



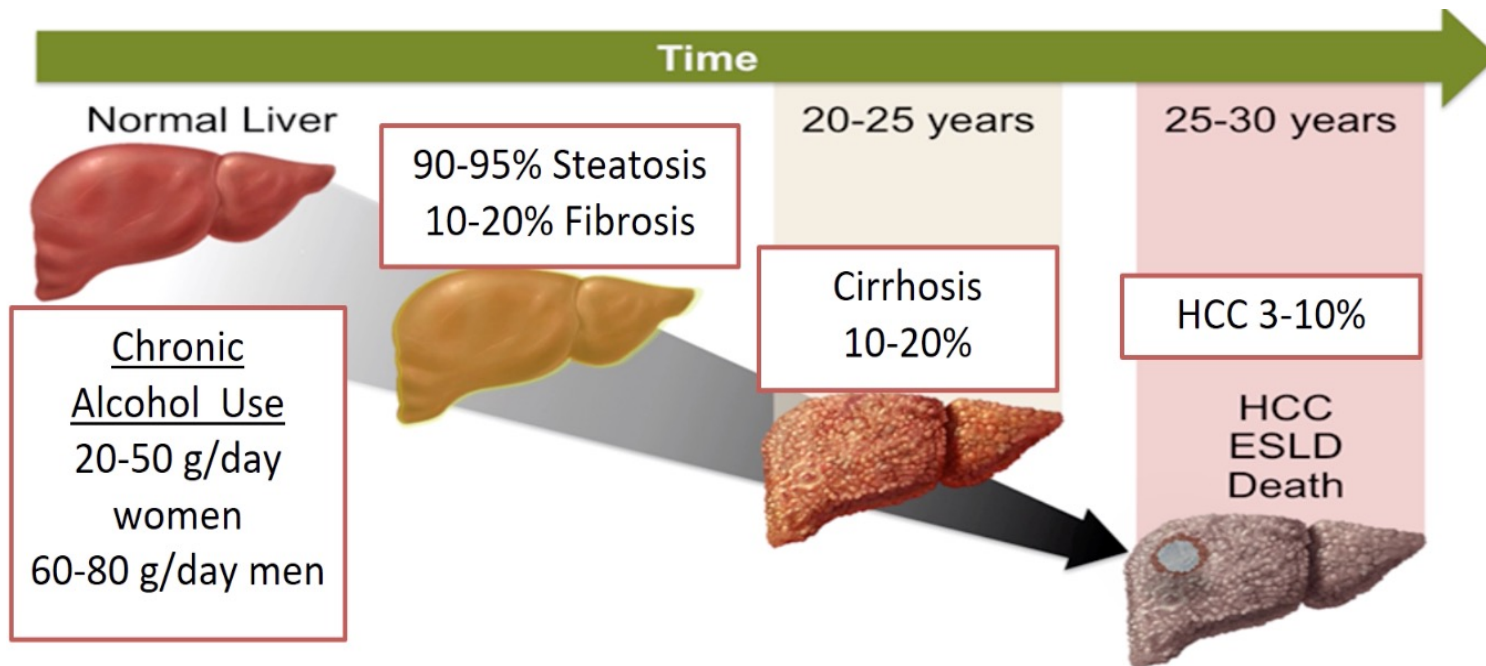
Liver Transplantation for Alcohol-Associated Liver Disease

Northern California Society for
Clinical Gastroenterology (NCSCG)
Liver Symposium

Allison Kwong MD

Saturday, Jan 29, 2022

Spectrum of ALD

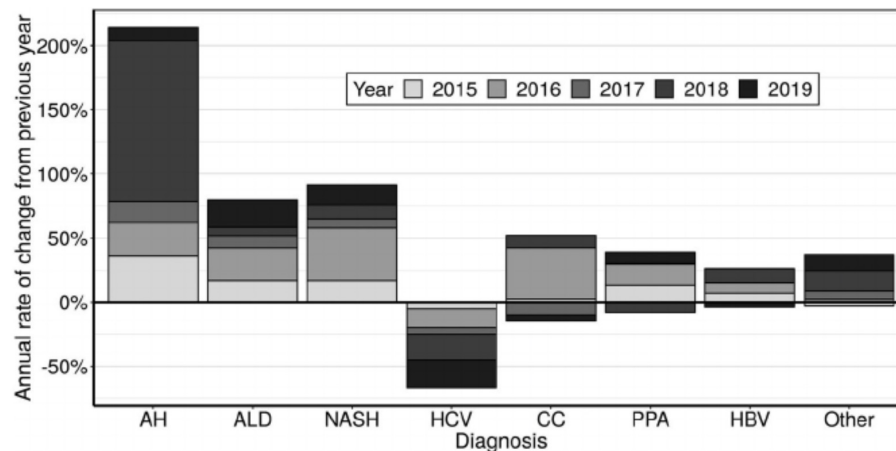
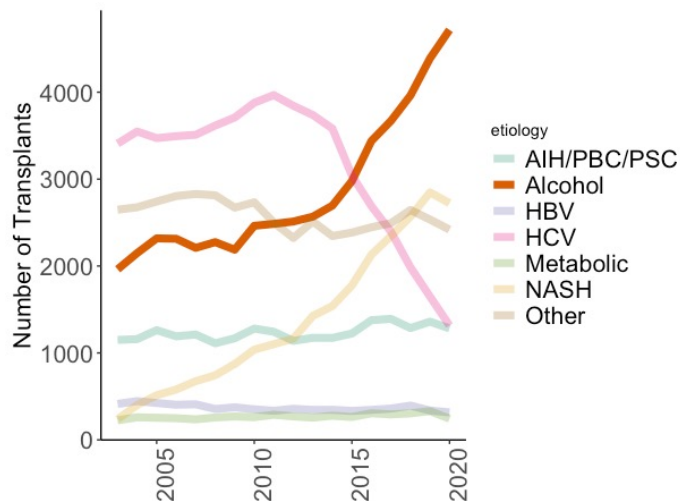


- Steatosis (“fatty liver”)
- Steatohepatitis (“alcoholic hepatitis”)
- Fibrosis
- Cirrhosis



Liver transplantation

- ALD now the leading indication for liver transplant in the United States
- >50% of all liver transplants in the US for ALD in 2020
- Sharp rise in recent years correlating with ↑ LT for AH



Cotter LT 2020

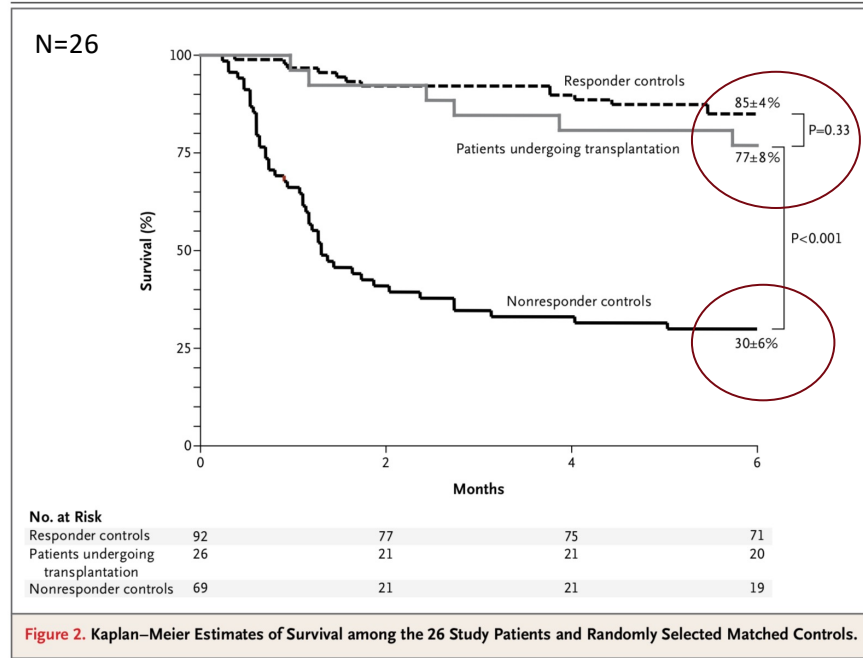
Early Liver Transplantation for Severe Alcoholic Hepatitis

Philippe Mathurin, M.D., Ph.D., Christophe Moreno, M.D., Ph.D., Didier Samuel, M.D., Ph.D., Jérôme Dumortier, M.D., Ph.D., Julia Salleron, M.S., François Durand, M.D., Ph.D., Hélène Castel, M.D., Alain Duhamel, M.D., Ph.D., Georges-Philippe Pageaux, M.D., Ph.D., Vincent Leroy, M.D., Ph.D., Sébastien Dharancy, M.D., Ph.D., Alexandre Louvet, M.D., Ph.D., *et al.*

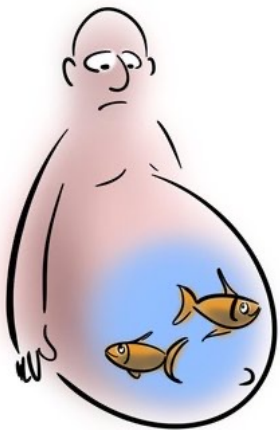
Criteria

1. Non-response to medical therapy
2. Severe AH as first liver-decompensating event
3. Presence of close supportive family members
4. Absence of severe coexisting or psychiatric disorders
5. Agreement (with support from family) to adhere to lifelong total alcohol abstinence

>90% *excluded* due to “predisposition to addiction or unfavorable social or familial profiles”



Liver transplantation for ALD

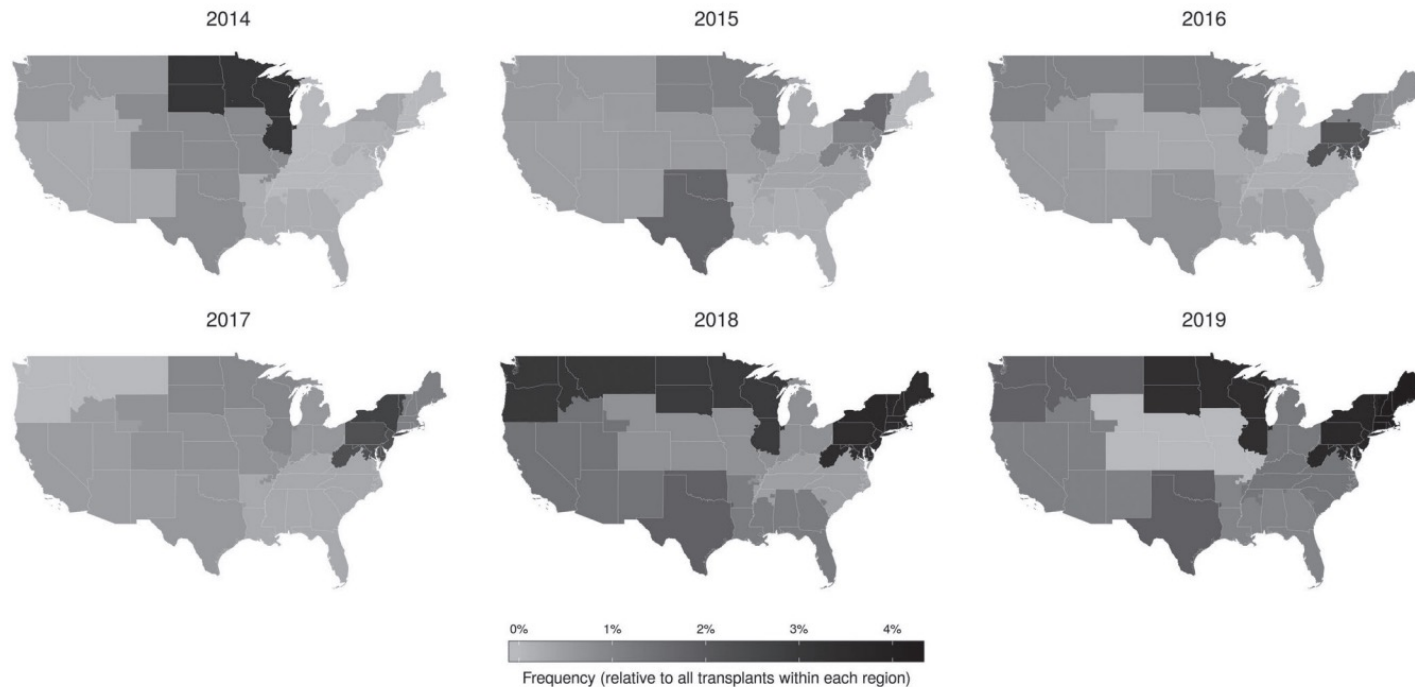


6-month “rule” (1997): At least 6 months of sobriety

- Provided 6 months for patients to demonstrate commitment to abstinence, and potentially hepatic recovery
- Many did not survive 6 months
- Now acknowledged to be rather arbitrary:
 - 6 months is a weak predictor of post-LT relapse; other methods of identifying relapse risk
 - Neurobiological component to alcohol use disorder; addiction is a disease, similar to obesity (NAFLD), AIH, HCV



Geographic variation

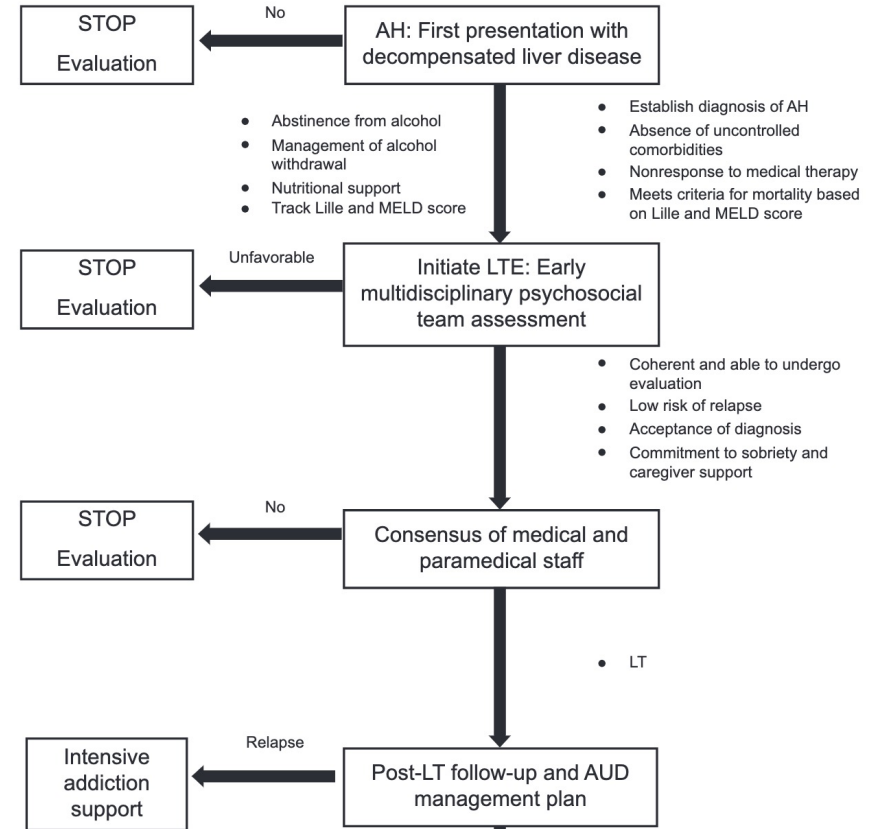


Meeting Report: The Dallas Consensus Conference on Liver Transplantation for Alcohol Associated Hepatitis

October 2019

Convened to standardize peri-LT care

- Recipient selection
- Post-LT care and relapse prevention

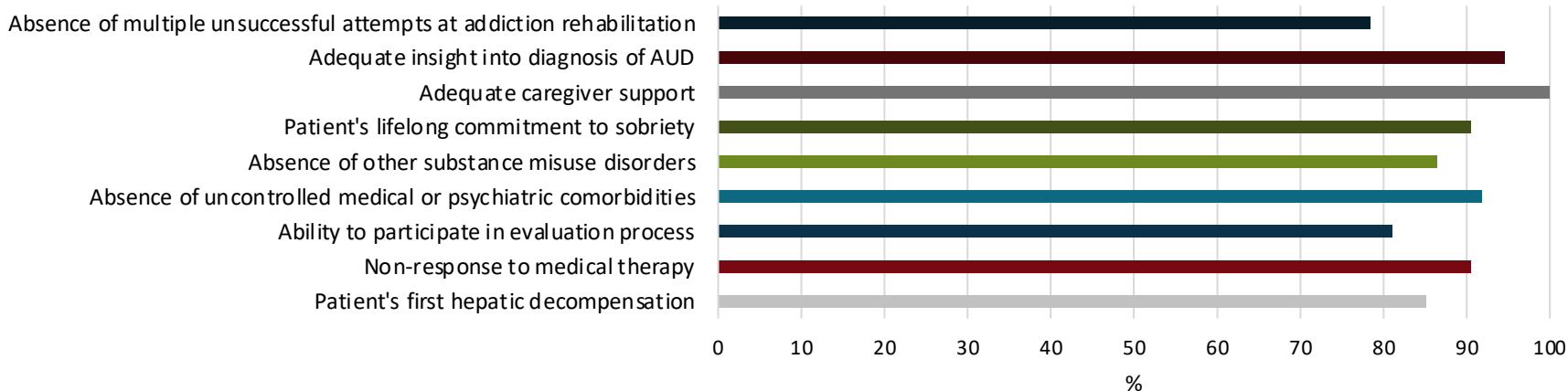


US experience

2020 national survey of 100/117 liver transplant centers (unpublished data)

- 70% of centers reported no sobriety requirement; 21% still require 6 months of sobriety
- 85% of centers reported doing LT for severe AAH (65 started within the past 5 years)

Center protocols for evaluation and listing of patients with severe alcohol-associated hepatitis



US experience

American Consortium of Early Liver Transplantation for Alcoholic Hepatitis: ACCELERATE-AH

12 centers in 8 UNOS regions

Early Transplant
= no specific sobriety
period (n=147)

*Mortality without
transplant up to
70% at 6 months*

→ Survival

→ Sustained
Alcohol Use
After
Transplant

Post-Transplant Outcomes

1 Year

3 Year

94%

84%

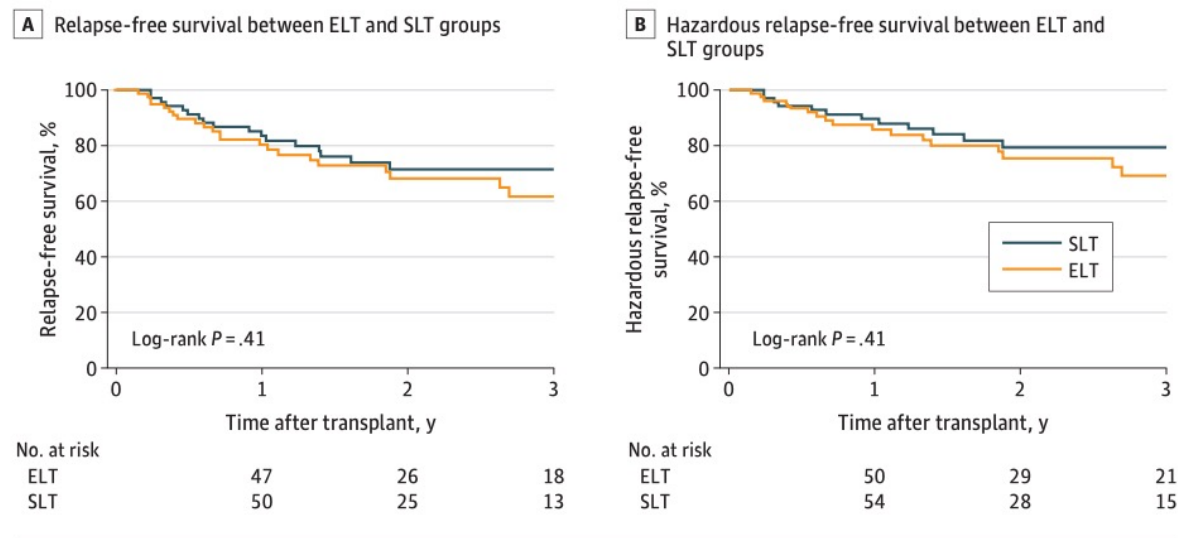
10%

17%

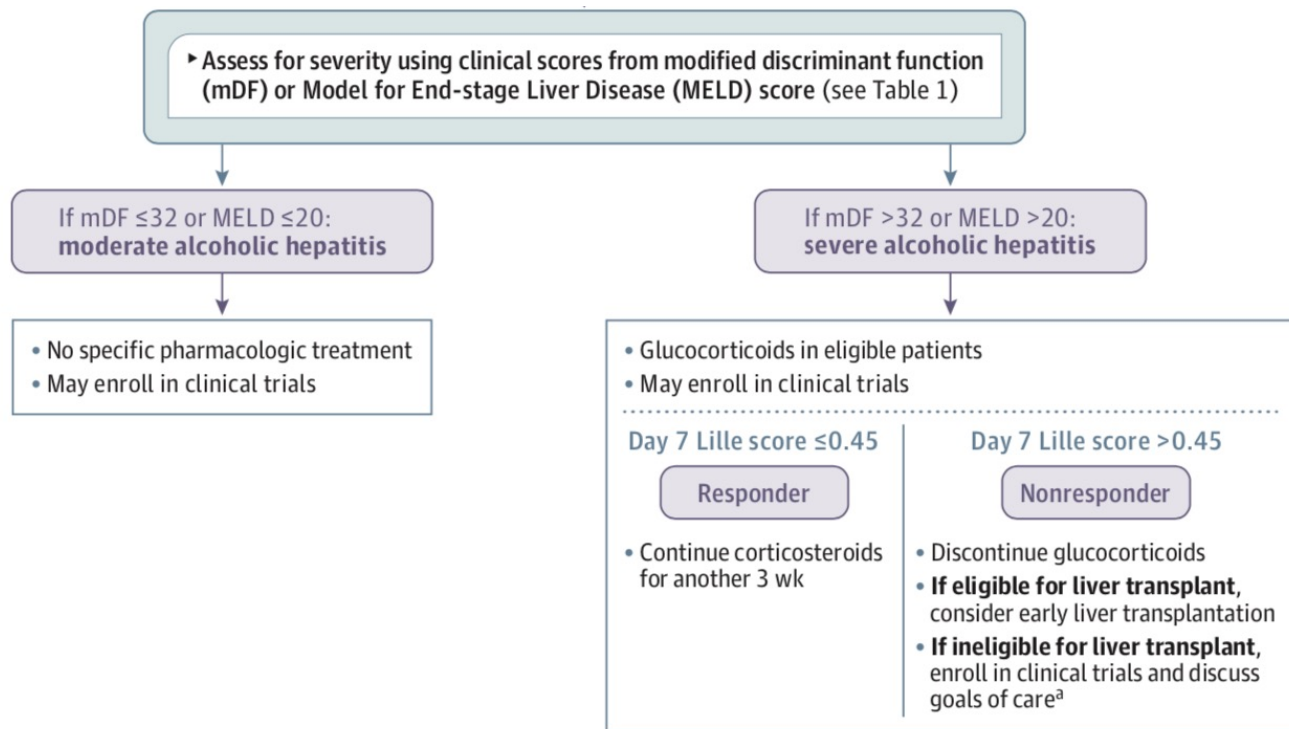
Gastroenterology

US experience

Figure 2. Kaplan-Meier Estimates of Relapse-Free Survival and Hazardous Relapse-Free Survival Among Patients Who Underwent Early Liver Transplant (ELT) vs Standard Liver Transplant (SLT)



Treatment algorithm for AH



Alcohol relapse after LT

- Reported at a rate of 10-30% post-LT
 - 10-15% return to hazardous drinking
- Associated with mortality and rejection

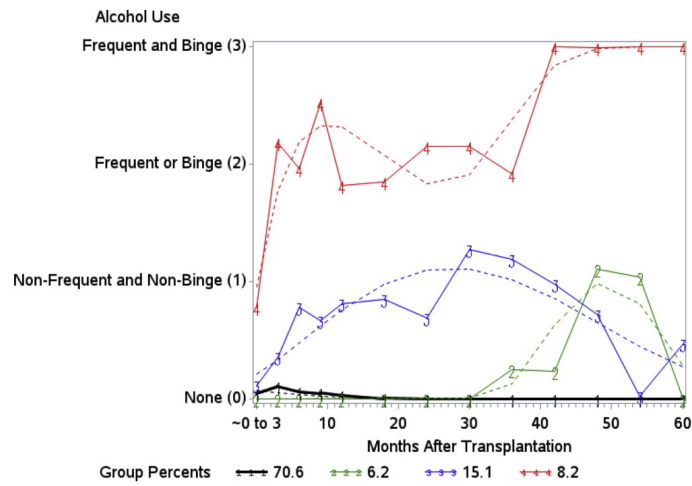
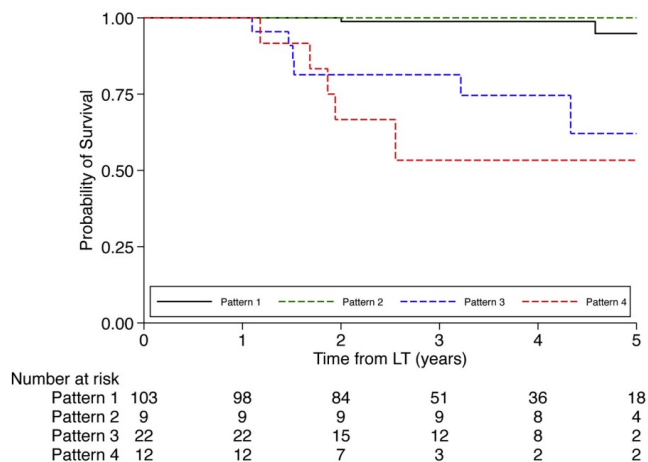


Figure 1. Patterns of post-transplant alcohol use. Pattern 1 (black) (n = 103, 70%) represents patients with abstinence post-LT. Pattern 2 (green) (n = 9, 6.2%) represents patients with abstinence, then late-onset nonbinge or nonfrequent alcohol use (late/nonheavy use). Pattern 3 (blue) (n = 22, 15%) represents patients with early-onset sustained nonbinge or nonfrequent alcohol use (early/nonheavy use). Pattern 4 (red) (n = 12, 8.2%) represents patients with early onset sustained binge or frequent alcohol use (early heavy use).



Predicting alcohol relapse

■ Scores

- SIPAT Stanford Integrated Psychosocial Assessment Tool
- SALT ≥ 5 Sustained Alcohol use post Liver Transplant
- HRAR ≥ 4 High-Risk Alcoholism Relapse

■ Other risk factors

- Absence of a life partner
- Psychiatric comorbidities
- <6 months of abstinence from alcohol

De Gottardi JAMA 2007

Lee Hepatology 2019

SALT Score* to Predict Sustained Alcohol Use Post-LT

Variable	Points
>10 Drinks/day at Presentation	+4
≥ 2 Prior Failed Rehabilitation Attempts	+4
Any History of Prior Alcohol-Related Legal Issues	+2
History of Non-THC Illicit Substance abuse	+1

Table 1. High-Risk Alcoholism Relapse Scale

Item	Score
Duration of heavy drinking, y	
≤ 11	0
11-25	1
≥ 25	2
Daily drinks, No.*	
≤ 9	0
9-17	1
≥ 17	2
Prior alcoholism inpatient treatments, No.	
0	0
1	1
≥ 1	2



Stanford
MEDICINE

Predicting alcohol relapse

Fig. 2 a Kaplan–Meier curve of alcohol relapse by SIPAT score.

Note: SIPAT=Stanford Integrated Psychosocial Assessment for Transplant. **b** Kaplan–Meier curve of alcohol relapse by SALT score. *Note:* SALT=Sustained Alcohol Use Post-Liver Transplant

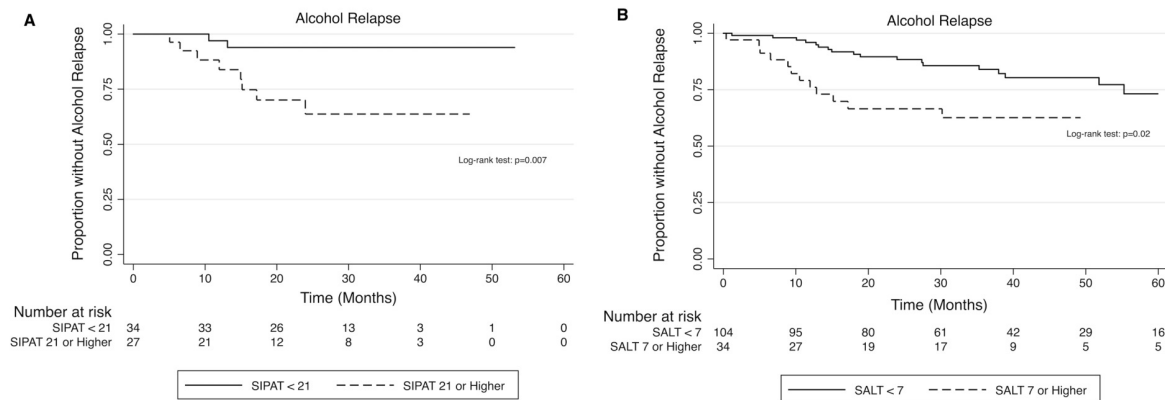


Table 6 Multivariable model of factors associated with post-transplant alcohol relapse

Variables selected	Hazard ratio	95% CI	P
Declined to participate in IOP despite recommendation	3.66	1.73–7.73	0.001
Relapse after initial attempt at sobriety	3.06	1.35–6.93	0.007
Stopped drinking when diagnosed with liver disease	.43	.20–.92	0.03

Number of observations: 150

Harrel's C concordance statistic = .769

IOP intensive outpatient program

Stanford experience

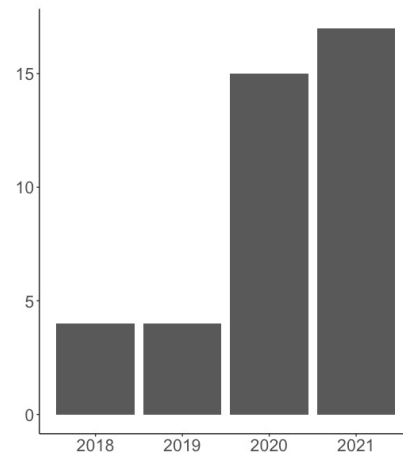
Limited Sobriety Pathway (est. 2017) with < 6 months of sobriety

1. Failed medical management with high risk of mortality without liver transplant, expected survival \leq 6 months
2. FIRST hepatic decompensation in a candidate who just learned that his/her pattern of alcohol use is the cause of end-stage liver disease
3. Commitment of patient and family/support to sobriety and formalized agreement to adhere to lifelong complete alcohol abstinence
 - Cannot be encephalopathic
 - Must agree to pre- and post-transplant alcohol rehabilitation + all other standard requirements for liver transplant

Stanford experience

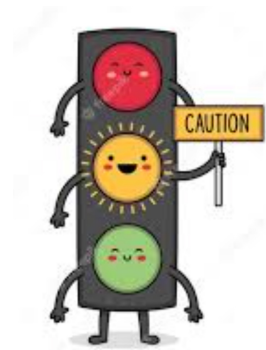
“Limited sobriety” pathway

- **121** referrals
- **40** transplants
 - Median age 43 (IQR 37-49)
 - Median MELD 39 (IQR 35-40)
 - AAH and ACLF
 - 100% survival
 - 1 re-transplant for graft failure (transplant-related)
 - 2 alcohol relapses (monitor with monthly PETH)



Caveats

- **Hepatic recovery: is it possible?**
 - Yes
 - Probably not if hepatorenal \rightarrow dialysis
- **Health disparities**
 - Selection favors patients with demographic and socioeconomic advantages
 - Insurance and provider bias
- **Public perception and trust**
 - Organ donation
 - Equity



Summary

- Alcohol now the leading indication for LT in the US
- Early LT for ALD and AH can be life-saving
- Consider liver transplant in select candidates
 - Should not be based on fixed interval of abstinence
 - Many will not qualify medically or psychosocially
 - Requires programmatic support including transplant psychiatry, addiction medicine resources
- Addiction must be treated in addition to the liver disease
 - Detect and treat alcohol use disorder after LT





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Public perception

TABLE 2. POTENTIAL IMPACT OF CHANGE IN POLICY ON PUBLIC TRUST AND DONATION

Would knowing that liver transplantation was offered to patients with alcoholic liver disease who are still actively drinking alcohol or have not shown a period of abstinence affect your trust in the process of transplantation?

Increase, 3.9% Decrease, 42.8% No impact, 53.3%

If liver transplantation were offered to patients with alcoholic liver disease who are still drinking alcohol, would you be more or less likely to become an organ donor?

All respondents

More likely, 1.8% Less likely, 34.8% No impact, 63.5%

Respondents who have considered becoming organ donors

More likely, 0.8% Less likely, 36% No impact, 63.2%

Would you support a change in the current criteria for liver transplantation to transplant patients with alcoholic liver disease who are still consuming alcohol or have not been abstinent for 6 months?

Yes, 30.5% No, 39.3% Undecided, 30.2%