Generalitat de Catalunya
Agència de Salut Pública de Catalunya

CAMFiC

AIFICC | ASSOCIACIÓ D'INFERMERIA FAMILIAR I COMUNITÀRIA DE CATALUNYA

PROGRAMA:

Actualització en diagnòstic, tractament farmacològic i psicològic de l'alcoholisme

25 maig de 2016
Horari: de 09:00 a 14:00 h
Lloc: Agència Salut Pública

Red de Trastornos Adictivos

IDIBAPS

CLÍNIC Corporació Sanitària

Antoni Gual
Unitat de Conductes Addictives
Servei de Psiquiatria. ICN.
Hospital Clínic. Barcelona

Conflictes d'interés

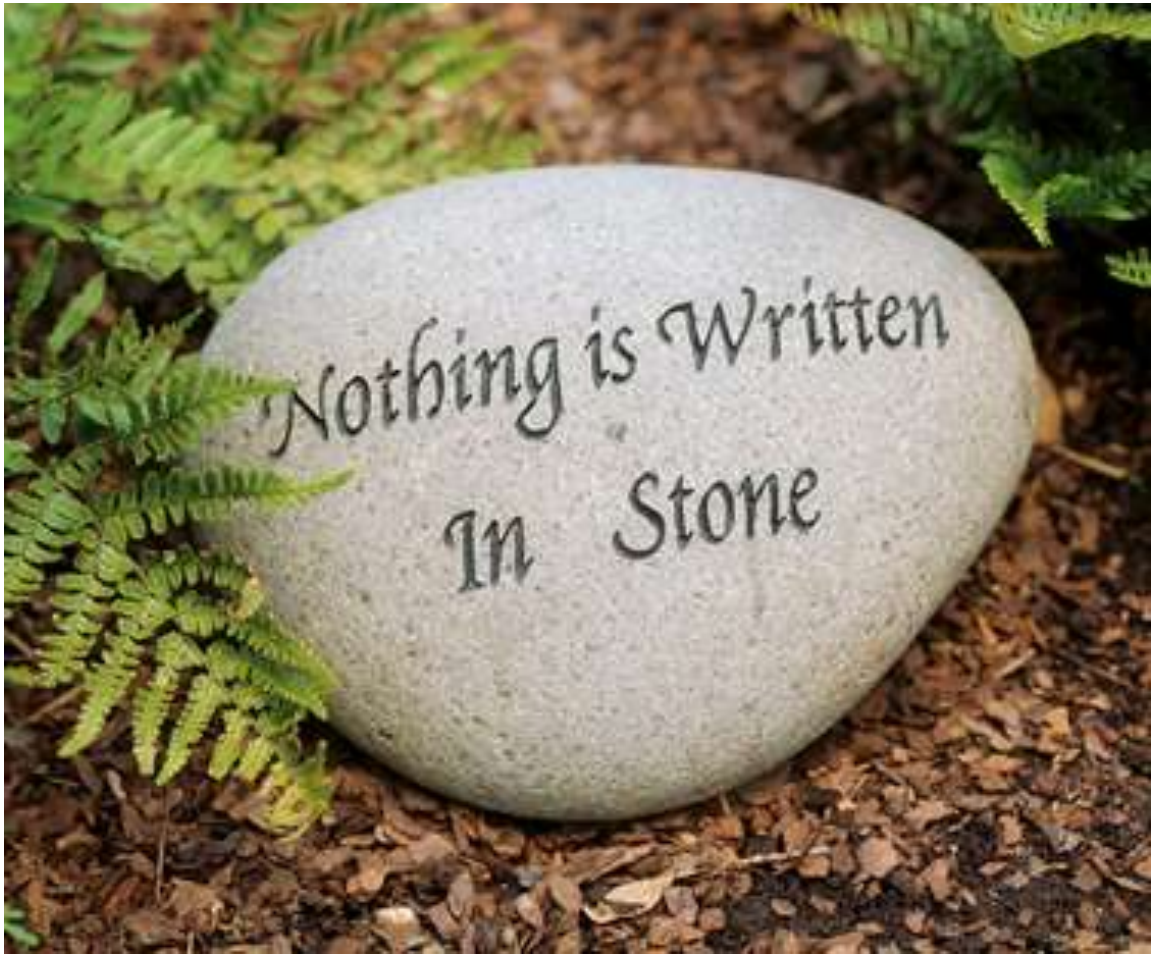
Interest	Name of organisation
Current roles and affiliations	Addictions Unit, Psychiatry Dept, Neurosciences Institute, Hospital Clinic, University of Barcelona; IDIBAPS; RTA; Vice President of INEBRIA, President of GETEM, President of EUFAS
Grants	Lundbeck, D&A Pharma, FP7, SANCO
Honoraria	Lundbeck, D&A Pharma, Servier, Lilly, Abbvie
Advisory board/consultant	Lundbeck, D&A Pharma, Socidrogalcohol (Alcohol Clinical Guidelines) 2013

Índex

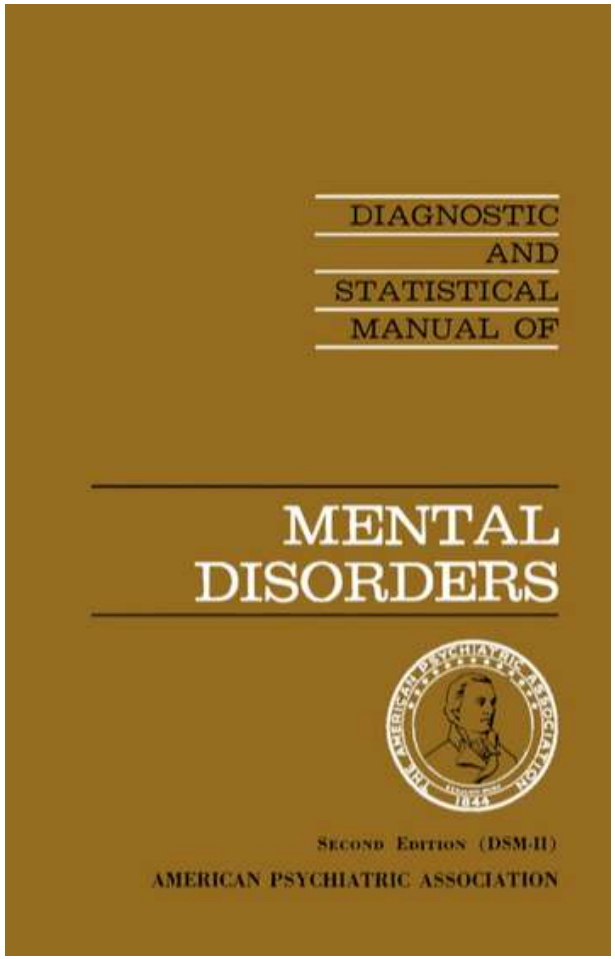
09:30h-11:00h	**Nous paradigmes en alcohol. Superant l'estigma i els prejudicis.** - Reconceptualització de l'addicció: Consum Excessiu Reiterat (CER) - Atenció centrada en el pacient - Presa de decisions compartida
11:00-11:30h	**Descans**
11:30h-13:30h	**Abordatge clínic del pacient amb Consum Excessiu Reiterat (CER)** - Estratègies per introduir l'alcohol a l'agenda - Avaluació diagnòstica. Elements prioritaris i accessoris. - El disseny del pla terapèutic - Atenció a la família - Maneig clínic de les situacions de crisi
13:30h-14:00h	**Debat sobre casos pràctics i aspectes de coordinació amb l'AP**

Reconceptualització de l'addicció: Consum Excessiu Reiterat (CER)

Nova definició d'addicció: Consum Excessiu Reiterat (CER)



DSM – II (1968)



V. PERSONALITY DISORDERS AND CERTAIN OTHER NON PSYCHOTIC MENTAL DISORDERS (301-304)

301. Personality disorders
302. Sexual deviations
303. Alcoholism
304. Drug dependence

EXPERT COMMITTEE ON ADDICTION-PRODUCING DRUGS

Seventh Report

		Page
1.	Report on the eleventh session of the Commission on Narcotic Drugs of the United Nations Economic and Social Council	3
2.	Resolutions of the United Nations Economic and Social Council	4
3.	Reports of the Permanent Central Opium Board and the Drug Supervisory Body	4
4.	Morphine and its derivatives	5
5.	Synthetic substances with morphine-like effect	6
6.	2,4-Diamino-5-phenylthiazole and β-ethyl-β-methylglutarimide	8
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Annex.	Habit-forming drugs	12

WORLD HEALTH ORGANIZATION

PALAIS DES NATIONS

GENEVA

1957

Addiction vs Habituation??

Drug addiction

Drug addiction is a state of periodic or chronic intoxication produced by the repeated consumption of a drug (natural or synthetic). Its characteristics include :

(1) an overpowering desire or need (compulsion) to continue taking the drug and to obtain it by any means ;

(2) a tendency to increase the dose ;

(3) a psychic (psychological) and generally a physical dependence on the effects of the drug ;

(4) detrimental effect on the individual and on society.

Drug habituation

Drug habituation (habit) is a condition resulting from the repeated consumption of a drug. Its characteristics include :

(1) a desire (but not a compulsion) to continue taking the drug for the sense of improved well-being which it engenders ;

(2) little or no tendency to increase the dose ;

(3) some degree of psychic dependence on the effect of the drug, but absence of physical dependence and hence of an abstinence syndrome ;

(4) detrimental effects, if any, primarily on the individual.

Consum Excessiu Reiterat (CER)

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. Samokhvalov[2,5], E. Scafato[15], K.D. Shield[2,3], M. Trapencieris[16], R.W. Wiers[17] and G. Gmel[2,11,18,19]

doi: 10.1093/alcalc/agt171
Advance Access publication 12 November 2013

Rehm, J. & Room, R. (2015). Cultural specificity in measurement and in clinical responses to alcohol use disorders. The Lancet dx.doi.org/10.1016/S0140-6736(15)00123-3

Alcohol and Alcoholism Vol. 48, No. 6, pp. 633–640, 2013
Advance Access Publication 7 August 2013

doi: 10.1093/alcalc/agt127

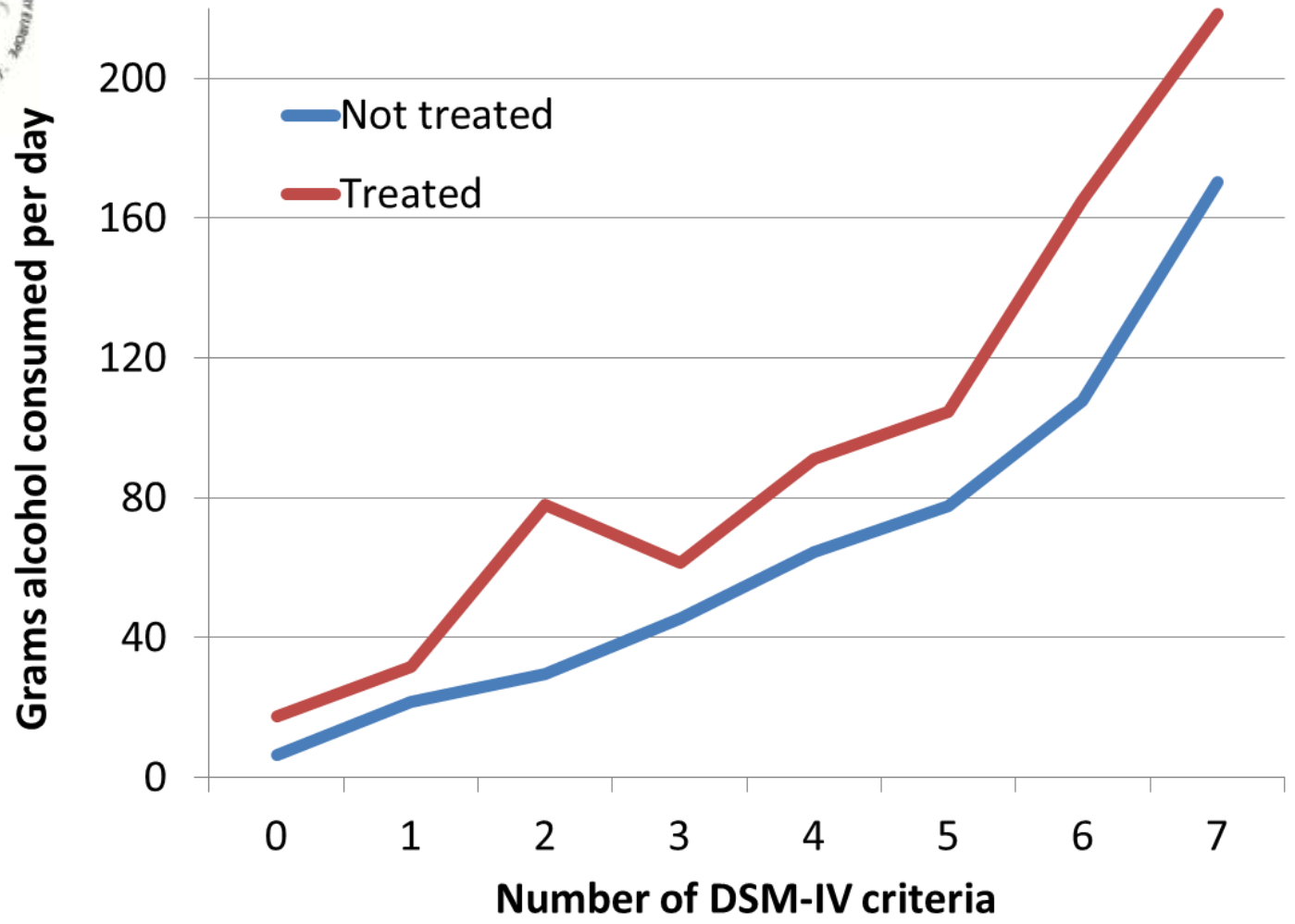
FOR DEBATE

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]

Perqué usar el CER?

- Les definicions de ‘addicció’ han canviat en el temps i l’espai, són subjectes a biaixos culturals, i tenen mancances rellevants
- La visió dicotòmica (addictes vs no addictes) no es correspón amb la realitat social i clínica, i és altament estigmatitzant
- Hi ha una molt alta correlació entre el consum excessiu reiterat i el nombre de criteris de dependència que es compleixen



Number of DSM-IV criteria for alcohol dependence by grams alcohol per day (NESARC data)

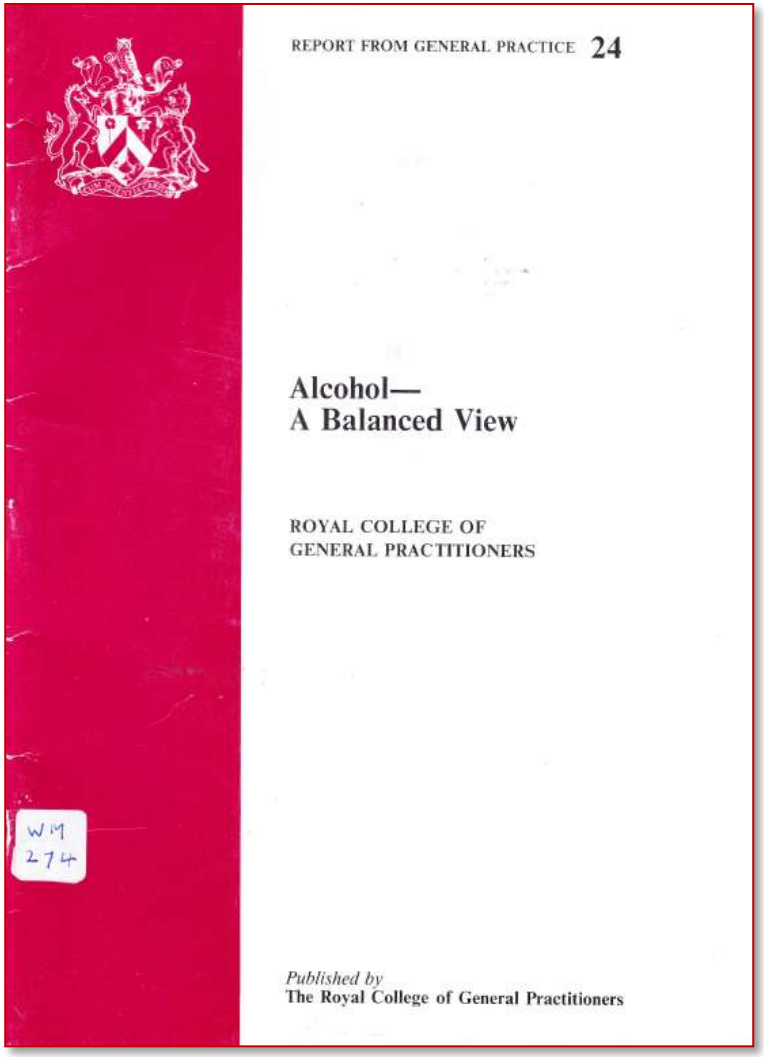
Source: Rehm et al 2013

Perqué usar el CER?

- El CER és responsable dels canvis cerebrals i les alteracions fisiològiques en les Trastorns per Consum de Substàncies (TCS)
- El CER és responsable dels fenòmens d'intoxicació, tolerància i abstinència, considerats centrals en la definició dels TCS
- El CER és responsable de la major part de les conseqüències socials dels TCS
- El CER és responsable de la major part de la morbi-mortalitat associada als TCS
- El CER encaixa millor amb les dades empíriques, redueix l'estigma, i evita que ens oblidem dels pacients de més alt risc

Alcohol. A Balanced View

Royal College of General Practitioners. London. 1986.



Alcohol. A Balanced View

Royal College of General Practitioners. London. 1986.

alcohol is similar both to blood pressure and to serum cholesterol, which both exist within continua and are risk factors for disease. The higher the level of blood pressure, the greater the risk of cerebrovascular disease and the higher the serum cholesterol level, the greater the risk of coronary heart disease.

Alcohol. A Balanced View

Royal College of General Practitioners. London. 1986.

That the Royal College of General Practitioners accept that a practical, preventive approach will entail the abandonment of the concept of 'alcoholism and the alcoholic' as the core of the problem and that concepts of addiction and dependence furnish few clues to the solution of the problem.

Atenció centrada en la persona i presa de decisions compartida

Review

Patient-Centered Approaches to Health Care: A Systematic Review of Randomized Controlled Trials

Medical Care Research and Review
70(6) 567–596
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DOI: 10.1177/1077558713496318
mcr.sagepub.com
SAGE

ann. behav. med. (2009) 37:335–342
DOI 10.1007/s12160-009-9108-5

RAPID COMMUNICATION

Brief Patient-Centered Clinician-Delivered Counseling for High-Risk Drinking: 4-Year Results

Judith K. Ockene, Ph.D., M.Ed. ·
George W. Reed, Ph.D. · Sarah Reiff-Hekking, Ph.D.

EDITORIAL

Editorials represent the opinions of the authors and *JAMA* and not those of the American Medical Association.

Bringing Patient-Centered Care to Patients With Alcohol Use Disorders

Katharine A. Bradley, MD, MPH; Daniel R. Kivlahan, PhD

Atención Centrada en la Persona (ACP)

Atención que es respetuosa con el paciente y responde a sus preferencias, necesidades y valores, asegurándose de que los valores del paciente guian el proceso de toma de decisiones

Institute of Medicine, 2001

Atributos que definen la ACP:

- **Holistica**
- **Individualizada**
- **Respetuosa**
- **Empoderadora**

Morgan & Yoder (2012)

"No decision about me, without me."

EDITORIAL

Editorials represent the opinions of the authors and *JAMA* and not those of the American Medical Association.

Bringing Patient-Centered Care to Patients With Alcohol Use Disorders

Katharine A. Bradley, MD, MPH; Daniel R. Kivlahan, PhD

jama.com

JAMA May 14, 2014 Volume 311, Number 18

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Clínicos y pacientes deben discutir:

- Sobre la ambivalencia hacia el cambio;
- Objetivos del paciente (abstinencia vs reducción vs no cambiar);
- Preferencia por un abordaje psicoterapéutico grupal o individual
- Diferencias en coste y privacidad de las distintas opciones
- Tratamientos farmacológicos

Principios de la atención centrada en el cliente (1)

- Nuestro servicio existe para beneficiar al cliente (y no viceversa).Las necesidades de los clientes tienen prioridad
- El cambio es fundamentalmente ‘auto-cambio’. Nuestros servicios facilitan procesos naturales de cambio.
- Los clientes son expertos en si mismos.
- No podemos provocar el cambio nosotros solos.
- No somos los únicos con buenas ideas. Las del cliente pueden ser mejores.

Principios de la atención centrada en el cliente (2)

- El cliente tiene capacidades, fuerzas y habilidades imprescindibles para que el cambio ocurra
- El cambio por tanto requiere la colaboración entre dos expertos
- Es importante por tanto incorporar la perspectiva del cliente.
- No es una lucha por el poder donde si el cambio se produce nosotros ganamos. Es una danza, no boxeo.
- La motivación no se insufla, se evoca.
- La gente toma sus decisiones, y el cambio sólo es un objetivo cuando el cliente lo decide.

Psychotherapy and Psychosomatics

Regular Article

Psychother Psychosom 2009;78:245–253
DOI: 10.1159/000219524

Received: July 9, 2008
Accepted after revision: September 29, 2008
Published online: May 21, 2009

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[a]Novadic-Ke
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and [d]Julius
[e]Departme

Shared Decision Making and Motivational Interviewing: Achieving Patient-Centered Care Across the Spectrum of Health Care Problems

Glyn Elwyn,
Christine Debl
Ronald M. Ep
Katy Marrin,
James White,
Dominick L. F

[1]The Dartmouth
Delivery Science,

[3]Departments of
Medicine, Obstet
ductive Sciences,
statistics, UCSF,

JGIM

PERSPECTIVE

Shared Decision Making: A Model for Clinical Practice

Glyn Elwyn, PhD[1,2], Dominick Frosch, PhD[3,4], Richard Thomson, MD[5], Natalie Joseph-Williams, MSc[1], Amy Lloyd, PhD[1], Paul Kinnersley, MD[1], Emma Cording, MB BCh[1], Dave Tomson, BM BCh[6], Carole Dodd, MSc[7], Stephen Rollnick, PhD[1], Adrian Edwards, PhD[1], and Michael Barry, MD[8,9]

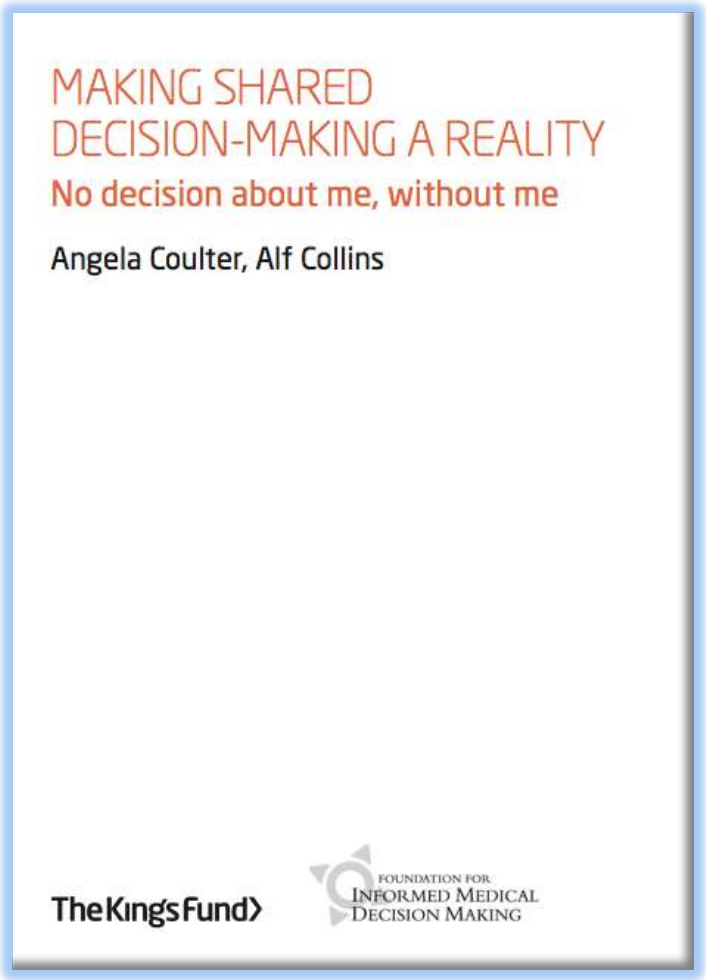
[1]Cochrane Institute of Primary Care and Public Health, Neuadd Meirionydd, Cardiff University, Cardiff, UK; [2]The Dartmouth Center for Health Care Delivery Science, Dartmouth College, New Hampshire, NH, USA; [3]Department of Health Services Research, Palo Alto Medical Foundation Research Institute, Palo Alto, CA, USA; [4]Department of Medicine, University of California, Los Angeles, Los Angeles, CA, USA; [5]Institute of Health and Society, Newcastle University, Newcastle upon Tyne, UK; [6]Collingwood Health Group, New York Surgery, North Shields, UK; [7]Clinical Governance & Risk department, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK; [8]General Medicine Division, Massachusetts General Hospital, Boston, MA, USA; [9]Informed Medical Decisions Foundation, Boston, MA, USA.

Principios éticos de la toma de decisiones compartida

- **Teoría de la autodeterminación**: la autodeterminación es deseable porque tendemos intrínsecamente a proteger y preservar nuestro bienestar
- **Teoría de la autonomía relacional**: nunca somos enteramente libres, pues nuestras decisiones están condicionadas por nuestras relaciones e interdependencias.

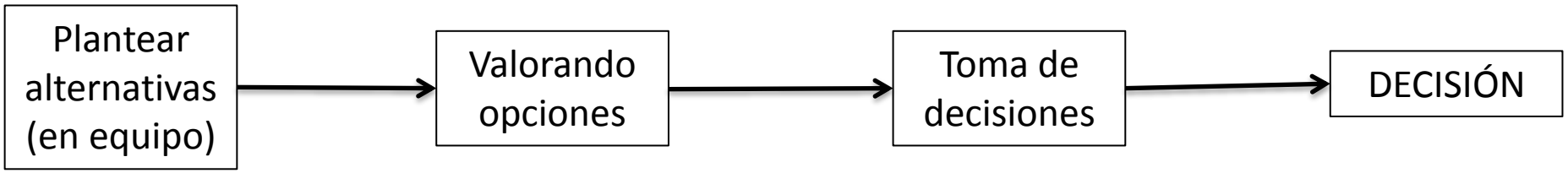
Toma de Decisiones Compartida (TDC)

- Ayudar a los pacientes a entender mejor su condición médica;
- Ofrecer información sobre los beneficios y efectos adversos de las distintas opciones terapéuticas;
- Apoyar a los pacientes mientras clarifican sus valores y preferencias;
- Apoyar al paciente en el proceso de implementación de sus decisiones;
- Trabajar con la familia y los cuidadores si el paciente tiene deterioradas sus capacidades cognitivas.



Un modelo para la práctica clínica

- Plantear alternativas en equipo (Choice talk /Team talk)
- Valorando opciones (Option talk)
- Toma de decisiones (Decision talk)



Adaptado de Elwyn et al, 2012

Plantear alternativas en equipo
(Considerar conjuntamente las posibilidades)

- Construir relación para trabajar en equipo
- Resumir el problema identificado. ¿Es tiempo de pensar cómo lo abordamos?
- Justificar la necesidad de involucrarle en la elección:
  - Preferencias individuales
  - Incertidumbre
- Evaluar respuesta y no cerrar el tema rápido

Adaptado de Elwyn et al, 2012

Valorando opciones
(Análisis de pros y contras)

- Evaluar conocimientos del paciente
- Hacer una lista de las opciones viables
- Describir con sencillez cada opción, incluyendo pros y contras.
- Facilitar instrumentos para decidir (material informativo)
- Resumir y/o pedir que el paciente reformule lo hablado

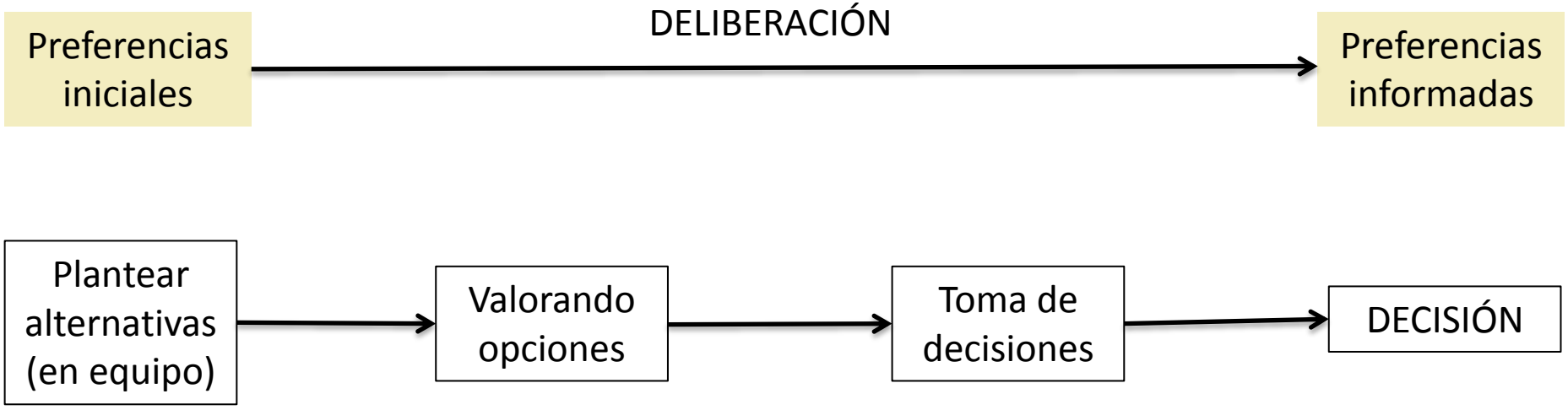
Adaptado de Elwyn et al, 2012

Toma de decisiones
(Concretando preferencias)

- Enfatizar las preferencias del paciente
- Chequear disponibilidad para tomar una decisión
- Concretar y confirmar la decisión tomada y las motivaciones para la elección realizada
- Ofrecer la posibilidad (cuando exista) de revisar la decisión.
- Agradecer el esfuerzo y el compromiso.

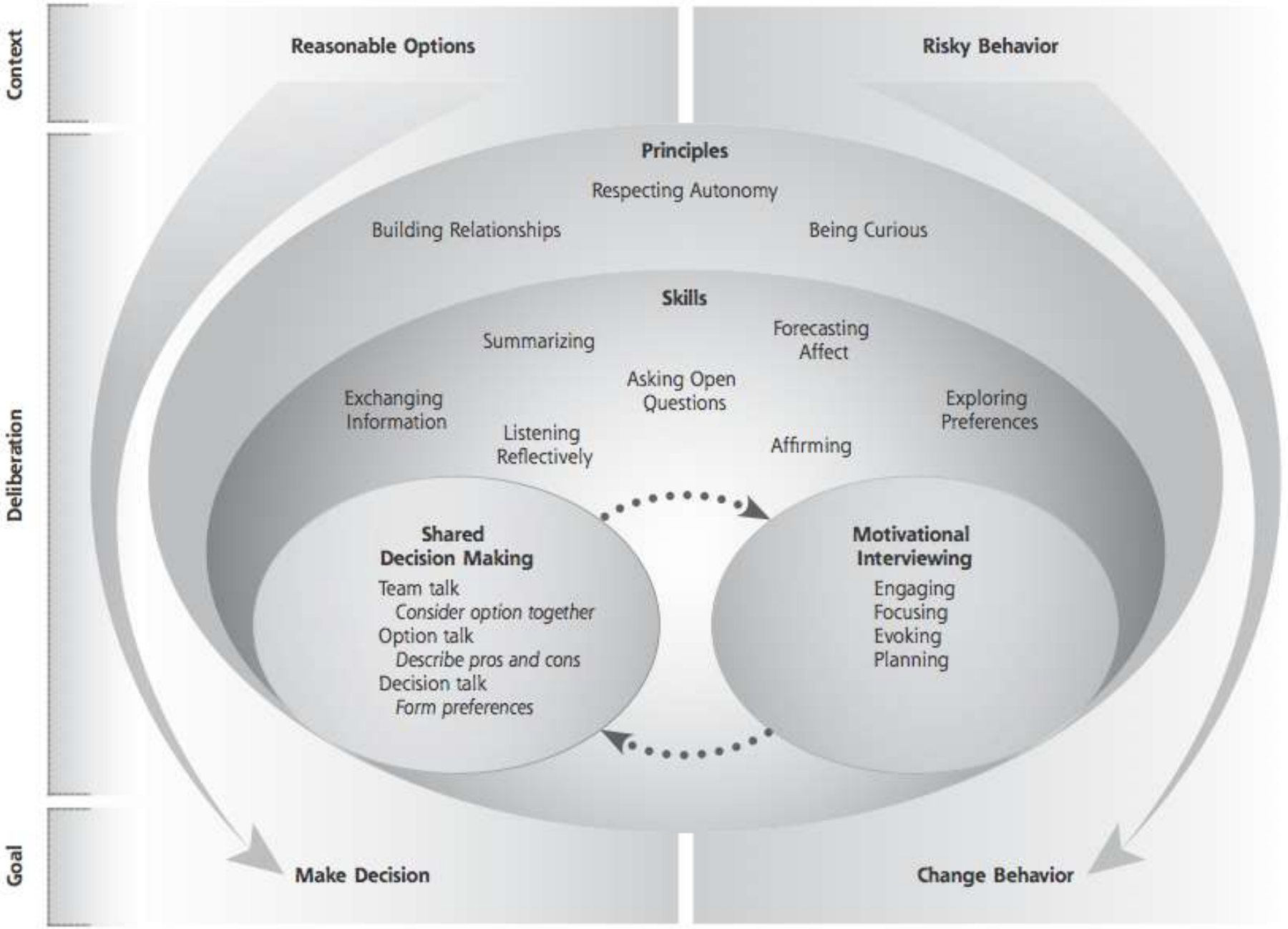
Adaptado de Elwyn et al, 2012

Toma de decisiones compartida y entrevista motivacional



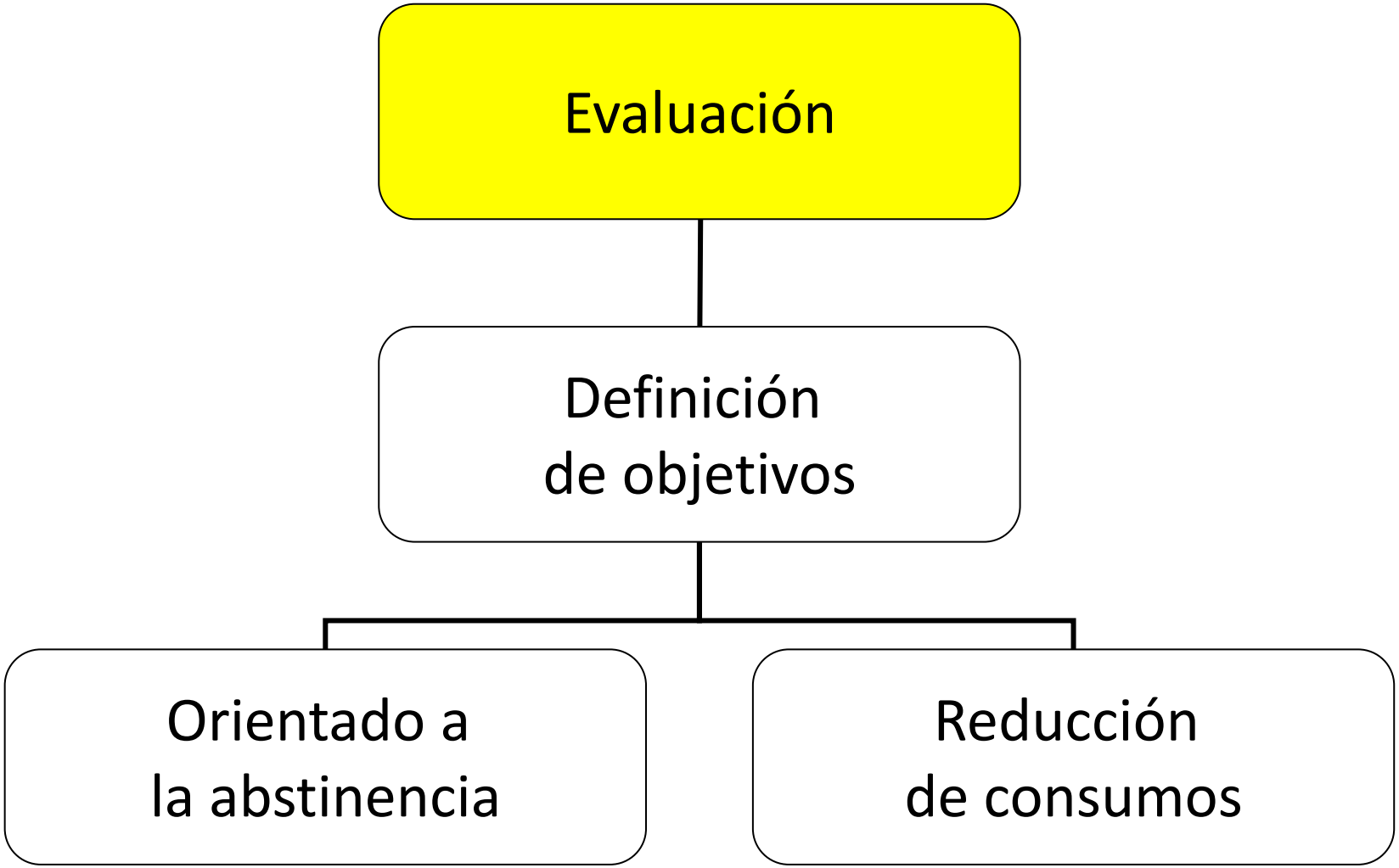
Traducido de Elwyn et al, 2014

Figure 3. The relationship of shared decision making and motivational interviewing.



Avaluació diagnòstica. Elements prioritaris i accessoris.

Manejo clínico



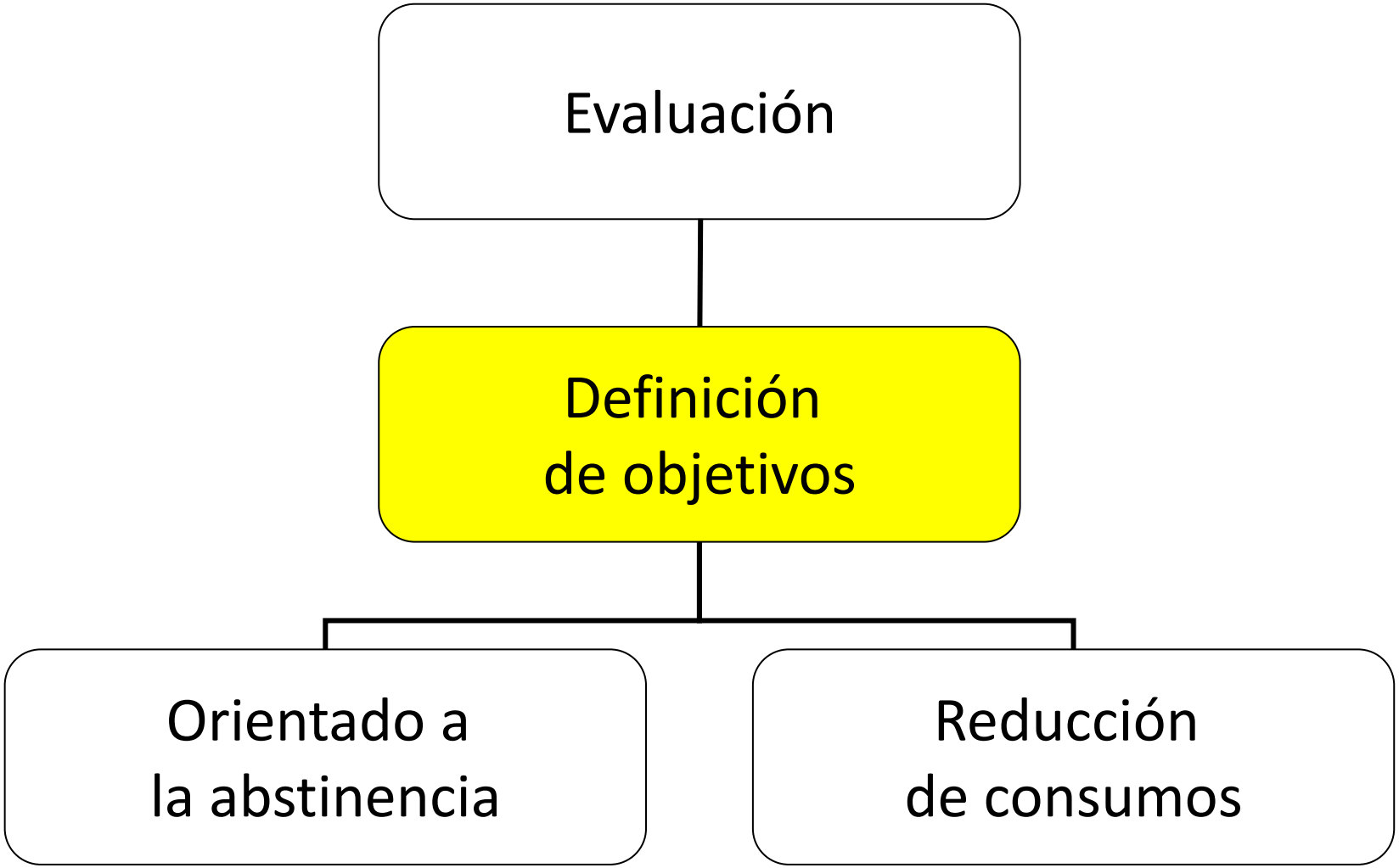
AUD. Assessment dimensions.

DIMENSION	DIAGNOSTIC CRITERIA
Drinking	Quantity & Frequency Tolerance & Withdrawal Craving
Medical harm	Continued use despite medical problems Recurrent drinking (physically hazardous)
Behavioural	Uncontrolled intake Unsuccessful efforts to stop Time spent around alcohol
Social harm	Given up or reduced activities Use despite social or interpersonal problems Failure to fulfil major role obligations

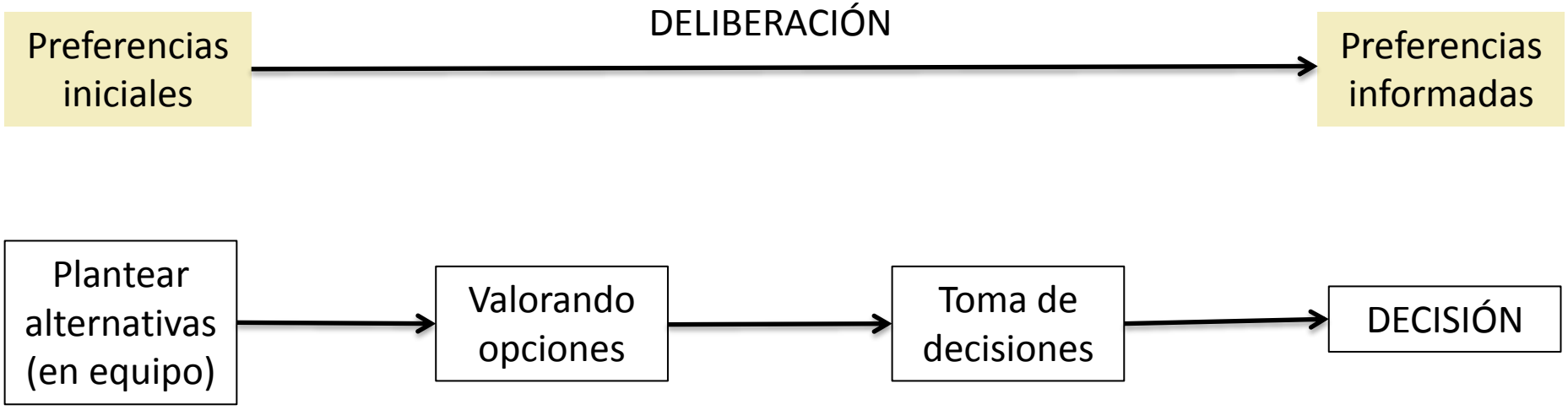
How to do it

- Empathic style
- Avoid judgmental attitudes
- Stick to facts. Do not discuss why.
- Don’t ask just about alcohol. Tobacco, BZD and illicit drugs are also relevant.
- Try to understand the story and the dilemma behind
- Try to identify strengths of the patient

Manejo clínico

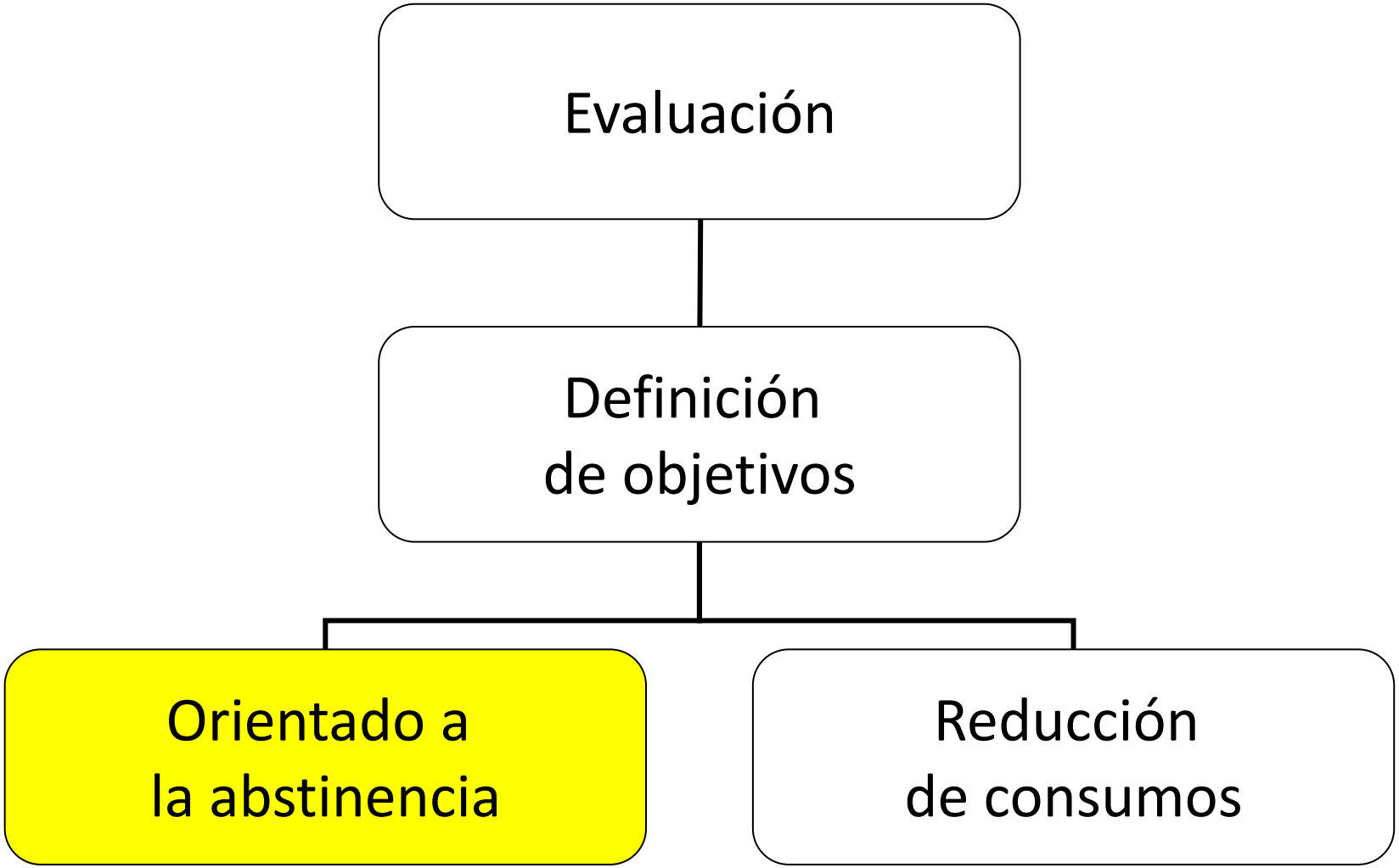


Toma de decisiones compartida y entrevista motivacional



Traducido de Elwyn et al, 2014

Manejo clínico



Tratamiento orientado a la abstinencia

- Desintoxicación
- Rehabilitación

DESINTOXICACIÓN

Conjunto de medidas ambientales y farmacológicas que permiten conseguir que el enfermo alcohólico interrumpa su consumo habitual de alcohol sin presentar signos ni síntomas de abstinencia

Gual et al, 1999

CRITERIOS PARA INDICAR UNA DESINTOXICACIÓN

- Presencia de signos o síntomas de abstinencia en el momento de la exploración (CIWA)
- Consumo continuado en las últimas semanas de cantidades superiores a los 120 gr de alcohol

Rodríguez Martos et al, 1999

CONTRAINDICACIONES DE LA DESINTOXICACIÓN

- Bebedor intermitente con abstinencia superior a 72 horas y ausencia de signos y/o síntomas de abstinencia
- Paciente que no acepta mantenerse abstinente en el curso de la desintoxicación

Gual et al, 1999

Clinical Institute Withdrawal Assessment (CIWA)

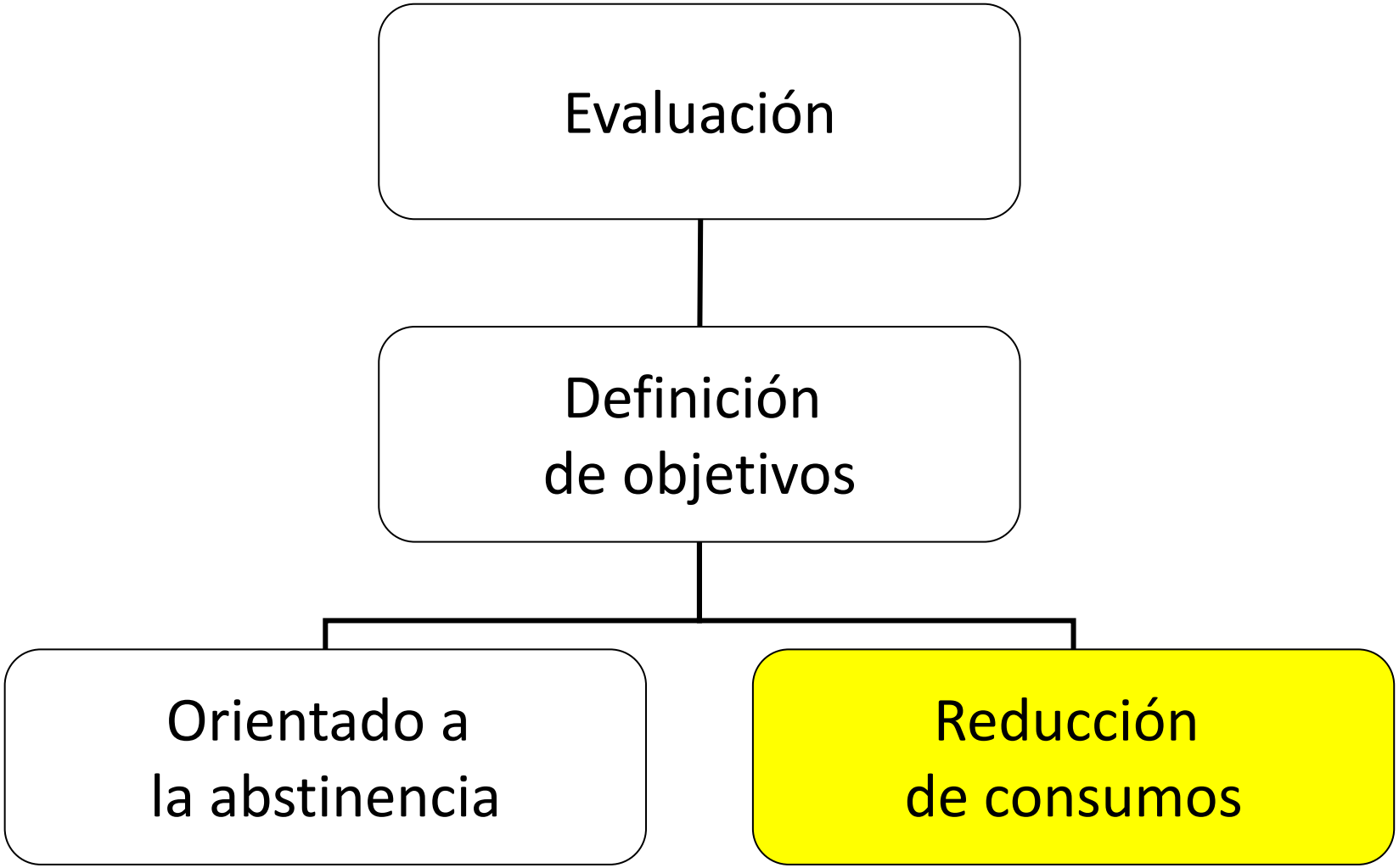
- Náuseas y Vómitos
- Temblor (brazos extendidos y dedos separados)
- Sudoración paroxística
- Ansiedad
- Agitación
- Alteraciones táctiles
- Trastornos auditivos
- Alteraciones visuales
- Cefaleas, sensación de plenitud cefálica.
- Orientación auto-alopsiquica

Sullivan et al, 1989

Tratamiento farmacológico

- Se deben usar benzodicepinas de vida media larga: Diacepam, cloracepato y clordiacepóxido son las mas usadas en pauta descendente, no superior a 10-12 dias.
- Permiten la técnica de ‘carga’ (loading dose): 20 mg cada hora hasta conseguir sedación
- Buena actividad anticomicial
- Elevado riesgo de adicción yatrogénica
- En caso de hepatopatia severa hay que usar oxacepam o loracepam
- Fármacos alternativos: clormetiazol, tiapride, oxcarbacepina

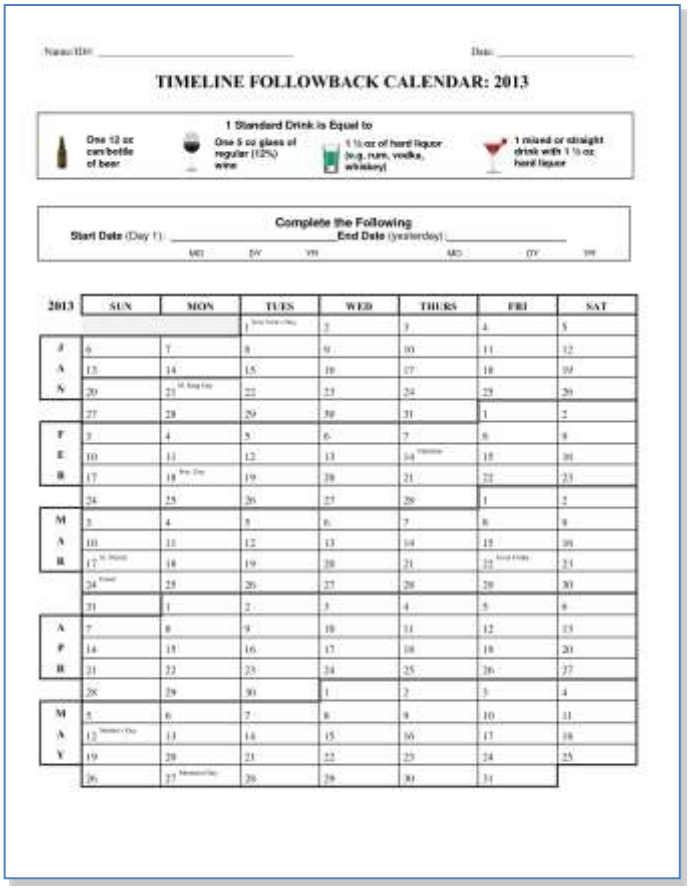
Manejo clínico



Reducción de Consumos

- No precisa desintoxicación
- La monitorización de consumos es imprescindible
- Facilitar estrategias de reducción de consumos
- Ofrecer tratamiento farmacológico

Monitorización de consumos



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): _____

2013	SUN	MON	TUES	WED	THURS	FRI	SAT
			1 New Year's Day	2	3	4	5
JAN	6	7	8	9	10	11	12
	13	14	15	16	17	18	19
	20	21 M. King Day	22	23	24	25	26
	27	28	29	30	31	1	2
FEB	3	4	5	6	7	8	9
	10	11	12	13	14 Valentine	15	16
	17	18 Pres. Day	19	20	21	22	23
	24	25	26	27	28	1	2
MAR	3	4	5	6	7	8	9
	10	11	12	13	14	15	16
	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
APR	7	8	9	10	11	12	13
	14	15	16	17	18	19	20
	21	22	23	24	25	26	27
	28	29	30	1	2	3	4
MAY	5	6	7	8	9	10	11
	12 Mother's Day	13	14	15	16	17	18
	19	20	21	22	23	24	25
	26	27 Memorial Day	28	29	30	31	

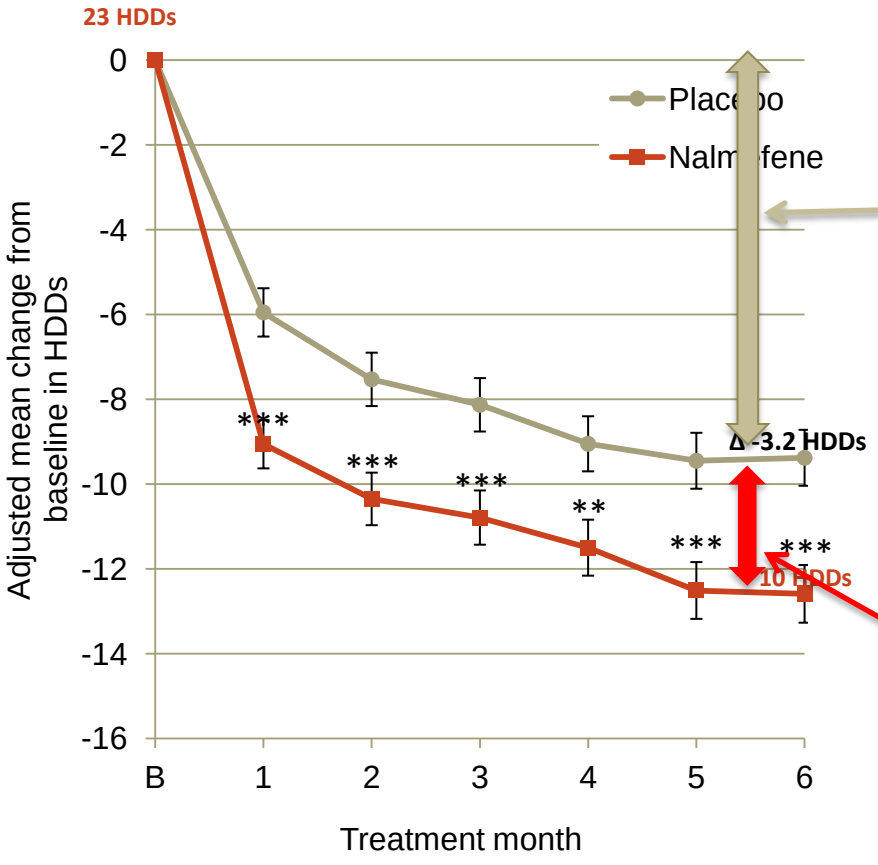
Estrategias de reducción de consumos

- No beber sin ingerir alimentos
- Beber lentamente, paladeando
- Intercalar bebidas con y sin alcohol
- Planificar actividades alternativas en las horas en que se suele beber
- Hacer ejercicio físico
- Evitar bares y encuentros con personas que beban mucho

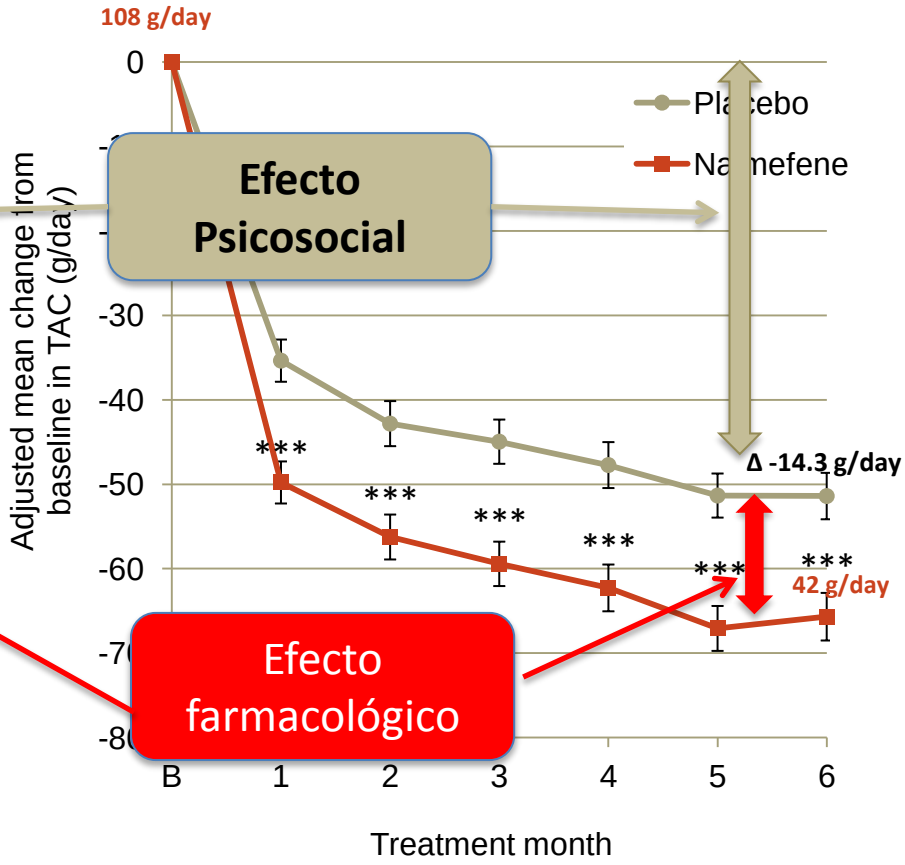
Tratamientos farmacológicos del trastorno por consumo de alcohol

Relevancia de los tratamientos no farmacológicos

Change in heavy drinking days (HDDs)



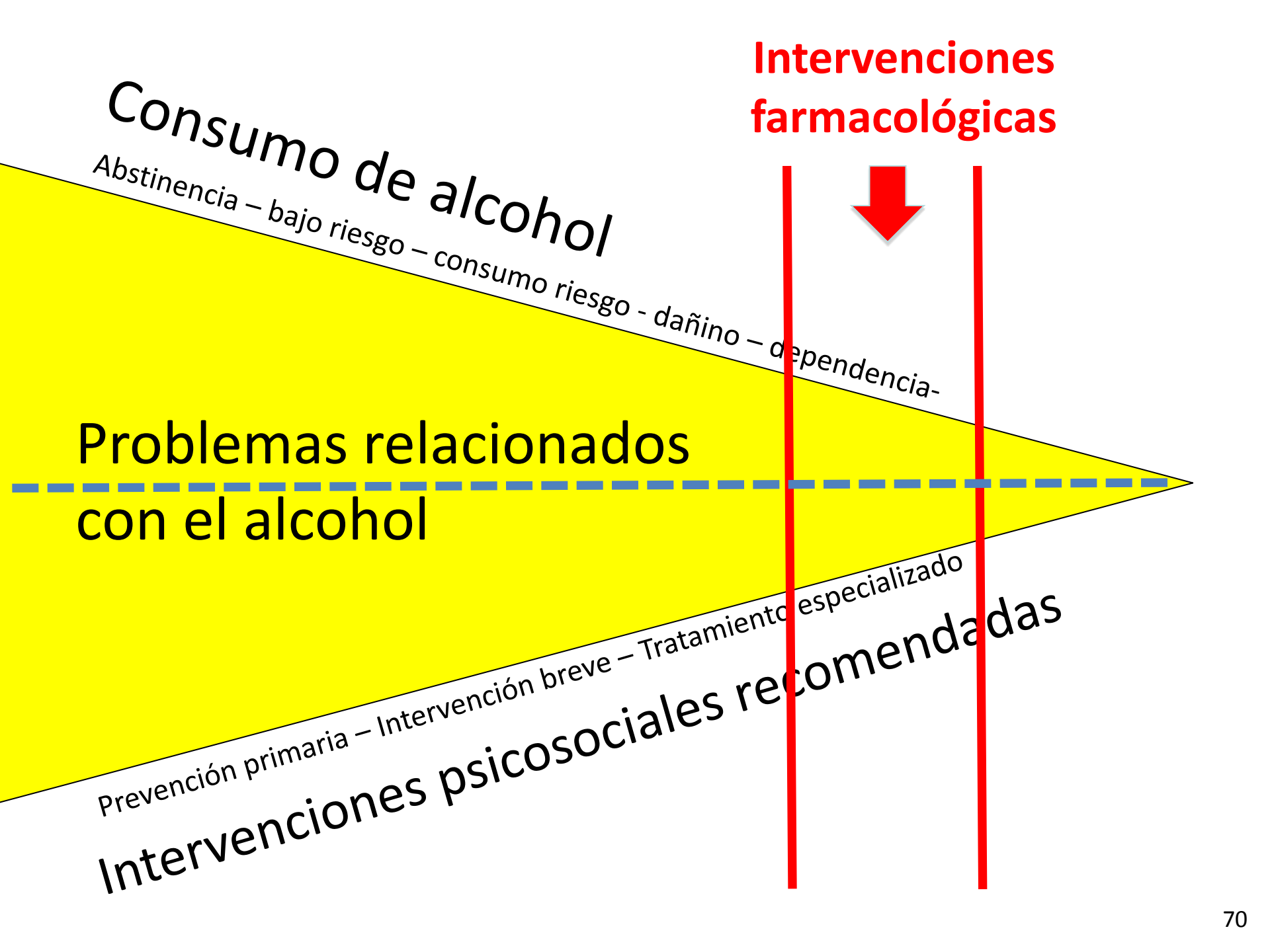
Change in total alcohol consumption (TAC)

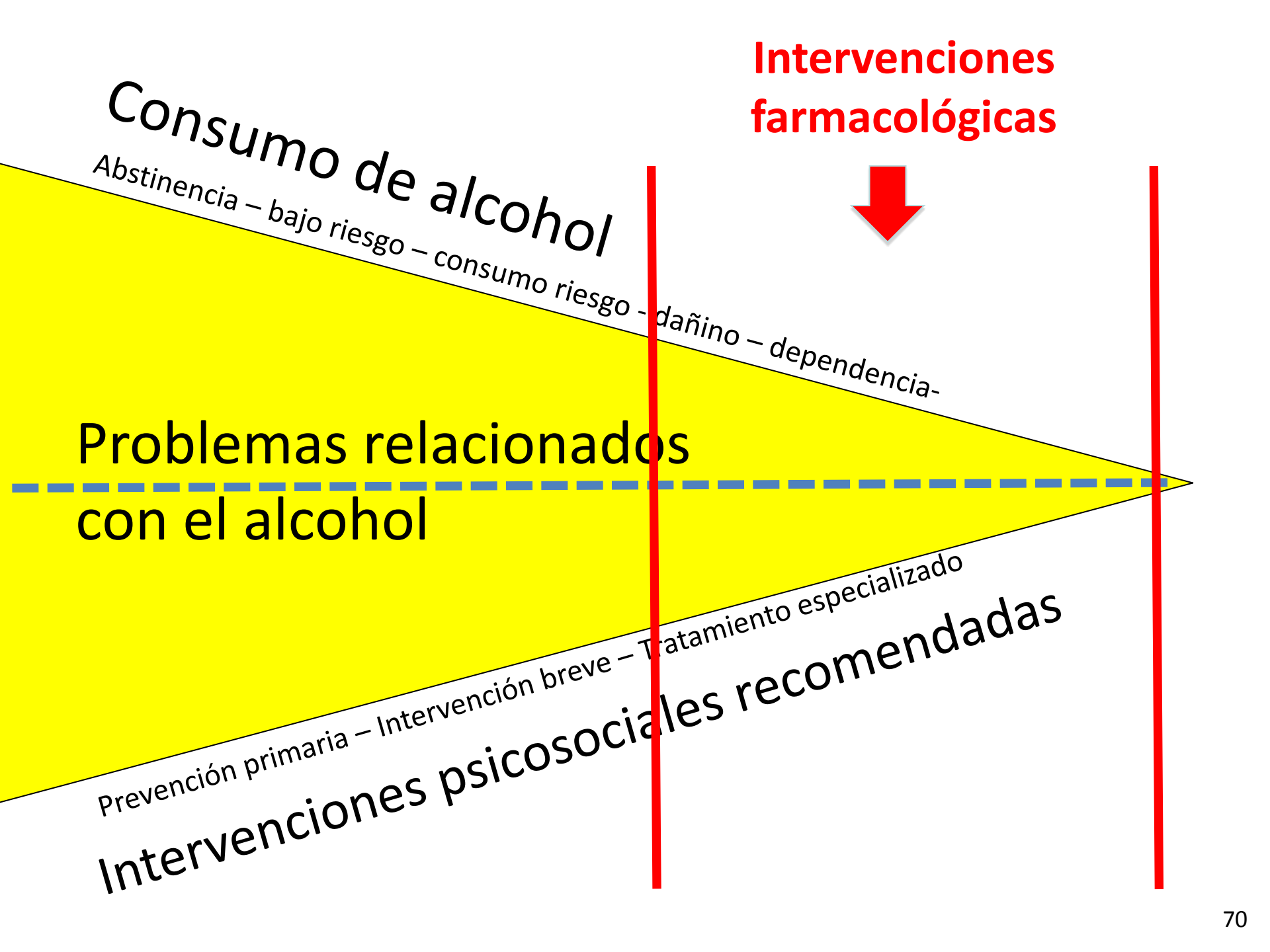


Efecto Psicosocial

Efecto farmacológico

van den Brink et al. 2013


Intervenciones farmacológicas
Consumo de alcohol
Abstinencia – bajo riesgo – consumo riesgo - dañino – dependencia-
Problemas relacionados con el alcohol
Prevención primaria – Intervención breve – Tratamiento especializado
Intervenciones psicosociales recomendadas


Intervenciones farmacológicas
Consumo de alcohol
Abstinencia – bajo riesgo – consumo riesgo - dañino – dependencia-
Problemas relacionados con el alcohol
Prevención primaria – Intervención breve – Tratamiento especializado
Intervenciones psicosociales recomendadas

Ampliando el ámbito de actuación farmacológica

- Clásico: Orientado a la abstinencia (disulfiram*, acamprosato*, naltrexona*, topiramato)
- Terapia substitutiva: BZD, oxibato sódico, baclofeno
- Reducción de consumos: nalmefeno*, naltrexona, topiramato, gabapentina.

* Indicación autorizada

Dianas de los tratamientos farmacológicos

Objetivo	Ejemplo
Reducir craving	Acamprosato
Reducir priming	Nalmefeno
Reducir impulsividad	Topiramato
Reacción aversiva	Disulfiram

Tratamientos farmacológicos orientados a la abstinencia

Table 1. Summary of Findings and Strength of Evidence From Trials Assessing Efficacy of FDA-Approved Medications for Alcohol Use Disorders

Medication	Outcome	No. of Studies	No. of Participants[a]	Results Effect Size (95% CI)[b]	NNT (95% CI)[c]	Strength of Evidence
Acamprosate	Return to any drinking	16	4847	RD: −0.09 (−0.14 to −0.04)	12 (8 to 26)	Moderate
	Return to heavy drinking	7	2496	RD: −0.01 (−0.04 to 0.03)	NA	Moderate
	% DDs	13	4485	WMD: −8.8 (−12.8 to −4.8)	NA	Moderate
	% HDDs	1	100	WMD: −2.6 (−11.4 to 6.2)	NA	Insufficient
Disulfiram	Return to any drinking	2	492	RD: −0.04 (−0.11 to 0.03)	NA	Low
	Return to heavy drinking	0	0	NA	NA	Insufficient
	% DDs	2	290	NSD[d]	NA	Insufficient
	% HDDs	0	0	NA	NA	Insufficient
Naltrexone, 50 mg oral	Return to any drinking	16	2347	RD: −0.05 (−0.10 to −0.002)	20 (11 to 500)	Moderate
	Return to heavy drinking	19	2875	RD: −0.09 (−0.13 to −0.04)	12 (8 to 26)	Moderate
	% DDs	15	1992	WMD: −5.4 (−7.5 to −3.2)	NA	Moderate
	% HDDs	6	521	WMD: −4.1 (−7.6 to −0.61)	NA	Moderate
Naltrexone injection	Return to any drinking	2	939	RD: −0.04 (−0.10 to 0.03)	NA	Low
	Return to heavy drinking	2	615	RD: −0.01 (−0.14 to 0.13)	NA	Low
	% DDs	1	315	WMD: −8.6 (−16.0 to −1.2)	NA	Insufficient
	% HDDs	2[e]	926	WMD: −4.6 (−8.5 to −0.56)	NA	Low

Jonas, D. E., Amick, H. R., Feltner, C., et al (2014). Pharmacotherapy for adults with alcohol use disorders in outpatient settings: a systematic review and meta-analysis. *Jama*, *311*(18), 1889–900. doi:10.1001/jama.2014.3628

Disulfiram

OPEN ACCESS Freely available online

PLOS | ONE

Disulfiram Efficacy in the Treatment of Alcohol Dependence: A Meta-Analysis

Marilyn D. Skinner[1]*, Pierre Lahmek[2], Héloïse Pham[3], Henri-Jean Aubin[4]

1 Centre de Traitement des Addictions, Hôpital Emile Roux, Assistance Publique-Hôpitaux de Paris, Institut National de la Santé et de la Recherche Médicale U669, Limeil-Brévannes, France, **2** Centre de Traitement des Addictions, Hôpital Emile Roux, Assistance Publique-Hôpitaux de Paris, Limeil-Brévannes, France, **3** Centre Médical Marmottan Paris, France, **4** Centre d'Enseignement, de Recherche et de Traitement des Addictions, Hôpital Paul Brousse, Assistance Publique-Hôpitaux de Paris, Université Paris-Sud, Institut National de la Santé et de la Recherche Médicale U669, Villejuif, France

Table 3. Success Rates on Primary Outcomes.

Study Mean (SD) or %	Disulfiram success Rate	Disulfiram N	Control success rate	Control N
Bardeleben et al 1999	93.3 (16.6)	20	89.6 (18.04)	40
Carroll et al 1993	2.4 (2.3)	9	10.4 (7.7)	9
Carroll et al 1998	53.00%	78	16.00%	44
Carroll et al 2004	87.50%	38	82.60%	25
Chick et al 1992	100 (70)	47	69 (67)	46
De Sousa & De Sousa 2004	82.00%	50	42.00%	50
De Sousa & De Sousa 2005	88.00%	50	46.00%	50
De Sousa et al 2008	90.00%	50	56.00%	50
De Sousa & De Sousa 2008	79.31%	29	51.72%	29
De Sousa & Jagtap 2009	81.25%	16	43.75%	16
Fuller & Roth 1979	21.00%	43	18.58%	85
Fuller et al 1986	18.80%	202	19.34%	403
Gerrein et al 1973	23.07%	26	8.70%	23
Grassi et al 2007	100.00%	4	12.50%	8
Laaksonen et al 2008	46.6 (27.5)	33	17,87 (21,03)	91
Ling et al 1983	9.80%	41	24.40%	41
Nava et al 2006	90.00%	31	80.11%	55
Niederhofer & Staffen 2003	53.80%	13	15.40%	13
Petrakis et al 2000	100.00%	8	57.00%	9
Petrakis et al 2005	77.30%	66	65.02	123
Pettinati et al 2008	17.00%	53	16.13%	106
Ulrichsen et al 2010	26.00%	19	20.00%	20

doi:10.1371/journal.pone.0087366.t003

Review

Current Findings and Mechanisms of Action of Disulfiram in the Treatment of Alcohol Dependence

Authors J. Mutschler[1, 3], M. Grosshans[2], M. Soyka[3, 4], S. Rösner[5]

Affiliations Affiliation addresses are listed at the end of the article

- Posición excepcional
- Relevancia de las expectativas
- Imposibilidad de demostrar eficacia en doble ciego
- Eficacia demostrable en estudios abiertos

Alcohol and Alcoholism Advance Access published October 27, 2007

Alcohol & Alcoholism Page 1 of 9
doi:10.1093/alcalc/agm136, available online at www.alcalc.oxfordjournals.org

A RANDOMIZED, MULTICENTRE, OPEN-LABEL, COMPARATIVE TRIAL OF DISULFIRAM, NALTEREXONE AND ACAMPROSATE IN THE TREATMENT OF ALCOHOL DEPENDENCE

E. LAAKSONEN[1], A. KOSKI-JÄNNES,[4] M. SALASPURO,[2,3] H. AHTINEN,[5] and HANNU ALHO[2,3]*

[1]University of Turku and Turku Health Centre
[2]National Public Health Institute, Department of Mental Health and Alcohol Research, Helsinki
[3]Research Unit of Substance Abuse Medicine, Helsinki University
[4]Department of Sociology and Social Psychology, University of Tampere, Finland
[5]Medikalla Oy, Medfiles, Turku, Finland

(*Received* 05 *April* 2007; *first review notified* 21 *May* 2007; *in revised form* 15 *August* 2007; *accepted* 23 *August* 2007)

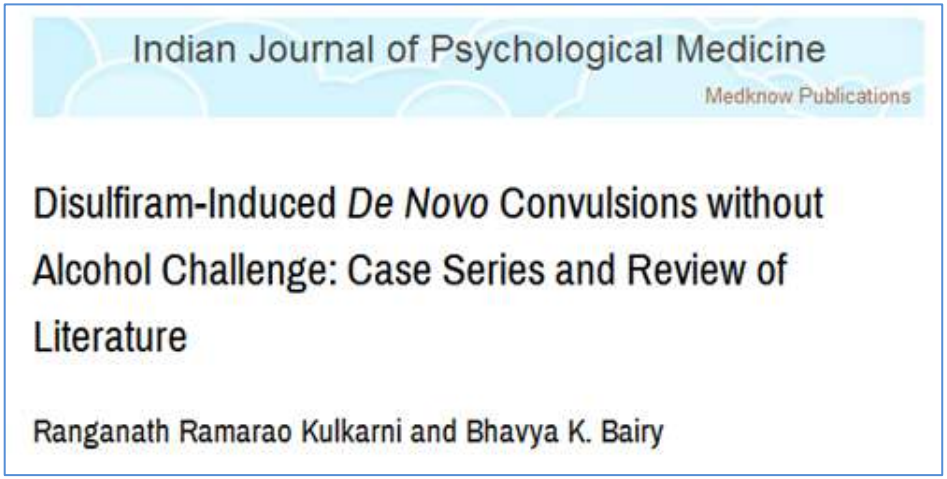
Table 2. Drinking outcomes during continuous medication period (up to 12 weeks)

	ACA	DIS	NTX
Time (days) to first HDD, mean ± SD (n)	17.6 ± 22.0 (44)	46.6 ± 27.5 (33)**	22.0 ± 22.0 (47)
Time (days) to first drinking, mean ± SD (*N*)	11.4 ± 17.0 (50)	30.4 ± 27.8 (39)*	16.2 ± 20.2 (50)
Abstinence days/week, mean ± SD (*N*)	4.5 ± 2.1 (52)	6.3 ± 0.9 (54 ***)	4.6 ± 2.0 (53)

* Significance DIS > NTX and ACA; $P = 0.0002$.
** Significance DIS > NTX and ACA ($P < 0.0001$).
*** Significance DIS > NTX and ACA ($P < 0.0001$); difference between weeks ($P = 0.001$).

Laaksonen et al, Alcohol Alcohol. 2008 Jan-Feb;43(1):53-61.

Efectos secundarios del disulfiram



Indian J Psychol Med. 2015 Jul-Sep;37(3):345-8

J Med Case Rep. 2016 Mar 31;10(1):72

Acamprosato

Addiction

SSA SOCIETY FOR THE STUDY OF ADDICTION

REVIEW

doi:10.1111/add.12875

The efficacy of acamprosate and naltrexone in the treatment of alcohol dependence, Europe versus the rest of the world: a meta-analysis

Kim Donoghue[1], Catherine Elzerbi[1], Rob Saunders[2], Craig Whittington[2], Stephen Pilling[2] & Colin Drummond[1]

National Addiction Centre, Addictions Department, King's College London, UK[1] and Centre for Outcomes Research and Effectiveness, Research Department of Clinical, Educational and Health Psychology, University College London, London, UK[2]

- Eficacia similar en todo el mundo
- Adherencia al tratamiento mayor en Europa que en el resto del mundo

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The article you requested is

Efficacy of Acamprosate for the Treatment of Alcohol Dependence Long After Recovery From Withdrawal Syndrome: A Randomized, Double-Blind, Placebo-Controlled Study Conducted in Japan (Sunrise Study)

Susumu Higuchi, MD, PhD, for the Japanese Acamprosate Study Group

J Clin Psychiatry 2015;76(2):181–188
10.4088/JCP.13m08940

Efficacy of acamprosate in Japan

- RCT in 327 Japanese patients with alcohol dependence
- Acamprosate (1,998 mg/d orally) or placebo for 24 weeks.
- Primary endpoint: complete abstinence after 24 weeks.
- Acamprosate demonstrated superior efficacy vs placebo on the primary endpoint (abstinence after 24 weeks):
  - 47.2% in the acamprosate group
  - 36.0% in the placebo group (P = .039).

Otros fármacos para tratamientos orientados a la abstinencia

Baclofeno

- Muy controvertido
- Muchos ensayos clínicos a punto de ser publicados
- Dosis bajas no son efectivas. Dosis altas sí.

Oxibato Sódico

- Autorizado en Austria y Italia
- Eficaz para la desintoxicación
- Resultados del ensayo europeo a punto de ser publicados

Alcohol & Alcoholism Vol. 40, No. 2, pp. 147–150, 2005
Advance Access publication 13 December 2004
doi:10.1093/alcalc/agh130

CASE REPORT

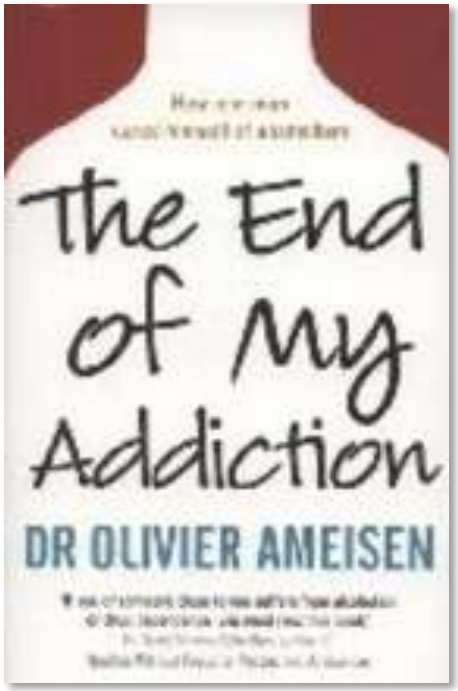
COMPLETE AND PROLONGED SUPPRESSION OF SYMPTOMS AND CONSEQUENCES OF ALCOHOL-DEPENDENCE USING HIGH-DOSE BACLOFEN: A SELF-CASE REPORT OF A PHYSICIAN

OLIVIER AMEISEN*

23 rue du Départ BP37, 75014 Paris, France

(*Received* 2 *October* 2004; *first review notified* 19 *October* 2004; *in revised form* 10 *November* 2004; *accepted* 11 *November* 2004)

Abstract — **Aims:** To test whether the dose-dependent motivation-suppressing effect of baclofen in animals could be transposed to humans, and suppress craving and sustain abstinence. **Methods:** Neurologists safely use up to 300 mg/day (10 times the dosage currently used for alcohol dependence) of high-dose oral baclofen, to control spasticity, in order to avoid invasive therapy. I am a physician with alcohol dependence and comorbid anxiety. I self-prescribed high-dose baclofen, starting at 30 mg/day, with 20 mg increments every third day and an (optional) additional 20–40 mg/day for cravings. **Results:** Cravings became easier to combat. After reaching the craving-suppression dose of 270 mg/day (3.6 mg/kg) after 5 weeks, I became and have remained free of alcohol dependence symptoms effortlessly for the ninth consecutive month. Anxiety is well controlled. Somnolence disappeared with a dosage reduction to 120 mg/day, now used for the eighth consecutive month. **Conclusions:** High-dose baclofen induced complete and prolonged suppression of symptoms and consequences of alcohol dependence, and relieved anxiety. This model, integrating cure and well-being, should be tested in randomized trials, under medical surveillance. It offers a new concept: medication-induced, dose-dependent, complete and prolonged suppression of substance-dependence symptoms with alleviation of comorbid anxiety.



European Neuropsychopharmacology (2015) 25, 1167-1177

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www.elsevier.com/locate/euroneuro

High-dose baclofen for the treatment of alcohol dependence (BACLAD study): A randomized, placebo-controlled trial

Christian A. Müller[a,*], Olga Geisel[a], Patricia Pelz[a], Verena Higl[a], Josephine Krüger[a], Anna Stickel[a], Anne Beck[a], Klaus-Dieter Wernecke[b], Rainer Hellweg[a], Andreas Heinz[a]

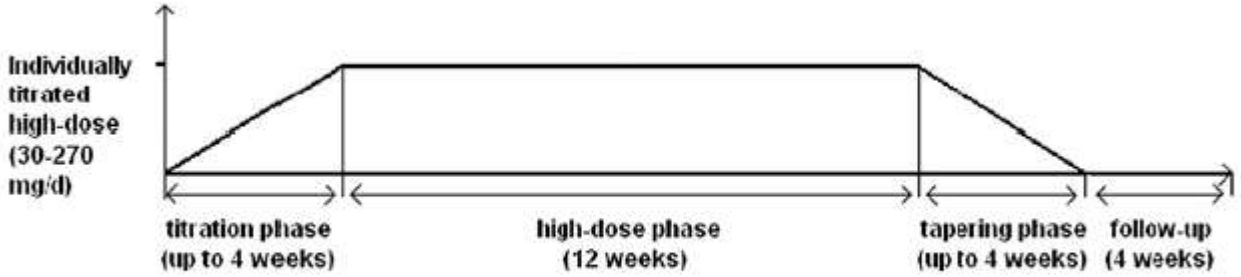
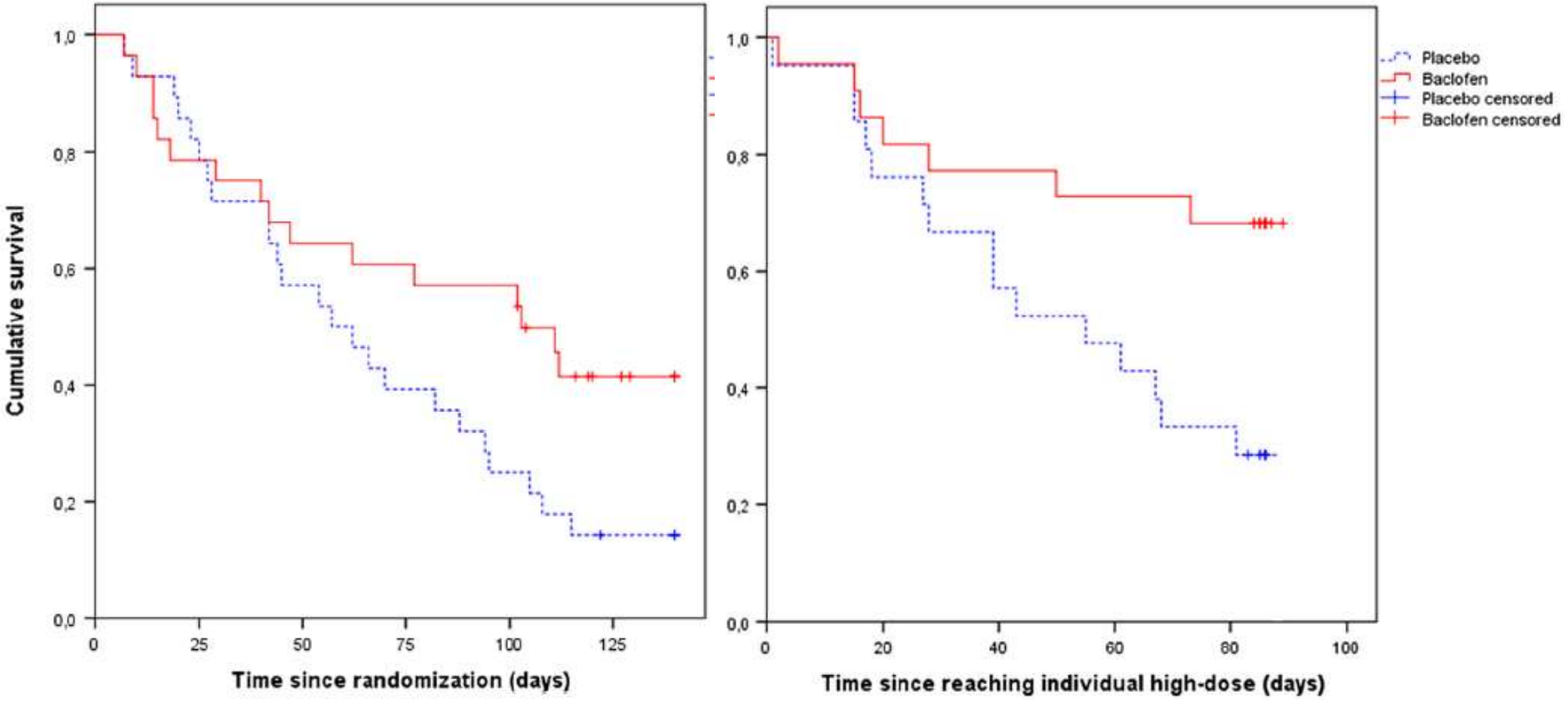


Figure 1 BACLAD trial profile.

Table 1 Dose titration schedule.

Days of treatment	Total daily dose (mg)	5 mg capsules	10 mg capsules	30 mg capsules
Day 1-3	15	1-1-1	-	-
Day 4-6	30	-	1-1-1	-
Day 7-9	60	-	2-2-2	-
Day 10-12	90	-	-	1-1-1
Day 13-15	120	-	1-1-1	1-1-1
Day 16-18	150	-	2-2-2	1-1-1
Day 19-21	180	-	-	2-2-2
Day 22-24	210	-	1-1-1	2-2-2
Day 25-27	240	-	2-2-2	2-2-2
Day 28-114	270	-	-	3-3-3
Day 115-117	240	-	2-2-2	2-2-2
Day 118-120	210	-	1-1-1	2-2-2
Day 121-123	180	-	-	2-2-2
Day 124-126	150	-	2-2-2	1-1-1
Day 127-129	120	-	1-1-1	1-1-1
Day 130-132	90	-	-	1-1-1
Day 133-135	60	-	2-2-2	-
Day 136-138	30	-	1-1-1	-
Day 139-141	15	1-1-1	-	-

Baclad study



Otros fármacos para tratamientos orientados a la abstinencia

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- Muy controvertido
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- Dosis bajas no son efectivas. Dosis altas sí.

Oxibato Sódico

- Autorizado en Austria y Italia
- Eficaz para la desintoxicación
- Resultados del ensayo europeo a punto de ser publicados

Naltrexona

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The article you requested is

Reduction of Alcohol Drinking in Young Adults by Naltrexone: A Double-Blind, Placebo-Controlled, Randomized Clinical Trial of Efficacy and Safety

Stephanie S. O'Malley, PhD; William R. Corbin, PhD; Robert F. Leeman, PhD; Kelly S. DeMartini, PhD; Lisa M. Fucito, PhD; Jolomi Ikomi, MD; Denise M. Romano, APRN; Ran Wu, MS; Benjamin A. Toll, PhD; Kenneth J. Sher, PhD; Ralitza Gueorguieva, PhD; and Henry R. Kranzler, MD

J Clin Psychiatry 2015;76(2):e207–e213
10.4088/JCP.13m08934

Reduction of alcohol drinking in young adults

- RCT in an outpatient center with 140 patients aged 18-25, who reported ≥ 4 HDD in the prior 4 weeks.
- Intervention: naltrexone 25 mg daily plus 25 mg targeted (at most daily) in anticipation of drinking (n = 61) or daily/targeted placebo (n = 67).
- **Primary outcome**: Percent HDD (21.60 vs 22.90) and percent days abstinent (56.60 vs 62.50) did not differ by group.
- **Secondary outcome**: Naltrexone reduced the number of DDD (4.90 vs 5.90; P = .009) and % of drinking days with estimated BAC ≥ 0.08 g/dL (35.4 vs 45.7; P = .042).

ORIGINAL CONTRIBUTION

Topiramate for Treating Alcohol Dependence

A Randomized Controlled Trial

Bankole A. Johnson, DSc, MD, PhD
Norman Rosenthal, MD
Julie A. Capece, BA
Frank Wiegand, MD
Lian Mao, PhD
Karen Beyers, MS
Amy McKay, PharmD
Nassima Ait-Daoud, MD
Raymond F. Anton, MD
Domenic A. Ciraulo, MD

Context Hypothetically, topiramate can improve drinking outcomes among alcohol-dependent individuals by reducing alcohol's reinforcing effects through facilitation of γ-aminobutyric acid function and inhibition of glutaminergic pathways in the corticomesolimbic system.

Objective To determine if topiramate is a safe and efficacious treatment for alcohol dependence.

Design, Setting, and Participants Double-blind, randomized, placebo-controlled, 14-week trial of 371 men and women aged 18 to 65 years diagnosed with alcohol dependence, conducted between January 27, 2004, and August 4, 2006, at 17 US sites.

Interventions Up to 300 mg/d of topiramate (n=183) or placebo (n=188), along with a weekly compliance enhancement intervention.

JAMA, October 10, 2007—Vol 298, No. 14

Topiramate vs placebo at week 14th

Outcome	Study End (Week 14) Topiramate (n = 183)	Placebo (n = 188)	Mean Difference Between Study Groups (95% CI)[b]	*P* Value
Baseline Value for All Dropouts				
Self-reported and laboratory drinking measures[c]				
Heavy drinking days, %	43.81 (40.43)	51.76 (37.43)	8.44 (3.07 to 13.80)	.002
Days abstinent, %	37.56 (39.66)	29.06 (32.35)	−7.68 (−12.49 to −2.87)	.002
Drinks/drinking day	6.53 (5.44)	7.46 (4.93)	0.88 (0.25 to 1.51)	.006
Log GGT ratio[d]	−0.05 (0.09)	−0.02 (0.09)	0.03 (0.01 to 0.04)	<.001
Model Analytic Approach	(n = 113)	(n = 144)		
Self-reported and laboratory drinking measures[e]				
Heavy drinking days, %	20.00 (30.46)	42.44 (36.38)	16.19 (10.79 to 21.60)	<.001
Days abstinent, %	54.94 (40.10)	34.48 (33.89)	−13.39 (−18.65 to −8.14)	<.001
Drinks/drinking day	3.62 (3.66)	6.33 (4.45)	1.77 (1.19 to 2.36)	<.001
Log GGT ratio[d]	−0.09 (0.12)	−0.02 (0.10)	0.05 (0.03 to 0.07)	<.001

JAMA, October 10, 2007—Vol 298, No. 14

Table 4. Adverse Events During Treatment Occurring in 10% or More of Participants[a]

	No. (%) of Participants With Adverse Events		
	Topiramate (n = 183)	Placebo (n = 188)	*P* Value[b]
Paresthesia	93 (50.8)	20 (10.6)	<.001
Headache	44 (24.0)	60 (31.9)	.09
Taste perversion	42 (23.0)	9 (4.8)	<.001
Fatigue	41 (22.4)	33 (17.6)	.24
Anorexia	36 (19.7)	13 (6.9)	<.001
Insomnia	35 (19.1)	30 (16.0)	.42
Difficulty with concentration/attention	27 (14.8)	6 (3.2)	<.001
Nervousness	26 (14.2)	14 (7.5)	.04
Difficulty with memory	23 (12.6)	13 (6.9)	.07
Somnolence	22 (12.0)	19 (10.1)	.56
Diarrhea	22 (12.0)	16 (8.5)	.27
Dizziness	21 (11.5)	10 (5.3)	.03
Pruritus	19 (10.4)	2 (1.1)	<.001

JAMA, October 10, 2007—Vol 298, No. 14

HHS Public Access
Author manuscript
Am J Addict. Author manuscript; available in PMC 2016 March 14.

Published in final edited form as:
Am J Addict. 2016 March ; 25(2): 94–98. doi:10.1111/ajad.12346.

Brief Report: A Randomized, Placebo-Controlled Proof-of-Concept Trial of Adjunctive Topiramate for Alcohol Use Disorders in Bipolar Disorder

Louisa G. Sylvia, PhD[1,2], Alexandra K. Gold, BA[1], Jonathan P. Stange, MA[3], Andrew D. Peckham, MA[4], Thilo Deckersbach, PhD[1,2], Joseph R. Calabrese, MD[5], Roger D. Weiss, MD[2,6], Roy H. Perlis, MD, MSc[1,2], Andrew A. Nierenberg, MD[1,2], and Michael J. Ostacher, MD, MPH, MMSc[7]

- RCT, 12 pacientes y 12 semanas
- Problemas de reclutamiento y de adherencia
- Placebo mejor que topiramato

Research

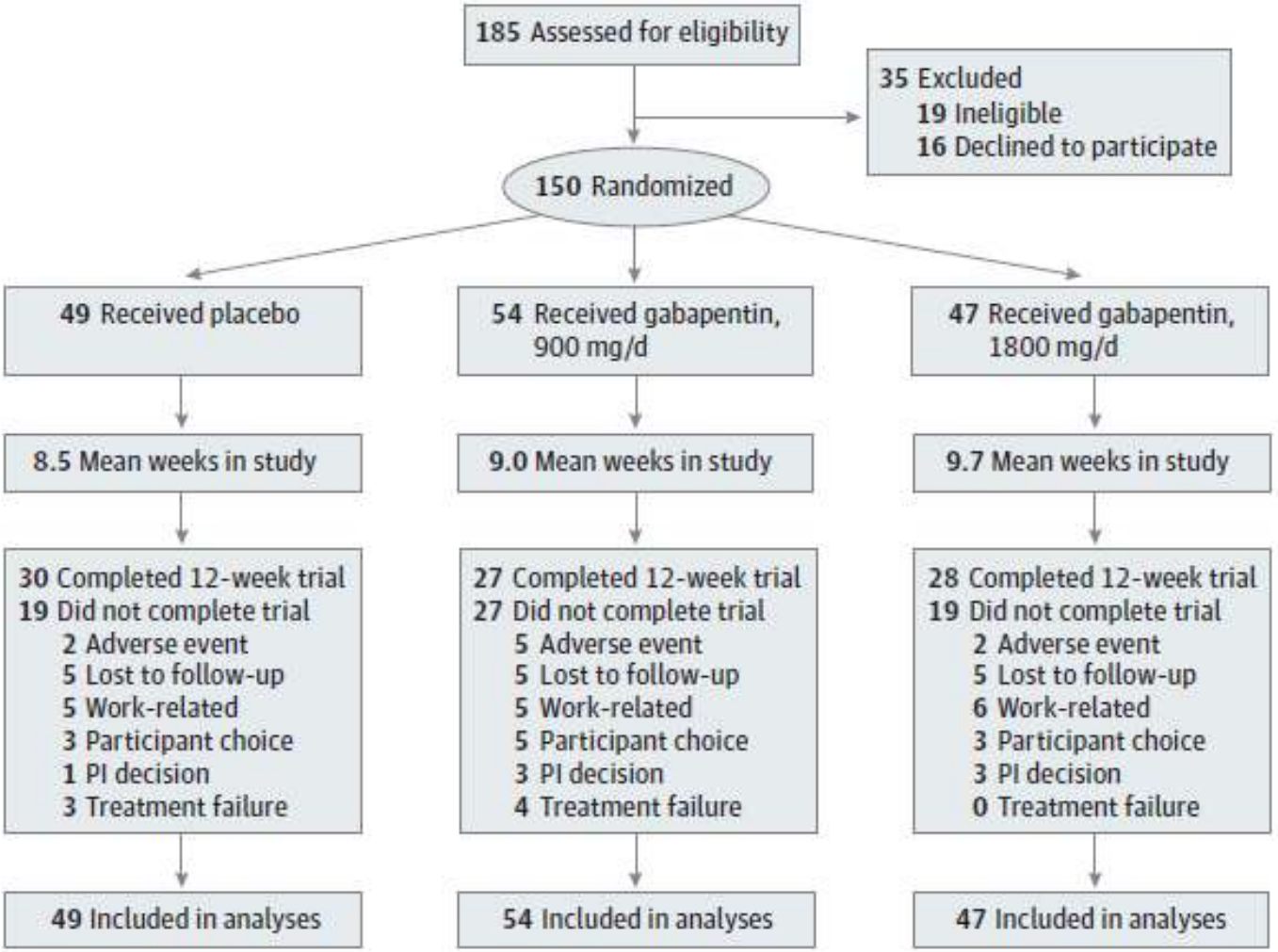
Original Investigation

Gabapentin Treatment for Alcohol Dependence
A Randomized Clinical Trial

Barbara J. Mason, PhD; Susan Quello, BA, BS; Vivian Goodell, MPH; Farhad Shadan, MD; Mark Kyle, MD; Adnan Begovic, MD

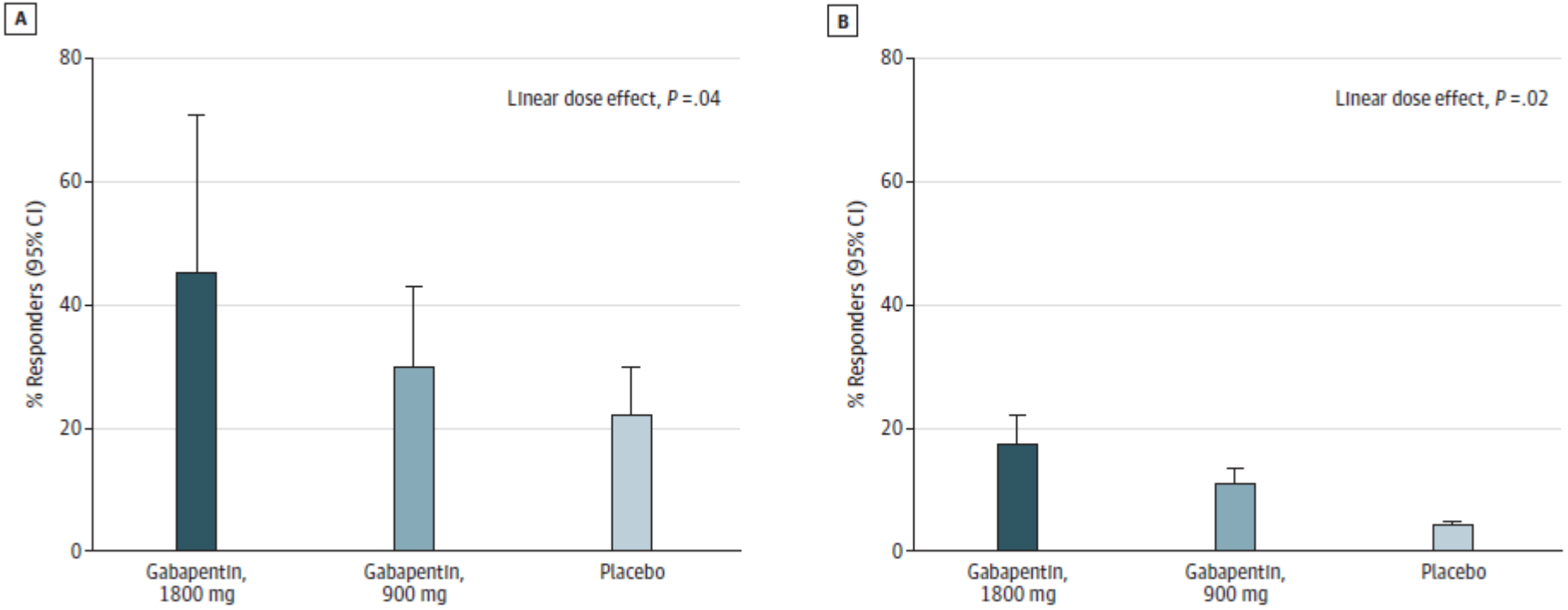
JAMA Intern Med. 2014;174(1):70-77. doi:10.1001/jamainternmed.2013.11950
Published online November 4, 2013.

Figure 1. Flow of Participants Through the Trial



JAMA Intern Med. 2014;174(1):70-77. doi:10.1001/jamainternmed.2013.11950
Published online November 4, 2013.

Figure 2. Gabapentin Effects on Rates of No Heavy Drinking and Complete Abstinence During the 12-Week Study in the Intention-to-Treat Population



A, No heavy drinking; B, complete abstinence. Error bars indicate 95% confidence intervals (N = 150).

JAMA Intern Med. 2014;174(1):70-77. doi:10.1001/jamainternmed.2013.11950
Published online November 4, 2013.

Nalmefeno

Nalmefene. Evolución de los dias de consumo excesivo. Población diana

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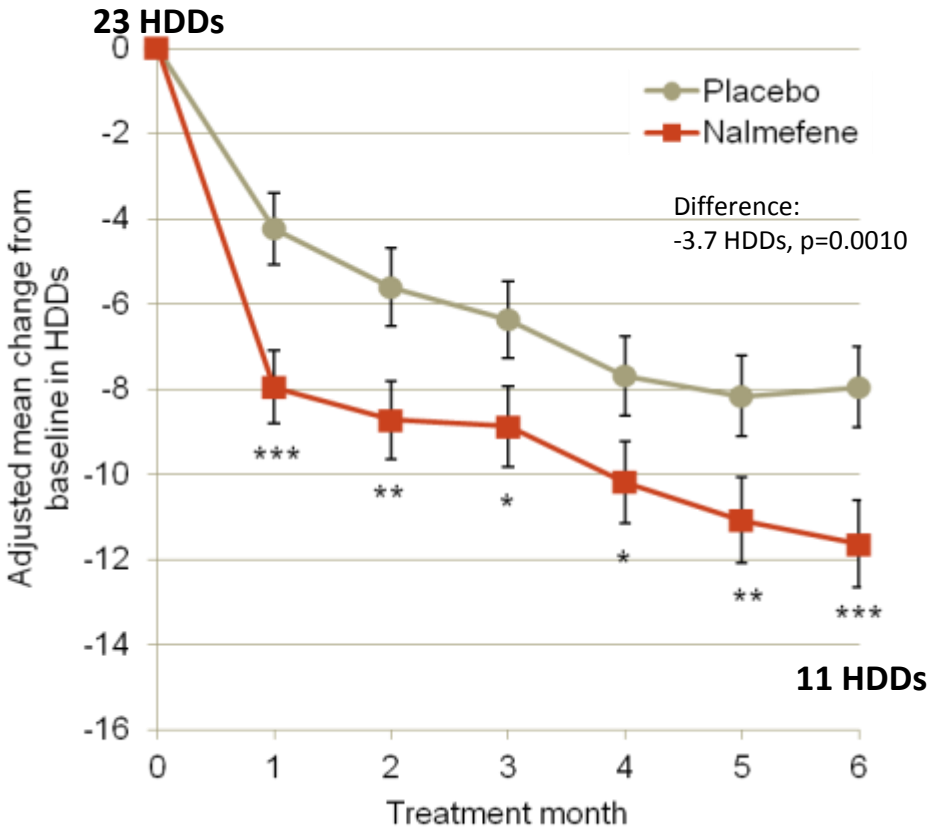
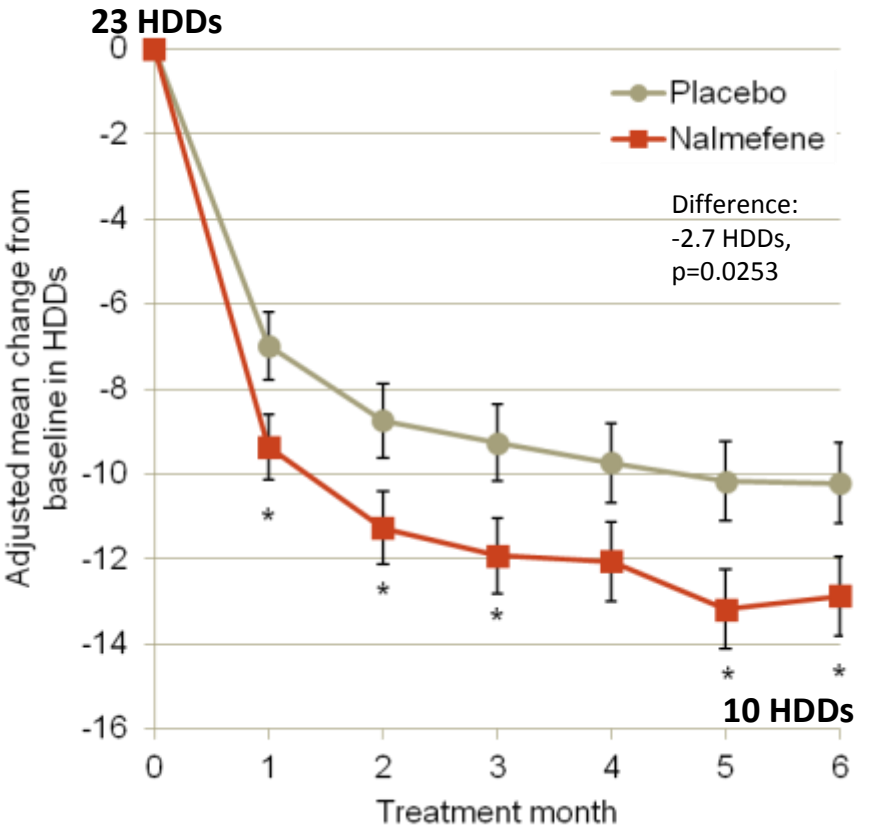


ESENSE 2



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

PLOS | MEDICINE

RESEARCH ARTICLE

Risks and Benefits of Nalmefene in the Treatment of Adult Alcohol Dependence: A Systematic Literature Review and Meta-Analysis of Published and Unpublished Double-Blind Randomized Controlled Trials

Clément Palpacuer[1], Bruno Laviolle[1,2], Rémy Boussageon[3], Jean Michel Reymann[1,2], Eric Bellissant[1,2], Florian Naudet[1,2]*

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Conclusions

The value of nalmefene for treatment of alcohol addiction is not established. At best, nalmefene has limited efficacy in reducing alcohol consumption.

Accepted Manuscript

Lipophilic nalmefene prodrugs to achieve a one-month sustained release

Tim Gaekens, Michel Guillaume, Herman Borghys, Loeckie L. De Zwart, Ronald de Vries, Roger C.A. Embrechts, An Vermeulen, Anton A.H.P. Megens, Josée E. Leysen, Piet Herdewijn, Pieter P. Annaert, John R. Atack

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DOI: doi: 10.1016/j.jconrel.2016.04.029
Reference: COREL 8232

To appear in: *Journal of Controlled Release*

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J Psychopharmacol. 2016 Apr;30(4):402-9. doi: 10.1177/0269881116629126. Epub 2016 Feb 9.

Sodium oxybate plus nalmefene for the treatment of alcohol use disorder: A case series.

Caputo F[1], Maremmani AG[2], Addolorato G[3], Domenicali M[4], Zoli G[5], D'Amore A[6], Maremmani I[2], Bernardi M[4].

Author information

- Serie de casos (7) que no responden a Oxibato sódico
- Elevada comorbilidad
- Al incorporar nalmefene, se produce abstinencia o reducción/supresión de HDD
- Nalmefene reduce el craving por oxibato

A modo de resumen sobre los tratamientos farmacológicos

- El principal componente del tratamiento es el manejo clínico o abordaje psicosocial
- La medicación incrementa de forma significativa y modesta los resultados terapéuticos
- No existe evidencia que demuestre la superioridad incontestable de un fármaco sobre otros
- La comparación entre fármacos es compleja puesto que se dirigen a objetivos distintos y mediante mecanismos de acción distintos
- Los tratamientos farmacológicos deben ser discutidos con el paciente, usando modelos de toma de decisiones compartida.

Generalitat de Catalunya
Agència de Salut Pública de Catalunya

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PROGRAMA:

Actualització en diagnòstic, tractament farmacològic i psicològic de l'alcoholisme

25 maig de 2016
Horari: de 09:00 a 14:00 h
Lloc: Agència Salut Pública

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