



# 9<sup>TH</sup> ANNUAL ***DIGESTIVE DISEASES: NEW ADVANCES***

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**W Hotel  
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# Alcoholic Liver Disease and COVID

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# Disclosures

- **Paul Martin MD, FRCP, FRCPI**
  - **Consultant:**
    - AbbVie, Mallinckrodt, Theratechnologies
  - **Research:**
    - Genfit, Durect, Grifols, Sera Trials, Viking, Enanta

# Terminology

- The term 'alcoholic' is stigmatizing
  - Undermines patient dignity and self-esteem
- These guidelines use the following terms

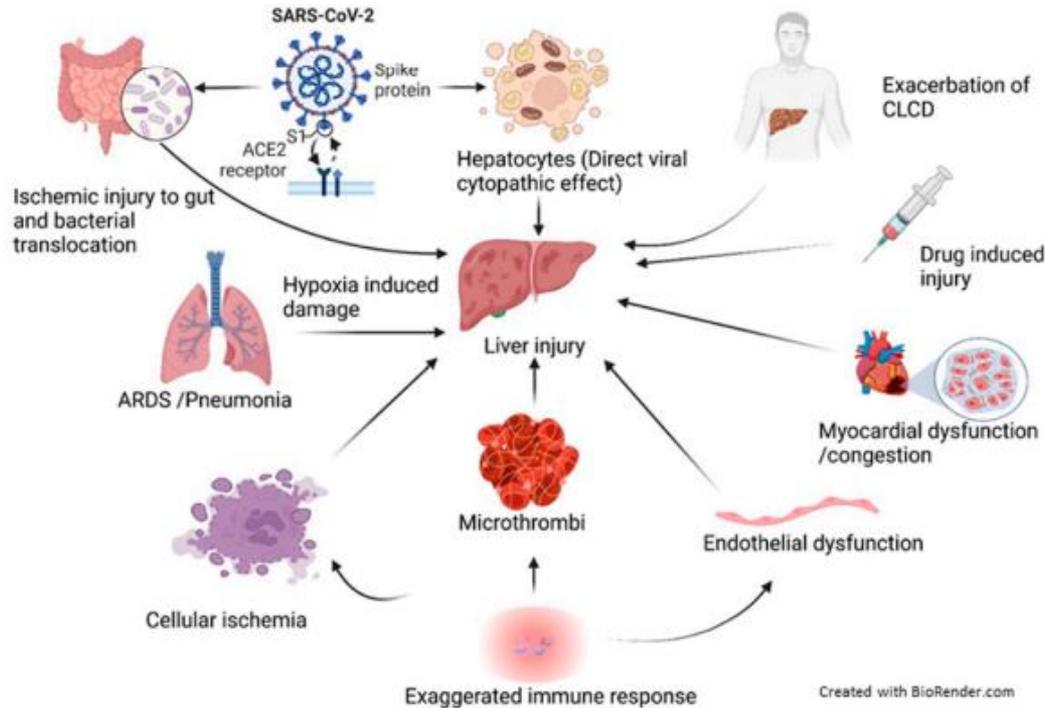
Previous term	Current term	Abbreviation
Alcoholic	Alcohol use disorder	AUD
Alcoholic liver disease	Alcohol-related liver disease	ALD
Alcoholic cirrhosis	Cirrhosis due to alcohol-related liver disease	ALD cirrhosis
Alcoholic steatohepatitis*	Steatohepatitis due to ALD	ASH
Alcoholic fibrosis	Fibrosis due to ALD	ALD fibrosis
Alcoholic hepatitis	Alcoholic hepatitis†	AH

\*Histologically-defined lesion;

†At this point the term alcoholic hepatitis has become too standardized to change (may be reviewed in future guidelines)

EASL CPG ALD. *J Hepatol.* 2018;69:154–81.

# COVID and The Liver



Kariyawasam 2022

The background is a light blue, futuristic scene. A human figure is visible, overlaid with several glowing hexagonal panels. Each panel contains a different icon: a heart with an ECG line, a stethoscope, a pill, a virus, a globe, and a bar chart. The overall aesthetic is clean and high-tech, with a focus on health and data.

**ALD:**

**Background**

# Public Health Aspects: Alcohol-Related Morbidity and Mortality

- Worldwide, harmful use of alcohol is associated with:
  - ~3.3 million deaths every year 1
    - 5.9% of all deaths overall (7.6% in men, 4.0% in women)<sup>1</sup>
  - ~139 million disability-adjusted life years
    - 5.1% of the global burden of disease and injury
- Alcohol has an impact on over 200 diseases and types of injuries
- Most deaths attributable to alcohol consumption from:
  - Cardiovascular diseases
  - Injuries
  - Gastrointestinal diseases
    - Mainly cirrhosis
  - Cancers
- Alcohol-attributable fraction is highest for liver diseases and foetal alcohol syndrome

WHO. Global status report on noncommunicable diseases 2014.

Available at: <http://www.who.int/nmh/publications/ncd-status-report-2014/en/>. Accessed August 2018;

EASL CPG ALD. *J Hepatol*. 2018;69:154–81.

# Public Health Issues: Definitions of “Drink” and “Drinking”

- Quantification of alcohol consumption is not easy in clinical practice
- Grams of alcohol is more precise, but:
  - Time consuming and frequently difficult to obtain
  - Patients cannot recall the different amounts and types of drink

Term	Definition
One standard drink	10 g of alcohol
Harmful drinking	Where alcohol use is causing damage to either physical or mental health
Heavy episodic drinking	Consumption of more than 60 g of pure alcohol on one occasion
Binge drinking	Consumption within about 2 hours of four or more drinks for women and five or more drinks for men

# Public Health Aspects: Data Are Conflicting Around a Safe Alcohol Limit

- Light–moderate intake: reduced risk of coronary artery disease
- Heavy chronic alcohol intake: increased risk of cardiomyopathy, hypertension, atrial arrhythmias and haemorrhagic stroke
- Alcohol is a recognized carcinogen
  - No threshold level of consumption known for cancer risk
- Chronic use of alcohol is a risk factor for cirrhosis
  - Unclear whether there is a continuous dose–response relationship
  - Unclear whether there is a threshold at which the risk emerges
- Risks of binge drinking vs. daily drinking remain controversial
- Cessation of drinking at any point reduces risk of disease progression and occurrence of complications

## Recommendation

Limit daily intake to  $\leq 2$  standard drinks for women and  $\leq 3$  for men.  
This amount is not associated with significant increase in cirrhosis mortality

# Threshold for Alcoholic Liver Disease

- 50-60 g alcohol/day for men, >20 g/day for women
- Low risk for alcoholic cirrhosis even at this level of consumption (4.2-5.9% in Italy, Denmark)
- Binge drinking, drinking between meals and alcohol type (wine risk less?) implicated

# Alcohol Use Disorders: Screening Tools: AUDIT

- Developed by the WHO in 1982 and remains the gold standard
- Good sensitivity and specificity in clinical settings across countries

Question	Score				
	0	1	2	3	4
1. How often do you have a drink containing alcohol?					
2. How many drinks containing alcohol do you have on a typical day when you are drinking?					
3. How often do you have five or more drinks on one occasion?					
4. How often during the last year have you found that you were not able to stop drinking once you had started?					
5. How often during the last year have you failed to do what was normally expected of you because of drinking?					
6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?					
7. How often during the last year have you had a feeling of guilt or remorse after drinking?					
8. How often during the last year have you been unable to remember what happened the night before because of your drinking?					
9. Have you or someone else been injured because of your drinking?					
10. Has a relative, friend, doctor or other healthcare worker been concerned about your drinking or suggested you cut down?					

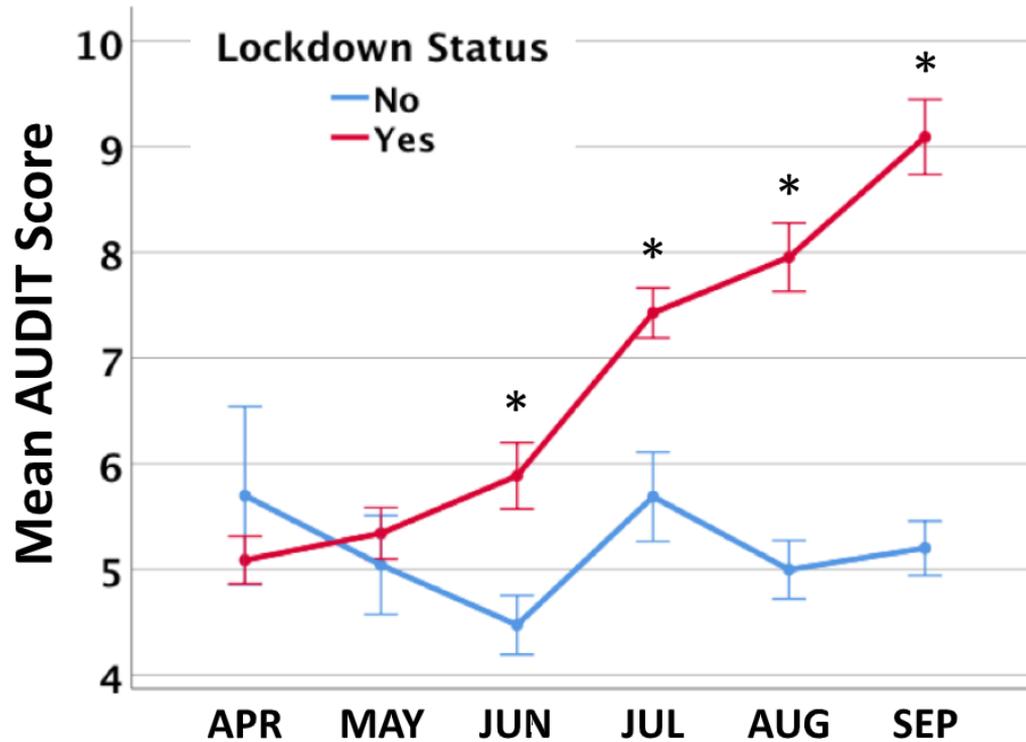
Total scores of  $\geq 8$  indicate hazardous and harmful alcohol use  
 Scores of  $\geq 20$  or above clearly warrant evaluation for alcohol dependence

Scores  $\geq 1$  on Q2 or Q3:  
 hazardous level of alcohol consumption

Scores  $> 0$  on Q4–6:  
 alcohol dependence

Points scored on Q7–10:  
 alcohol-related harm

# Alcohol Use and COVID

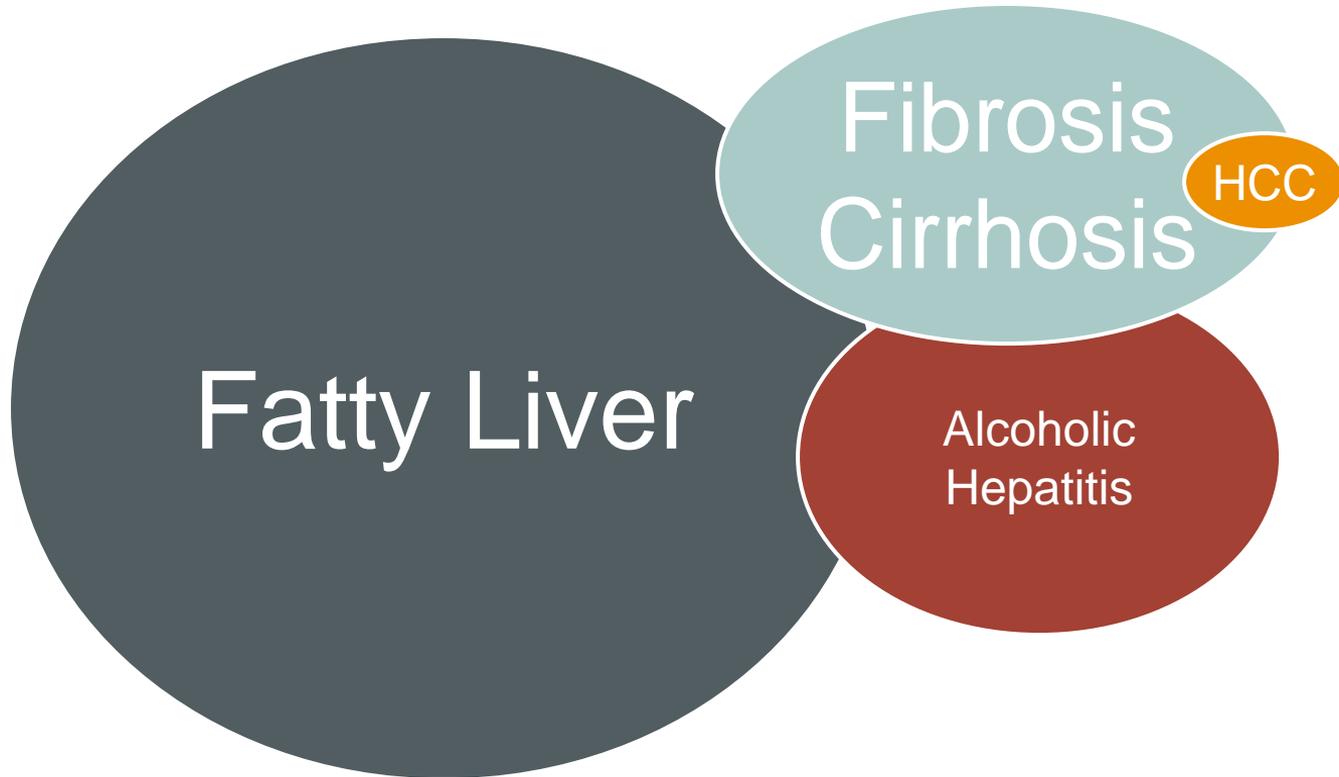




**ALD:**

**Clinical Features**

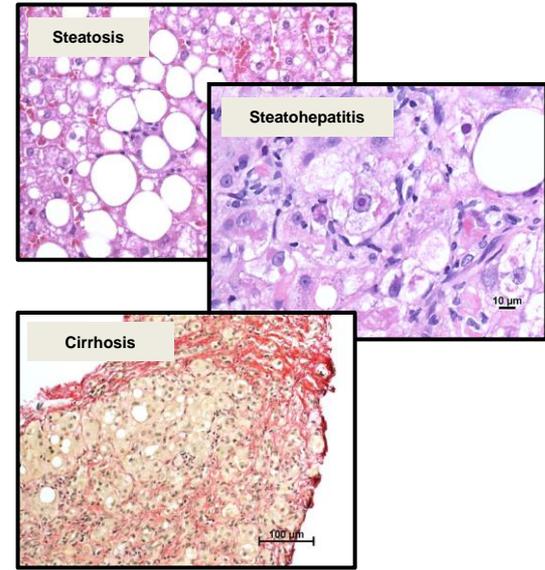
# Alcoholic Liver Disease



# Diagnostic Tests in the Management of ALD: Histological Features and Diagnosis of ALD Types

- Lesions predominate in centrilobular regions (in pre-cirrhotic stages)
  - **Alcoholic steatosis**
    - Macro and eventually variable blend of macro- and microvesicles
  - **Alcoholic steatohepatitis (ASH)**
    - Variable degree of macrovesicular steatosis
    - Hepatocellular injury with ballooning, potentially necrosis
    - Lobular inflammation
  - **Alcoholic fibrosis/cirrhosis**
    - Pericellular fibrosis (PCF) and/or septal F in precirrhotic stage
    - Micronodular cirrhosis ± PCF
- A single lesion or any combination may be found in a given individual

## Main histological diagnoses:



# ALD: Spectrum

- Hepatic Steatosis: present in 90% of heavy drinkers, rapidly reversible with abstinence
- Alcoholic Hepatitis: occurs in 10-35% of heavy drinkers, precursor of cirrhosis
- Cirrhosis: develops in subset of heavy drinkers
- HCC

# Cofactors in Alcoholic Cirrhosis

- Concomitant HCV
- Obesity
- ? Etoh increases penetrance of primary hemochromatosis
- Gene polymorphisms: PNPLA, TNF  $\alpha$  etc.

The background is a complex, futuristic digital composition. It features a central human torso rendered in a glowing blue, semi-transparent style. Overlaid on this are numerous hexagonal frames, some containing icons like a heart with an ECG line, a water drop, pills, a stethoscope, and a virus. There are also various data visualization elements such as bar charts, line graphs, and network maps. The overall aesthetic is clean, high-tech, and medical in theme.

# Alcoholic Hepatitis

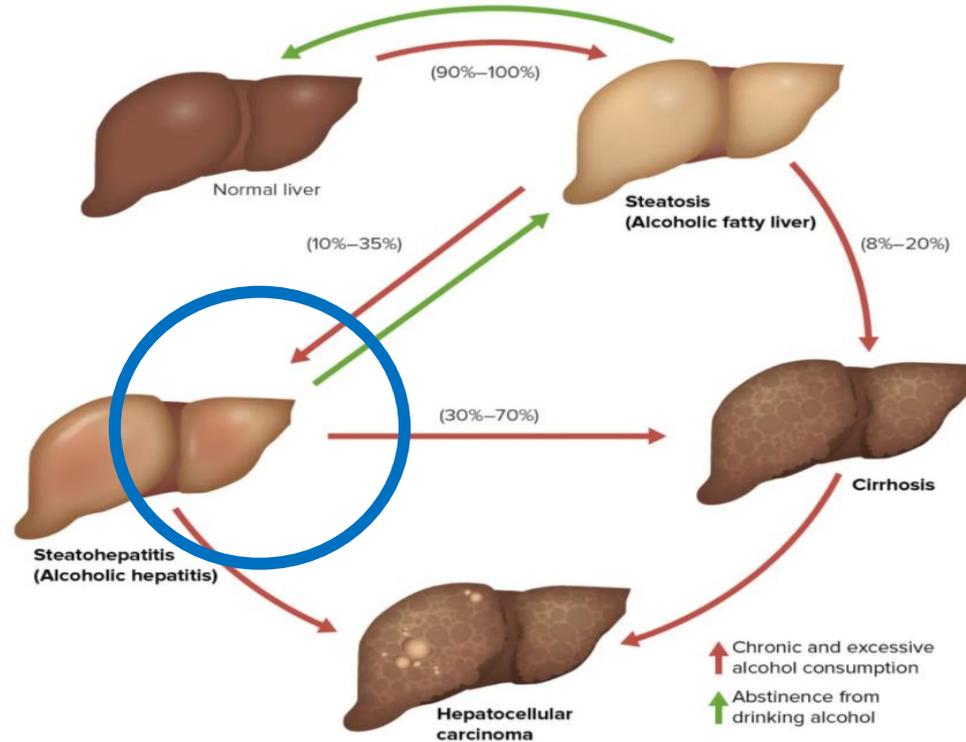
# Alcoholic Fatty Liver

- Treatment
  - Abstinence
  - Fat resolves in several weeks to several months
- Natural history
  - Can progress to cirrhosis if patients continue to drink alcohol
    - Women at higher risk of cirrhosis than men

# Alcoholic Hepatitis

- Long history of alcohol use
  - Decades, >6 drinks per day
  - Abstinence for <6 weeks
- **Jaundice**
- Fever
- Tender hepatomegaly, hepatic bruit
- Ascites
- $AST > ALT$ ;  $AST < 200$  (usually)
- INR prolonged
- Leukocytosis ( $WBC > 10,000$ ;  $PMN's > 6000$ )

# Alcoholic Hepatitis May Be Reversible With Abstinence



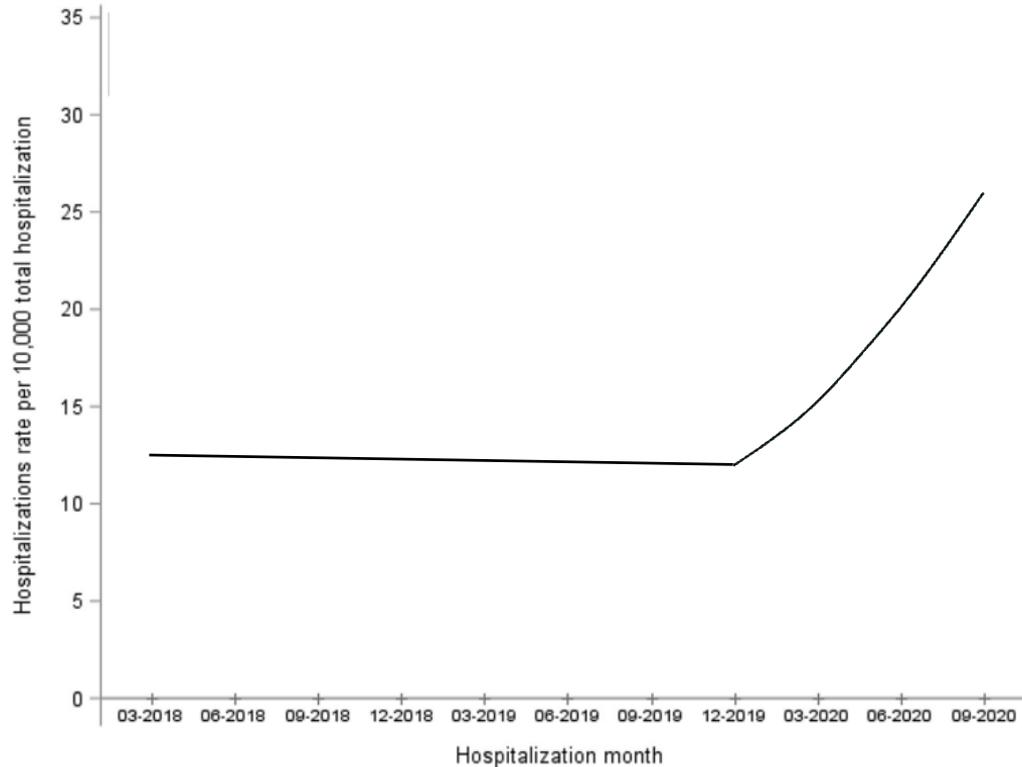
# Severity of Alcoholic Hepatitis

- Discriminate Function (Maddrey)
  - Bilirubin (mg/dL) + [4.6 x prothrombin time] (seconds prolonged)
  - >32 has high short term mortality
  - >55 has very high mortality
- MELD (<http://unos.org>)
  - Creatinine, bilirubin, INR (prothrombin)
  - MELD >22 predicts high 30-day mortality
    - Sensitivity 0.75; specificity 0.75

# Management of Alcoholic Hepatitis

- Hospitalize patients with  $DF > 32$  or  $MELD > 20$
- Exclude infection
- Norfloxacin if ascites albumin  $< 1.0$  g/dl
- Adequate nutrition
  - $> 2000$  Cal/day (enteral feeding if necessary)
  - Multivitamins (thiamine, etc)

# Alcoholic Hepatitis Hospitalizations Increased During the COVID-19 Pandemic

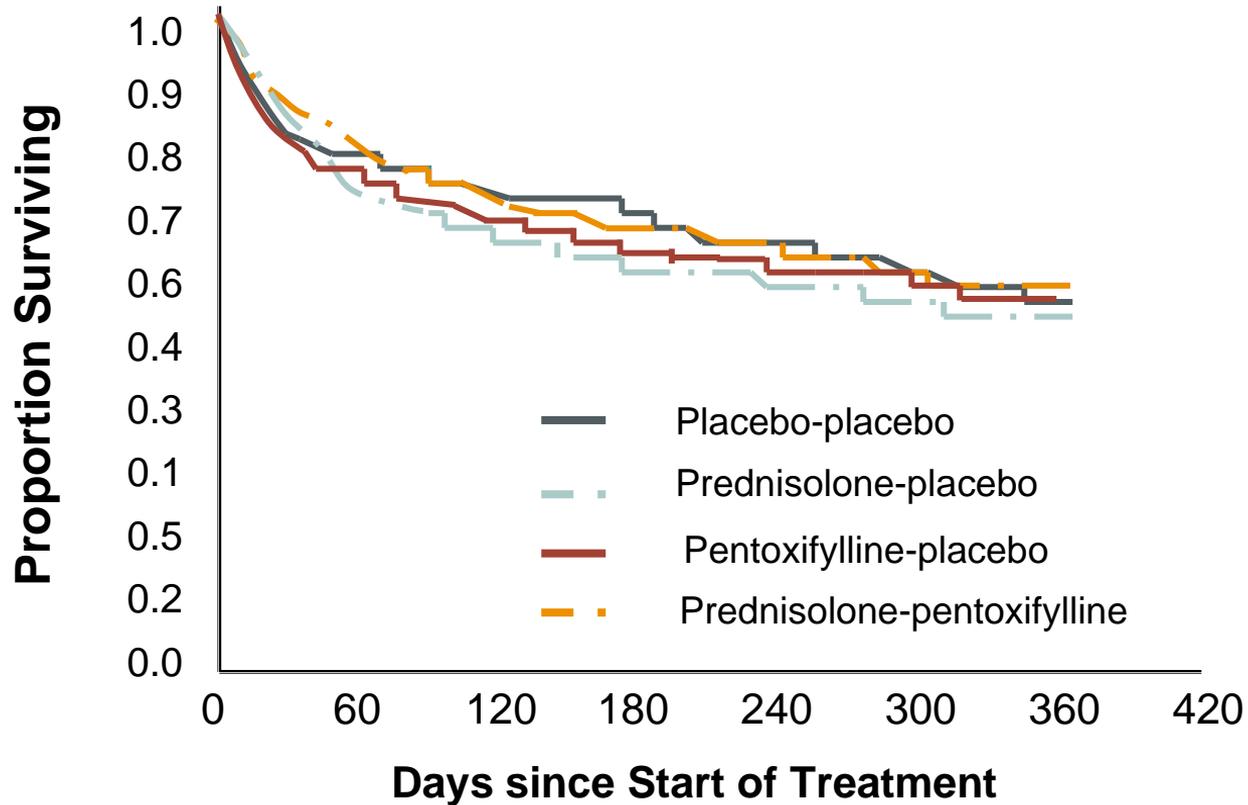




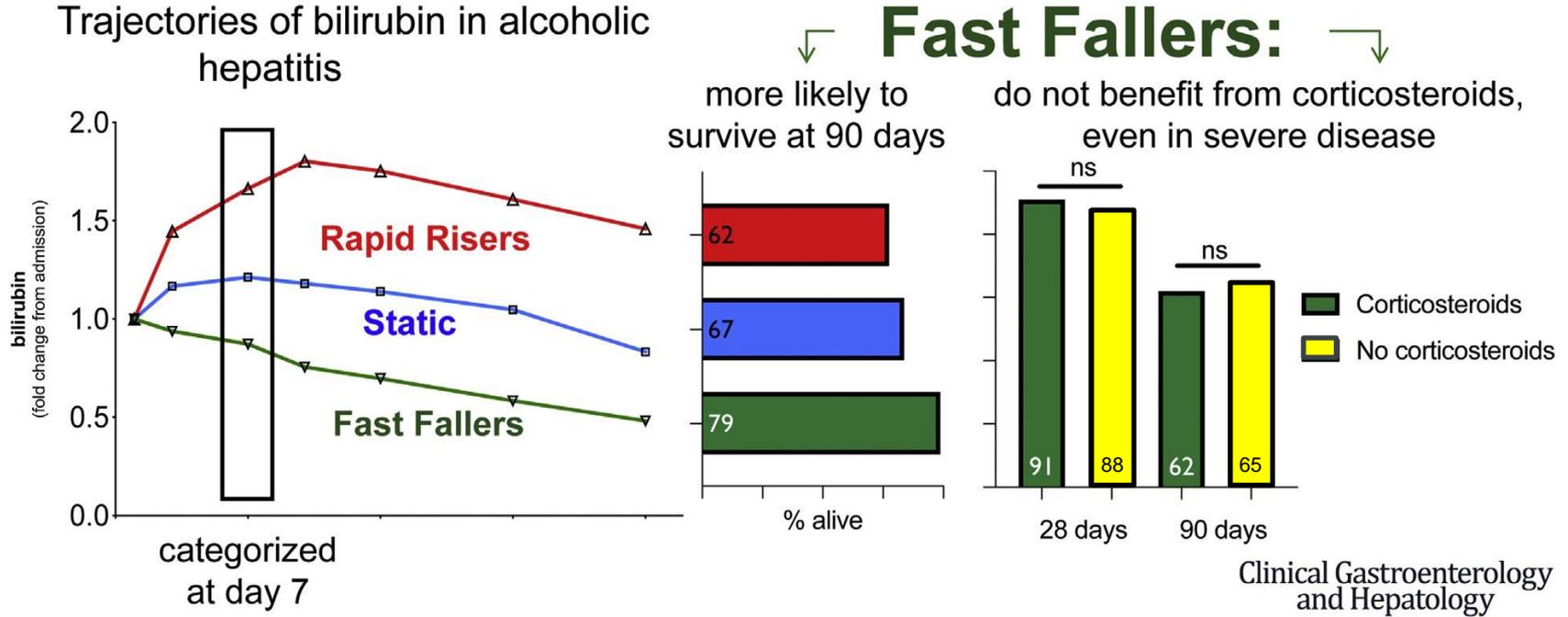
**ALD:**

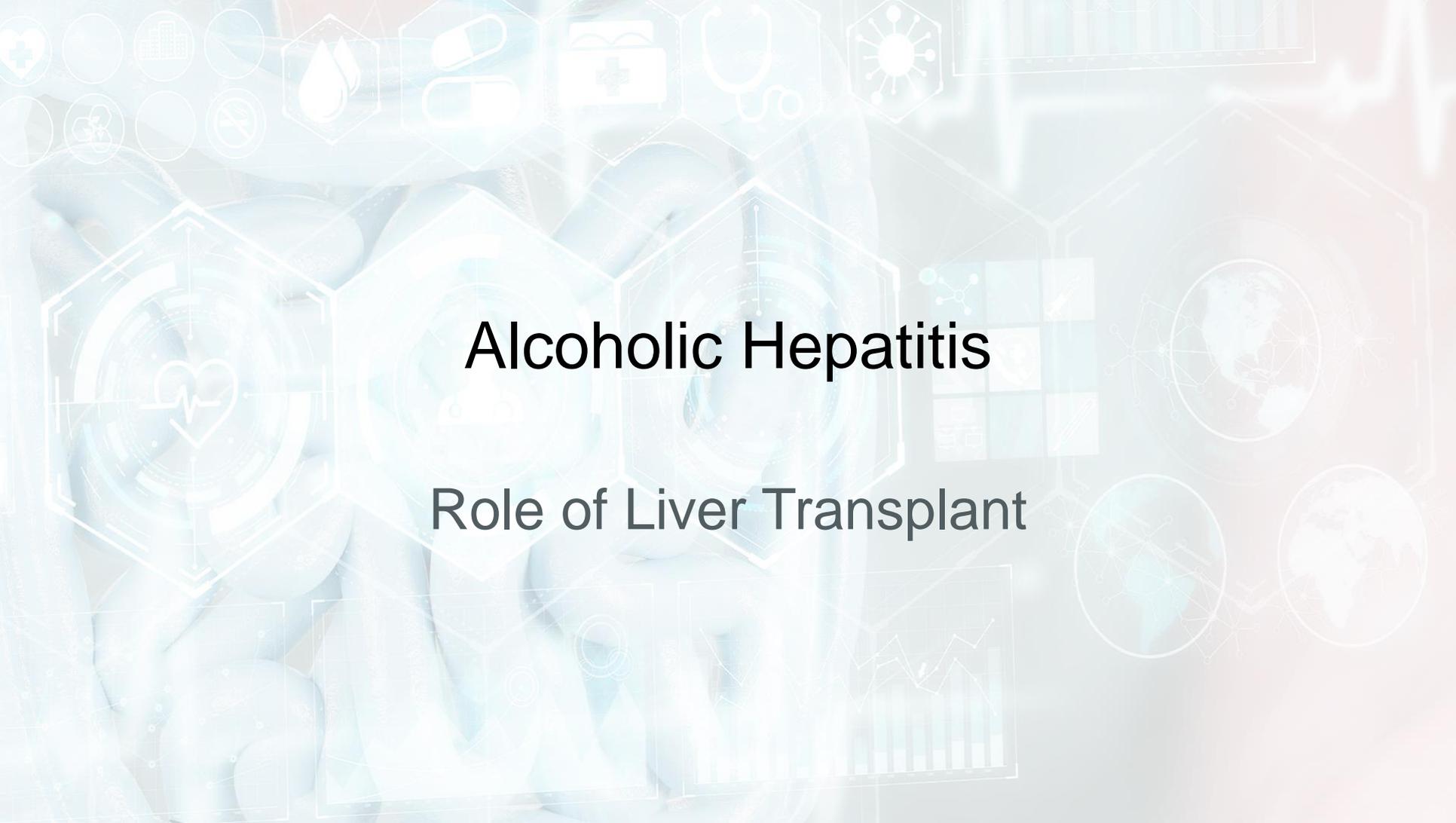
**? Role for Steroids in Alcoholic  
Hepatitis**

# One-Year Survival in Alcoholic Hepatitis



# Trajectory of Bilirubin Predicts Spontaneous Recovery in Patients With AH

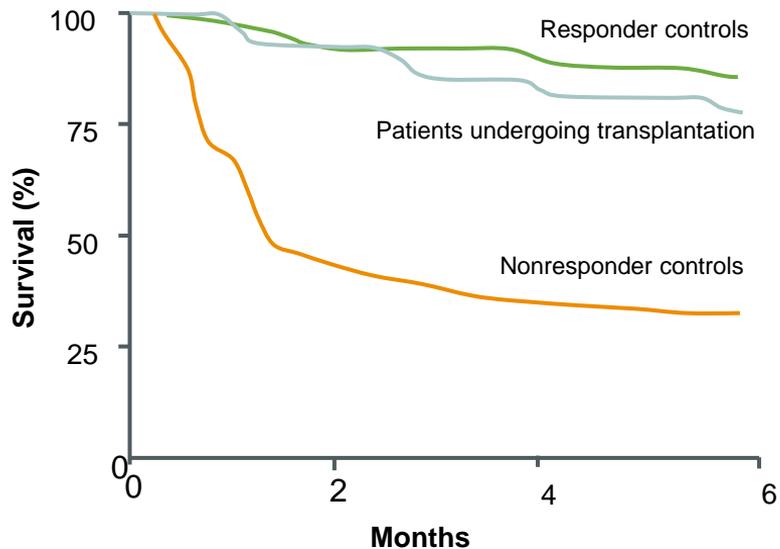




# Alcoholic Hepatitis

## Role of Liver Transplant

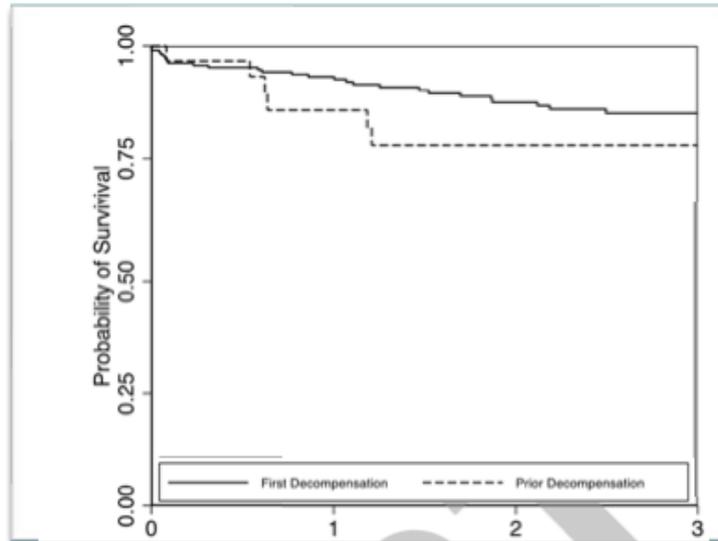
# Liver Transplant for Alcoholic Hepatitis (N=26)



$P < .001$

	<b>No. at Risk</b>			
	0	2	4	6
Responder controls	92	77	75	71
Patients undergoing transplantation	26	21	21	20
Nonresponder controls	69	21	21	19

# Prior Decompensation and Liver Transplant Outcomes



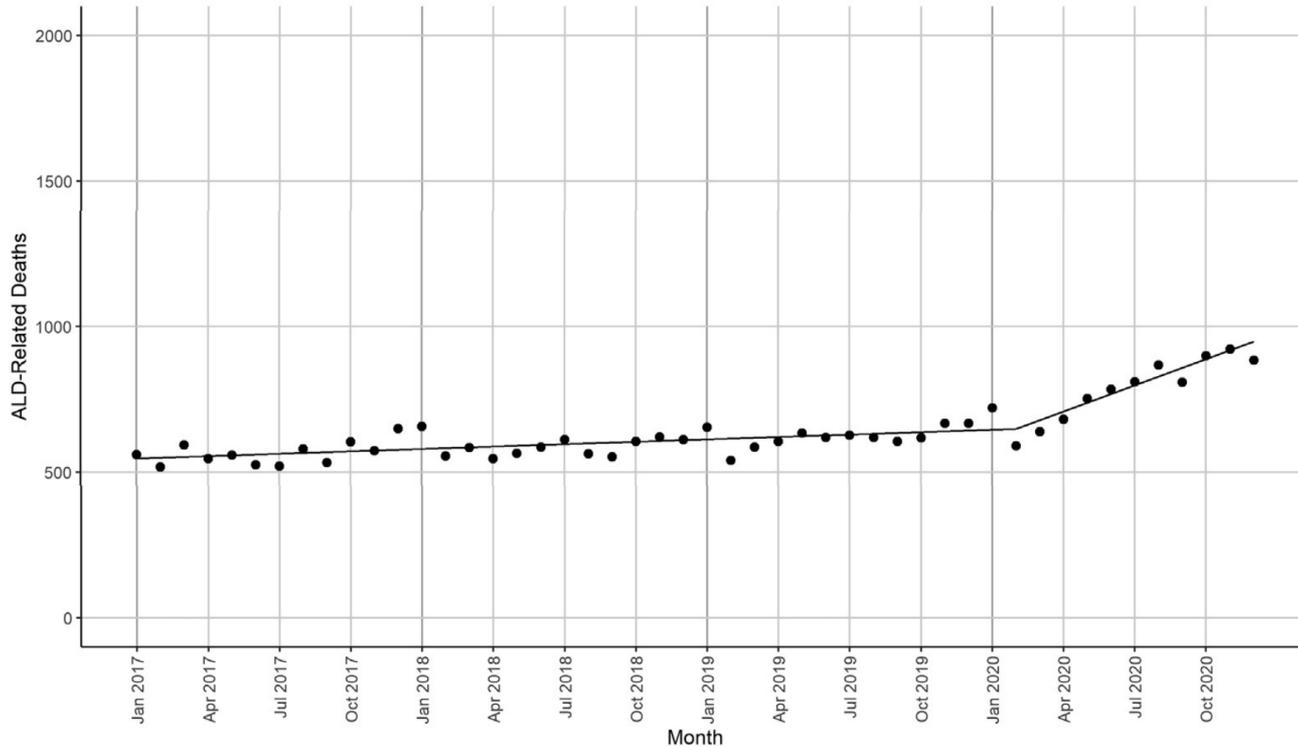
Number at risk				
First Decompensation	210	165	122	71
Prior Decompensation	31	23	13	7

**Weinberg 2022**

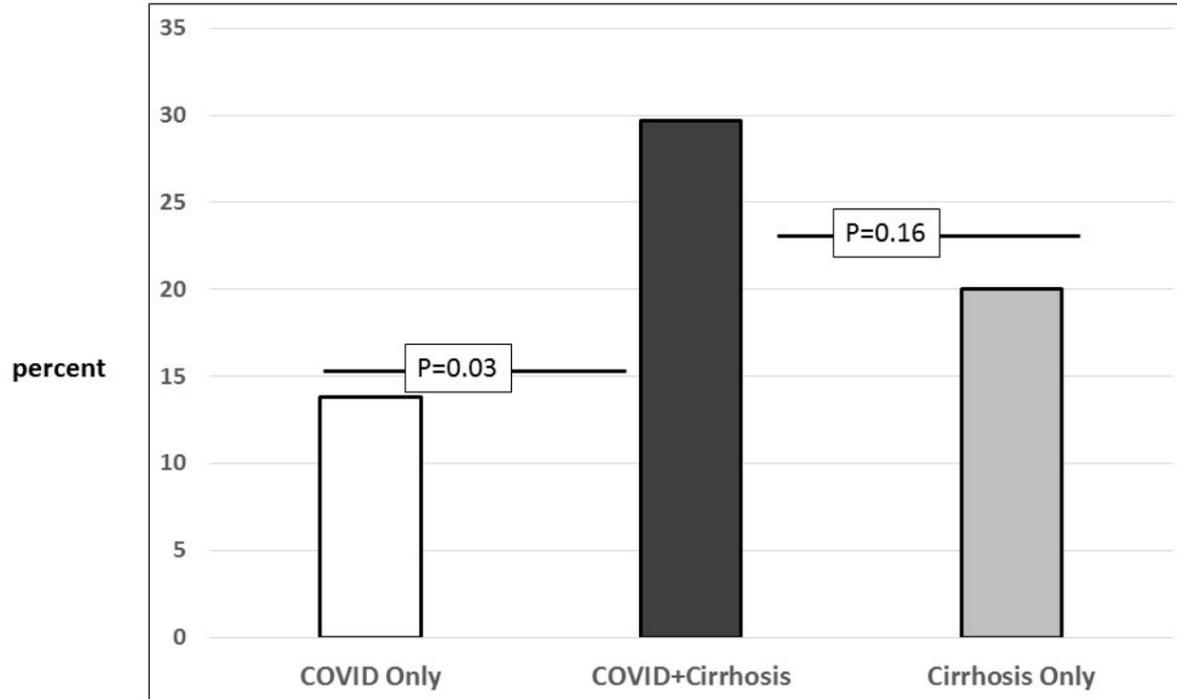
The background is a complex, futuristic composition. It features a central human figure, possibly a man, rendered in a light blue, almost ethereal style. Overlaid on this figure and the entire scene are numerous glowing hexagonal shapes, some containing circular patterns or data points. Scattered throughout are various icons: a heart with a pulse line, a water drop, pills, a first aid kit, a stethoscope, a virus particle, a bar chart, a globe, and a network diagram. The overall color palette is dominated by light blues and whites, with a soft, hazy glow that gives it a high-tech, medical, and scientific feel.

# Alcoholic Liver Disease and COVID

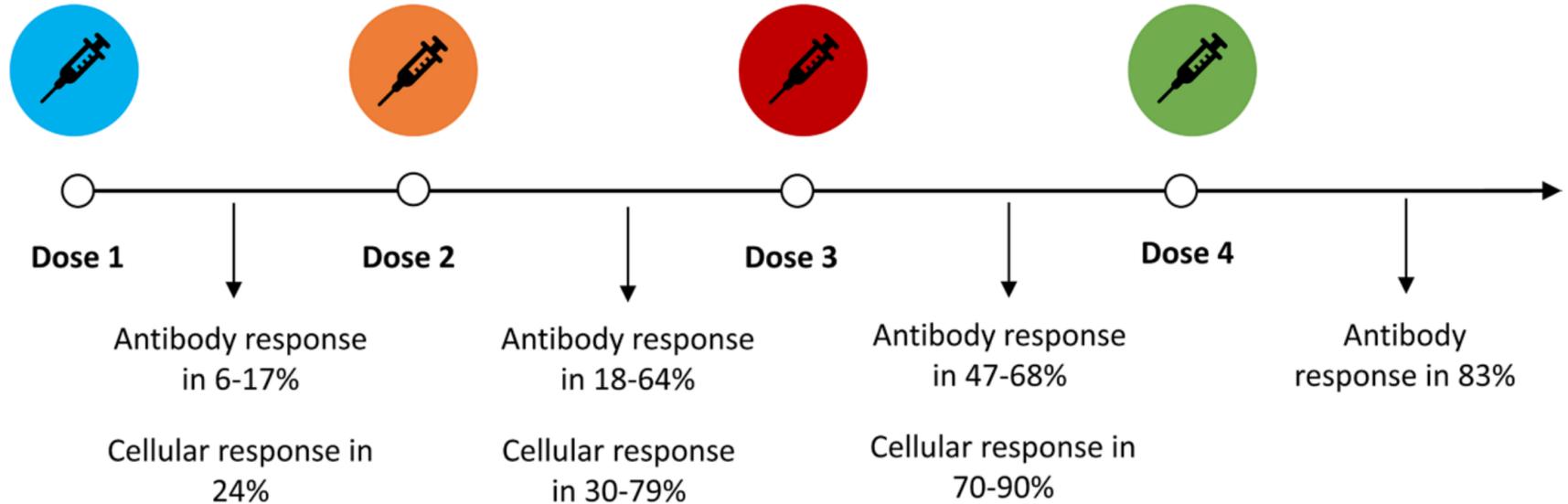
# ALD-Related Mortality for January 2017 to December 2020



# Mortality (In-Hospital Mortality and Hospice) Comparison



# COVID Vaccination Post-Transplant



# Alcoholic Liver Disease and COVID

- Increase in alcohol use
- Increase in hospitalizations for ALD
- Increased mortality
- Highlights controversies in ALD