Alcolismo: nuovi modelli di consumo e possibilità terapeutiche

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New steps for treating alcohol use disorder

Erin J. Campbell[1,2] · Andrew J. Lawrence[1,2] · Christina J. Perry[1,2]

A huge milestone for the treatment of alcohol use disorder across several countries in the last 10 years was

l'introduzione di lineeguida pratiche che integrano l'esperienza clinica e le evidenze della ricerca.
L'analisi di queste lineeguida mostrano buona consistenza, ma poche evidenze di progresso nell'approccio al disturbo da uso di alcol nell'ultimo decennio

In this mini-review, we discuss emerging treatments for alcohol use disorder that may supplement or improve the evidence-based treatments that are currently recommended.

New medications, the emergence of digital technology, and other novel approaches such as transcranial magnetic stimulation are all discussed with reference to treatments already in practice.

Le diverse posizioni

OMS ICD-10

- **DEPENDENCE**
  AUDIT > 20
- **HARMFUL USE**
  (CONSUMO DANNOS
  AUDIT > 16
- **HAZARD**
  (CONSUM SCHIOSO)
  AUDIT > 8

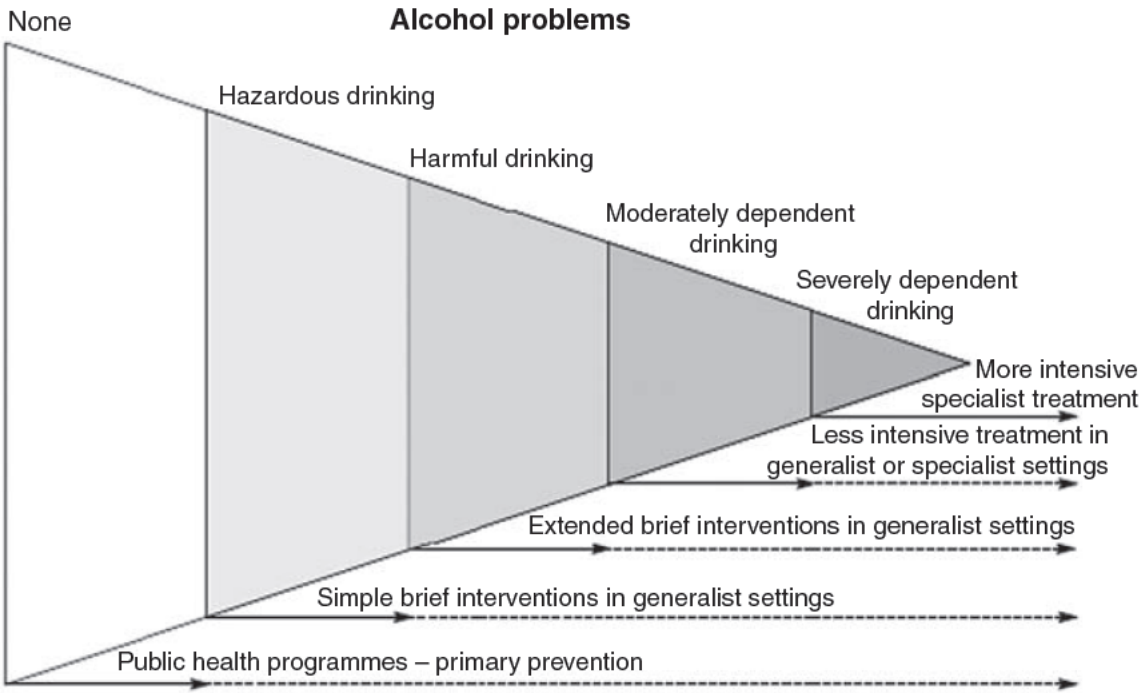
APA DSM-5

- **A ION**
  cohol Use Disorder)

BINGE DRINKING?

Rischio basso Consumo inferiore a 2 UA per maschi e 1 UA per femmine die

Figure 3: A spectrum of responses to alcohol problems. Reproduced from a review of the effectiveness of treatment for alcohol problems (Raistrick *et al.*, 2006)



ALCOHOL-USE DISORDERS

THE NICE GUIDELINE ON DIAGNOSIS, ASSESSMENT AND MANAGEMENT OF HARMFUL DRINKING AND ALCOHOL DEPENDENCE

Text Box 2: Levels of care for addiction treatment (Mee-Lee *et al., 2001)*

Level I – Outpatient treatment
Level II – Intensive outpatient treatment/partial hospitalisation
Level III – Residential (medically-monitored) treatment
Level IV – Medically-managed intensive inpatient treatment

Alcohol-use disorders: diagnosis, assessment and management of harmful drinking and alcohol dependence

NICE National Institute for Health and Care Excellence

Clinical guideline
Published: 23 February 2011
nice.org.uk/guidance/cg115

Interventions for harmful drinking and mild alcohol dependence

- **a psychological intervention focused specifically on alcohol-related cognitions, behaviour, problems and social networks**
- who have a regular partner **behavioural couples therapy**
- **who have not responded to psychological interventions alone, or who have specifically requested a pharmacological intervention acamprosate or oral naltrexone in combination with an individual psychological intervention or behavioural couples therapy**

Alcohol-use disorders: diagnosis, assessment and management of harmful drinking and alcohol dependence

NICE National Institute for Health and Care Excellence
Clinical guideline
Published: 23 February 2011
nice.org.uk/guidance/cg115

Interventions for moderate and severe alcohol dependence

After a successful withdrawal consider offering

- **acamprosate or oral naltrexone + an individual psychological intervention** (cognitive behavioural therapies, behavioural therapies or social network and environment-based therapies) **focused specifically on alcohol misuse**
- **consider offering acamprosate or oral naltrexone + behavioural couples therapy to service users who have a regular partner and whose partner is willing to participate in treatment**
- **consider offering disulfiram + a psychological intervention to service users who:**
  - **have a goal of abstinence but for whom acamprosate and oral naltrexone are not suitable or prefer disulfiram and understand the relative risks of taking the drug**

Psicosociale in Alcologia: lo stato dell'arte

Lancet 2016; 387: 988–98

Alcohol use disorders

Jason P Connor, Paul S Haber, Wayne D Hall

	Description	Level of evidence*
Cognitive behaviour therapy	This approach addresses cognitive, affective, and interpersonal triggers for alcohol use. It enhances drinking refusal self-efficacy† skills; identifies and modifies alcohol expectancies‡; improves problem-solving skills; and develops more effective coping strategies, including relaxation approaches.	High[20–24]
Motivational enhancement therapy	This therapy is a patient-centred approach that enhances motivation to change behaviour. It uses a collaborative therapeutic approach to assist patients to recognise and resolve ambivalence, and develop their own reasons to reduce or abstain from drinking. Key strategies include collaborative identification of the gap between the patient's present and desired health (ie, goal–status discrepancy), recognition of their resistance to change, avoidance of confrontational communication, and guided assessment of the pros and cons for change.	High[20–22]
Behavioural therapies based on conditioning	Cue exposure: repeated exposure to conditioned cues (eg, image or smell of alcohol, or associated emotion) can induce habituation or craving. Exposure to cues during treatment in the absence of drinking (with or without coping skill practice) is thought to reduce habituation. It is often combined with other cognitive therapy or skills. Contingency management: this approach introduces a tangible reinforcer, such as money or vouchers, to increase session attendance or abstinence. It is more suitable for inpatient and residential settings, and needs more translatable evidence.	Low;[23] Moderate[25,26]
12-step facilitation	This approach offers continuous mutual peer support, usually in the form of self-help groups run by Alcoholics Anonymous. Participation is free of charge. Participants need to "surrender to a higher power" to facilitate change. Some groups use a buddy system (a sponsor) to provide support between group meetings.	Mixed[21,33,37]

*Summary based on authors' narrative review of the highest level of evidence for each treatment. †Individuals' beliefs about their ability to refrain from drinking. ‡Individuals' expectations about the effects of alcohol consumption.

Table 1: **Non-pharmacological behavioural treatments**

Diagnosis and Pharmacotherapy of Alcohol Use Disorder: A Review. **Kranzler H.R. and Soyka M. *JAMA*, 320, 8, 815-824 28/08/2018**

Table 1. Food and Drug Administration–Approved Medications for Treating Alcohol Use Disorder

	Medication[a]			
	Disulfiram	Naltrexone	Long-Acting Injectable Naltrexone	Acamprosate
Indication	Management of selected chronic alcohol patients who want to remain in a state of enforced sobriety	Treatment of alcohol dependence	Treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting	Maintenance of abstinence from alcohol in patients with alcohol dependence who are abstinent
Dosage	FDA-approved dosage: 250-500 mg/d orally Dosage used in clinical trials: 125-500 mg/d	FDA-approved dosage: 50 mg/d orally Dosage used in clinical trials: 50-100 mg/d, with an initial dosage of 25-50 mg/d	FDA-approved dosage: 380 mg/mo intramuscularly Dosage used in clinical trials: 190 mg or 380 mg/mo	FDA-approved dosage: 1998 mg/d orally Dosage used in clinical trials: 1000-3000 mg/d
Effect size(s)	A meta-analysis of 22 studies (N = 2414)[13] showed an association of disulfiram with sustained abstinence from alcohol compared to control conditions only in open-label studies (Hedges g = 0.70, 95% CI, 0.46 to 0.93); there was not a significant association in blinded trials (Hedges g = 0.01, 95% CI, −0.29 to 0.32).[b] Disulfiram was associated with a better response than control conditions when medication adherence was supervised (N = 13 studies; Hedges g = 0.82, 95% CI, 0.59 to 1.05), but not when it was unsupervised (N = 9 studies; Hedges g = 0.26, 95% CI, −0.02 to 0.53).[13]	A meta-analysis (N = 16 studies and 2347 patients) showed a risk decrease (RD) for a return to any drinking associated with naltrexone 50 mg/d (RD = −0.05 (95% CI, −0.10 to −0.002); number needed to treat (NNT) = 20]. Naltrexone was also associated with reduced risk of binge drinking [19 studies; N = 2875; RD = −0.09 (95% CI, −0.13 to −0.04); NNT = 12).[11]	In the only placebo-controlled trial of long-acting naltrexone, the median monthly number of binge drinking days declined by 13.3 in the placebo group (to 6.0/mo), 14.8 in the 190-mg group (to 4.5/mo), and 16.2 in the 380-mg group (to 3.1/mo).[20]	In a meta-analysis of 16 studies (N = 4827),[11] acamprosate treatment was associated with a greater reduction in the risk of drinking among abstinent patients [RD = −0.09 (95% CI, −0.14 to −0.04); NNT = 12], but no reduction in the likelihood of binge drinking.
Most common adverse effects	Moderate or severe drowsiness occurred in 8% of patients treated with disulfiram 250 mg.[37] More severe adverse events associated with disulfiram (hepatitis, neuropathy, optic neuritis, psychosis, and confusional states) are rare.[48]	Somnolence (29.5%), nausea (25.8%), vomiting (16.9%), decreased appetite (17.7%), abdominal pain (15.9%), insomnia (16.4%), and dizziness (11.9%)[14]	Same adverse events as oral naltrexone and also injection site reactions	The only adverse event that was more common with acamprosate than placebo was diarrhea (24.9%).[15]
Clinical notes	Because the disulfiram-ethanol interaction can present as an emergency, use of disulfiram to reduce drinking, rather than sustain abstinence, is not advised.	Naltrexone can block the effects of opioid analgesics and precipitate withdrawal in a patient physically dependent on opioids.	Naltrexone can block the effects of opioid analgesics and precipitate withdrawal in a patient physically dependent on opioids.	Not metabolized; can be used in patients with hepatic disease.

Abbreviations: FDA, Food and Drug Administration; NNT, number needed to treat; RD, risk decrease.

[a] None of these medications has psychotropic effects or abuse potential.

[b] Hedges g: 0.2 = small effect, 0.5 = medium effect, and 0.8 = large effect.

Disufiram
Inibitore della ALD
n.s. in double blind
s.s. solo se supervisionato

Naltrexone
Antagonista nonselettivo
dei recettori oppioidi
μ-, κ-, and δ
Riduce il rischio di ricaduta
in qualsiasi uso (NNT=20)
e di BD (NNT =12)

Acamprosato
Modulatore glutammato
Riduce rischio di ricaduta
(NNT=12) - Non reduce BD

Table 2. Non-Food and Drug Administration–Approved Medications for Treating Alcohol Use Disorder

	Medication			
	Nalmefene	Baclofen	Gabapentin	Topiramate
Indication(s)	United States: Complete or partial reversal of opioid drug effects European Union: Help reduce alcohol consumption in adults with alcohol dependence who consume >60 g (≈4 drinks) per day (men) or >40 g (≈3 drinks/ day) (women).	Alleviation of signs and symptoms of spasticity resulting from multiple sclerosis	Management of postherpetic neuralgia in adults and adjunctive therapy in the treatment of partial seizures in patients age 3 and older.	Monotherapy for partial onset or primary generalized tonic-clonic seizures, adjunctive therapy for partial onset seizures or primary generalized tonic-clonic seizures and seizures associated with Lennox-Gastaut syndrome; migraine prophylaxis; weight loss and chronic weight management (in combination with phentermine)
Dosage	Approved dosage for AUD (in the European Union): 18 mg/d (as needed) Dosage in clinical trials for AUD: 5-80 mg/d in 1 dose or 2 divided doses	Dosage in clinical trials for AUD: 30-180 mg/d in up to 4 divided doses	Dosage in clinical trials for AUD: 600-1800 mg/d in 3 divided doses	Dosage in clinical trials for AUD: 75-300 mg/d in 2 divided doses
Effect size(s)	In a meta-analysis of 5 RCTs (N = 2567),[16] nalmefene treatment was associated with a reduction in binge drinking of 1.65 d (95% CI, 0.89 to 2.41) more per month at 6 mo and by 1.60 d more per month (95% CI, 0.35 to 2.85) at 1 y, and with a reduction in total alcohol consumption of 20% (95% CI, 0.10 to 0.30) at 6 mo.	In a meta-analysis of 13 RCTs (N = 1492),[17] baclofen was associated with a significantly greater time to first lapse to drinking [SMD = 0.42 (95% CI, 0.19 to 0.64)] and a greater likelihood of abstinence during treatment [odds ratio = 1.93 (95% CI, 1.17 to 3.17)], with no greater difference at a higher dosage (>60 mg/d). Persons who drank very heavily at study entry had a greater association of abstinence with baclofen.	Of 3 peer-reviewed, placebo-controlled RCTs (total N = 231), the largest (N = 150) showed that gabapentin resulted in a rate of abstinence of 11.1% (95% CI, 5.2 to 22.2) in the 900-mg/d group and 17.0% (95% CI, 8.9 to 30.1) in the 1800-mg/d group, compared with 4.1% (95% CI, 1.1 to 13.7) for placebo. The rate of no binge drinking was 22.5% (95% CI, 13.6 to 37.2) in the placebo group, 29.6% (95% CI, 19.1 to 42.8) in the gabapentin 900 mg/d group, and 44.7% (95% CI, 31.4 to 58.8) in the 1800 mg/d group.[20] Preliminary findings from a multi-center trial of enacarbil ER (N = 346)[52] showed no treatment effect on the primary outcome measure, percent of subjects with no binge drinking (28.3% vs 21.5% for placebo) or any other drinking measures.	In a meta-analysis of 7 RCTs (N = 1125), there were small-to-medium effects of topiramate on abstinent days (Hedges g = 0.468)[a] and binge drinking days (Hedges' g = 0.406).[18]
Most common adverse effects	Nausea (22.1%), dizziness (18.2%), insomnia (13.4%), headache (12.3%), vomiting (8.7%), fatigue (8.3%), somnolence (5.2%)[21]	With low-dose treatment (30 mg/d): drowsiness (39.1%), dizziness (26.4%), headache (25.3%), confusion (23.0%), muscle stiffness (16.1%), excessive perspiration (14.9%), itching/pruritus (14.9%), abnormal muscle movements (13.8%), numbness (12.6%), slurred speech (10.3%)[24]	Dizziness (19.1%), somnolence (14.1%), ataxia or gait disorder (14.0%), peripheral edema (6.6%)[22]	Paresthesia (50.8%), dysgeusia (23.0%), anorexia (19.7%), difficulty with concentration/ attention (14.8%), nervousness (14.2%), dizziness (11.5%), pruritis (10.4%).[25] Transient mental slowing and modest reductions in verbal fluency and working memory are generally dose related.[53]
Clinical notes	Not approved in the United States for treating AUD	Temporary recommendation in France for use in the management of alcohol dependence at a maximum recommended dosage of 80 mg/d	Potential bias due to high rate of treatment non-completion in the largest trial.[53] Additional studies needed to validate medication effects.	To reduce risk/severity of adverse effects, begin treatment at 25-50 mg/d, with 25-50 mg/d increases at weekly intervals. Contraindicated in patients with a predisposition or history of metabolic acidosis, renal calculi, and secondary angle closure glaucoma.

Abbreviations: AUD, alcohol use disorder; RCT, randomized clinical trial.

[a] Hedges g: 0.2 = small effect, 0.5 = medium effect, and 0.8 = large effect.

Diagnosis and Pharmacotherapy of Alcohol Use Disorder: A Review. **Kranzler H.R. and Soyka M. *JAMA*, 320, 8, 815-824 28/08/2018**

Nalmefene
μ- and δ-opioid receptor antagonist and a κ-opioid receptor partial agonist
Diminuisce consumo e BD

Baclofen
γ-aminobutyric acid–B receptor agonist
Maggior tempo sino alla ricaduta in ogni uso (per dose < a 60 mg/die)
Maggiore probabilità di astensione durante il trattamento
Maggior effetto se uso elevato
n.s. sui gg di astinenza

Gabapentina
Topiramato

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DOI: 10.1002/npr2.12028

INVITED REVIEW

WILEY NEUROPSYCHOPHARMACOLOGY REPORTS

Anticraving therapy for alcohol use disorder: A clinical review

Winston W. Shen[1,2]

TABLE 1 Possible mechanisms implicated for anticraving actions in treating alcohol use disorder patients

Mechanism of action of anticraving drugs	Applicable drugs
Opioid modulation	Naltrexone, Nalmefene
Dopamine neurotransmission	Naltrexone, Nalmefene
Serotonin neurotransmission	Ondansetron
GABA neurotransmission	Gabapentin
Glutamate neurotransmission	Acamprosate
Blockage of GIRK channel	Ifenprodil

GABA, γ-aminobutyric acid; GIRK channel, G protein-activated inwardly rectifying potassium channel.

Shen, W. W. (2018). **Anticraving therapy for alcohol use disorder: A clinical review**. *Neuropsychopharmacology reports*, *38*(3), 105-116.

TABLE 2 Representing anticraving drugs for patients with alcohol drinking disorder

Drug	Drug profile responsible for anticraving properties	Representing human anticraving studies	Other medical use besides anticraving therapy
Naltrexone[a]	A glutamate agonist, is derived from amino acid, taurine	Weinstein et al (2003)[5]	
Naltrexone[a]	A main μ and δ (lesser extent) opioid receptor antagonist	Volpicelli et al (1992)[11] O'Malley et al (1992)[12]	Opioid overdose
GHB[b]	A precursor to GABA, glutamate, and glycine	Addolorato et al (1996)[14]	Narcolepsy
Nalmefene[b]	A μ-opioid receptor antagonist & κ-opioid partial agonist	Gual et al (2013)[19] van den Brink et al (2014)[20]	
Topiramate	An antagonist for kainate/AMPA, a subtype of the glutamate	Johnson et al (2003)[22] Johnson et al (2004)[23] Johnson et al (2007)[24]	Epilepsy Migraine Lennox-Gastaut syndrome
Gabapentin	A drug to facilitate GABA transmission	Furieri & Nakamura-Palacio (2007)[27] Mason et al (2014)[28]	Epilepsy Nerve pain
Ondansetron	A 5-HT_3 reuptake inhibitor	Johnson et al (2000)[29]	Antiemetic for cancer patients receiving chemotherapy
Ifenprodil	A GIRK channel inhibitor	Sagaya et al (2018)[35]	Dizziness in poststroke patients

The Arab numbers in superscripts denote the reference entries cited in the article.
AMPA receptors, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors; GABA, gamma-aminobutyric acid; GHB, gamma-hydroxybutyate; GIRK channel, G protein-activated inwardly rectifying potassium channel.
[a]Approved by US Food and Drug Administration for anticraving indication in patients with alcohol use disorder.
[b]Approved by European Medicines Agency for anticraving indication in patients with alcohol use disorder.

EXPERT OPINION ON PHARMACOTHERAPY, 2017
VOL. 18, NO. 12, 1187–1199
https://doi.org/10.1080/14656566.2017.1349098

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REVIEW

Check for updates

Pharmacotherapy of alcoholism – an update on approved and off-label medications

Michael Soyka[a,b] and Christian A. Müller[c]

Article highlights

- Only a few drugs with clear evidence but modest effects are approved for treatment of AUDs, including naltrexone (oral, depot) and acamprosate.
- Supervised disulfiram administration represents a second-line treatment in AUDs.
- Nalmefene is approved for the reduction of alcohol intake, but its use is controversial.
- Encouraging results have been reported for topiramate, gabapentin and varenidine.
- Baclofen has shown mixed results; further studies are needed to evaluate baclofen and new formulations of this compound.
- Some recent unpublished studies have shown positive results for gabapentin and in the USA it may be close to approval for the treatment of AUDs.
- A 'magic bullet' is not in sight, but progress is being made.

This box summarizes key points contained in the article.

CNS Drugs (2018) 32:13–31
https://doi.org/10.1007/s40263-017-0484-2

CrossMark

SYSTEMATIC REVIEW

Systematic Review of Combined Pharmacotherapy for the Treatment of Alcohol Use Disorder in Patients Without Comorbid Conditions

Andrew C. Naglich[1] · Austin Lin[2] · Sidarth Wakhlu[2] · Bryon H. Adinoff[1,2]

Nx – acamprosato
Nx – setralina
Nx – GHB
Nx – Ondansetron
Nx – gabapentina
Nx – quetiapina
Acamprosato – disulfiram
Quetiapina – mirtazapina
5 OH triptofano – carbidopa – levodopa
Disulfiram – GHB
Nx/GHB - escitalopram

Key Points

Naltrexone was the drug most frequently combined with other agents to reduce alcohol consumption.

No combination of drugs has demonstrated a significantly larger treatment effect when compared with the individual components of the combination.

Targeting combined pharmacological interventions to address specific symptoms of alcohol use disorder known to be influenced by combination components may prove more successful than initiating treatment for alcohol consumption only.

Guerzoni, S., Pellesi, L., Pini, L. A., & Caputo, F. (2018). **Drug-drug interactions in the treatment for alcohol use disorders: a comprehensive review**. *Pharmacological research*, *133*, 65-76.

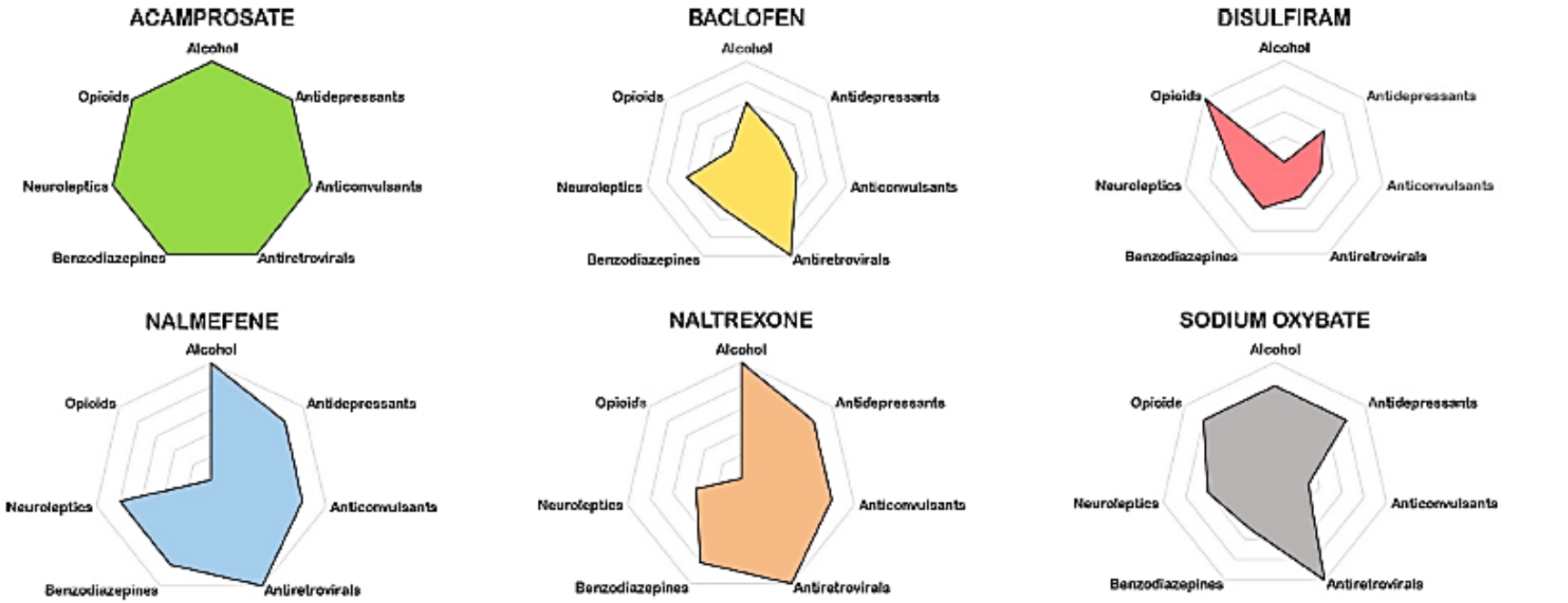

Fig. 1. Radar charts showing the potential combination of pharmacological treatments of alcohol dependence with several classes of medications. The data length of a spoke is proportional to the magnitude of the potential association between the two drugs. A line connect the data values for each spoke.

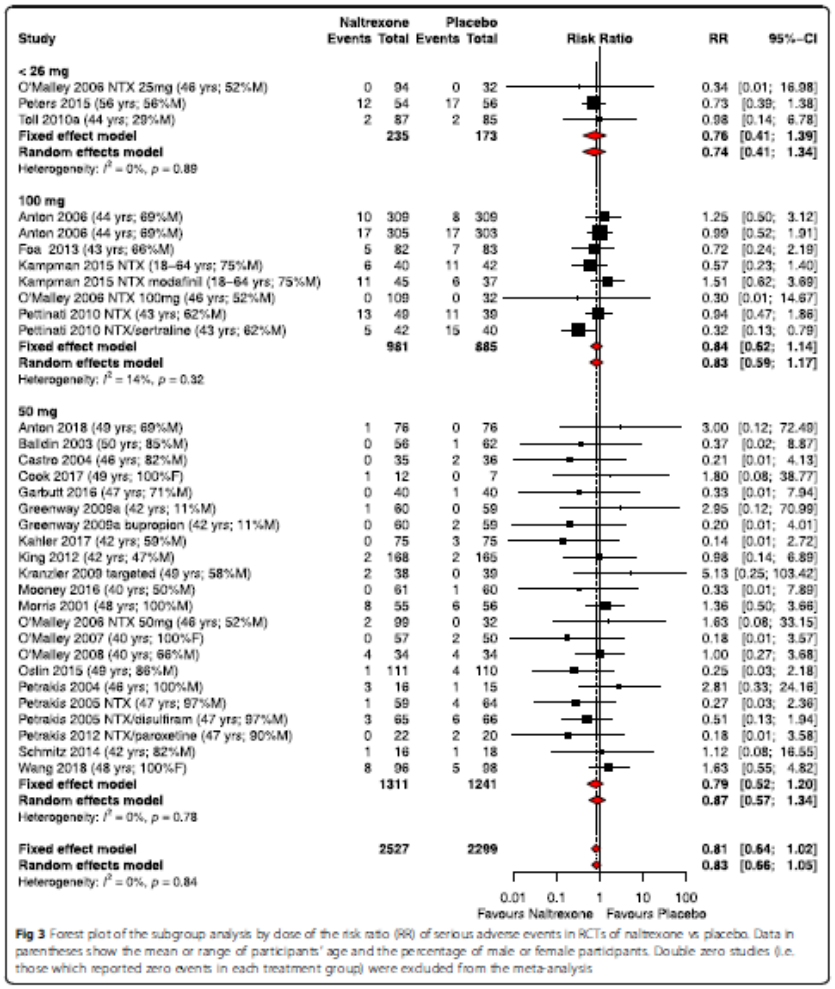

Fig 3 Forest plot of the subgroup analysis by dose of the risk ratio (RR) of serious adverse events in RCTs of naltrexone vs placebo. Data in parentheses show the mean or range of participants' age and the percentage of male or female participants. Double zero studies (i.e. those which reported zero events in each treatment group) were excluded from the meta-analysis

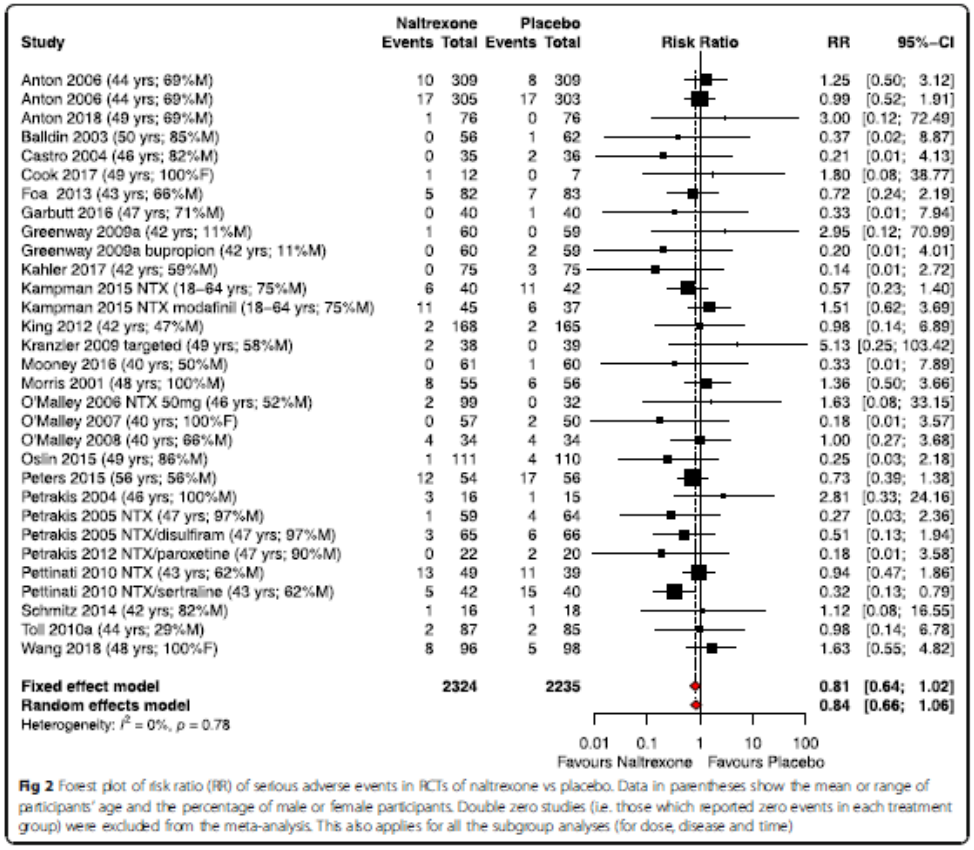

Fig 2 Forest plot of risk ratio (RR) of serious adverse events in RCTs of naltrexone vs placebo. Data in parentheses show the mean or range of participants' age and the percentage of male or female participants. Double zero studies (i.e. those which reported zero events in each treatment group) were excluded from the meta-analysis. This also applies for all the subgroup analyses (for dose, disease and time)

Bolton *et al. BMC Medicine* (2019) 17:10
https://doi.org/10.1186/s12916-018-1242-0

BMC Medicine

RESEARCH ARTICLE Open Access

Serious adverse events reported in placebo randomised controlled trials of oral naltrexone: a systematic review and meta-analysis

CLINICAL GUIDELINES
CNS Neuroscience & Therapeutics

Pharmacotherapy for Alcohol Dependence: The 2015 Recommendations of the French Alcohol Society, Issued in Partnership with the European Federation of Addiction Societies

Benjamin Rolland,[1,2] François Paille,[1,3] Claudine Gillet,[1,4] Alain Rigaud,[1,5,6] Romain Moirand,[1,7,8] Corine Dano,[1,9] Maurice Dematteis,[1,10] Karl Mann[11,12] & Henri-Jean Aubin[1,12,13]

CNS Neuroscience & Therapeutics 22 (2016) 25–37

Table 5 Recommendations issued on the management of abstinence maintenance (question 12 of the GPRs)

#	Recommendation	Grade
12.4	Medications for relapse prevention should be automatically associated with adapted psychosocial support in patients with alcohol-dependence	A
12.5	Increased compliance with medications improves therapeutic efficacy	EC
12.6	Acamprosate or naltrexone are the first-line treatment for supporting relapse prevention	A
12.7	Disulfiram can be proposed as second-line treatment in patients motivated to sustain abstinence, correctly informed of the risk of the antabuse effect, and adequately supervised	EC
12.8	The second-line prescription of baclofen for preventing relapse among alcohol-dependent patients has been authorized by a "temporary recommendation for use" (TRU) up to the dose of 300 mg/day, and requires the online reporting of patients' follow-up on the TRU portal. Doses should be increased and decreased slowly according to efficacy and tolerability	EC

Each recommendation was graded from A to C using the methodological tool published by the Haute Autorité de Santé (HAS), i.e., the French High Authority for Health [14], according to the level of evidence of the studies on which the recommendation was based (see Table 1). EC = 'expert consensus', i.e., recommendations based on consensual expert opinion when no study was available; GPRs = 'good practice recommendations'.

- **Farmaci e intervento psico-sociale devono essere associati**
- **Acamprosato e natrexone sono la prima linea**
- **Disulfiram è una seconda linea**
- **Baclofene è una seconda linea soggetta a restrizioni**

Quali novità?

- Non nelle terapie farmacologiche o non farmacologiche

ma

Nel modo di usare gli elementi nel trattamento dei diversi modelli del bere:

- Nella differenziazione degli obiettivi (astensione, riduzione, bere controllato, riduzione del danno)
- Nel diverso utilizzo dei biomarkers
- Nell'introduzione della tecnologia nel trattamento

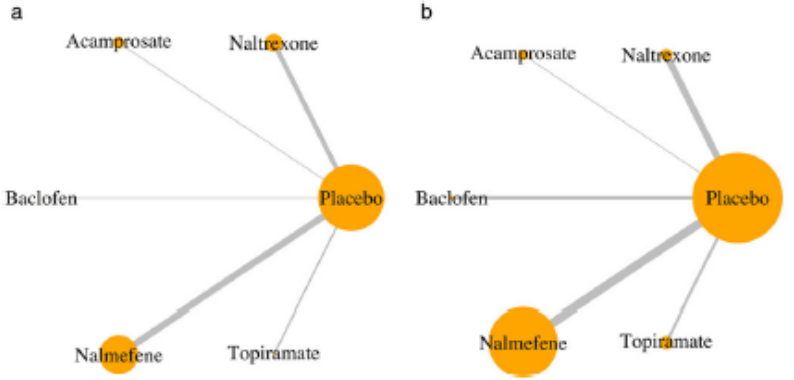

Figure 3 Network geometry for the total alcohol consumption outcome (a) and the withdrawals for safety reasons outcome (b). Each node is proportional to the number of patients for whom the outcome is available. Each edge is proportional to the number of studies for which the comparison is available.

There is currently **no high-grade evidence for pharmacological treatment to control drinking using nalmefene, naltrexone, acamprosate, baclofen or topiramate in patients with alcohol dependence or alcohol use disorder.** Some treatments show low to medium efficacy in reducing drinking across a range of studies with a high risk of bias. None demonstrates any benefit on health outcomes.

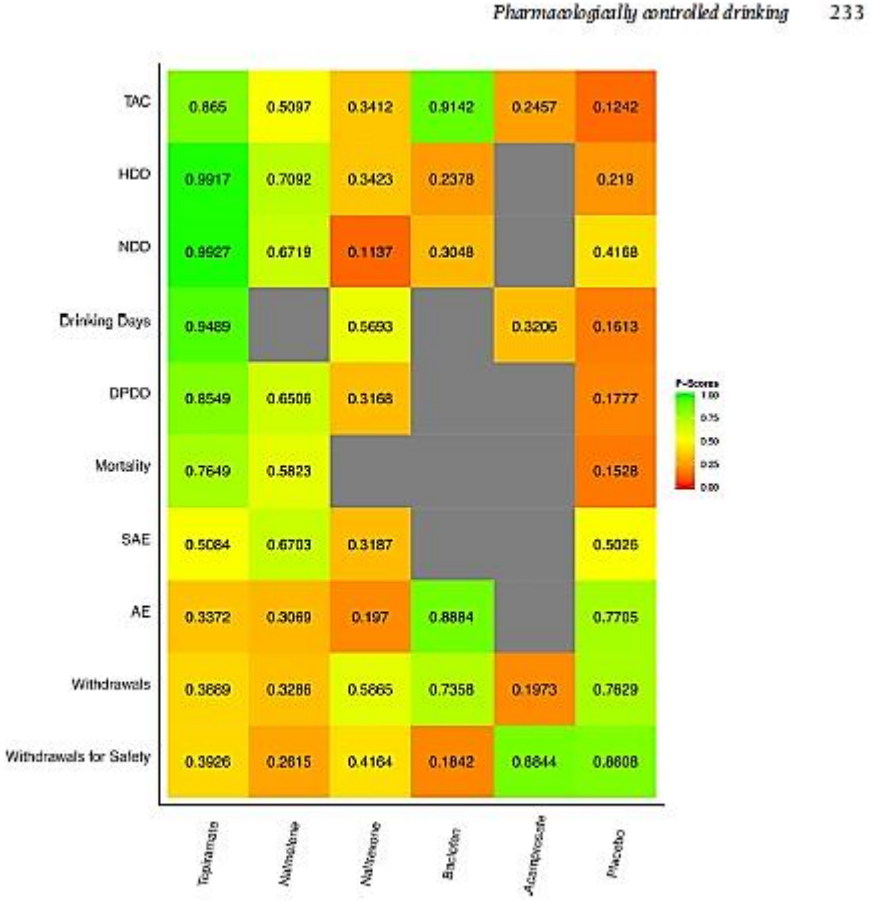

Figure 4 P-scores estimations. P-scores are values comprised between 0 and 1 that measure the mean extent of certainty that a treatment is better than the competing treatments. The closer to 1 the P-score, the better the treatment. TAC = Total alcohol consumption; HDD = Heavy drinking days; NDD = Non drinking days; DPDD = Drinks per drinking day; SAE = Serious adverse events; AE = Adverse events.

Palpacuer, C., Duprez, R., Huneau, A., Locher, C., Boussageon, R., Laviolle, B., & Naudet, F. (2018). **Pharmacologically controlled drinking in the treatment of alcohol dependence or alcohol use disorders: a systematic review with direct and network meta-analyses on nalmefene, naltrexone, acamprosate, baclofen and topiramate.** *Addiction*, *113*(2), 220-237.

CLINICAL GUIDELINES
CNS Neuroscience & Therapeutics

Pharmacotherapy for Alcohol Dependence: The 2015 Recommendations of the French Alcohol Society, Issued in Partnership with the European Federation of Addiction Societies

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CNS Neuroscience & Therapeutics 22 (2016) 25–37

Table 7 Recommendations issued on the management of treatment for alcohol dependence in specific populations, i.e., pregnant women, children and adolescents, elderly adults, and individuals with comorbid alcohol-related physical conditions or comorbid psychiatric and substance use disorders (question 16 of the GPRs)

#	Recommendation	Grade
16.2	Abstinence throughout pregnancy is recommended for any pregnant women	EC
16.4	If medically assisted withdrawal is necessary during pregnancy, using BZDs is recommended	B
16.5a	No treatments other than those for alcohol withdrawal should be initiated in pregnant or breastfeeding women	EC
16.5b	In the event of a pregnancy occurring in a patient obviously stabilized by a medication for supporting abstinence, the continuation of the drug should be considered on a case by-case basis, weighing up the benefit/risk ratio.	EC
16.5c	Disulfiram is an exception, and it should be always stopped during pregnancy, to the unknown risks on the fetus of the antabuse effect	EC
16.7a	Any adolescent with alcohol dependence under the age of 16 should undergo a pediatric psychiatric assessment	C
16.7b	In the case of alcohol dependence occurring under the age of 16, the objective of abstinence should be preferred	EC
16.7c	First line treatments to help maintain abstinence or reduce drinking are off-label, and should thus be considered on a case-by-case basis, after repeated failure of psychosocial measures alone.	EC
16.8a	In elderly patients with alcohol-dependence, it is preferable to conduct the detoxification process in a hospital setting	EC
16.8b	Short half-life benzodiazepines should be preferred for detoxification in elderly patients	B
16.8c	Initial doses of benzodiazepines should be reduced by 30 to 50% in elderly patients	EC
16.8d	Psychosocial support should be particularly emphasized in elderly patients with alcohol dependence	B
16.10	In patients with chronic alcohol-related physical disorders, a goal of abstinence is recommended	EC
16.11	Antidepressants or anxiolytic medication should be introduced only after reassessment of the psychiatric state, after 2–4 weeks of alcohol abstinence or low-risk use	B
16.12	A smoking cessation program should be systematically offered to smokers when they are giving up alcohol, in either a hospital or an outpatient setting	B

Each recommendation was graded from A to C using the methodological tool published by the Haute Autorité de Santé (HAS), i.e., the French High Authority for Health [14], according to the level of evidence of the studies on which the recommendation was based (see Table 1). EC = 'expert consensus', i.e., recommendations based on consensual expert opinion when no study was available; GPRs = 'good practice recommendations'.

Margret, C. P., & Ries, R. K. (2016). **Assessment and treatment of adolescent substance use disorders: alcohol use disorders.** *Child and Adolescent Psychiatric Clinics*, *25*(3), 411-430.

The pharmacotherapy of alcohol use disorders is a less travelled path for adolescents, unlike the aggressive options available for adult population owing to the

(i) Differential patterns of use including binge drinking patterns that offset withdrawal or dependence states,
(ii) emergence of disordered drinking in later adolescence or young adulthood,
(iii) **developing brain systems**, and
(iv) **limited research on safety and efficacy of drug trials among adolescents**.

However, medications are still considered pertinent because of alcohol-related plasticity on reward function, frontal lobe–related inhibition, and a limbic system that succumbs easily to cues and results in relapse. Medication precludes toxic states like withdrawal and detoxification, reduces craving, prevents relapse, and manages comorbid psychiatric and medical problems, which tend to perpetuate chronic alcohol use. The use of medications among adolescents is a judicious call, with caution to not replicate use on the basis of treating adolescents like “miniature adults.”

"Naltrexone, acamprosate, and disulfiram are US Food and Drug Administration-approved for treating AUD in adults over age 18, and the Substance Abuse and Mental Health Services Administration recommends considering medications for adolescents under age 18"

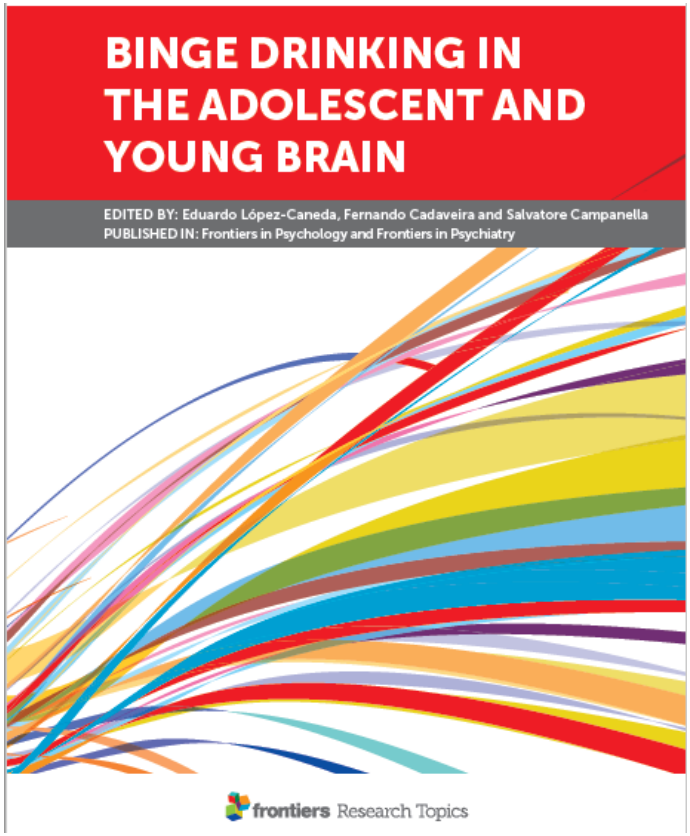
MEDICATIONS FOR ALCOHOL USE DISORDER AMONG MEDICAID ENROLLED YOUTH, 2011-2016
Joel Earlywine, BA, Sarah Bagley, MD, MSc , Jonathan Rodean, MPP , Bonnie T. Zima, MD, MPH, Nicholas Chadi, MD, MPH, Douglas Leslie, PhD , Scott E. Hadland, MD, MPH, MS Platform Research Presentations / Journal of Adolescent Health 66 (2020) S1eS22

4,064,195 Medicaid-enrolled youth using Truven MarketScan data from 16 states between January 2011 and December 2016. We included youth aged 13-22 years with 6 months continuous enrollment who received a diagnosis of AUD.

10,426 youth diagnosed with AUD
4.3% (n 168) were dispensed an AUD medication. Of those receiving medication, 86.3% received naltrexone, 8.9% received acamprosate, and 4.8% received disulfiram.

Solo 1:3 riceve un trattamento
1:45 un trattamento farmacologico

AOR rispetto ai > 21 aa. 13-15 aa 0.25 16-17 aa. 0.36
Maggiore tra i non ispanici neri
Maggiore nelle femmine
Maggiore tra coloro con un altro DUS (il più basso per la cannabis)



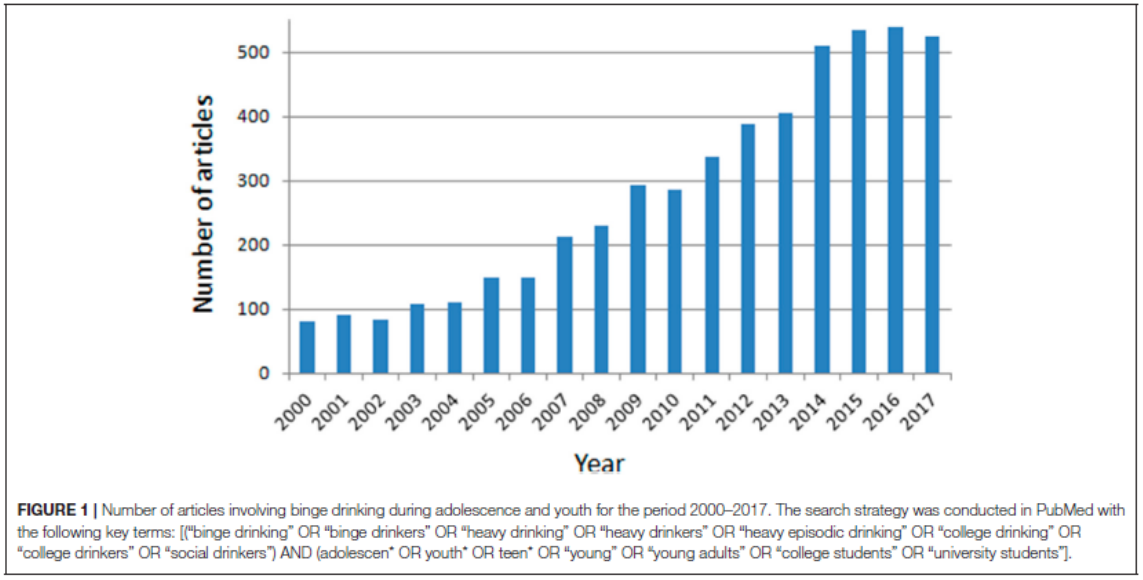


FIGURE 1 | Number of articles involving binge drinking during adolescence and youth for the period 2000–2017. The search strategy was conducted in PubMed with the following key terms: [("binge drinking" OR "binge drinkers" OR "heavy drinking" OR "heavy drinkers" OR "heavy episodic drinking" OR "college drinking" OR "college drinkers" OR "social drinkers") AND (adolescen* OR youth* OR teen* OR "young" OR "young adults" OR "college students" OR "university students"].

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

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[1,2], William R. Corbin, PhD[3], Robert F. Leeman, PhD[1], Kelly S. DeMartini, PhD[1], Lisa M. Fucito, PhD[1], Jolomi Ikomi, MD[1], Denise M. Romano, APRN[1], Ran Wu, MS[1], Benjamin A. Toll, PhD[1,2], Kenneth J. Sher, PhD[4], Ralitza Gueorguieva, PhD[5], and Henry R. Kranzler, MD[6]

Naltrexone did not reduce frequency of drinking or heavy drinking days, but reduced secondary measures of drinking intensity. While effects were modest, the risk-benefit ratio favors offering naltrexone to help young adult heavy drinkers reduce their drinking (anni 18-25)

Alcohol—There are only a handful of published reports on pharmacotherapy for adolescent drinking. Most are case studies or open label trials, and all reports bear substantial limitations that preclude inferences about the efficacy of the medication studies. In terms of RCTs, there are no adequately powered trials with adolescents younger than 18 years. One recent well-designed RCT of naltrexone with young adult drinkers, ages 18 to 25 years, showed naltrexone (25mg daily + 25mg targeted) plus a brief motivational intervention reduced the number of drinks per drinking day by the end of the 8-week treatment period (38). At the 12-month follow-up assessment, there were no differences between conditions but drinking reductions observed during the active treatment phase were maintained (39).

Curr Addict Rep. 2016 June ; 3(2): 145–156. doi:10.1007/s40429-016-0098-7.

Emerging Pharmacologic Treatments for Adolescent Substance Use: Challenges and New Directions

Robert Miranda Jr. and Hayley Treloar
Center for Alcohol and Addiction Studies, Brown University.

Addiction è un circolo a 3 stadi:
Binge/intossicazione
Astinenza/sentimenti negativi
Preoccupazione/anticipazione

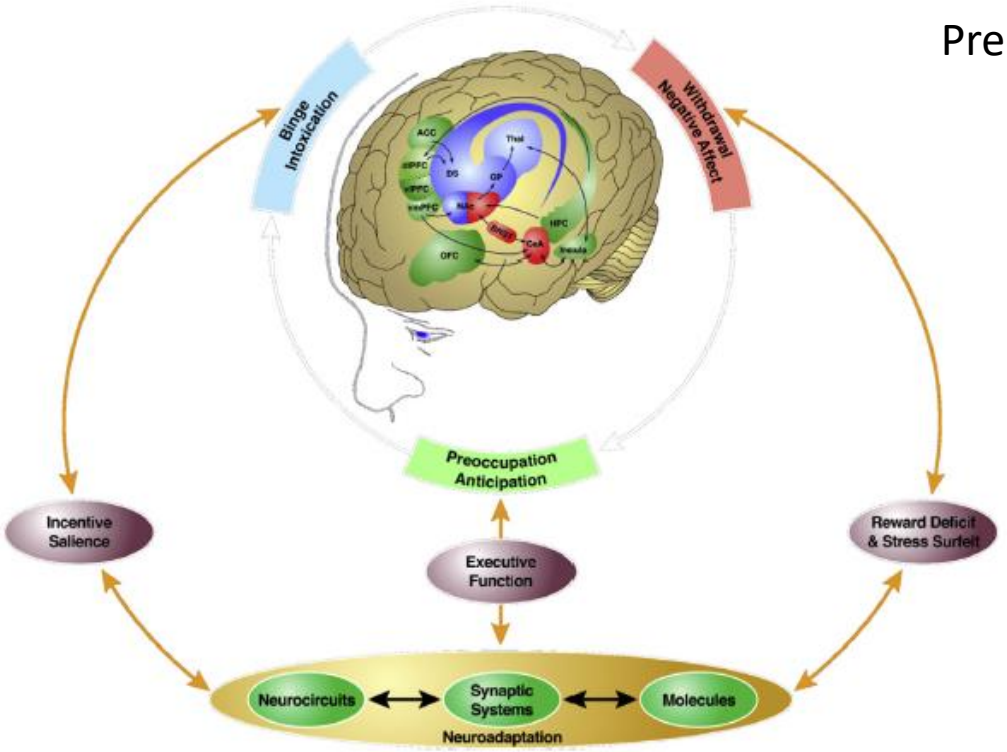
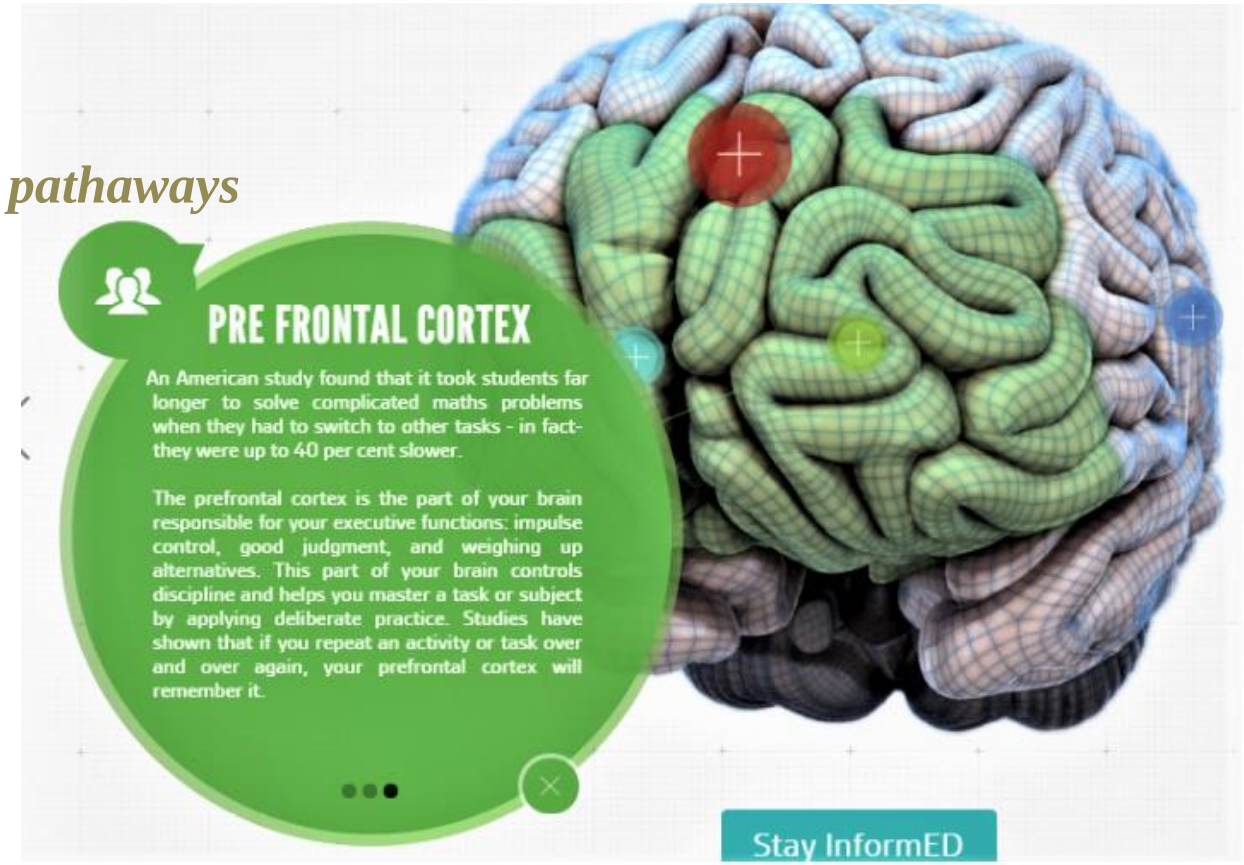


Fig. 1. Neurobiological-based framework for the stages of addiction. A three-stage cycle of alcohol addiction, affecting synaptic-neurocircuitry and molecular-genetic systems, is shown. The brain regions are color coded to correspond to the relevant stage. ACC, anterior cingulate cortex; PFC, prefrontal cortex; DS, dorsal striatum; GP, globus pallidus; Thal, thalamus; NAc, nucleus accumbens; BNST, basal nucleus of the stria terminalis; CeA, central nucleus of the amygdala; HPC, hippocampus; OFC, orbitofrontal cortex; Insula, insular cortex. (The figure was modified from Volkow ND and Koob G, Brain disease model of addiction: why is it so controversial? *Lancet Psychiatry*, 2: 677–679, 2015).

it's the place of cognitive executive functions

That regulates and control

- *Impulsivity*
- *judgment*
- *Alternative options*
- *Projects to memory pathaways (voluntary and procedural)*



Limbic System

It is a set of cortical and subcortical areas related to emotional regulations, motivation, learning and memory

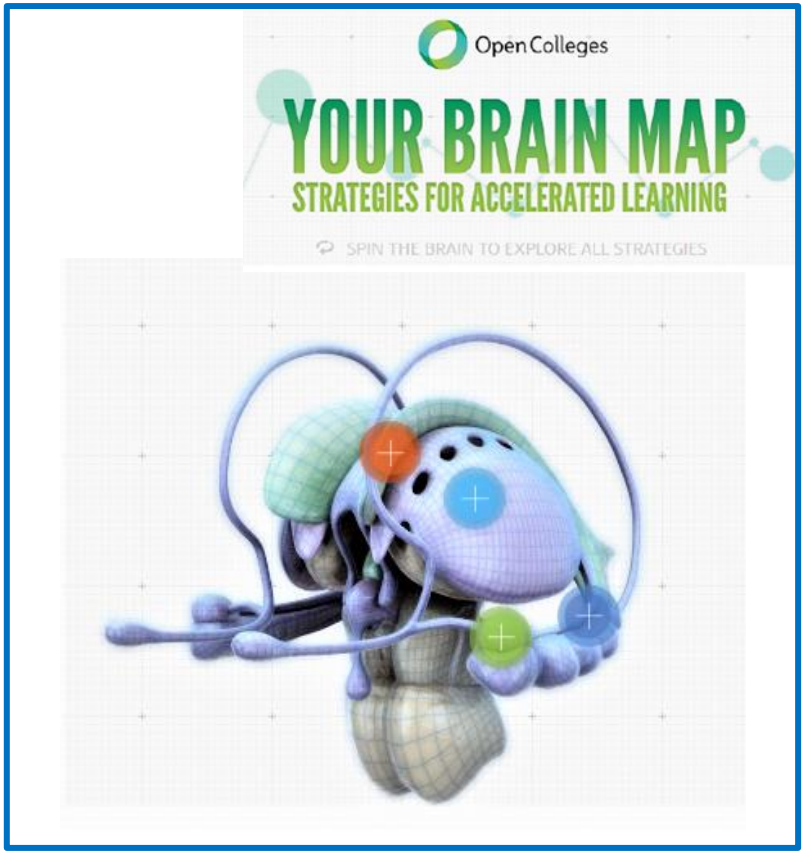
Lobo limbico

Ippocampo

- *learnig*
- *Memories formation and retrieval*
- *Adult neurogenesis*

Amigdala

- *Alearning and emotional learning*
- *fear*
- *reward*



Neuron 69, February 24, 2011 ©2011 Elsevier Inc.

600 Neuron 69, February 24, 2011 ©2011 Elsevier Inc.

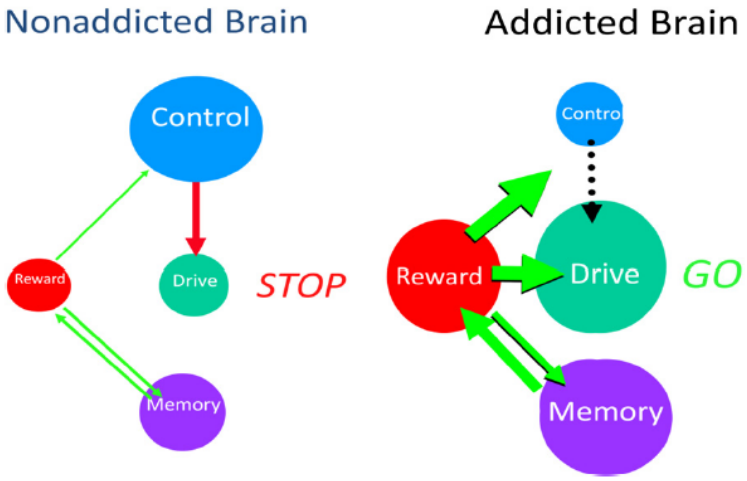
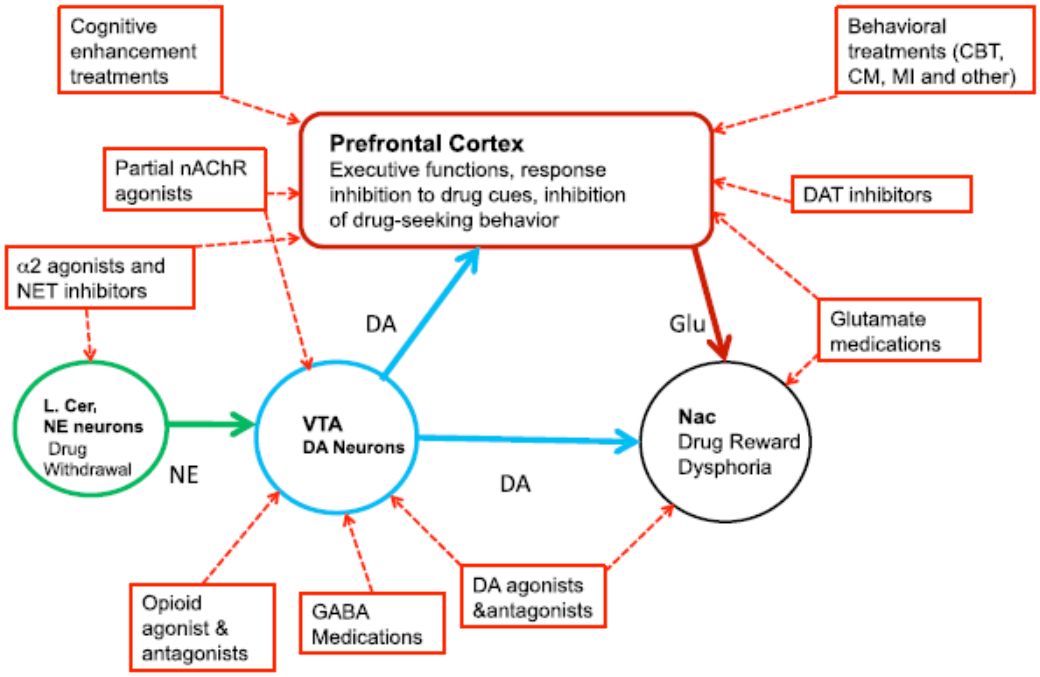


Figure 1. Model Proposing a Network of Four Circuits Involved with Addiction: Reward, Motivation/Drive, Memory, and Control

These circuits work together and change with experience. Each is linked to an important concept: reward (value of positive and negative reinforcers), drive (incentive motivation), memory (learned associations conditioning), and control (conflict resolution). During addiction, the enhanced value of the drug in the reward, motivation, and memory circuits overcomes the inhibitory control exerted by the prefrontal cortex, thereby favoring a positive-feedback loop initiated by the consumption of the drug and perpetuated by the enhanced activation of the motivation/drive and memory circuits (reprinted with permission [Volkow et al., 2003]).



Definizioni di binge drinking

- NIAAA pattern che porta la BAC > 0.08% 4 UA per F e 5 UA per M in 2 h (considera la velocità)
- SAMSHA 4 UA per F e 5 UA per M nella stessa occasione, almeno 1 volta negli ultimi 30 g

  Heavy drinking: binge drinking in 5 o più giorni sugli ultimi 30
- WHO heavy episodic drinking consumo superiore a 60 gr o più in almeno una occasione negli ultimi 30 gg (almeno 1 volta al mese)

- I criteri del NIAAA sembra tendano a identificare pattern e gravità maggiori (Rolland, 2017)

Binge Drinking: Predictors, Patterns, and Consequences. Alcohol Research: *Current Reviews* **Vol. 39, No. 1, 2018**

binge behaviour

- ***Extreme binge drinking o high-intensity drinking***

  oltre 2 o più volte la soglia del binge secondo il genere (Level II e III)

FOR IMMEDIATE RELEASE - NIAAA

Wednesday, May 17, 2017

Study finds tens of millions of Americans drink alcohol at dangerously high levels (Hingson, RW, Zha, W, White, A. M. Drinking Beyond the Binge Threshold: Predictors, Consequences, and Changes in the U.S. Am. J. Prev. Med. Online May 17, 2017)

The current study analyzed three levels of past-year binge drinking – Levels I, II, and III.

- **Level I** were defined as four to seven drinks per F, and five to nine drinks per M (56-98g and 70-126g)
- **Level II** eight to 11 drinks per F, 10-14 drinks per M (112-154g and 140-196g)
- **Level III** 12 or more drinks per F and 15 or more drinks on a single occasion for men(>168g and >210g)

- The researchers found that in the 2012–2013 survey, 39% of adult males and 27 % of adult females reported binge drinking during the previous year.
- 11% dei maschi riportavano Level II binge drinking almeno 1 volta nell'anno e 7% riportavano Level III binge drinking. 5% delle femmine riportavano un Level II binge drinking e 3% un Level III binge drinking

Table 3
Gender- and age-adjusted bivariable logistic regression analyses comparing subjects meeting the NIAAA (BD2 group) vs. the exclusive WHO (BD1 group) criteria for binge drinking.

	aOR [95%CI]	p-value
Marital status *(vs. having with a partner)*		
– separated/divorced/widowed	1.81 [1.31–2.50]	< 0.0001
– single	1.64 [1.36–1.98]	< 0.0001
Educational status *(vs. UPE)*		
–USE	0.76 [0.68–0.99]	0.041
–CSE	0.64 [0.50–0.82]	0.001
Occupational status *(vs. active)*		
–unemployed	1.57 [1.27–1.90]	< 0.0001
–retired	0.51 [0.23–0.79]	< 0.0001
Drinking frequency * (AUDIT-C) *(vs. less than once per month)*		
– 2-4 times per month	1.23 [1.01–1.50]	0.043
– 2-3 times per weeks	1.79 [1.44–2.23]	< 0.0001
Average drinks per occasion (AUDIT-C) *(vs. 1–2 drinks)*		
– 3 or 4 sds	1.47 [1.20–1.80]	< 0.0001
– 5 or 6 sds	2.50 [2.00–3.14]	< 0.0001
– 7–9 sds	5.38 [3.88–7.45]	< 0.0001
– 10 sd or more	6.53 [4.63–9.21]	< 0.0001
HDD Frequency (AUDIT-C) *(vs. less than once a month*		
– once a month	2.69 [2.07–3.21]	< 0.0001
– once a week but less than 4 times a week	5.67 [4.04–7.15]	< 0.0001
Average drinking > 15/10 drinks per week *(Yes vs. No)*	5.25 [3.13–7.33]	< 0.0001
Positive CAGE questionnaire *(Yes vs. No)*	2.09 [1.75–2.50]	< 0.0001
Previous guilt or remorse (RAPS4) *(Yes vs. No)*	1.83 [1.54–2.18]	< 0.0001
Previous remarks from family (RAPS4) *(Yes vs. No)*	3.00 [2.53–3.56]	< 0.0001
Ever failed to do what expected (RAPS4) *(Yes vs. No)*	2.49 [1.92–3.24]	< 0.0001
Ever alcohol use on waking-up (RAPS4) *(Yes vs. No)*	2.05 [1.37–2.72]	< 0.0001
Medical reason for admission *(vs. other cause)*		
– Physical (injury, fall, aggression, …)	1.34 [1.14–1.58]	0.001
– Behavioral (psychiatric, drunkenness, …)	2.27 [1.68–3.07]	< 0.0001

Subjects with ≥4 drinking episodes per week were excluded from the analyses, using the AUDIT-C questionnaire. This procedure aimed to exclude subjects with regular heavy

Comparison between the WHO and NIAAA criteria for binge drinking on drinking features and alcohol-related aftermaths: Results from a crosssectional study among eight emergency wards in France,Benjamin Rolland et al., *Drug and Alcohol Dependence 175 (2017) 92–98*

	NoBD n = 6657	BD1 n = 1826	BD2 n = 1042
Age (years) m ± SD	47.7 ± 21.8	33.4 ± 13.8 29	29.0 ± 12.3
n = 9525 med [IQR]	45 [29–65]	30 [23–42]	24 [20–35]
Gender (% females) *n = 9525*	42.9%	31.1%	29.9%
Under 18 s (%) *n = 450*	4.4%	3.5%	8.7%

BD vs noBD

Più giovani, più maschi, più disturbi psichiatrici

NIAAA-BD vs WHO-BD

- **Frequenza, quantità media, frequenza di HDD**
- **Conseguenze**
- **frequenza di accesso in PS per problematiche psichiatriche e comportamentali**

Target diversi con diverse vulnerabilità?

Pattern di assunzione

Binge behaviour episodi di BD alternati a periodi di astensione più o meno lunghi (episodic heavy use)

Binge Drinking: Predictors, Patterns, and Consequences Alcohol Research: *Current Reviews* **Vol. 39, No. 1, 2018**

valid definitions of BD require not only specific features of the drinking patterns, such as **drinking intensity per drinking occasion**, but also **frequency** of BD behaviors and periods of abstinence between binging episodes. Moreover, recent data suggest that **BD is a heterogeneous phenotype**. Consequently, binge drinkers should not be considered as a unitary group, but rather as a **heterogeneous population of individuals displaying particular gender and personality dimensions** (Gierski et al., 2017), **as well differences in drinking motives and impulsivity** (Lannoy et al., 2017a).

Jeanblanc J, Rolland B, Gierski F, Martinetti MP, Naassila M, Animal models of binge drinking, current challenges to improve face validity, *Neuroscience and Biobehavioral Reviews, 106,* (2019),

Elementi di ambiguità per i modelli animali di BD

- Quantità (diversa metabolizzazione che richiede diverse quantità per intox)
- Frequenza (esclusione del criterio dipendenza)
- Durata (criterio più importante per distinguere BD da HD)

A cosa si può servire lo studio di modelli animali di BD

- vulnerabilità allo sviluppo di dipendenza
- compromissioni delle funzioni cognitive (funzioni esecutive, memoria)
- differenze di genere in queste aree
- compromissioni epatiche

Jeanblanc J, Rolland B, Gierski F, Martinetti MP, Naassila M, Animal models of binge drinking, current challenges to improve face validity, *Neuroscience and Biobehavioral Reviews, 106,* (2019),

Jeanblanc J, Rolland B, Gierski F, Martinetti MP, Naassila M, Animal models of binge drinking, current challenges to improve face validity, *Neuroscience and Biobehavioral Reviews, 106,* (2019),

Table 1. *Title*: Criteria for an animal model of BD.

Items	Criteria for an animal model of BD
1.	Voluntary intake / oral ingestion (without food deprivation or sugar adulteration)
2.	Quantity (>0.08g/dl) / visible signs of behavioral intoxication
3.	Fast intake
4.	Duration (at least subchronic)
5.	Frequency / intermittence (few days off)
6.	Brain damages/cognitive deficits and somatic damages (such as on liver)
7.	Large inter-individual variability

CNS Drugs (2017) 31:181–186
DOI 10.1007/s40263-017-0413-4

CrossMark

CURRENT OPINION

Binge Drinking: Current Diagnostic and Therapeutic Issues

Benjamin Rolland[1] · Mickaël Naassila[1]

Key Points

The concept of BD is increasing worldwide but actually encompasses very heterogeneous populations.

The official BD definitions do not address the psychosocial and medical consequences of the type of alcohol use seen in BD, which determine the diagnosis and the required type of intervention.

Early occurrence of harmful alcohol use is associated with poorer outcome and could thus warrant early pharmacotherapy; however, only naltrexone has been investigated in harmful use of alcohol to date, but not in adolescents.

The case of BD is paradoxical, especially among adolescents and young adults. Situations of BD that meet the criteria for HUA or alcohol abuse theoretically indicate a less severe disorder than a diagnosis of alcohol dependence.
However, when it occurs in adolescents or very young adults, HUA is known to be associated with many more risk factors than in adults

Principi del Contingency Management

- CM-based treatments for SUDs originate in basic behavioral science, namely the operant-conditioning literature. Operant conditioning is a type of learning where the operant (ie, behavior) is maintained or modified via behavioral consequences (positive/negative reiforcement, positive/negative punishment).

- Grado del rinforzo
- Immediatezza del rinforzo
- importanza del rinforzo

} Delay discounting

- Dare un rinforzo tangibile ed immediato in presenza di un comportamento positivo/negativo verificabile

J Subst Abuse Treat. 2017 January ; 72: 10–18. doi:10.1016/j.jsat.2016.09.008.

Contingency management: New directions and remaining challenges for an evidence-based intervention

Carla J. Rash, PhD[1,*], Maxine Stitzer, PhD[2], and Jeremiah Weinstock, PhD[3]

Highlights

- Contingency management (CM) is an efficacious intervention for substance use disorders.
- Clinical uptake is not commensurate with evidence for efficacy.
- CM is appropriate for and generalizable to a wide range of patient characteristics.
- Technology and designs sensitive to clinic constraints may further speed adoption efforts.

Open Access Full Text Article REVIEW

A review of contingency management for the treatment of substance-use disorders: adaptation for underserved populations, use of experimental technologies, and personalized optimization strategies Substance Abuse and Rehabilitation 2018:9 43–57

ETG urinario

Applicabilità migliorata con utilizzo tecnologia sperimentale:

Monitoraggio alcol trandermico
Monitoraggio via breathanalyzer e registrazione via cell
Monitoraggio aderenza via remoto etc…

Ghosh et al. Int Arch Subst Abuse Rehabil 2019, 1:002

Biomarker di consumo

Table 1: Sensitivity, specificity, drinking behaviour and window of assessment of alcohol biomarkers [7,8,23,65,73].

Biomarkers	Sample Source	Sensitivity%	Specificity%	Drinking Behaviour	Window of Assessment
GGT	Serum/Plasma	40-50	80-90	Chronic Heavy Drinking	2-3 weeks
MCV	Blood	60-90	30-75	Chronic Heavy Drinking	2-4 months
ALT/AST	Serum/Plasma	15-69	50-95	Chronic Heavy Drinking	2-3 weeks
CDT	Serum/Plasma	80-90	85-95	Heavy alcohol use	2-3 weeks
5-HTOL	Urine	n/a**	n/a**	Recent Use	5-20 hours
PEth	Blood	80-90	90-95	Heavy alcohol use*	2-4 weeks
FAEE	Serum	> 75	> 75	Recent Use	2-3 days
FAEE	Hair	100	90	Chronic Heavy Drinking	Several Months depending upon hair length
EtG	Urine	73-75	55-60	Recent Use	2-5 days
EtG	Hair	70-90	80-95	Chronic Heavy Drinking	Several Months depending upon hair length

*= more than 60 grams per day (4-5 standard drinks); **n/a = data not available.

Rilevazioni di consumo. What's new?

Self report

- **Retrospettivi** **TLFB** (Timeline Followback)
  più utile a definire il pattern di uso che il consumo in sé
- **Prospettici** **EMA** (Ecological Momentary Assesment)
  diari giornalieri
  ESM (Experience Sampling Method)

Sostanzialmente validi, ma soggetti a imprecisa valutazione del grado di intossicazione (variabili di rilevazione, variabili metaboliche etc.) e del pattern del suo sviluppo (cinetica del BAC)

Simons, J. S., Wills, T. A., Emery, N. N., & Marks, R. M. (2015). **Quantifying alcohol consumption: Self-report, transdermal assessment, and prediction of dependence symptoms.** *Addictive behaviors*, *50*, 205-212.

Addictive Behaviors 50 (2015) 205–212

Contents lists available at ScienceDirect

Addictive Behaviors

ELSEVIER

Quantifying alcohol consumption: Self-report, transdermal assessment, and prediction of dependence symptoms☆

Jeffrey S. Simons [a,*], Thomas A. Wills [b], Noah N. Emery [a], Russell M. Marks [a]

H I G H L I G H T S

- Research participants can provide valid self-reports of alcohol use.
- Transdermal alcohol assessment (WrisTAS) provides objective alcohol monitoring.
- Individual drinking dynamics are associated with alcohol use disorder.
- Experience sampling, TLFB , and WrisTAS assessments show convergent validity.

Rilevazione in setting naturalistico - EMA

EMA ⟹ collezione di dati attraverso auto-rilevazioni frequenti e ripetute associate o meno a rilevazione di altri parametri

- Schedulazioni fisse (time based)
- Schedulazioni correlate ad evento (event based)

Rilevazione uso:

Calcolo in base alla rilevazione di eBAC (estimated BAC)

- app su smartphone
- Breathanalyzer connesso allo smartphone
- Validità della rilevazione in funzione del eBAC?
- Validità della correlazione con self-report retrospettivo?

Piasecki, T. M. (2019). Assessment of alcohol use in the natural environment. *Alcoholism: clinical and experimental research*, *43*(4), 564-577.

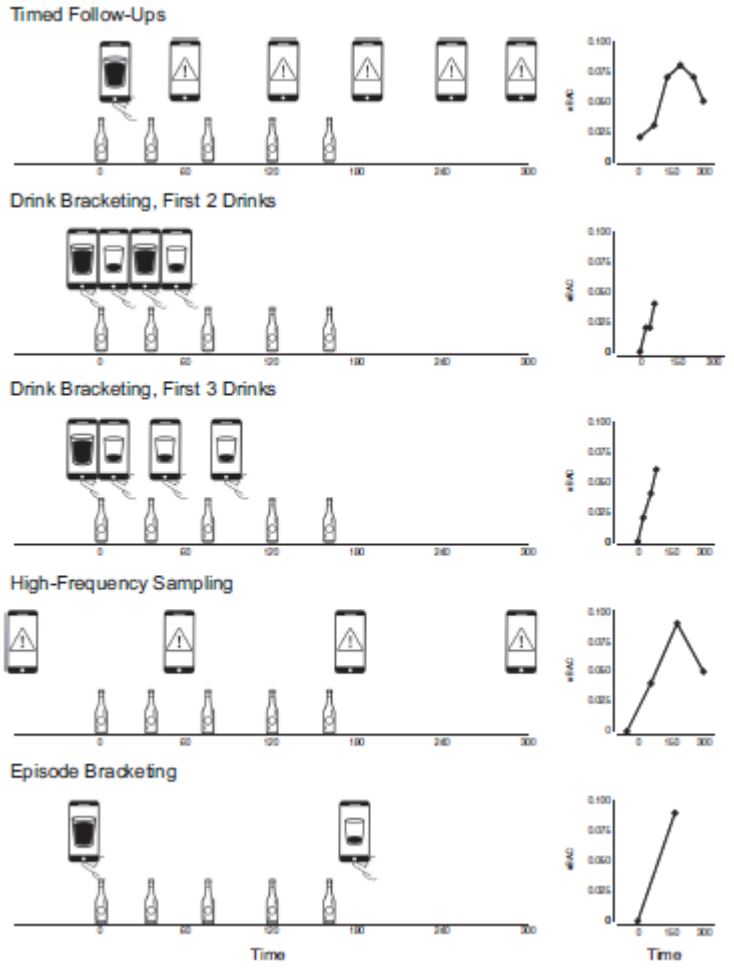
High-Resolution EMA Designs

- timed follow-ups (primo drink poi prompt su allarme)
- drink bracketing (promt prima e dopo il drink)
- high-frequency sampling (promt ravvicinati in funzione della probabilità)
- episode bracketing (prompt pre-post)

Lower-Resolution EMA Designs

- Prompt a tempi predeterminati a tempi distanziati

Molte informazioni missed vengono in genere richieste nel report post-episodio



Piasecki, T. M. (2019). Assessment of alcohol use in the natural environment. *Alcoholism: clinical and experimental research*, *43*(4), 564-577.

- La compliance è in genere abbastanza alta
- La comparazione tra EMA drinking data in adolescenti rispetto a TLFB ha mostrato forte correlazione per numero totale di drink, numero per DD e numero di HDD
- Viene spesso accoppiato con un incentive
- Utilizzato in studi clinici sino ad ora con qualche risultato

L'associazione degli EMA con device è un'area nascente di grande interesse : TAS è in grado di descrivere con precisione la curva discendente della BAC stimata perché non si interrompe di notte e fa un monitoraggio passivo e continuo

Piasecki, T. M. (2019). Assessment of alcohol use in the natural environment. *Alcoholism: clinical and experimental research*, *43*(4), 564-577.

sensori transdermici (TAS)

- Metodo passivo
- Relazione complessa di TAC con BAC e BrAC
- Variabilità per caratteristiche cute
- Variabilità per caratteristiche device

- Logoramento/errore sensore
- Manomissioni sensore
- Esposizione ad alcol ambientale
- Rimozione del device
- Tende a non rilevare bassi consumi

Sensori transdermici per la rilevazione dell'alcol (TAS)

Compliance

Nei pochi studi
- non viene indossato (6-10%)
- viene manomesso (34%)
- Si rifiuta di indossarlo (9%)
- non funziona (5-18% dei gg)

scomodità
interferenza con attività fisica
stigma

Various parameters of TAS data
- peak TAC level
- time to peak
- area under the TAC curve

are robustly related to BrAC measures and number of drinks consumed in laboratory challenge conditions and in EMA reports

Available evidence is mixed, however, concerning the ability to detect drinking events on the basis of TAC readings alone

Monitoraggio passivo tramite sensori da mobile device

presunzione di eBAC tramite algoritmi formulati su dati di sensori presenti nei device

Piasecki, T. M. (2019). Assessment of alcohol use in the natural environment. *Alcoholism: clinical and experimental research*, *43*(4), 564-577.

The supporting literature indicates that EMA, TAS, and sensor-based approaches are all valid, and tend to produce convergent information when used in conjunction with one another. Each has a unique profile of advantages, disadvantages, and threats to validity.

Piasecki, T. M. (2019). Assessment of alcohol use in the natural environment. *Alcoholism: clinical and experimental research*, *43*(4), 564-577.

Adolescent and young-adult alcohol abuse is an emerging area for integration of sensor technology and EMA.

Despite the potential for scientific discovery, careful research is needed to address ethical and feasibility issues with using alcohol sensors in youth at risk.

Russell, M. A., & Gajos, J. M. (2020). Annual Research Review: Ecological momentary assessment studies in child psychology and psychiatry. Journal of Child Psychology and Psychiatry.

conclusioni

- Il trattamento dell'alcolismo ha al momento pochi ma abbastanza solidi trattamenti riconosciuti dalle principali linee guida internazionali sia farmacologici che non farmacologici come label
- Pochi progressi sono stati fatti comunque per bypassare la «valley of death» e rendere disponibili farmaci attualmente off label per indicazione, per target, per diagnosi

conclusioni

- Il miglioramento dei modelli preclinici, la precisione diagnostica, la modificazione degli obiettivi del trattamento, l'utilizzo alternativo delle componenti del trattamento alla luce delle interpretazioni neuroscientifiche e delle nuove tecnologie possono portarci a modificare più che le terapie in sé, l'approccio alla cura e al modo di interpretarla…..

Grazie per l'attenzione!