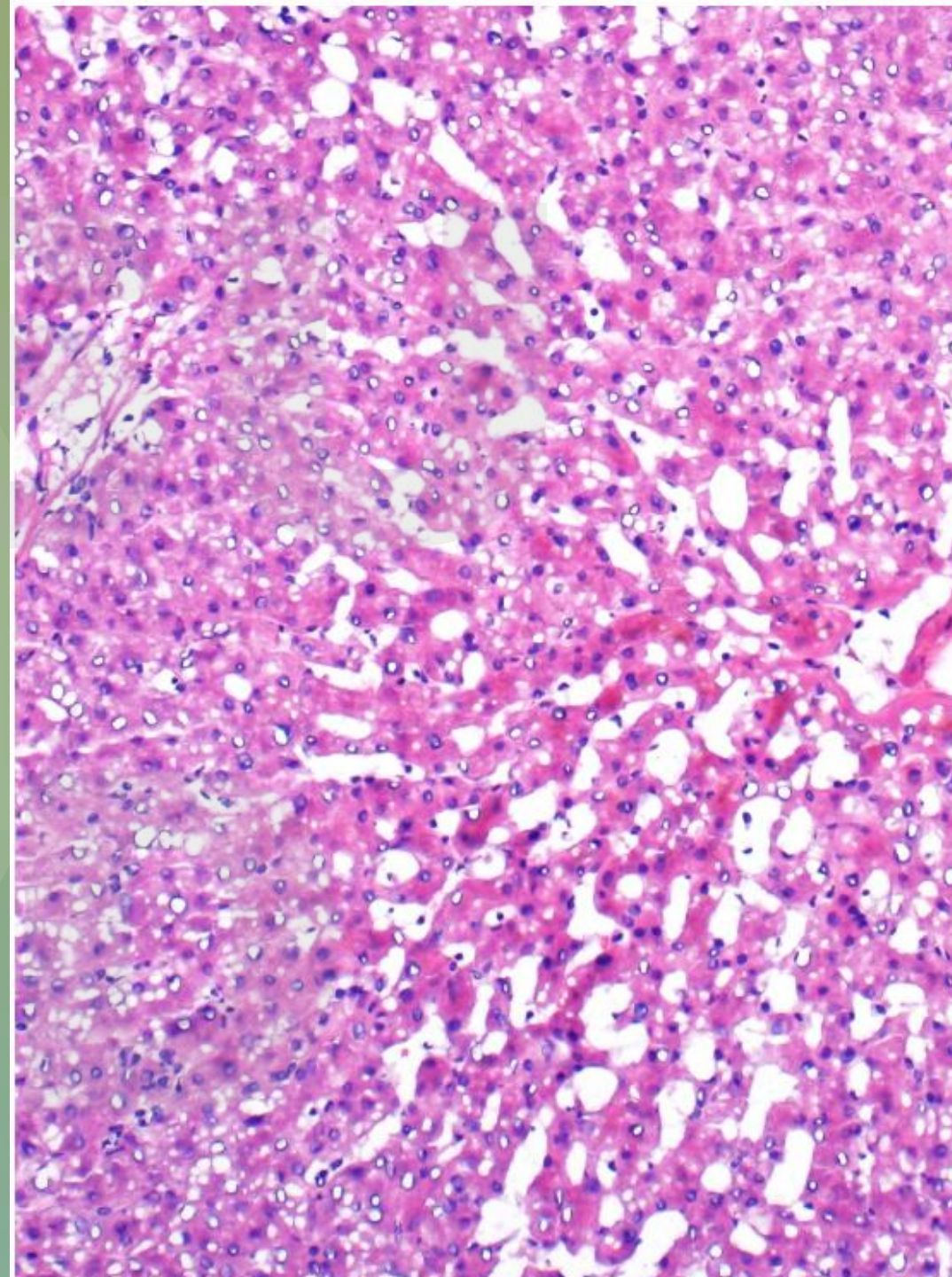


LIVER HEALTH IN PRIMARY CARE

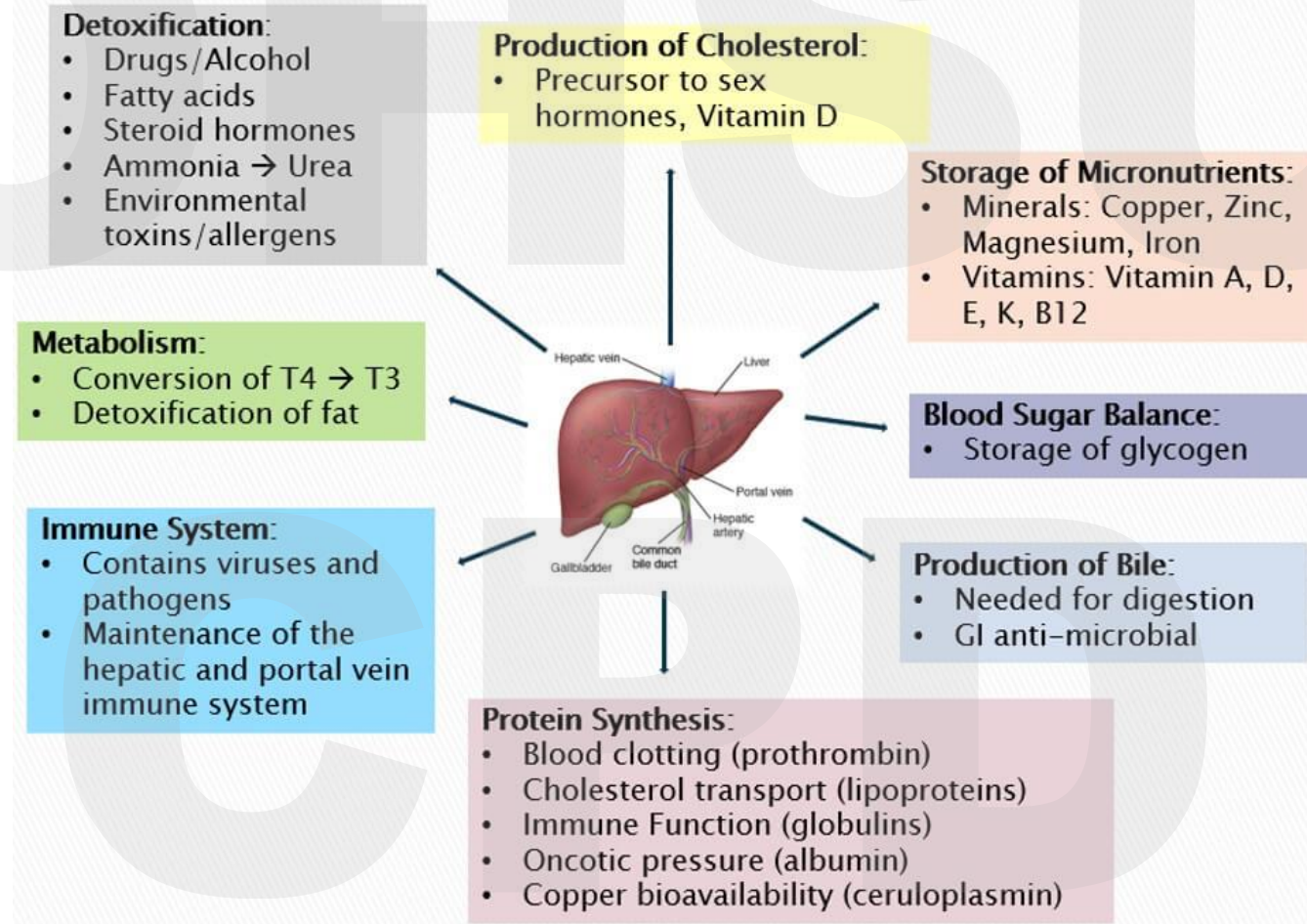
ALINE GOTTLIEB, MD PHD,
RASHA NAKHLEH, MD AGSF
OHSU HILLSBORO MEDICAL CENTER,
FEBRUARY 11TH, 2025



OUTLINE

- Why should we care about the liver in general?
- What liver diseases should be considered?
- How common are liver diseases in the primary care office?
- Is there a difference amongst different populations regarding liver health, it's incidence and outcomes?
- How can you diagnose liver diseases in the primary care setting?
- How to monitor and treat liver diseases in the primary care setting?
- When should you refer to a hepatologist?

WHY SHOULD WE CARE ABOUT THE LIVER?



WHAT LIVER DISEASES SHOULD YOU CONSIDER?

- Alcoholic liver disease (ALD)
- Drug-induced-liver-injury (DILI)
- Hep C (cirrhosis)
- **Metabolic dysfunction- associated fatty liver disease (MAFLD)**
- More rare: acute liver diseases, genetic liver diseases, AIH, PBC, PSC

HOW COMMON ARE LIVER DISEASES?

Prevalence	ALD	Alcohol-associated cirrhosis	Dili
General population	3.5%	0.3%	14-19 cases per 100.000 population
In primary care	2.6% (0.5%–11.7%)	1.7% (0.3%–10.2%)	

MAFLD:

- US prevalence 35%
- Patient with T2DM, up to 52% in US affected by MASLD
- MAFLD presents in 40% of Veterans in primary care; 9.4% had at least moderate hepatic fibrosis
- Does anyone want to take a guess what the reported percentage is of MAFLD in primary care? 2-5% for PCPs

HOW DO LIVER HEALTH, INCIDENCE, AND OUTCOMES VARY ACROSS DIFFERENT POPULATIONS

ALD:

prevalence of the full spectrum of ALD was 9.3% in Hispanic, 4.1% in White, 3.4% in Black, and 2.7% in other populations

General:

- Neighborhood-level Social Determinants Of Health are associated with mortality, incidence of LREs and incident CVD in patients with steatotic liver disease (Chen et al, Sept 2023)
- Study: Evaluating the prevalence and severity of NAFLD in Diabetes in primary care: the EPSONIP study protocol, Nasr 2021

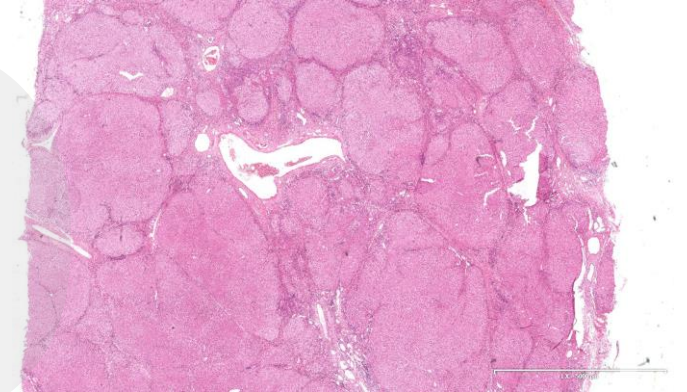
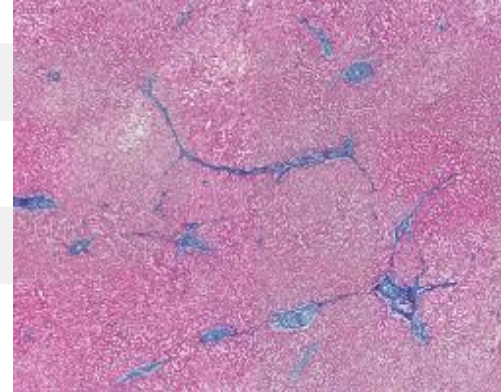
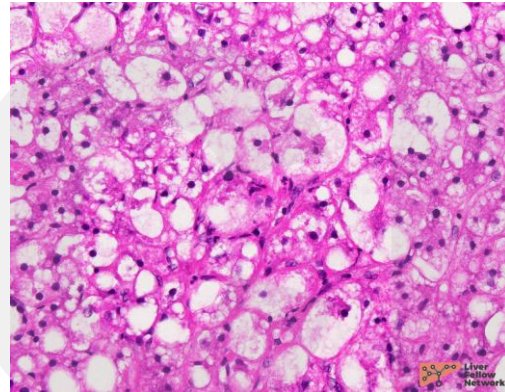
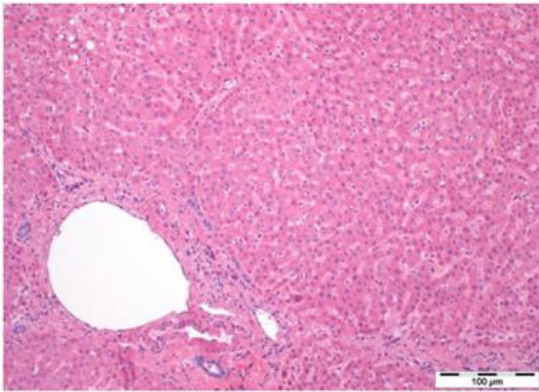
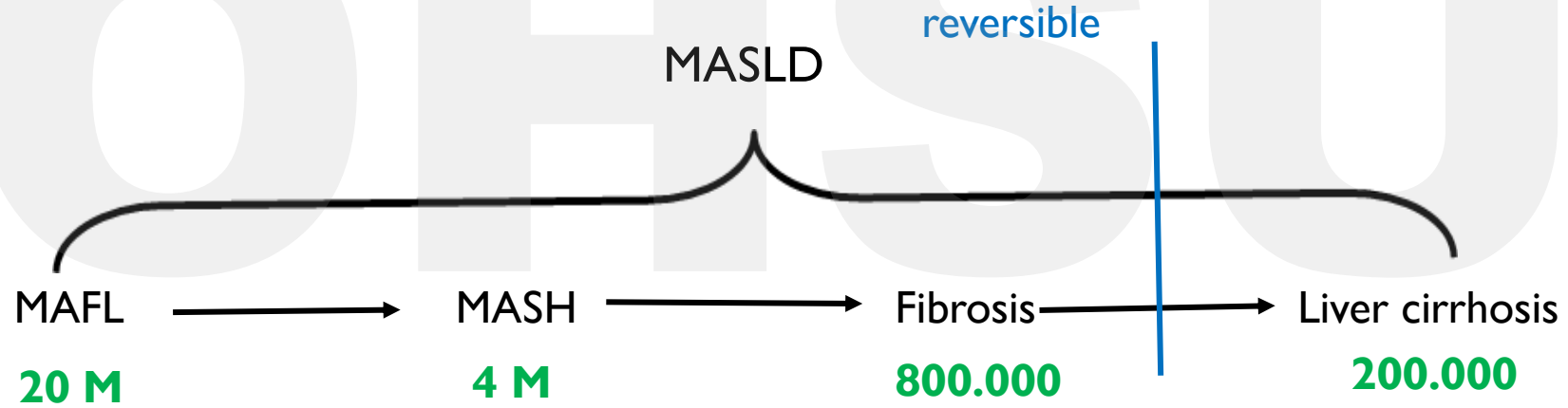
HOW DO LIVER HEALTH, INCIDENCE, AND OUTCOMES VARY ACROSS DIFFERENT POPULATIONS? - CONT'D

MASLD:

- Hispanic persons are disproportionately affected (RR 1.36 compared to white people)
- Black people had a lower risk (RR 0.68 compared to white persons)
- No difference amongst groups for fibrosis severity
- Women >50
- People experiencing food insecurity
- Data were limited and discordant on racial or ethnic disparities in outcomes of patients

LIVER DISEASE SPECTRUM

Germany
82 M



AN EXAMPLE : HERBERT



Symptoms before diagnosis

- Abdominal pain and bloating
- Decreased strength
- Fatigue
- Malaise
- Weight gain

Other symptoms

- Impaired memory
- Poor sleep quality
- Reduced focus

Patients with symptoms (versus those without) experienced worse overall and liver-related HRQoL and a higher work impairment



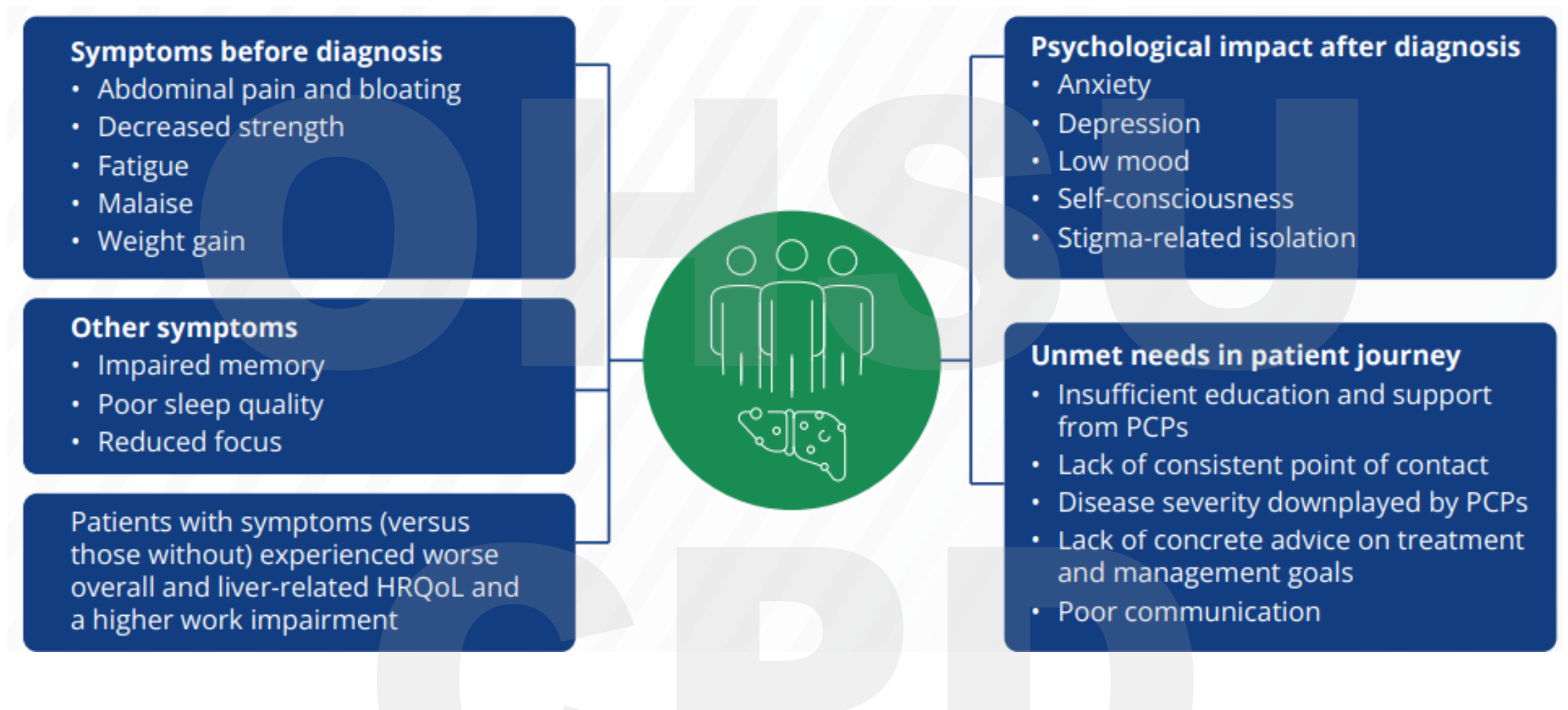
SYMPTOMS OF MAFLD

Metabolic Dysfunction-Associated
Steatotic Liver Disease

Clark, J. M., Cryer, D. R. H., Morton, M., & Shubrook, J. H. (2023).

PATIENT'S PERCEPTION

Emerging pattern	Patient quotes
Embarrassment at NASH diagnosis	'I felt embarrassed because I had an unhealthy lifestyle—I put on a lot of weight.' (UK patient)
	'I felt embarrassed that this happened to me because I felt it is my fault.' (US patient)
Perceived lack of physician support	'I was concerned of course and confused as to why my doctor wasn't doing more.' (US patient, fibrosis stage F1)
	'I felt let down that they expect you to go away and be OK with no information as they say fatty liver is common.' (UK patient)
	'Someone sitting me down and talking me through what I should and shouldn't do, like caring support to give me hope, that's all I want.' (UK patient)
	'Doctors should not wait until the condition gets to stage 3 to start taking it seriously.' (US patient)
Need for more education on NASH	'I really think I'm missing medical support. No one has really explained my prognosis or any treatment options. I am kind of in the dark.' (US patient)
	'Better education would be good, guidance to eating habits and foods to help improve or reduce the issue. I have been taking the pills long enough now not to need reminding. I think mainly support from GP or specialist.' (UK patient)
	'A NASH information pack would be nice, also with plenty of information about the drug and how it works.' (UK patient)
	'Detailed information about NASH, how to care for your liver, dietary info, supplement info, who to contact if you need support. I would like a physical copy, but also an online format.' (UK patient)
	'What is missing is a(n) educational course designed for those with NASH because I have had to do a lot of research on my own to seek and gather knowledge about NASH. I would like a(n) educational DVD designed for people dealing with NASH.' (US patient)



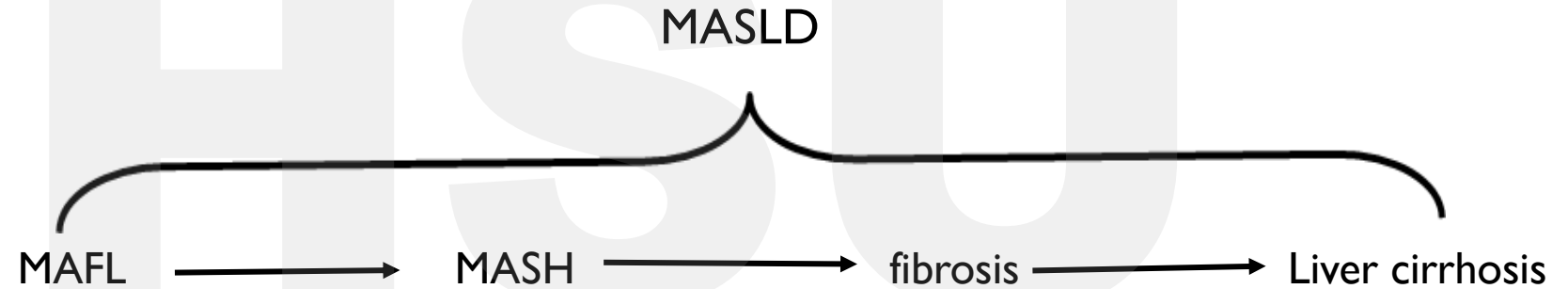
SYMPTOMS OF MAFLD CONT'D

DIAGNOSING LIVER DISEASE

- Ask. Consider. Investigate
- labs:
 - Liver injury: ALT, AST, ALP
 - Liver function: INR, Bilirubin, Albumin, Platelets
 - Hepatitis C antibody, hepatitis B core and surface antigen, alpha-1 antitrypsin, and ferritin +/- transferrin saturation
 - GGT
- imaging: US Abdomen, transient elastography

ALT > 25 (female)
and > 33 (male) is
associated with
higher liver morbidity

WHAT MAKES THE SITUATION SO CHALLENGING?



- underutilized cost effective screening
- no option to determine who is at risk to develop a liver cirrhosis or HCC
- most people with MASLD die because of complications of diabetes or CVD

HCC

DIAGNOSING LIVER DISEASE

CTN'D

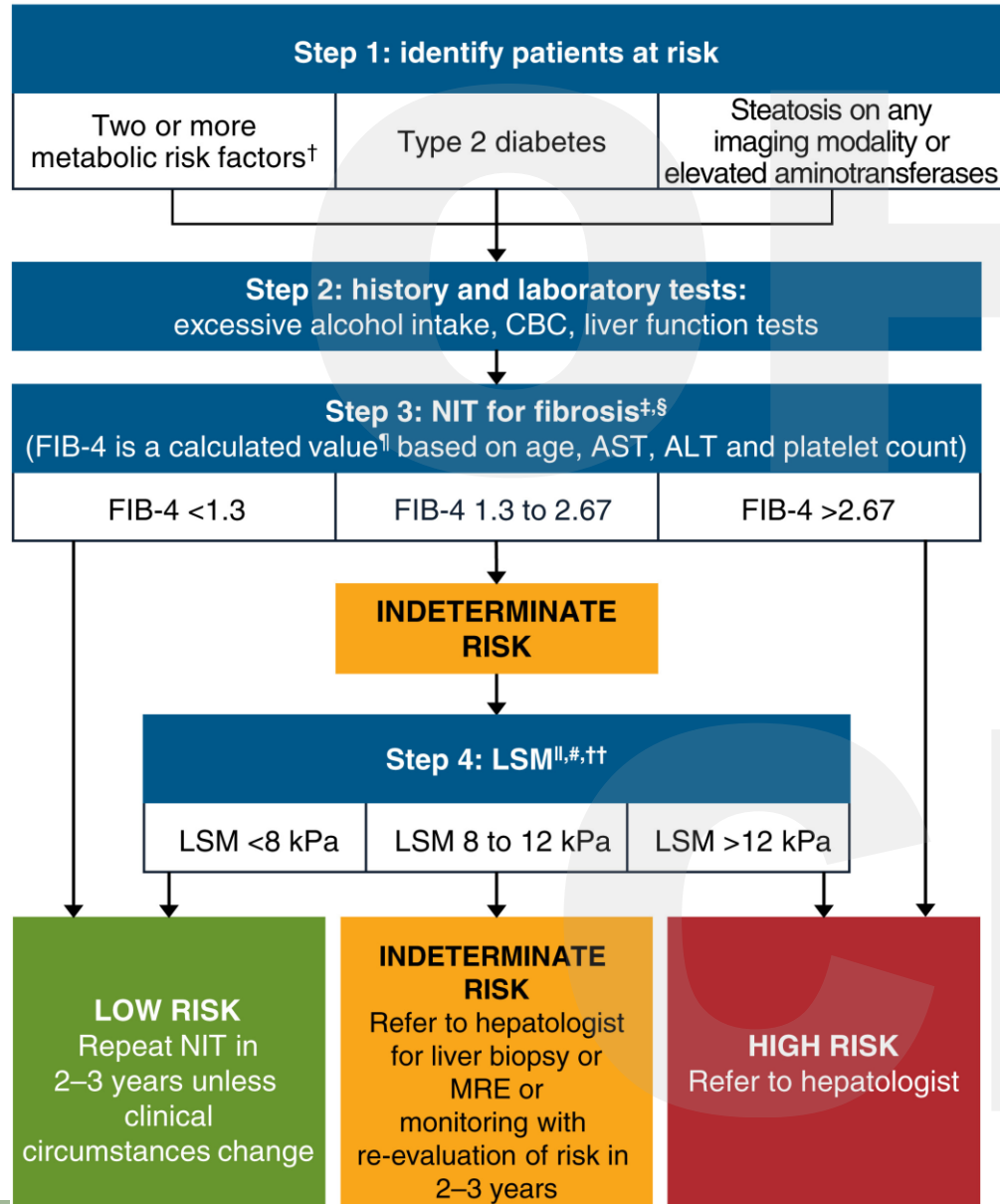
Unclear liver enzyme
elevation

R value: $(\text{ALT}/\text{ULN ALT}) / (\text{ALP}/\text{ULN ALP})$
>5: hepatocellular
2-5: mixed
<2 cholestatic

MAFLD

Fib4	NFS (NAFLD Fibrosis Score)
Age	Age
AST/ALT	AST/ALT
Platelet	Platelet
	Diabetes y/n
	Albumin
	BMI

Primary care, endocrinologists, gastroenterologists and obesity specialists should screen for NAFLD with advanced fibrosis



RISK STRATIFICATION

71% of primary care patients had a non-invasive fibrosis score (Fibrosis-4 Index [FIB-4] and NAFLD Fibrosis Score) in the indeterminate-risk or high-risk category for advanced fibrosis*

*Identifying Patients at Risk for Fibrosis in a Primary Care NAFLD Cohort, Andrew D Schreiner, , J Clin Gastroenterol. 2023 Jan

STAGING - CIRRHOSIS

2 Minute Medicine® Child-Pugh Score 2minutemedicine.com			
Factor	1 point	2 points	3 points
Total bilirubin (μmol/L)	<34	34-50	>50
Serum albumin (g/L)	>35	28-35	<28
PT INR	<1.7	1.71-2.30	>2.30
Ascites	None	Mild	Moderate to Severe
Hepatic encephalopathy	None	Grade I-II (or suppressed with medication)	Grade III-IV (or refractory)
	Class A	Class B	Class C
Total points	5-6	7-9	10-15
1-year survival	100%	80%	45%

Table I. Child-Pugh score.

TREATMENT

ALD

Treat AUD

MAFLD

- 10% weight loss
- Meds: GLP-1 Agonists , SGLT2, Tirzepatide
- (bariatric surgery and liver transplantation)

Dili

- Stop agent
- Check livertox.nih.gov

Cirrhosis: Treat complications of cirrhosis + US q6 months for HCC surveillance

TREATMENT OF MAFLD

- MASH and fibrosis are associated with 3 major outcomes:

1) cardiovascular disease mortality

2) liver-related morbidity and mortality

3) malignancy (HCC and others)

Statins are safe in chronic liver disease

	LOW RISK FIB-4 < 1.3 or LSM < 8 kPa or liver biopsy F0-F1	INDETERMINATE RISK FIB-4 1.3-2.67 and/or LSM 8-12 kPa and liver biopsy not available	HIGH RISK [†] FIB-4 > 2.67 or LSM > 12 kPa or liver biopsy F2-F4
	Management by PCP, dietitian, endocrinologist, cardiologist, others	Management by hepatologist with multidisciplinary team (PCP, dietitian, endocrinologist, cardiologist, others)	
Lifestyle intervention [‡]	Yes	Yes	Yes
Weight loss recommended if overweight or obese [§]	Yes May benefit from structured weight loss programmes, antiobesity medications, bariatric surgery	Yes Greater need for structured weight loss programmes, antiobesity medications, bariatric surgery	Yes Strong need for structured weight loss programmes, antiobesity medications, bariatric surgery
Pharmacotherapy for NASH	Not recommended	Yes ^{¶,}	Yes ^{¶,}
CVD risk reduction [#]	Yes	Yes	Yes
Diabetes care	Standard of care	Prefer medications with efficacy in NASH (pioglitazone, GLP-1RA)	Prefer medications with efficacy in NASH (pioglitazone, GLP-1RA)

WHEN TO REFER TO A HEPATOLOGIST

Most patients with MAFLD DO NOT REQUIRE A REFERRAL

- people with decompensated liver disease
- clinically significant portal hypertension
- advanced fibrosis
- severe alcohol-associated hepatitis
- patients with unclear diagnosis or those with other risk factors for liver disease
- Patients who have progressive liver disease that might require liver transplantation evaluation

TAKE - AWAYS

- Frequency: it is common, underdiagnosed
- Diagnosis/ workup: Liver enzymes, risk profile
- Patient perspective: might struggle with shame/ self-worth after diagnosis of MAFLD
- Triaging: using NFS or Fib4 to identify at-risk patients
- Treatment:
 - Mild disease can be treated by PCP
 - Focus on treatment of CVD and diabetes
 - Statins are safe in chronic liver diseases

RESULTS WITH LIFESTYLE CHANGES ALONE



SOURCES

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- 2) Clin Gastroenterol Hepatol . 2023 May;21(5):1252-1260.e5. doi: 10.1016/j.cgh.2022.05.046. Epub 2022 Jul 8. The Prevalence and Determinants of NAFLD and MAFLD and Their Severity in the VA Primary Care Setting Aaron P Thrift
- 3) Nonalcoholic fatty liver disease from a primary care perspective Jeanne M. Clark MD, Donna R. H. Cryer JD, Michelle Morton MSN, Jay H. Shubrook DO First published: 15 February 2023
- 4) Effects of social determinants of health on mortality and incident liver-related events and cardiovascular disease in steatotic liver diseasem Chen at al, Sept 2023,
- 5) Racial and Ethnic Disparities in Non-alcoholic Fatty Liver Disease Prevalence, Severity, and Outcomes in the United States: A Systematic Review and Meta-analysis Rich et al, 2018, Clin Gastroenterol Hepatol.
- 6) The Curbsiders Podcast, episodes #73, #227, #452
- 7) Management of NAFLD in primary care setting. Vincent W.S. Wong, 20 August 2022, Liver international
- 8) Prevalence of steatotic liver disease, MASLD, MetALD and significant fibrosis in people with HIV in the United States, Samer Gawrieh, Dec 2023
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**THANK YOU FOR YOUR
ATTENTION**

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