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Regione Emilia Romagna

SIA

Società Italiana di Alcologia (SIA)

PERCHE' E' STATA REVOCATA LA INDICAZIONE AIFA PER IL MANTENIMENTO?

MA QUINDI ADESSO LO POSSIAMO PRESCRIVERE O NO?

E SE LO POSSIAMO PRESCRIVERE CON QUALI INDICAZIONI E CONTROINDICAZIONI?

Caputo F, Skala K, Walter H, et al. "Sodium Oxybate in the prevention of alcohol relapses in alcohol dependent patients (GATE 2 study). Alcohol Alcohol 2013; 48:S1-i33

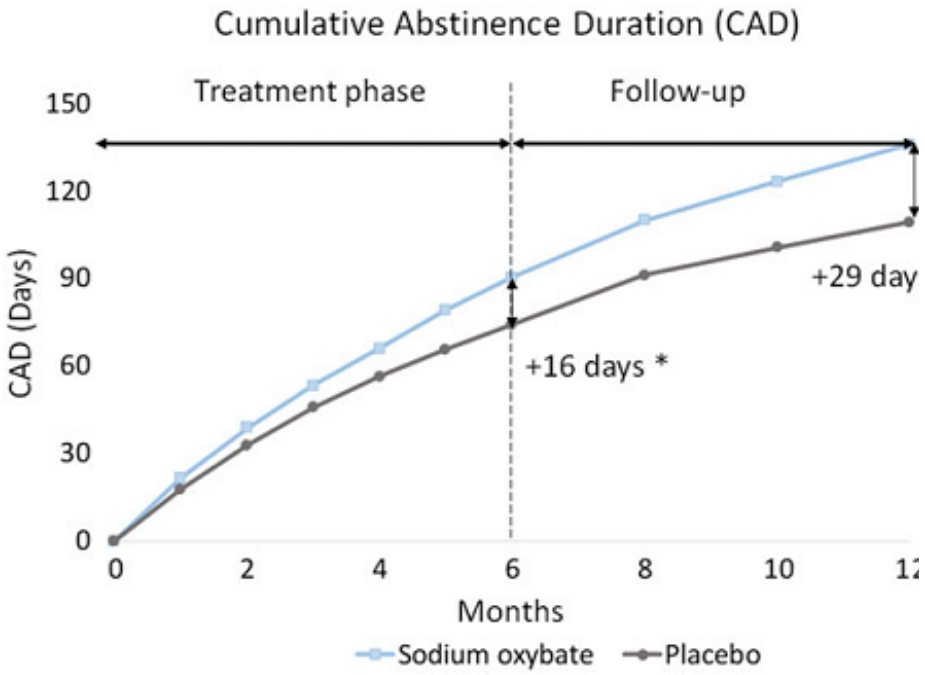

Figure 7 GATE 2 is a randomized, international, double-blind placebo-controlled trial with 314 patients. During the 6-month treatment period, patients in the sodium oxybate arm received between 3 and 4 g/day sodium oxybate syrup and were then followed up for an additional 6 months without medication. The primary endpoint was cumulative abstinence duration at month 6 (+16 days ($P < 0.05$)). This effect was further augmented during the follow-up period. The statistical significance was also confirmed by sensitivity analysis (EMA 2017)

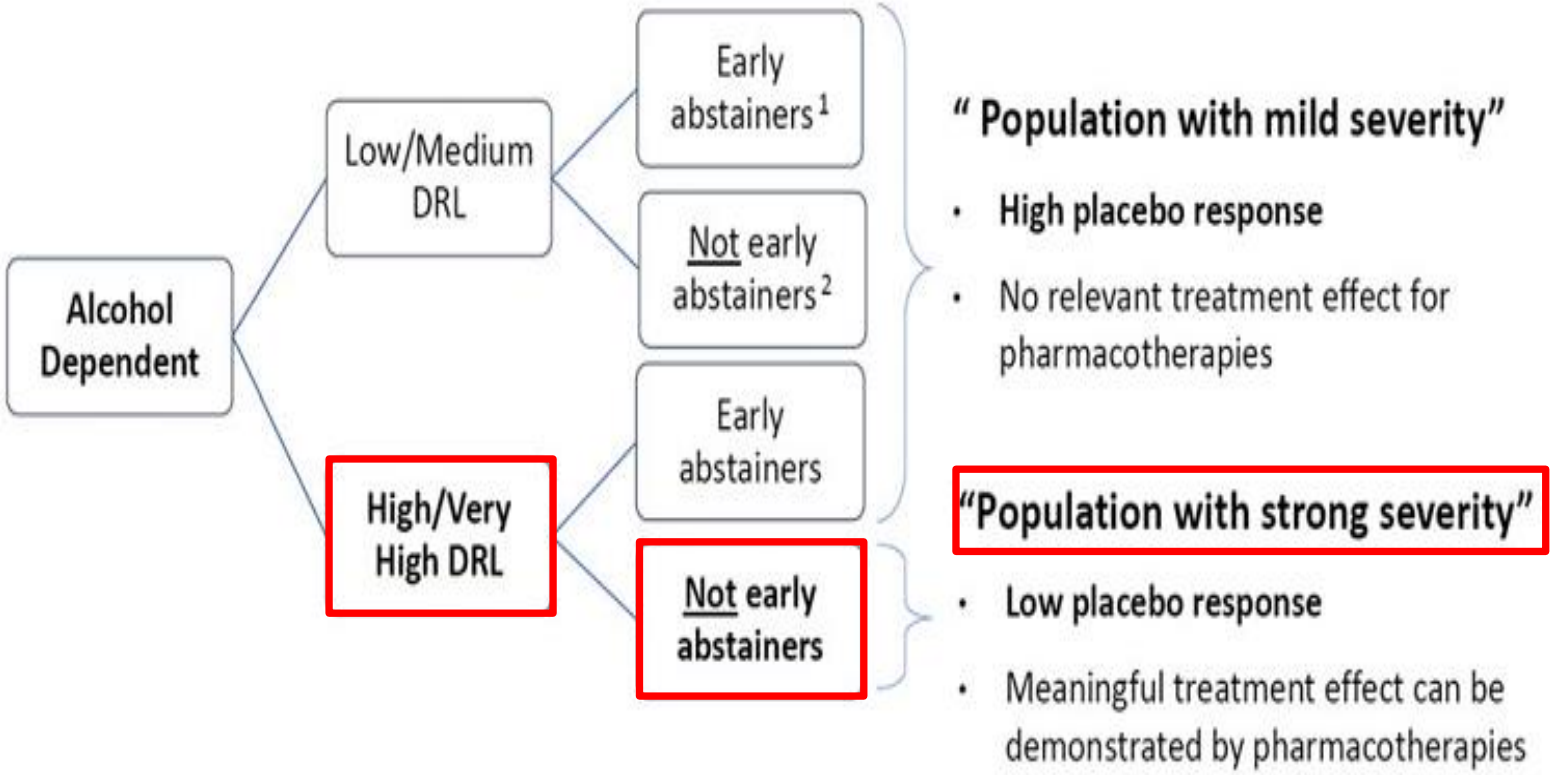

Fig. 3 Mean Percentage of Days Abstinent per week in severe and mild population. Bars indicate standard errors.

Treating alcohol dependence with an abuse and misuse deterrent formulation of sodium oxybate: Results of a randomised, double-blind, placebo-controlled study

(Guiraud etr Al, Eur. Neuropsychopharmacol 2021)

Incidence of abuse/misuse, central nervous system depression and dependence to sodium oxybate in alcohol-dependent patients (EMA 2017)

Number of events (incidence)	*Clinical trials, N = 3436*	*Pharmacovigilance database, N = 260 000*
Abuse/misuse	100 (2.91%)	6 (0.002%)
CNS depression	19 (0.55%)	14 (0.005%)
Dependence/withdrawal	4 (0.12%)	2 (0.001%)

CNS depression refers to 'depressed level of consciousness' and 'sedation' cases.

Importantly, no deaths attributable to the use of sodium oxybate have ever been reported in the pharmacovigilance database or in the clinical database

EXPERT OPINION ON DRUG SAFETY
https://doi.org/10.1080/14740338.2020.1709821

Taylor & Francis
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REVIEW

Check for updates

Post-marketing and clinical safety experience with sodium oxybate for the treatment of alcohol withdrawal syndrome and maintenance of abstinence in alcohol-dependent subjects

Giovanni Addolorato [a,b], Otto-Michael Lesch[c], Icro Maremmani[d], Henriette Walter[c], Felice Nava[e], Quentin Raffaillac[f] and Fabio Caputo[g,h]

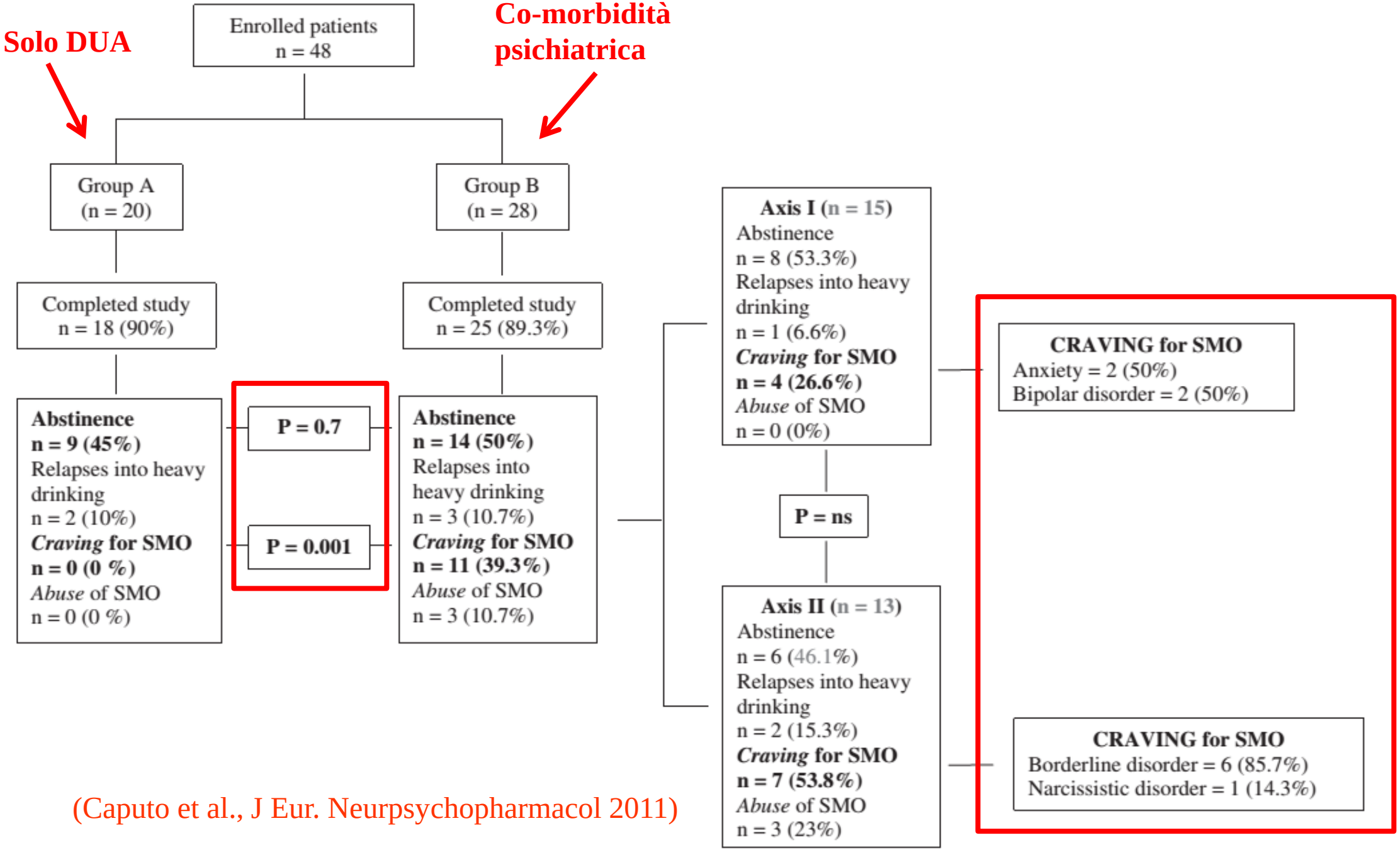
Risk	Alcover Liquid	Granules
Number of subjects	2250	397
Abuse/Misuse	36 (1.60%)	0 (0%)
Diversion	0 (0%)	0 (0%)

*Data from the clinical trial database (recent RCT and early clinical studies). Patients were exempt of psychiatric comorbidities or poly-addictions.

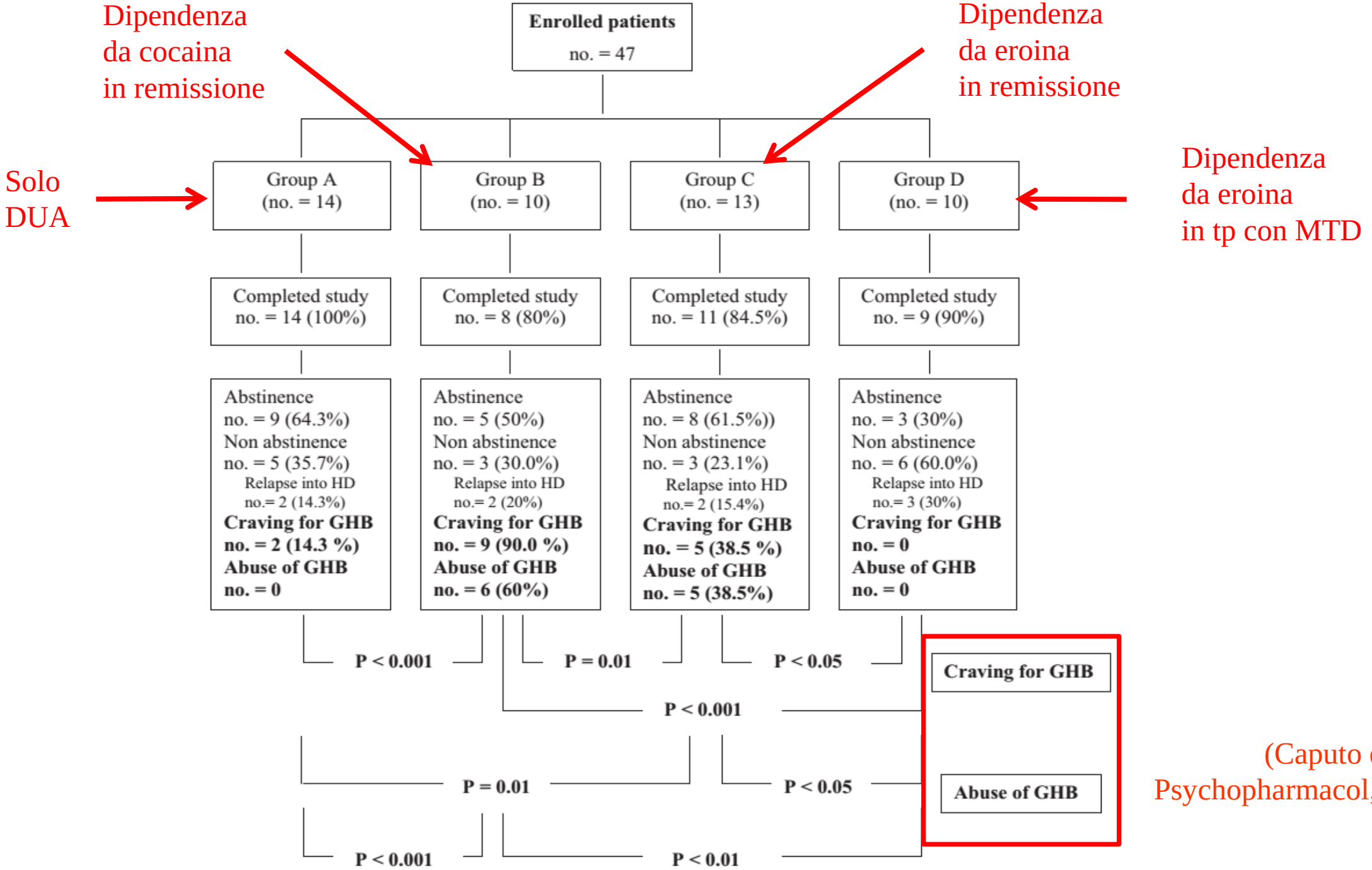
Pharmacological Treatment in γ-Hydroxybutyrate (GHB) and γ-Butyrolactone (GBL) Dependence: Detoxification and Relapse Prevention

Kamal et Al, CNS Drug 2016

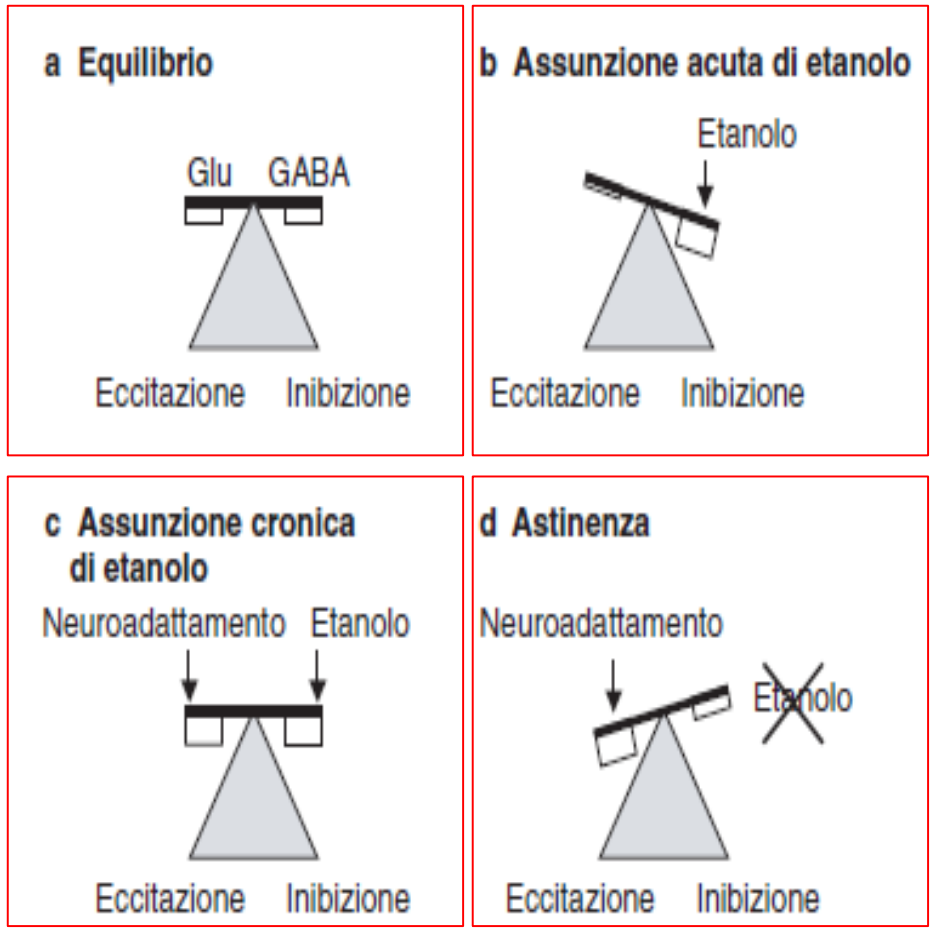
Across Europe, higher levels of GHB misuse and related problems have been reported, particularly in the Netherlands, Norway, Spain and the UK [20, 38, 41]. In Europe, it



(Caputo et al., J Eur. Neurpsychopharmacol 2011)



(Caputo et al., J Psychopharmacol, 2009)

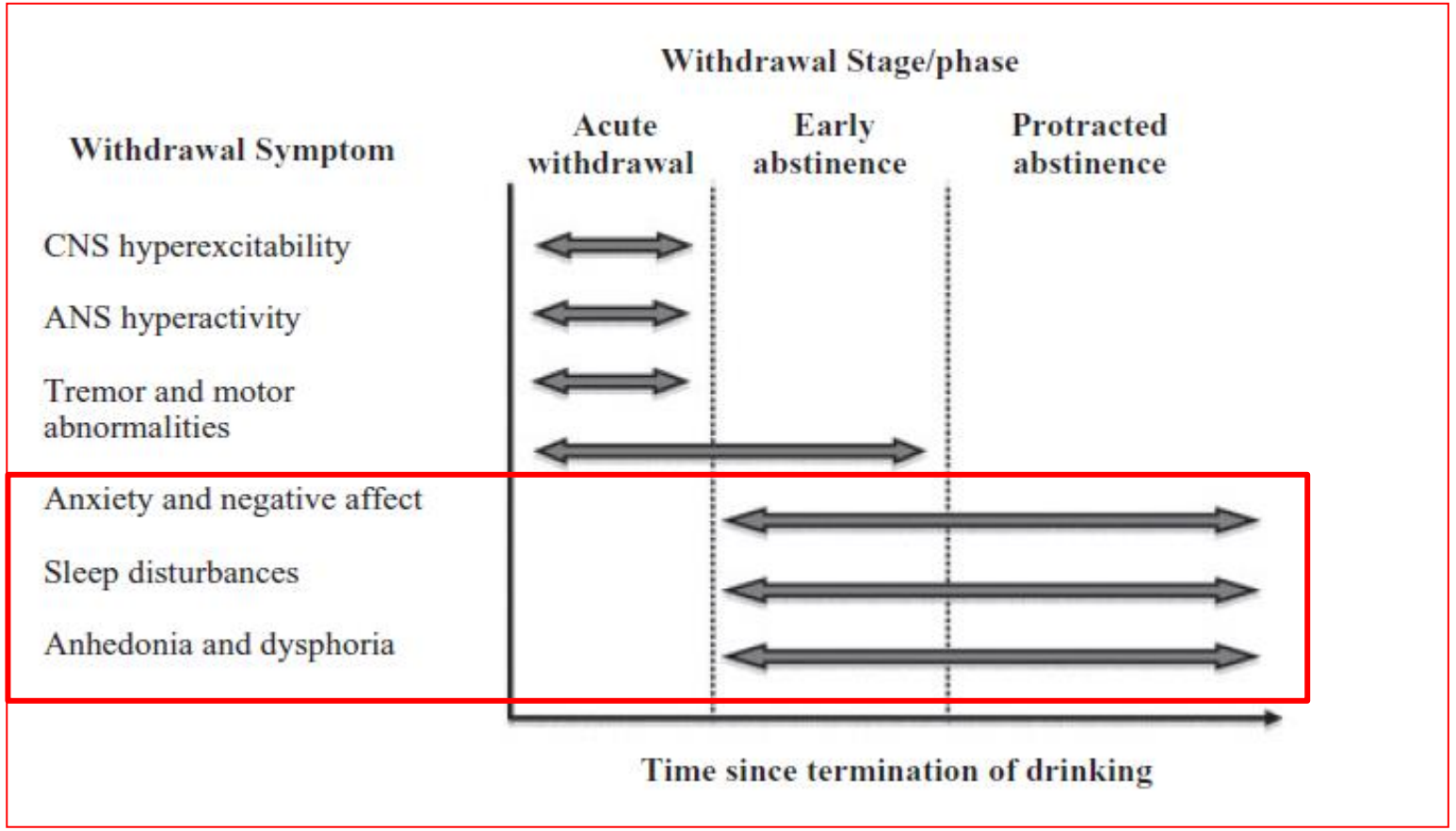


(Himmelsbach, Ann Int Med, 1941

Ipertono Glutamatergico
Ipotono GABAergico

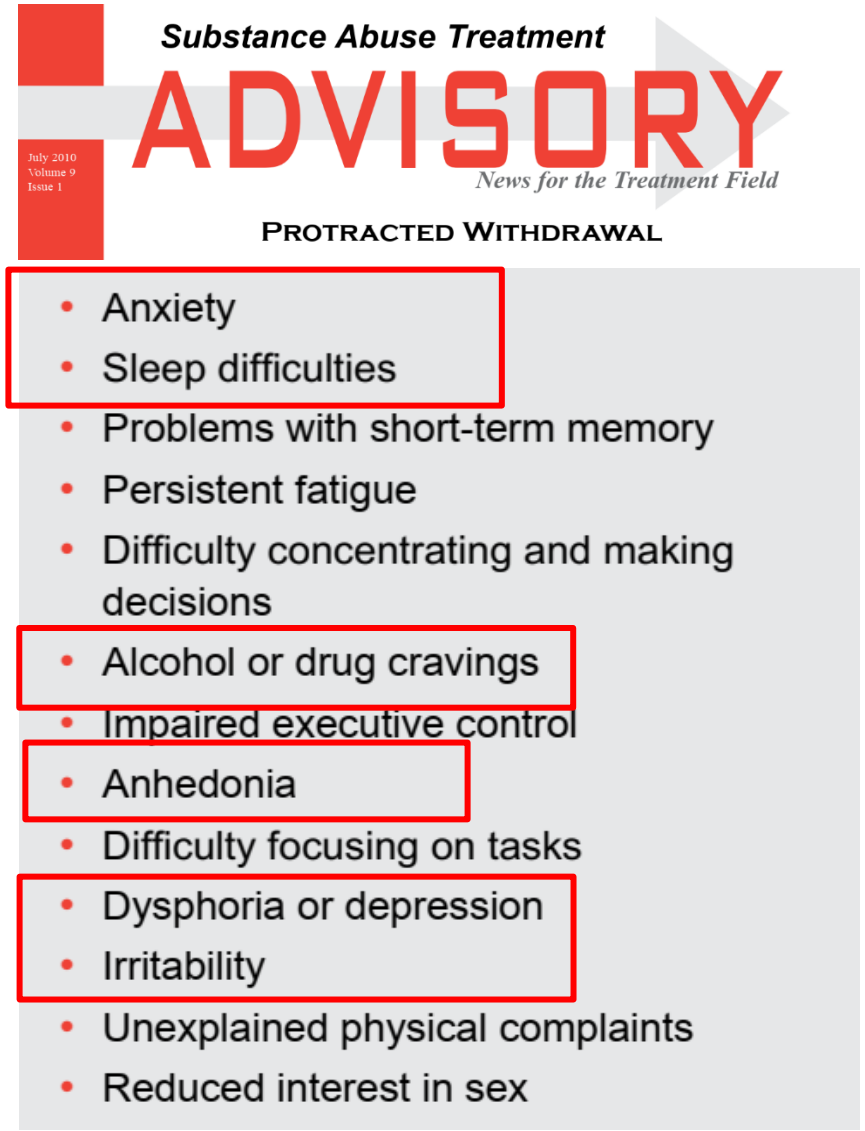
SINDROME DI ASTINENZA DA ALCOL

Acute withdrawal phase: humans (48–72 hours);
Early abstinence phase: humans (2-3 weeks)
Protracted abstinence phase: humans (> 3 months)



(Heilig et al., Add Biol, 2010)

SINDROME DI ASTINENZA PROTRATTA



(U.S. Department of Health and Human Service, 2010)

Sindrome da astinenza protratta da alcol: il ruolo del sodio ossibato...e non solo

MDD 37 - Marzo 2020

di Fabio Caputo, Teo Vignoli, Mauro Cibin, Roberto De Giorgio e Giorgio Zoli

Newsletter "Clinica dell'Alcolismo"

Anno VII, n. 29 MISSION n. 53

La sindrome da astinenza alcolica protratta

*a cura di Alfio Lucchini**

The recognition and management of protracted alcohol withdrawal may improve and modulate the pharmacological treatment of alcohol use disorder

Fabio Caputo[1,2], Mauro Cibin[3], Antonella Loche[4], Roberto De Giorgio[5] and Giorgio Zoli[5]

Psychopharm

Journal of Psychopharmacology
2020, Vol. 34(11) 1171–1175

DOI: 10.1177/0269881120936483
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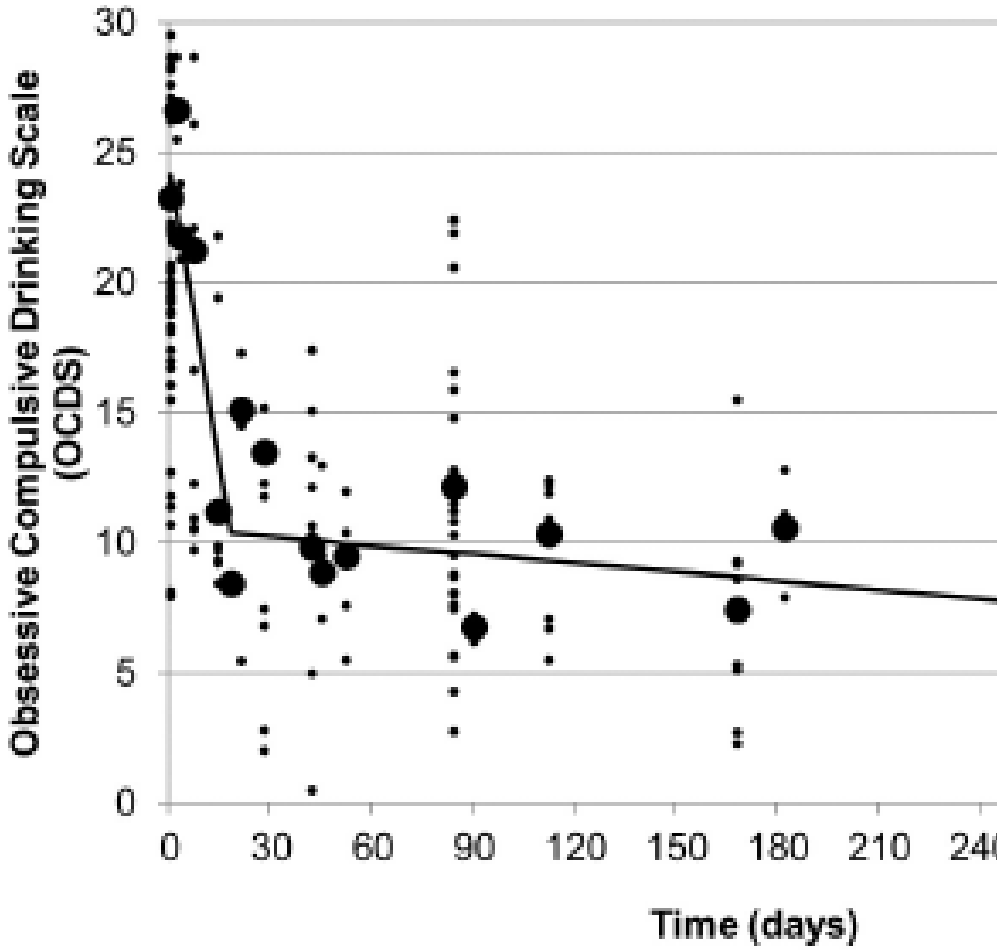
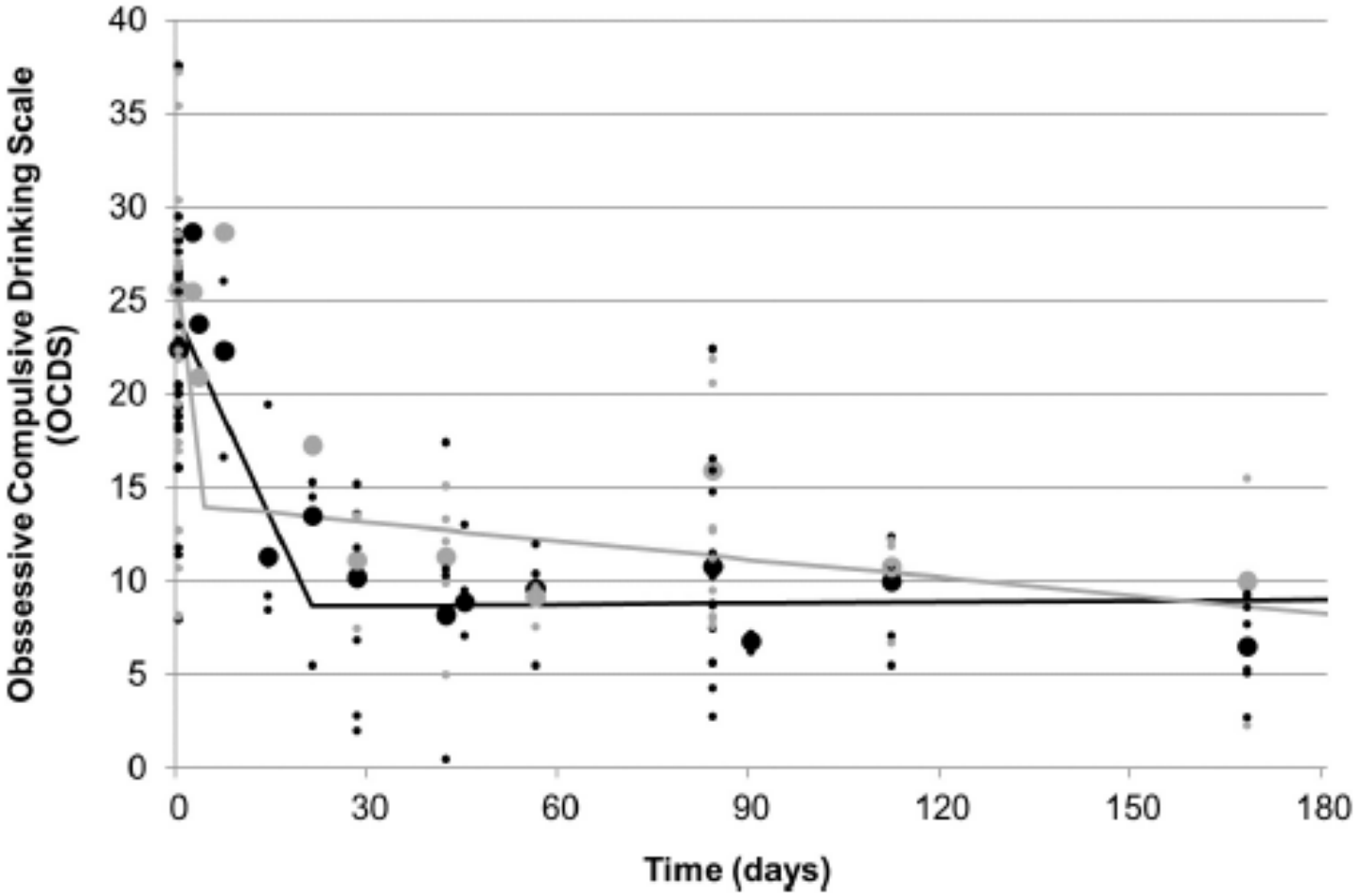
Current Neuropharmacology, 2023, *21*, 409-416

SYSTEMATIC REVIEW ARTICLE

Symptoms of Protracted Alcohol Withdrawal in Patients with Alcohol Use Disorder: A Comprehensive Systematic Review

Silvano Gallus[1], Alessandra Lugo[1], Elisa Borroni[1], Teo Vignoli[2], Lisa Lungaro[3], Giacomo Caio[3], Roberto De Giorgio[3], Giorgio Zoli[3,4] and Fabio Caputo[3,4,*]





Valutazione quantitativa del craving e dei disturbi del sonno nel periodo dell'astinenza protratta

Outcomes	Number of studies	Time (days) of the possible knot#	Mean estimates of various scales at different time points						
			Baseline	1 week	2 weeks	3 weeks	1 month	2 months	3 months
Craving									
OCDS	34	18	24·2	18·8	13·5	11·4	10·3	9·9	9·7
OCDS (GABA)	21	20	24·7	19·2	13·6	8·8	8·9	8·6	8·3
OCDS (non-GABA)	14	39	22·7	18·7	15·8	12·3	8·8	4·6	6·6
OCDS (non-treated)	16	4	25·3	13·9	13·7	13·4	13·2	12·3	11·4
PACS	11	4	16·1	8·6	8·6	8·7	8·8	9·1	9·3
VAS	11	28	4·4	3·5	2·7	1·9	1·1	1·3	1·5
Sleep disorders									
ESS	3	NA	7·3	7·3	7·3	7·3	7·2	7·2	7·1

The recognition and management of protracted alcohol withdrawal may improve and modulate the pharmacological treatment of alcohol use disorder

Fabio Caputo[1,2], Mauro Cibin[3], Antonella Loche[4], Roberto De Giorgio[5] and Giorgio Zoli[5]

Psychopharm

Journal of Psychopharmacology
1–5

DOI: 10.1177/0269881120936483
journals.sagepub.com/home/jop
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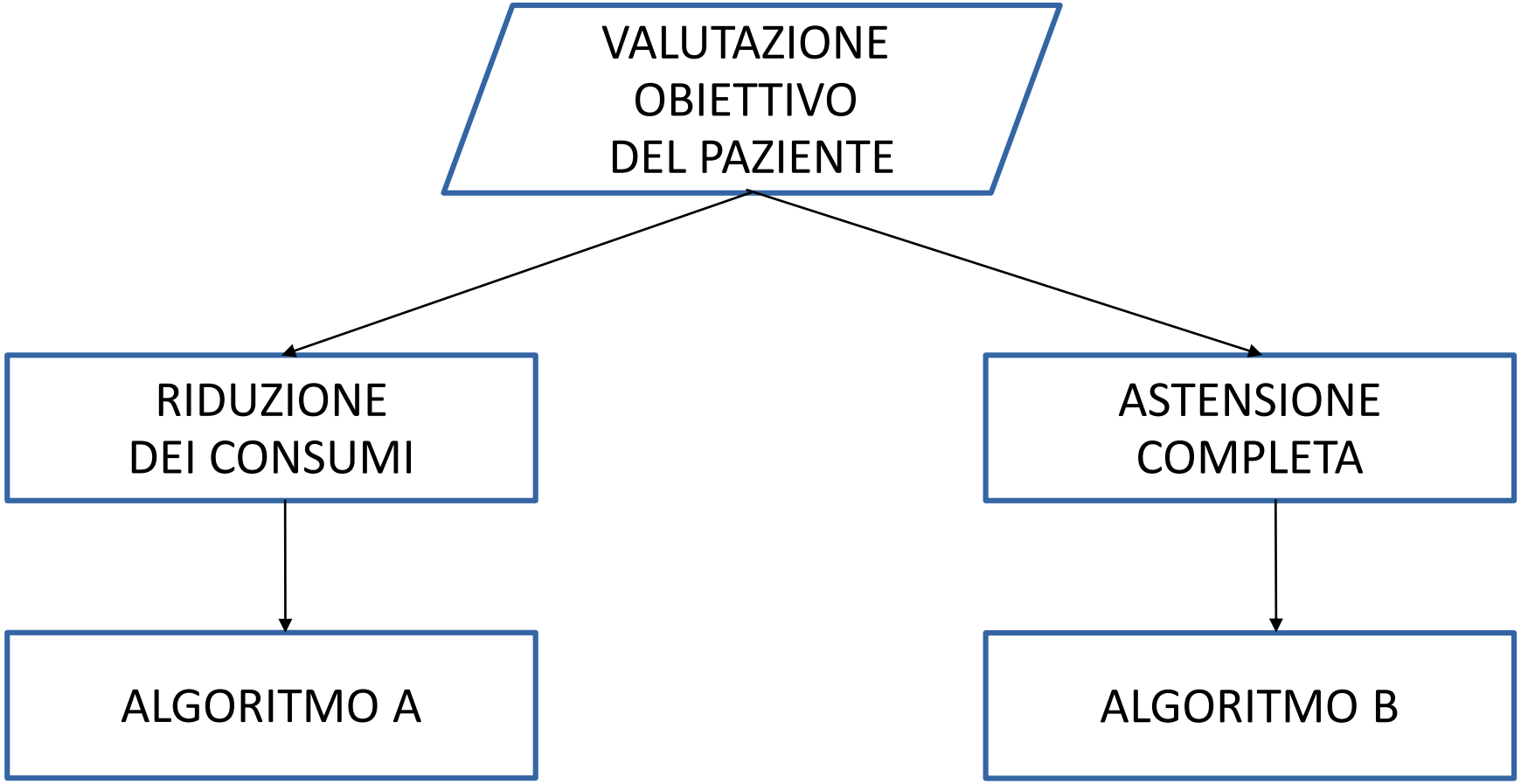
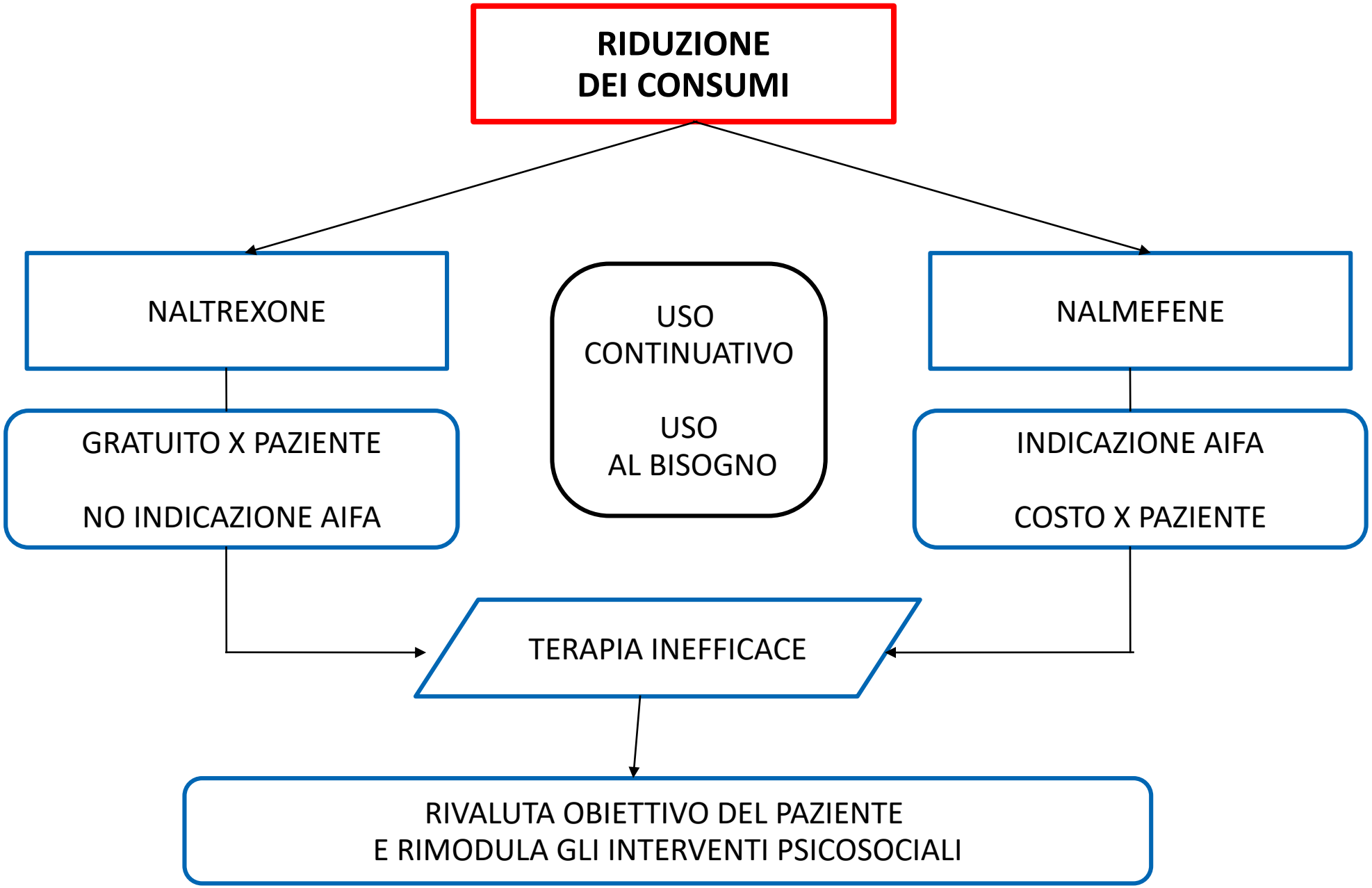
SODIO OXIBATO
BACLOFENE
GABAPENTIN
ACAMPROSATO

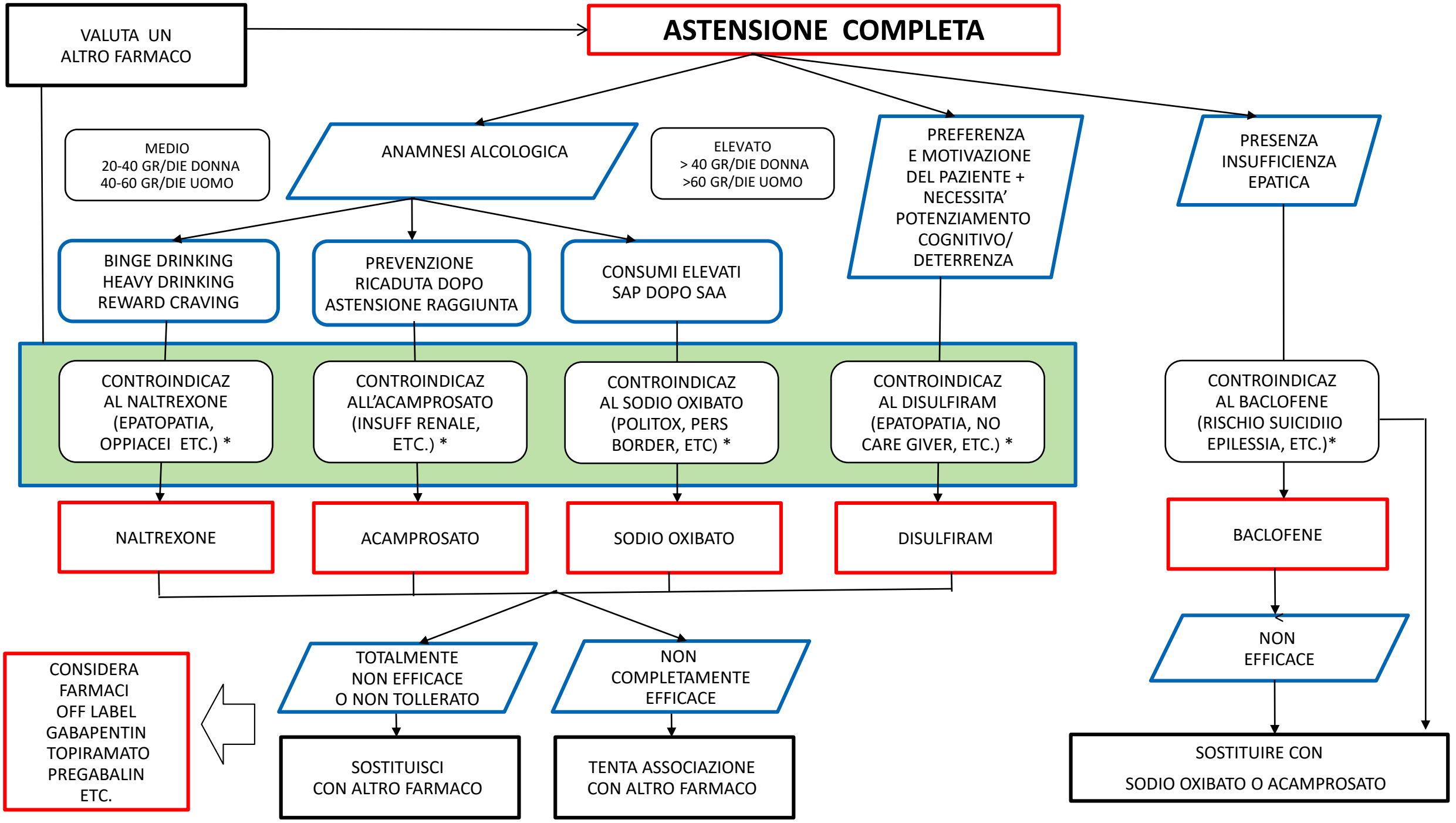
Stages of alcohol withdrawal syndrome (AWS)	Acute alcohol withdrawal	Early abstinence, protracted alcohol withdrawal
Medications	Bezodiazepines (or sodium oxybate§) plus (if indicated) symptomatic drugs^	NMDA antagonist* plus GABA agonist*
Period of treatment	7–10 days	To be defined*

(Caputo et al., J Psychopharmacol, 2020)

DIAGNOSI DI DISTURBO DA USO DI ALCOL
DI GRADO MODERATO O SEVERO




RIDUZIONE
DEI CONSUMI
NALTREXONE
USO
CONTINUATIVO
USO
AL BISOGNO
NALMEFENE
GRATUITO X PAZIENTE
NO INDICAZIONE AIFA
INDICAZIONE AIFA
COSTO X PAZIENTE
TERAPIA INEFFICACE
RIVALUTA OBIETTIVO DEL PAZIENTE
E RIMODULA GLI INTERVENTI PSICOSOCIALI


VALUTA UN ALTRO FARMACO
ASTENSIONE COMPLETA
MEDIO 20-40 GR/DIE DONNA 40-60 GR/DIE UOMO
ANAMNESI ALCOLOGICA
ELEVATO > 40 GR/DIE DONNA >60 GR/DIE UOMO
PREFERENZA E MOTIVAZIONE DEL PAZIENTE + NECESSITA' POTENZIAMENTO COGNITIVO/ DETERRENZA
PRESENZA INSUFFICIENZA EPATICA
BINGE DRINKING HEAVY DRINKING REWARD CRAVING
PREVENZIONE RICADUTA DOPO ASTENSIONE RAGGIUNTA
CONSUMI ELEVATI SAP DOPO SAA
CONTROINDICAZ AL NALTREXONE (EPATOPATIA, OPPIACEI ETC.) *
CONTROINDICAZ ALL'ACAMPROSATO (INSUFF RENALE, ETC.) *
CONTROINDICAZ AL SODIO OXIBATO (POLITOX, PERS BORDER, ETC) *
CONTROINDICAZ AL DISULFIRAM (EPATOPATIA, NO CARE GIVER, ETC.) *
CONTROINDICAZ AL BACLOFENE (RISCHIO SUICIDIIO EPILESSIA, ETC.)*
NALTREXONE
ACAMPROSATO
SODIO OXIBATO
DISULFIRAM
BACLOFENE
NON EFFICACE
TOTALMENTE NON EFFICACE O NON TOLLERATO
NON COMPLETAMENTE EFFICACE
CONSIDERA FARMACI OFF LABEL GABAPENTIN TOPIRAMATO PREGABALIN ETC.
SOSTITUISCI CON ALTRO FARMACO
TENTA ASSOCIAZIONE CON ALTRO FARMACO
SOSTITUIRE CON SODIO OXIBATO O ACAMPROSATO

Gamma-Hydroxybutyric Acid in the Treatment of Alcohol Dependence: A Double-Blind Study

Table 2. Effect of Gamma-Hydroxybutyric acid (GHB) on Ethanol Consumption in Alcoholics

Response	During the 3 months before treatment		p	During the 3 months of treatment period		p
	Placebo	GHB		Placebo	GHB	
Daily drinks (mean ± SEM)	11.4 ± 0.6	12.1 ± 0.5	NS	9.3 ± 0.7	4.7 ± 0.4	<0.01
% of abstinent days (mean ± SEM)	4.9 ± 0.4	5.6 ± 0.5	NS	8.4 ± 1.6	25.9 ± 3.1	<0.001

Each value is the mean ± SEM from 35 placebo and 36 GHB treated subjects. Values of alcohol intake prior to treatment were based on a single interview, while those during treatment were obtained by weekly interviews (means ± SEM). Therefore, the statistical significance of the results was calculated by comparing the values of GHB versus placebo, during the 3-month treatment period (Student's *t* test).

reducing relapses into heavy drinking ($p < 0.00032$)

Table 3. Effect of Gamma-Hydroxybutyric Acid on Ethanol Craving

Month of treatment	Craving score	
	Placebo	GHB
Prior to treatment	8.5 ± 0.3	8.9 ± 0.5
1st month	5.1 ± 0.6†	2.1 ± 0.1†
2nd month	7.5 ± 0.4	3.3 ± 0.4*,†
3rd month	7.6 ± 0.3	3.1 ± 0.6*,†

71 partients double blind placebo controlled Gallimberti Alcohol Clin Exp Res 1992

ELSEVIER Alcohol 20 (2000) 285–291

Gamma-hydroxybutyric acid and alcohol-related syndromes

M. Moncini, E. Masini, F. Gambassi, P.F. Mannaioni*

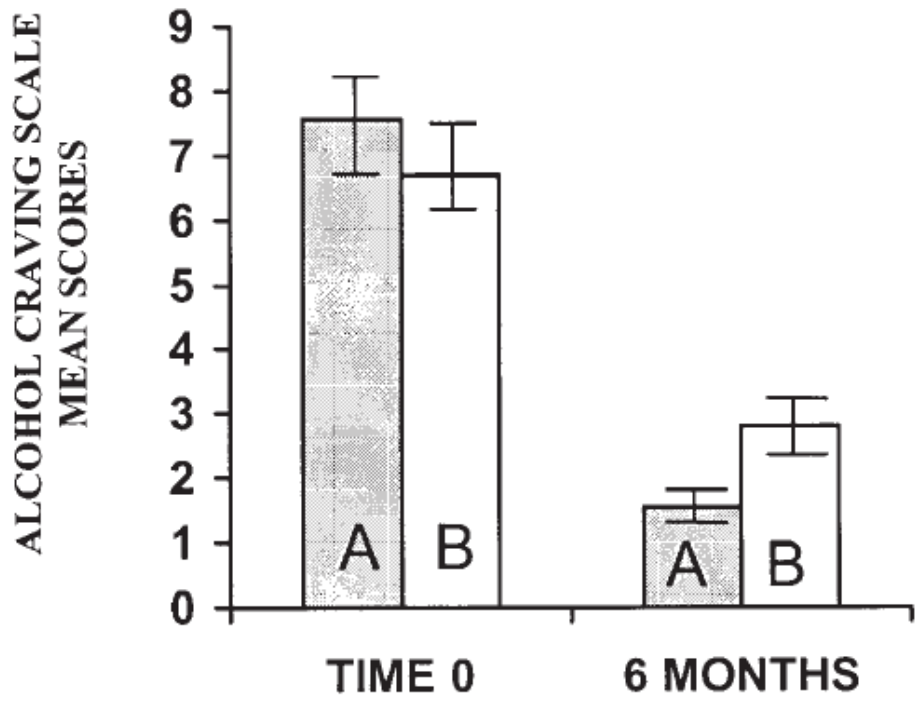


Fig. 1. Mean scores of Alcohol Craving Scale in GHB-treated and placebo-treated patients. Student's *t-test: at time o, A vs. B not significantly different (n.s.);*
A at time o vs. A at 6 months, *p , o.o5; B at time o vs. B at 6 months, n.s.; at 6 months, A vs. B, p , o.o5.*

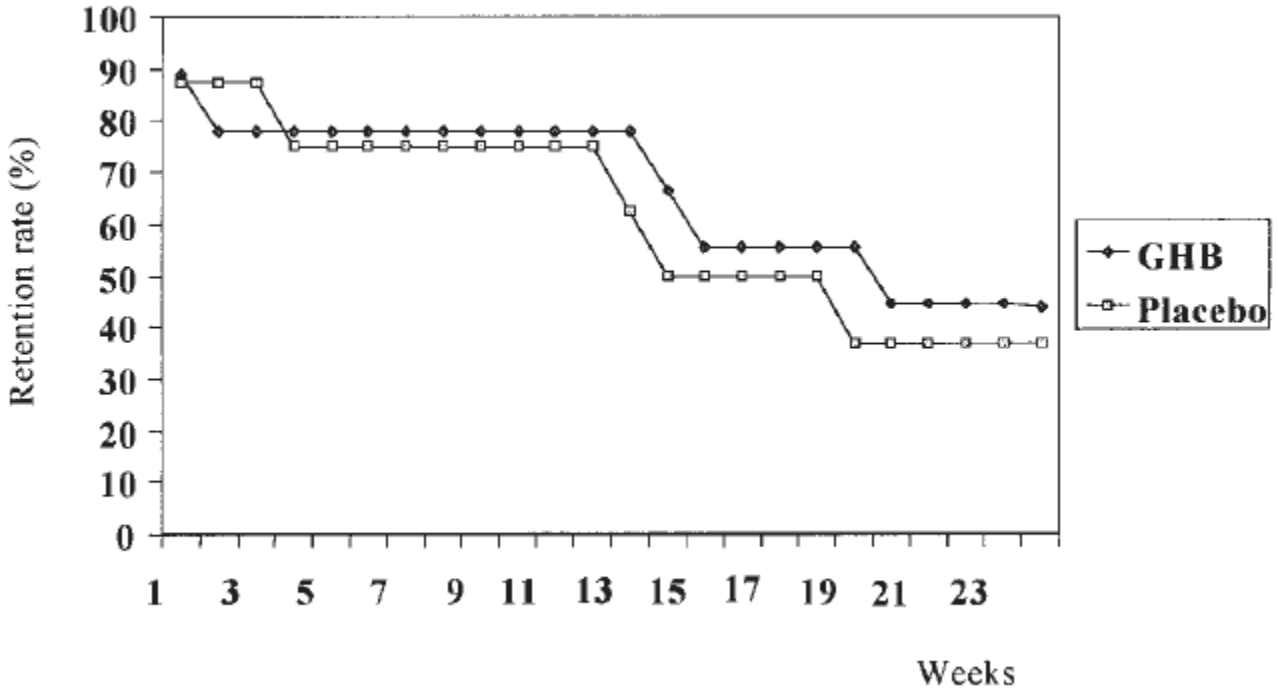


Fig. 2. Retention rate (%) in the program within GHB- and placebo-treated groups. Two-way ANOVA: GHB vs. placebo, *p , o.o5*