

Early diagnosis of Liver disease in
Alcohol use disorder
Safe Addictions prescribing in Liver
disease

Naina Shah

Consultant Hepatologist

- I have no disclosures

Case history

- 41 year old male accountant-Croydon University Hospital March 22
 - jaundice, distention of abdomen, confusion
 - Drinking since the age of 17 years socially, escalated to dependence for 8 years
 - 30 units/day during COVID pandemic
 - Stress, anxiety
- Clinically was markedly icteric, moderate ascites, grade 2 hepatic encephalopathy

Investigations

- Bilirubin **550** (<21)
- Albumin **25** (35-50)
- INR **2.1** (<1.3)
- Sodium **128** (135-145)
- Creatinine **300** (61-123)

Severe Alcoholic Hepatitis with 4 organ failure

Intubated and ventilated, inotropic support, haemofiltration

Treated with Prednisolone- responder

Protracted stay on ICU- discharged after 2 months

Referred to Kings College Hospital to manage his ArLD on patient's request

- Reviewed in the integrated Alcohol Liver clinic-Naina Shah and Nicky Kalk
- Remained abstinent of Alcohol since his discharge in May 22
 - Supportive partner, family, manager.
 - Got married
 - Work provided distraction from craving and anxiety
 - Referred to Croydon IAPT and self guided help to manage anxiety
- Fibroscan August 22 LSM 14 kPA, CAP 187

- Decompensation



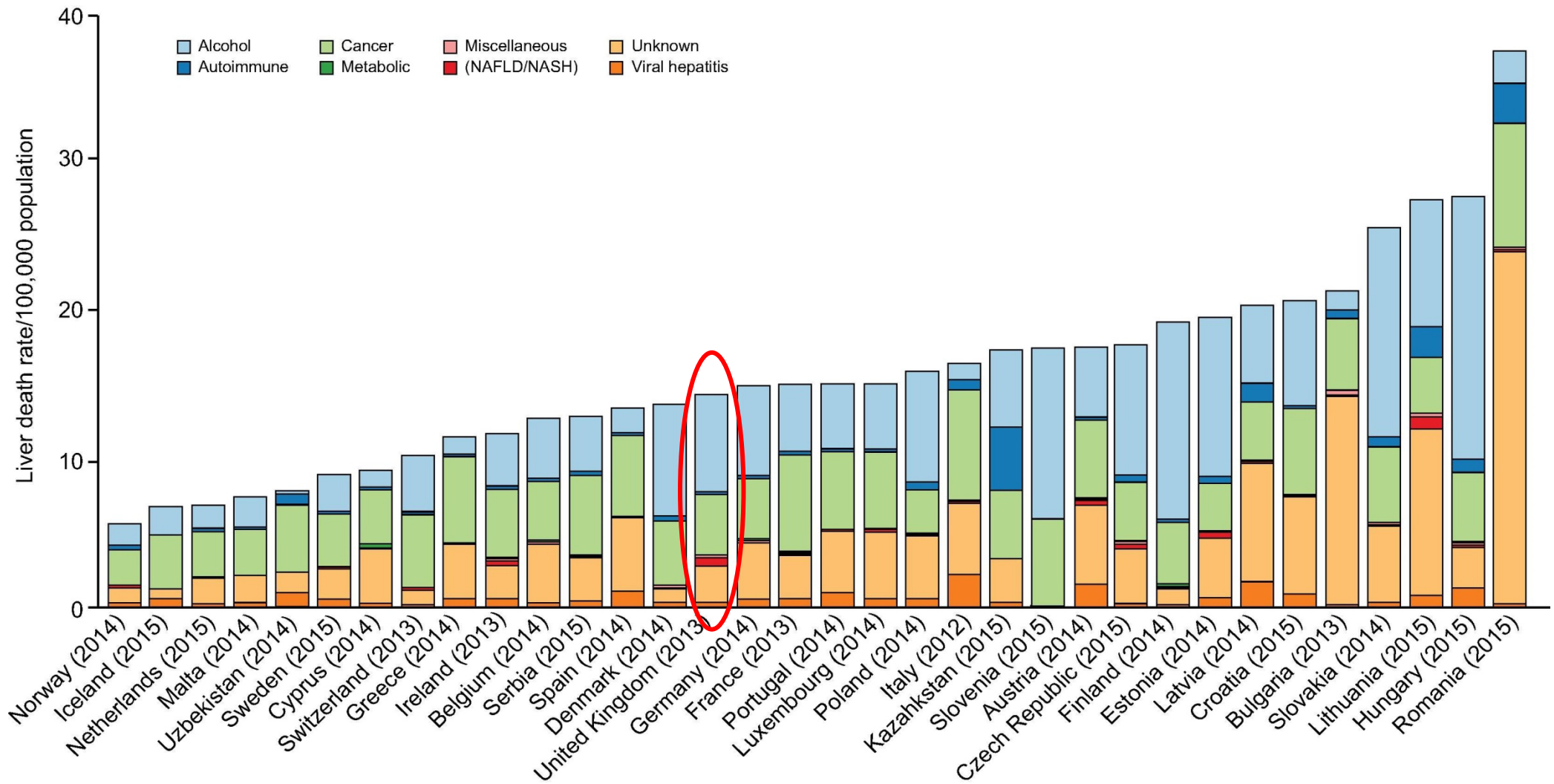
Fibroscan August 22 LSM 14 kPA, CAP 187

- Recompensation

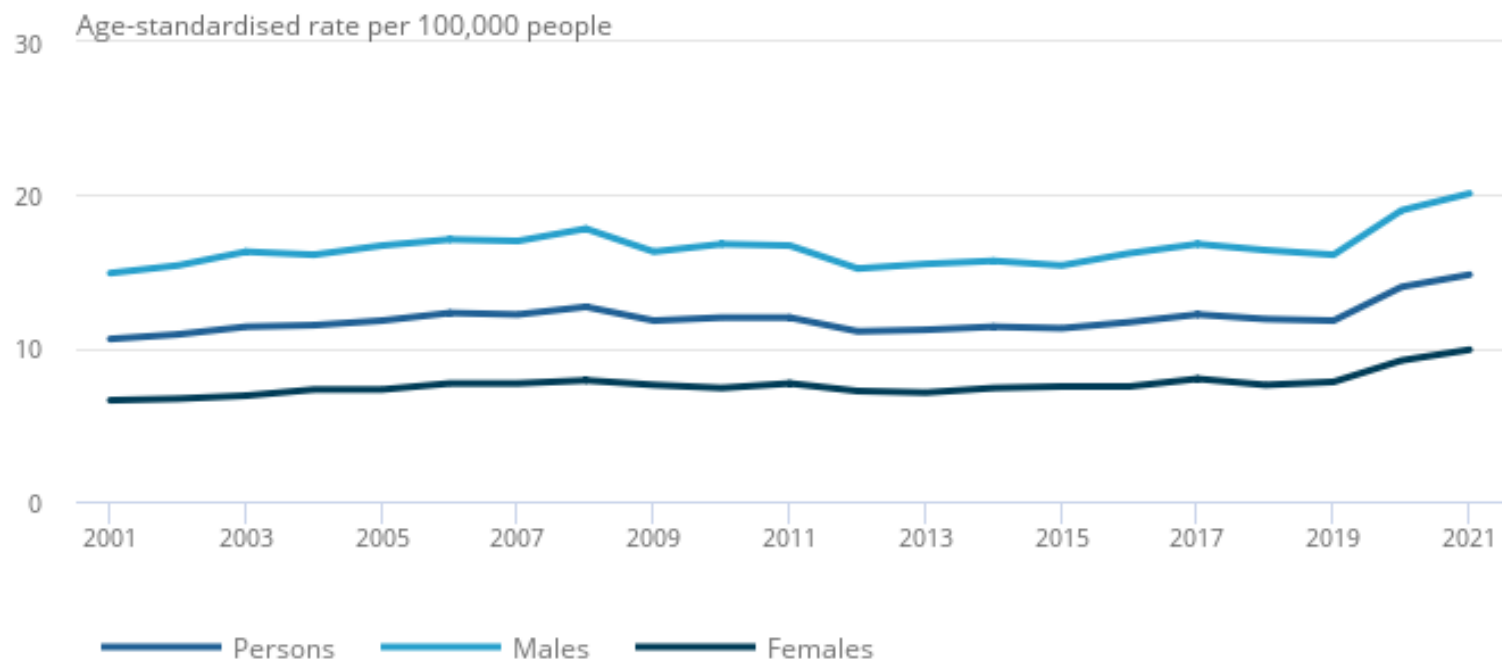


Fibroscan April 23 LSM 6.9 kPA, CAP 153

No Cirrhosis but life threatening clinical presentation.
Excellent recovery with sustained abstinence



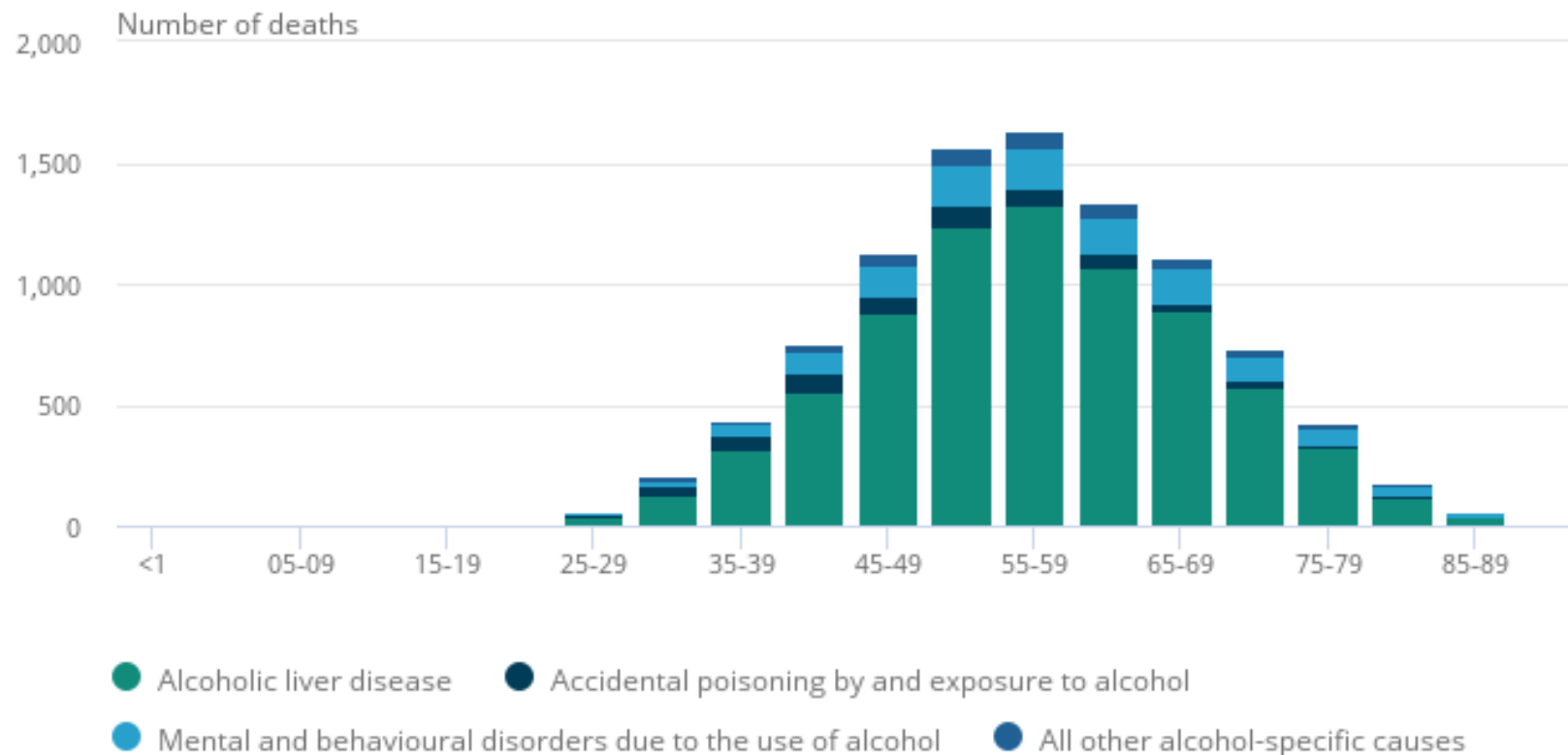
Age-standardised alcohol-specific death rates per 100,000 people, by sex, UK, deaths registered between 2001 and 2021



Source: Office for National Statistics – Alcohol-specific deaths in the UK: registered in 2021, National Records of Scotland and the Northern Ireland Statistics and Research Agency

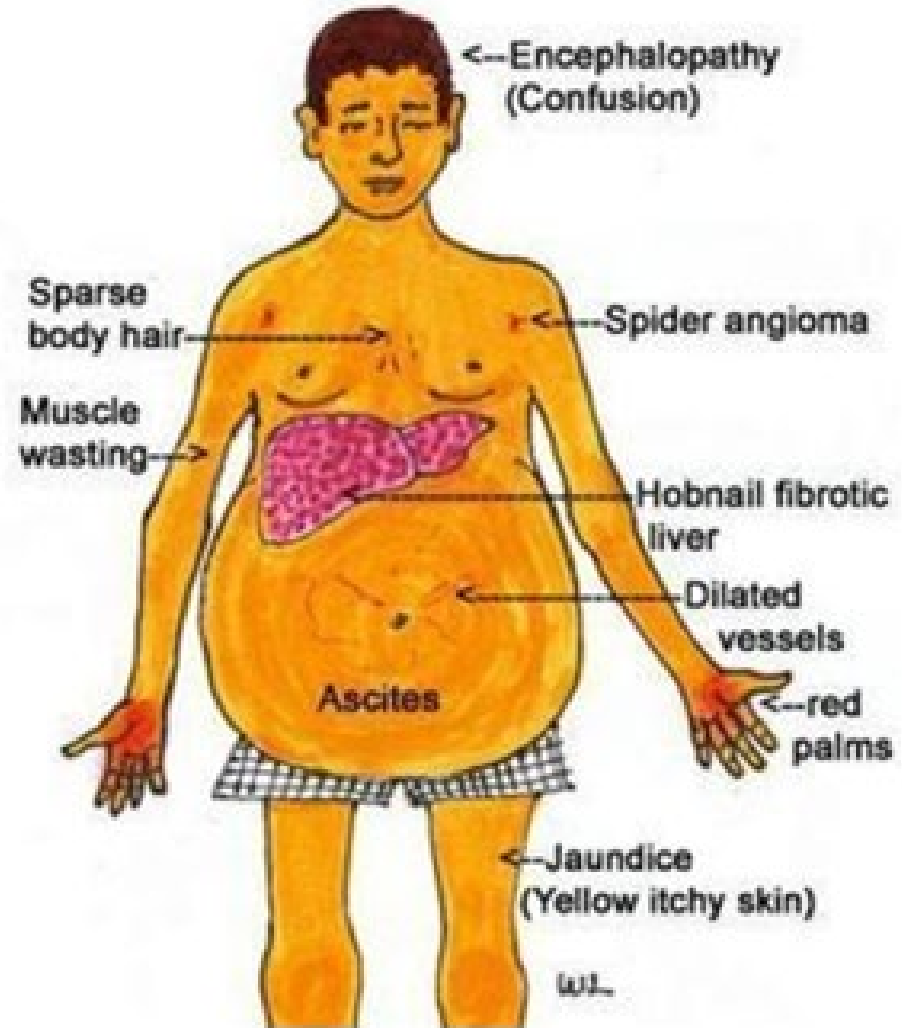
The alcohol specific death rate in 2021 was 25.4% higher than 2019

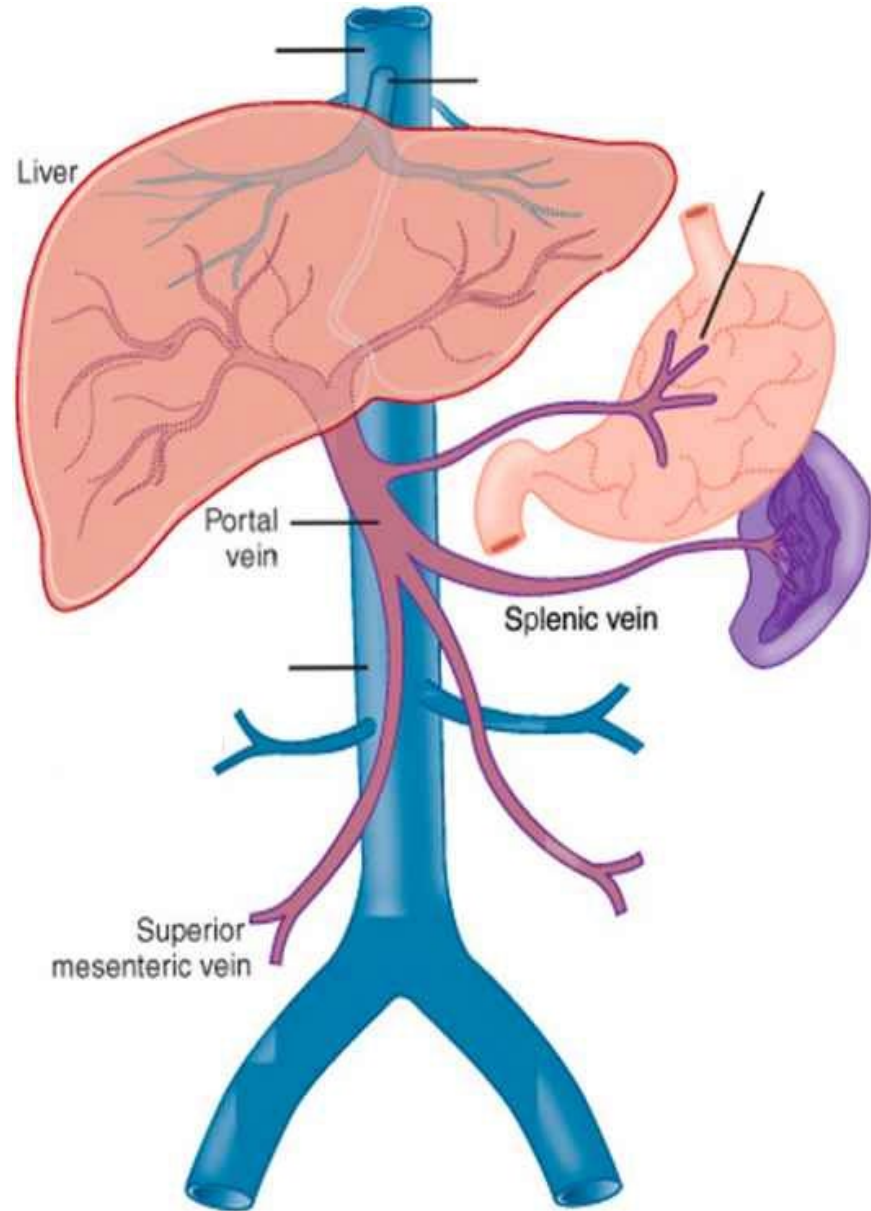
Numbers of alcohol-specific deaths, by five-year age group and individual cause, UK, deaths registered in 2021



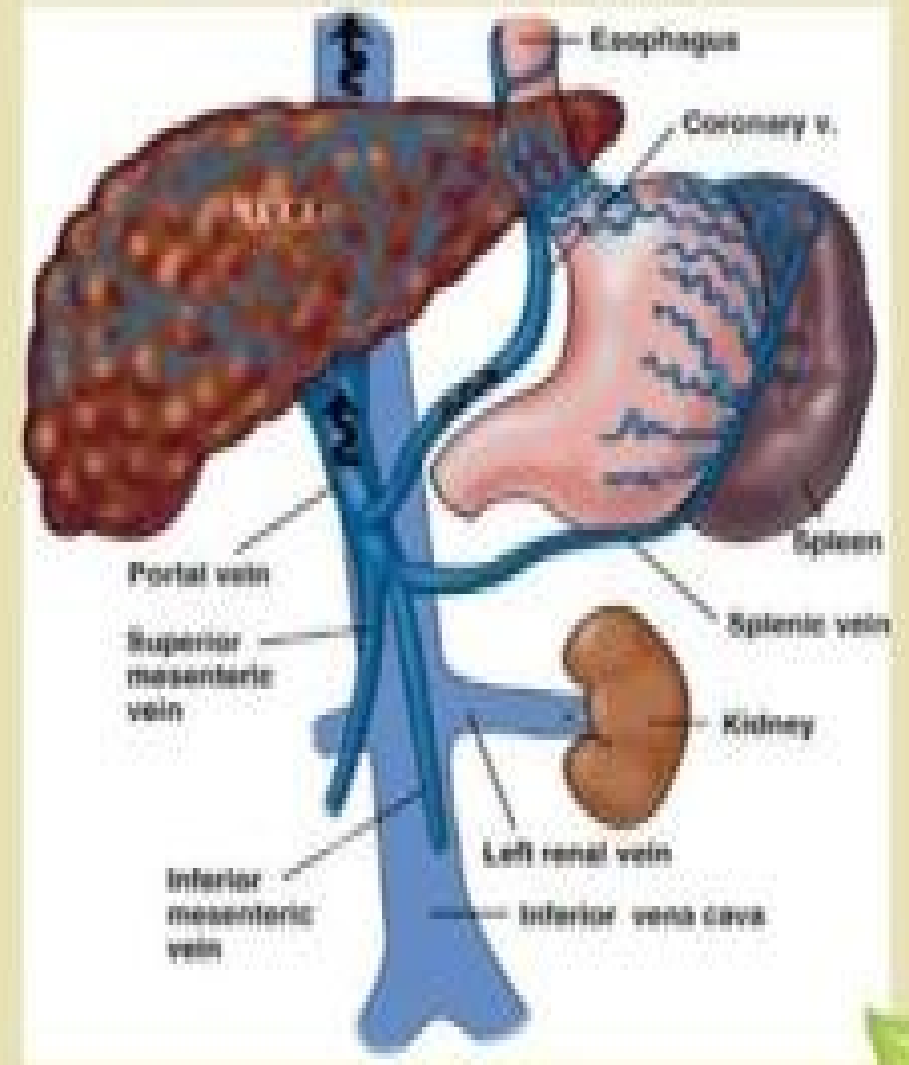
Source: Office for National Statistics – Alcohol-specific deaths in the UK: registered in 2021, National Records of Scotland and the Northern Ireland Statistics and Research Agency

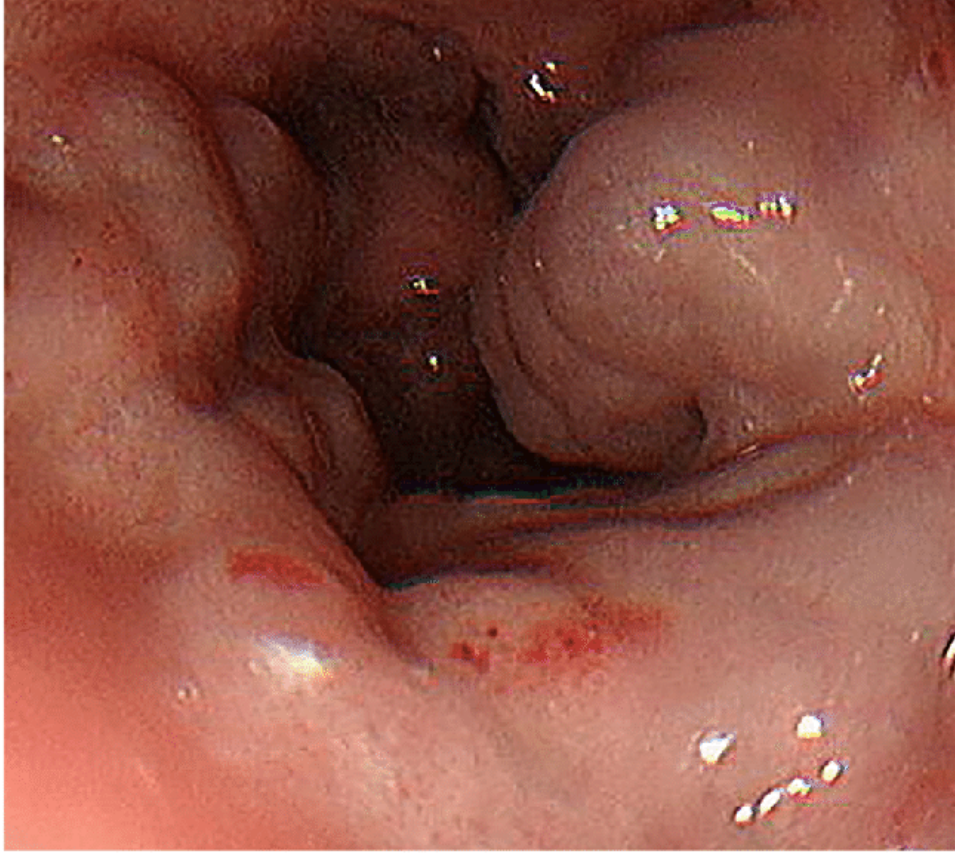
Three-quarters of alcohol-specific deaths were caused by alcoholic liver disease

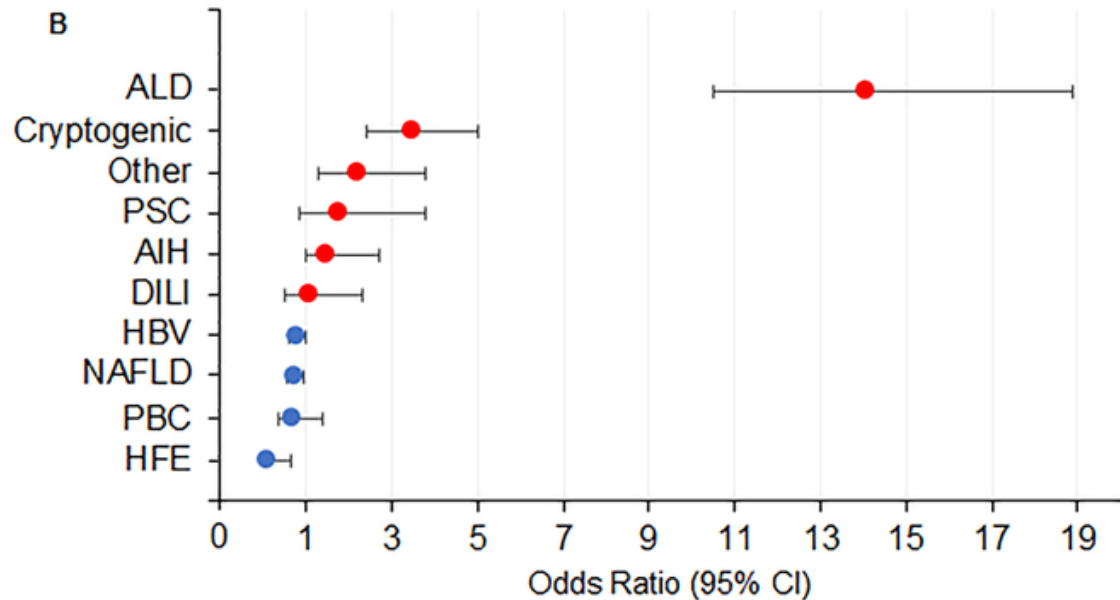
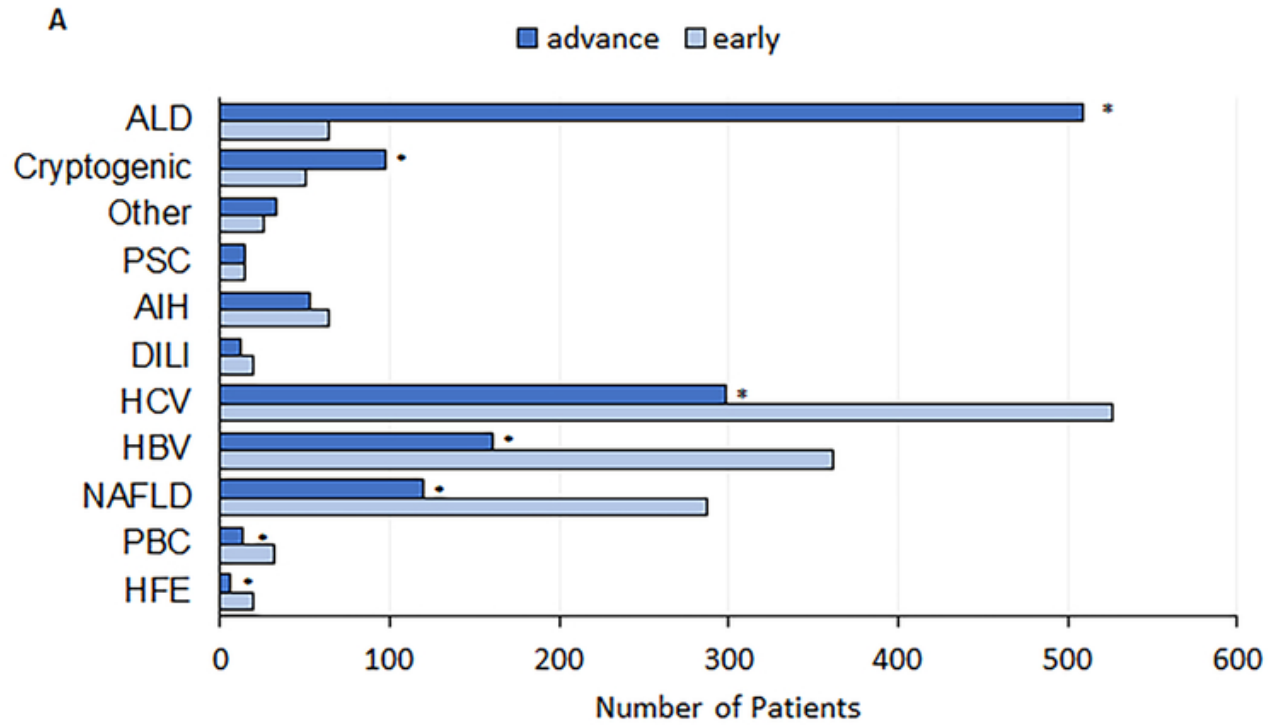




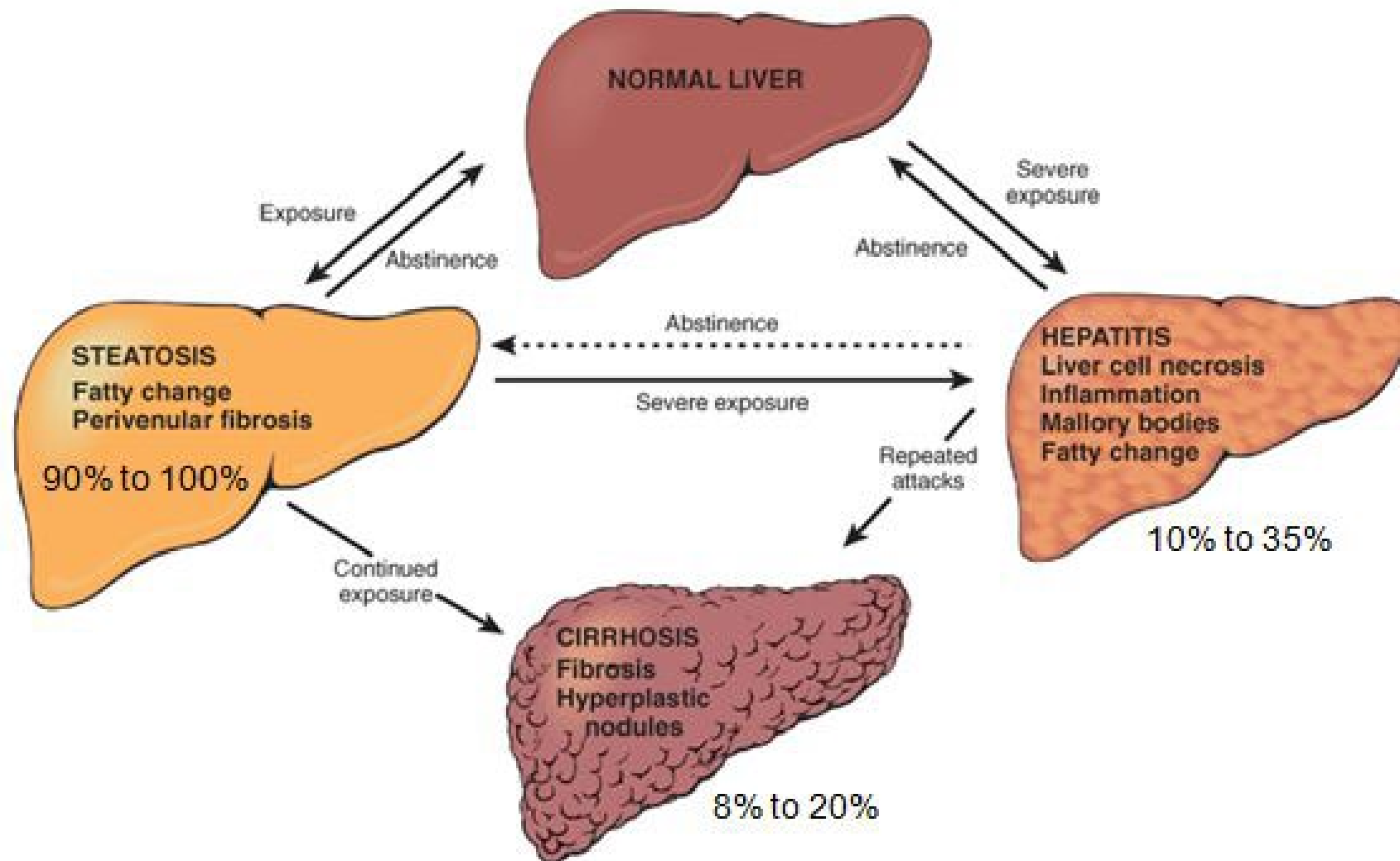
Portal Hypertension

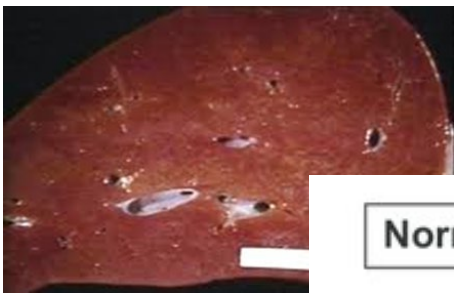




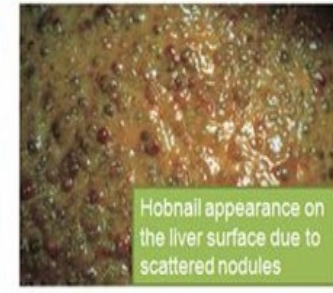


Medical Visits at Specialized Centers of Patients with Single Etiology.
 Panel A: Number of Patients with Medical Visits at Advanced vs. Early Liver Stages.
 Panel B: Odds Ratio of being seen at Advanced stage.



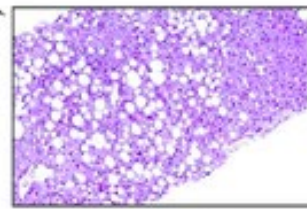


Normal liver



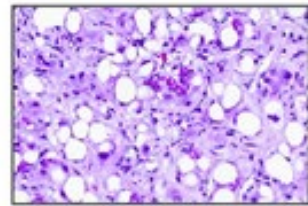
Hobnail appearance on the liver surface due to scattered nodules

80-90%



Steatosis

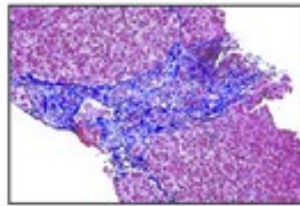
Contributes to disease progression



Alcoholic steatohepatitis

SILENT

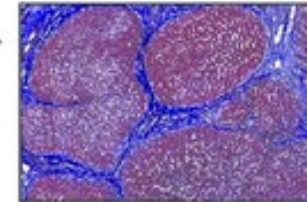
20-40%



Fibrosis

AH

8-20%



Cirrhosis

20-40%



Decompensation (+ infections)

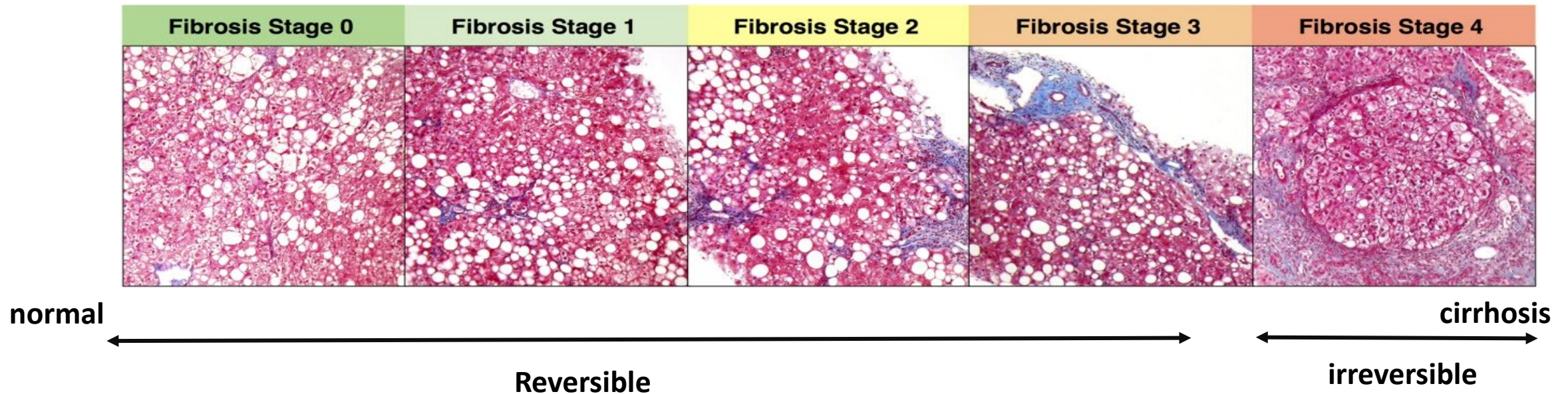
JAUNDICE and COMPLICATIONS

3-10%

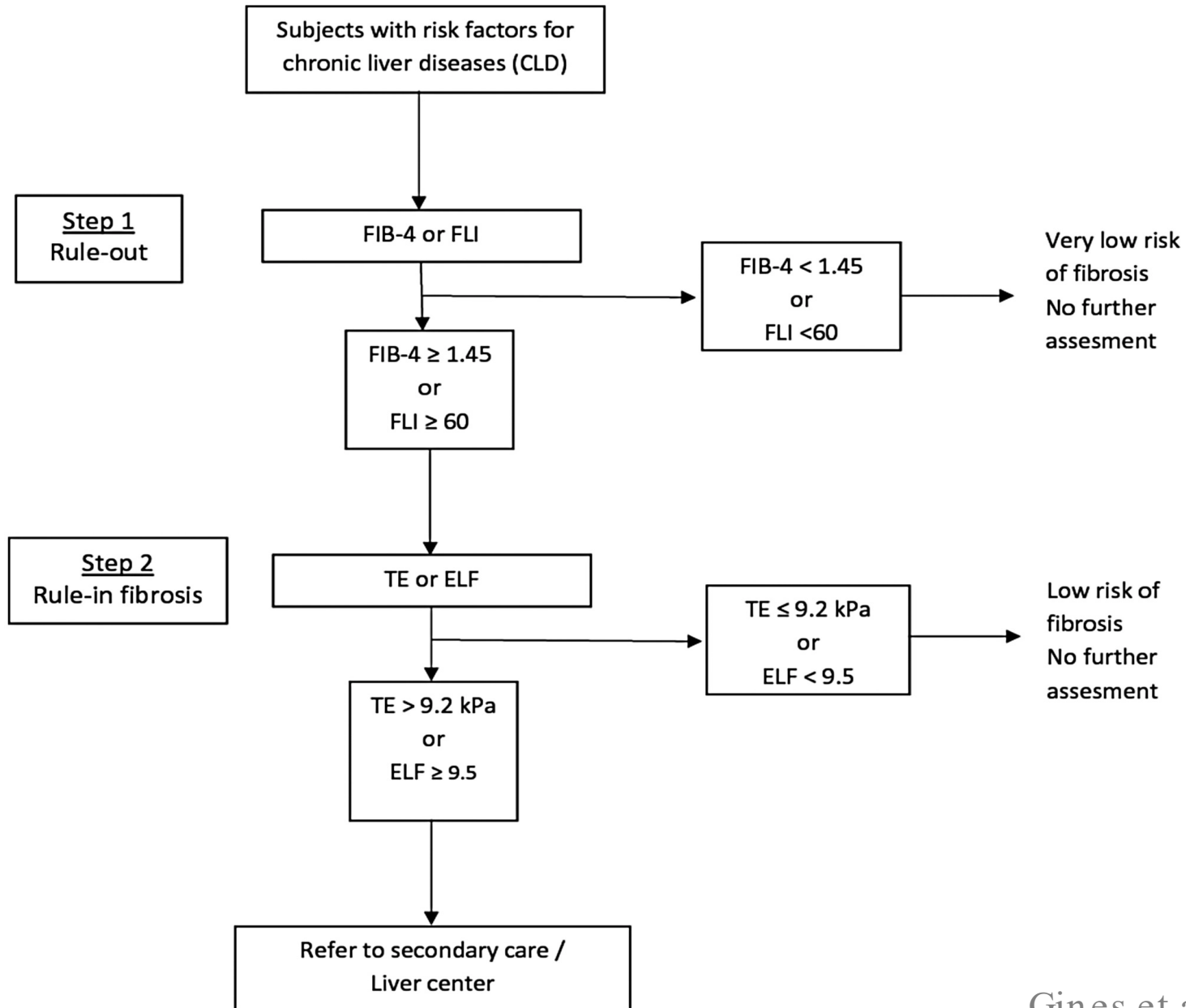
HCC

Screen for underlying Liver disease

- Late presentation with fatal complications of cirrhosis.
- harmful levels—more than 50 (men) and 35 (women) units a week- to be offered transient elastography (Fibroscan) to exclude cirrhosis.




A proposed framework for early diagnosis of chronic Liver disease



Fibrosis-4 (FIB-4) Index for Liver Fibrosis

Noninvasive estimate of liver scarring in HCV and HBV patients, to assess need for biopsy.

When to Use 

Pearls/Pitfalls 

Why Use 

Age

Use with caution in patients <35 or >65 years old, as the score has been shown to be less reliable in these patients

Norm: 0 - 0

years

AST

Aspartate aminotransferase

Norm: 15 - 41

U/L

ALT

Alanine aminotransferase

Norm: 1 - 35

U/L

Platelet count

Norm: 150 - 350

$\times 10^9/L$ 

Result:

Please fill out required fields.

A score - <1.45 has a negative predictive value of over 90% for advanced liver fibrosis of multiple aetiologies

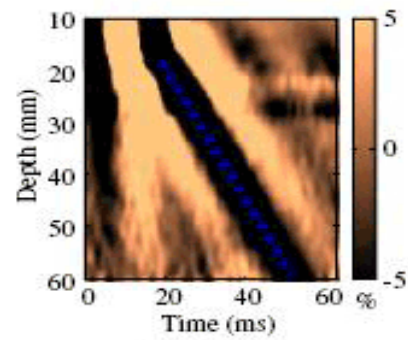
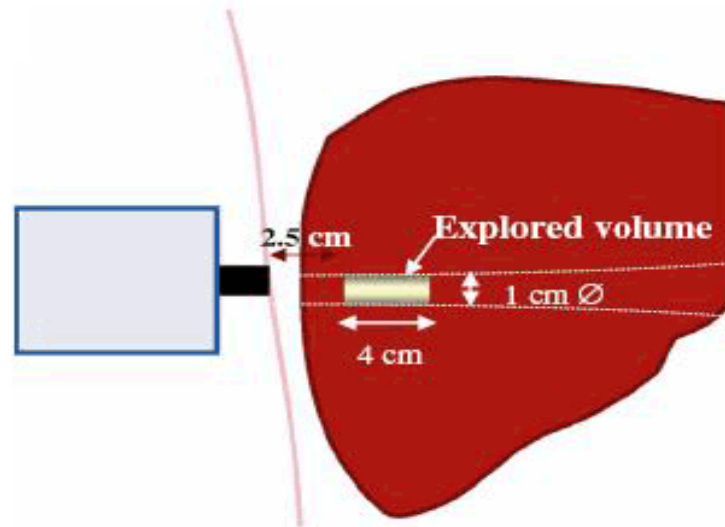
ELF

- The Enhanced Liver Fibrosis (ELF) score is an ECM marker
 - tissue inhibitor of metalloproteinases 1 (TIMP-1),
 - amino-terminal propeptide of type III procollagen (PIIINP) and
 - hyaluronic acid (HA)
- shows good correlation with fibrosis stages in chronic liver disease.

ELF Test Score	Interpretation	Action plan
>9.8	Likely severe fibrosis	Biopsy may not be required for liver fibrosis assessment
7.7-9.8	Uncertain may be moderate fibrosis	Biopsy may be recommended
<7.7	Likely no or mild fibrosis	Biopsy may not be required for fibrosis assessment

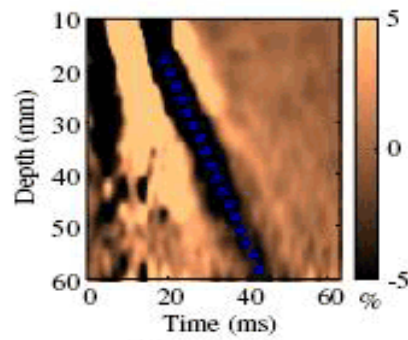
Fibroscan, Echosens, Paris





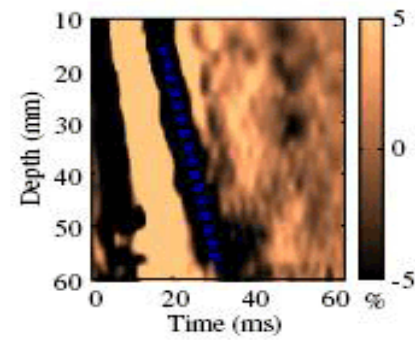
$V_s = 1.0$ m/s
 $E = 3.0$ kPa

F0



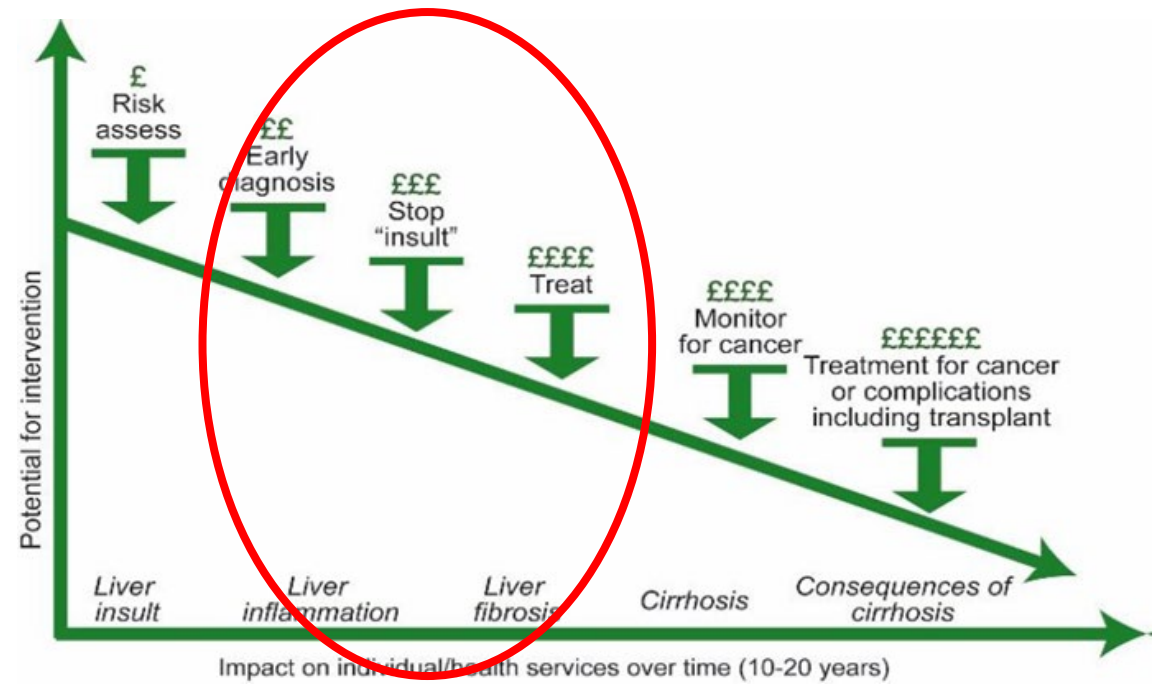
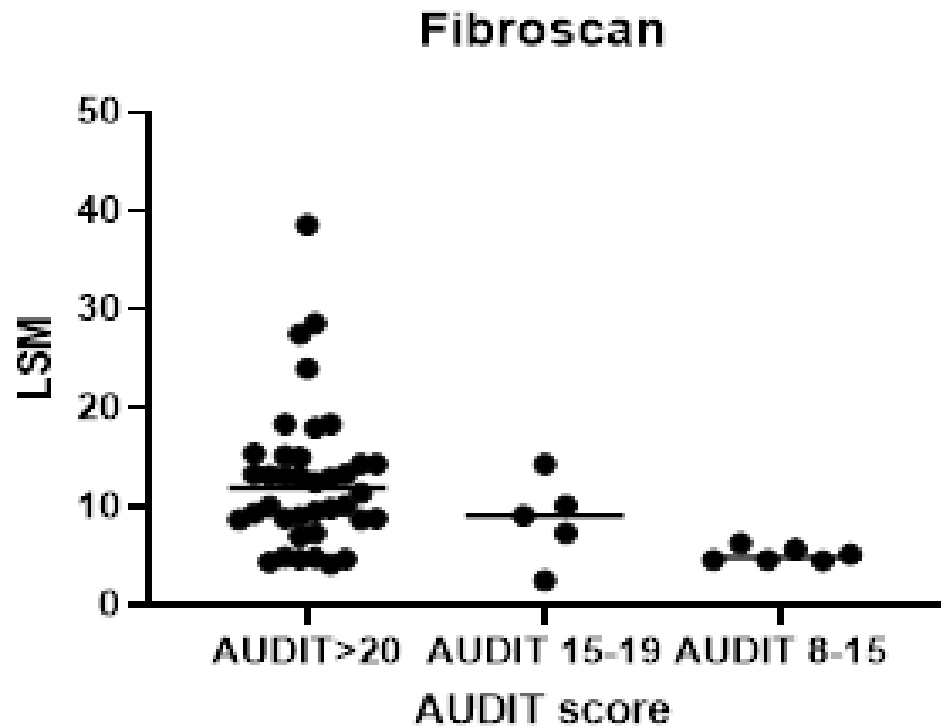
$V_s = 1.6$ m/s
 $E = 7.7$ kPa

F2



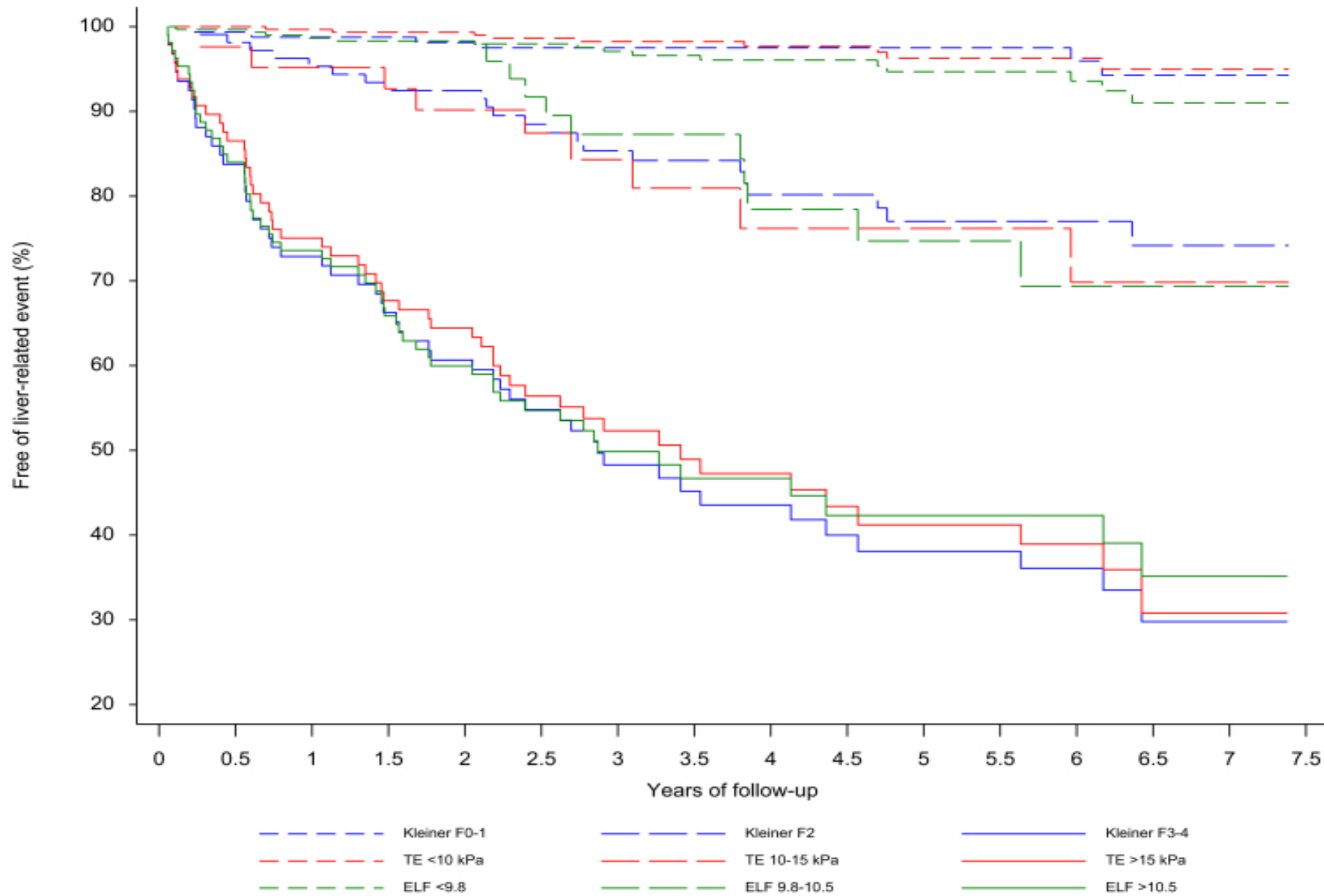
$V_s = 3.0$ m/s
 $E = 27.0$ kPa

F4

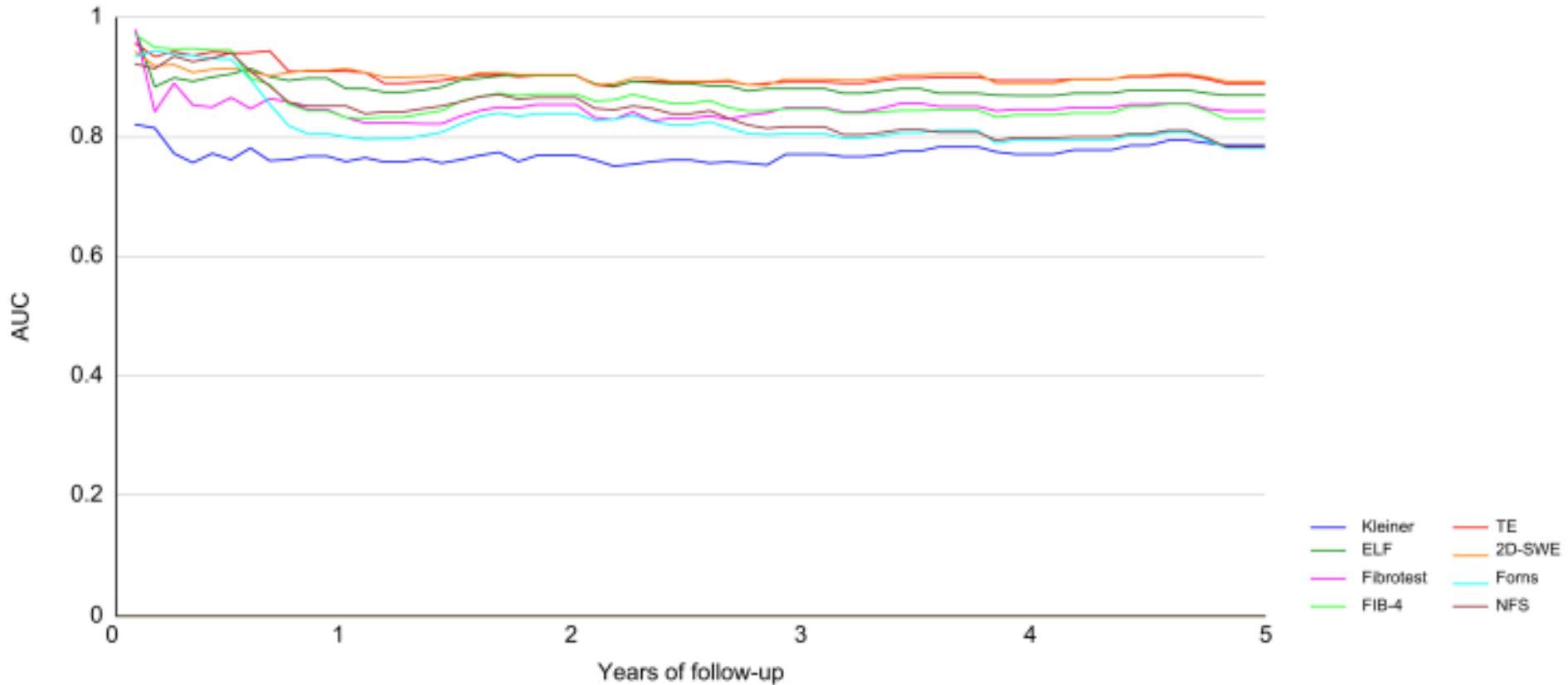


‘The estimated lifetime cost of a patient with alcohol-related liver disease is between £47000 and £124000, so early interventions are likely to be highly cost-effective’
 ‘Cost of transplant’

Risk of Liver related events for 3 risk groups

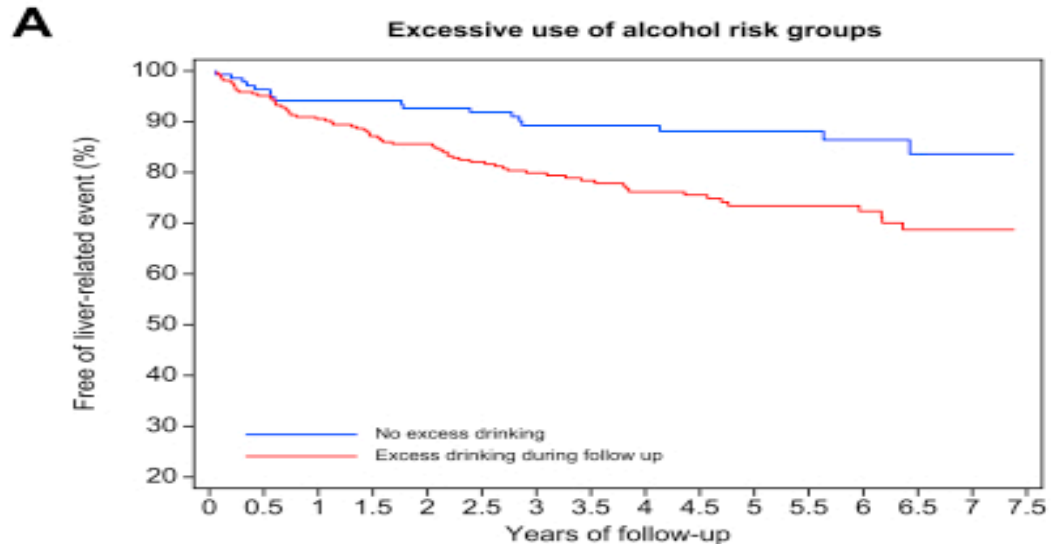


Time-dependent AUC for prediction of liver-related events during 5 years of follow-up

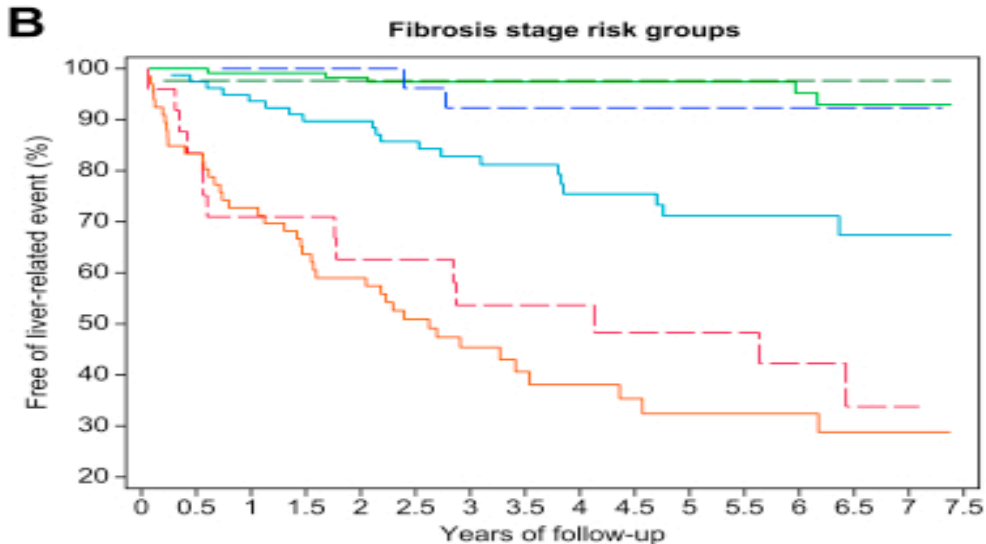


Model performance measures	Kleiner	ELF	TE	2D-SWE	FibroTest	FIB-4	Forns	NFS
Time-dependent AUC	0.786	0.870	0.889	0.893	0.843	0.830	0.781	0.783
Integrated AUC	0.868	0.890	0.890	0.909	0.859	0.855	0.810	0.812
Harrell's C	0.819	0.859	0.876	0.868	0.808	0.821	0.783	0.794

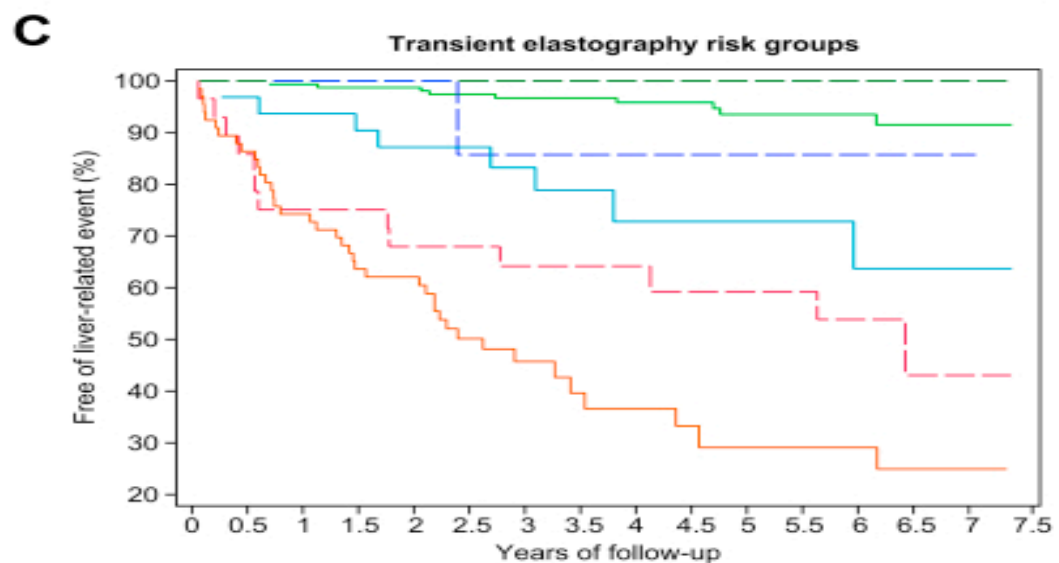
Kaplan-Meier survival curves from univariable Cox regression for liver-related events



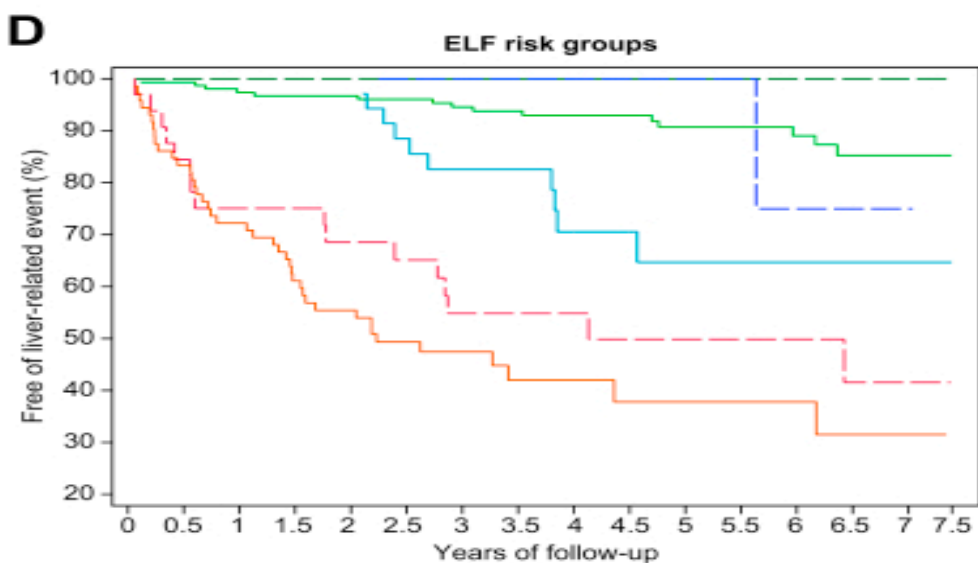
Risk table								
No overuse	140	126	124	98	84	71	40	8
Overuse	265	239	223	171	134	97	66	13



—	Kleiner 0/1 & no overuse	—	Kleiner 0/1 & overuse
—	Kleiner 2 & no overuse	—	Kleiner 2 & overuse
—	Kleiner 3/4 & no overuse	—	Kleiner 3/4 & overuse



—	TE <10 kPa & no overuse	—	TE <10 kPa & overuse
—	TE 10-15 kPa & no overuse	—	TE 10-15 kPa & overuse
—	TE >15 kPa & no overuse	—	TE >15 kPa & overuse



—	ELF <9.8 & no overuse	—	ELF <9.8 & overuse
—	ELF 9.8-10.5 & no overuse	—	ELF 9.8-10.5 & overuse
—	ELF >10.5 & no overuse	—	ELF >10.5 & overuse

	Total cohort	F0-1	F2	F3-4	TE <10	TE 10-15	TE >15	ELF <9.8	ELF 9.8-10.5	ELF >10.5
Any excessive drinking during follow-up, n	265	116	78	66	155	32	66	154	35	72
No evidence of excessive drinking during follow-up, n	140	42	28	26	95	8	30	93	12	34

Fibroscan as a motivational intervention

	Whole Cohort (<i>n</i> = 86)	Raised Liver Stiffness (<i>n</i> = 33)	Normal Liver Stiffness (<i>n</i> = 53)	<i>p</i> *
Age (years)	46.3 (±9.8)	46.6 (±8.6)	46.0 (±10.9)	0.79
Gender (male)	53 (70.0)	17 (51.2)	35 (66.0)	
Liver stiffness score (kPa)	6.9 (3.1–75.0)	13.5 (8.1–75)	5.8 (3.1–8)	<0.01
ALT (units/litre)	64.5 (±52.5)	83.1 (±60.8)	53.0 (±43.4)	0.01
GGT (units/litre)	568.6 (±757.4)	1033.6 (±949.7)	226.7 (±260.8)	<0.01
Alcohol intake (units/week)				
Baseline (<i>n</i> = 57)	145 (24–420)	149 (39–420)	126 (24–378)	0.338
≥Six months (<i>n</i> = 47)	80 (0–315)	65 (0–300)	90.7 (0–315)	

Alcohol related Liver disease

- Late presentation
- 50% of patients will stop drinking after Liver consultation, 25% die and 25% survive long term.
- High risk drinkers in the primary care: 10% of patients reduce drinking by a significant degree.
- Alcohol intoxication within the last 3 months of presentation and infection were the most common PE's: **CANONIC** study.

Clària J et al. Hepatology. 2016

Thursz MR et al. N Engl J Med. 2015

Sheron N et al. Br J Gen Pract. 2013

Severe Alcoholic (Alcohol related) Hepatitis

- **Clinical**

- Jaundice

- Drinking until admission or stopped within 4 weeks of presentation

- (daily consumption of 80 grams for at least 5 years)*

- **Biochemical**

- Bilirubin > 85umol/L, INR 1.5 or more, AST>ALT *(but AST <400)

- Maddrey discriminant factor >32 poor prognosis, 30% mortality at 28 days.

- **Treatment**

- Steroids but no benefit beyond 28 days

- Clinical trials: immuno-modulators

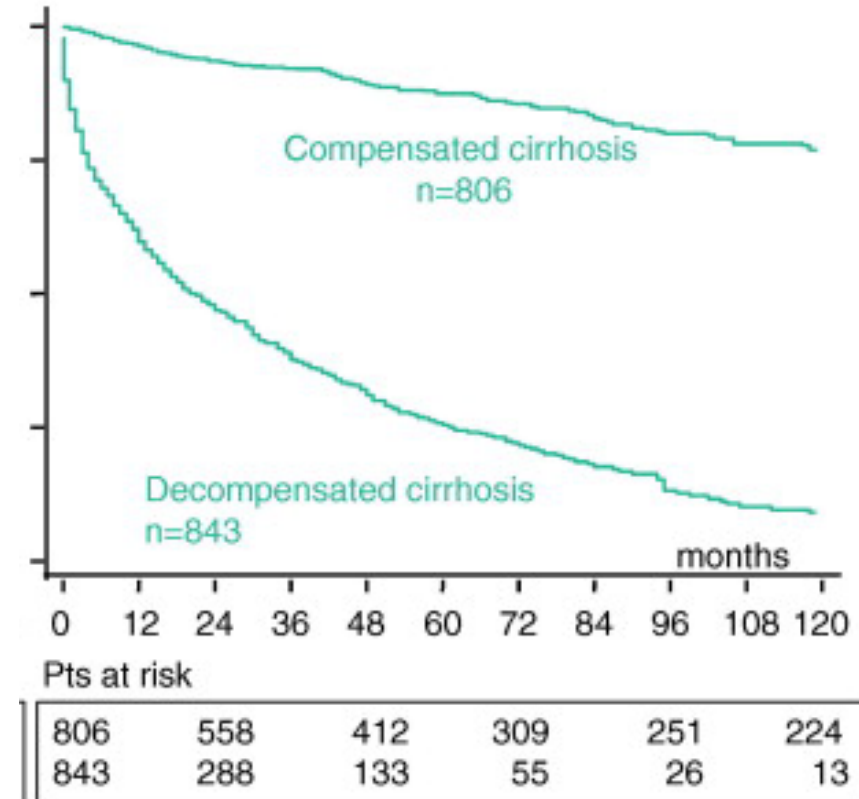
- Best clinical care

- * ***Alcohol abstinence improves long term prognosis***

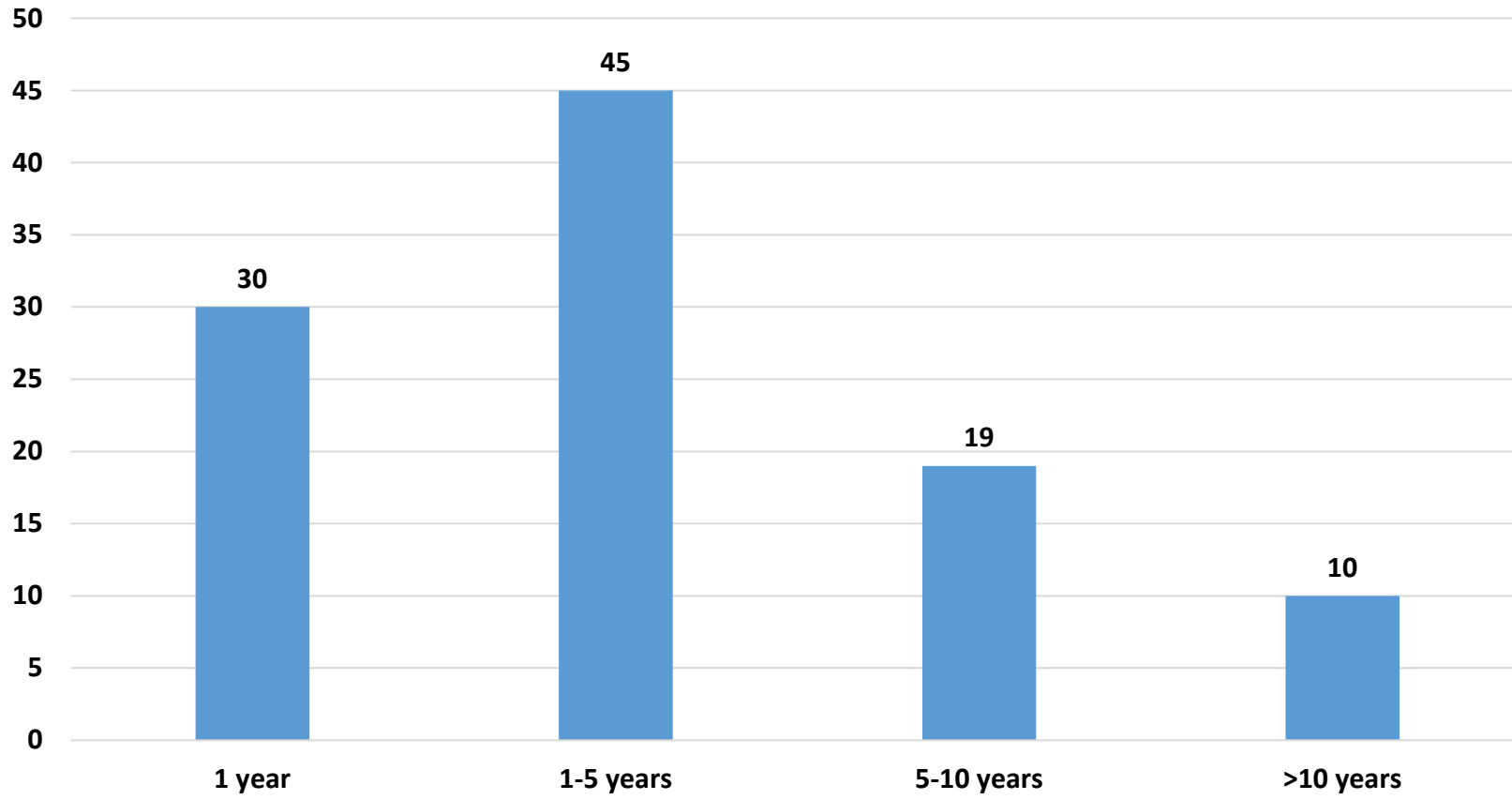
Stratification- AUDIT score

- Low risk
- Increasing risk
- **Higher risk**
- **Possible dependence**

priority



duration of abstinence



ACT



	Abstinent	Drinking	Harm reduction
ACLF grade 1 (n=7)	5	2	0
ACLF grade 2 (n=15)	6	5	4
ACLF grade 3 (n=7)	6	1	1
Decompensated ArLD (n=61)	51	6	4
recompensated (n=51) 83%			
Cirrhosis compensated (n=69)	36	18	15
mortality (n=22)	4	18	0

The overall abstinence rate is 65%

Alcohol recovery>>> Liver recovery>>> reduced Hospital readmission>>>>reduce mortality

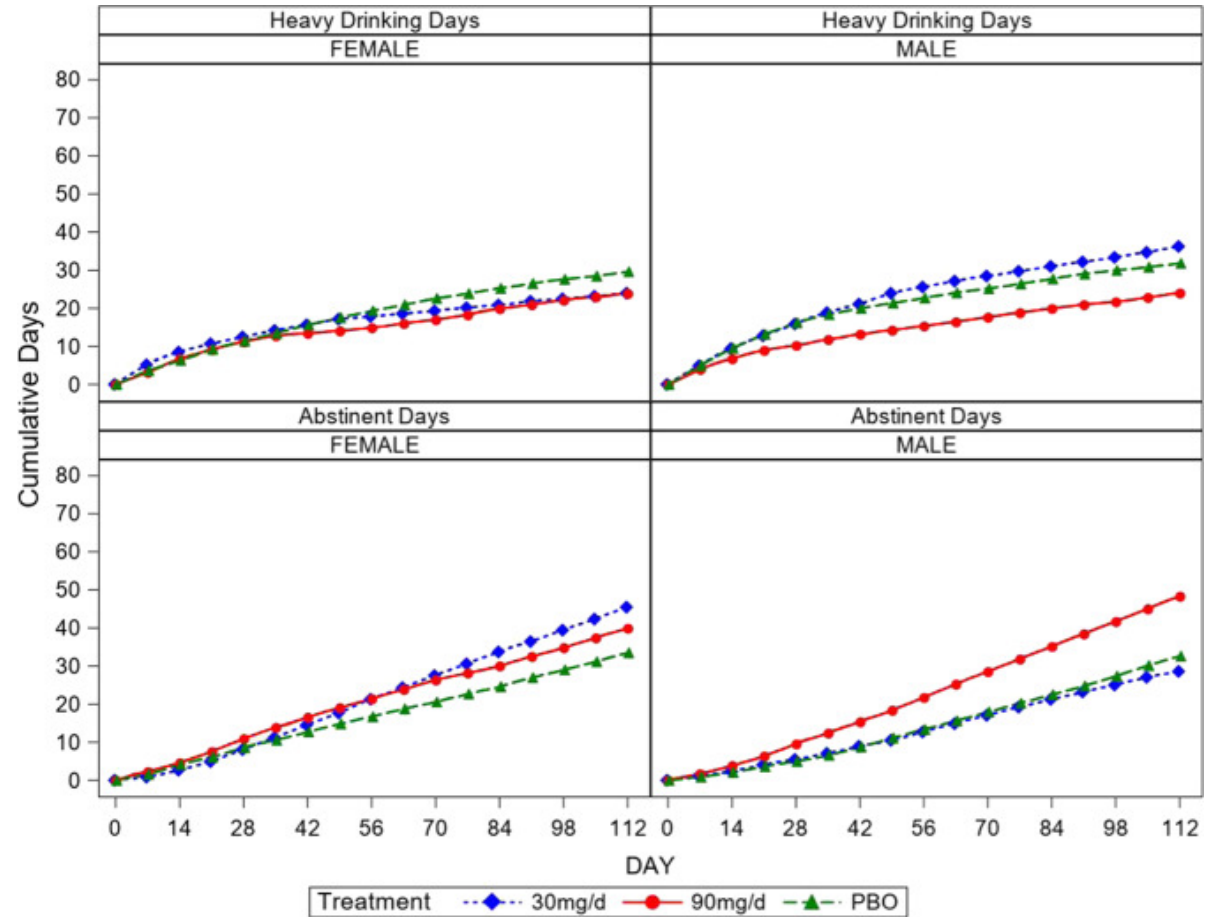
Acamprosate

- Possibly NMDA receptor agonist
- Safe in Alcohol related cirrhosis- no hepatic metabolism
- Need to monitor eGFR

Naltrexone

- a μ -opioid antagonist- moderates dopamine surges and reduces alcohol consumption
- Black box warning
- Safe in cirrhosis

Baclofen





Funding

Addictions Psychiatrist

Hepatologist

Psychologist

Social worker

Family support network

Community recovery services

Pharmacist

Residential rehabilitation

Take home messages

- Abstinence
- Abstinence
- Abstinence
- Alcohol dependence for 5 years or more- consider referral for Fibroscan/ELF.
- Fibrosis is reversible
- Complications related to portal hypertension can be stabilised following abstinence



Love your Liver!

Any Q/comments