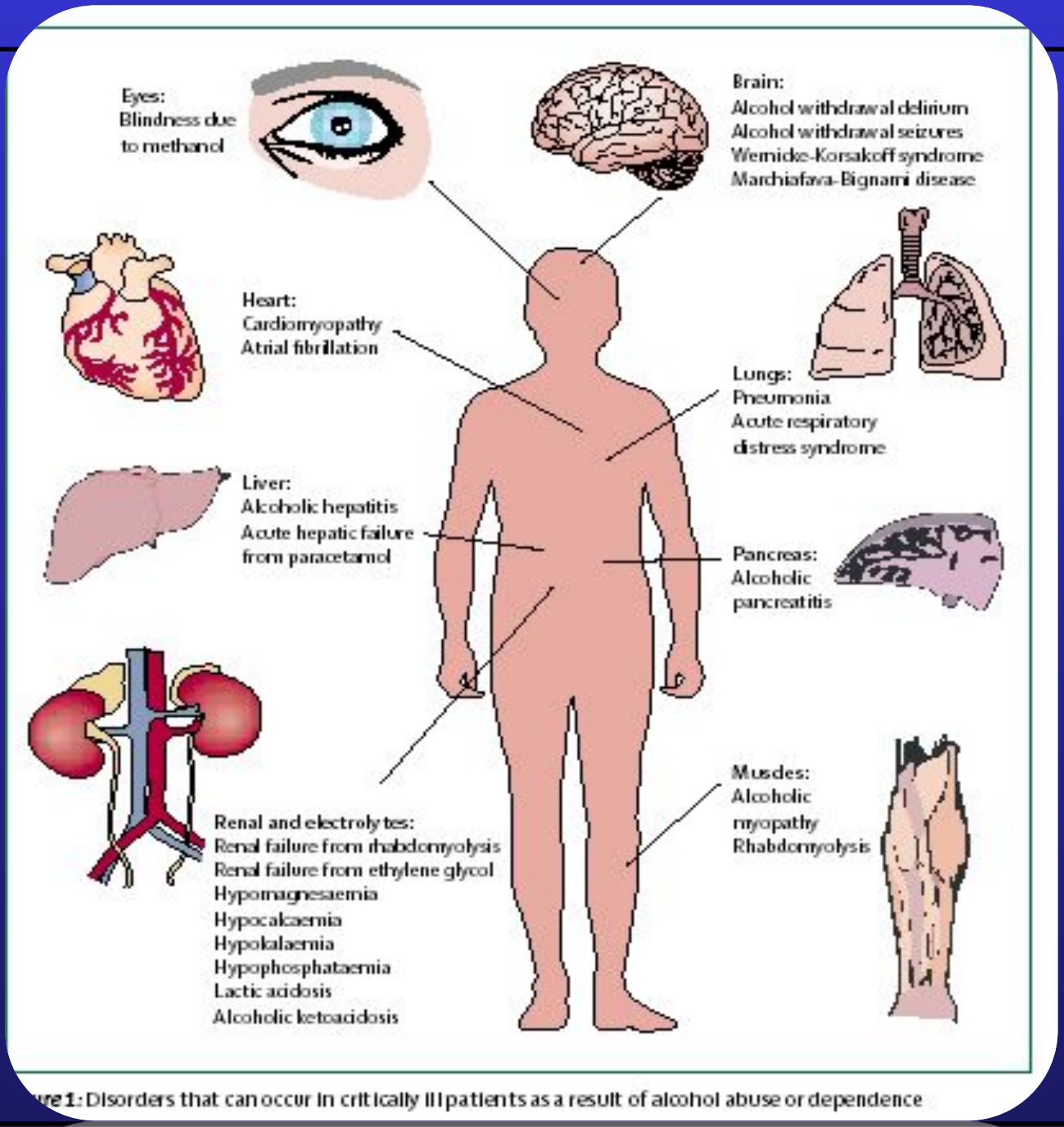
PATOLOGIE ALCOL CORRELATE

Gianni Testino
SC Pat. Dipendenze ed Epatologia
ASL3 c/o Osp. Policlinico
San Martino, Genova

Società Italiana di Alcologia (SIA)



ure 1: Disorders that can occur in critically ill patients as a result of alcohol abuse or dependence

Moss M. and Burnham E. L., The Lancet 2006

Consumatori (11+)	(M=77,4% - F=57,5%)	36 milioni M=20 milioni - F=16 milioni
Consumatori giornalieri (18+)	(M = 30,7% - F=11,4%)	10,2 milioni M = 7,3 milioni - F = 2,9 milioni
Consumatori a rischio (11+)	(M = 21,1% - F = 9,1%)	8 milioni M = 5,5 milioni- F = 2,5 milioni
Consumatori a rischio (11-24)		1.310.000
Consumatori a rischio (11-17)		*650.000*
Consumatori a rischio (18-24)		*660.000*
Consumatori a rischio (65+)		2,55 milioni
Consumatori a rischio (65-74)		*1.350.000*
Consumatori a rischio (75-84)		*920.000*
Consumatori a rischio (85+)		*280.000*
Binge drinkers (11+)	(M = 10,5% - F = 3,7%)	3,7 milioni M = 2,7 milioni - F = 1 milione
Binge drinkers (11-24)		728.000
Binge drinkers (11-17)		*104.000*
Binge drinkers (18-24)		*624.000*
Eccedenti le linee guida su base abituale (11+)	(M = 13,0% - F = 6,1%)	5,0 milioni M = 3,4 milioni - F = 1,6 milioni
Consumatori dannosi (18+)	(M = 2,04% - F = 1,13)	770.000 M = 480.000 - F = 290.000
Alcoldipendenti	(M = 76,1% - F = 23,9%)	62.886 in carico
Accessi in PS per Patologie Alcol Attribuibili (PAA)	(M = 67,7% - F = 32,3%)	39.590

E. Scafato 2024

Osservatorio Nazionale Alcol - SISMA – Sistema Monitoraggio Alcol (DPCM 3/3/2017)
Centro Nazionale Dipendenze e Doping – ISS

E. Scafato, ISS, 2024

ALCOL SCREENING SCORES
(CAGE e AUDIT)

RISCHIO DI COMPLICANZE GASTROINTESTINALI

Pazienti al di sotto di 50 anni
con CAGE > 2 o AUDIT > 4

hanno un rischio aumentato sino a 7 volte,
dopo un periodo di osservazione di 4/5 anni,
di sviluppare complicanze come:

- **Cirrosi epatica scompensata**
- **Sanguinamento da varici gastro-esofagee**
- **Pancreatite**

Au DH et al, Alcoholism: Clinical and Experimental Research 2007; 31:443

Table 1. The fifth edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria for the framing of patients with alcohol use disorder (AUD).

1.	Alcohol is often taken in larger amounts or over a longer period than was intended.
2.	There is a persistent desire or unsuccessful efforts to cut down or control alcohol use.
3.	A great deal of time is spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects.
4.	Craving, or a strong desire or urge to use alcohol.
5.	Recurrent alcohol use resulting in a failure to fulfill major role obligations at work, school, or home.
6.	Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol.
7.	Important social, occupational, or recreational activities are given up or reduced because of alcohol use.
8.	Recurrent alcohol use in situations in which it is physically hazardous.
9.	Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol.
10.	Tolerance, as defined by either of the following: (a) A need for markedly increased amounts of alcohol to achieve intoxication or desired effect; (b) A markedly diminished effect with continued use of the same amount of alcohol.
11.	Withdrawal, as manifested by either of the following: (a) The characteristic withdrawal syndrome for alcohol (refer to criteria A and B of the criteria set for alcohol withdrawal); (b) Alcohol is taken to relieve or avoid withdrawal symptoms.

all the criteria in Table 1). The presence of two or three symptoms indicate a mild disorder, four or five symptoms a moderate one, and six or more symptoms a severe disorder. Notably, DSM-5 removes "legal problems" between the diagnostic criteria adding the craving [11].

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed.; American Psychiatric Association: Washington, DC, USA, 2013; pp. 154–196.

Alcohol Use Disorder (AUD)

-About 20% of men and 10% of women in most Western societies have an alcohol use disorder (AUD), which is defined as repetitive alcohol-related problems in at least 2 of 11 areas of life (see DSM-V criteria)

-Alcohol-related conditions affect more than 20% of patients in most medical settings

-About 50% of persons with AUD have symptoms of alcohol withdrawal when they reduce or discontinue their alcohol consumption; in 3 to 5% of these persons, grand mal convulsions, severe confusion (a delirium), or both develop *(Schuckit, NEJM,*

PATOLOGIA ALCOL CORRELATA ED OSPEDALIZZAZIONE

- 7-24% prevalenza ricoveri in ambiente internistico (Kennel-Webb et al, QJM 1999; Smothers et al, Arch Intern Med 2003)
- 18.6% dei ricoveri (Cameron et al, Scott Med J 2006)
- 16% dei ricoveri in degenza ordinaria (Salvagnini et al., Intern Emerg Med 2008)
- 10% dei ricoveri in terapia intensiva (Moss and Burnham, Lancet 2006)
- 30% dei ricoveri complessivi (degenza ordinaria/ intensiva) (Addolorato, APD 2023)

ALCOLOGIA COINVOLTA IN NUMEROSE DISCIPLINE MEDICHE INTERNISTICHE

- Ricoveri ospedalieri (pronto soccorso, degenza ordinaria, terapia intensiva)
- Complicanze post-chirurgiche
- Importante fattore di trapianto d'organo

- *Non percepito il problema alcologico*
- *Se percepito non affrontato in modo adeguato*
- *Etica*

ALCOLOGIA OSPEDALIERA
CRITICITÀ

ACCETTAZIONE CON RISERVA DI UNA STRUTTURA DI ALCOLOGIA ALL'INTERNO DI UN OSPEDALE

DIFFICOLTÀ A FAVORIRE LA CULTURA ALCOLOGICA

STIGMA DA PARTE DEGLI OPERATORI

NON SEMPRE PRESENTE UN OTTIMALE COLLABORAZIONE CON I SERD
(costruzione di un linguaggio tecnico-scientifico comune)

RIDOTTA CAPACITÀ DI IDENTIFICARE UN EVENTUALE DISTURBO DA USO DI ALCOL SOTTOSTANTE (Alcohol Use Disorder Identification Test e altro)

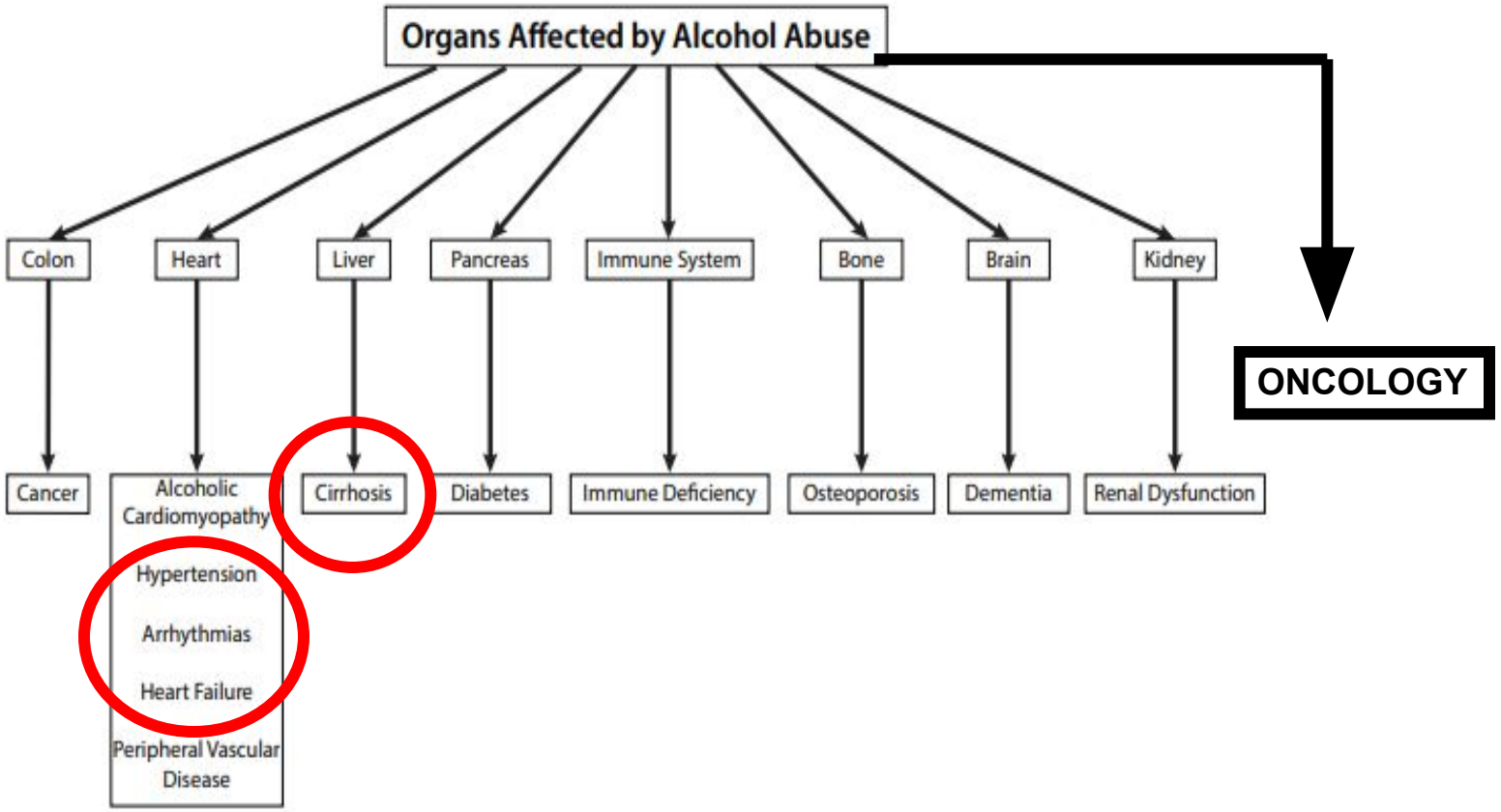


Figure 1. Known organs that show pathophysiological changes as a result of chronic alcohol abuse and the related clinical manifestations.

Dguzeh et al, Int J Environ Public Health, 2018

MEDICAL CONDITIONS AND BINGE DRINKING

Table 3. Systems and medical conditions affected by binge drinking

System	Conditions
Nervous	• Attenuated WM development and accelerated GM volume reductions have been evidenced in young binge drinkers. • BD has also been shown to produce oral microbiome dysbiosis, which may subsequently lead to changes in the blood brain barrier permeability and the development of Alzheimer's disease.
Cardiovascular	• BD has been associated with higher blood pressure and an increased risk of CHD. • It may also prompt different types of arrhythmias and prolong the QTc by causing a 'holiday heart syndrome'. • Furthermore, BD has been linked to a higher sudden cardiac death risk.
Digestive	• Although most of the evidence regarding liver diseases comes from studies of chronic consumption, BD may also represent a risk factor for advanced liver disease and alcoholic hepatitis. • Regarding intestinal disorders, BD has been shown to increase gastrointestinal symptoms in IBS patients.
Endocrine	• BD has been associated with an increased risk of T2D. • Moreover, hypoglycemia risk is higher in T2D patients with a history of BD.
Others	• BD may prompt the appearance of several hydroelectrolytic disorders, transient hematological disturbances and sleeping bruxism. • Furthermore, it tends to increase risky sexual behavior. Thus, it has been shown to double the risk of HIV infection. • BD has also been linked to higher rates of suicide in teenagers.

Abbreviations: QTc, QT interval corrected for heart rate; T2D, type 2 diabetes.

EMERGENCY DEPARTMENT

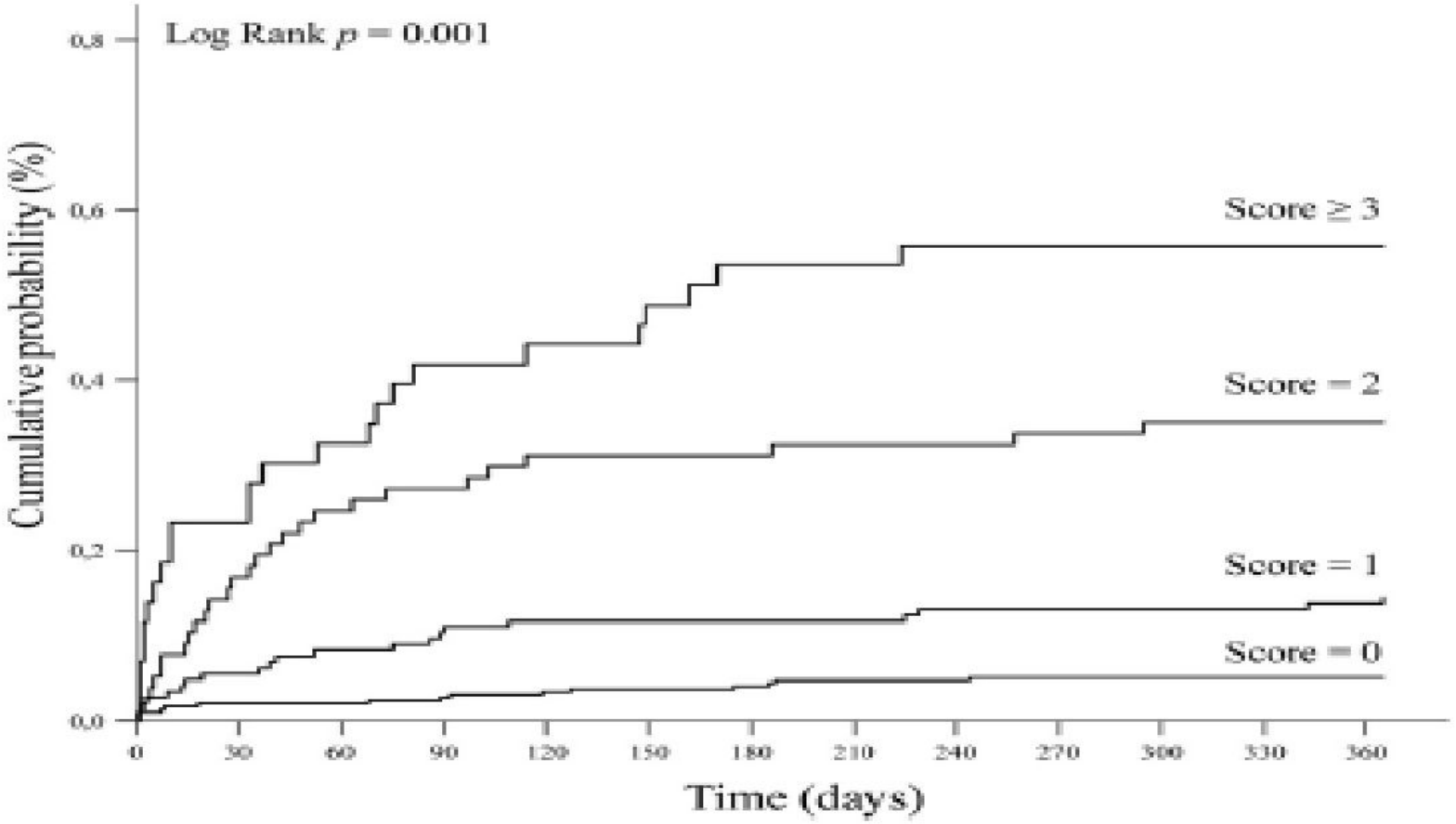


Fig. 2. Cumulative probability of readmission to the Emergency Department (ED) for Acute Alcohol Intoxication (AAI) within one year in patients presenting 0, 1, 2 or ≥ 3 risk factors at the first admission to the ED in the year 2014.

Past episodes of alcohol abuse

Social discomfort

Previous traumas

Psychiatric disorders

Baldassarre et al, Addictive Behaviors 2018

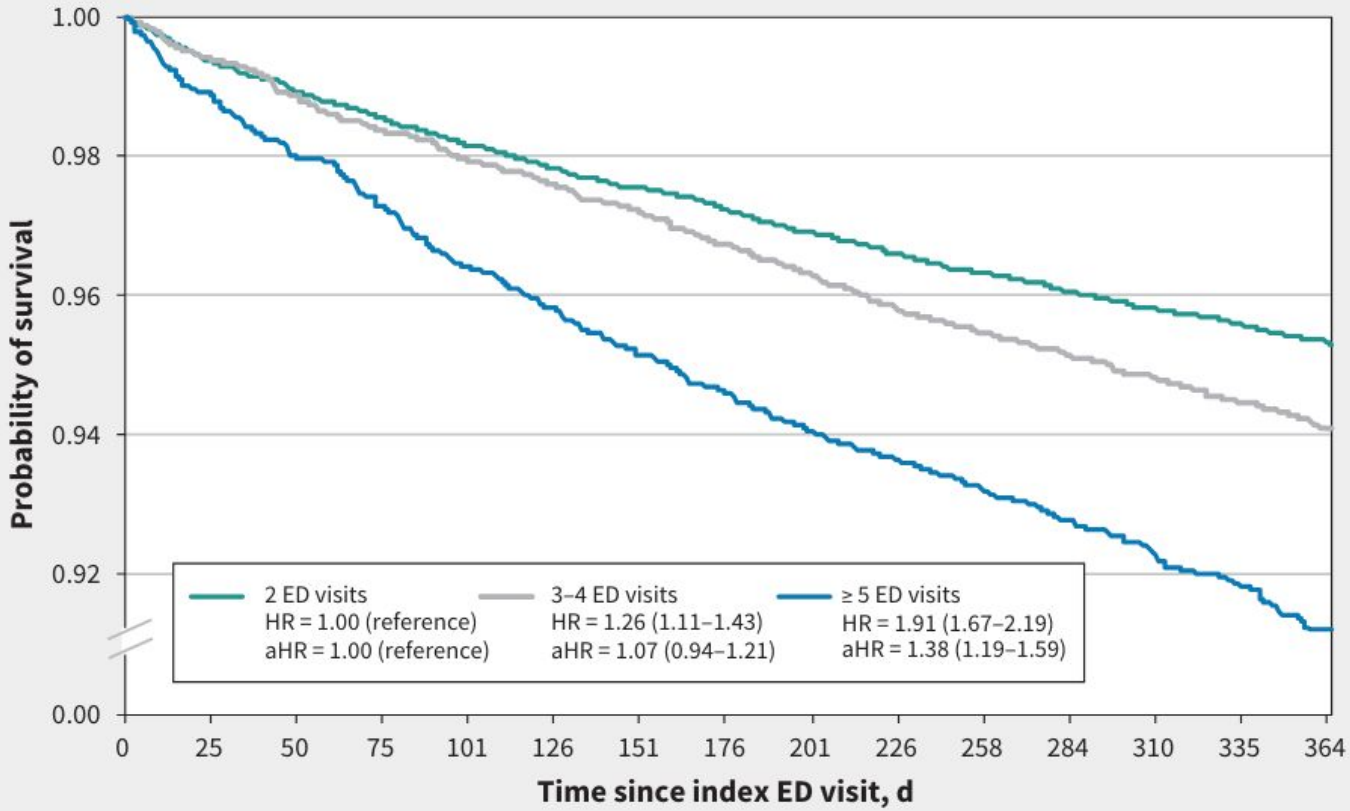


Figure 2: Kaplan–Meier survival plot 1 year after index emergency department (ED) visit. Adjusted and unadjusted hazard ratios are presented with 95% confidence intervals. Note: aHR = adjusted hazard ratio, HR = hazard ratio.

Diseases of the circulatory and digestive system; external causes…

Hulme et al, CMAJ 2020 November 23;192:E1522-31. doi: 10.1503/cmaj.191730

Emergency department initiation of pharmacotherapy for alcohol use disorder: A retrospective cohort study

Karlee S. De Monnin BS[1] | Emily Terian BS[1] | Julianne Yeary PharmD[2] | Elizabeth Bathon MSW[2] | Phillip Asaro MD[3] | Carrie M. Mintz MD[4] | Kevin Baumgartner MD[5]

Emerging evidence suggests mAUD initiation in the ED is feasible[5,6] and may be associated with improved patient outcomes, including reduced alcohol consumption and higher quality of life.[5]

In summary, in this large retrospective study of more than 600 AUD-related ED visits, although 88% of encounters involved patients previously untreated for AUD, fewer than 1% were associated with initiation of a recommended first-line mAUD. Initiation rates

In practice, EM physicians cite several barriers to initiating mAUD, including limited familiarity with prescribing, difficulty identifying appropriate candidates, a sense of futility, and stigma.[11]

De Monnin KS, American Emergency Medicine 2024

Online version at https://www.minervamedica.it

Panminerva Medica 2022 September;64(3):311-3
DOI: 10.23736/S0031-0808.22.04689-4

EDITORIAL

Proposal for the enhancement of alcohology (prevention, treatment and rehabilitation of alcohol problems): the position of Società Italiana di Alcologia (SIA), Federazione Italiana degli Operatori dei Dipartimenti e dei Servizi delle Dipendenze (FeDerSerD) and Società Italiana Tossicodipendenze (SITD)

Teo VIGNOLI [1, 2], Valeria ZAVAN [3, 4], Edoardo COZZOLINO [5], Giovanni ADDOLORATO [4, 6, 7], Maria F. AMENDOLA [2, 8], Fabio CAPUTO [2, 9, 10], Mauro CIBIN [4, 11], Alfio LUCCHINI [5], Felice A. NAVA [5, 12, 13], Rinaldo PELLICANO [14], Guido FAILLACE [5, 15], Luigi STELLA [4, 16, 17], Gianni TESTINO [2, 18] *

competence has not helped to reduce. Thus, it is recommended the presence of alcohol dedicated beds in hospitals and of an Alcohology Unit in hospitals that represent a hub in each of the 20 Italian regions; it is also recommended that each healthcare authority provide the presence of an Alcohology Outpatient Treatment Unit to supervise alcohology local network. Moreover, in the contest of territorial medicine, alcohology should be considered a part of the addiction medicine, with his specific peculiarity, converging in the Addiction Department and avoiding the combination with psychiatry or disciplines other than addiction medicine, in order to preserve the over mentioned cultural peculiarity in everyday work.

Gestione Ospedaliera

Attività di consulenza

– Consulenze al pronto soccorso

– Consulenze nei reparti ed eventuale trasferimento

(se posti letto) o inserimento nel percorso day service

– Valutazione alcologica della candidabilità al trapianto di fegato

(team integrato epato-alcologia/trapiantologia)

Internal and Emergency Medicine (2019) 14:143–160
https://doi.org/10.1007/s11739-018-1933-8

CE - ORIGINAL

Diagnosis and treatment of acute alcohol intoxication and alcohol withdrawal syndrome: position paper of the Italian Society on Alcohol

Fabio Caputo[1,2] · Roberta Agabio[3] · Teo Vignoli[4] · Valentino Patussi[5] · Tiziana Fanucchi[5] · Paolo Cimarosti[6] · Cristina Meneguzzi[6] · Giovanni Greco[7] · Raffaella Rossin[8] · Michele Parisi[9] · Davide Mioni[10] · Sarino Arico'[11] · Vincenzo Ostilio Palmieri[12] · Valeria Zavan[13] · Pierluigi Allosio[14] · Patrizia Balbinot[15] · Maria Francesca Amendola[16] · Livia Macciò[17] · Doda Renzetti[18] · Emanuele Scafato[19] · Gianni Testino[15]

Received: 26 April 2018 / Accepted: 22 August 2018 / Published online: 5 September 2018

Abstract

The chronic use of alcohol can lead to the onset of an alcohol use disorder (AUD). About 50% of subjects with an AUD may develop alcohol withdrawal syndrome (AWS) when they reduce or discontinue their alcohol consumption and, in 3–5% of them, convulsions and delirium tremens (DTs), representing life-threatening complications, may occur. Unfortunately, few physicians are adequately trained in identifying and treating AWS. The Italian Society on Alcohol has, therefore, implemented a task force of specialists to draw up recommendations for the treatment of AWS with the following main results: (1) while mild AWS may not require treatment, moderate and severe AWS need to be pharmacologically treated; (2) outpatient treatment is appropriate in patients with mild or moderate AWS, while patients with severe AWS need to be treated as in-patients; (3) benzodiazepines, BDZs are the "gold standard" for the treatment of AWS and DTs; (4) alpha-2-agonists, beta-blockers, and neuroleptics may be used in association when BDZs do not completely resolve specific persisting symptoms of AWS; (5) in the case of a refractory form of DTs, the use of anaesthetic drugs (propofol and phenobarbital) in an intensive care unit is appropriate; (6) alternatively to BDZs, sodium oxybate, clomethiazole, and tiapride approved in some European Countries for the treatment of AWS may be employed for the treatment of moderate AWS; (7) anti-convulsants are not sufficient to suppress AWS, and they may be used only in association with BDZs for the treatment of refractory forms of convulsions in the course of AWS.

Pharmacological treatment of Alcohol Use Disorder (AUD)

- *-ACUTE ALCOHOL INTOXICATION*
- **-ALCOHOL WITHDRAWAL SYNDROME (AWS)**
- **-RELAPSE PREVENTION**
  1. **MAINTENANCE OL ALCOHOL ABSTINENCE**
  2. **REDUCTION OF EPISODES OF HEAVY DRINKING/ REDUCTION OF HEAVY DRINKING DAYS (HDDs)**

Intensity of acute alcohol intoxication

Stages of Acute Intoxication in Nontolerant Individuals

Approximate Number of Drinks	Blood Alcohol Concentration	Typical Appearance of Individuals Consuming Alcohol*
1-2	less than 0.05	Virtually Sober; Only slight changes noticeable below 0.04%
2-5	0.03-0.12	Feeling Good; Decreased Inhibitions, Some loss of judgment, Mild impairment
4-10	0.09-0.25	Noticeably Impaired; "Feeling No Pain", Muscular Incoordination, Increased Reaction Time, Diminished Comprehension
7-12	0.18-0.30	Confused, Disoriented, Uncoordinated, Staggering, Slurred Speech
10-16	0.27- 0.40	Stuporous; Not Moving Much, Apathetic, Difficult to Stand; Falling Asleep
14+	0.35+	Unconscious, Coma, Absent Reflexes, Approaching Respiratory Depression, Circulatory Collapse and Death

*The appearance and onset of intoxication is quite variable among individuals and is dependent not only on the rate and amount of alcohol consumed, but also on the setting in which it is used, and the expectation of the person. These descriptions are a general guideline only and certainly do not describe everyone's response to alcohol all of the time.

Benowitz, McGraw-Hill, 1992

Management of acute alcohol intoxication in adults

–no drugs are generally necessary: monitor vital function, liquids administration, observe patient for the onset of alcohol withdrawal symptoms

–in the case of coma, support ventilation mechanically, correct hypoglycaemia with 5% glucose solution, hydro-electrolyte imbalance and base acid balance, administer vitamin B and vitamin C supplements, perform gastro-lavage and administer activated charcoal only within 2 h of drinking a considerable amount of alcohol

–in the case of the simultaneous use of other sedative drugs, antidotes should be administered: naloxone (0.4 mg i.v. or i.m. repeated, if necessary, every 30 min) for the use of opioids and flumazenil (0.2 mg, repeated, if necessary, every minute up to 3 mg) for the use of benzodiazepines

–metadoxine 900 mg i.v. reduces BAC and leads to a more rapid resolution of the symptoms (Grade A2)

–alcohol hangover: fruit and fruit juice, sleep and physical rest, anti-acid drugs, acetylsalicylic acid, and caffeine may be helpful

(Caputo et al., Int Emerg Med, 2018

Management of acute alcohol intoxication in adolescents

–adolescents do not show tolerance to the effects developed by repeated exposure to ethanol and they have *immature hepatic alcohol deydrogenase activity: more exposed to the toxic effect of alcohol and rapid onset of coma*

–the lethal dose of alcohol varies as widely among children and adolescents as it does among adults: lethal BAC for infants and adolescents is not certain

–hypoglycaemia and hypothermia tend to be more severe in young individuals than in adults: management for all adolescents should be focused on the prompt correction of hypoglycaemia, hypothermia and restlessness (haloperidol)

–the administration of antiemetics is preferred to gastric content aspiration, as well as maintaining airway patency; venous access is necessary to ensure fluid administration

–so far, no studies have been performed on metadoxine use for the improvement of symptoms of AAI in the paediatric population

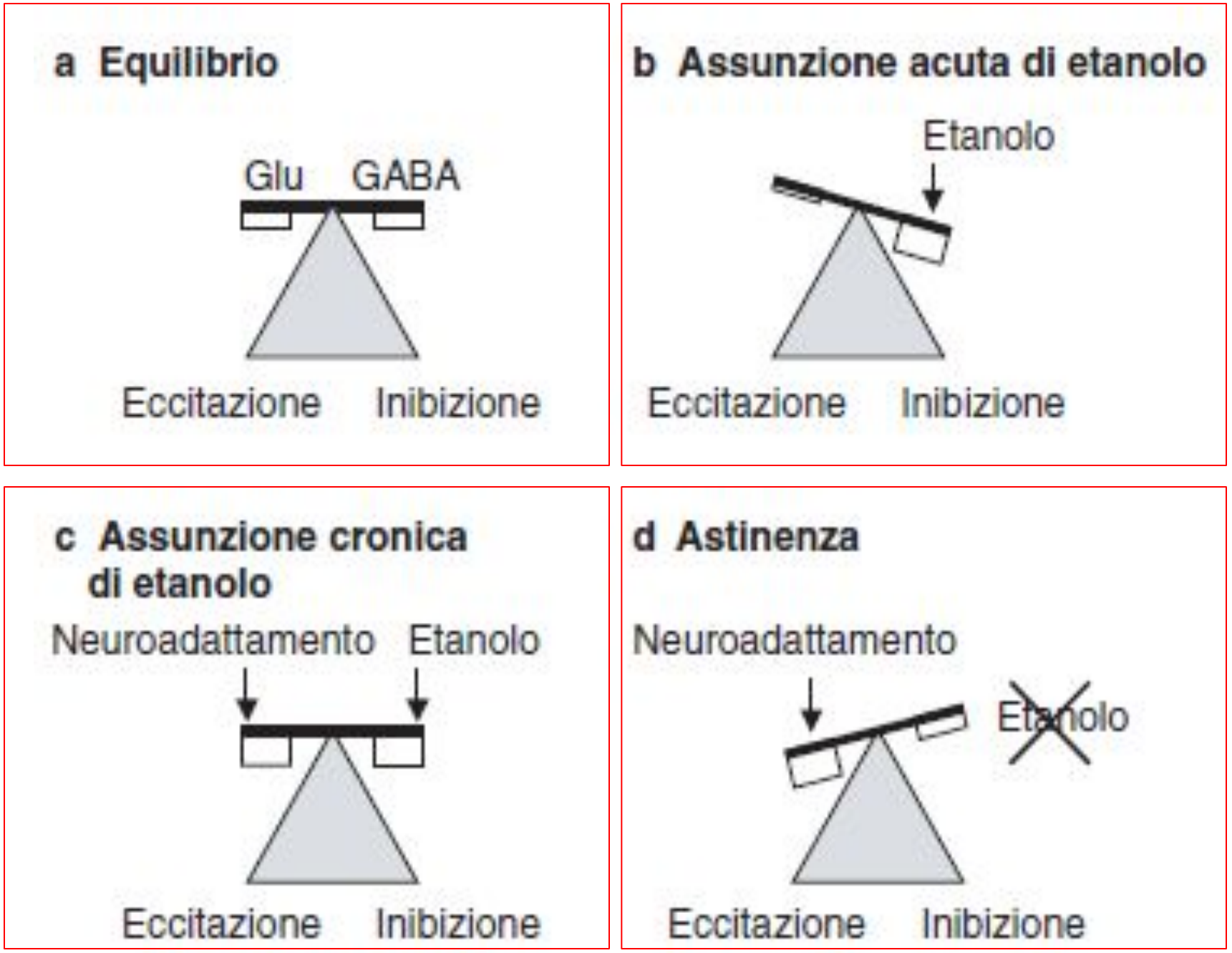
Caputo et al., Int Emerg Med, 2018

Pharmacological treatment of Alcohol Use Disorder (AUD)

- **-ACUTE ALCOHOL INTOXICATION**
- ***-ALCOHOL WITHDRAWAL SYNDROME (AWS)***
- **-RELAPSE PREVENTION**

  1. MAINTENANCE OL ALCOHOL ABSTINENCE

  2. REDUCTION OF EPISODES OF HEAVY DRINKING / REDUCTION OF HEAVY DRINKING DAYS (HDDs)



(Himmelsbach, Ann Int Med, 1941)

Criteria for alcohol withdrawal

Cessation of or reduction in heavy and prolonged use of alcohol

At least two of eight possible symptoms after reduced use of alcohol:

- Autonomic hyperactivity
- Hand tremor
- Insomnia
- Nausea or vomiting
- Transient hallucinations or illusions
- Psychomotor agitation
- Anxiety
- Generalized tonic–clonic seizures

Criteria for delirium

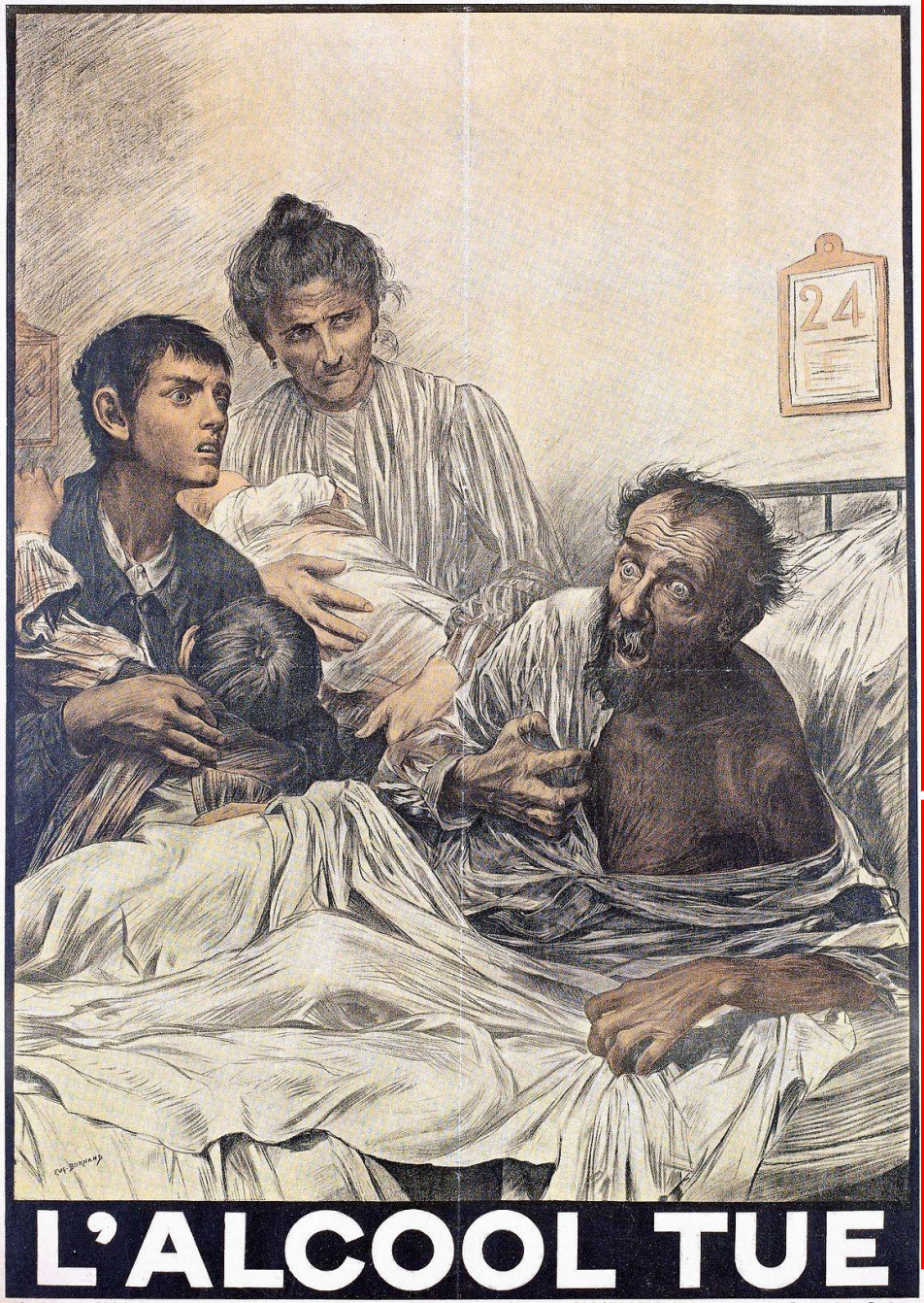
Decreased attention and awareness

Disturbance in attention, awareness, memory, orientation, language, visuo-spatial ability, perception, or all of these abilities that is a change from the normal level and fluctuates in severity during the day

Disturbances in memory, orientation, language, visuospatial ability, or perception

No evidence of coma or other evolving neurocognitive disorders

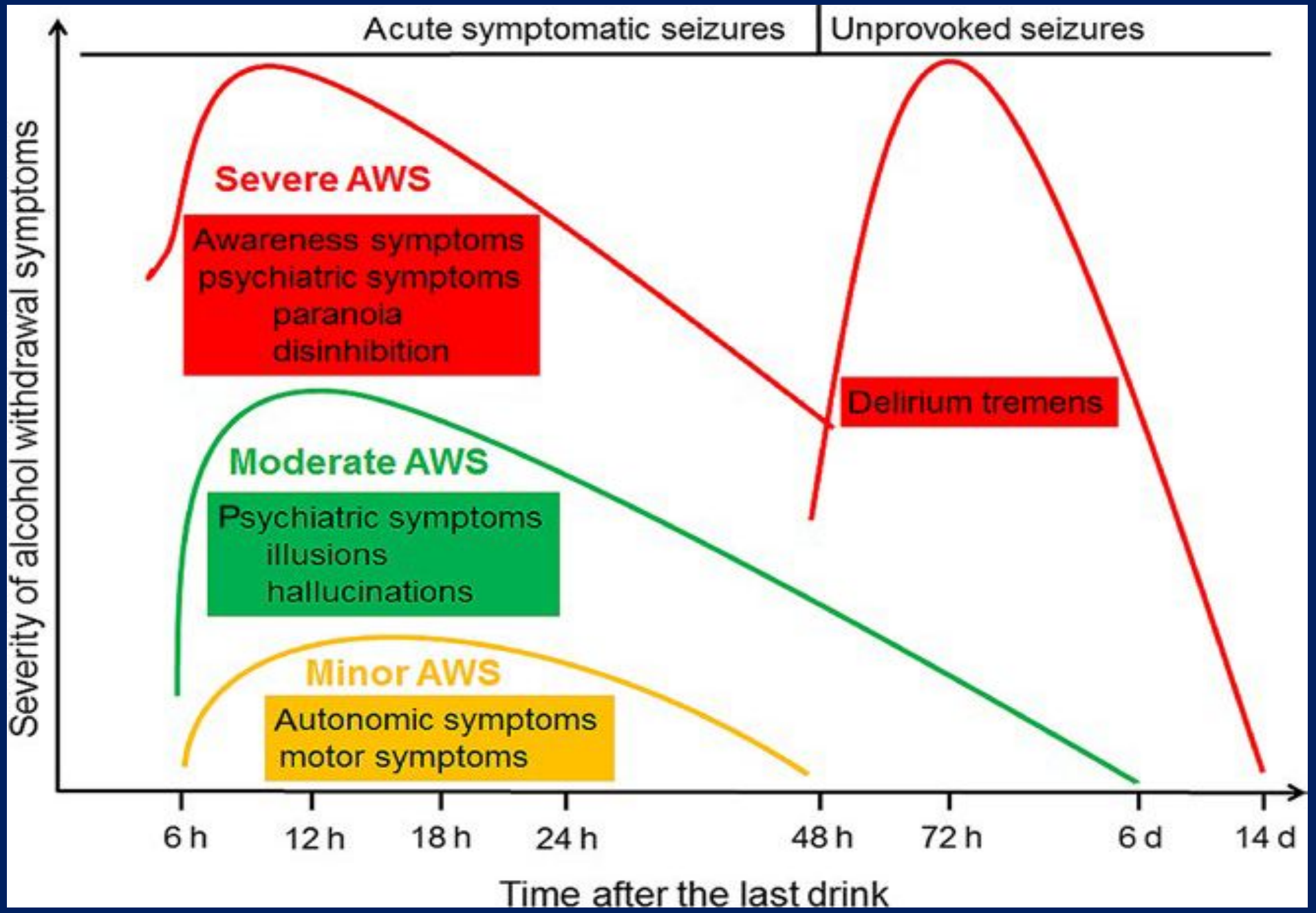
(American Psychiatric Association, 2013)



In particolare, il Delirium Tremens (DTs) è una condizione clinica caratterizzata da disturbo cognitivo e dell'attenzione ad insorgenza rapida e fluttuante, talvolta caratterizzata da allucinazioni

Fino a qualche anno fa, la mortalità per DTs era del 5-15% (ipertermia, aritmie, collasso cardiocircolatorio).
Dopo l'avvento dei farmaci specifici, la mortalità si è ridotta a non più dell'1% .

(Schuckit, NEJM, 2014)



(*Jesse et al., Acta Neurol*

Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar)

Symptoms	Range of scores
Nausea or vomiting	0 (no nausea, no vomiting): 7 (constant nausea and/or vomiting)
Tremor	0 (no tremor): 7 (severe tremors, even with arms not extended)
Paroxysmal sweats	0 (no sweat visible): 7 (drenching sweats)
Anxiety	0 (no anxiety, at ease): 7 (acute panic states)
Agitation	0 (normal activity): 7 (constantly thrashes about)
Tactile disturbances	0 (none): 7 (continuous hallucinations)
Auditory disturbances	0 (not present): 7 (continuous hallucinations)
Visual disturbances	0 (not present): 7 (continuous hallucinations)
Headache	0 (not present): 7 (extremely severe)
Orientation/clouding of sensorium	0 (orientated, can do serial additions): 4 (disorientated for place and/or person)

<8 mild withdrawal
8-15 moderate withdrawal
> 15 severe withdrawal

If initial score < 8, assess q 4 h x 72 hrs
If score < 8 for 72 hrs, discontinue assessment

(Sullivan et al., Br J Addict, 1989)

PREDICTORS OF COMPLICATED AWS

1. Previous episodes of AWS
2. Previous alcohol withdrawal seizures
3. History of DT
4. History of alcohol rehabilitation treatment
5. Previous episodes of blackouts
6. Concomitant use of CNS-depressant agents, such as benzodiazepine or barbiturates
7. Concomitant use of other illicit substances
8. Recent episode of alcohol intoxication
9. Blood alcohol level (BAL) on admission > 200 mg/dl
10. Evidence of increased autonomic activity (tremor, sweating, agitation, nausea, HR > 120)

≥4 criteria suggest HIGH RISK to develop moderate to severe AWS; prophylaxis and/or treatment may be indicated

(Maldonado et al, Alcohol, 2014)

Mechanism of kindling

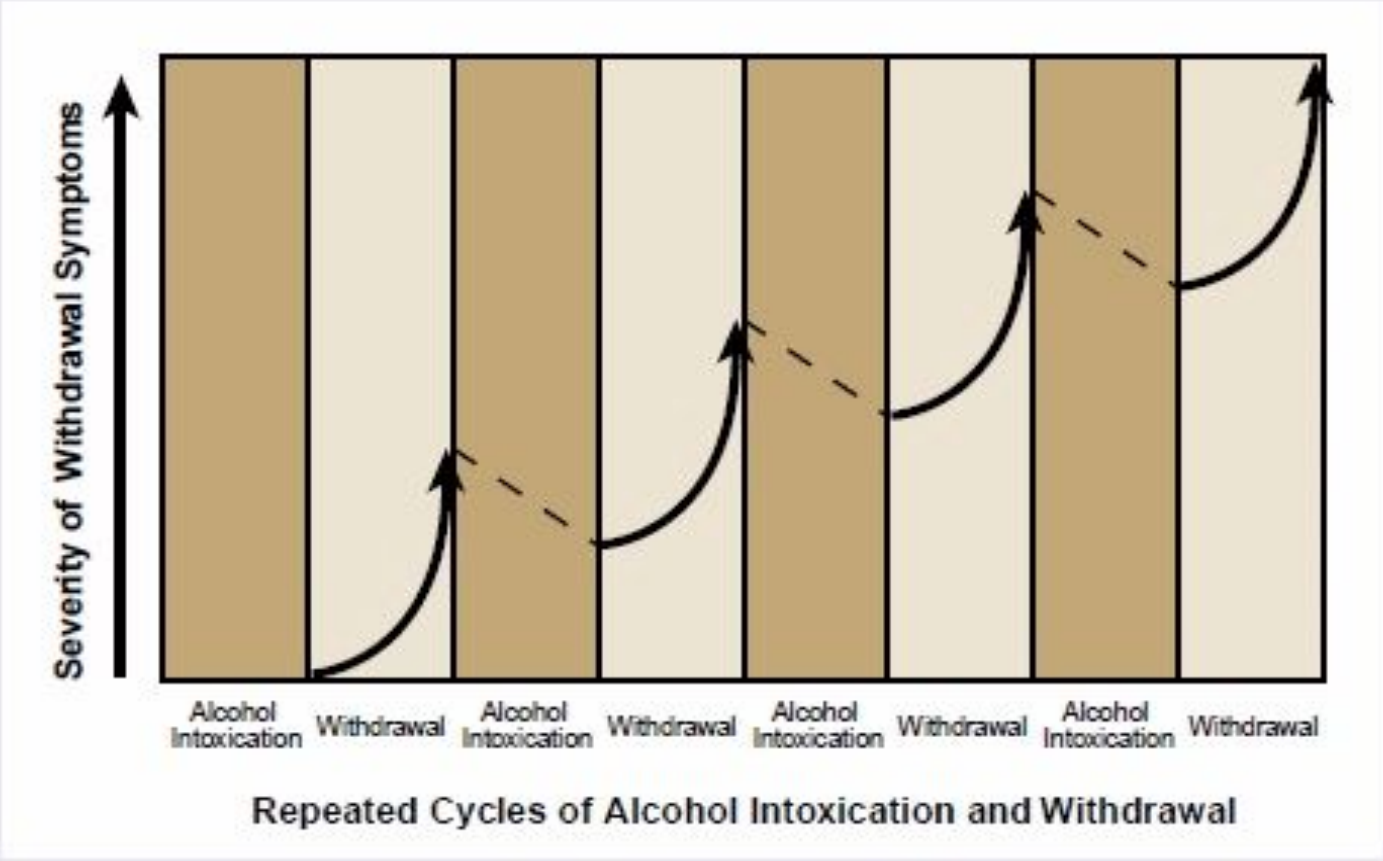


Fig aphic representation of the kindling concept during alcohol withdrawal. e term "kindling" refers to the phenomenon that people undergoing repeated cycles of intoxication followed by abstinence and withdrawal will experience increasingly severe withdrawal symptoms with each successive cycle.

(Gonzales et al., ACER, 2001)

Trattamento non-farmacologico della SAA

-monitoraggio parametri vitali, continua rassicurazione del paziente e, se disponibile, una stanza tranquilla senza rumore non eccessivamente illuminata o eccessivamente scura

-idratazione fino a 1500-2000 cc (soluzioni glucosata al 5% e salina)

-complessi vitaminici per prevenire l'insorgenza del quadro clinico di encefalopatia di Wernicke (oftalmoplegia del VI nervo cranico, atassia e confusione mentale):

-Vit B_1 (tiamina) (250 mg di Vit B_1 i.m./die, per 3-5 gg.)

-Vit B_6 e B_{12}, vitamina C e folati

NB: in caso di encefalopatia di Wernicke il trattamento prevede l'utilizzo di una dose maggiore di tiamina:

-500 mg i.m. o e.v. tre volte al giorno per almeno 2 giorni insieme a Vit B_6 e B_{12} e Vit C (Agabio, 2005)

-tiamina va somministrata prima di ogni infusione di glucosio per evitare l'insorgenza o la progressione della sindrome di Wernicke

-controllare i valori sierici di magnesio e, se ridotti, integrarli in quanto l'uso cronico di bevande alcoliche e la SAA sono strettamente correlate al prolungamento dell'intervallo QT con rischio di aritmie (Espay, 2014)

(Schuckit, NEJM, 2014)

The two methods of treatment for alcohol withdrawal syndrome (treat only if CIWA-Ar > 8 points)

Treatment with a symptom-triggered regimen

Chlordiazepoxide: 50–100 mg orally[a]

Diazepam: 10–20 mg orally or i.v.[a]

Lorazepam: 2–4 mg orally, i.v. or i.m.[a]

Oxazepam: 60–90 mg orally[a]

Treatment with a fixed-schedule regimen

Chlordiazepoxide: 50–100 mg every 6 h (day 1), then 25–50 mg every 6 h (days 2 and 3)[b]

Diazepam: 10 mg orally or i.v. every 6 h (day 1), then 5 mg every 6 h (days 2 and 3)[b]

Lorazepam: 2 mg orally or i.v. every 6 h (day 1), then 1 mg every 6 h (days 2 and 3)[b]

Oxazepam: 60–90 mg orally or i.v. every 6 h (day 1), then 30–60 mg every 6 h (days 2 and 3)[b]

Tiapride: 400–1200 mg orally i.m. or i.v. every 4–6 h from day 1 to day 3[c]

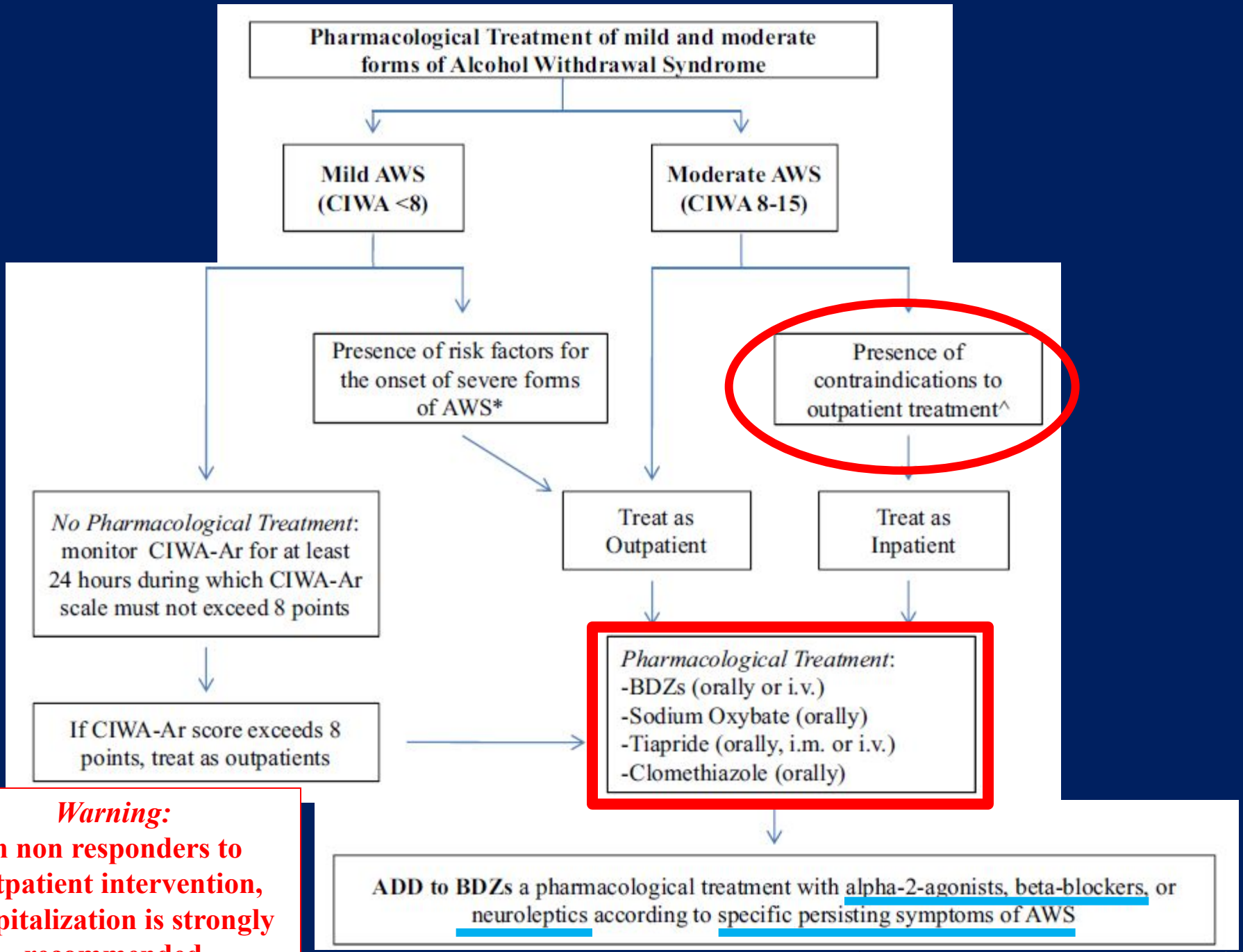
Sodium oxybate: 50–100 mg/kg fractioned into 3 or 6 daily administrations (every 4 or 6 h) from day 1 to day 3[c]

[a]Administer CIWA-Ar every hour, and if score persists > 8 points, repeat the administration of the drug

[b]On day 4, start to gradually reduce the dose by 25% every day until day 7, then suspend

[c]On day 4, follow a tapering procedure according to the attenuation of symptoms: you may then decide to continue the administration of the drugs in the maintenance of alcohol abstinence at the dosages of 50 mg/kg per day for sodium oxybate and 300 mg/day for tiapride

(Caputo et al., Int Emerg Med, 2018)



Warning:
in non responders to outpatient intervention, hospitalization is strongly recommended

(SIA, Int Emerg Med, 2018)

Only in association with BDZs

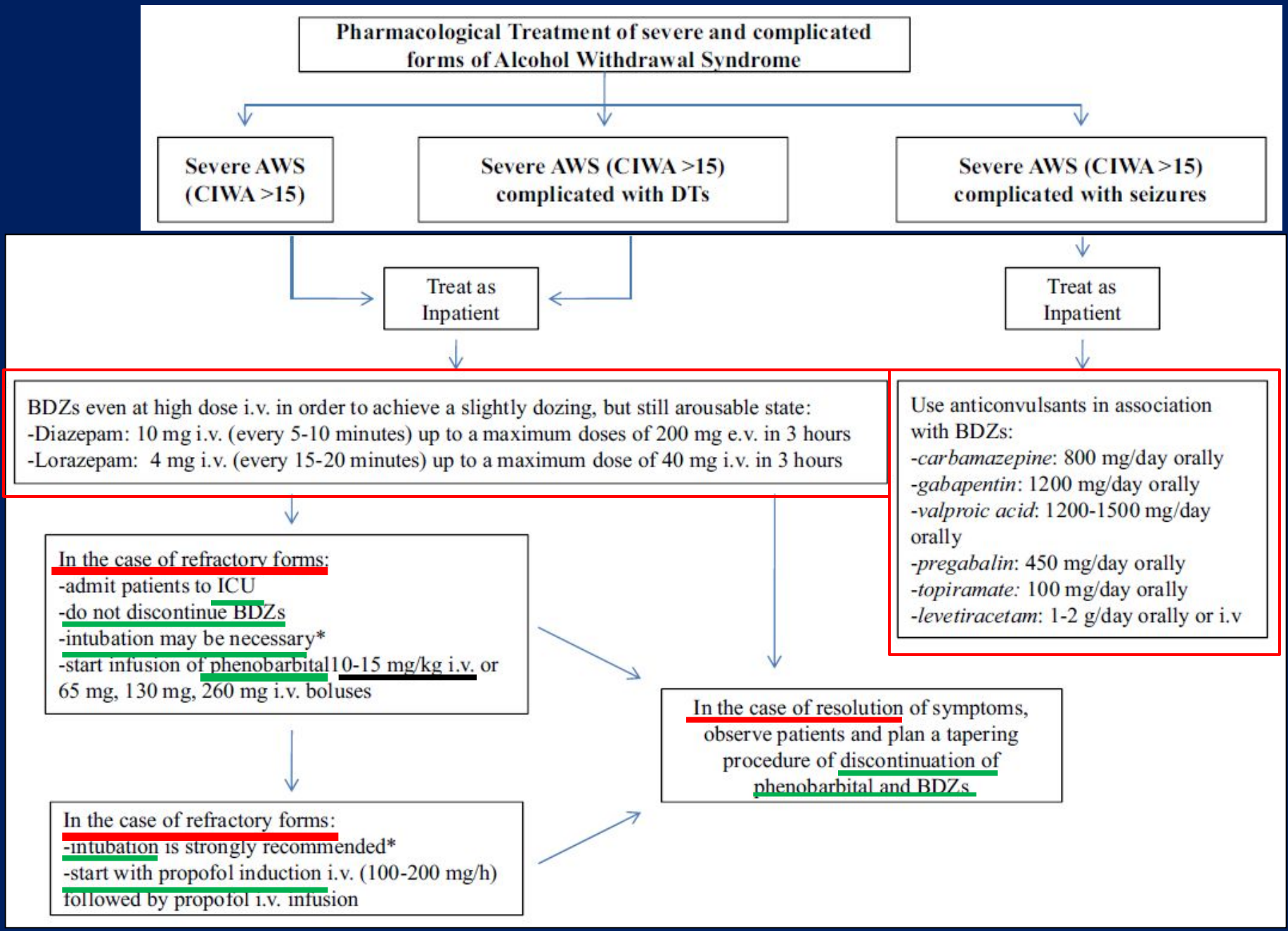
(when high dosages of BDZs are inadequate to control AWS)

- **Neuroleptic agents (haloperidol: 0.5-5 mg orally every 4 hs or 0.5-5 mg i.v./i.m. every 30-60 minutes)**

- **beta-blockers (atenolol: 100 mg/day orally) or central sympatholytics (clonidine: 0.150-0.300 mg/day orally)**

- **Anticonvulsants (carbamazepine: 800 mg/day orally the first 3 days, than 600 mg/day from 4 to 7 day, than 400 mg/day on day 8, than 200 mg/day on day 9)**

(Mayo-Smith MF et al., Arch Intern Med, 2004)



(*Caputo et al., Int Emerg Med, 2018*

Internal and Emergency Medicine
https://doi.org/10.1007/s11739-018-1933-8

CE - ORIGINAL

Diagnosis and treatment of acute alcohol intoxication and alcohol withdrawal syndrome: position paper of the Italian Society on Alcohol

Fabio Caputo[1,2] · Roberta Agabio[3] · Teo Vignoli[4] · Valentino Patussi[5] · Tiziana Fanucchi[5] · Paolo Cimarosti[6] · Cristina Meneguzzi[6] · Giovanni Greco[7] · Raffaella Rossin[8] · Michele Parisi[9] · Davide Mioni[10] · Sarino Arico'[11] · Vincenzo Ostilio Palmieri[12] · Valeria Zavan[13] · Pierluigi Allosio[14] · Patrizia Balbinot[15] · Maria Francesca Amendola[16] · Livia Macciò[17] · Doda Renzetti[18] · Emanuele Scafato[19] · Gianni Testino[15]

-BDZs are the "gold standard" for the treatment of AWS and DTs (Grade A1)

-alternatively to BDZs, sodium oxybate, clomethiazole, and tiapride approved in some European Countries for the treatment of AWS may be employed for the treatment of moderate AWS (Grade A1)

-alpha-2 agonists, beta-blockers, neuroleptics, and anticovulsants may be used in association with BDZs when BDZs do not completely resolve specific persisting symptoms of AWS and the refractory forms of convulsions in the course of AWS (Grade A1)

(Caputo et al., Int Emerg Med, 2019)

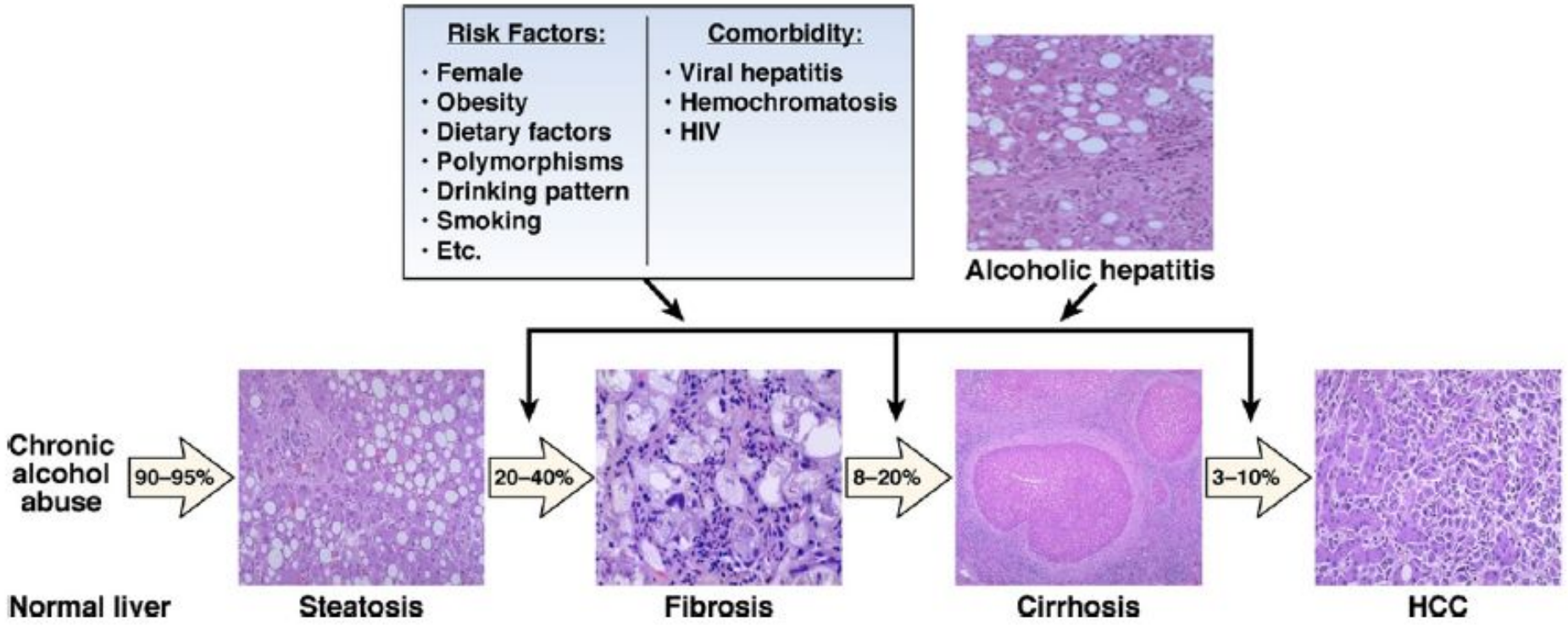
GASTROENTEROLOGY 2011;141:1572–1585

REVIEWS IN BASIC AND CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

Robert F. Schwabe and John W. Wiley, Section Editors

Alcoholic Liver Disease: Pathogenesis and New Therapeutic Targets

BIN GAO* and RAMON BATALLER‡



EPATOLOGIA

↓

EPATO - ALCOLOGIA

DISTURBO DA USO DI ALCOL

- 80% dei decessi per epatopatia

- 60% dei decessi per cirrosi epatica in Italia

- prima causa di inserimento in lista/ trapianto di fegato

- prognosi estremamente sfavorevole (mortalità a 5 anni del 71% e a 15 anni del 91%)

Frenette et al, Dig Disc Sci 2021

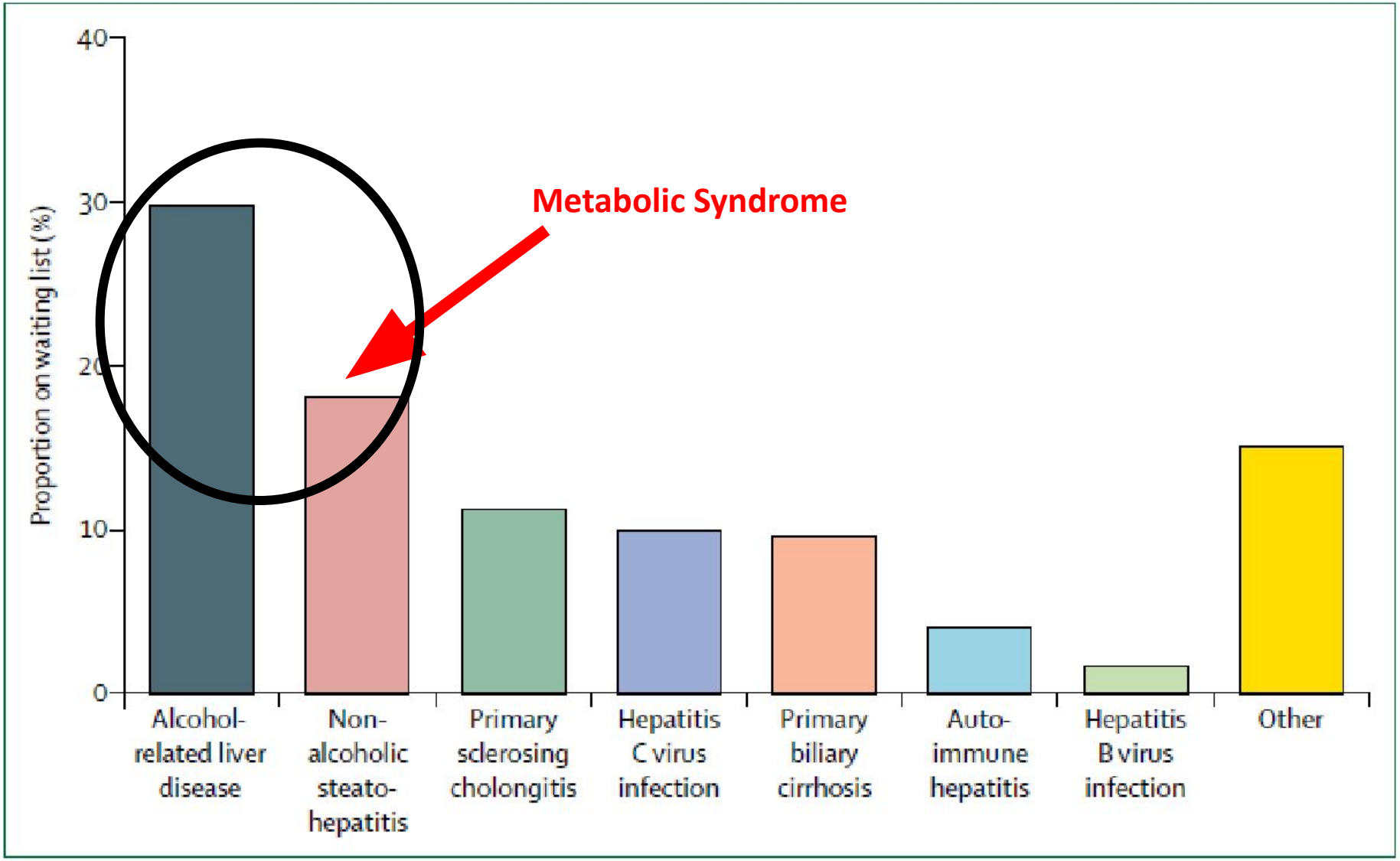


Figure 6: Causes of liver disease in patients on liver transplantation waiting list as of January, 2017

Williams et al, The Lancet, Vol 391 March 17, 2018

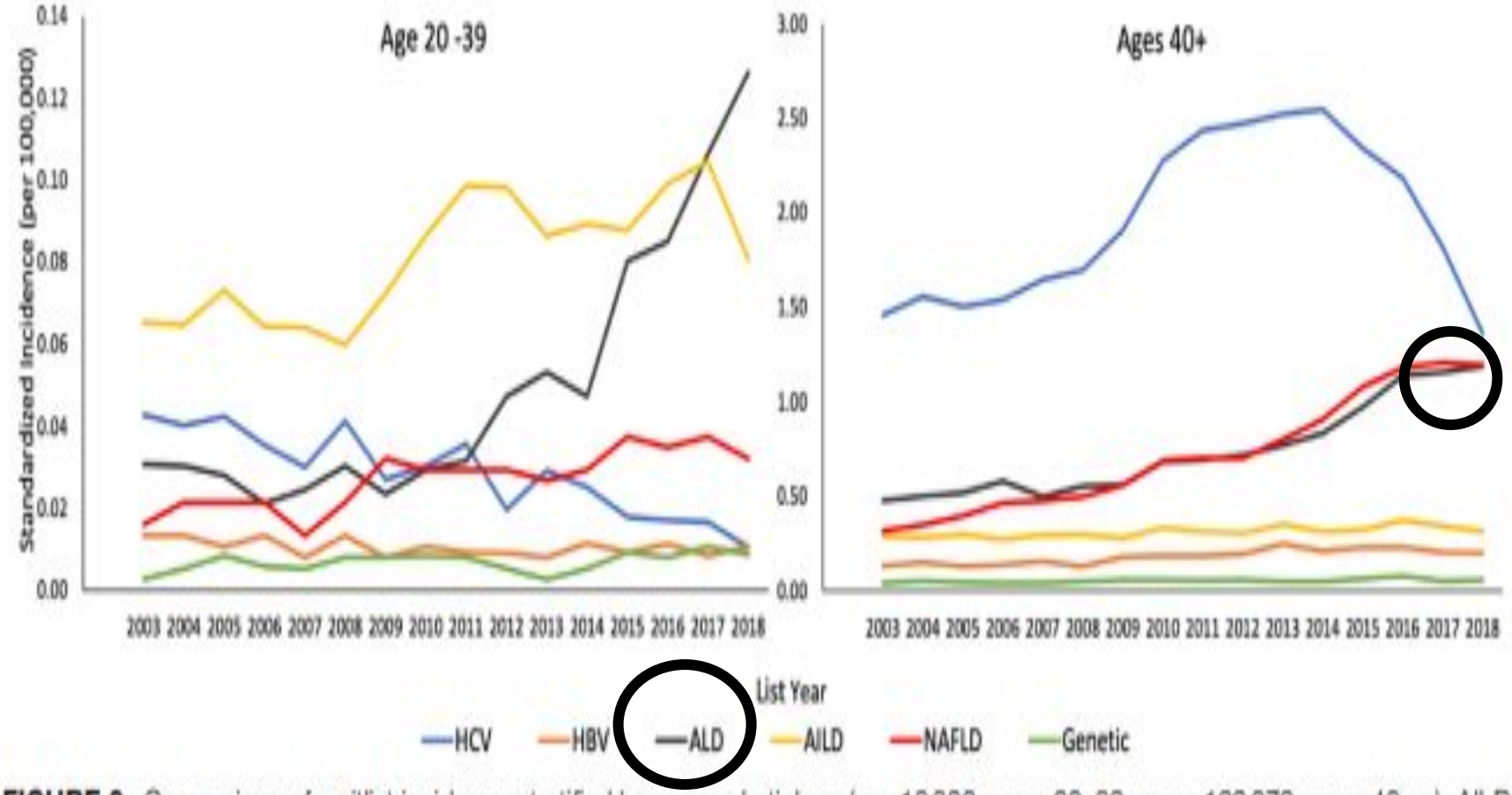


FIGURE 2. Comparison of waitlist incidence stratified by age and etiology (n = 10326: ages 20–39 y; n = 199073: ages 40+ y). AILD, autoimmune liver disease; ALD, alcohol-associated liver disease; HBV, hepatitis B virus; HCV, hepatitis C virus; NAFLD, nonalcoholic fatty liver disease.

Philip et al, Transplantation 2022; doi: 10.1097/TP.0000000000004202

Digestive and Liver Disease 52 (2020) 21–32

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

Guidelines

Management of end-stage alcohol-related liver disease and severe acute alcohol-related hepatitis: position paper of the Italian Society on Alcohol (SIA)

Gianni Testino[a], Teo Vignoli[b], Valentino Patussi[c], Emanuele Scafato[d], Fabio Caputo[e,f,*], on behalf of the SIA board (Appendix A) and the external expert supervisors (Appendix B)

[a] *Unit of Addiction and Hepatology ASL3 Liguria, San Martino Hospital, Genova, Italy*
[b] *Unit of Addiction Treatment, Lugo, Ravenna, Italy*
[c] *Regional Centre on Alcohol, Careggi Hospital, Firenze, Italy*
[d] *National Observatory on Alcohol, National Institute of Health, Roma, Italy*
[e] *Department of Internal Medicine, SS Annunziata Hospital, Cento, Ferrara, Italy*
[f] *"G. Fontana" Centre for the Study and Multidisciplinary Treatment of Alcohol Addiction, Department of Medical and Surgical Sciences, University of Bologna, Italy*

Recommendations 3

- DSM-V is the accepted diagnostic method to identify patients with AUD (Grade A1)
- Patients with AUD on the transplant waiting list should be checked for alcohol use by regular clinical interviews and use of laboratory tests to confirm abstinence (Grade A1).
- AUDIT or AUDIT-C should be used to screen patients for AUD (Grade A1)
- Metadoxine, due to its efficacy in rapidily reducing the half-life of ethanol, should be used to rapidily improve symptoms of AAI (Grade A2)
- Abstinence can be accurately monitored by measurement of EtG in urine (Grade A2)
- Short acting benzodiazepines should be used to treat AWS with a symptoms trigger approach in order to avoid drug accumulation due to reduced hepatic clearance (Grade A1)
- Pharmacotherapy to reduce craving for alcohol should be considered in patients with AUD and ESALD or SAAH (Grade A1) in accordance with the presence or absence of HE, and liver and renal impairment; baclofen seems to be the safest medication to be used as first line therapy in patients with ESALD and SAAH (Grade B2).

HEPATOLOGY

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

CONCISE REVIEW | HEPATOLOGY, VOL. 0, NO. 0, 2019

Diagnosis and Treatment of Alcohol Use Disorder in Patients With End-Stage Alcoholic Liver Disease

General indications (CIWA-Ar score > 8 points)

-Benzodiazepines (BDZs) with short half-life: lorazepam (1 or 2 mg once a day [qd] or twice daily [bid]) or oxazepam (15 mg qd or bid), with subsequent titration up to the dose achieving complete symptom remission

***Caution**: A trigger-dose approach (administration only at the onset of symptoms) to avoid the risk of drug accumulation is preferable, starting with the lowest therapeutic doses. Close medical supervision is needed.*

-Parenteral thiamine (200 mg/day for 3-5 days) to prevent Wernicke encephalopathy

-Haloperidol (0.5 mg-5 mg every 30-60 minutes intravenously or intramuscularly or 0.5 mg-5 mg every 4 hours orally) to treat hallucinations

-α_2-agonists or β-blockers to reduce autonomic hyperactivity

(Caputo et al., Hepatology, 2019)

Drugs (2015) 75:353–365
DOI 10.1007/s40265-015-0358-1

THERAPY IN PRACTICE

Identification and Management of Alcohol Withdrawal Syndrome

Antonio Mirijello · Cristina D'Angelo · Anna Ferrulli · Gabriele Vassallo · Mariangela Antonelli · Fabio Caputo · Lorenzo Leggio · Antonio Gasbarrini · Giovanni Addolorato

Drug	Half-life	Active metabolites	Metabolism	Excretion
Diazepam	20–80 h (metabolites 30–100 h)	Yes	Hepatic	Hepatic: urinary (metabolites)
Chlordiazepoxide	5–30 h (metabolites 30–200 h)	Yes	Hepatic	Hepatic: urinary (metabolites)
Lorazepam	10–20	No	Hepatic	Urinary, fecal
Oxazepam	10–20	No	Hepatic	Urinary
Midazolam	2–6	Yes	Hepatic, gut	Urinary

(Mirijello et al., Drugs, 2015)

EPATITE ALCOLICA ACUTA

La manifestazione clinica copre un largo spettro di segni e sintomi che vanno dall'ittero asintomatico a forme più severe caratterizzate dalla combinazione di encefalopatia, febbre, astenia, coagulopatia, leucocitosi

Wells JT, Liver Transplantation 2007

Mortalità a 30 giorni: 35-40% dei casi; a 6 mesi: 70% dei casi

Day CP, Liver Transplantation 2007; Burroughs AK, Int Hepatol 2012
Lanthier and Starkel, Eur J Clin Invest 2017; Marot et al, PLoS ONE 2018

Scoring system	Calculation				Severe disease score
Maddrey discriminant function (mDF)	4.6 × [patient's prothrombin time (seconds) − control prothrombin time (seconds)] + bilirubin (mg/dL)				32
Model for end-stage liver disease (MELD) **MELD-sodio**	3.8 × $\log_e$ bilirubin (mg/dL) + 11.2 × $\log_e$ INR + 9.6 × $\log_e$ creatinine (mg/dL) + 6.4				21
Glasgow Alcoholic Hepatitis Score (GAHS)		1	2	3	
	Age (years)	<50	≥50	–	
	WCC (10^9/L)	<15	≥15	–	
	Urea (mmol/L)	<5	≥5	–	9
	PT ratio	<1.5	1.5–2.0	>2.0	
	Bilirubin (μmol/L)	<125	125–250	>250	
	- Sum the points assigned for each of the 5 variables				
ABIC (age, serum bilirubin, INR, and serum creatinine)	Age (years) × 0.1 + bilirubin (mg/dL) × 0.08 + creatinine (mg/dL) × 0.3 + INR × 0.8				9
Lille score	3.19 − 0.101 × age (years) + 0.147 × albumin on day 0 (g/L) + 0.0165 × the change in bilirubin between day 0 and day 7 of corticosteroid treatment (μmol/L) − 0.206 × renal insufficiency (rated as 0 if absent and 1 if present) − 0.0065 × bilirubin on day 0 (μmol/L) − 0.0096 × prothrombin time (seconds)				0.45

(Dugum & McCullough, J Clin Translat Hepatol, 2015)

ACUTE ON CHRONIC LIVER FAILURE

Acute on chronic liver failure (ACLF) can occour during the course of chronic liver disease

Acute decompensation* (ascites, encephalopaty, hemorrhage and/or infection) *along with at least one failure of the following organs or systems: kidney, brain, coagulation, circulation, lungs

Table 1. CLIF-SOFA Score

Organ/system	0	1	2	3	4
Liver (bilirubin, *mg/dL*)	<1.2	≥1.2 to ≤2.0	≥2.0 to <6.0	≥6.0 to <12.0	**≥12.0**
Kidney (creatinine, *mg/dL*)	<1.2	≥1.2 to <2.0	**≥2.0 to <3.5**	**≥3.5 to <5.0**	**≥5.0**
				or use of renal replacement therapy	
Cerebral (HE grade)	No HE	I	II	**III**	**IV**
Coagulation (international normalized ratio)	<1.1	≥1.1 to <1.25	≥1.25 to <1.5	≥1.5 to <2.5	**≥2.5 or platelet count ≤20×10³/L**
Circulation (mean arterial pressure, *mm Hg*)	≥70	<70	**Dopamine ≤5 or dobutamine or terlipressin**	**Dopamine >5 or E ≤0.1 or NE ≤0.1**	**Dopamine >15 or E >0.1 or NE >0.1**
Lungs					
PaO_2/FIO_2 or	>400	>300 to ≤400	>200 to ≤300	**>100 to ≤200**	**≤100**
SpO_2/FIO_2	>512	>357 to ≤512	>214 to ≤357	**>89 to ≤214**	**≤89**

NOTE. The original SOFA score is described by Vincent et al.[21] Like the SOFA score, the CLIF-SOFA score includes subscores ranging from 0 to 4 for each of 6 components (liver, kidneys, brain, coagulation, circulation, and lungs), with higher scores indicating more severe organ impairment. Aggregated scores range from 0 to 24 and provide information on overall severity. The text in bold indicates the diagnostic criteria for organ failures (see also Supplementary Materials and Methods).

HE, hepatic encephalopathy; E, epinephrine; NE, norepinephrine; PaO_2, partial pressure of arterial oxygen; FIO_2, fraction of inspired oxygen; SpO_2, pulse oximetric saturation.

MORTALITY often exceeding 50%

Acute-on-chronic liver failure

William Bernal, Rajiv Jalan, Alberto Quaglia, Kennet

Acute-on-chronic liver failure combines
chronic liver disease and hepatic and e
mortality. Common precipitants include
than 40% of patients, no precipitating ev

Review

Acute-on-chronic

Vicente Arroyo[1], Ricl
of the investigatc

[1]Liver Unit, Hospital Clinic, University of Barcelon
Paris, UMR S_1149, Université Paris Diderot, Paris, DHU UNITY, Service d'Hepatologie, Hopital Beaujon, APHP, Clichy, France; Liver Failure Group, Institute for Liver and Digestive Health, Royal Free Hospital, UCL, London, United Kingdom; [4]Liver Unit, Hospital Clinic, University of Barcelona, Insitut d'Investigacions Biomediques August Pi I Sunyer (IDIBAPS), Centro de Investigacion Biomedica en Red Enfermedades Hepaticas y Digestivas (CIBEReHD), Instituto Reina Sofia de Investigacion en Nefrologia (IRSIN), Spain

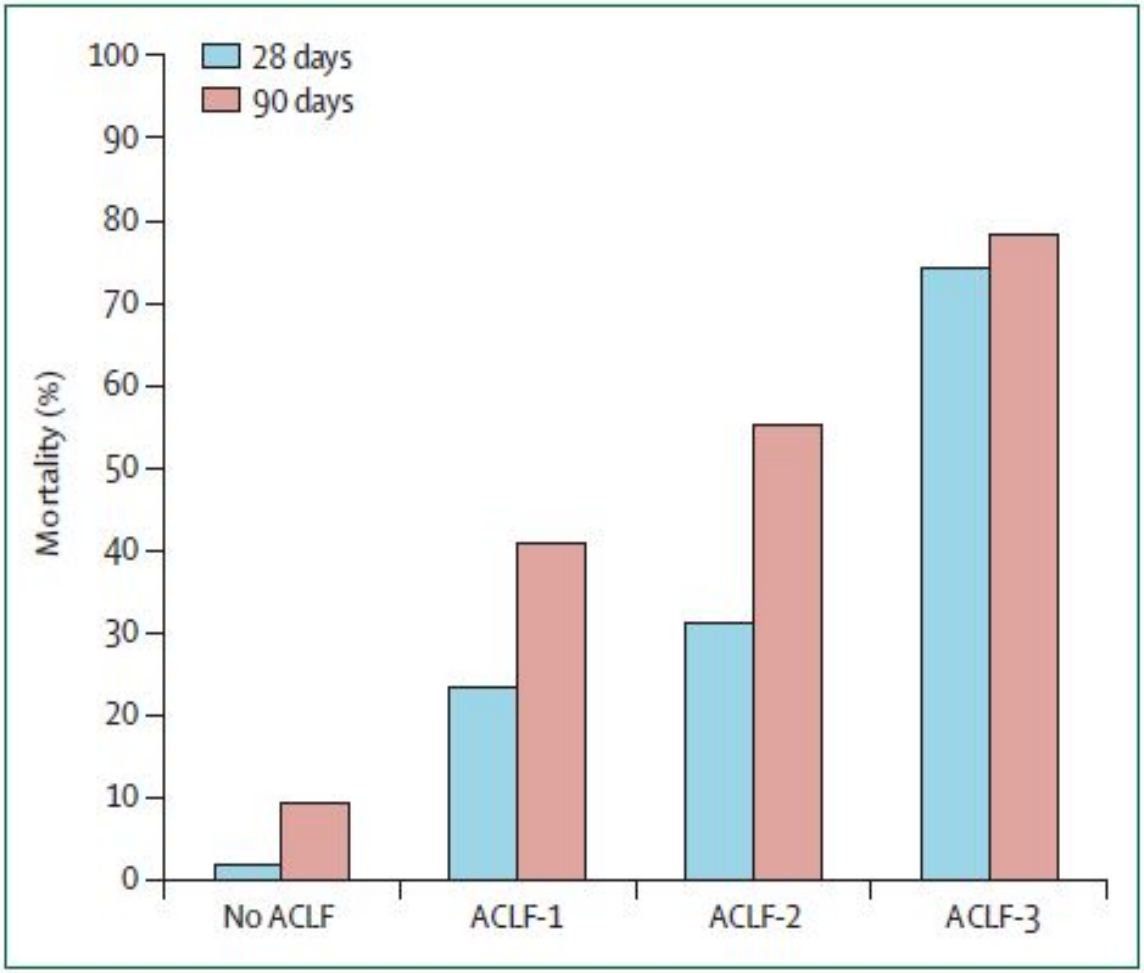
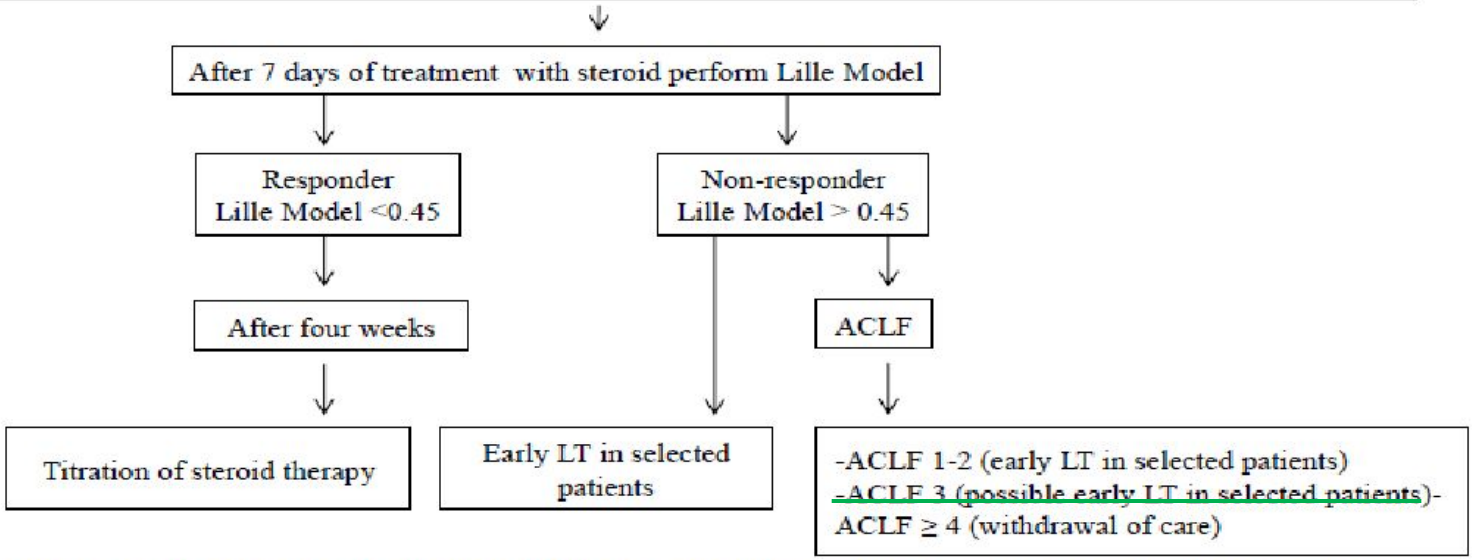


Table 4: Therapeutic pathway in patients with SAAH or ACLF and AUD

-management of ESALD complications (i.e. HE: lactulose / lactilol and rifamixin 400 mg t.i.d. or 550 mg b.i.d. in case of refractary form of HE)
-nutritional status (>35-40 kcal/kg BW, 1.2-1.5 g/kg proteins)
-management of AWS with short acting benzodiazepines (lorazepam 1-2 mg q.d or b.i.d orally or i.v. or oxazepam 15 mg q.d or b.i.d orally) following a trigger symptoms regimen
-vitamins supplementation (Vit B1: 200 mg/day for 3-5 days to prevent Wernicke encephalopathy); haloperidol (0.5-5 mg every 30-60 minutes iv or 0.5-5 mg every 4 hours orally) to treat hallucinations; alpha-2 agonists or beta-blockers to reduce autonomic hyperactivity
-maintenance of alcohol abstinence with multi-disciplinary treatment: psychosocial-therapy, family support, self-help groups, and pharmacotherapy (i.e. baclofen 10 mg t.i.d.)*
-identification and management of infections
-in case of mDF≥32: prednisolone 40 mg/day or methylprednisolone 32 mg/day** for 28 days plus N-acetyl-cysteine for 5 days (day 1: 150 mg/kg in 250 ml of 5% glucose solution over a period of 30 minutes, then 50 mg/kg in 500 ml of glucose solution over a period of 4 hours, and 100 mg/kg in 1000 ml of glucose solution over a period of 16 hours; days 2-5, 100 mg/kg/day in 1000 ml of glucose solution) ± antibiotic therapy in case of sepsis°



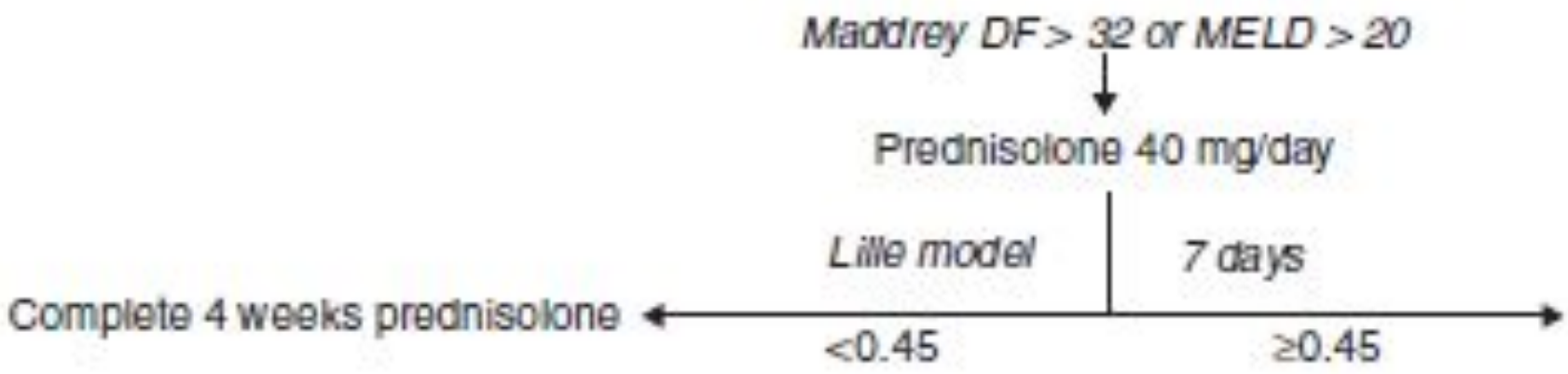
*not in case of hepato-renal syndrome (HRS), hepatic encephalopathy (HE), and neuro-psychiatric contraindications; **not in case of bleeding, infections, renal failure; °in case of sepsis, corticosteroid needs to be collegially discussed evaluating risks and benefits.

Position Paper of the Italian Society on Alcohol, Dig Liver Dis 2020

SAAH: severe acute alcoholic hepatitis; ACLF: acute-on-chronic liver failure

ACG Clinical Guideline: Alcoholic Liver Disease

Ashwani K. Singal, MD, MS, FACG[1], Ramon Bataller, MD, PhD, FACG[2], Joseph Ahn, MD, MS, FACG (GRADE Methodologist)[3], Patrick S. Kamath, MD[4] and Vijay H. Shah, MD, FACG[4]



Stop prednisolone and consider

- Early OLT among select patients
- Clinical trials
- Discussion on goals of care if ≥4 organsfailure

(Singal et al., Am J Gastroenterol, 2018)

Encefalopatia Epatica

20% dei pazienti affetti da cirrosi epatica ospedalizzati in Italia presentano EE

Quasi il 40% dei pazienti ospedalizzati per EE saranno nuovamente ospedalizzati entro 1 anno per cause correlate all'encefalopatia

Necessità di gestione a breve e a lungo termine.

(Bass et al. N Engl J Med 2010)

Encefalopatia Epatica

Non tutte le encefalopatie sono epatiche

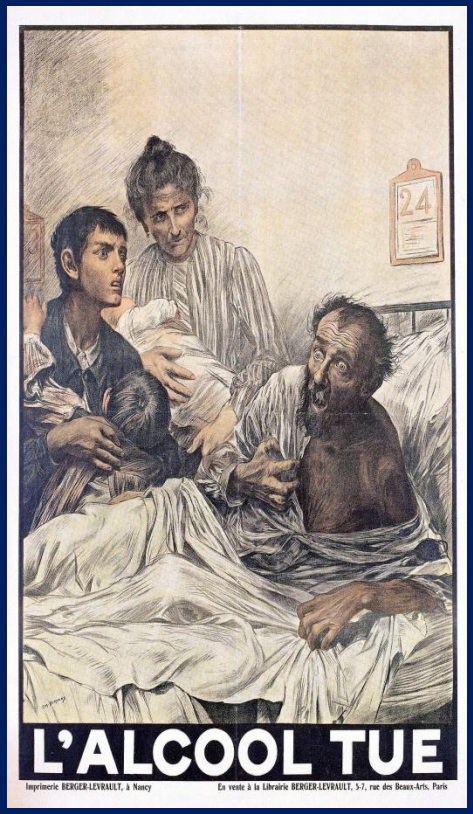
(da ricordare ancor di più in pazienti con epatopatia alcolica nei quali le comorbidità neuropsichiatriche sono frequenti)

- **Delirium tremens**

-Dovuto a sospensione o intossicazione da alcol.

-Può includere agitazione, terrore, insonnia, febbricola e instabilità autonomica. Allucinazioni possono essere uditive e di natura persecutoria o kinesthetiche (tattili-insetti)

-Appare gradualmente 2-3 giorni dopo la cessazione dell'alcol con un picco di intensità al 4° o 5° giorno



(Mack et al., American Psychiatric Publishing 2010; Caputo et l., Int Emerg Med, 2019)

Encefalopatia Epatica

Non tutte le encefalopatie sono epatiche

(da ricordare ancor di più in pazienti con epatopatia alcolica nei quali le comorbidità neuropsichiatriche sono frequenti)

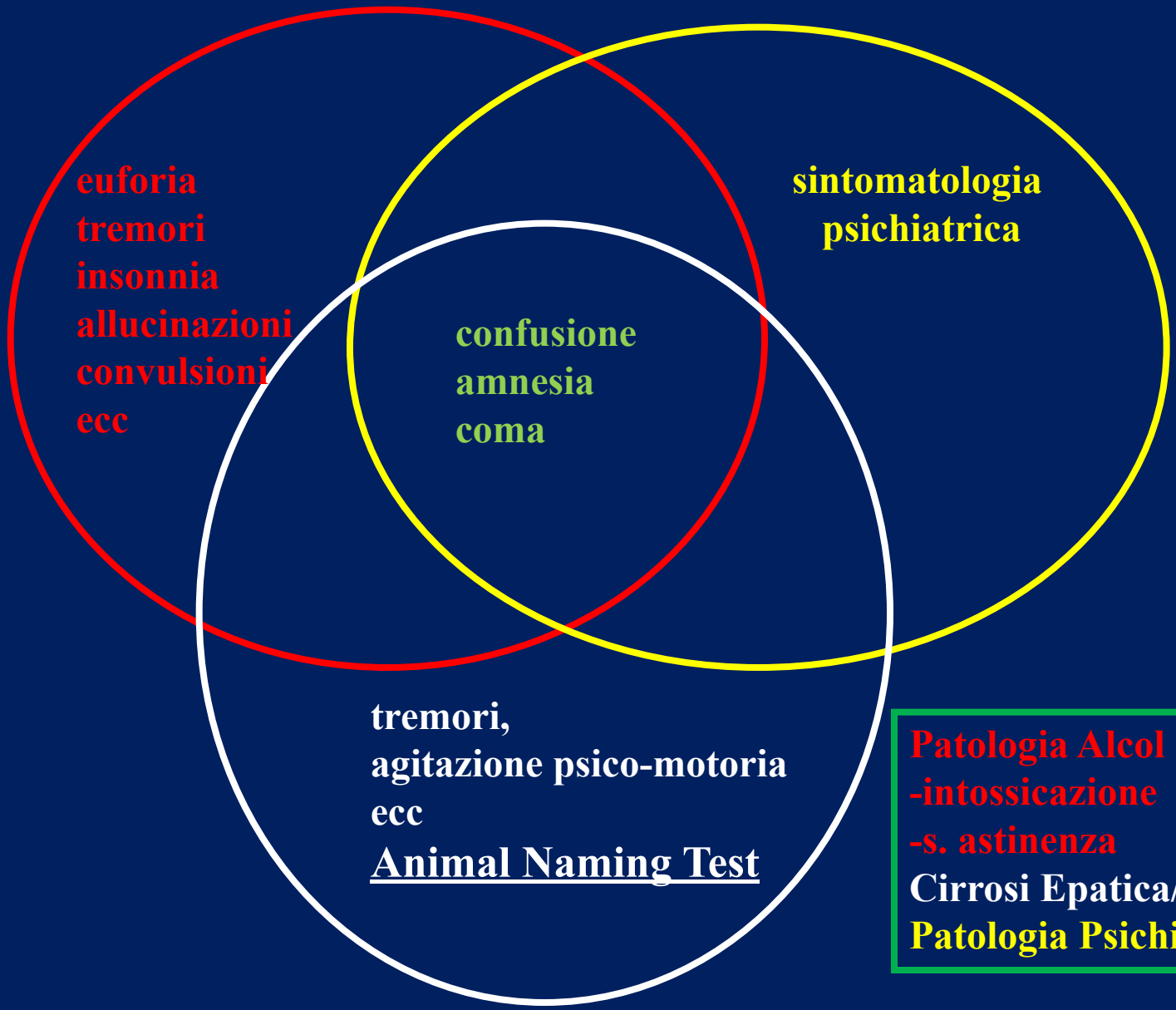
- **Sindrome di Wernicke-Korsakoff**

Disordine amnesico persistente indotto dall'alcol

dovuto a deficit di vitamina B1 con amnesia e neuropatia periferica, atassia cerebellare e miopatia

(Mack et al, American Psychiatric Publishing 2010; Caputo et al, Int Emerg Med, 2019)

CAREGIVER: OSSERVAZIONE



Patologia Alcol Correlata
-intossicazione
-s. astinenza
Cirrosi Epatica/Encefalopatia
Patologia Psichiatrica

Testino, Balbinot; Il ruolo del Caregiver, Speciale Famiglie, ASL3 2021

HEPATOLOGY

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

CONCISE REVIEW | HEPATOLOGY, VOL. 0, NO. 0, 2019

Diagnosis and Treatment of Alcohol Use Disorder in Patients With End-Stage Alcoholic Liver Disease

Treatment in specific settings

-*HE:* Prompt treatment should be pursued; then treatment of AWS can be initiated.

-*Ascites, hepatorenal syndrome, and variceal hemorrhage:* Ascites *per se* does not contraindicate short-acting BDZs. In patients with hepatorenal syndrome, BDZs should be used with great caution due to the simultaneous impairment of liver and kidney functions. Intravenous short-acting BDZs such as lorazepam (oxazepam is not available in intravenous formulation) can be used in patients with variceal hemorrhage.

(Caputo et al., Hepatology, 2019)

Digestive and Liver Disease 52 (2020) 21–32

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

Guidelines

Management of end-stage alcohol-related liver disease and severe acute alcohol-related hepatitis: position paper of the Italian Society on Alcohol (SIA)

Gianni Testino[a], Teo Vignoli[b], Valentino Patussi[c], Emanuele Scafato[d], Fabio Caputo[e,f,*], on behalf of the SIA board (Appendix A) and the external expert supervisors (Appendix B)

-management of complications (i.e. HE: lactulose / lactilol and rifaximin 400 mg t.i.d. or 550 mg b.i.d. in cases of refractary forms of HE)
-management of AWS (short acting benzodiazepines; trigger symptoms regimen)
-vitamin supplementation

(Testino et al., Dig Liv Dis,

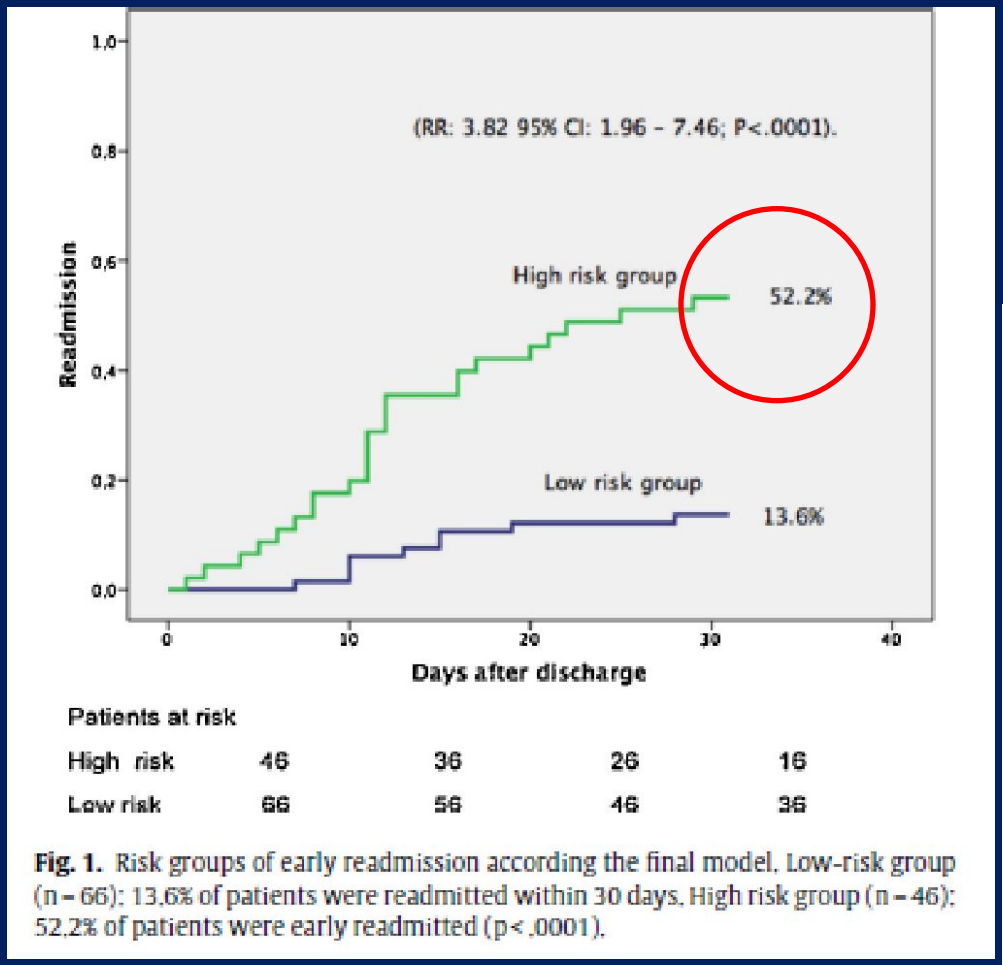


Fig. 1. Risk groups of early readmission according the final model. Low-risk group (n = 66): 13.6% of patients were readmitted within 30 days. High risk group (n = 46): 52.2% of patients were early readmitted (p < .0001).

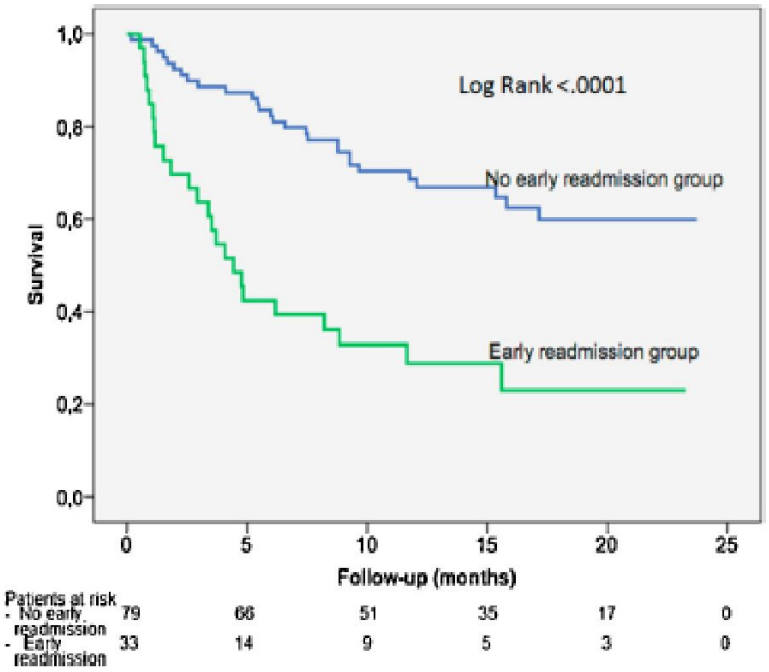


Fig. 2. Survival at the end of follow-up between patients with & without early readmission.

-Aderenza terapeutica (1/3)
-Assenza di relazione con il servizio di appartenenza
-«burnout» familiare caregiver

Morales BP et al, Dig Liver Dis 2017; 49: 903-9

Comment > Dig Liver Dis. 2020 Mar;52(3):358-359. doi: 10.1016/j.dld.2019.12.002.
Epub 2019 Dec 23.

Hospital readmission of patients with hepatic encephalopathy: Is the introduction of the formal caregiver useful in care management?

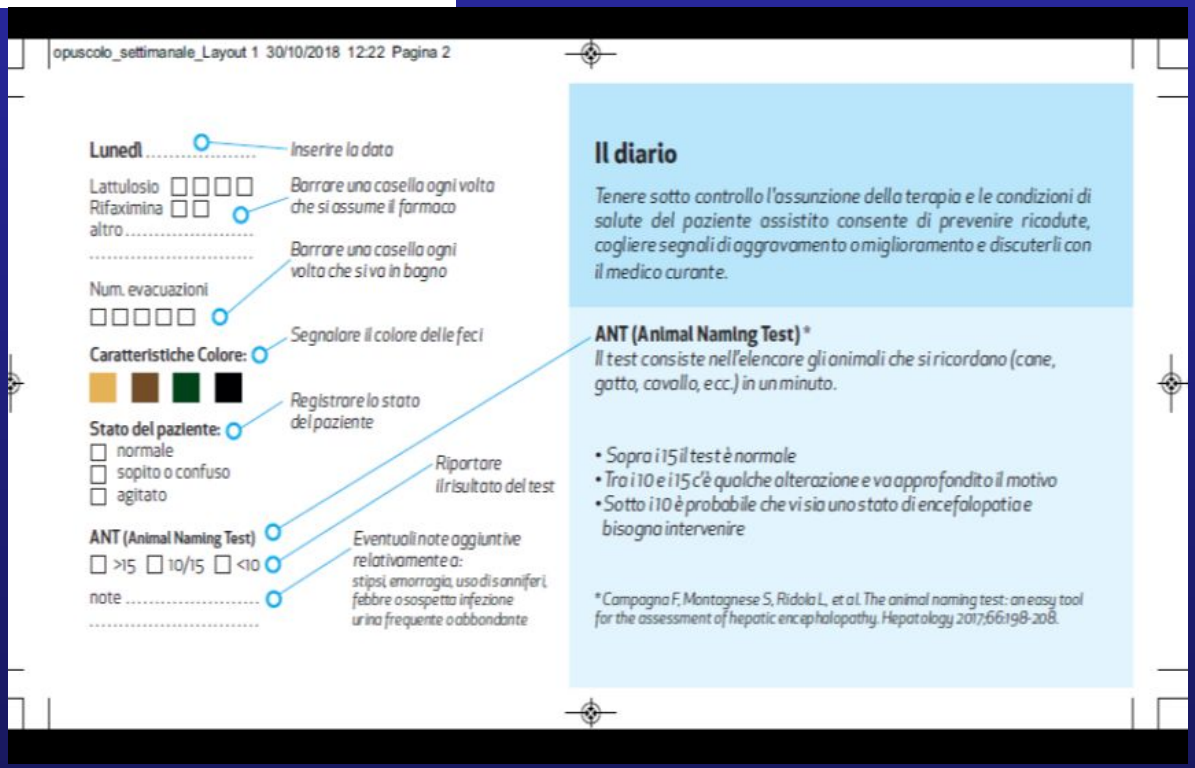
Patrizia Balbinot [1], Silvia Leone [1], Gianni Testino [2], Fabio Caputo [3]

Affiliations – collapse

Affiliations

1 Unit of Addiction and Hepatology, ASL3 Liguria c/o San Martino Hospital, Genova, Italy.
2 Unit of Addiction and Hepatology, ASL3 Liguria c/o San Martino Hospital, Genova, Italy. Electronic address: gianni.testino@hsanmartino.it.
3 Department of Internal Medicine, SS Annunziata Hospital, Cento, Ferrara, Italy; "G. Fontana" Centre for the Study and Multidisciplinary Treatment of Alcohol Addiction, Department of Medical and Surgical Science, University of Bologna, Italy.

Diario e Animal Naming Test



Asl3

Sistema Sanitario Regione Liguria

IL RUOLO DEL CAREGIVER NELLA GESTIONE DEL PAZIENTE CON ENCEFALOPATIA EPATICA

SPECIALE FAMIGLIE

a cura di Gianni Testino (medico epatologo)
e Patrizia Balbinot (caregiver formale)
del Centro Alcologico/SC Patologie delle Dipendenze ed Epatologia
ASL3 Liguria e Centro Studi del Centro Alcologico ASL3
"Auto Mutuo Aiuto, Programmi di Comunità e Formazione Caregiver"

Asl3

Sistema Sanitario Regione Liguria

IL RUOLO DEL CAREGIVER NELLA GESTIONE DEL PAZIENTE CON ENCEFALOPATIA EPATICA

SPECIALE MEDICI

a cura di Gianni Testino (medico epatologo)
e Patrizia Balbinot (caregiver formale)
del Centro Alcologico/SC Patologie delle Dipendenze ed Epatologia
ASL3 Liguria e Centro Studi del Centro Alcologico ASL3
"Auto Mutuo Aiuto, Programmi di Comunità e Formazione Caregiver"

C. A. T.
CLUB
degli ALCOLISTI
in TRATTAMENTO

Associazione
Italiana dei
Club
Alcologici
Territoriali
(metodo hudolin)


GRAZIE