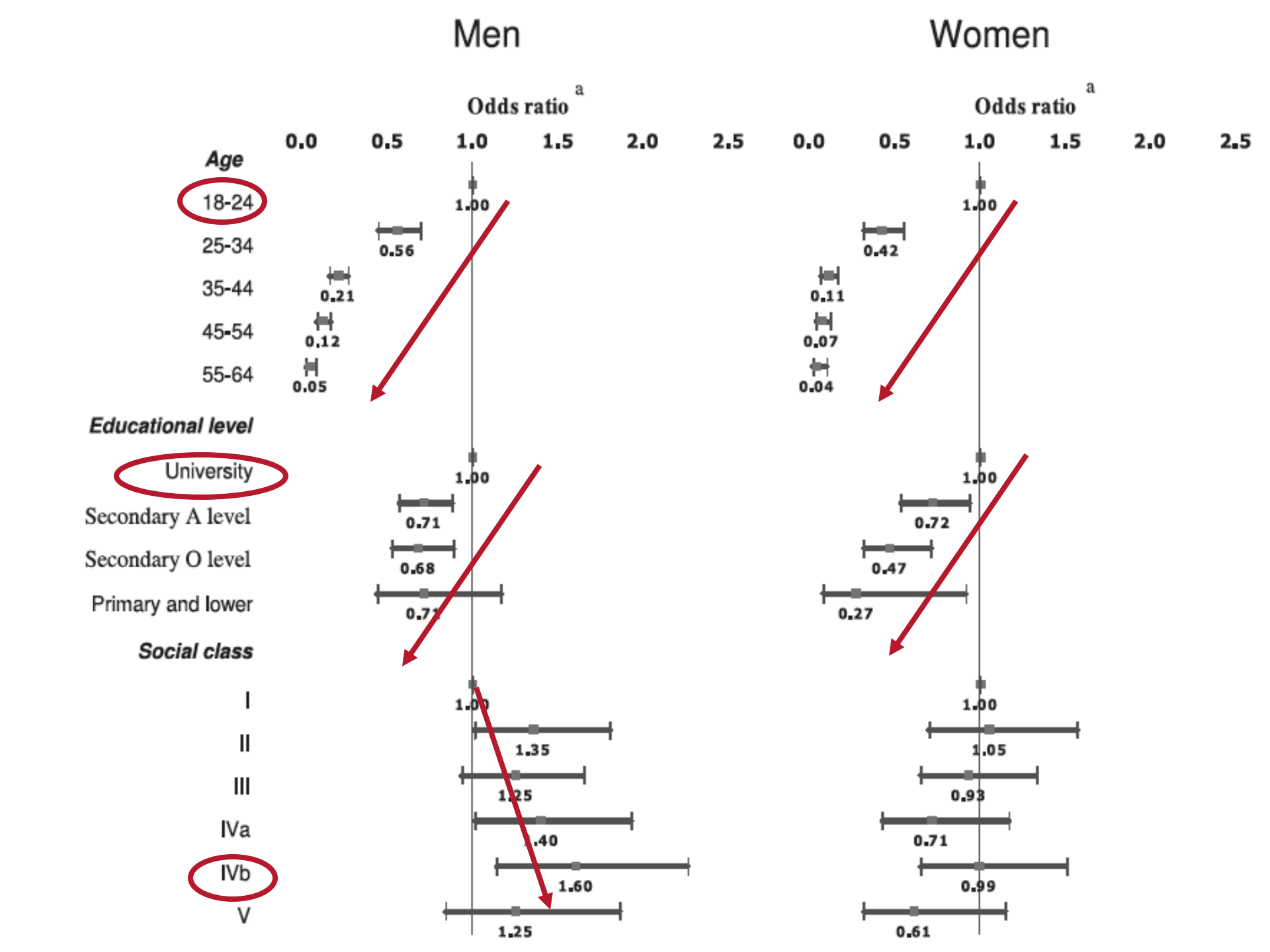
- 12.037 encuestados en Madrid
- 14,4% de hombres y 6,5% de mujeres refieren uno o mas episodios de ‘binge drinking’ en el último mes (> 80gr en varones y > 60gr en mujeres por ocasión de consumo)
- Las bebidas de alta graduación generaron el 72% del consumo

Binge drinking y edad

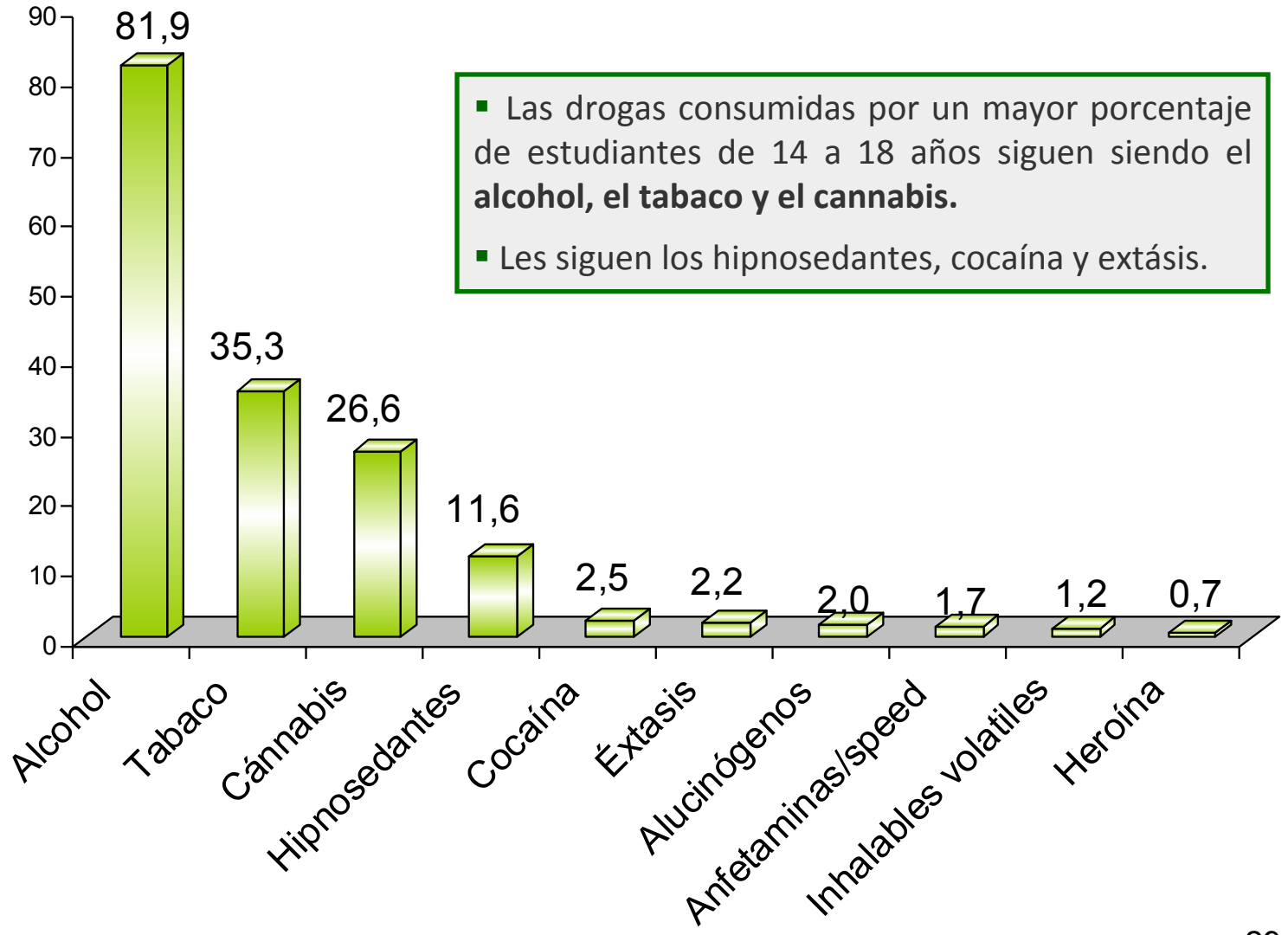


Lorenzo et al, 2007

Esporádico = 1-2 mes
Frecuente = >2 mes


Men
Women
Odds ratio a
0.0
0.5
1.0
1.5
2.0
2.5
Age
18-24
25-34
35-44
45-54
55-64
1.00
0.56
0.21
0.12
0.05
1.00
0.42
0.11
0.07
0.04
Educational level
University
Secondary A level
Secondary O level
Primary and lower
1.00
0.71
0.68
0.71
1.00
0.72
0.47
0.27
Social class
I
II
III
IVa
IVb
V
1.00
1.35
1.25
1.40
1.60
1.25
1.00
1.05
0.93
0.71
0.99
0.61

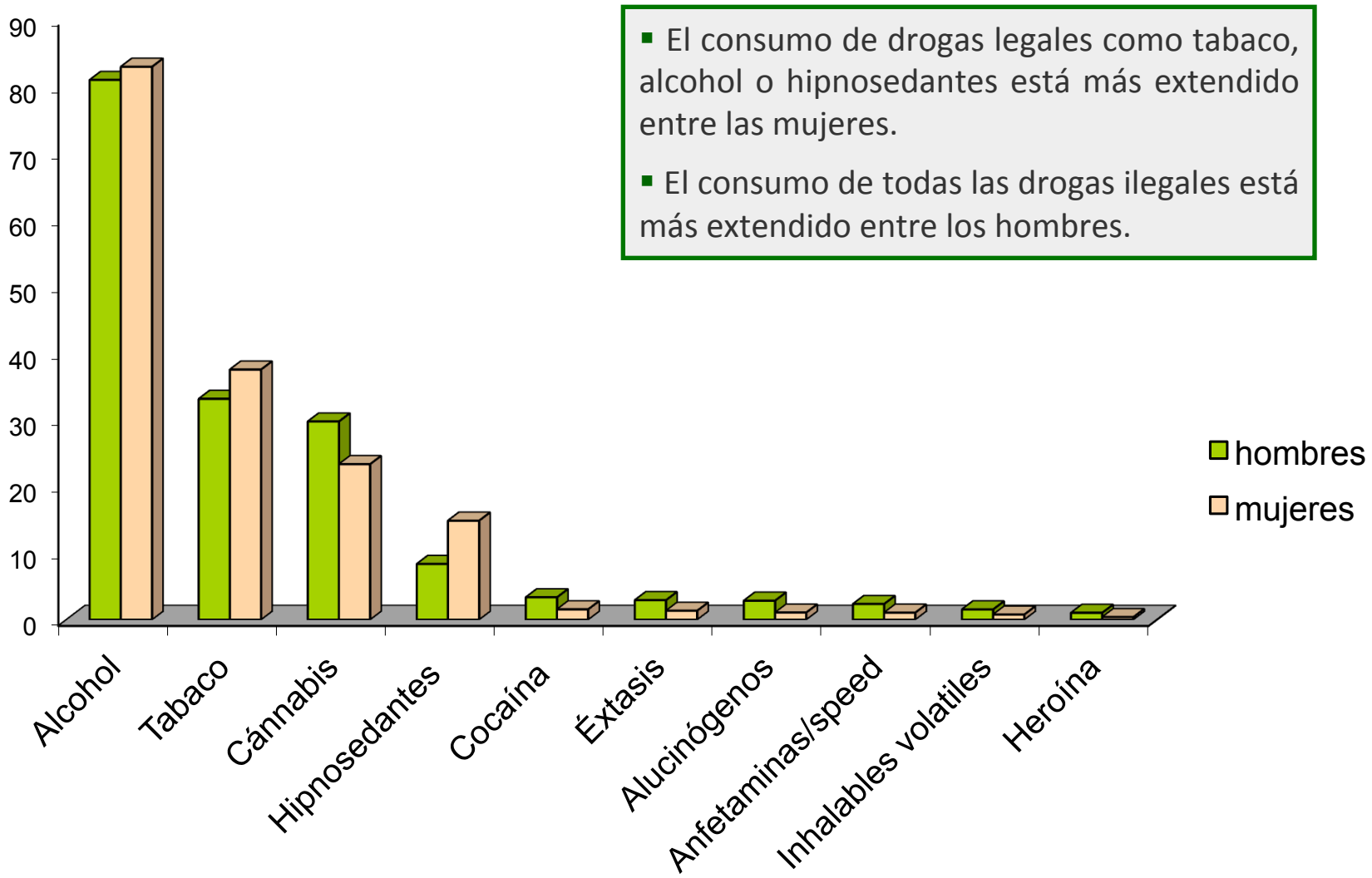
Porcentaje de consumidores de drogas en el último año. ESTUDES (14-18 años), 2012/2013.



- Las drogas consumidas por un mayor porcentaje de estudiantes de 14 a 18 años siguen siendo el **alcohol, el tabaco y el cannabis.**
- Les siguen los hipnosedantes, cocaína y extásis.

FUENTE: ESTUDES 2013. Observatorio Español sobre Drogas. DGPNSD. MSSSI.

Porcentaje de consumidores de drogas en el último año, según SEXO. ESTUDES (14-18 años), 2012/2013.



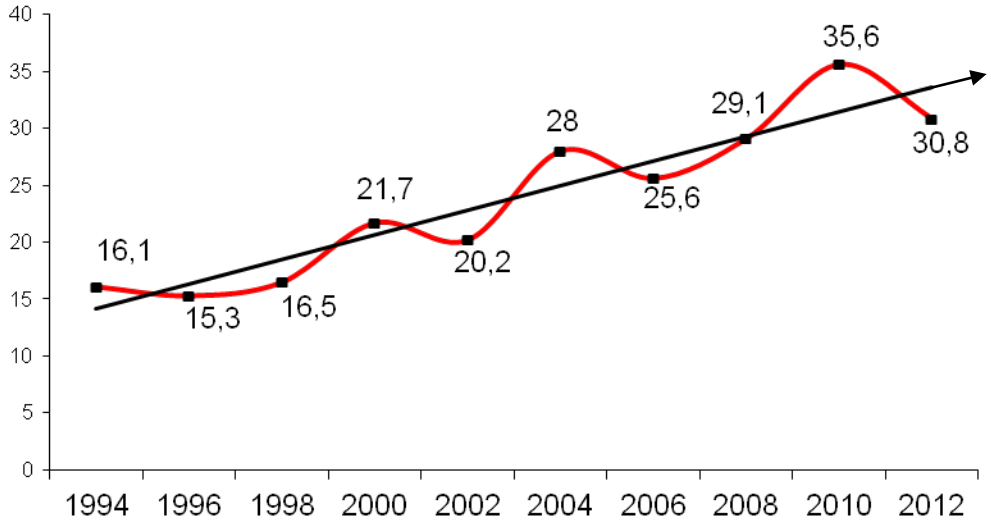
- El consumo de drogas legales como tabaco, alcohol o hipnosedantes está más extendido entre las mujeres.
- El consumo de todas las drogas ilegales está más extendido entre los hombres.

FUENTE: ESTUDES 2012/2013. Observatorio Español sobre Drogas. DGPNSD. MSSSI.

Evolución y porcentaje de "BORRACHERAS". ESTUDES (14-18 años) , 1994-2012/2013.

- A pesar de la tendencia global ascendente de las borracheras, en 2013 desciende el % de jóvenes que se emborracha.
- El % de jóvenes que se emborracha se mantiene en niveles altos: 3 de cada 10 en el último mes.

Evolución del % de jóvenes de 14 a 18 años que se han emborrachado en el último mes.



% de jóvenes de 14 a 18 años que se han emborrachado, en 2012, por edad y sexo.

	Alguna vez	Último año	Último mes
Total	60,7	52,0	30,8
Chicos	59,9	51,7	31,3
Chicas	61,5	52,3	30,3
14 años	31,5	26,1	12,7
16 años	62,3	53,4	30,9
18 años	80,4	70,5	46,5

FUENTE: ESTUDES 1994-2012/013. Observatorio Español sobre Drogas. DGPNSD. MSSSI.

Nuevas formas de expresión clínica

- Mayor comorbilidad psiquiátrica
- Policonsumo (cannabis, cocaina, BZD)
- Mayor patología conductual (y neurológica: W-K)

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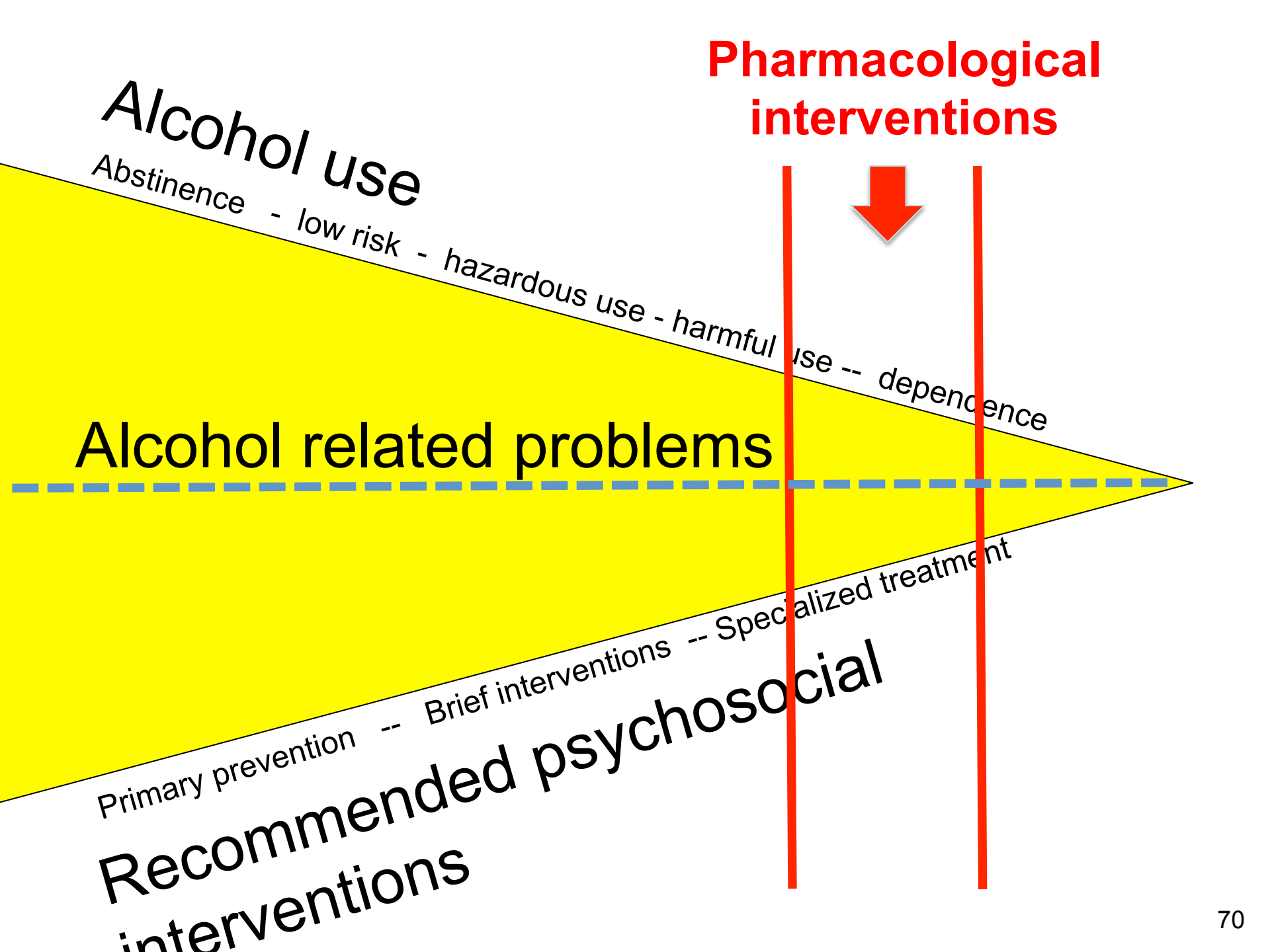
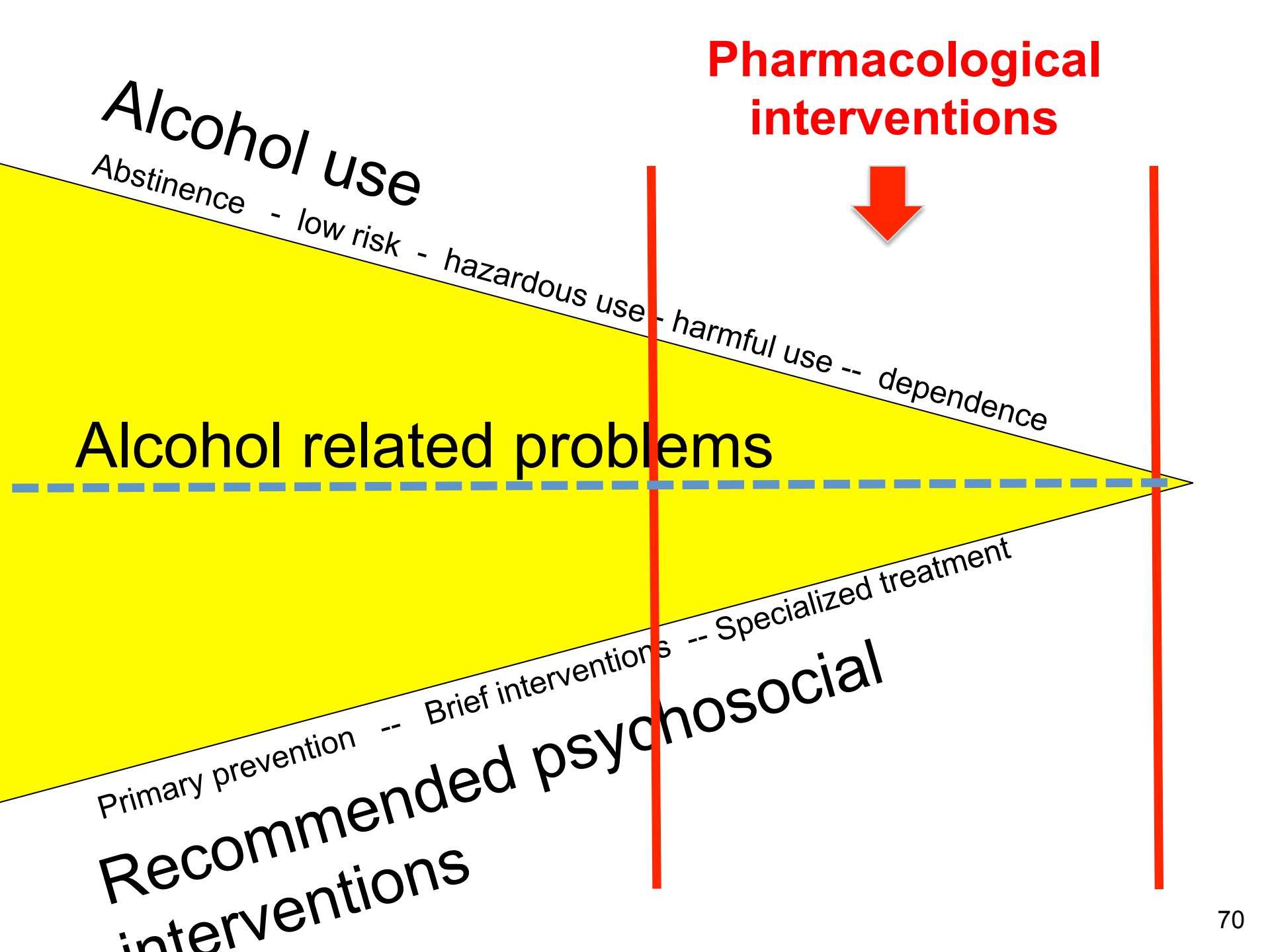

Pharmacological interventions
Alcohol use
Abstinence - low risk - hazardous use - harmful use -- dependence
Alcohol related problems
Primary prevention -- Brief interventions -- Specialized treatment
Recommended psychosocial interventions


Pharmacological interventions
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Recommended psychosocial interventions

Widening the scope of pharmacological treatments

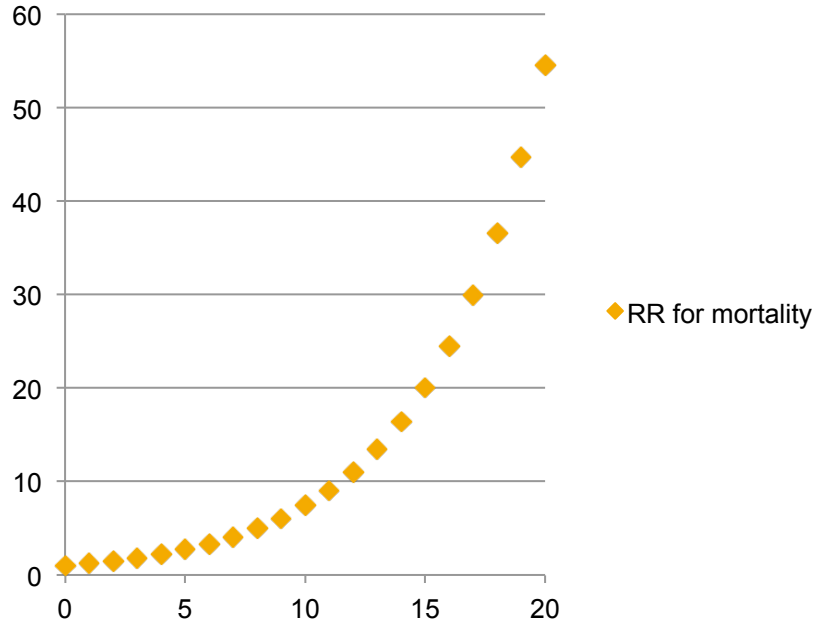
- Classical approach: Abstinence oriented (disulfiram, naltrexone, acamprosate)
- Substitution therapy: BZD, sodyum oxibate, baclofen
- Reduction approach: nalmefene

Estrategias de reducción de consumos

Why is alcohol dependence treatment successful?

It reduces level of consumption either to abstinence or by sizable reduction of heavy drinking.

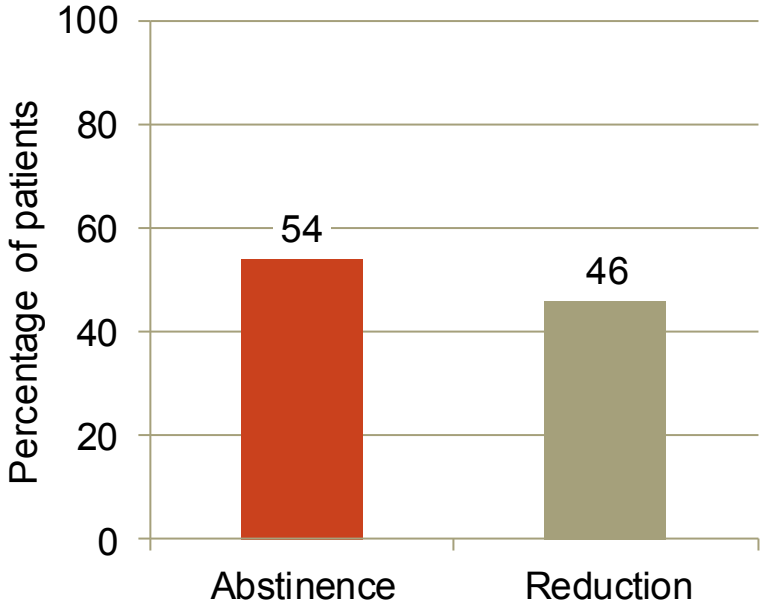
Typical risk curve for alcohol (e.g., liver cirrhosis mortality)



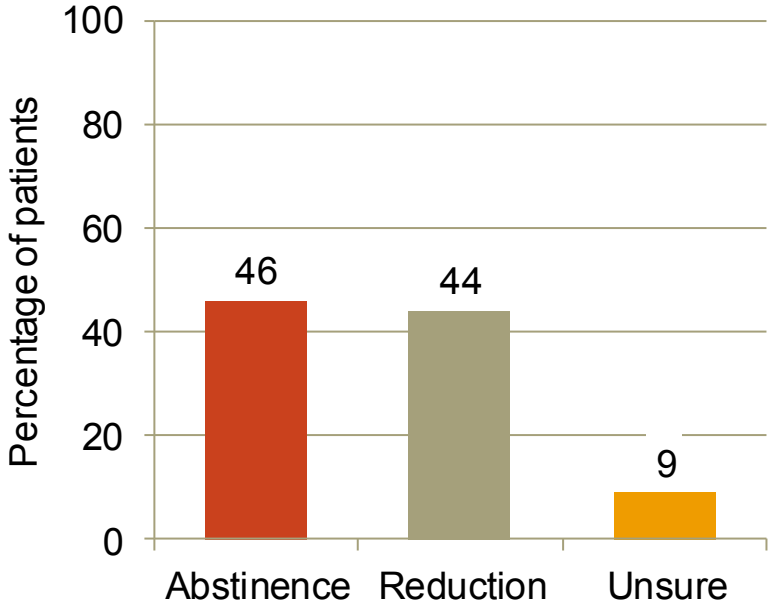
Relative gain in risk for mortality of reducing by three drinks/day for different levels of drinking

Treatment goal preference among patients

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



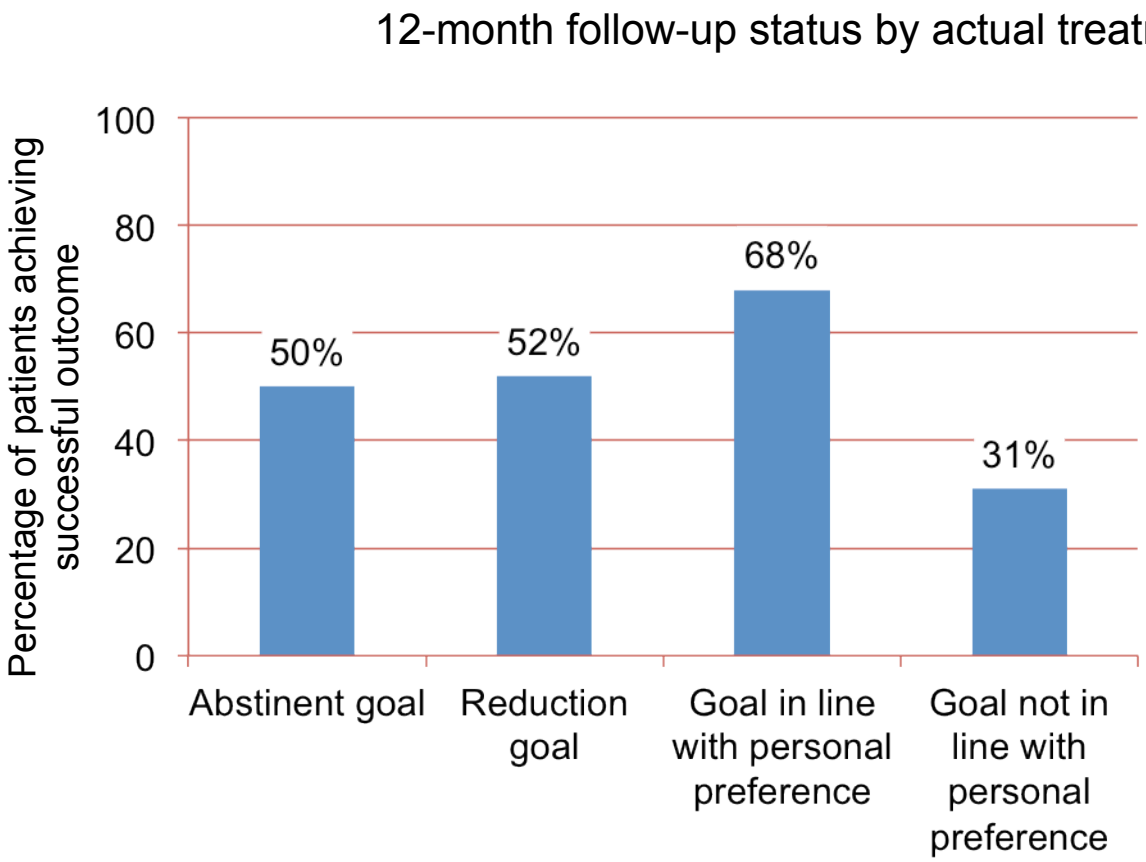
Canadian study of patients with chronic alcoholism (n=106)[2]



Approximately half of patients would choose reduction rather than abstinence as a treatment goal

1. Heather et al. Alcohol Alcohol 2010;45(2):128–135;
2. Hodgins et al. Addict Behav 1997;22(2):247–255

Patient involvement in treatment goals



Success achieved during one year was virtually identical, at around 50%, for goals of abstinence and controlled drinking

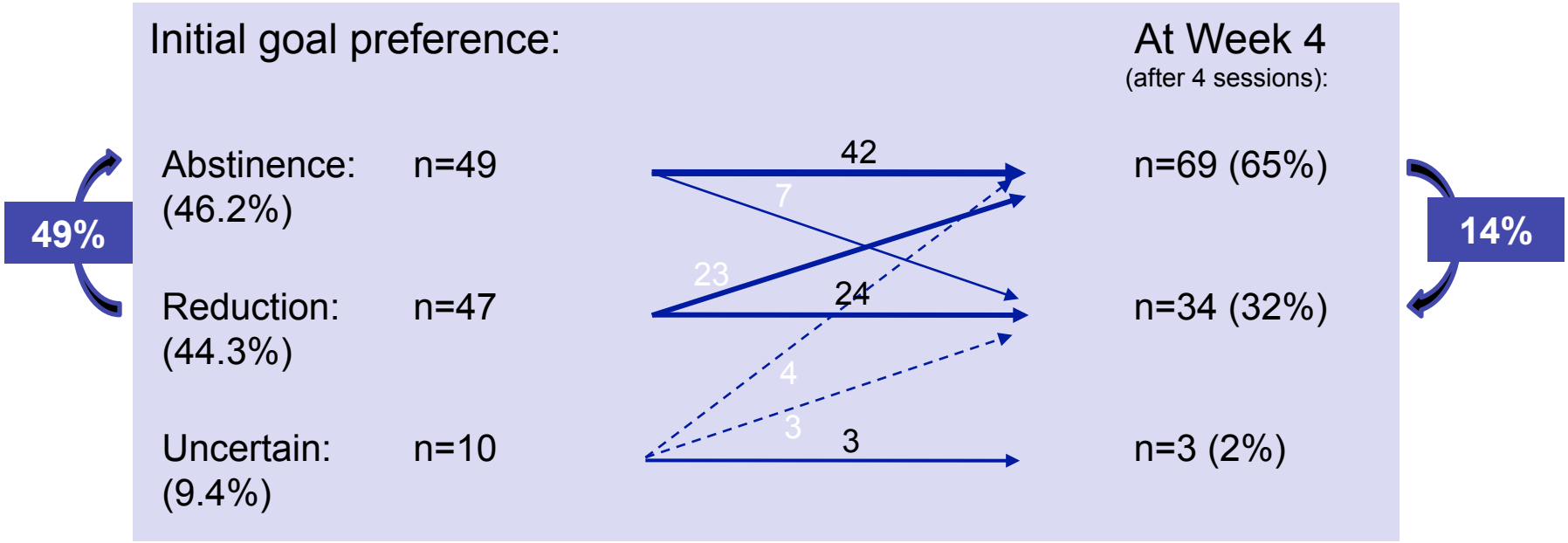
This supports the view that controlled drinking oriented treatment is an acceptable and effective alternative to abstinence-oriented treatment, particularly when it is compatible with the individual's beliefs and preferences

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

Orford & Keddie. Br J Addict 1986;81(4):495–504

Movement from reduction goal to abstinence goal

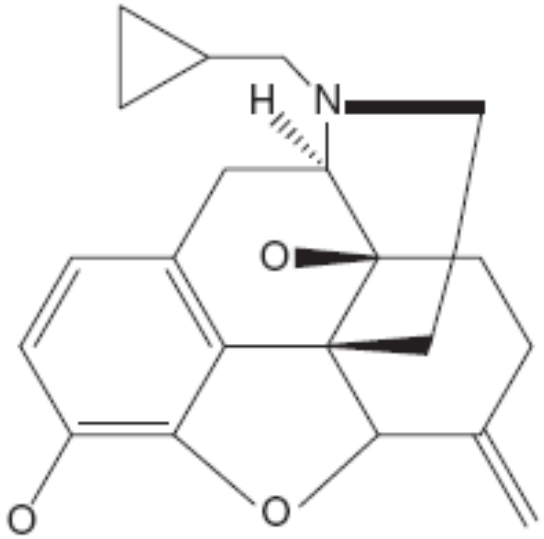
Initial goal preferences and changes at 4 weeks



- 49% of patients with an initial preference for a reduction goal changed to an abstinence goal within 4 weeks.
- Many patients who initially have reduction as a treatment goal may decide to become abstinent after initial experience with reduction

Hodgins et al. Addict Behav 1997;22(2):247–255

Características del nalmefeno



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

In vitro receptor profile

Antagonist at μ opioid receptors

Antagonist at δ opioid receptors

Partial agonist at k opioid receptors

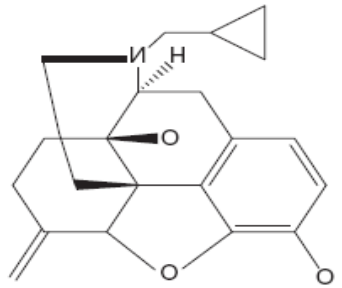
- Equal high potency on μ and k opioid receptors
- Lower potency on δ opioid receptors

Bart et al. Neuropsychopharmacology 2005;30:2254–2262

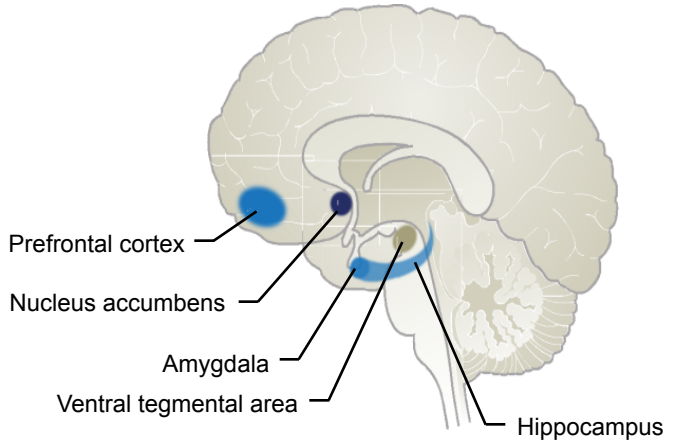
Nalmefene – What it does!

- Nalmefene diminishes the reinforcing effects of alcohol, helping the patient to reduce drinking possibly by modulating cortico-mesolimbic functions.

Nalmefene



Areas in the brain affected by alcohol, including the mesolimbic dopamine system



Nalmefene Summary of Product Characteristics;
Nalmefene European Public Assessment Report, 2012; Clapp et al. Alcohol Res Health 2008;31(4):310–339

Clinical pharmacology

- t_{max} 0.5-3 h
- $t_{½}$ approximately 11 h
- Oral availability >50%
- Effect of food unlikely to be clinically significant
- Metabolites pharmacologically inactive
- Minimum involvement of CYP isozymes
- Maximum μ-opioid-receptor occupancy reached after 3 h
  - 94-100% after single and repeated dosing with 20mg
  - 83-100% 26 h after single and repeated dosing with 20 mg

Phase III Programme overview

Three randomised, double-blind, placebo-controlled, parallel-group studies in patients with alcohol dependence

Active compound: 20 mg nalmefene hydrochloride (~18 mg base)

Dose regimen: as needed

Study Name	Study duration	Patients enrolled
ESENSE 1 (12014A)	24-week plus 4-week run-out	604 (306 NMF + 298 PBO)
ESENSE 2 (12023A)	24-week plus 4-week run-out	718 (358 NMF + 360 PBO)
SENSE (12013A)	52-week	675 (509 NMF + 166 PBO)

Ensayos clínicos pivotales

PRIORITY COMMUNICATION

Extending the Treatment Options in Alcohol

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Metho

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4 week

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Week 2

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Alcohol and Alcoholism Advance Access published July 19, 2013

Alcohol and Alcoholism pp. 1–9, 2013 doi: 10.1093/alcalc/agt061

ORIGINAL ARTICLE

Efficacy of As-Needed Nalmefene in Alcohol-Dependent Patients with at Least a High Drinking Risk Level: Results from a Subgroup Analysis of Two Randomized Controlled 6-Month Studies

Wim van den Brink[1,*], Henri-Jean Aubin[2], Anna Bladström[3], Lars Torup[3], Antoni Gual[4,†] and Karl Mann[5,†]

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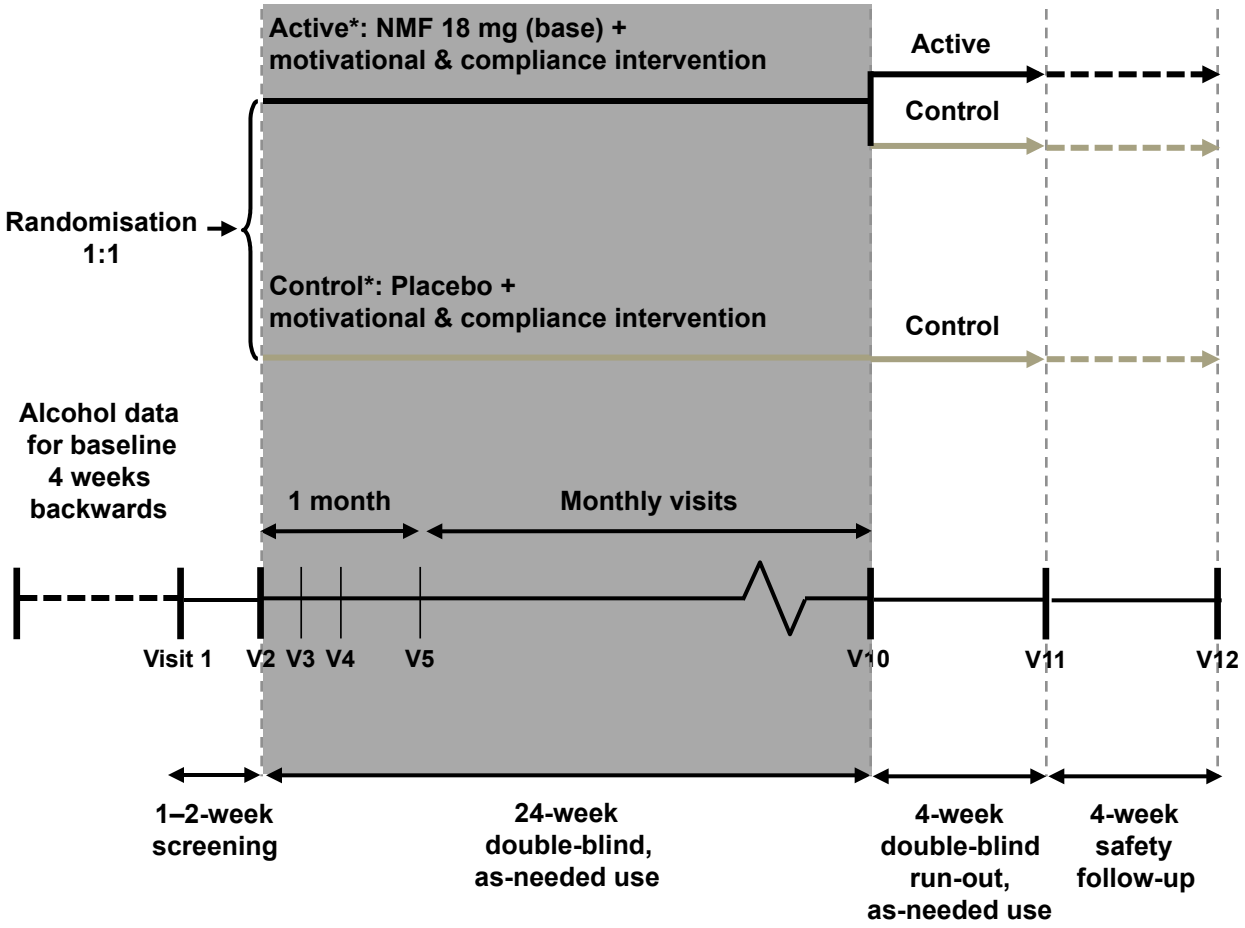
†Denotes equal contribution.

(*Received* 3 *May* 2013; *first review notified* 2 *June* 2013; *in revised form* 5 *June* 2013; *accepted* 6 *June* 2013)

Study design 6-month studies: ESENSE 1 & 2



Main exclusion criteria:

- **Patients with below medium EMA/WHO drinking risk level (DRL) at baseline**
- **Patients with <6 HDDs in previous 4 weeks**
- **S-ASAT and/or S-ALAT levels >3 times upper normal limit**
- **Psychiatric comorbidities**
- **CIWA-Ar score ≥10**

*Planned for enrolment: ESENSE 1, n=300; ESENSE 2, n=350
NMF=nalmefene; V=visit; S-ASAT=aspartate aminotransferase; S-ALAT=alanine transaminase; CIWA-Ar=Revised Clinical Institute Withdrawal Assessment for Alcohol

Mann et al. Biol Psychiatry 2013;73(8):706–713;
Gual et al. Eur Neuropsychopharmacol 2013; Data on file

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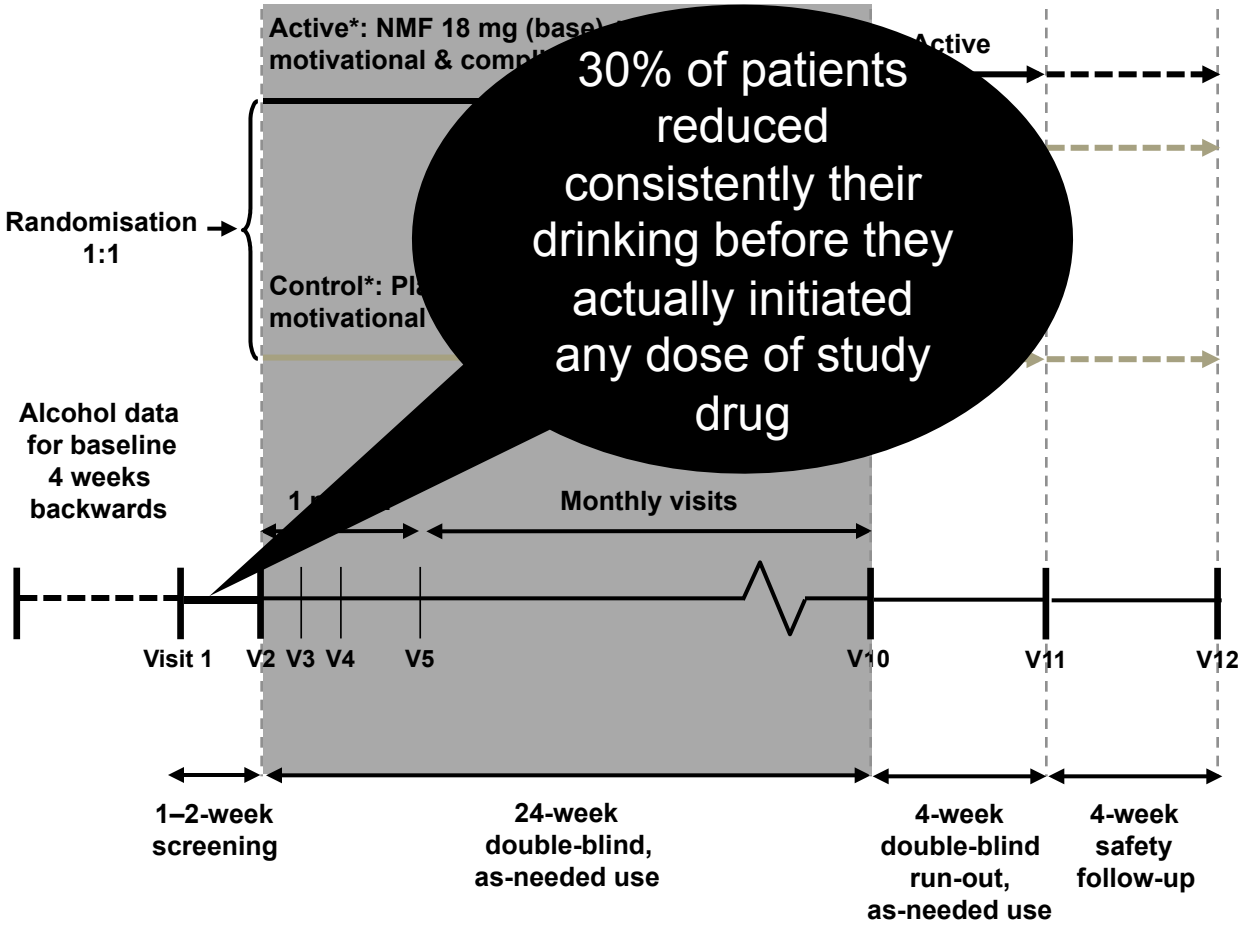

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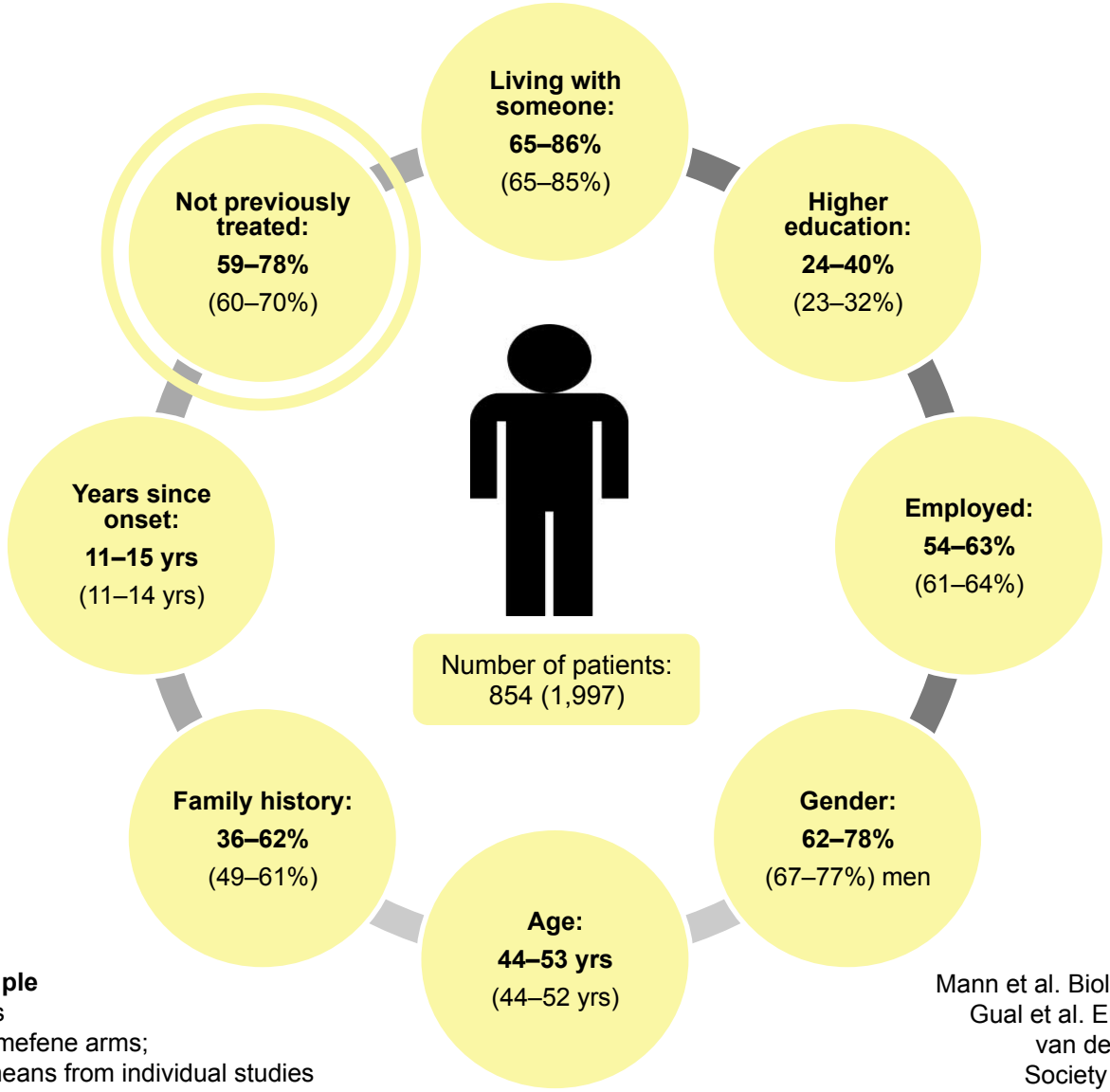
Heavy Drinking Days (HDDs) and Total Alcohol Consumption (TAC) as study endpoints

- HDDs (≥60 grams/day ♂; ≥40 grams/day ♀)
- TAC (average daily consumption in grams of pure alcohol)[1]
- WHO Drinking Risk Levels[1,2]

	♂	♀
Consumption categories	**TAC (g/day)**	**TAC (g/day)**
Very high-risk consumption	>100 g	>60 g
High-risk consumption	60–100 g	40–60 g
Medium-risk consumption	40–60 g	20–40 g
Low-risk consumption	1–40 g	1–20 g

1. WHO International guide for monitoring alcohol consumption and related harm. © WHO, 2000; 2. Rehm et al. Eur Addict Res 2001;7:138–147

High and very high drinking-risk levels at baseline and randomisation – demographics*

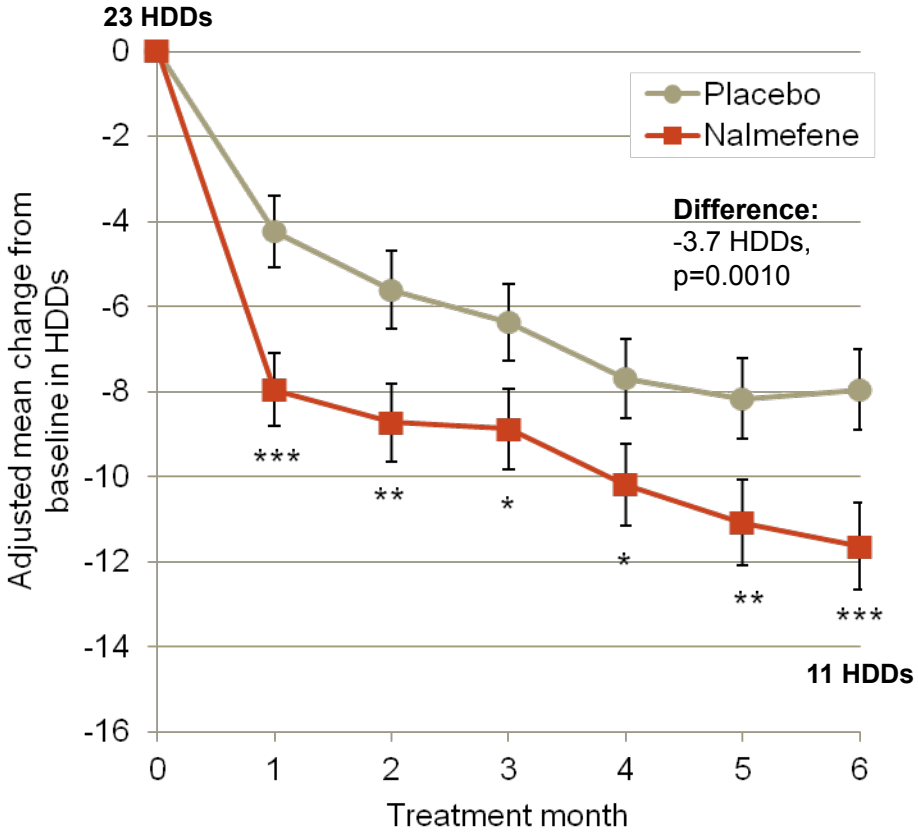


Numbers in ()=total sample
*No significant differences between placebo and nalmefene arms;
Data show range of the means from individual studies

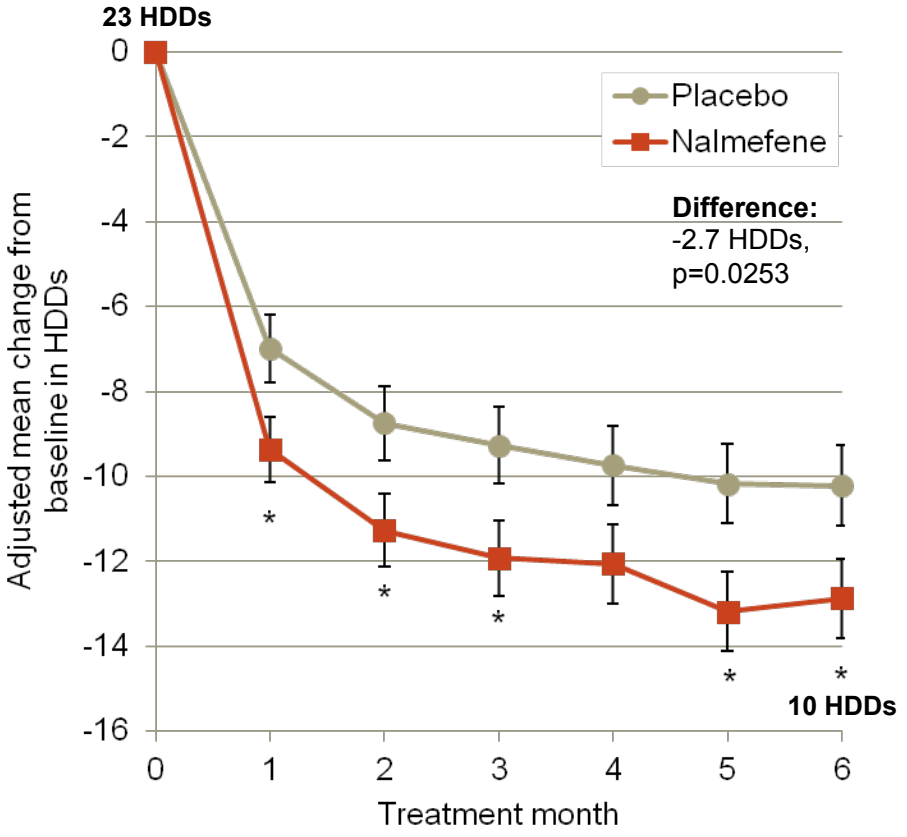
Mann et al. Biol Psychiatry 2013;73(8):706–713;
Gual et al. Eur Neuropsychopharmacol 2013;
van den Brink et al. Poster at Research Society on Alcoholism 2012; Data on file

HDD: change from baseline in the 6-month studies – patients with at least high DRL at baseline and randomisation

ESENSE 1



ESENSE 2

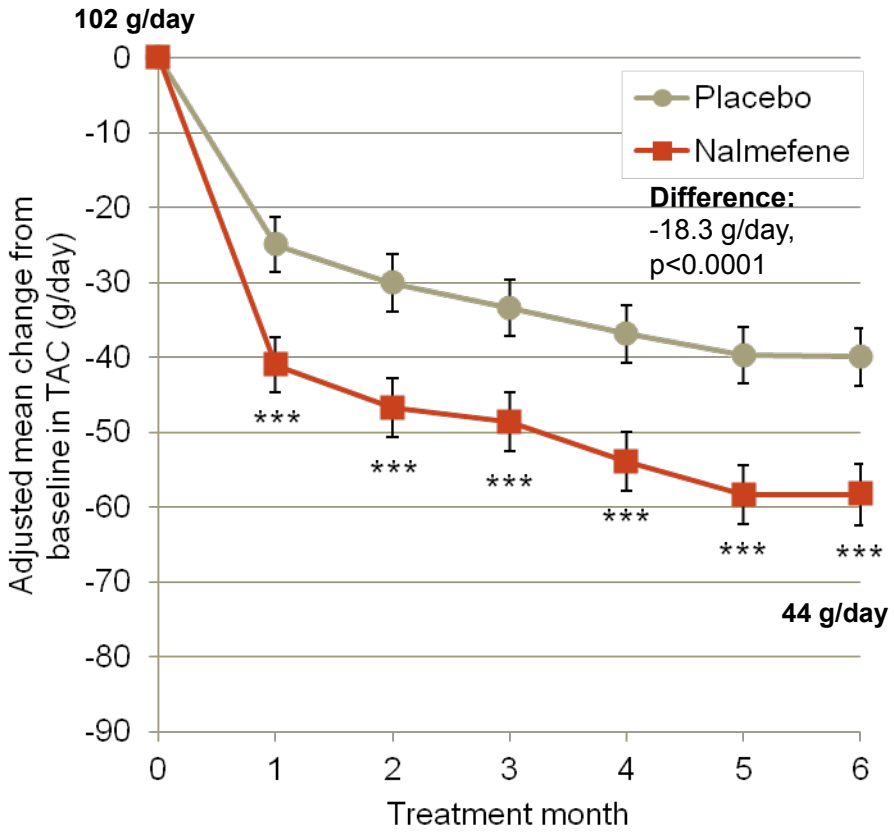


MMRM (OC) FAS estimates and SE; *p<0.05, **p<0.01, ***p≤0.001;
MMRM=mixed-effect model repeated measure;
OC=observed cases; FAS=full analysis set; SE=standard error

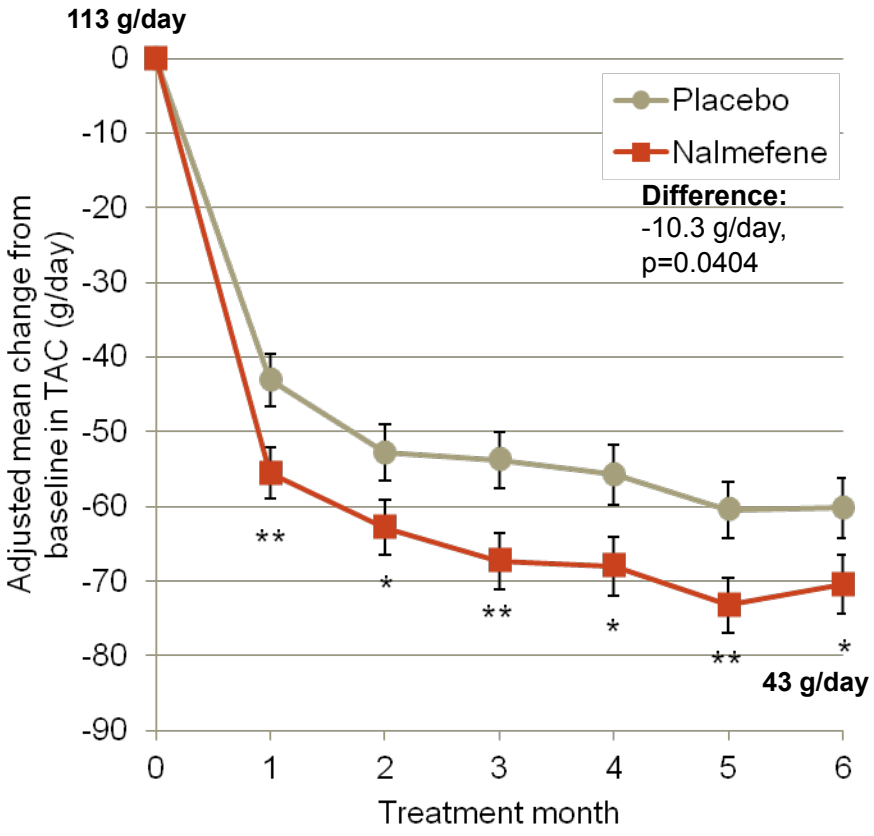
van den Brink et al. Alcohol Alcohol 2013;48(5):570–578; Data on file

TAC: change from baseline in the 6-month studies – patients with at least high DRL at baseline and randomisation

ESENSE 1



ESENSE 2



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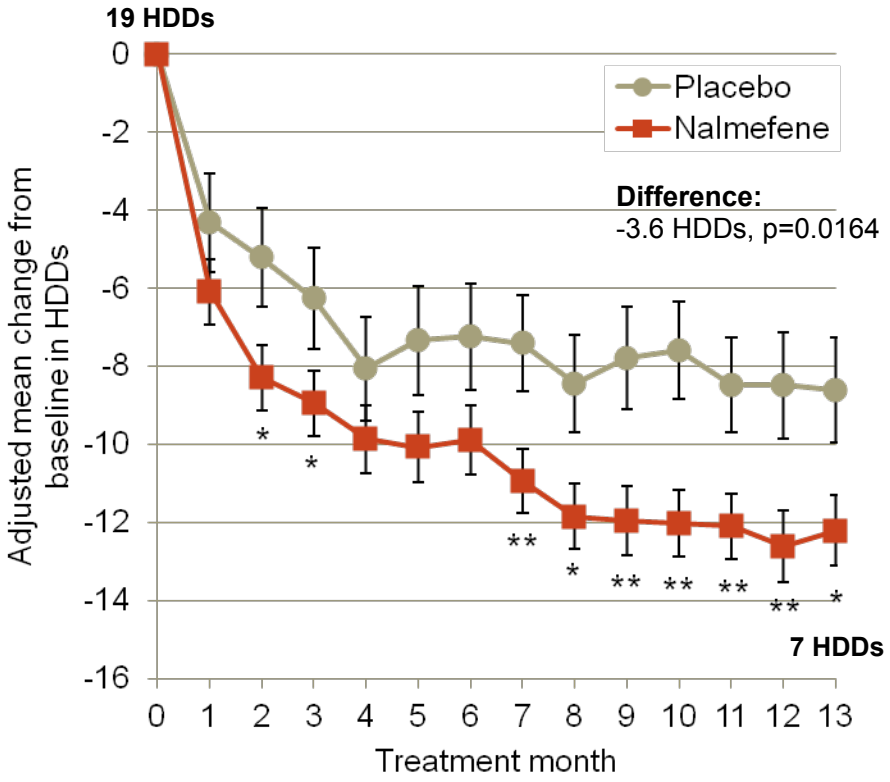
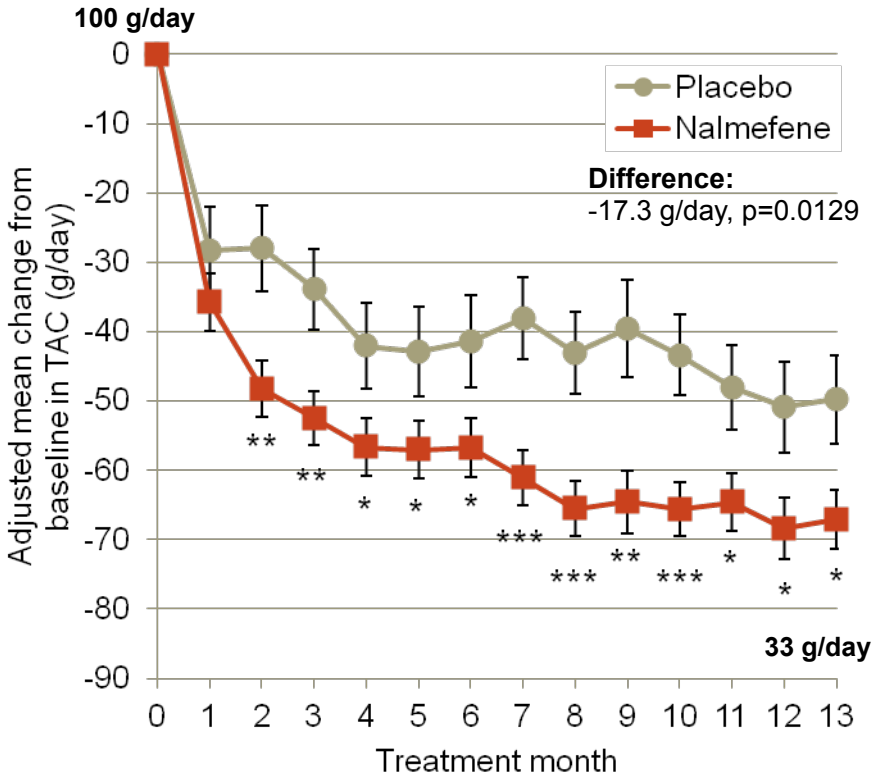
van den Brink et al. Alcohol Alcohol 2013;48(5):570–578; Data on file

HDD/TAC: change from baseline in the 1-year study – patients with at least high DRL at baseline and randomisation

SENSE – change in HDDs



SENSE – change in TAC



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MMRM=mixed-effect model repeated measure;
OC=observed cases; FAS=full analysis set; SE=standard error

van den Brink et al. SENSE. Poster at EPA 2013; Data on file

Clinical efficacy across all three studies
– patients with at least a high DRL at screening and randomisation

	ESENSE 1		ESENSE 2		SENSE	
	PBO (n=167)	NMF (n=171)	PBO (n=155)	NMF (n=148)	PBO (n=42)	NMF (n=141)
HDDs per month						
Difference vs placebo	-3.7 (1.1) p=0.001		-2.7 (1.2) p=0.025		-3.6 (1.5) p=0.0164	
TAC (g/day)						
Difference vs placebo	-18.3 (4.4) p<0.001		-10.3 (5.0) p=0.040		-17.3 (6.8) p=0.0129	

Adjusted mean (SE) change from baseline in drinking scores in the target patient population at Month 6 (ESENSE 1 & 2), and at Month 13 (SENSE), MMRM, OC; FAS; HDD=heavy drinking day; TAC=total alcohol consumption

Mann et al. Biol Psychiatry 2013;73(8):706–713;
Gual et al. Eur Neuropsychopharmacol 2013, Epub ahead of print;
van den Brink et al. Poster at Research Society on Alcoholism 2012; van den Brink et al. ESENSE 1. Poster at EPA 2013;
van den Brink et al. ESENSE 2. Poster at EPA 2013; van den Brink et al. SENSE. Poster at EPA 2013

Markers of alcohol consumption in the weeks leading up to the 6 month assessment – serum GGT and ALAT in patients with at least high DRL at baseline and randomisation (pooled 6-month studies)

Efficacy variable	Placebo		Nalmefene		Ratio to placebo		
	n	Geometric mean	n	Geometric mean	Ratio	95% CI	p-value
GGT (IU/L)							
Baseline	320	57.6	319	55.8			
Adjusted geometric mean at Week 24	220	53.0	187	43.5	0.82	0.73–0.92	0.0005
ALAT (IU/L)							
Baseline	319	29.2	319	29.3			
Adjusted geometric mean at Week 24	218	30.7	187	26.0	0.85	0.78–0.92	<0.0001

MMRM;
GGT=γ-glutamyltransferase; ALAT=alanine aminotransferase;
CI=confidence interval

Gual et al. Poster at WONCA 2013;
van den Brink et al. Alcohol Alcohol 2013;48(5):570–578

Most common adverse events – all patients treated (incidence ≥5%)

- Adverse events were transient, mostly mild or moderate, occurred shortly after the first dose and did not re-occur
- Adverse events as expected based on nalmefene's pharmacological properties

	Placebo (n=797)		Nalmefene (n=1,144)	
Preferred term	**n**	**%**	**n**	**%**
Patients with AEs	500	62.7	855	74.7
Nausea	47	5.9	253	22.1
Dizziness	44	5.5	208	18.2
Insomnia	43	5.4	153	13.4
Headache	66	8.3	141	12.3
Nasopharyngitis	73	9.2	107	9.4
Vomiting	18	2.3	100	8.7
Fatigue	37	4.6	95	8.3
Somnolence	23	2.9	59	5.2

Pooled data ESENSE 1, ESENSE 2, and SENSE

Data on file

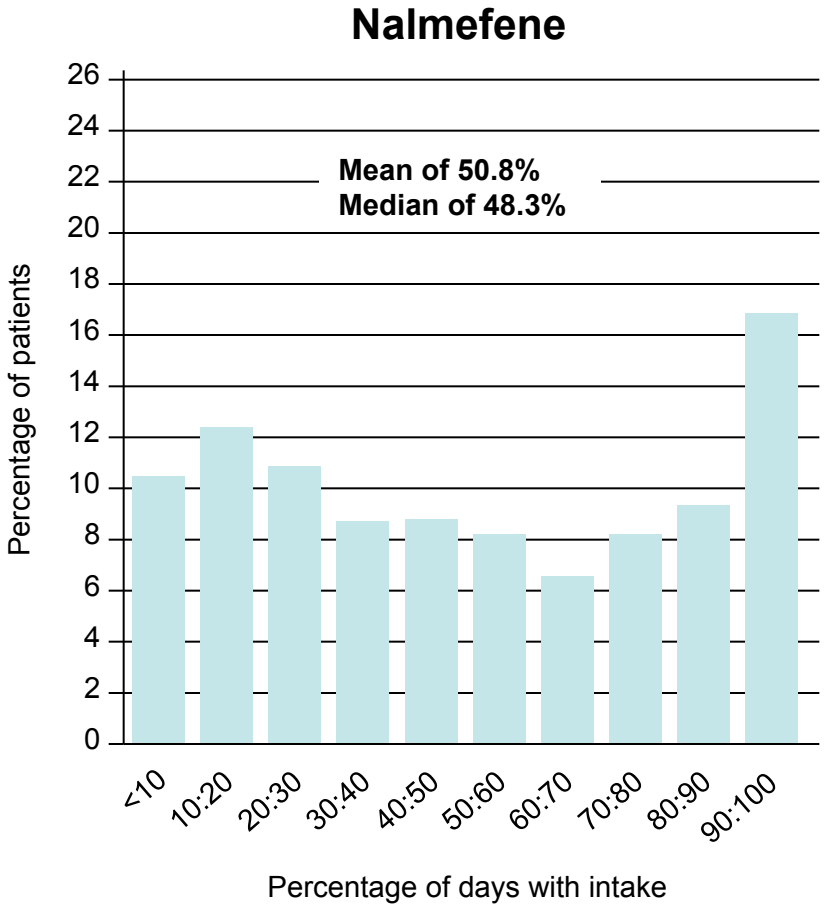
Study medication: ‘as-needed’ use

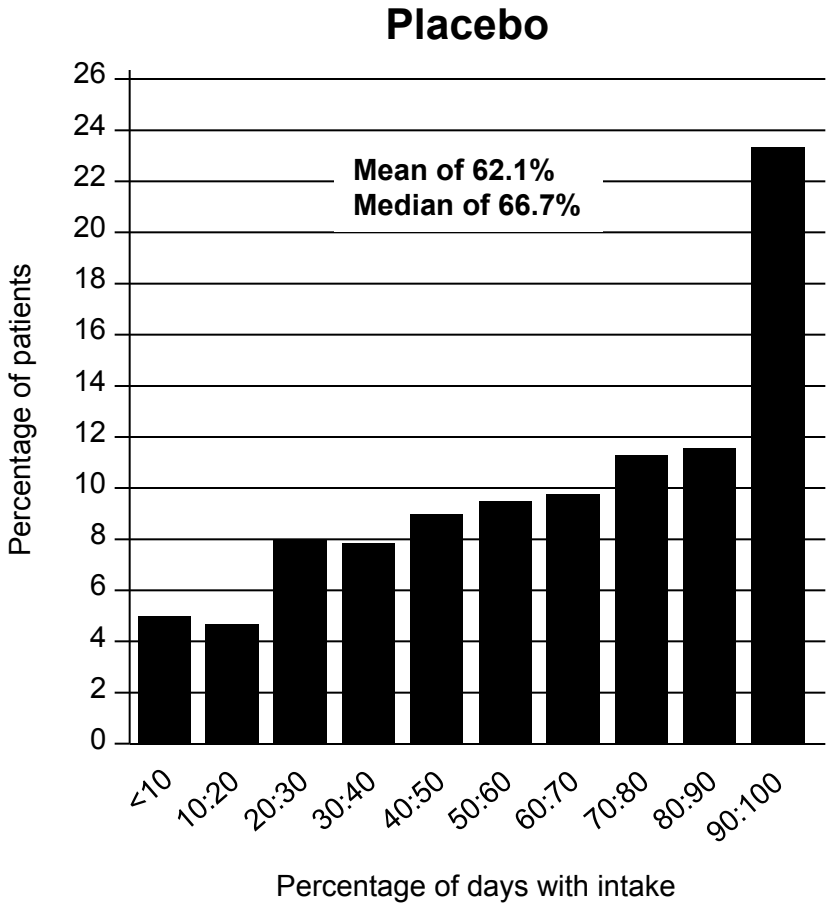
‘As-needed’ dosing regimen:

- One tablet to be taken on days where the patients anticipate a risk of drinking
- Can be used daily when patients feel a risk of drinking every day
- Not more than one tablet per day

Mann et al. Biol Psychiatry 2013;73(8):706–713;
Gual et al. Eur Neuropsychopharmacol 2013, Epub ahead of print;
van den Brink et al. Poster at Research Society on Alcoholism 2012

Medication intake





Adherence to ‘as-needed’ dosing was greater than 80% in 1,513 out of 1,923 patients

All patients treated set

Data on file

Responder analyses

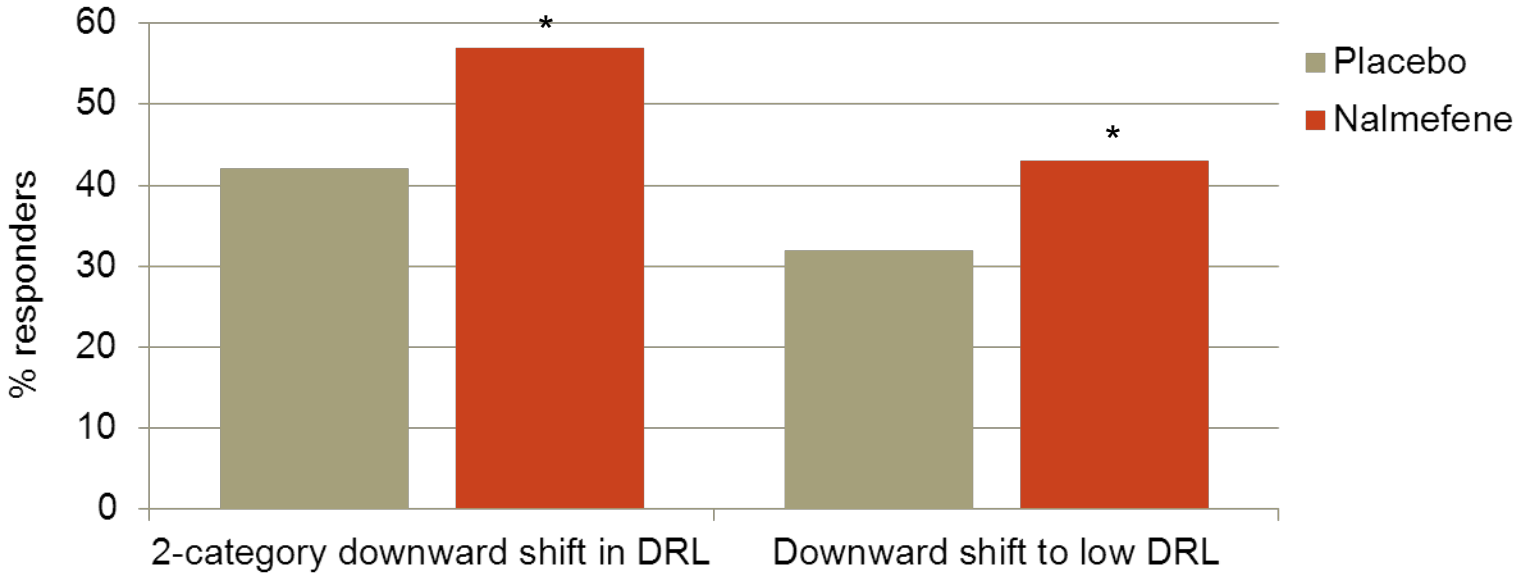
- 2-category downward shift in DRL
- Downward shift to low DRL

Consumption categories	TAC (g/ day) men	TAC (g/ day) women
Very high-risk consumption	>100 g	>60 g
High-risk consumption	60–100 g	40–60 g
Medium-risk consumption	40–60 g	20–40 g
Low-risk consumption	1–40 g	1–20 g

DRL=drinking risk level; TAC=total alcohol consumption

Gual et al. Poster at WONCA 2013

WHO defined DRL at Month 6 in sub-group who did not reduce to low risk after screening (pooled 6-month studies)

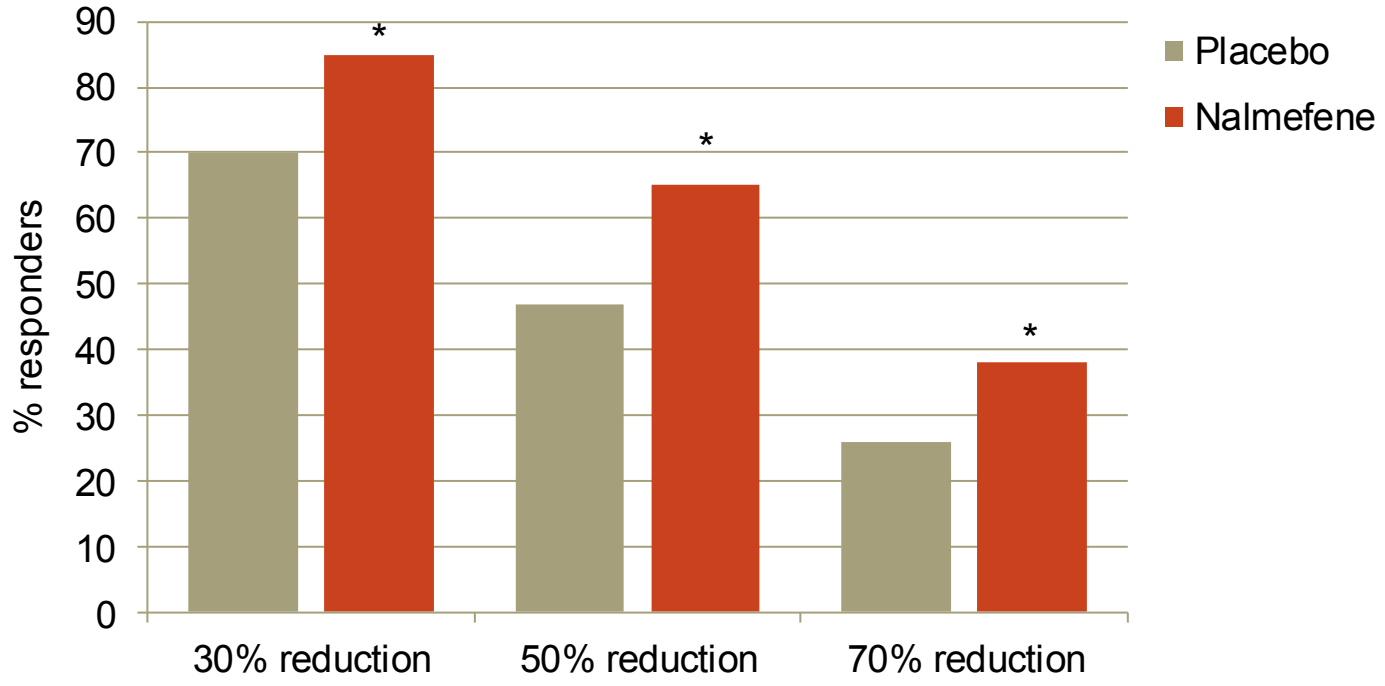


Responder analysis (MMRM)	Odds ratio	95% CI	NNTB
2-category downward shift in DRL	1.87	1.35–2.59	7
Downward shift to low DRL	1.79	1.27–2.53	9

*p<0.05;
WHO=World Health Organization; DRL=drinking risk level;
MMRM=mixed model repeated measures; CI=confidence interval;
NNTB=number-needed-to-treat-to-benefit;
data pooled from ESENSE 1 and ESENSE 2

Gual et al. Poster at WONCA 2013

Responder analysis: pooled data at 6 months (ESENSE 1 & ESENSE 2) – patients with at least high DRL at baseline and randomisation



Responder analysis	Odds ratio	95% CI	NNT
>30% reduction	2.44	1.64–3.66	7
>50% reduction	2.15	1.54–3.00	6
>70% reduction	1.88	1.32–2.70	9

*p<0.05;
Based on MMRM imputed TAC values; CI=confidence interval;
NNT=number-needed-to-treat

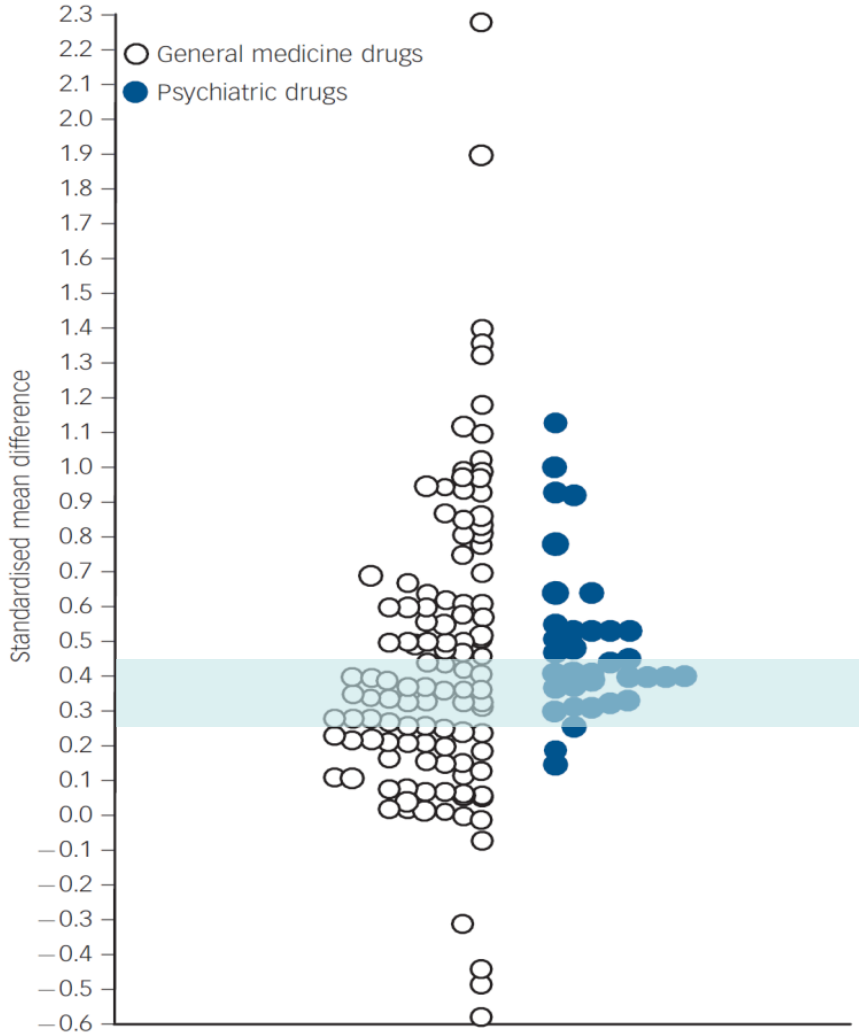
Data on file

Clinical relevance: effect sizes for nalmefene are comparable to treatments for other mental disorders

	Standardized effect size (Cohen's d)	
Nalmefene[1]	**HDDs**	**TAC**
ESENSE 1	0.37	0.46
ESENSE 2	0.27	0.25
Alcohol treatment[2,3]	0.12 to 0.33	
Antidepressants[4]	0.24 to 0.35	
Antipsychotics[4]	0.30 to 0.53	

1. Data on file;
2. Kranzler & Van Kirk. Alcohol Clin Exp Res 2001;25:1335–1341;
3. NICE. CG115. Alcohol dependence and harmful alcohol use: appendix 17d – pharmacological interventions forest plot. 2011;
4. Leucht et al. Br J Psychiatry 2012;200:97–106

Putting the efficacy of psychiatric and general medicine medication into perspective: review of meta-analyses



Nalmefene
standardised effect size range

Leucht et al. Br J Psychiatry 2012;200:97–106

Perspectives

Substitution therapy for alcoholism: time for a reappraisal?

Jonathan Chick[1] and David J Nutt[2]

Psychopharm

Journal of Psychopharmacology
0(0) 1–8

DOI: 10.1177/0269881111408463
jop.sagepub.com
SAGE

- BZD
- Sodium oxybate
- Baclofen

Criterios para un tratamiento de sustitución

1. Debe reducir el uso de alcohol y así reducir los daños relacionados .
2. Idealmente debería estar libre de daños .
3. Hay que demostrar que se puede sustituir por el alcohol y no se utilizarán junto con el alcohol.
4. Debería ser más seguro en caso de sobredosis .
5. Idealmente no debería potenciar los efectos del alcohol si cualquiera de los fármacos se toman en sobredosis.
6. Debe ofrecer beneficios económicos significativos para la salud .

Chick & Nutt, 2011

HISTORIA

En 2008 el Dr. Oliver Ameisen publica un libro, “Le Dernier Verre” (La última copa)

Clinical Pharmacology: Advances and Applications

Dovepress

open access to scientific and medical research

Open Access Full Text Article

REVIEW

Clinical effectiveness of baclofen for the treatment of alcohol dependence: a review

This article was published in the following Dove Press journal:
Clinical Pharmacology: Advances and Applications
2 July 2013

Table 2 Description of randomized controlled trials

Source	Addolorato et al[16]	Garbutt et al[18]	Addolorato et al[19]
Setting	**Single inpatient site**	**Outpatients recruited from community**	**Single inpatient site**
Subjects			
Number	84	80	39
Age (y)	49.0 (range 43.0–61.0)	47.5 ± 7.6	45.8 ± 10.6
Male gender	76%	55%	Not reported
Daily drinks	Not reported	7.3 ± 3.7 (baclofen group)	14.2 ± 7.9 (all subjects)
Duration of use (y)	22.0 (range 17.0–27.0)	23.5 ± 9.9	12.6 ± 4.8
Comorbidities	Cirrhosis (Child-Pugh A, B, or C)	No medical/psychiatric	No medical/psychiatric
Intervention	Baclofen 10 mg po tid for 12 weeks	Baclofen 10 mg po tid for 12 weeks	Baclofen 10 mg po tid for 4 weeks
Primary outcome/ results	Percentage of patients maintaining abstinence: 71% vs 29% ($P = 0.0001$)	Percentage of heavy drinking days: 19.3% vs 24.7% ($P = 0.73$)	Percentage of patients maintaining abstinence: 70% vs 21.2% ($P < 0.005$)
	Cumulative abstinent days: 62.8 ± 5.4 vs 30.8 ± 5.5 ($P = 0.001$)	Percentage of abstinent days: 51.7% vs 51.6% ($P = 0.61$)	Cumulative abstinent days: 19.6 ± 2.6 vs 6.3 ± 2.4 ($P < 0.005$)

Note: Reported as mean + standard deviation unless noted otherwise.
Abbreviations: po, orally; tid, three times daily; vs, versus; y, years.

ESTUDIOS EN CURSO
Deshabituación

- Naltrexona y Baclofeno para la Dependencia del Alcohol : Un estudio piloto .
  Naltrexona vs baclofeno vs Placebo vsTerapia de Conducta. Completo
- Eficacia y seguridad de baclofeno para el mantenimiento de la abstinencia en pacientes dependientes del alcohol
  Baclofeno vs Placebo. Reclutando
- Eficacia y tolerabilidad de baclofeno para la Dependencia del Alcohol
  baclofeno vs placebo vs terapia conductual. Reclutando
- Baclofeno para el tratamiento de la dependencia al alcohol
  baclofeno vsPlacebo
- Baclofen para reducir el consumo de alcohol en los veteranos con el VHC
  Baclofeno vs placebo
- Eficacia y seguridad de altas dosis de baclofeno para la Dependencia del Alcohol
  baclofeno vsPlacebo. Reclutando

Gamma-hydroxybutyrate (GHB) for treatment of alcohol withdrawal and prevention of relapses (Review)

Leone MA, Vigna-Taglianti F, Avanzi G, Brambilla R, Faggiano F

Conclusions - Detox

- Thirteen randomised controlled trials involving 648 participants were included in this review. Eleven were conducted in Italy. Six trials with a total of 286 participants evaluated the effectiveness of GHB in reducing withdrawal syndrome.
- Single studies showed that GHB could reduce withdrawal symptoms when compared to a placebo and Chlormethiazole but with more side effects. No strong differences were observed between GHB and benzodiazepines. In the other comparisons the differences were not statistically significant.

Conclusions - Rehab

- Seven trials involving 362 participants tested the use of GHB to treat alcohol dependence or prevent relapses if a person was already detoxified (mid-term outcomes).
- GHB was better than naltrexone and Disulfiram in maintaining abstinence and had a better effect on craving than placebo and Disulfiram.
- Sample sizes in individual trials were generally small (range 17 to 98 participants).
- The most consistently reported side effect of GHB was dizziness and vertigo, which was clearly dose dependent.

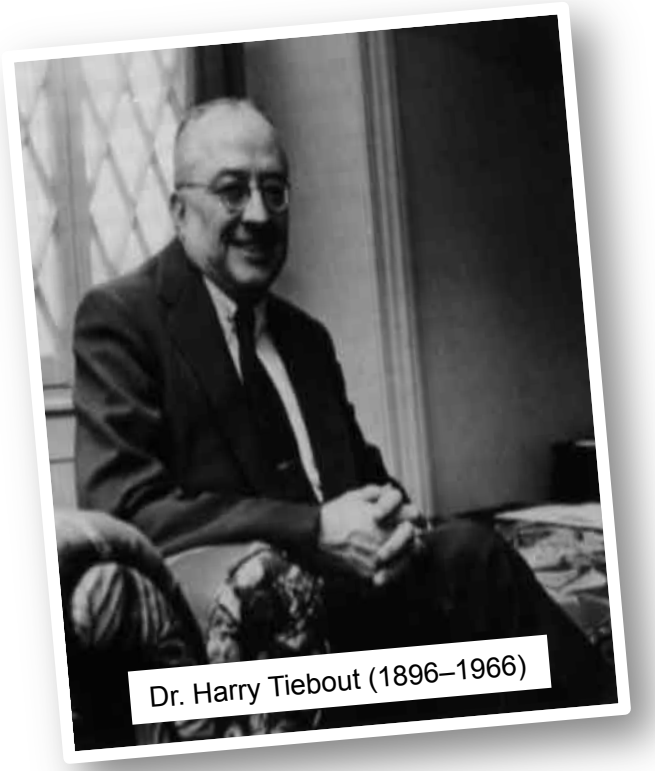
Sodium Oxybate trial

Randomized, multicenter, double-blind, placebo-controlled study of the safety and efficacy of 4 dose regimens of SMO.IR, an oral solid formulation of sodium oxybate, in the maintenance of alcohol abstinence in recently abstinent alcohol-dependent patients.

Índice

- Nuevos conceptos
- Impacto del alcohol en la sociedad y el individuo en los tiempos actuales
- Las nuevas formas de expresión clínica
- Nuevos paradigmas de tratamiento y nuevos fármacos
- El abordaje psicosocial en el siglo XXI
- Conclusiones

‘Old’ psychosocial treatments


Dr. Harry Tiebout (1896–1966)

- Alcoholic
  - Incapable of accurate self-perception (e.g., denial, projection of blame)
  - **Defence mechanisms** entrenched over the long term until the alcoholic hit bottom and experienced full surrender
- Professional helper moves alcoholic
  - Surrender
  - Personality reconstruction
- **“Break ‘em down to build ‘em up”**

Psychoanalytic observations on alcoholics
→ Confrontational therapies

The confrontational approach

- Addiction is rooted in an immature, defective character encased within an armour-plated defence structure
- The alcoholic can therefore be reached only by a **“dynamite charge”** that breaks through this protective shield
- Verbal confrontation is the most effective means of engaging and changing addictive behaviour

Bassin, 1975

The confrontational approach: the evidence

- Review of 4 decades of treatment outcome research
- A large body of trials found no therapeutic effect relative to control or comparison treatment conditions
- Several reported harmful effects, including increased drop-out, and elevated and more rapid relapse
- Pattern consistent across a variety of confrontational techniques
- There is not (and never has been) a scientific evidence base for the use of confrontational therapies

WR. Miller & W. White. 2007

New psychosocial approach

- Motivational interviewing
- Brief interventions

New psychosocial treatments: motivational interviewing

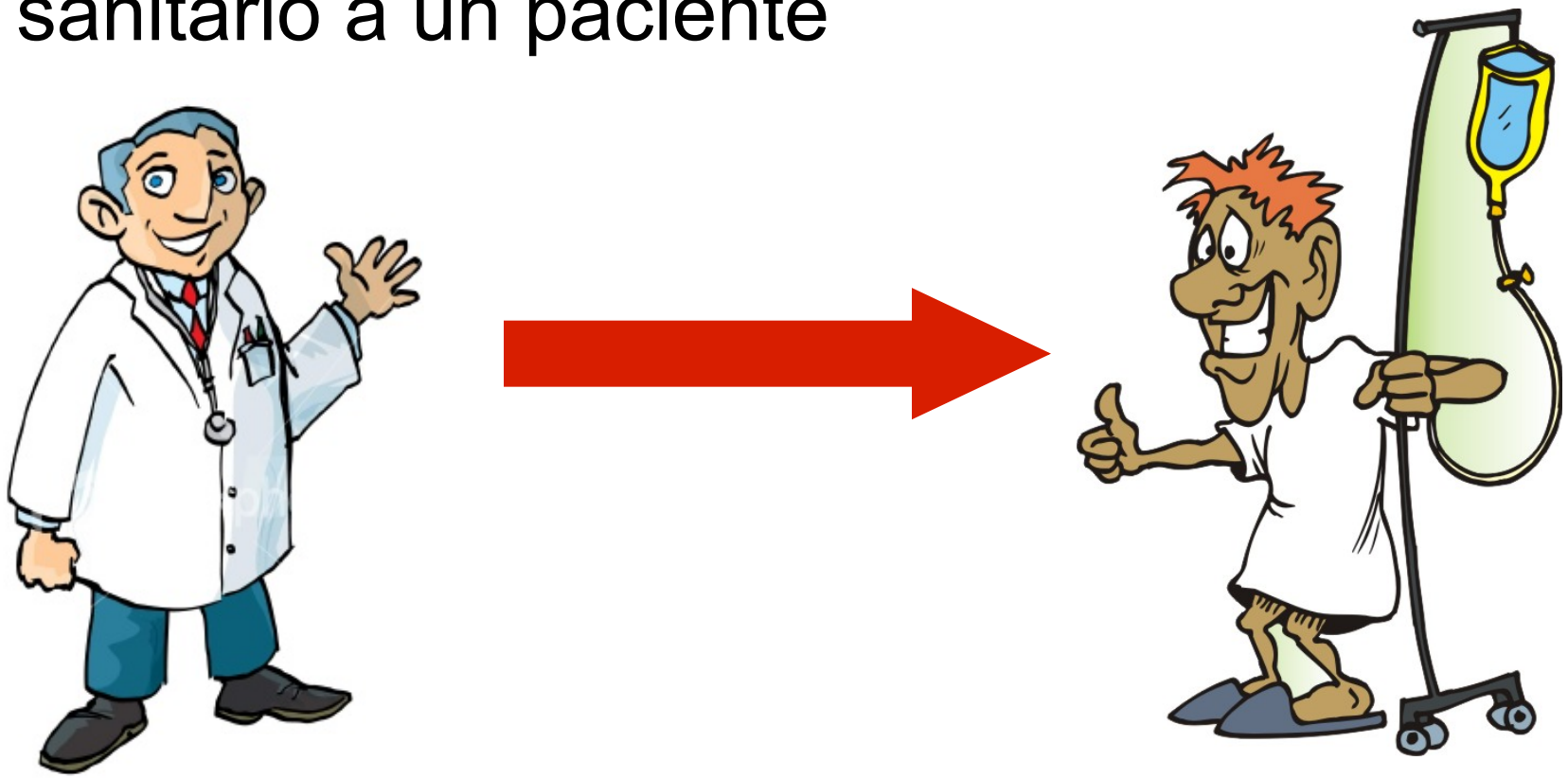
- New golden standard for the psychological approach to addictive behaviours
- Radical change:
  - Patient centred
  - Ambivalence as a core concept
  - External confrontation as a technique vs. internal confrontation as a goal
  - Spirit: partnership, acceptance, evocation, compassion
  - Processes: engaging, focusing, evoking, planning
  - Communication style: guidance

New psychosocial treatments: brief interventions

- Consistent evidence of its effectiveness to reduce alcohol consumption in risky drinkers and heavy drinkers
- The motivational component increases its efficacy
- Two types: opportunistic & specialised
- Two styles: feed back & conversational

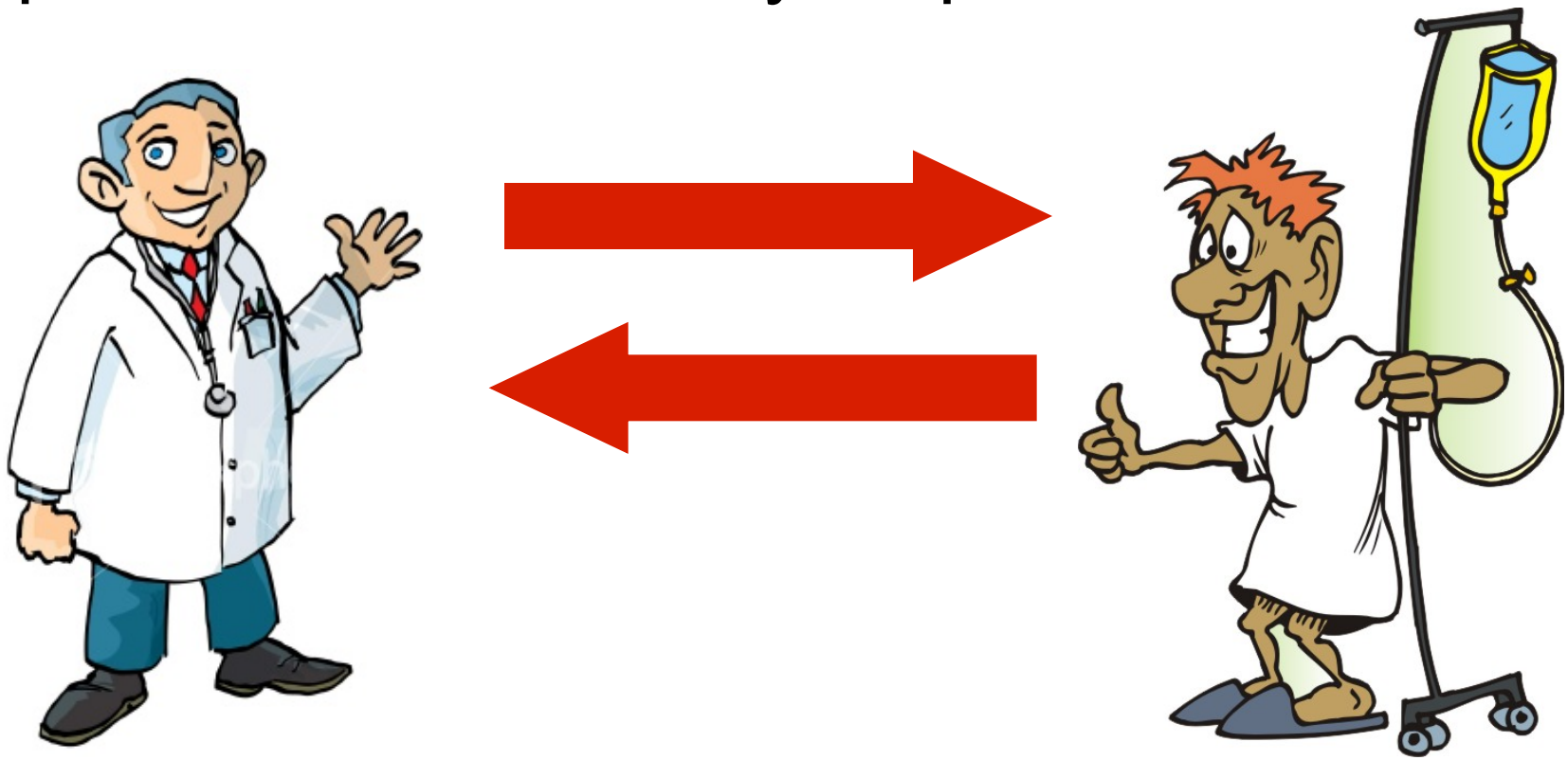
Qué es una intervención breve?

- Un consejo breve dado por un profesional sanitario a un paciente



Y una intervención motivacional breve?

- Una corta conversación entre un profesional sanitario y un paciente



Two different MBI approaches

Assessment feedback

- Feedback of assessment as the primary means of structuring the conversation and as the basis for exploration of areas in which change talk may be elicited

Conversational style

- Series of conversational exercises expected to be helpful in eliciting change talk on relevant material

Opportunistic MBI

Specialist MBI

McCambridge J, 2002

Components of MBI

Communicate empathy

Promote self-efficacy

Evaluate stage of change

Give feed back on health status

Give advice (Ask for permission)

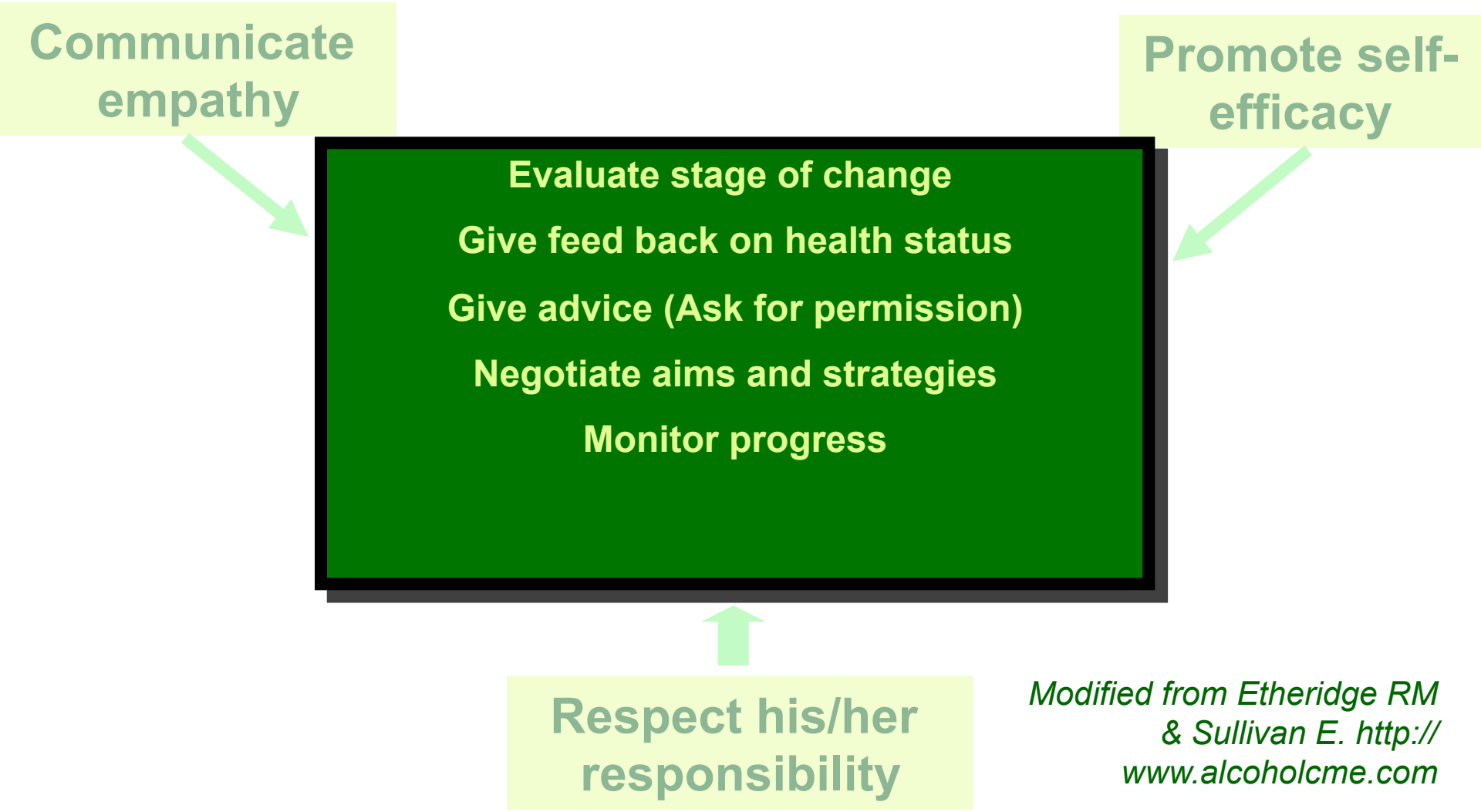
Negotiate aims and strategies

Monitor progress

Respect his/her responsibility

Modified from Etheridge RM & Sullivan E. http://www.alcoholcme.com

Opportunistic MBI



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Specialist MBI

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Modified from Etheridge RM & Sullivan E. http://www.alcoholcme.com

Timeline followback

- Retrospective assessment of drinking behaviour.
- Reliable and valid for a variety of populations for time frames of up to one year.

(Sobell & Sobell, 1992, 1996)

Name/ID#: _____ Date: _____

TIMELINE FOLLOWBACK CALENDAR: 2013

1 Standard Drink is Equal to


One 12 oz can/bottle of beer


One 5 oz glass of regular (12%) wine


1 ½ oz of hard liquor (e.g. rum, vodka, whiskey)

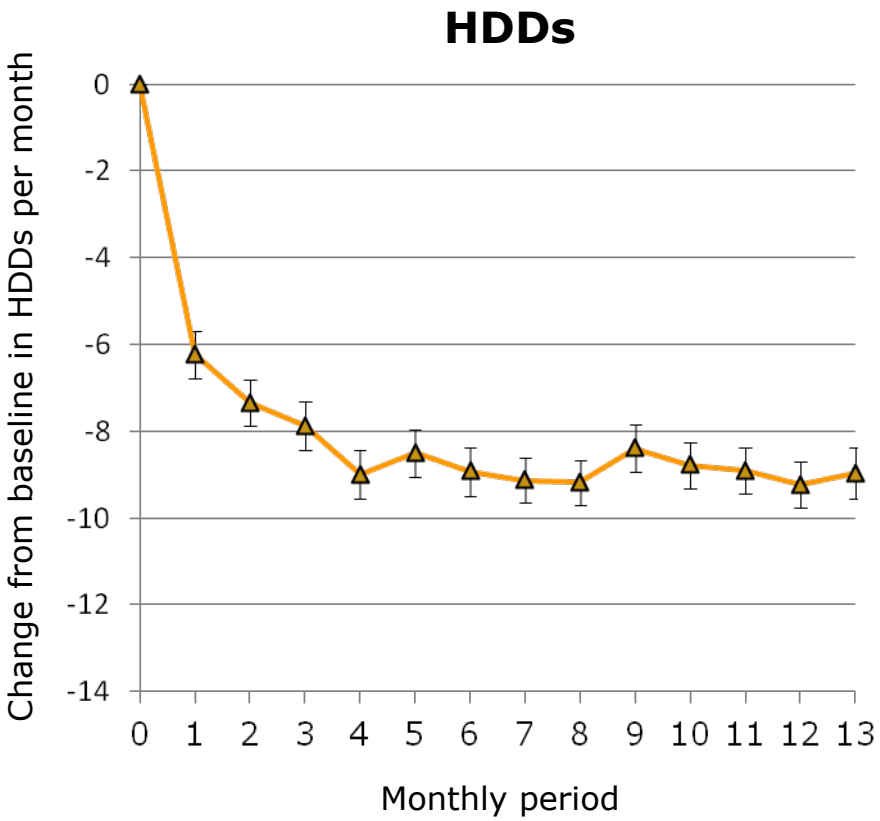

1 mixed or straight drink with 1 ½ oz hard liquor

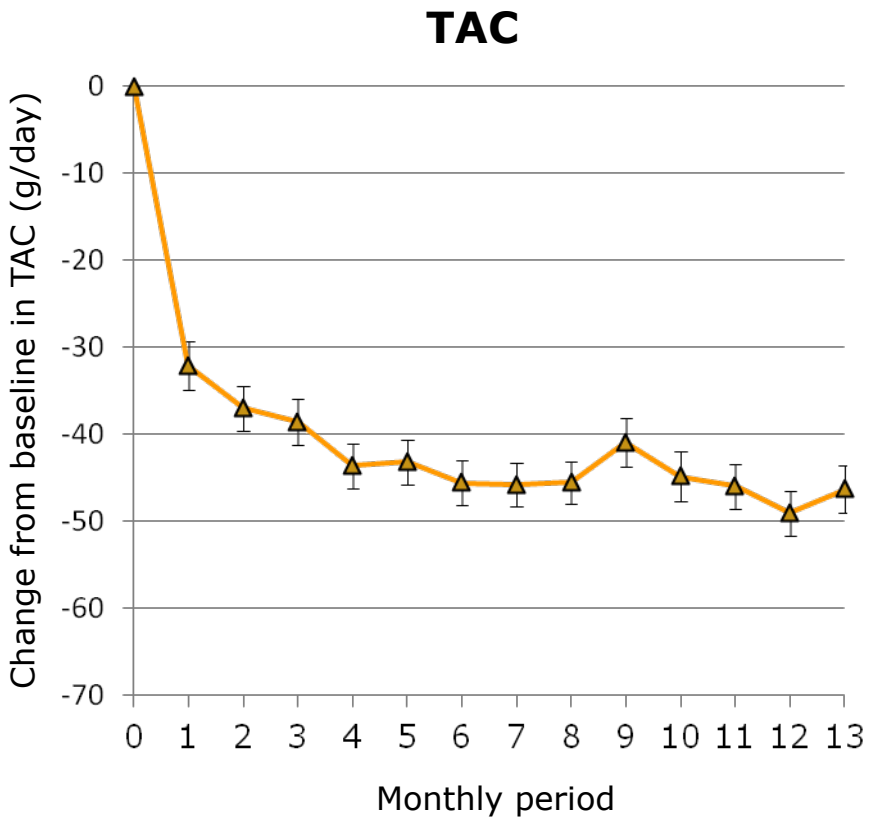
Complete the Following

Start Date (Day 1): _____ **End Date** (yesterday): _____
MO DY YR MO DY YR

2013	SUN	MON	TUES	WED	THURS	FRI	SAT
			1 New Year's Day	2	3	4	5
J	6	7	8	9	10	11	12
A	13	14	15	16	17	18	19
N	20	21 M. King Day	22	23	24	25	26
	27	28	29	30	31	1	2
F	3	4	5	6	7	8	9
E	10	11	12	13	14 Valentine	15	16
B	17	18 Pres. Day	19	20	21	22	23
	24	25	26	27	28	1	2
M	3	4	5	6	7	8	9
A	10	11	12	13	14	15	16
R	17 St. Patrick	18	19	20	21	22 Good Friday	23
	24 Easter	25	26	27	28	29	30
	31	1	2	3	4	5	6
A	7	8	9	10	11	12	13
P	14	15	16	17	18	19	20
R	21	22	23	24	25	26	27
	28	29	30	1	2	3	4
M	5	6	7	8	9	10	11
A	12 Mother's Day	13	14	15	16	17	18
Y	19	20	21	22	23	24	25
	26	27 Memorial Day	28	29	30	31	

Reducción de consumos usando Brenda y TLFB (Sense study)





Resultados del grupo placebo

Índice

- Nuevos conceptos
- Impacto del alcohol en la sociedad y el individuo en los tiempos actuales
- Las nuevas formas de expresión clínica
- Nuevos paradigmas de tratamiento y nuevos fármacos
- El abordaje psicosocial en el siglo XXI
- Conclusiones

Conclusiones

- El TUA es una patología cerebral y el CEC la mejor manera de definirlo
- Los problemas derivados del alcohol son un gran problema de salud pública
- Los patrones de consumo y las formas de expresión del TUA han cambiado
- La mayoria de pacientes no son diagnosticados ni tratados
- Disponemos de nuevos modelos de tratamiento que amplian la oferta terapéutica

Muchas gracias

Antoni Gual
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