Addiction Treatment in Alcohol Associated Liver Disease

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Disclosures

- No disclosures for:
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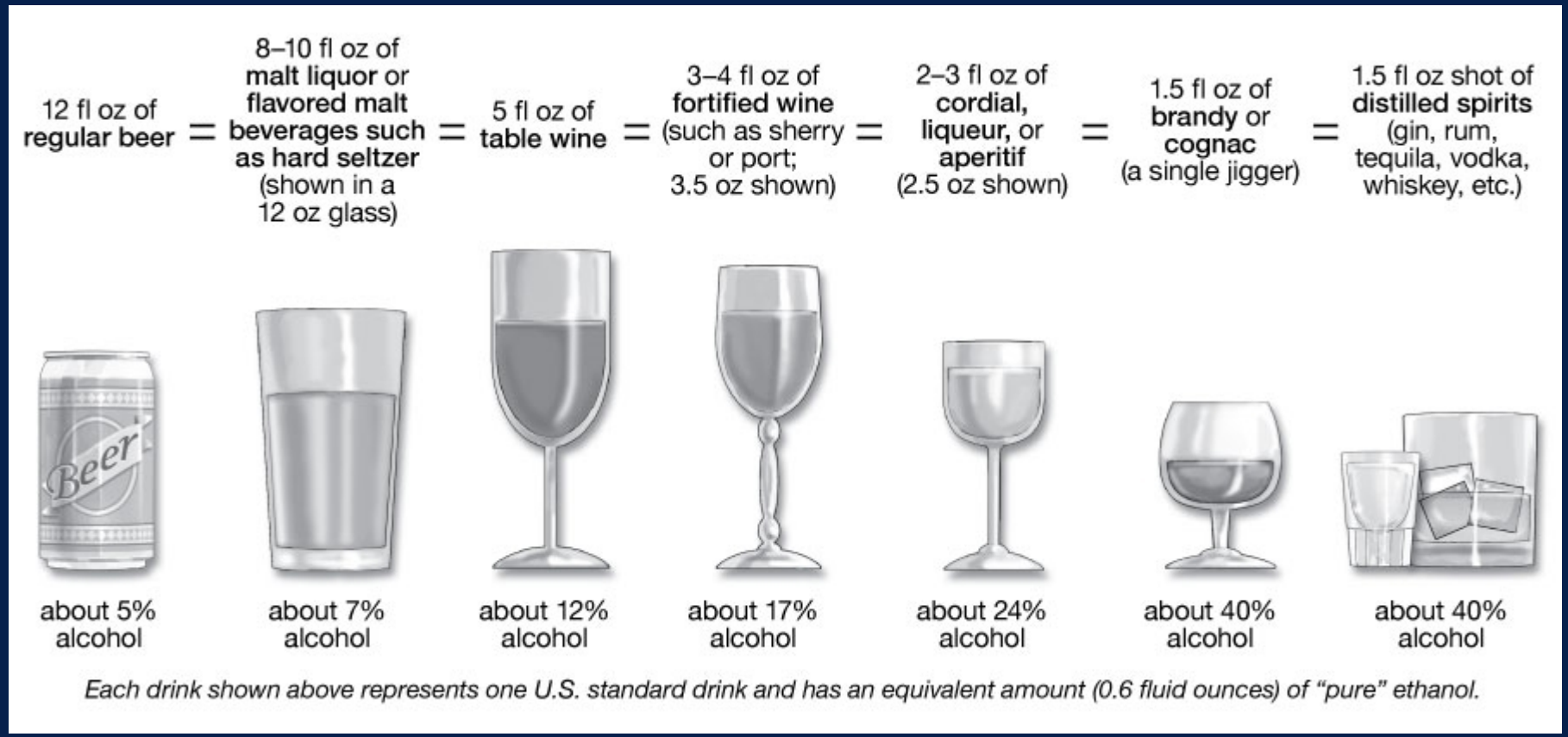
Learning Objectives

- Review harms related to alcohol use
- Explore alcohol-associated liver disease (ALD)
- Explore alcohol use disorder (AUD)
- Discuss challenges in treating AUD with ALD
- Discuss ALD specific addiction treatment

Alcohol

- 63% of US adults consumed alcohol in 2022
- Associated with >200 diseases
  - Excessive use linked to 1 in 8 deaths among 20-64 in 2015-19
  - Linked to 30% of homicides, 22% of suicides, 33% MVAs
- COVID-19 has only intensified alcohol use

A “standard drink”



U.S. Guidelines

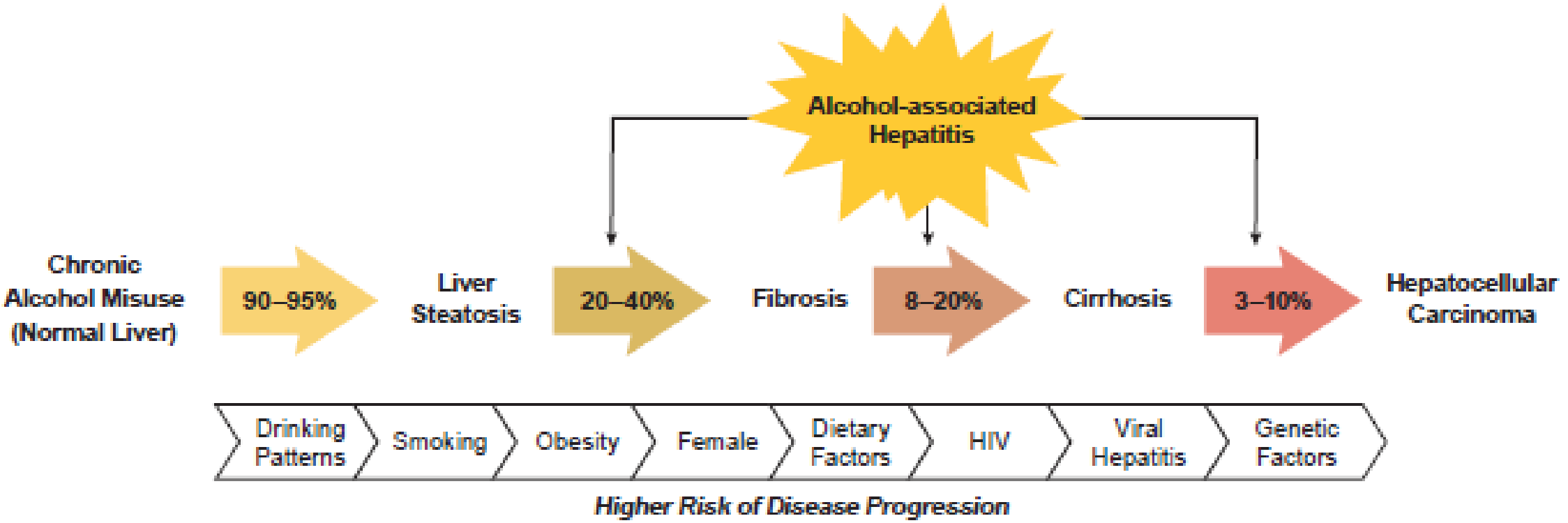
NIAAA

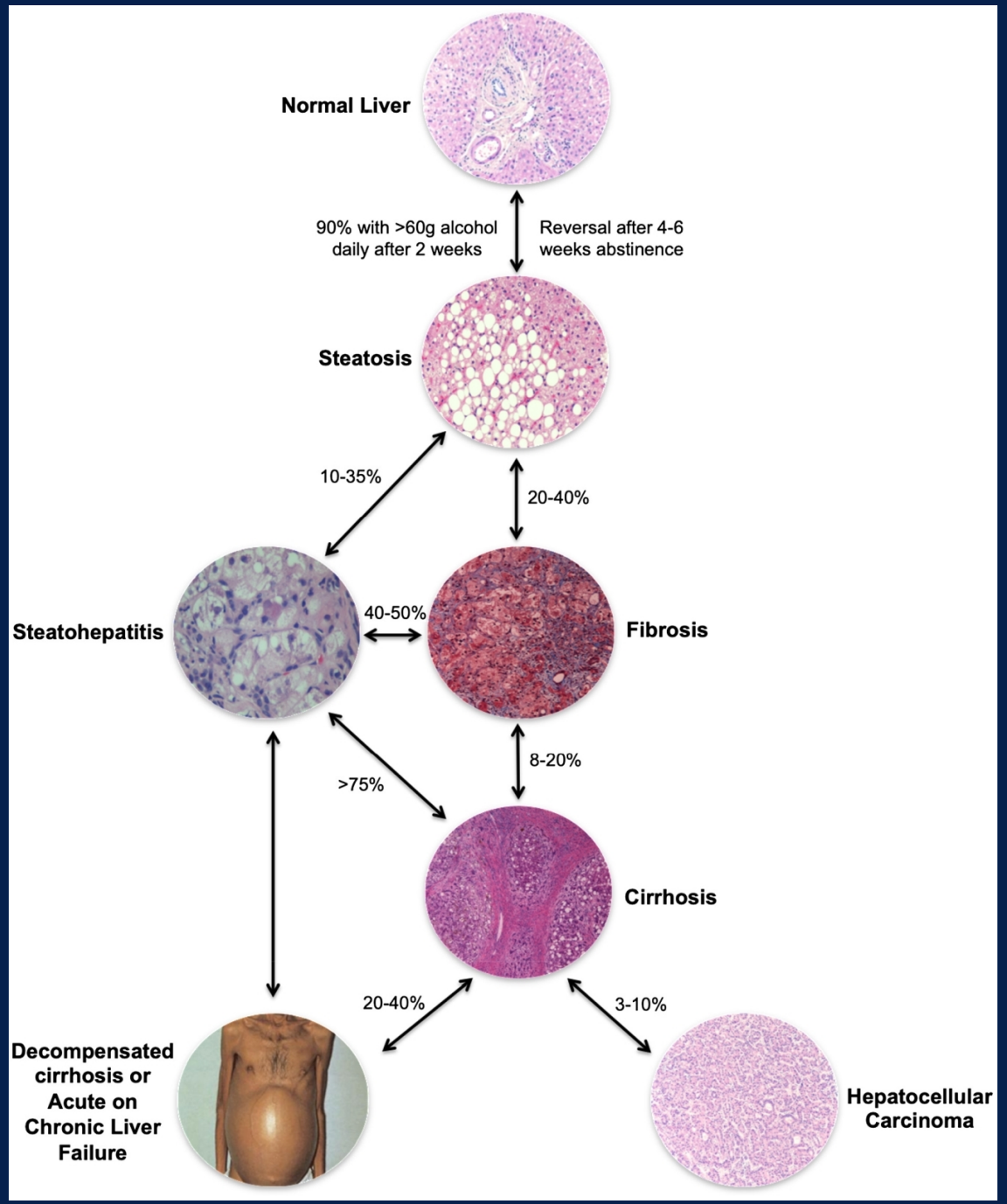
Demographic	Daily Maximum	Weekly Maximum
Women (21+)	3 drinks	7 drinks
Men 21-64	4 drinks	14 drinks
Men 65+	3 drinks	7 drinks

USDA

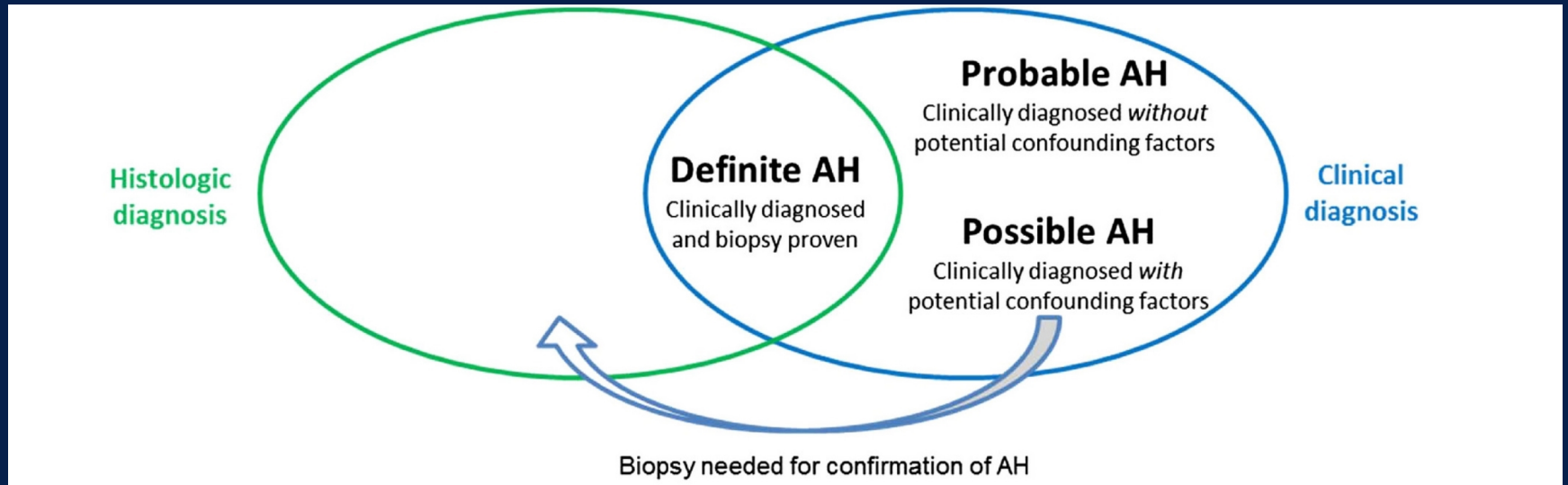
Demographic	Daily Maximum
Women (21+)	1 drink
Men (21+)	2 drinks

ALD


Alcohol-associated Hepatitis
Chronic Alcohol Misuse (Normal Liver)
90–95%
Liver Steatosis
20–40%
Fibrosis
8–20%
Cirrhosis
3–10%
Hepatocellular Carcinoma
Drinking Patterns
Smoking
Obesity
Female
Dietary Factors
HIV
Viral Hepatitis
Genetic Factors
Higher Risk of Disease Progression


Normal Liver
90% with >60g alcohol daily after 2 weeks
Reversal after 4-6 weeks abstinence
Steatosis
10-35%
20-40%
Steatohepatitis
40-50%
Fibrosis
>75%
8-20%
Cirrhosis
20-40%
3-10%
Decompensated cirrhosis or Acute on Chronic Liver Failure
Hepatocellular Carcinoma

Alcohol-associated hepatitis (AH)



Clinical diagnosis of AH

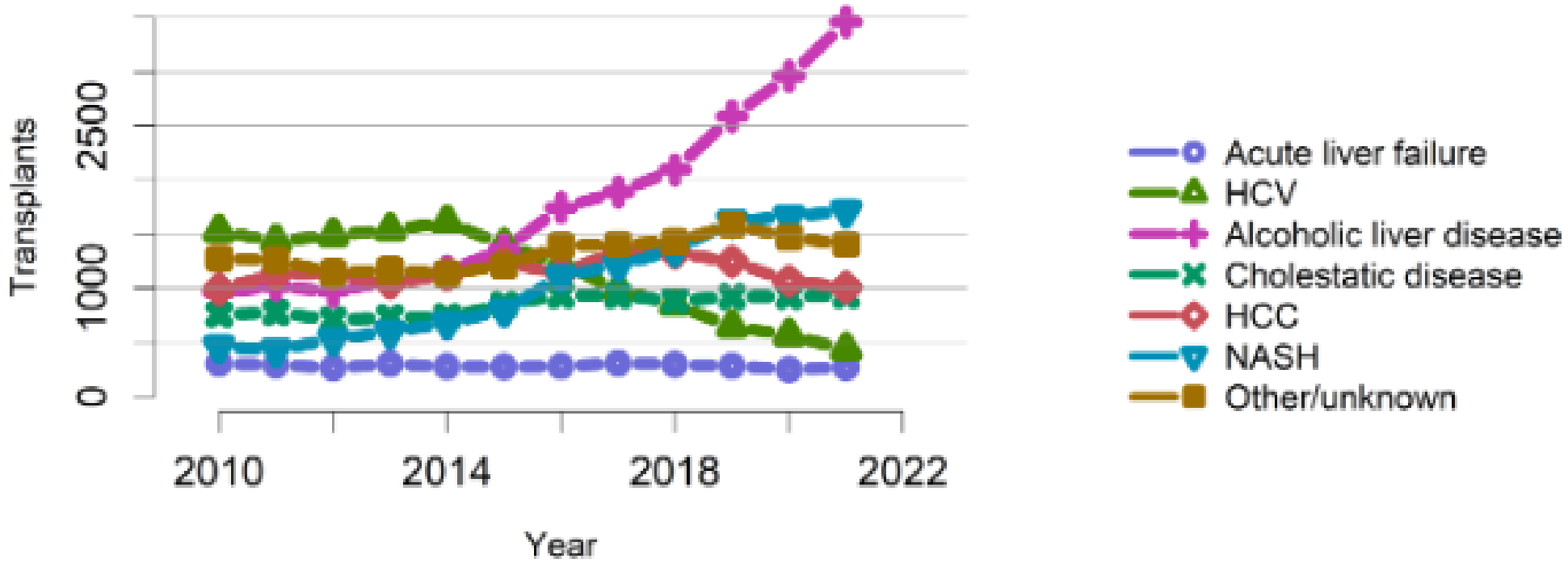
- Onset of jaundice within prior 8 weeks
- Ongoing consumption of >40 (female) or 60 (male) g alcohol/day for ≥6 months, with <60 days of abstinence before the onset of jaundice
- AST >50, AST/ALT >1.5, and both values <400 IU/L
- Serum total bilirubin >3.0 mg/dL

Potential confounding factors

- Possible ischemic hepatitis (e.g., severe upper gastrointestinal bleed, hypotension, or cocaine use within 7 days) or metabolic liver disease (Wilson disease, alpha 1 antitrypsin deficiency)
- Possible drug-induced liver disease (suspect drug within 30 days of onset of jaundice)
- Uncertain alcohol use assessment (e.g., patient denies excessive alcohol use)
- Presence of atypical laboratory tests (e.g., AST <50 or >400 IU/L, AST/ALT <1.5), ANA >1:160 or SMA >1:80.

ALD and Liver Transplant

Figure LI 59: Total liver transplants by diagnosis



OPTN/SRTR 2021 Annual Data Report

Patient Challenges

- Decision to stop drinking thrust upon them by medical event
- Pre-occupied with medical/transplant management
- Typically present with severe AUD
- Unwillingness to disclose alcohol use or high ambivalence

Patient Challenges

- Co-occurring biopsychosocial, medical, substance use, and psychiatric issues
- **Motivating patients to follow the treatment recommendations, monitor compliance, and preventing relapse are major obstacles**

		Public Stigma	Self-Stigma	Structural stigma
Stigma and its impact on health outcomes	Enacted stigma	Individual discrimination and devaluation	Loss of self-efficacy, loss of self-worth, shame	Discrimination in healthcare, in resource allocation
	Anticipated stigma Avoidance of labelling and stigma	Secrecy, avoidance of help, delayed help-seeking, social withdrawal	Denial of problem, misattribution of symptoms, delayed problem recognition and help-seeking	Non-disclosure in healthcare settings, avoidance of specialised addiction services, non-adherence
Result		Increased illness burden, failure or delay of seeking help, inferior healthcare, negative health outcomes		

Care Challenges

- Disconnected silo based care
  - Low multidisciplinary collaboration, affiliation, shared space
- Hesitancy and knowledge gaps
  - Medical and psychiatric complexity can be daunting
- Research gaps
  - Intentionally omitted from studies

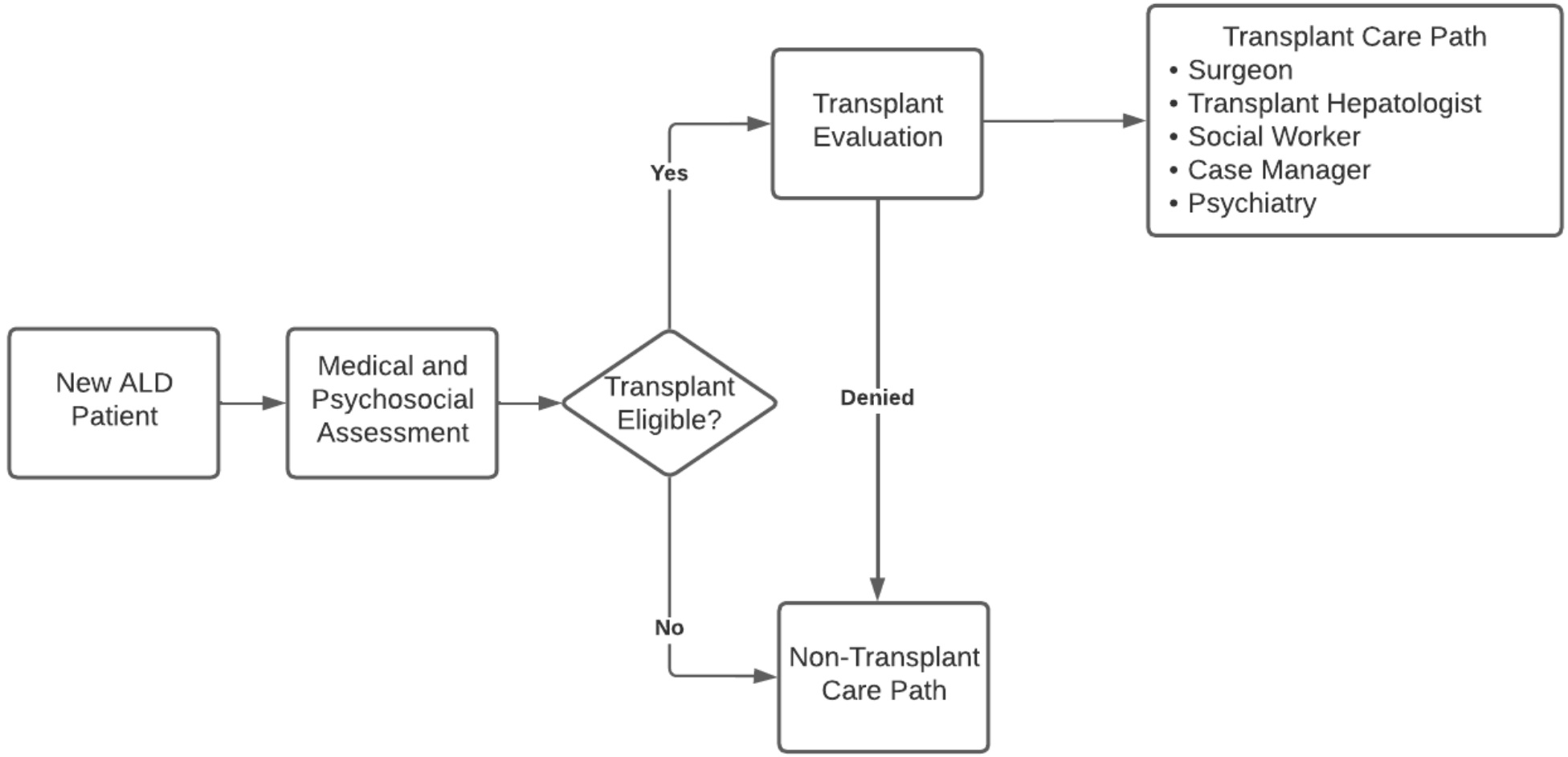
Care Challenges

- Divided treatment leads to lagging care time, poor show rates, low multidisciplinary collaboration, and overall worse treatment

Bottom line

Between 14%-30% of the world's population is affected by alcohol use disorder (AUD), and excessive alcohol consumption represents the most common cause of liver disease in the western world. The clinical picture of alcoholic end-stage liver disease is rendered extremely complex, as manifestations such as alcohol withdrawal syndrome, craving and physical dependence, as well as extrahepatic alcohol-related diseases merge with the complications of advanced cirrhosis. This makes AUD recognition and assessment difficult and its management arduous as many drugs commonly used to treat complications such as alcohol withdrawal syndrome are often contraindicated by the presence of hepatic encephalopathy or hepatorenal syndrome. Reaching and maintaining abstinence represents the mainstay of managing patients with AUD and end-stage liver disease. Psychosocial interventions are an essential component of treatment to reach these goals. However, these interventions alone often prove insufficient in AUD patients and even more frequently in those with end-stage liver disease because of inadequate adherence due to poor functional and physical status. Pharmacological treatments need to be associated, but the available options are greatly limited in end-stage liver disease because many GABA-Ergic drugs can favor the development of hepatic encephalopathy, whereas drugs undergoing extensive liver metabolism should be avoided or used with the greatest caution. Because of these limitations, the management of end-stage AUD is extremely challenging and requires an integrated multidisciplinary approach. (Hepatology 2019;70:410-417).

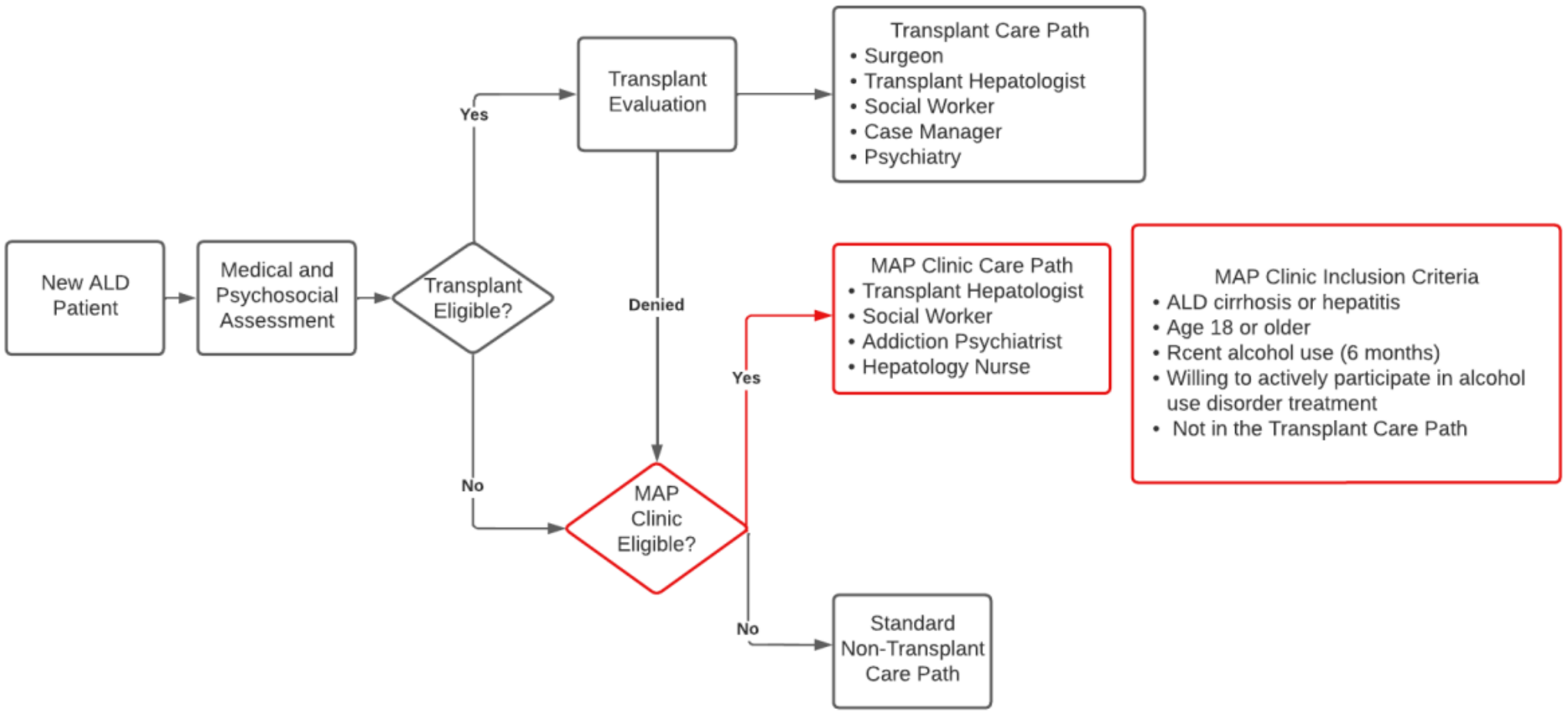
Classic CCF Care Model



Multidisciplinary Alcohol Program (MAP)

- Established June 2022
- ALD patients not in transplant care path
- Patients seen by:
  - Transplant hepatology (SS)
  - Addiction psychiatry (AA)
  - Addiction trained mental health SW (MR)
  - Care Coordinator RN (MY)
  - Support staff: Psychiatry pharmacist, informatics, research coordinator

New CCF model



Clinic Flow

Time	Patient 1	Patient 2	Patient 3	Patient 4
1:00pm	Hepatology	Psychiatry	Social Work	
1:30pm	Psychiatry	Hepatology	FibroScan and Routine Outcome Monitoring	Social Work
2:00pm	Social Work	Additional Testing	Hepatology	Psychiatry
2:30pm	Fibroscan and Routine Outcome Monitoring	Social Work	Psychiatry	Hepatology
3:00pm	Group Visit	FibroScan and Routine Outcome Monitoring	Additional Testing	Additional Testing
3:30pm	Additional Testing	Group Visit	Break	FibroScan and Routine Outcome Monitoring
4:00pm			Group Visit	Break
4:30pm				Group Visit
End	No Breaks	No Breaks	1 Break	1 Break

Preliminary Data

- Total patients referred: 141
  - 49 seen
  - 51 refused
  - 11 not appropriate
  - 6 scheduled and not yet seen
  - 6 no response
  - 7 deceased before contact
  - 10 new referrals
- Total patients deceased: 10
  - 3 established
  - 7 prior to contact

- Mean age: 49.2 years
- Female: 47% (23 patients)
- Male: 53% (26 patients)
- Ethnic origin/Race:
  - Hispanic: 4% (2 patients)
  - White: 78% (38 patients)
  - Black: 16% (8 patients)
  - Asian: 2% (1 patient)

Preliminary Data

- Addiction and psych:
- Severe alcohol use disorder: 82% (40 patients)
- Moderate alcohol use disorder: 12% (6 patients)
- Other: 6% (3 patients, 1 no disorder, 1 R/O disorder, 1 unspecified)
- Mild alcohol use disorder: 0
- Started on MAT: 69% (34 patients)
- Referred to formalized treatment (IOP/PHP, or rehab): 94% (46 patients)

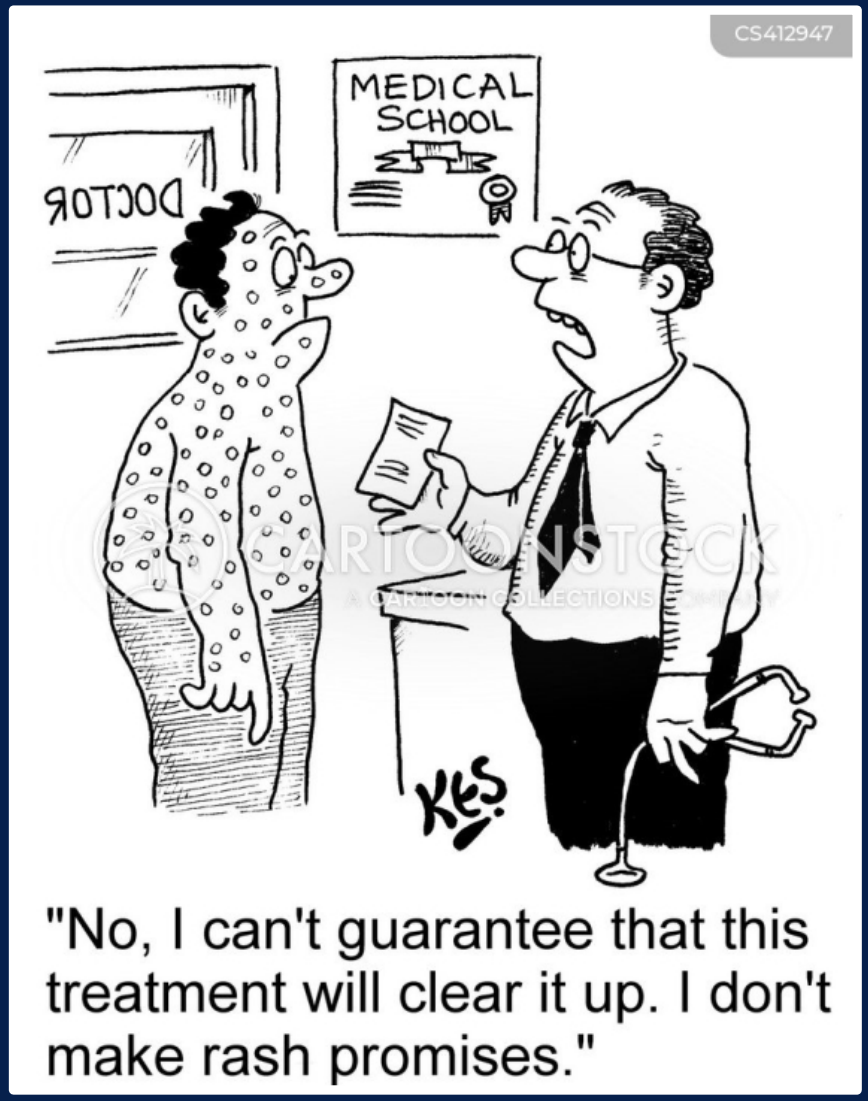
Preliminary Data

- Liver:
- Post-transplant with relapse: 16% (8 patients)
- Ascites: 35% (17 patients)
- Alcohol associated cirrhosis: 59% (29 patients)
- Referred for transplant: 6% (3 patients)
- Number transplanted: 2% (1 patient)

Early impressions

- Very medically, psychiatrically and addictively sick population
- Patients are rarely receiving any psychiatric and/or addiction medication and psychosocial treatment prior to MAP
- High patient and family satisfaction with clinic design
- Strong show rate
- Educational and professionally enjoyable setting to all clinic members
- Has strengthened bond between both NI and DDSI

AUD Treatment in ALD



Assessment & Follow-up

- Self-report, patient's behavior, collaterals
- Physical and neurological exam
- Chart records
- Psychometric and cognitive tests (PHQ-9, GAD-7, ISI, BAM; MMSE, Mini-Cog, MOCA, NCT, CHESS)
- Child-Pugh Score
- Labs and drug screens (UDS, EtG, Pain panel, Benzo panel and PEth)

Pay attention to: Patient and family understanding, Social stability, Substitute activities, Negative consequences, Trauma and Self-efficacy

Relevant Labs & Tests

BIOMARKER	MARKER CHARACTERISTIC
AST, ALT	- Used to detect acute and chronic excessive alcohol consumption.
GGT	- Used to detect chronic excessive alcohol consumption. - Takes 2 to 8 weeks to normalize after alcohol cessation
MCV	- Used to detect chronic excessive alcohol consumption.

Other labs: elevated bilirubin, decreased albumin, elevated INR and abnormal CMP levels

Relevant Labs & Tests

TEST	MARKER CHARACTERISTIC
Alcohol breath test	- Active alcohol consumption - Underestimates blood alcohol consumption by 10%
Blood alcohol level	- 80-100 mg/dl is OVI level - Non-tolerant metabolism rate is 20 mg/dl - DKA and starvation increase levels
EtG, EtS	- Ethanol metabolites formed in the non-oxidative alcohol metabolism pathway - Measurable in the urine for 2-5 days in excessive alcohol use - Sensitivity 75-93%; Specificity 82-99%
PEth	- Measurable in the blood for up to four weeks after last use - Sensitivity 91-100%; Specificity 77-96%

Frequency of testing is individualized to patient.

Psychosocial Interventions

WHAT WE DO	WHAT WE DON'T DO
Motivation Interviewing	Educational lectures and films
Cognitive behavioral therapy	Mandated 12-Step therapies
Coping Skills Intervention	"Scare tactics"
"Network Therapy"	
Twelve-Step Psychoeducation	
Addiction Psychoeducation	

Referral to formalized psychosocial interventions: Intensive Outpatient Program, Partial Hospitalization Program and Residential Treatment

AUD Pharmacotherapy

- FDA approved: disulfiram, naltrexone and acamprosate
- Non-FDA approved: gabapentin, pregabalin, baclofen, topiramate, ondansetron, varenicline, valproate acid, carbamazepine, oxcarbazepine

- ALD patients omitted from studies; only baclofen

Medication	Dosage	Mechanism of action	Advanced liver disease	Other features
Acamprosate	666 mg TID, 3g/d	NMDA receptor antagonist*	Yes; no hepatic metabolism	• Helpful in post-acute withdrawal
Naltrexone	PO: 50-150 mg/d IM: 380 mg SC/mon	Opioid receptor antagonist	Dose modification not needed with mild to moderate hepatic impairment	• Used in the treatment of cholestasis-pruritus
Baclofen	10-20mg TID	GABA-B receptor agonist	Yes; no hepatic metabolism	• Withdrawal when stopped abruptly • Misuse potential
Gabapentin	900-2400 mg/d	Modulates GABA deficits and glutamate excess	Yes; no hepatic metabolism	• Helpful in post-acute withdrawal, comorbid anxiety and insomnia • Additive efficacy when used with naltrexone
Topiramate	75-400 mg/d	Decreases DA activity after alcohol use through enhancement of GABA action, some	Yes but with dose modification because of reduction in clearance	• Helpful in post-acute withdrawal and impulsivity

Child-Pugh score

- CPS- A: 75-100%
- CPS-B: 50%
- CPS-C: avoid all meds that undergo hepatic oxidation

Clinical and Lab Criteria	Points*		
	1	2	3
Encephalopathy	None	Mild to moderate (grade 1 or 2)	Severe (grade 3 or 4)
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dL)	< 2	2-3	>3
Albumin (g/dL)	> 3.5	2.8-3.5	<2.8
Prothrombin time			
Seconds prolonged	<4	4-6	>6
International normalized ratio	<1.7	1.7-2.3	>2.3
Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points) Class A = 5 to 6 points (least severe liver disease) Class B = 7 to 9 points (moderately severe liver disease) Class C = 10 to 15 points (most severe liver disease)			

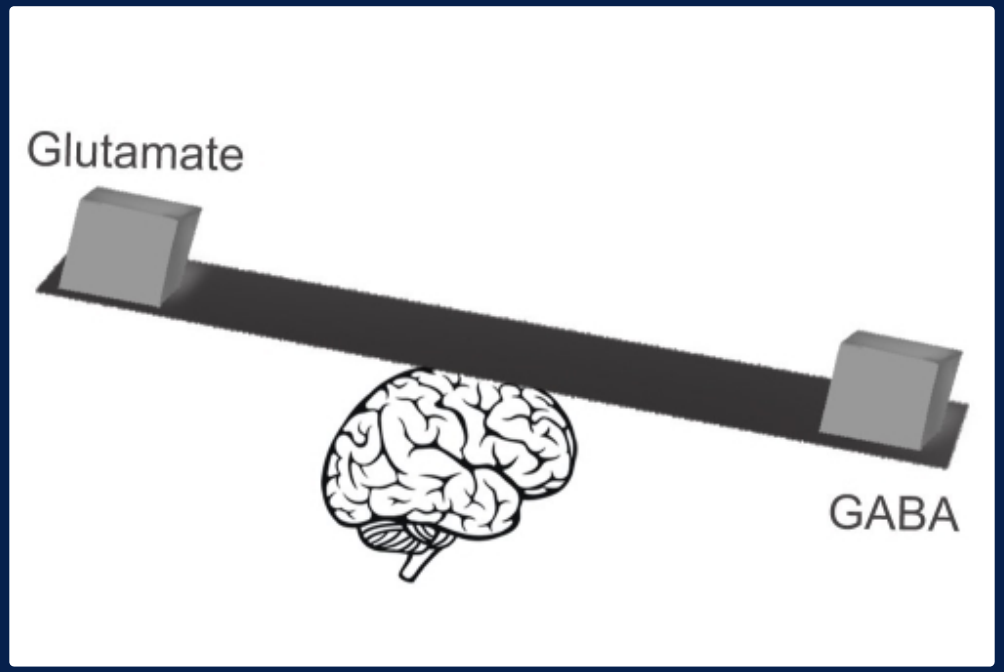
Post-acute withdrawal syndrome

- After acute alcohol withdrawal
- Non-specific symptoms
- Related to glutamate hyperactivity
- Not in DSM-5

Symptoms	
• Sleep difficulties • Problems with short-term memory, brain fog • Difficulty with cognitive tasks • Apathy • Persistent fatigue • Difficulty maintaining relationships	• Cravings • Dysphoria, depression, irritability, anhedonia • Panic disorders, anxiety • ↑↑ sensitivity to anxiety and stress • ↑↑ sensitivity to pain and sound • Autonomic disturbances

Post-acute withdrawal syndrome

- Psychosocial interventions: individual and group therapy
- Medication interventions: gabapentin, baclofen, acamprosate, topiramate



Final Takeaways

- ALD is on the rise
- Medication advancement is limited
- Treatment of ALD contingent on AUD treatment
- Bio-psychosocially complex patients
- MDP model more effective than typical disjointed care model
- Early lessons from MAP clinic: strong patient satisfaction, higher attendance/show rate, and increased prescribing of necessary AUD and psychiatric medications

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