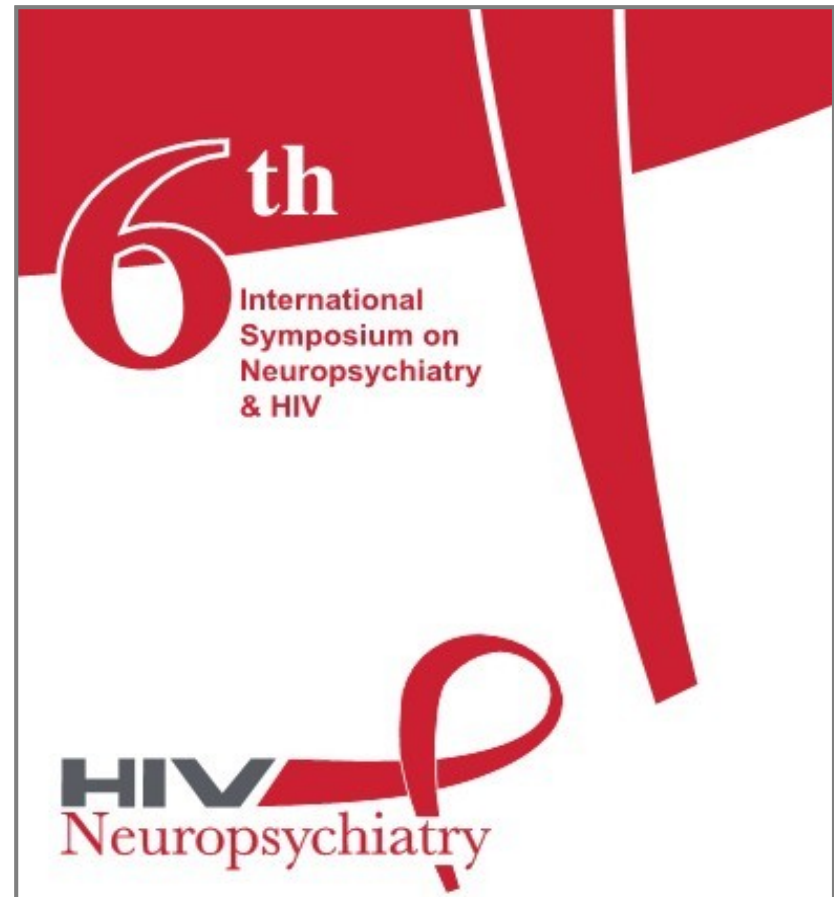


**Alcohol Use:
Impact on HAND and
Other Health Issues in
HIV-Infected Patients,
Screening and
Management**



Antoni Gual
Alcohol Unit
Psychiatry Department
Neurosciences Institute
Hospital Clínic de Barcelona. IDIBAPS.
Barcelona, May 9th, 2013

Conflicts of interest

Since 2009, Antoni Gual has received honoraria and travel grants from Lundbeck, Janssen, Servier, D&A Pharma, Lilly and Abbvie, and has received research grants from Bayer, Lundbeck and D&A Pharma.

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Prevalence of High-Risk Drinking By Gender, Age, and Region, 2000

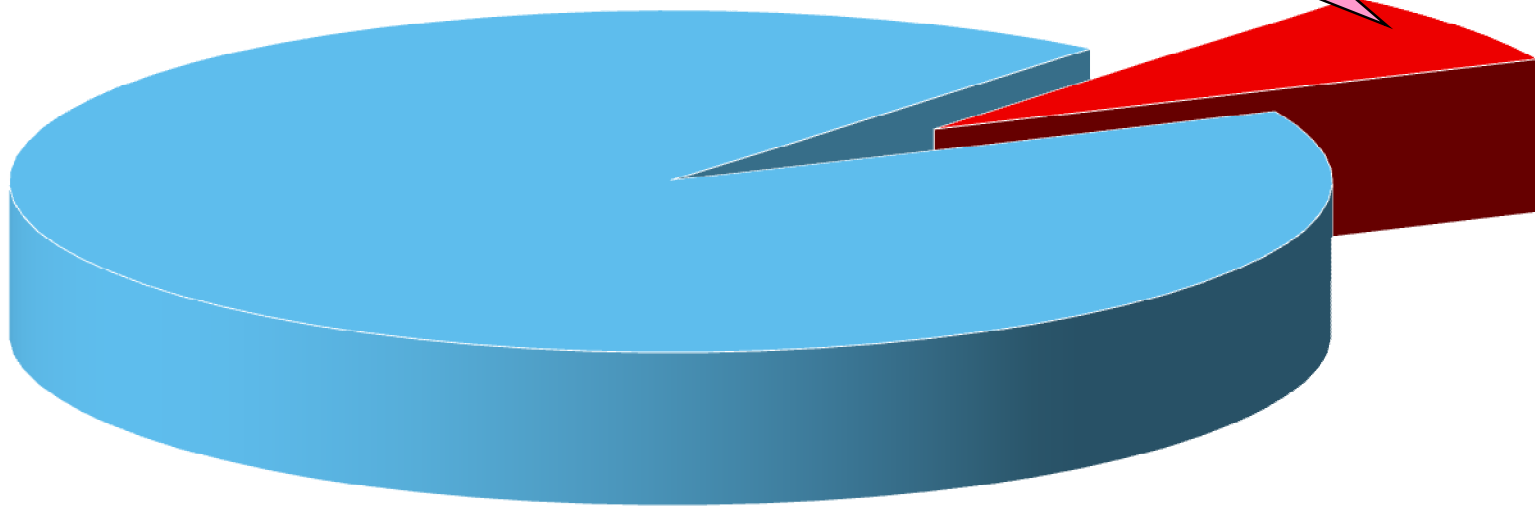
Region	<u>15-29 Years</u>		<u>30-44 Years</u>		<u>45-59 Years</u>	
	Men	Women	Men	Women	Men	Women
Europe and Central Asia	21	11	19	10	21	12
Latin America and the Caribbean	10	7	11	8	11	7
Sub-Saharan Africa	10	3	14	5	13	5
East Asia and the Pacific	6	<1	8	<1	7	<1
South Asia	<1	1	3	<1	<1	<1

Source: *Disease Control Priorities in Developing Countries*, second edition, 2006, Table 47.1

The World Health Organization uses a summary measure of ill-health, called the DALY (Disability Adjusted Life Year). One DALY is a year of premature death, or ill-health, adjusted for the severity of the ill-health.

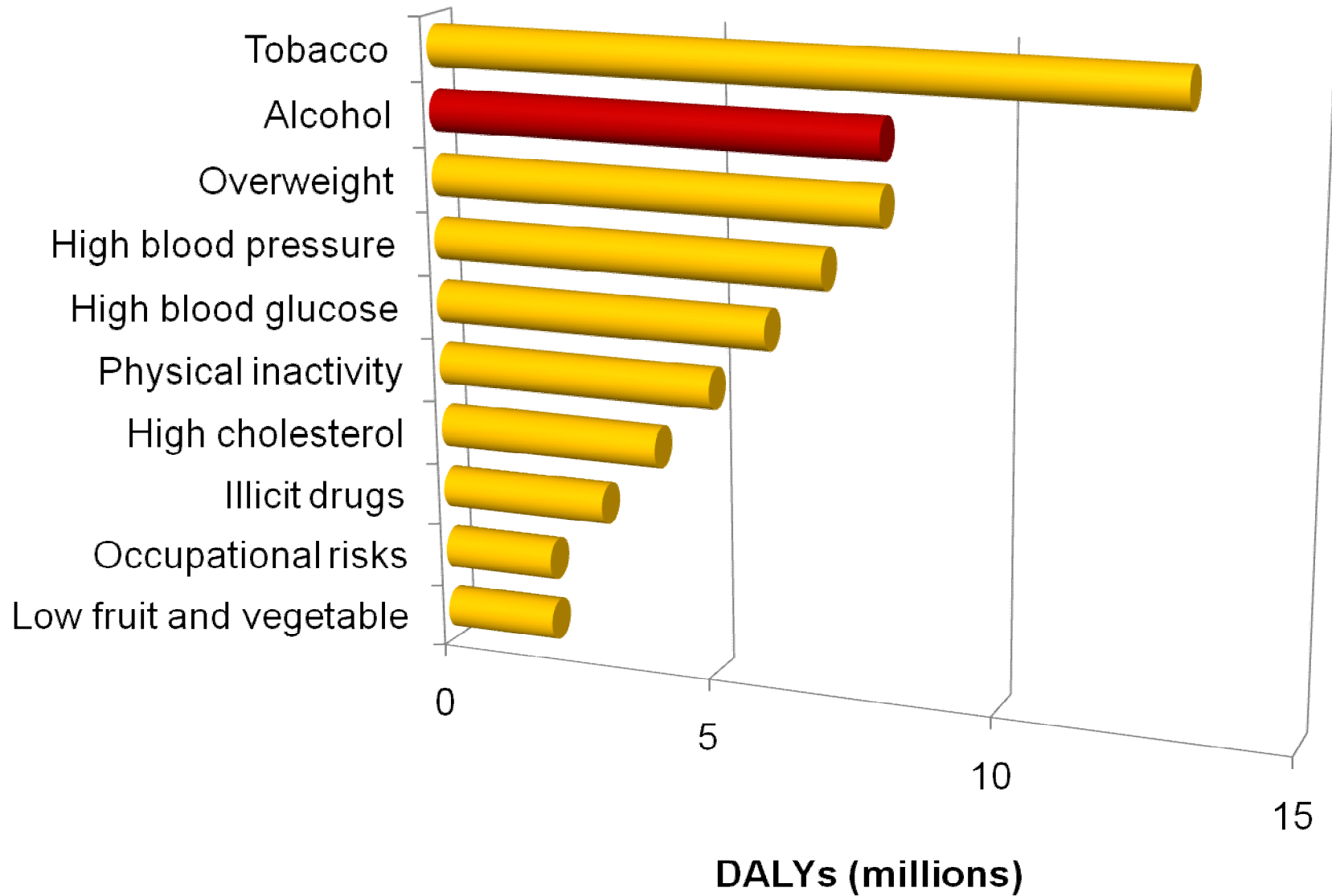
It measures the gap between current health status and what could be achieved.

Alcohol caused DALYs
= 4.5 million (7.4%)



EU Health Gap in 2000 = 61 million DALYs

Top 10 risk factors for DALYs (high income countries)



Peter Anderson, 2009

Alcohol & HIV

- Prevalence
- Alcohol increases the risk of infection
- Alcohol facilitates the progression of HIV
- Alcohol decreases ART compliance
- Alcohol decreases the proper use of health care resources

Prevalence

- Alcohol use disorders (AUDs) and HIV are both widespread, and result in intertwined global epidemics
- HIV/AIDS results in more than 2 million deaths annually (WHO, 2009).
- Similarly, there are 1.8 million alcohol-related deaths annually world-wide (WHO, 2007).
- AUDs alone cause significant impairment, and also exacerbate other co-morbid conditions like HIV due to:
 - Decreased adherence with medications (Hendershot et al., 2009),
 - Decreased health care utilization (Zarkin et al., 2004)
 - Increased HIV risk behaviors (Fisher et al., 2007; Justus et al., 2000).
- AUDs and HIV act synergistically at the individual and societal level to negatively impact health

Alcohol use among patients with HIV infection

Maurizio Bonacini*

* Department of Transplantation, California Pacific Medical Center, San Francisco CA, USA.

	Men n (371)	Women n (60)	p value
0-10 g/d	119 (32%)	28 (47%)	0.04
0-29 g/d	231 (62%)	42 (70%)	NS
30-49	57 (15%)	6 (10%)	NS
≥ 50 g/d	83 (22%)	12 (2 TG, 20%)	NS

Alcohol increases the risk of infection



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AIDS. Author manuscript; available in PMC 2012 January 14.

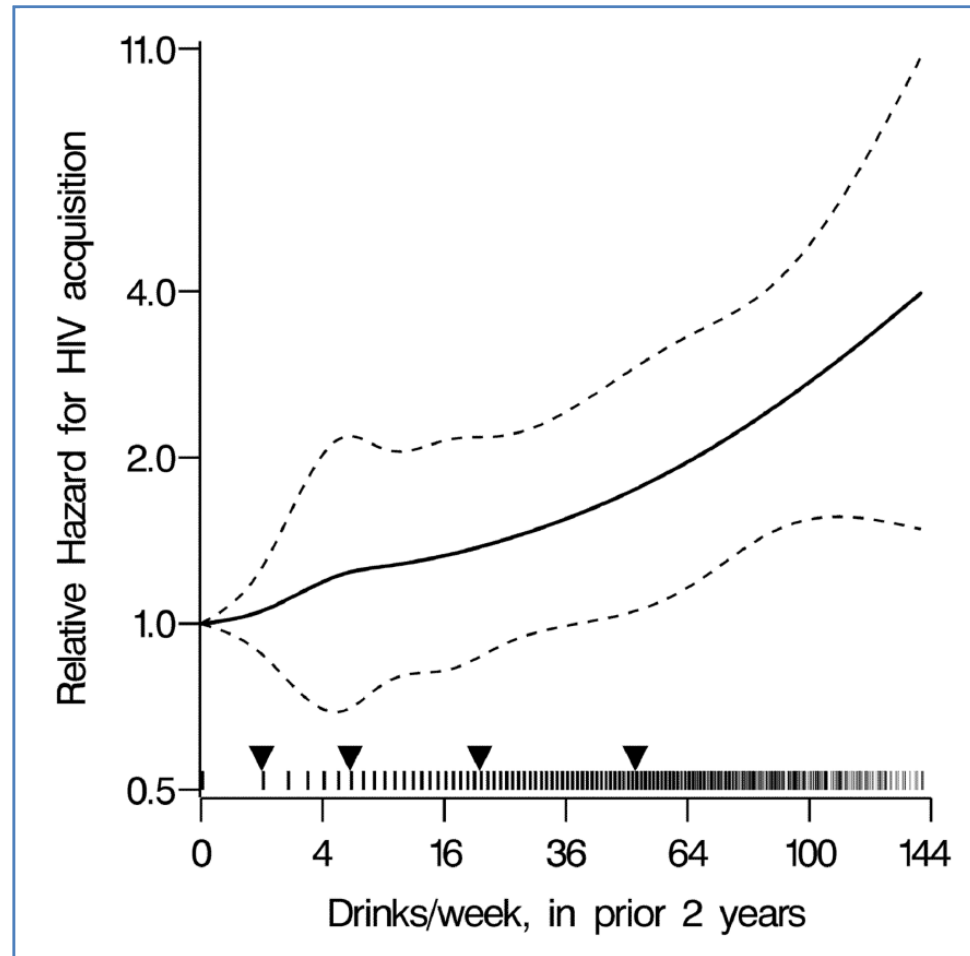
Published in final edited form as:

AIDS. 2011 January 14; 25(2): 221–228. doi:10.1097/QAD.0b013e328340fee2.

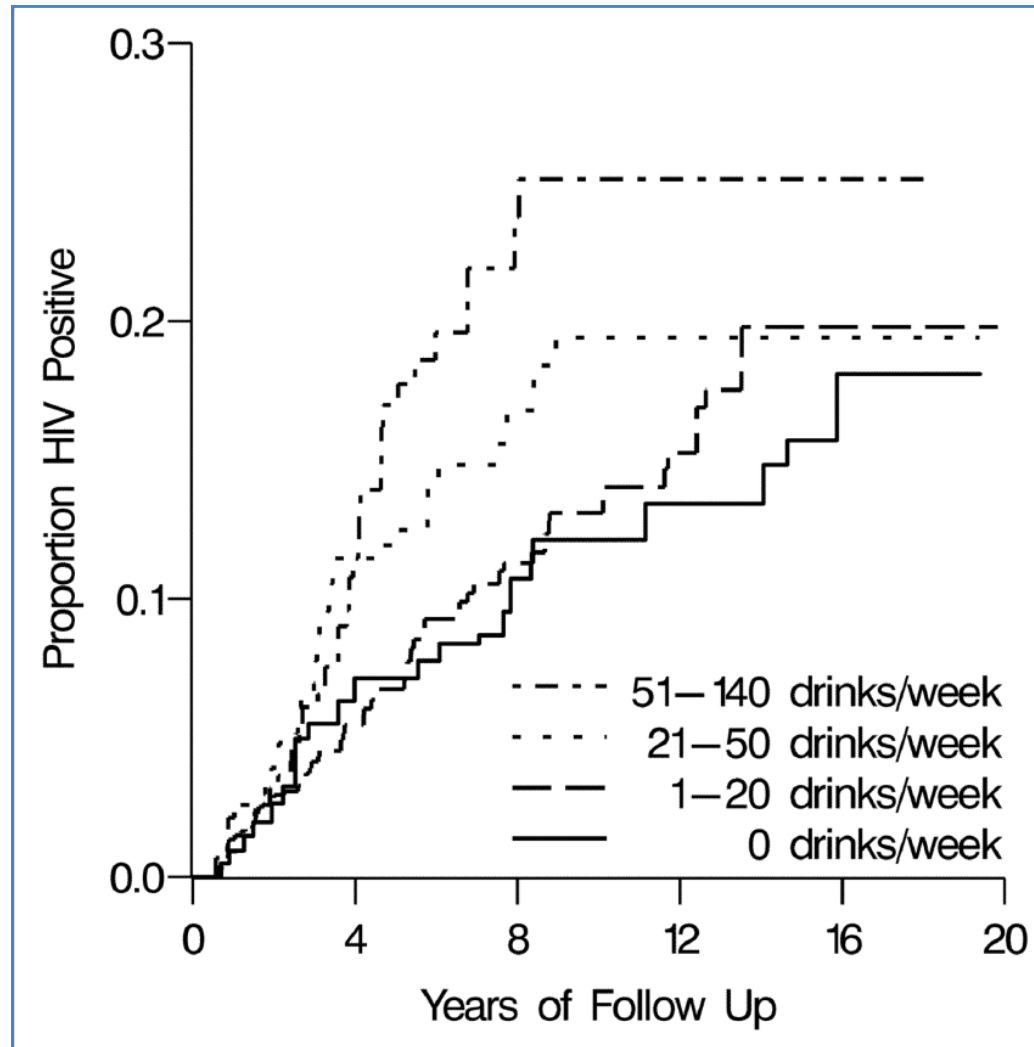
A prospective study of alcohol consumption and HIV acquisition among injection drug users

Chanelle J. HOWE^a, Stephen R. COLE^a, David G. OSTROW^b, Shruti H. MEHTA^c, and Gregory D. KIRK^{c,d}

Weighted relative hazard of HIV acquisition by alcohol consumption (ALIVE study, n=1525)



Proportion HIV positive by alcohol consumption (ALIVE study, n=1525)



Alcohol facilitates the progression of
HIV

ALCOHOL AND HIV INFECTION

STEVE NELSON, M.D., and (*by invitation*) GREGORY J. BAGBY Ph.D.

NEW ORLEANS, LOUISIANA

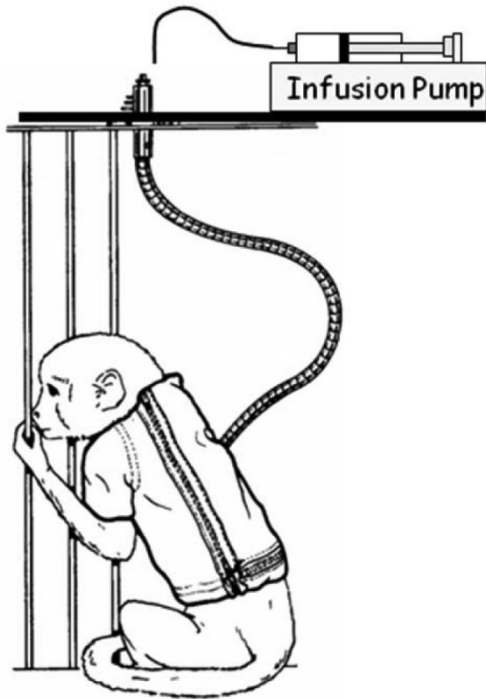


FIG. 1. Model for the controlled delivery of alcohol or sucrose in the home cage of conscious rhesus monkeys.

The median time of survival after SIV infection was (P 0.05):

- 374 days in ethanol-treated animals
- 900 days in the sucrose control group



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J Acquir Immune Defic Syndr. Author manuscript; available in PMC 2008 February 19.

Published in final edited form as:

J Acquir Immune Defic Syndr. 2007 October 1; 46(2): 194–199.

Alcohol Consumption and HIV Disease Progression

Jeffrey H. Samet, MD, MA, MPH^{*,†}, Debbie M. Cheng, ScD^{*,‡}, Howard Libman, MD[§], David P. Nunes, MD^{||}, Julie K. Alperen, DrPh^{*}, and Richard Saitz, MD, MPH^{*,¶}

**Clinical Addiction Research and Education Unit, Section of General Internal Medicine, Department of Medicine, Boston Medical Center, Boston University School of Medicine, Boston, MA*

†Department of Social and Behavioral Sciences, Boston University School of Public Health, Boston, MA

‡Department of Biostatistics, Boston University School of Public Health, Boston, MA

§Divisions of General Medicine and Primary Care and Infectious Diseases, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA

||Section of Gastroenterology, Department of Medicine, Boston Medical Center, Boston University School of Medicine, Boston, MA

¶Department of Epidemiology and Youth Alcohol Prevention Center, Boston University School of Public Health, Boston, MA.

Alcohol facilitates the progression of HIV

		CD4 Cell Count ^{*†}	
ART Status	Alcohol Consumption Status	Adjusted Mean Difference (vs. Abstinent) [*] (SE)	<i>P</i>
On ART [‡]	Abstinent	—	—
	Moderate	11.5 (13.8)	0.40
	Heavy	-1.2 (11.0)	0.92
Not on ART	Abstinent	—	—
	Moderate	-25.8 (17.7)	0.15
	Heavy	-48.6 (21.9)	0.03

Alcohol facilitates the progression of HIV

AIDS RESEARCH AND HUMAN RETROVIRUSES
Volume 26, Number 5, 2010
© Mary Ann Liebert, Inc.
DOI: 10.1089/aid.2009.0211

CLINICAL TRIALS/CLINICAL STUDIES

Alcohol Use Accelerates HIV Disease Progression

Marianna K. Baum,¹ Carlin Rafie,¹ Shenghan Lai,² Sabrina Sales,¹ John Bryan Page,³ and Adriana Campa¹

231 HIV+ adults followed up prospectively during 30
months

Alcohol facilitates the progression of HIV

TABLE 2. ALCOHOL USE AND RISK OF DECLINE OF CD4⁺ TO ≤ 200 CELLS/ μ l COMPARED TO ALCOHOL ABSTENTION

<i>Variable^a</i>	<i>HR^b</i>	<i>95% CI HR</i>	<i>p Value</i>
Moderate alcohol use (<1 drink/day)	0.795	0.332–1.904	0.607
Frequent alcohol use (≥ 2 drinks/day)	2.907	1.233–6.855	0.015
Alcohol and crack cocaine use	3.575	1.240–10.307	0.018

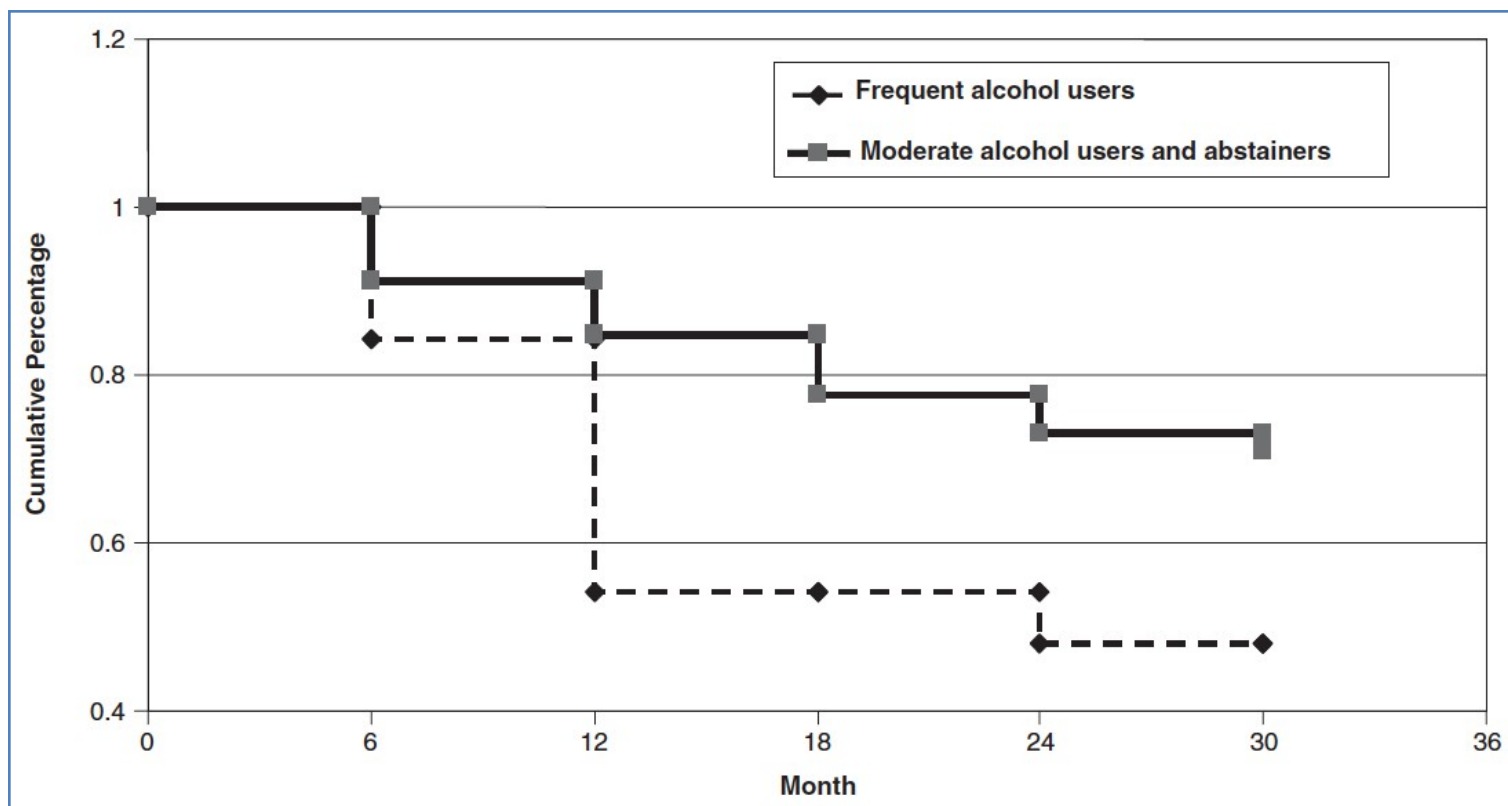
^aAll Cox regression models were controlled for ART over time, baseline HIV viral load and CD4 cell count, years since diagnosis of HIV, age, and gender.

^bHazard ratio.

231 HIV+ adults followed up prospectively during 30 months

Alcohol facilitates the progression of HIV

Rate of decline of CD4p cell count to $200 \text{ cells}/\mu\text{l}$



231 HIV+ adults followed up prospectively during 30 months

Alcohol facilitates the progression of HIV

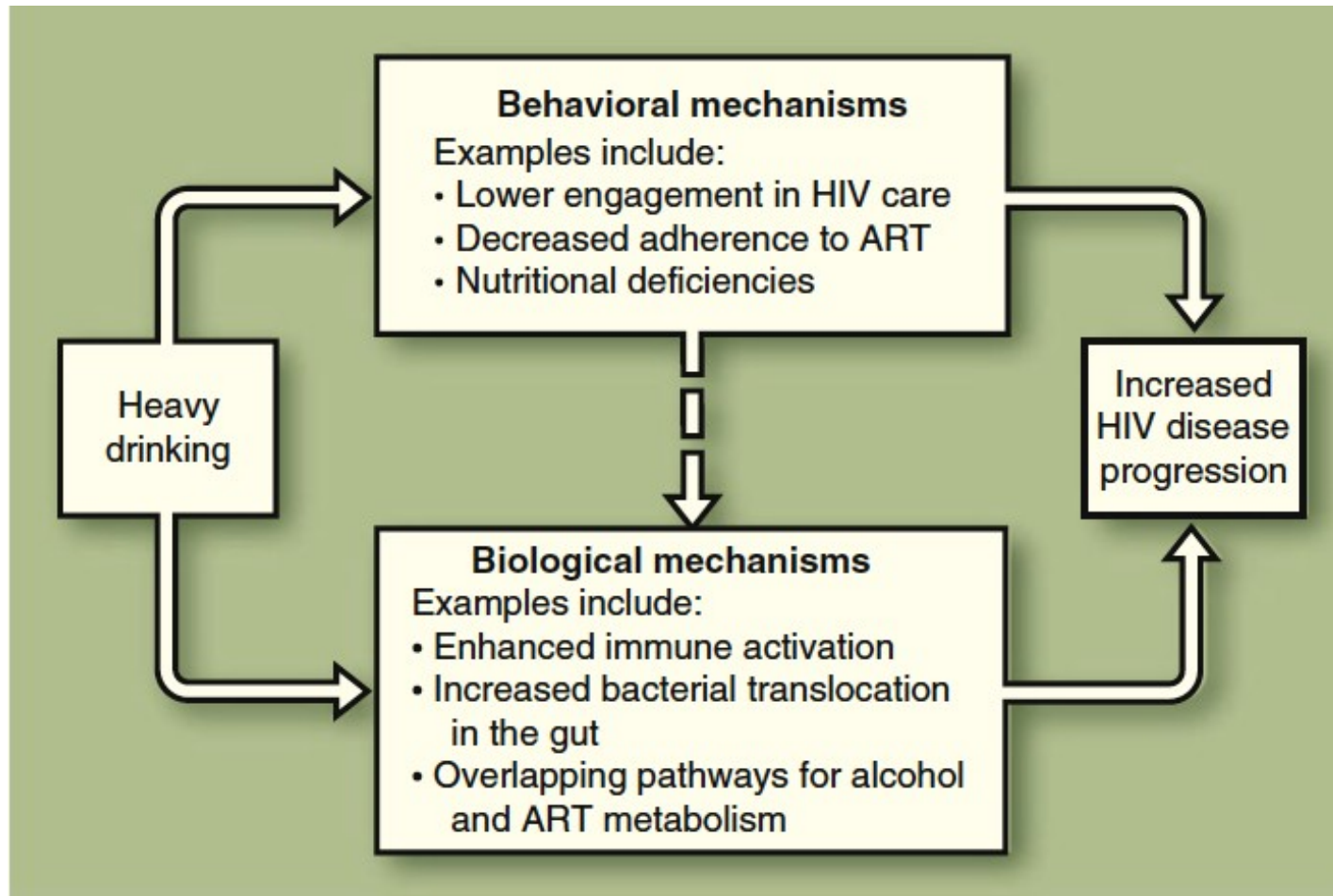
Curr HIV/AIDS Rep (2010) 7:226–233

DOI 10.1007/s11904-010-0060-6

Alcohol and HIV Disease Progression: Weighing the Evidence

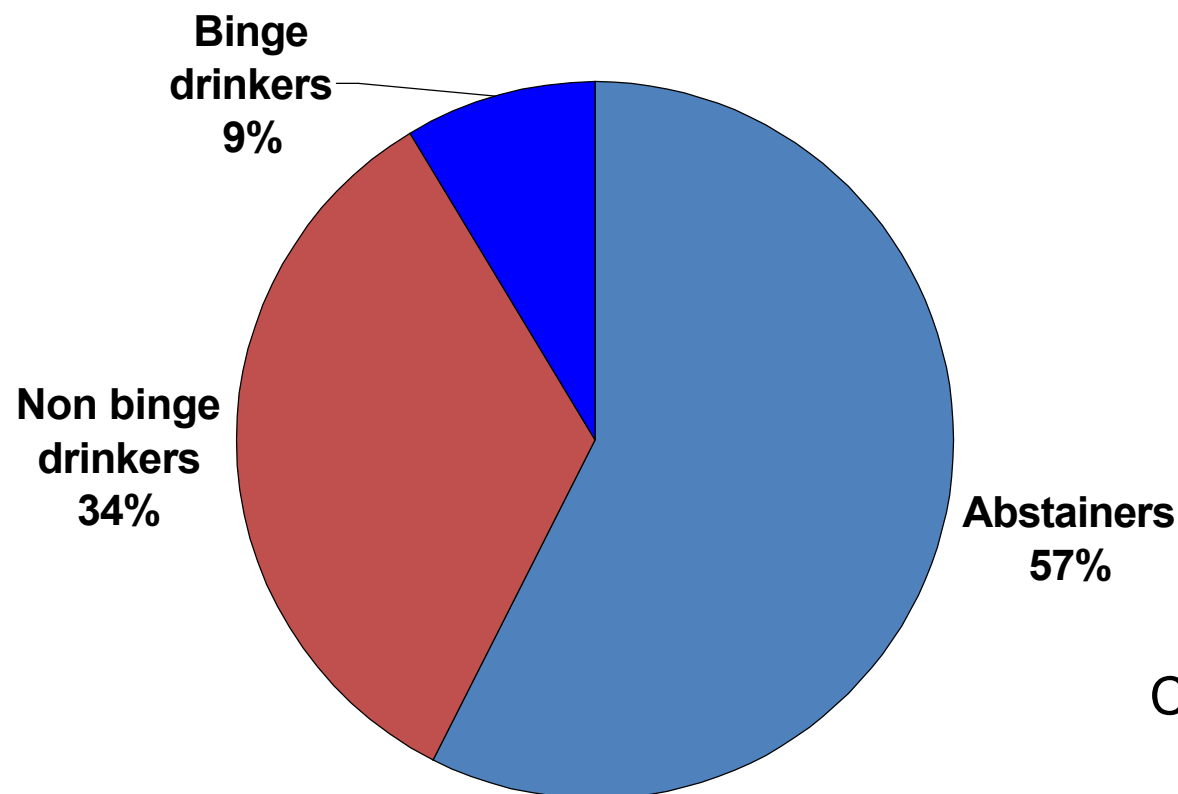
Judith A. Hahn • Jeffrey H. Samet

Alcohol facilitates the progression of HIV



A Temporal and Dose-Response Association Between Alcohol Consumption and Medication Adherence Among Veterans in Care

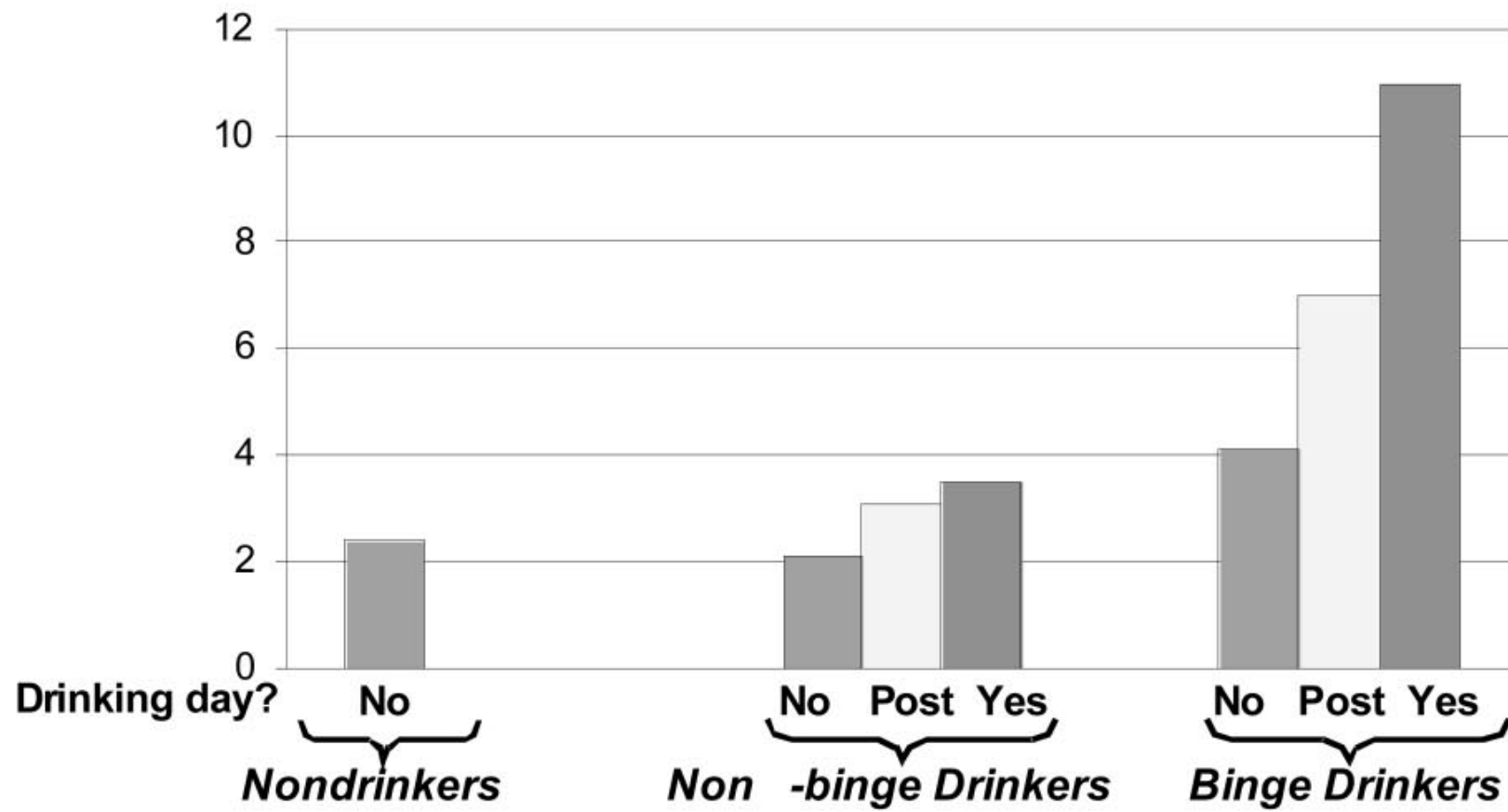
R. Scott Braithwaite, Kathleen A. McGinnis, Joseph Conigliaro, Stephen A. Maisto, Stephen Crystal, Nancy Day, Robert L. Cook, Adam Gordon, Michael W. Bridges, Jason F. S. Seiler, and Amy C. Justice



Contact attempted: 3,519

Surveyed: 2,774

% nonadherent



Alcohol and HIV treatment



NIH Public Access

Author Manuscript

Drug Alcohol Depend. Author manuscript; available in PMC 2011 December 1.

Published in final edited form as:

Drug Alcohol Depend. 2010 December 1; 112(3): 178–193. doi:10.1016/j.drugalcdep.2010.06.014.

A Systematic Review of the Impact of Alcohol Use Disorders on HIV Treatment Outcomes, Adherence to Antiretroviral Therapy and Health Care Utilization *

Marwan M. Azar, Sandra A. Springer, Jaimie P. Meyer, and Frederick L. Altice
Yale University School of Medicine, Department of Medicine, Section of Infectious Diseases,
AIDS Program, 135 College Street, Suite 323, New Haven, CT, USA, 06511

Alcohol and HIV treatment

- AUDs and HIV are prevalent and each independently contribute negatively to poor health outcomes.
- When combined, synergistic negative consequences result in increased morbidity and mortality.
- The literature is complicated further by the added contribution of co-morbid mental illness, which is highly prevalent among both groups.
- The systematic review assessed the impact of AUDs on adherence to ART (N=20), health care utilization (N=11) and HIV treatment outcomes (N=10).
- In general, and with some exceptions, AUDs negatively impact adherence to ART, health care utilization and HIV treatment outcomes.

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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:

- Moderate: 2-3 criteria positive
- Severe: 4 or more criteria positive

Specify Physiological Dependence:

- tolerance and/or withdrawal

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The need for early identification

Past Alcohol Dependence. Treatment History:

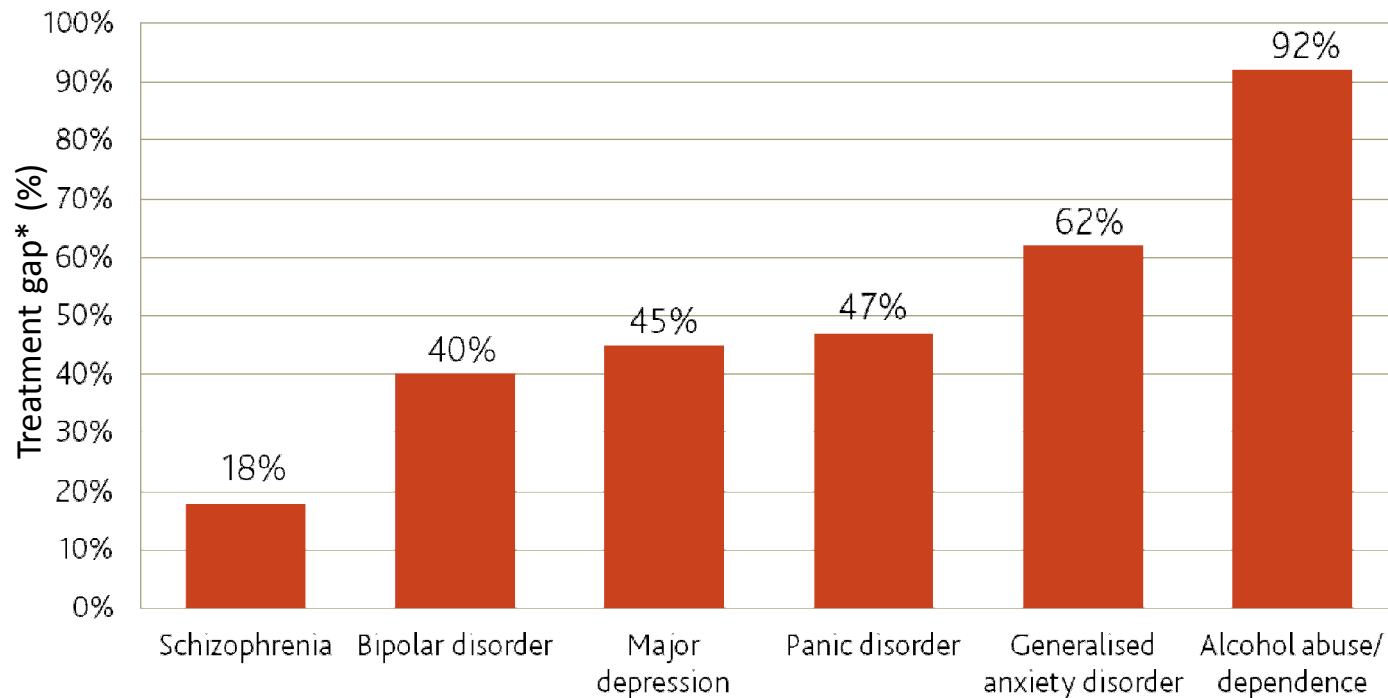
EVER had treatment	25.5%
NEVER had treatment	74.5%

Treatment Examples:

- Inpatient
- Outpatient
- Alcoholics Anonymous

Source: United States 2001-2002, NESARC data

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

The AUDIT

Alcohol Use Disorders Inventory Test

1. How often do you have a drink containing alcohol?
2. How many standard drinks containing alcohol do you have on a typical day when drinking?
3. How often do you have six or more drinks on one occasion?
4. During the past year, how often have you found that you were not able to stop drinking once you had started?
5. During the past year, how often have you failed to do what was normally expected of you because of drinking?
6. During the past year, how often have you needed a drink in the morning to get yourself going after a heavy drinking session?
7. During the past year, how often have you had a feeling of guilt or remorse after drinking?
8. During the past year, have you been unable to remember what happened the night before because you had been drinking?

0) Never **1) Less than monthly** **2) Monthly** **3) Weekly** **4) Daily or almost daily**

9. Have you or someone else been injured as a result of your drinking?
10. Has a relative or friend, doctor or other health worker been concerned about your drinking or suggested you cut down?

0) No **2) Yes, but not in the past year** **4) Yes, during the past year**

The AUDIT

Alcohol Use Disorders Inventory Test

1. How often do you have a drink containing alcohol?
2. How many standard drinks containing alcohol do you have on a typical day when drinking?
3. How often do you have six or more drinks on one occasion?
4. During the past year, how often have you found that you were not able to stop drinking once you had started?
5. During the past year, how often have you failed to do what was normally expected of you because of drinking?

6. Cut off points:

7.

8. Harmful or Hazardous drinking: 8 or more

Alcohol Dependence: 13 or more in women, and 15 or more in men

9. Have you or someone else been injured as a result of your drinking?
10. Has a relative or friend, doctor or other health worker been concerned about your drinking or suggested you cut down?
0) No 2) Yes, but not in the past year 4) Yes, during the past year

The AUDIT-C

1. How often do you have a drink containing alcohol?
2. How many standard drinks containing alcohol do you have on a typical day when drinking?
3. How often do you have six or more drinks on one occasion

0) Never 1) Less than monthly 2) Monthly
3) Weekly 4) Daily or almost daily

The AUDIT-C

1. How often do you have a drink containing alcohol?
2. How many standard drinks containing alcohol do you have on a typical day when drinking?

Cut off point for Hazardous drinking:

- 4 or more in women
- 5 or more in men

The AUDIT 3

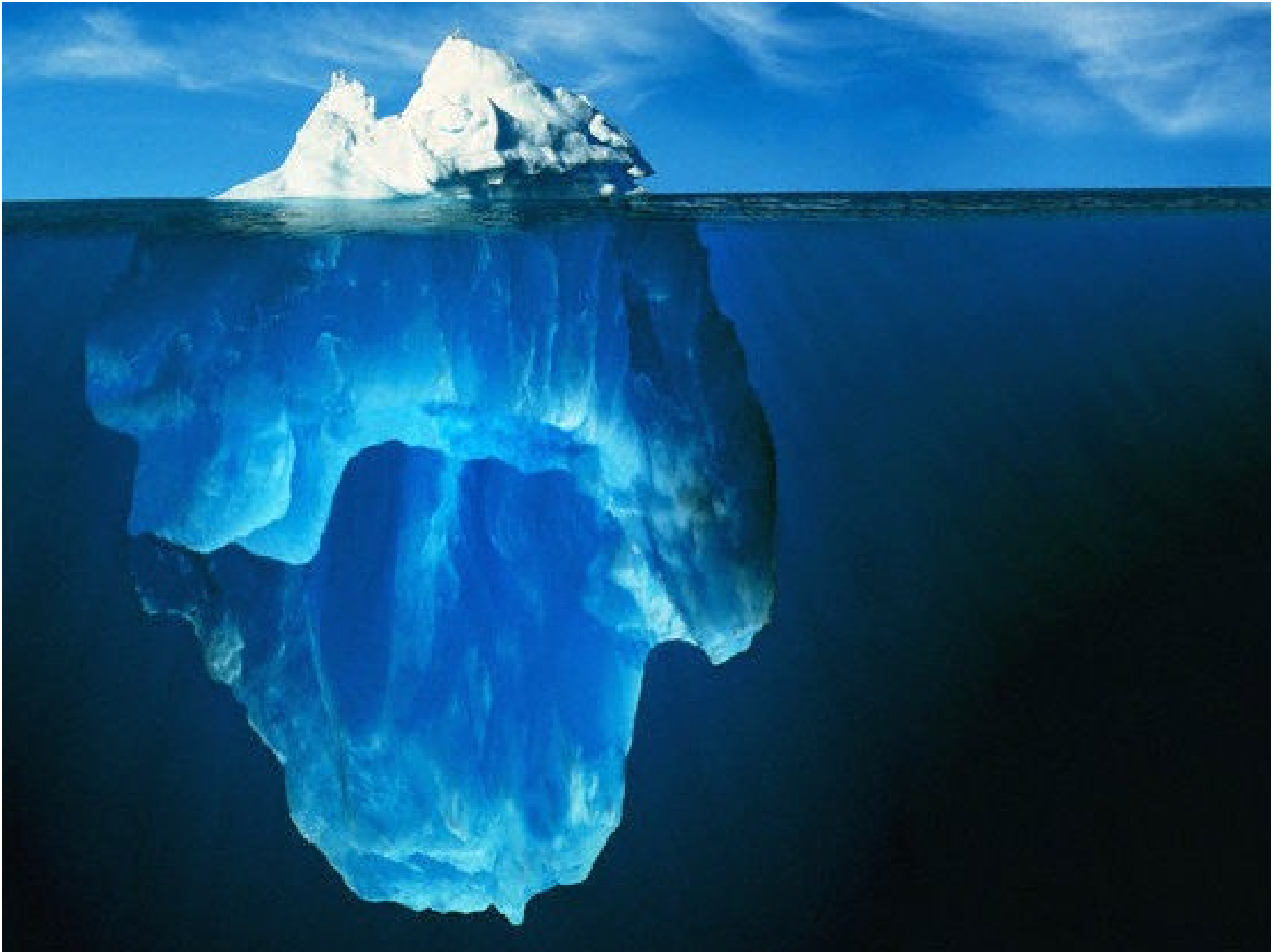
- How often do you have six or more drinks on one occasion?

Cut off point for Hazardous drinking:

If yes in the last 12 months, continue with full AUDIT

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Bio-psycho-social assessment (1)

Biological assessment

- Physical examination
- Blood tests (GGT, VCM, ASAT, ALAT, VHC, etc)
- Focussed Anamnesis (accidents, A&E and hospital admissions, alcohol –related diseases, etc)
- Drinking pattern
 - Use Standard drinks, measure in grams/week
 - Ask quantity & frequency specifically
 - Ask for labour & weekend days separately

Bio-**psycho**-social assessment (2)

Psychological Assessment

- Subjective perception of alcohol consumption (craving, priming, readiness to change, etc)
- Alcohol related distress (feeling guilty, irritability, insomnia, etc.)
- Psychiatric comorbidity (depression, suicidal thoughts, anxiety, etc)

Bio-psycho-**social** assessment (3)

Social Assessment

- Family status
- Work
- Economical situation
- Educational level

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.

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Clinical management phases

- Detoxification
- Rehabilitation

DETOXIFICATION

Alcohol detoxification, or detox, for individuals with alcohol dependence, is the abrupt cessation of alcohol intake coupled with the substitution of alcohol with cross-tolerant drugs that have similar effects in order to prevent alcohol withdrawal (AW).

DETOXIFICATION

Indicated when:

- Signs or symptoms of AW are present
- Patient drinks above 120gr of alcohol daily

Not indicated when:

- Patient is abstinent >72h and no signs of AW are present
- Patient does not agree to an abstinence goal

Clinical Institute Withdrawal Assessment (CIWA)

- Nausea and vomiting
- Tactile disturbances
- Tremor
- Auditory disturbances
- Paroxysmal sweats
- Visual disturbances
- Anxiety
- Headache, fullness in head
- Agitation
- Orientation and clouding of sensorium

BENZODIACEPINES (BZD)

- Long half-life BZD are preferred: Diazepam and chlordiazepoxide are the golden standard
- Loading dose Technique: a standard dose of the BZD is given every 2 hours until light sedation is reached.
- Tapering technique: initial dose of BZD based on history. Then adjust and taper.
- Lorazepam and oxazepam are indicated in patients with impaired liver function
- BZD should only be used short term to prevent risk of addiction

REHABILITATION

The process of treatment and help that leads to cessation of drinking or, rarely, to controlled drinking, with improved health and normal or stable social and economic functioning

A Dictionary of words about alcohol, 1982

Drug rehabilitation is an umbrella term for the processes of medical and/or psychotherapeutic treatment, for dependency on psychoactive substances.

Wikipedia, 2010

REHABILITATION: Group of therapeutic processes designed to help the patient to:

- S** • Accept and understand his disease
- S** **H** • Reduce his desire & craving for alcohol
- H** • Reduce the priming effects of alcohol if he resumes drinking
- S** **H** • Promote abstinence/reduction of alcohol
- S** • Improve coping skills
- H** **S** • Improve quality of life

H - pHarmacological

S - pSychosocial

Pharmacological treatments

Drugs for the treatment of alcohol dependence

- Disulfiram
- Naltrexone
- Acamprosate
- Nalmefene
- Topiramate
- Sodium Oxybate
- Baclofen

Disulfiram

- Not to be used in all patients
- Decreases the number of drinks and the number of drinking days.
- Does not influence abstinence rates
- Under supervision and framed in a psychosocial treatment
- Subcutaneous slow release presentations not efficacious

Disulfiram

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

	ACA	DIS	NTX
Time (days) to first HDD, mean \pm SD (n)	17.6 \pm 22.0 (44)	46.6 \pm 27.5 (33)**	22.0 \pm 22.0 (47)
Time (days) to first drinking, mean \pm SD (N)	11.4 \pm 17.0 (50)	30.4 \pm 27.8 (39)*	16.2 \pm 20.2 (50)
Abstinence days/week, mean \pm SD (N)	4.5 \pm 2.1 (52)	6.3 \pm 0.9 (54 ***)	4.6 \pm 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 ($P = 0.001$).

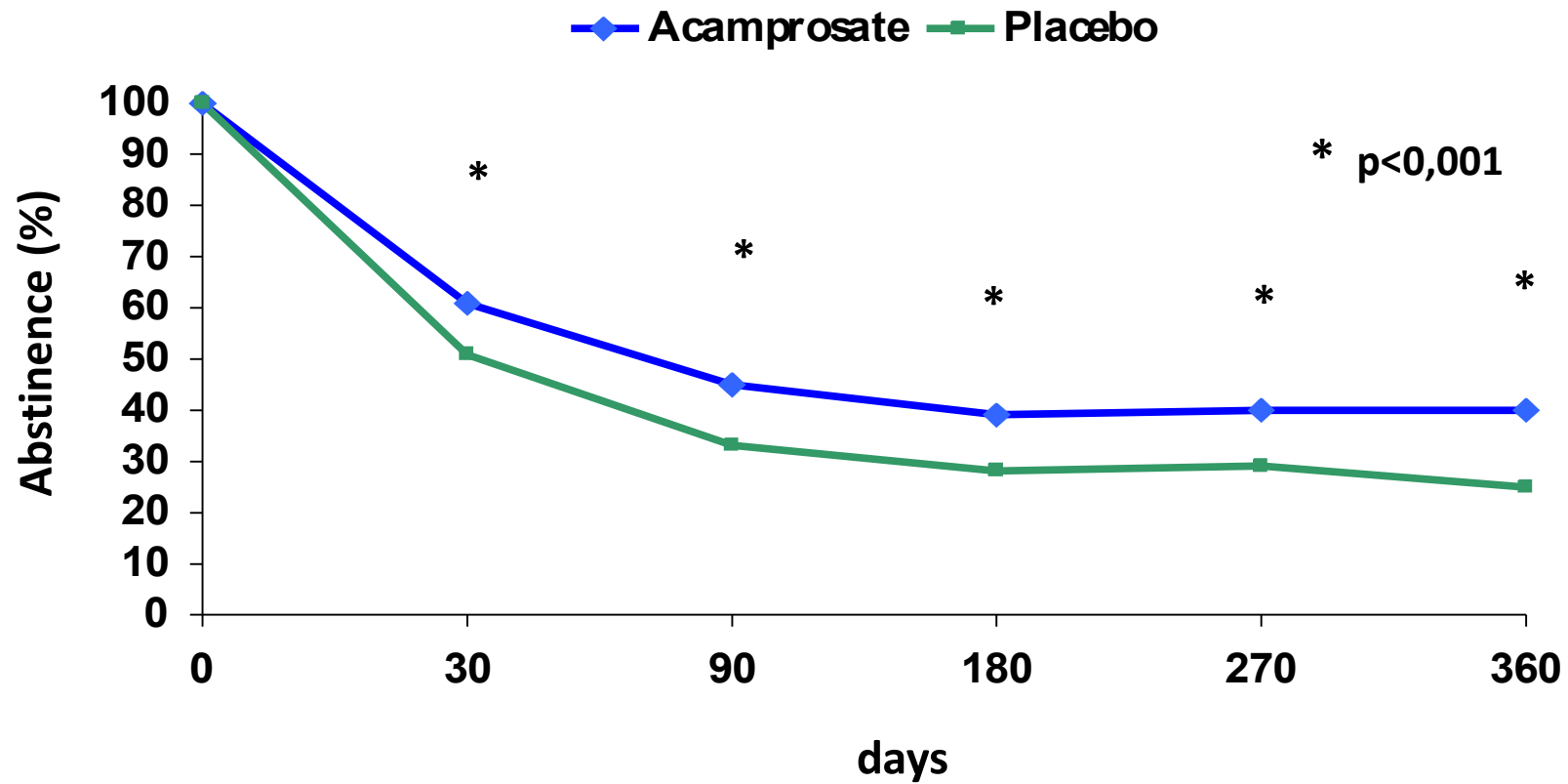
Laaksonen et al, Alcohol Alcohol. 2008 Jan-Feb;43(1):53-61.

ACAMPROSATE

- Increases the cummulated abstinence duration (percentage of abstinent days)
- Less clear data on time to first drink and time to first relapse.
- Difficult compliance because of dosage
- Weak results in the american trial

RESULTS:

Abstinence rate at each visit



Naltrexone

- Reduces relapse rates. No effect on abstinence rates.
- Decreases the rewarding effects of alcohol.
- Increased efficacy when used with CBT
- Long-acting injectable available in some countries
- When compared to acamprosate, better results.

RCTs with naltrexone

Table 2
Randomized, controlled clinical trials — naltrexone vs. placebo

Investigators (Year)	<i>N</i>	Alcoholism severity	Therapy	Relapse	Abstinence	DDD	Craving
Volpicelli, Alterman, Hayashida, and O'Brien (1992)	70	Severe ^a	Intensive multimodal	+	—	?	+
O'Malley et al. (1992)	97	Moderate	Coping skills or supportive	+	—	+	+/-
Volpicelli et al. (1997)	97	Moderate/severe ^a	Relapse prevention	+	—	?	—
Oslin, Liberto, O'Brien, Krois, and Norbeck (1997)	44	Moderate ^b	Supportive	+/-	—	—	—
Anton et al. (1999)	131	Moderate	CBT	+	—	+	+/-
Chick et al. (2000)	175	Moderate	TAU	+/-	—	+/-	+
Kranzler et al. (2000)	124	Moderate	Coping skills	—	—	—	—
Heinala et al. (2001)	121	Moderate	Coping skills or supportive	+	—	?	?
Monti et al. (2001)	128	Moderate	Cue-coping skills	—	?	+	+
Morris, Hopwood, Whelan, Gardiner, and Drummond (2001)	111	Moderate/severe	Coping skills (group)	+	—	+	?
Monterosso et al. (2001)	183	Moderate	Supportive	+	—	—	+
Krystal et al. (2001)	627	Moderate/severe	Twelve-step facilitation	—	?	—	—
Latt, Jurd, Houseman, and Wutzke (2002)	107	Moderate/severe ^a	TAU	+	?	?	—

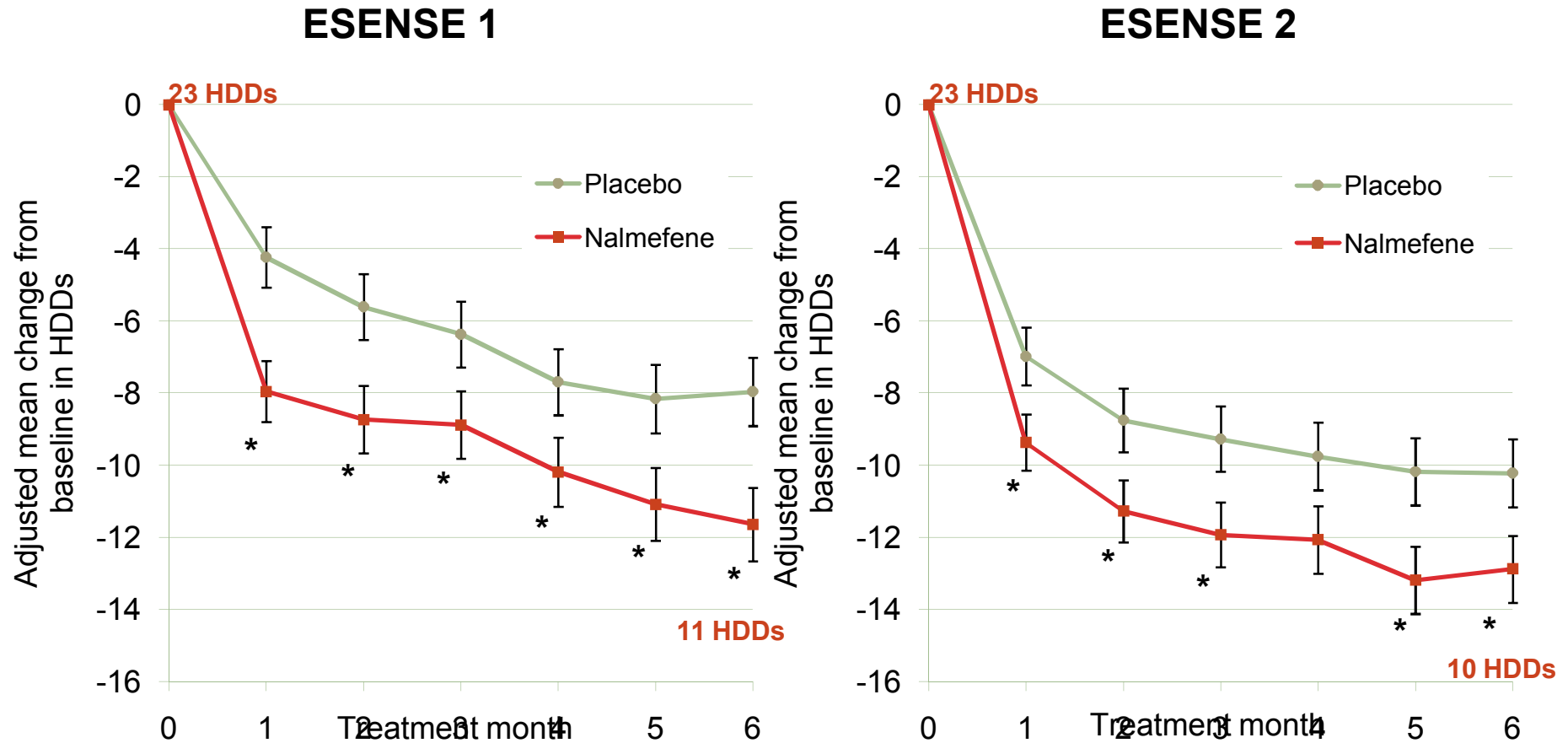
Ait-Daoud et al, 2006

Nalmefene

- Opioid modulator.
- Recently approved by the EMA
- Targeted use ('as needed')
- Focus on reduction
- Used jointly with psychosocial intervention

HDD – change from baseline in the 6-month studies

– patients with at least high DRL at baseline and randomisation



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

Psychosocial treatments

The confrontational model

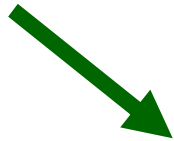
- Review of four decades of treatment outcome research.
- A large body of trials found **no therapeutic effect** relative to control or comparison treatment conditions.
- Several have reported **harmful effects** including increased **drop-out**, elevated and more rapid **relapse**.
- This pattern is consistent across a variety of confrontational techniques tested.
- In sum, there is not and never has been a scientific evidence base for the use of confrontational therapies.

Motivational Interviewing

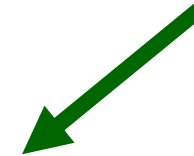
- New golden standard for the psychological approach to addictive behaviours
- Radical change:
 - external confrontation as a technique vs internal confrontation as a goal
 - Patient centered
 - Spirit: autonomy, evocation, empathy
 - Communication style: guiding

Brief Intervention

**Empathic
attitude**



**Promote
self-efficacy**



**Respect
Responsibility**

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

Alcohol Brief Interventions with HIV patients?

Huis in 't Veld *et al. Trials* 2012, **13**:190
<http://www.trialsjournal.com/content/13/1/190>



STUDY PROTOCOL

Open Access

The efficacy of a brief intervention to reduce alcohol misuse in patients with HIV in South Africa: study protocol for a randomized controlled trial

Diana Huis in 't Veld^{1,2,3*}, Linda Skaal^{4,5}, Karl Peltzer^{6,7}, Robert Colebunders^{1,3}, John V Ndimande⁸ and Supa Pengpid⁵

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Conclusions

- Alcohol and HIV are public health problems.
- Alcohol has a negative impact on the progression of HIV and its treatment.
- The prevalence of risky drinking in HIV population is high. Routine screening procedures are needed.
- Brief interventions, psychosocial treatments and various drugs have shown efficacy in the treatment of alcohol use disorders.

Thank you
(moltes gràcies)

Antoni Gual
tgual@clinic.cat

