

SANIT – FORUM INTERNAZIONALE DELLA SALUTE

Alcol e giovani, famiglia e società.

**Le priorità della prevenzione integrata sanitaria e sociale tra cultura del trattamento
e razionalizzazione dei servizi**

15 DICEMBRE 2014 – PALAZZO DEI CONGRESSI - EUR - ROMA

**VERSO UNA RINNOVATA CULTURA
DEL TRATTAMENTO:
DALLA PREVENZIONE ALLA TERAPIA**

dott. FABIO CAPUTO

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Multidisciplinare dell'Uso Inadeguato dell'Alcol
“G. Fontana”, U.O. Semeiotica Medica,
Università degli Studi di Bologna**

Presidente della Sezione Emiliano-Romagnola della SIA

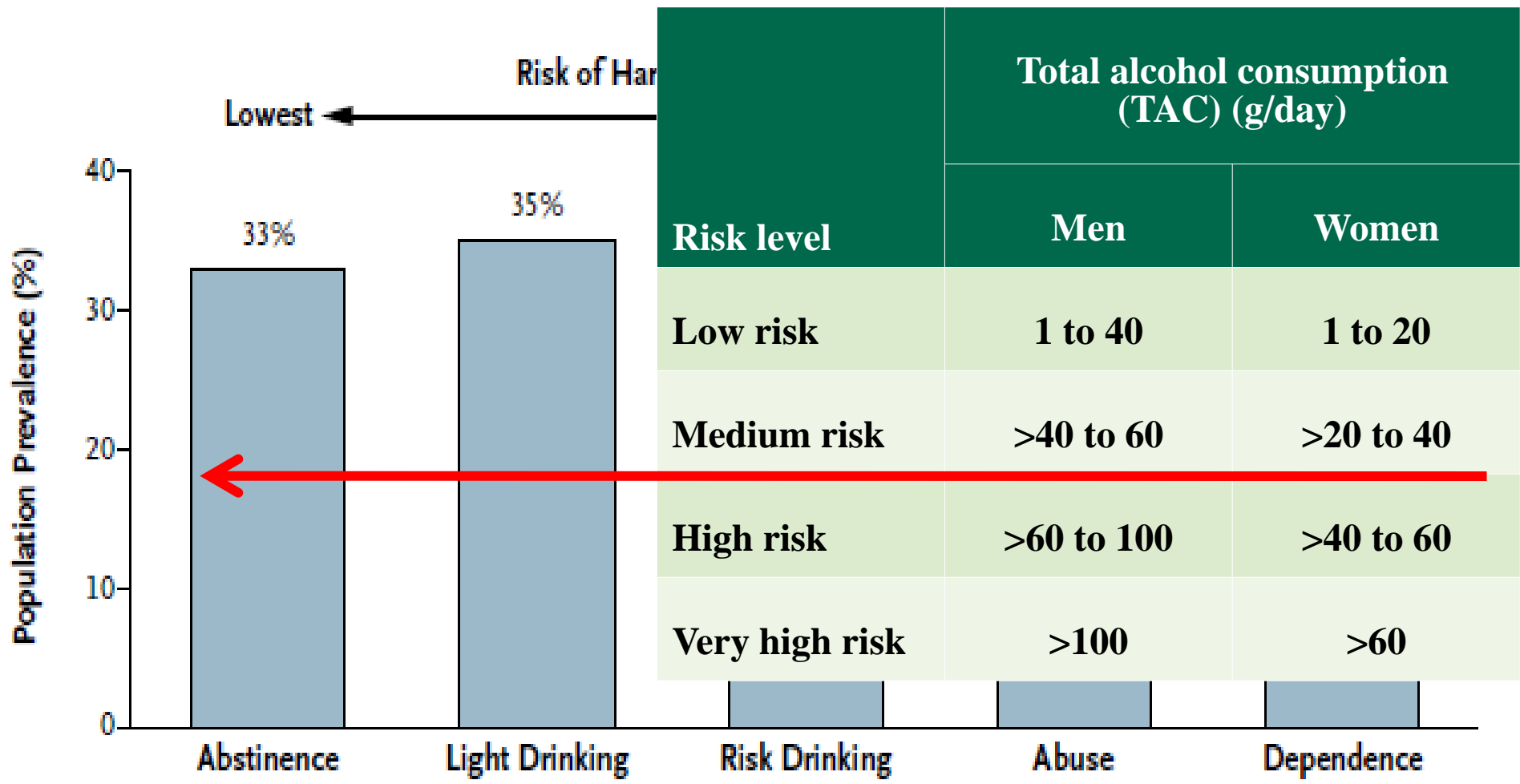


**SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA**
Azienda Unità Sanitaria Locale di Ferrara



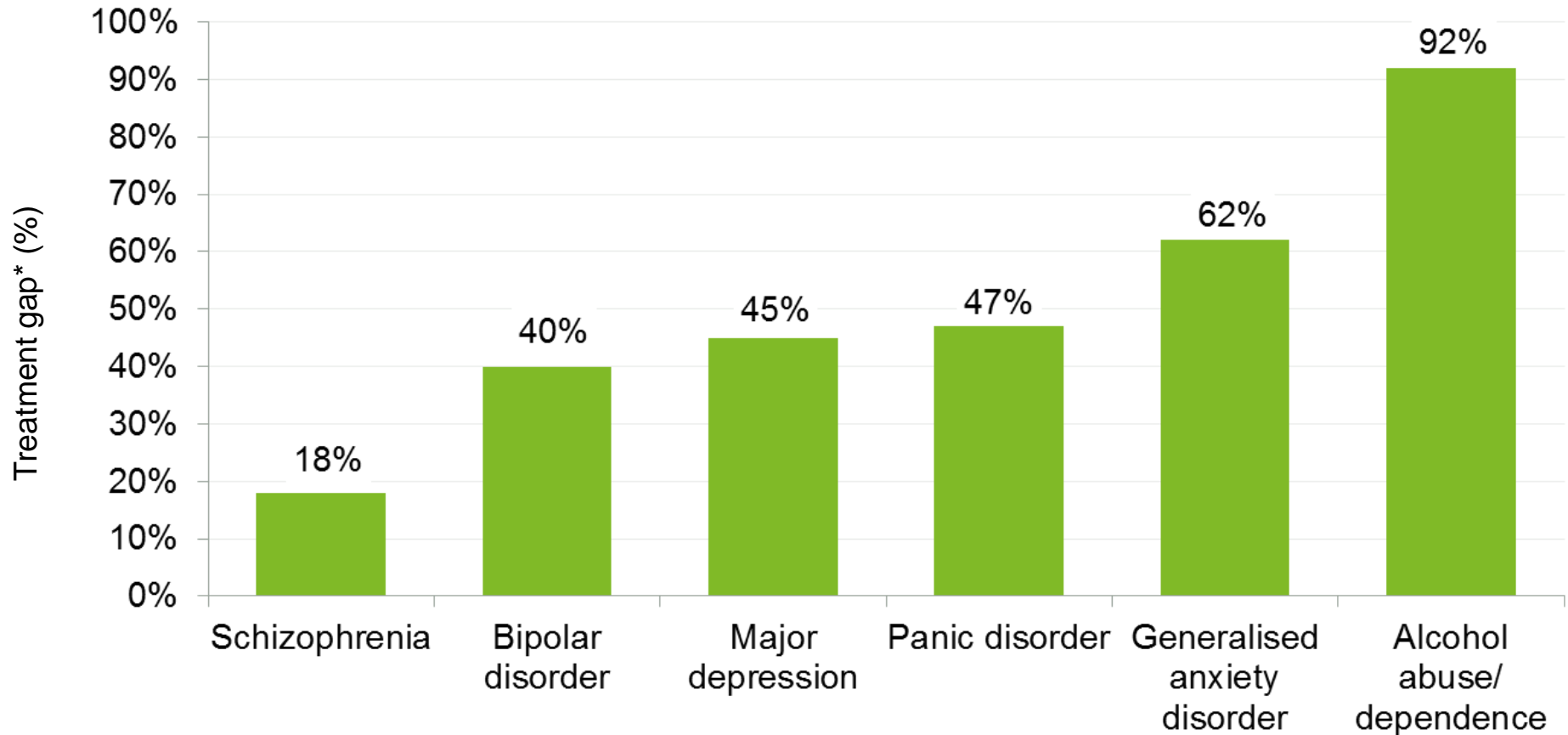
**SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA**
Azienda Ospedaliero - Universitaria di Bologna

Policlinico S. Orsola-Malpighi



Clinical Response	Abstinence	Light Drinking	Risk Drinking	Abuse	Dependence
	Primary prevention Inquiry about prior alcohol use Annual screening	Counsel about lower-risk limits Annual screening	Assessment Brief intervention Motivational interview	Assessment Brief intervention or motivational interview Referral to specialty treatment Pharmacotherapy and medical-management counseling Referral to mutual support groups	

Treatment gap in alcohol dependence



(Kohn et al., Bull World Health Organ 2004)

TRATTAMENTO ALCOLDIPENDENTI

% DI PAZIENTI TRATTATI PER TIPOLOGIA PROGRAMMA ospedalizzazione

Tab.13 - TRATTAMENTI EFFETTUATI DAI SERVIZI O GRUPPI DI LAVORO: percentuale di soggetti trattati per tipologia di programma - ANNO 2012

REGIONE	Medico farmacologico ambulatoriale	Psicoterapeutico		Counseling all'utente o alla famiglia	Inserimento nei gruppi di auto/muto aiuto	Trattamento socio- riabilitativo	Inserimento in comunità di carattere resid. o semiresid.	Ricovero ospedaliero o day hospital per:			Ricovero in casa di cura privata consenzionata per:			Altro
		individuale	di gruppo o familiare					sindrome di dipendenza da alcool	altre patologie alcolcorrelate	altro	sindrome di dipendenza da alcool	altre patologie alcolcorrelate	altro	
PIEMONTE	27,5	9,4	2,7	30,2	5,2	12,4	2,5	0,9	0,3	0,3	1,5	0,3	0,1	7,1
VALLE D'AOSTA	40,9	5,6	2,0	16,7	3,6	10,0	10,9	10,3	0,0	0,0	0,0	0,0	0,0	0,0
LOMBARDIA	22,2	8,6	3,6	23,7	1,3	20,5	2,2	0,8	0,1	0,2	0,2	0,0	0,0	16,7
PROV. AUTON. BOLZANO	18,7	11,4	2,6	21,2	4,8	1,3	5,1	4,0	0,0	0,0	2,8	0,0	0,0	28,1
PROV. AUTON. TRENTO	8,5	0,0	0,0	69,9	11,4	5,3	1,1	1,0	0,2	0,0	2,5	0,1	0,0	0,0
VENETO	25,7	5,1	3,9	25,3	10,6	11,6	2,0	2,6	1,4	0,0	0,3	0,2	0,0	11,3
FRIULI VENEZIA GIULIA	13,6	3,7	5,4	28,3	10,7	10,5	0,7	6,8	0,1	0,6	0,2	0,0	3,6	15,8
LIGURIA	40,9	12,7	5,6	22,4	4,4	7,4	2,9	1,7	0,4	0,0	1,4	0,1	0,0	0,0
EMILIA ROMAGNA	47,7	2,9	1,8	10,8	2,7	22,4	4,3	0,3	0,1	0,6	0,4	0,2	0,3	5,7
TOSCANA	35,4	3,2	1,4	26,7	11,2	12,2	4,0	2,2	0,6	0,4	0,4	0,2	0,0	1,9
UMBRIA	16,3	9,4	2,5	45,1	12,3	7,5	2,6	1,2	0,3	0,0	2,8	0,0	0,0	0,0
MARCHE	24,8	14,9	3,4	30,0	0,9	13,6	4,5	3,6	1,0	0,0	3,0	0,1	0,0	0,0
LAZIO	27,1	13,8	5,0	24,1	6,9	12,8	3,1	1,6	1,2	0,0	2,6	0,2	0,0	1,7
ABRUZZO	19,6	5,6	1,7	24,1	2,7	8,0	1,1	0,6	0,4	0,1	1,0	0,0	0,0	35,0
MOLISE	23,3	15,2	6,2	25,1	6,8	19,7	1,8	0,6	0,8	0,0	0,4	0,1	0,0	0,0
CAMPANIA	31,7	9,3	4,2	28,2	4,3	12,7	2,2	2,6	2,2	0,0	1,7	0,7	0,0	0,3
PUGLIA	19,1	14,2	6,4	24,3	1,3	22,4	5,3	2,6	2,8	0,0	1,3	0,0	0,0	0,2
BASILICATA	23,6	13,5	5,6	23,4	9,0	17,7	2,8	2,0	1,2	0,3	0,8	0,0	0,0	0,0
CALABRIA	36,7	5,1	3,4	34,7	1,0	15,5	1,3	2,0	0,3	0,0	0,0	0,0	0,0	0,0
SICILIA	28,7	12,3	4,8	26,3	3,3	17,8	2,7	1,5	1,5	0,0	0,8	0,3	0,0	0,0
SARDEGNA	34,7	6,9	5,2	26,7	10,9	8,2	3,2	1,9	1,6	0,0	0,6	0,1	0,0	0,1
ITALIA	27,3	7,5	3,5	26,5	6,3	13,5	2,6	1,9	0,7	0,2	0,9	0,1	0,2	8,8

OBIETTIVI DEL TRATTAMENTO FARMACOLOGICO NELLA DIPENDENZA DA ALCOL

ASTINENZA

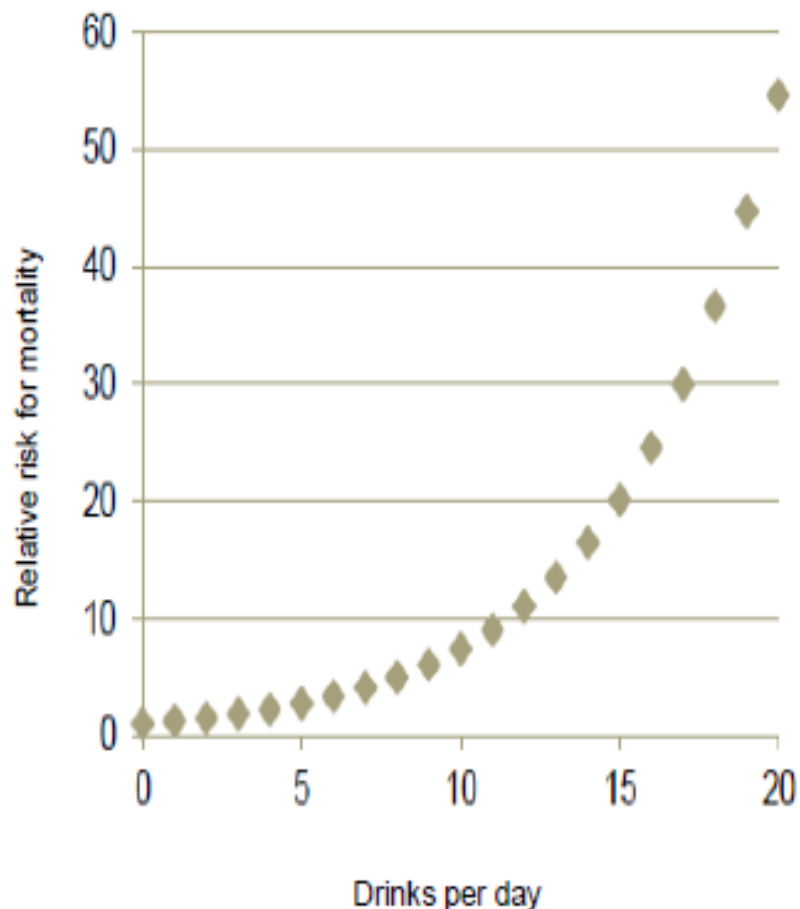
(Friedmann, N Engl J Med, 2013)

**RIDUZIONE DEL
CONSUMO**

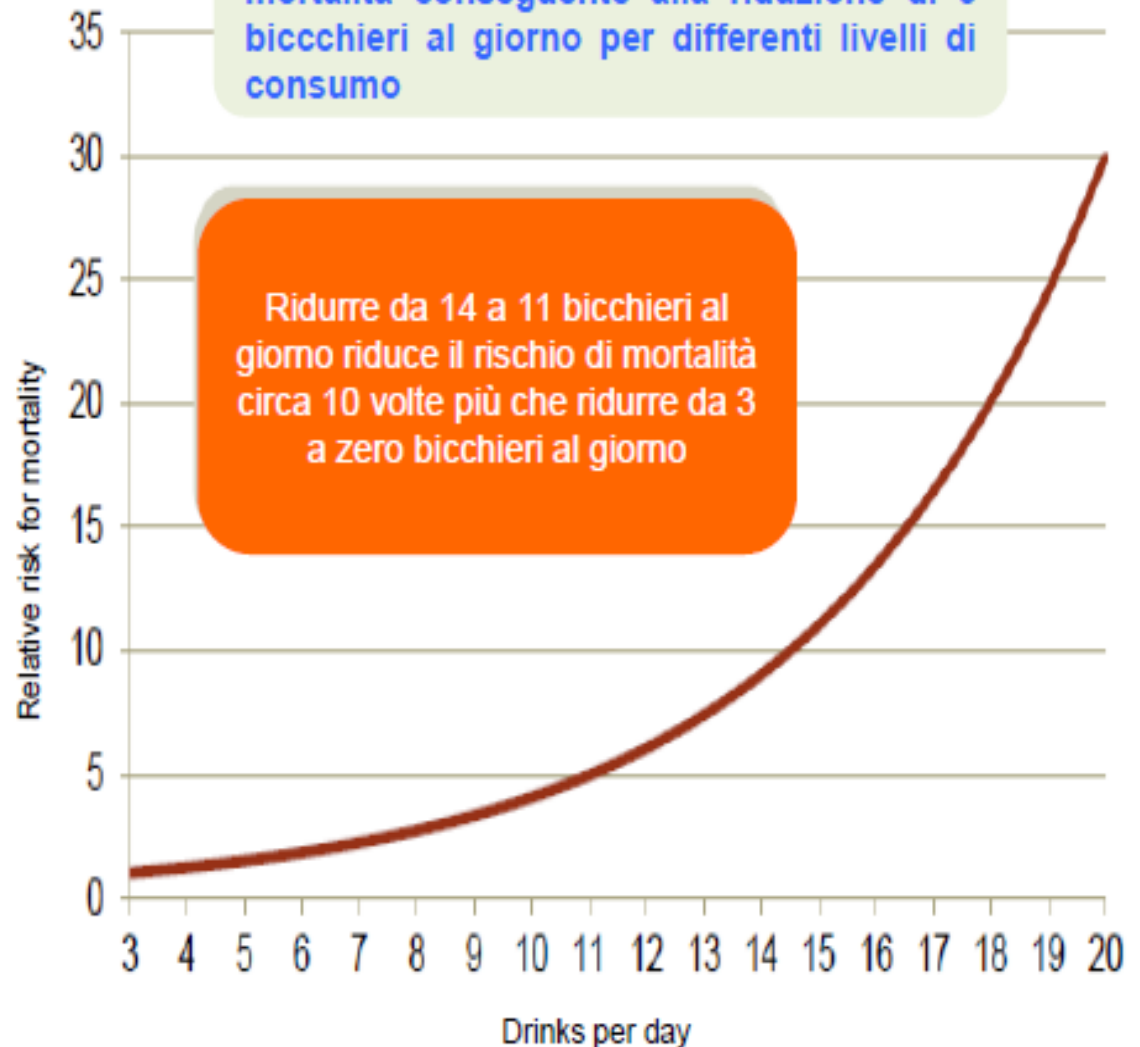
*(Aubin & Daeppen, Drug Alcohol Dep, 2013
van Amsterdam & van Den Brink, J Psychopharmacol, 2013)*

E' importante intervenire per "guadagnare" la maggior riduzione nel rischio

Rischio ALCOL , curva tipica
(ad es. Mortalità per cirrosi)



Guadagno relativo alla riduzione di mortalità conseguente alla riduzione di 3 bicchieri al giorno per differenti livelli di consumo



Ridurre da 14 a 11 bicchieri al giorno riduce il rischio di mortalità circa 10 volte più che ridurre da 3 a zero bicchieri al giorno

Reducing alcohol consumption has immediate health benefits

Improvements in:

Sleep disorders

Depression

Weight / nutrition

Blood pressure

(Anderson & Baumberg, Alcohol in Europe, 2006; Xin et al., Hypertension, 2001; Brown & Schuckit, J Stud Alcohol, 1988)

Reduction of alcohol consumption decreases the risk of morbidity

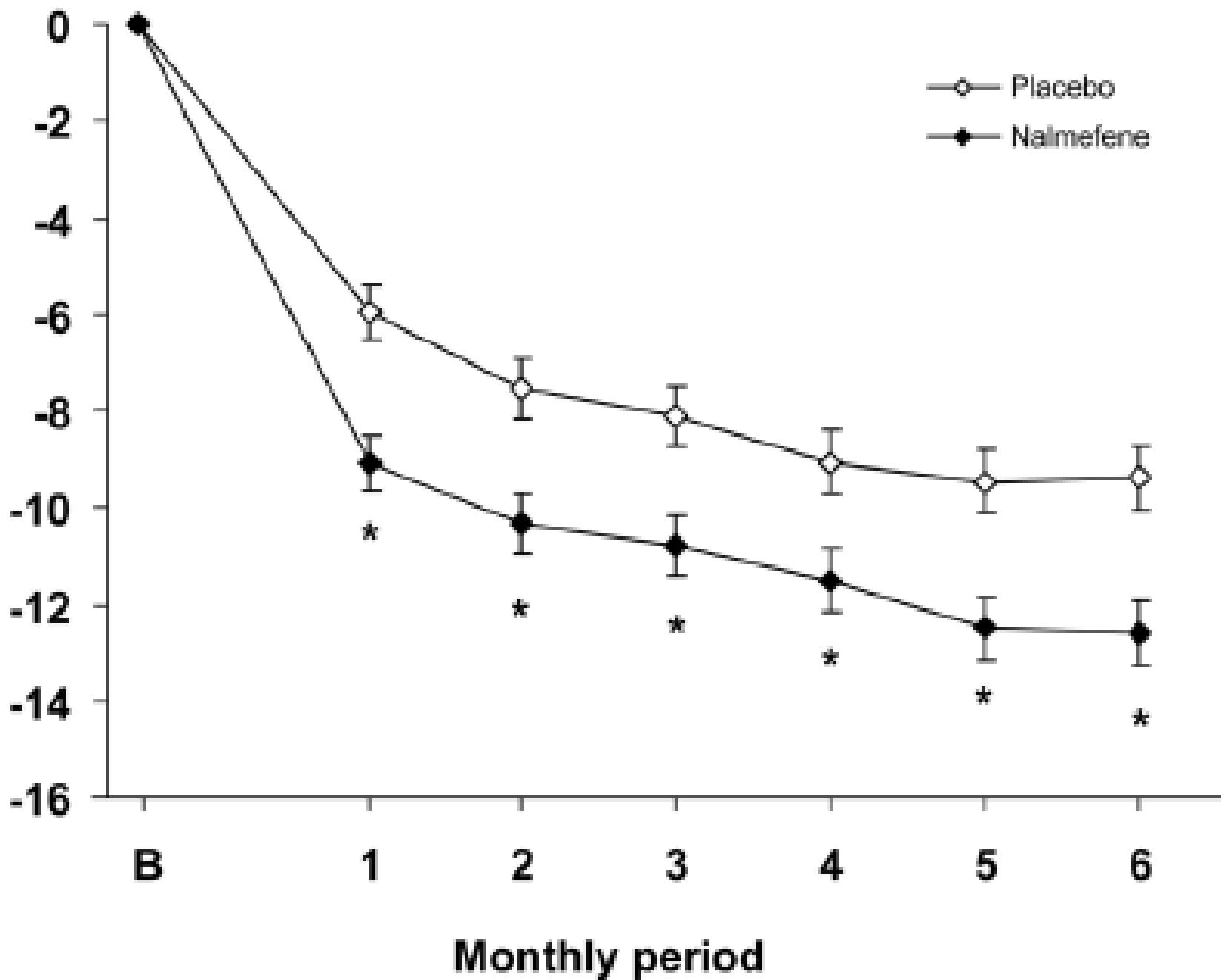
Lowers risks of:

Prenatal conditions

Liver cirrhosis

Lifetime development of:

- Cancer
- Cardiovascular disease
- Osteoporosis
- Pancreatitis

A**Adjusted mean change from baseline in
heavy drinking days**

(van den Brink, Alcohol Alcohol, 2013)

Table 1 Drugs currently approved for the treatment of AD: mechanisms of action, clinical use and dosages.

Disulfiram

- Aldehyde-dehydrogenase enzyme inhibitor
- Deterrent medication to be used in patients highly motivated to maintain abstinence from alcohol
- To be used in the presence of a family member to be entrusted with the drug and its administration
- It should be avoided in patients with severe liver disease, and peripheral neuropathy
- Dosages: 800-1200 mg/day until the 4th day, then 400 mg/day from the 5th to the 7th day, then 200 mg/day for 5-6 months

Acamprosate

- N-methyl-D-aspartate glutamate receptor antagonist
- Anti-craving medication to be used in patients with *relief* craving
- A reduction in the episodes of heavy drinking can be considered a positive result
- It should be avoided in patients with severe kidney disease
- Dosages: 1.3-2 g/day in 2-3 oral administrations for 12 months

Naltrexone

- μ and κ -opioid receptor antagonist
- Anti-craving medication to be used in patients with *reward* craving
- A reduction in the episodes of heavy drinking can be considered a positive result
- It should be avoided in patients with severe liver disease
- Dosages: 50-100 mg/day orally, for 3-6 months or an intramuscular injection of 380 mg of long-acting formulation every 30 days for 6 months

Nalmefene

- μ and δ -opioid receptor antagonist and κ -opioid receptor partial-agonist
- To be used during a program of alcohol reduction in patients with at least a high drinking risk level (defined as ≥ 60 g/day for men and ≥ 40 g/day for women of alcohol intake)
- It should be avoided in patients with alcohol withdrawal syndrome who need a symptomatic pharmacological approach (CIWA score > 10 points) and/or need immediate alcohol detoxification
- Dosages: 18 mg orally "as-needed" for 6-months

Sodium oxybate

- GABA_B receptors agonist
- Suppress alcohol withdrawal syndrome
- Anti-craving medication with alcohol-mimicking property to be used in patients with *reward* and *relief* craving
- To be used in the presence of a family member to be entrusted with the drug and its administration
- It should be avoided in patients with poly-drug addiction and Axis II borderline personality disorders
- Dosages: 50-100 mg/kg/day every 4-6 h for 7-10 days to treat alcohol withdrawal syndrome, and 50-75 mg/kg/day every 6-8 h for 3-12 months as anti-craving

FARMACI

TIPOLOGIA DI ALCOLISMO

CRAVING

CO-MORBIDITA' INTERNISTICA

CO-MORBIDITA' PSICHIATRICA

CO-DIPENDENZA

GENOTIPO

La tipologia di Cloninger.

Tipo I

Inizio tardivo, reattivo a eventi accaduti nel corso della vita (traumi lutti, situazioni "di passaggio")

Comportamento prevalente: evitamento (*harm avoidance*)

Base neurobiologica: deficit serotoninergico

Effetto ricercato: ansiolitico/ antidepressivo, rilassamento psicofisico

Craving: relief craving (desiderio di ridurre la tensione)

Capacità di gratificazione: buona

Capacità di contatto con gli altri: buona

Storia di vita: "vita vissuta" in cui l'alcolismo appare come un incidente o una complicanza

Tipo II

Geneticamente determinato

Inizio precoce, evoluzione rapida

Comportamento prevalente: ricerca sensazioni intense (*Novelty Seeking*)

Neurobiologia: deficit del sistema dopaminergico

Effetto ricercato: gratificazione

Craving: reward craving (desiderio di ricompensa)

Maggiore risposta ai potenziali auditivi evocati

Associazione con disturbi antisociale e borderline di personalità

Capacità di gratificazione: scarsa (cosiddetto *Reward Deficiency Syndrome*)

Capacità di contatto con gli altri: scarsa e problematica

Storia di vita: vita improntata dal rapporto con l'alcol e le sostanze

(Cloninger et al., *Arch Gen Psych.*, 1981)

TIPOLOGIE DI CRAVING

REWARD (*ricompensa*): disregolazione dopaminergica / oppioidergica (*deficit oppioidi*), alcolismo precoce e familiarità per alcolismo

RELIEF (*tensione*): disregolazione GABA-ergica / glutammatergica (*ipereccitabilità*), alcolismo tardivo

OBSESSIVE (*ossessione*): disregolazione serotoninergica (*deficit di serotonina*), bere ossessivo / compulsivo

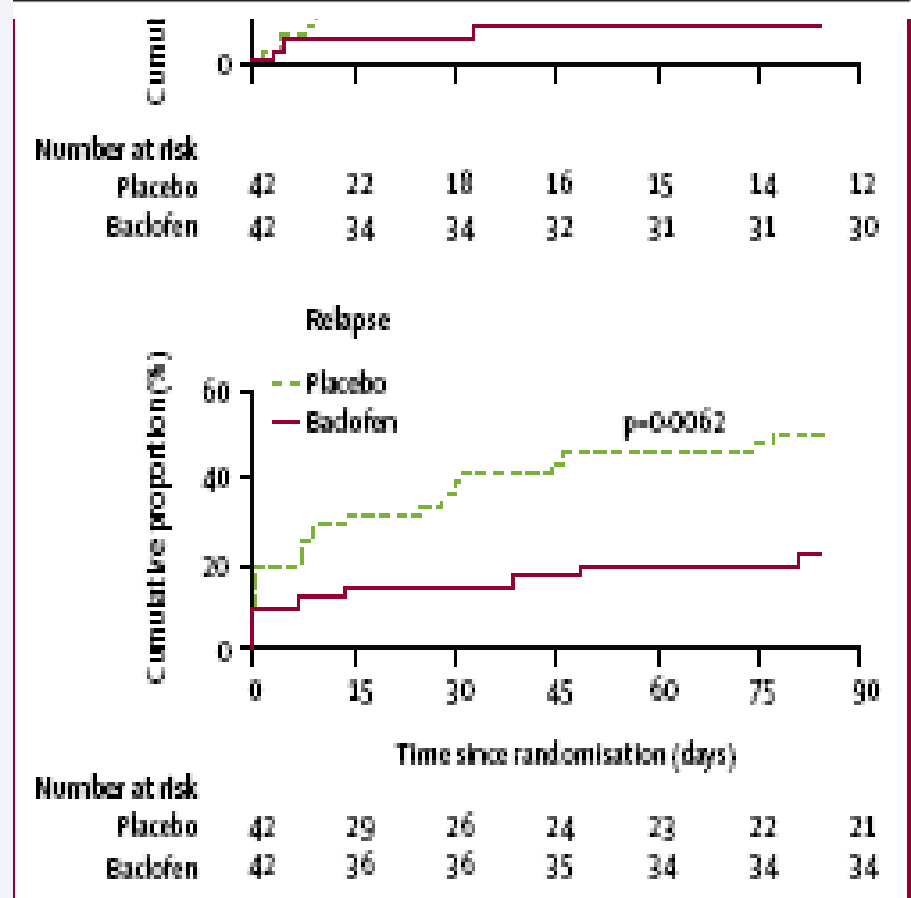


- Drinking habits of patients need to be routinely screened by physicians with tools which have proven their reliability
(**Recommendation A1**)
The AUDIT is the 'gold standard' screening test for alcohol abuse and dependence
(**Recommendation B1**)
- In patients with acute withdrawal syndrome and ALD, benzodiazepines are the treatment of choice
(**Recommendation A1**)
- In patients with ALD, persistent alcohol intake is associated with disease progression; therefore the most effective recommendation for these individuals is total alcohol abstinence
(**Recommendation A1**)
- Brief motivational interventions should be routinely used in the medical management of alcohol use disorders
(**Recommendation A1**)
- In alcohol-dependent patients without advanced ALD, disulfiram, naltrexone and acamprosate, combined with counseling, reduce alcohol consumption and prevent relapse
(**Recommendation A1**)
These drugs cannot be recommended in patients with advanced ALD because of the potential side-effects
(**Recommendation B1**)
- In patients with advanced ALD, recent studies suggest that baclofen is safe and effective to prevent alcohol relapse
(**Recommendation B2**)

Management of Alcoholic

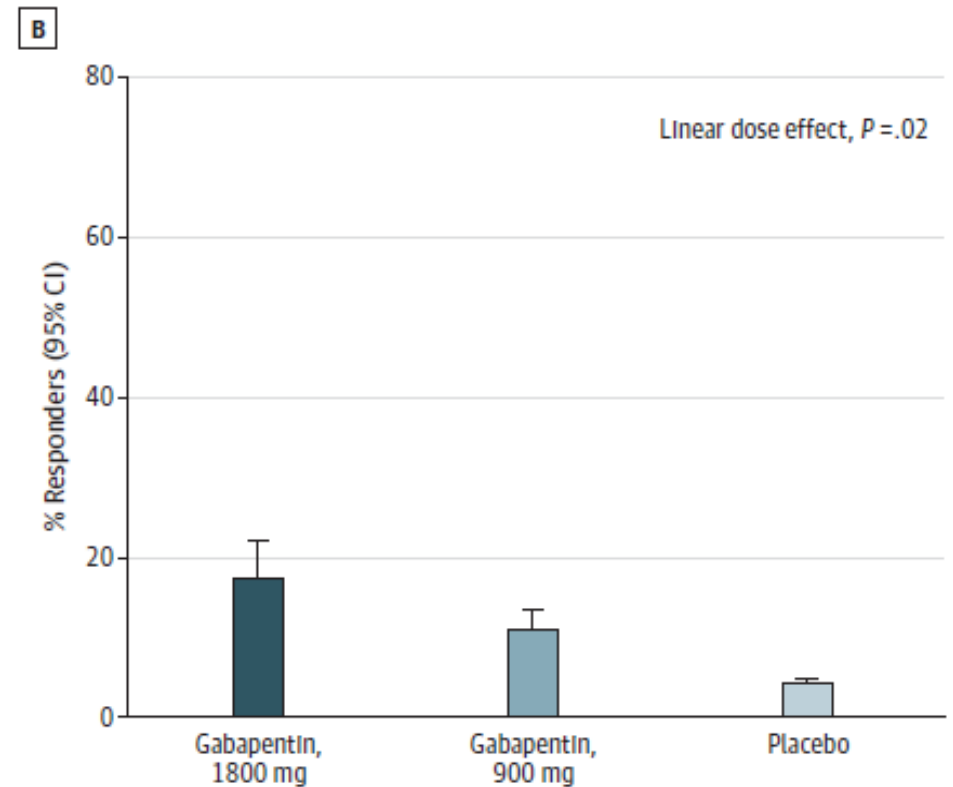
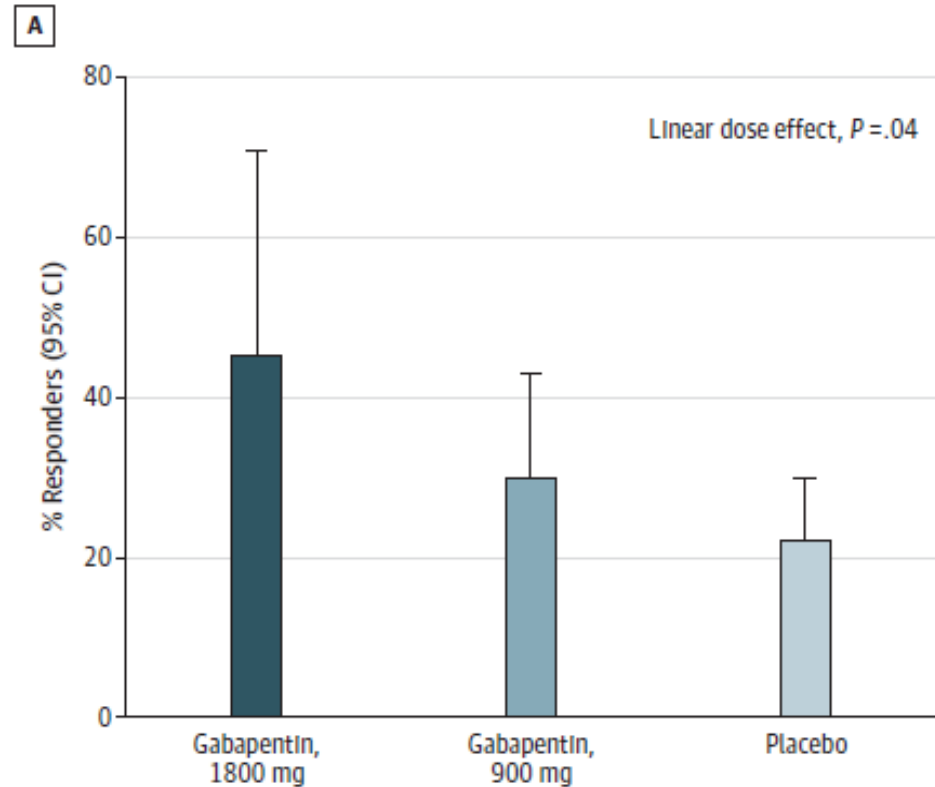
ase

Study of the Liver^{*,†}



(Addolorato et al, Lancet, 2007)

Original Investigation



CONCLUSIONS AND RELEVANCE Gabapentin (particularly the 1800-mg dosage) was effective in treating alcohol dependence and relapse-related symptoms of insomnia, dysphoria, and craving, with a favorable safety profile. Increased implementation of pharmacological treatment of alcohol dependence in primary care may be a major benefit of gabapentin as a treatment option for alcohol dependence.

Toward Personalized Medicine in the Pharmacotherapy of Alcohol Use Disorder: Targeting Patient Genes and Patient Goals

Medication	Genetic Variant	Outcome Moderated	Notable Studies
Topiramate	<i>GRIK1</i> (rs2832407)	Heavy drinking days (%); side effects	Kranzler et al., 2014 (2); Ray et al., 2009 (4)
Naltrexone	<i>OPRM1</i> (Asn40Asp), (rs1799971), <i>DRD4</i> VNTR	Heavy drinking days (%); abstinence rates; relapse to heavy drinking	Anton et al., 2008 (12); Kim et al., 2009 (13); Oslin et al., 2003 (14); Tidey et al., 2008 (15)
Ondansetron	LL/LS/SS (5-HTTLPR) (rs1042173), <i>SLC6A4</i> (5-HTTLPR)	Drinks per drinking day; days abstinent (%)	Johnson et al., 2011 (9)
Sertraline	5-HTTLPR triallelic <i>SLC6A4</i>	Heavy drinking days (%); drinking days (%)	Kranzler et al., 2011 (8)
Acamprosate	<i>GATA4</i> (rs1327367)	Relapse	Kiefer et al., 2011 (10)
Disulfiram	<i>DBH</i> (rs161115)	Adverse events	Mutschler et al., 2012 (11)

Medication Treatment of Different Types of Alcoholism

Bankole A. Johnson, D.Sc., M.D.

Alcoholism remains a serious cause of morbidity and mortality despite progress through neurobiological research in identifying new pharmacological strategies for its treatment. Drugs that affect neural pathways that modulate the activity of the cortico-mesolimbic dopamine system have been shown to alter drinking behavior, presumably because this dopaminergic system is closely associated

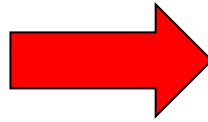
rewarding behavior. Ondansetron, naltrexone, topiramate, and baclofen are examples. Subtyping alcoholism in adults into an early-onset type, with chronic symptoms and a strong biological predis-

position to the disease, and a late-onset type, typically brought on by psychosocial triggers and associated with mood symptoms, may help in the selection of optimal therapy. Emerging adults with binge drinking patterns also might be aided by selective treatments. Although preliminary work on the pharmacogenetics of alcoholism and its treatment has been promising, the assignment to treatment still depends on clinical assessment. Brief behavioral interventions that encourage the patient to set goals for a reduction in heavy drinking or abstinence also are part of optimal therapy.

(Am J Psychiatry 2010; 167:630–639)

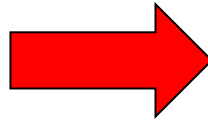
Choice of therapy can be guided by the patient's history of alcoholism and stage of life and, in the future, perhaps by pharmacogenetics.

DISULFIRAM



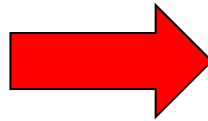
- Maintain (continuous) Abstinence
- Craving (“reward”?)
- High motivation

ACAMPROSATE



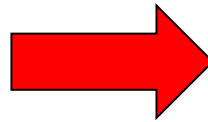
- Reduction in return to drink
- Craving (“relief”?)
- Lesch I and II
- Cloninger I

NALTREXONE



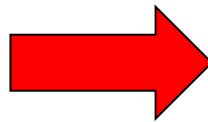
- Reduction in return to drink
- Craving (“reward”)
- Lesch III and IV
- Cloninger II

SODIUM OXYBATE

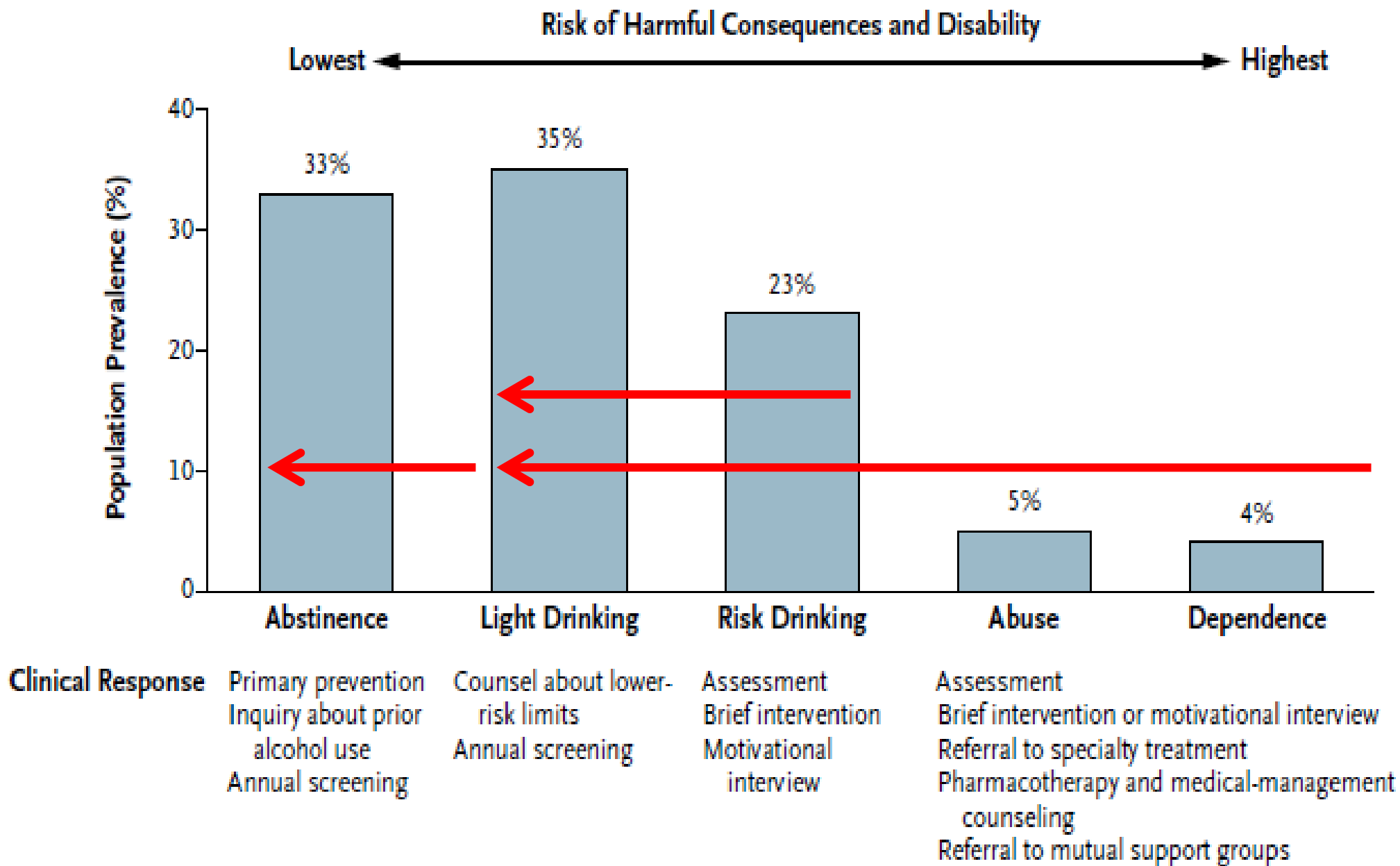


- Detox patients
- Maintain (continuous) Abstinence
- Craving (“relief”)
- Alcohol mimic effect (“reinforce”)
- Cloninger I e II; Lesch I and II
- High and very high DRL

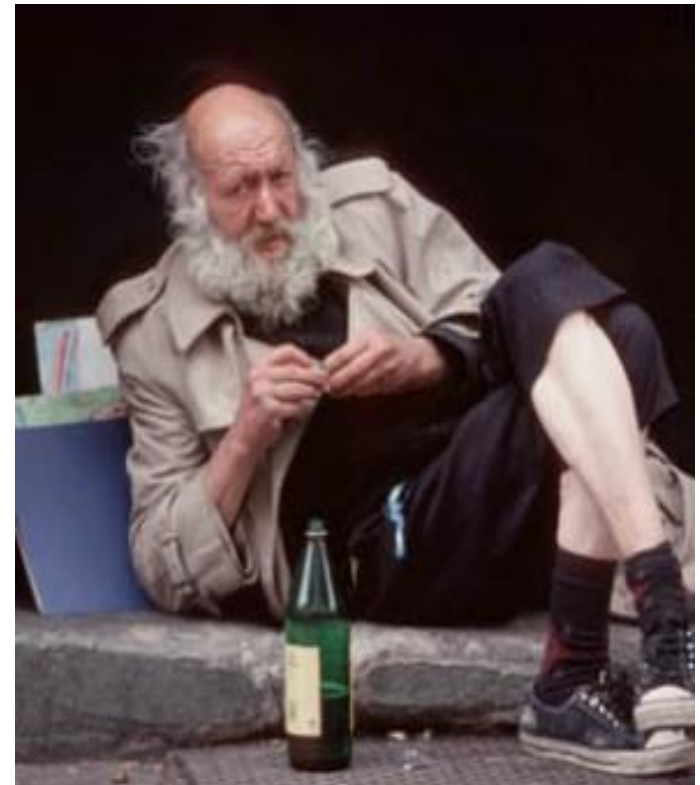
NALMEFENE



- Reduce Heavy Alcohol Consumption
- “as needed”
- Craving (“reward”?)



(Friedmann, N Engl J Med, 2013)



Grazie per l'attenzione