# LIVER HEALTH IN PRIMARY CARE

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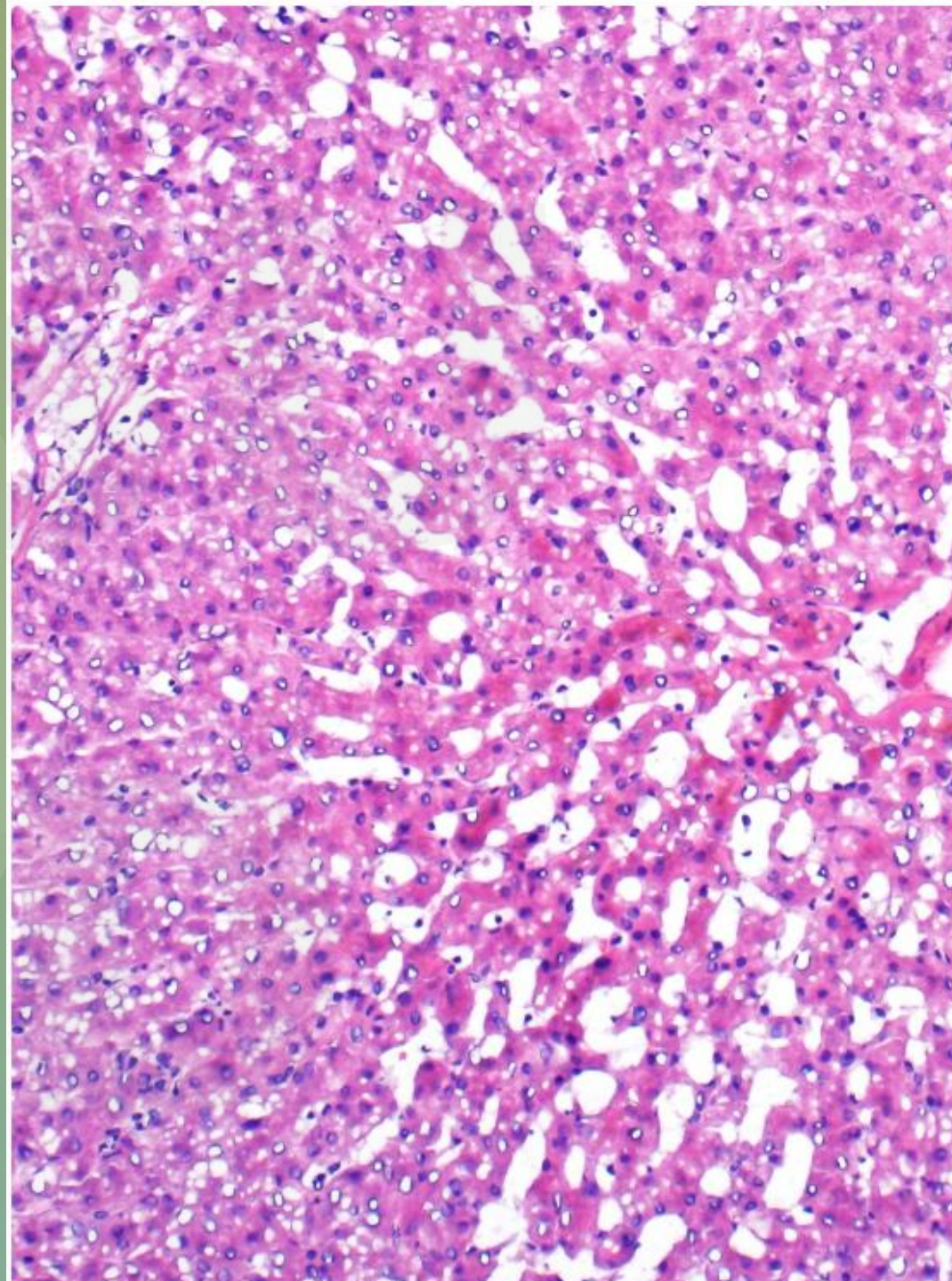


# OUTLINE

- 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?

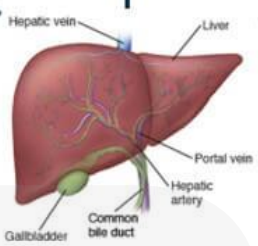
# WHY SHOULD WE CARE ABOUT THE LIVER?

**Detoxification**:
- Drugs/Alcohol
- Fatty acids
- Steroid hormones
- Ammonia → Urea
- Environmental toxins/allergens

**Production of Cholesterol**:
- Precursor to sex hormones, Vitamin D

**Storage of Micronutrients**:
- Minerals: Copper, Zinc, Magnesium, Iron
- Vitamins: Vitamin A, D, E, K, B12

**Metabolism**:
- Conversion of T4 → T3
- Detoxification of fat




**Blood Sugar Balance**:
- Storage of glycogen

**Immune System**:
- Contains viruses and pathogens
- Maintenance of the hepatic and portal vein immune system

**Production of Bile**:
- Needed for digestion
- GI anti-microbial

**Protein Synthesis**:
- Blood clotting (prothrombin)
- Cholesterol transport (lipoproteins)
- Immune Function (globulins)
- Oncotic pressure (albumin)
- Copper bioavailability (ceruloplasmin)

# 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


1) Prevalence of alcohol-associated liver disease: a systematic review and meta-analysis, Hepatol Commun. 2023 May; 7(5): e0133. 2023 Apr
2) The Prevalence and Determinants of NAFLD and MAFLD and Their Severity in the VA Primary Care Setting Aaron P Thrift, Clin Gastroenterol Hepatol . 2023 May;
3) Nonalcoholic fatty liver disease from a primary care perspective Jeanne M. Clark MD, First published: 15 February 2023
4) Loomba R, et al. Nonalcoholic fatty liver disease progression rates to cirrhosis and progression of cirrhosis to decompensation and mortality: a real world analysis of Medicare data. Aliment Pharmacol Ther. 2020;

# AN EXAMPLE : HERBERT

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

ALD:

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

General:

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

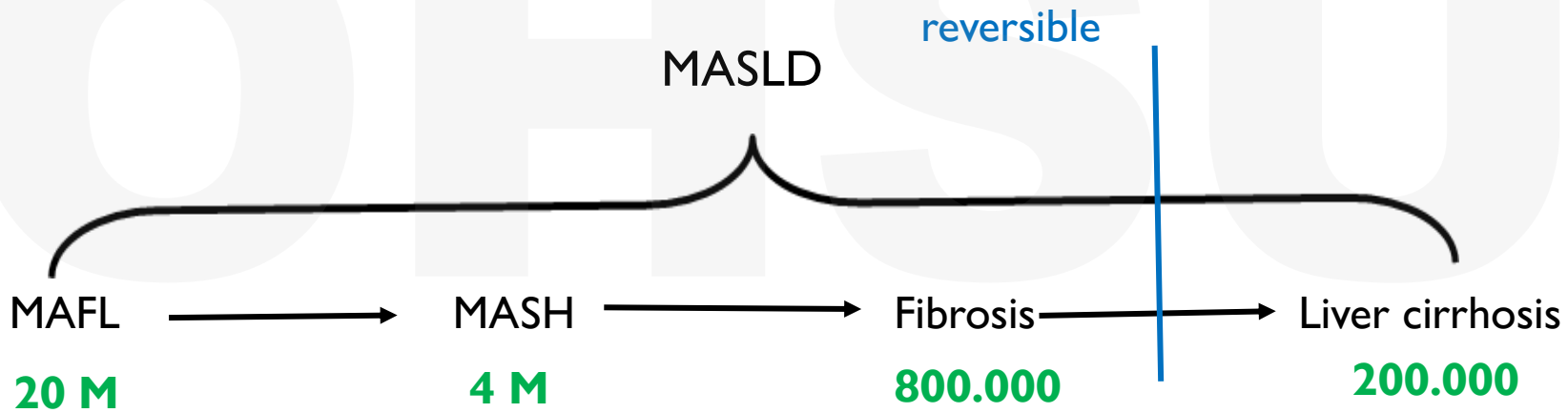
# HOW DO LIVER HEALTH, INCIDENCE, AND OUTCOMES VARY ACROSS DIFFERENT POPULATIONS?- CONT'D

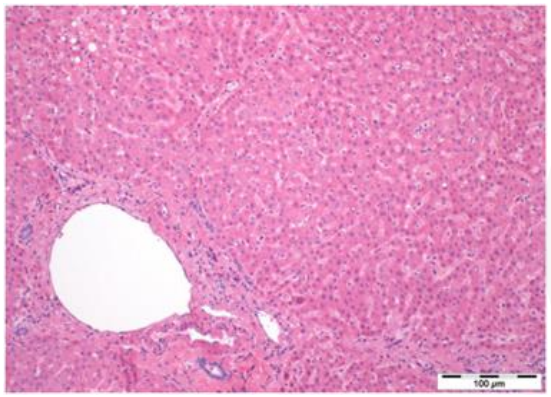
MASLD:

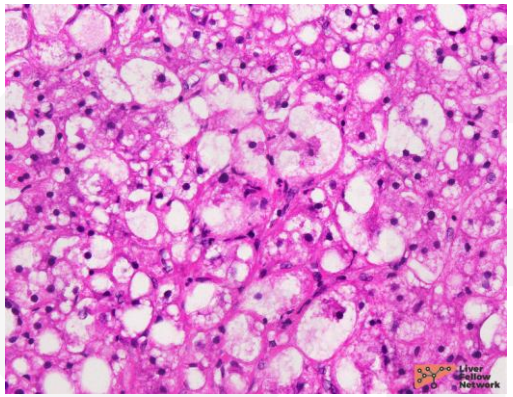
- Hispanic persons are disproportionately affected (RR 1.36 compared to white people)
- Black people had a lower risk (RR 0.68 compared to white persons)
- No difference amongst groups for fibrosis severity
- Women >50
- People experiencing food insecurity
- Data were limited and discordant on racial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

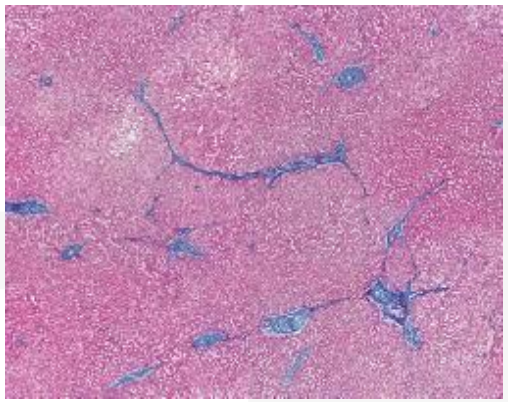
# LIVER DISEASE SPECTRUM

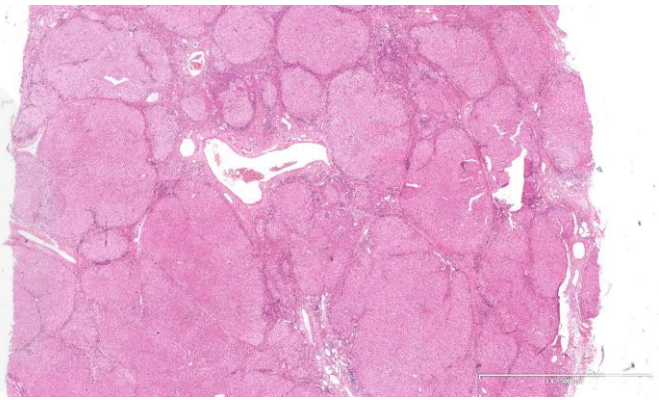
**Germany**
**82 M**









**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) |
| | '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) |
| Need for more education on NASH | '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) |

Nonalcoholic fatty liver disease from a primary care perspective, Jeanne M. Clark MD, Feb 2023

**Symptoms before diagnosis**
- Abdominal pain and bloating
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**Psychological impact after diagnosis**
- Anxiety
- Depression
- Low mood
- Self-consciousness
- Stigma-related isolation

**Unmet needs in patient journey**
- Insufficient education and support from PCPs
- Lack of consistent point of contact
- Disease severity downplayed by PCPs
- Lack of concrete advice on treatment and management goals
- Poor communication

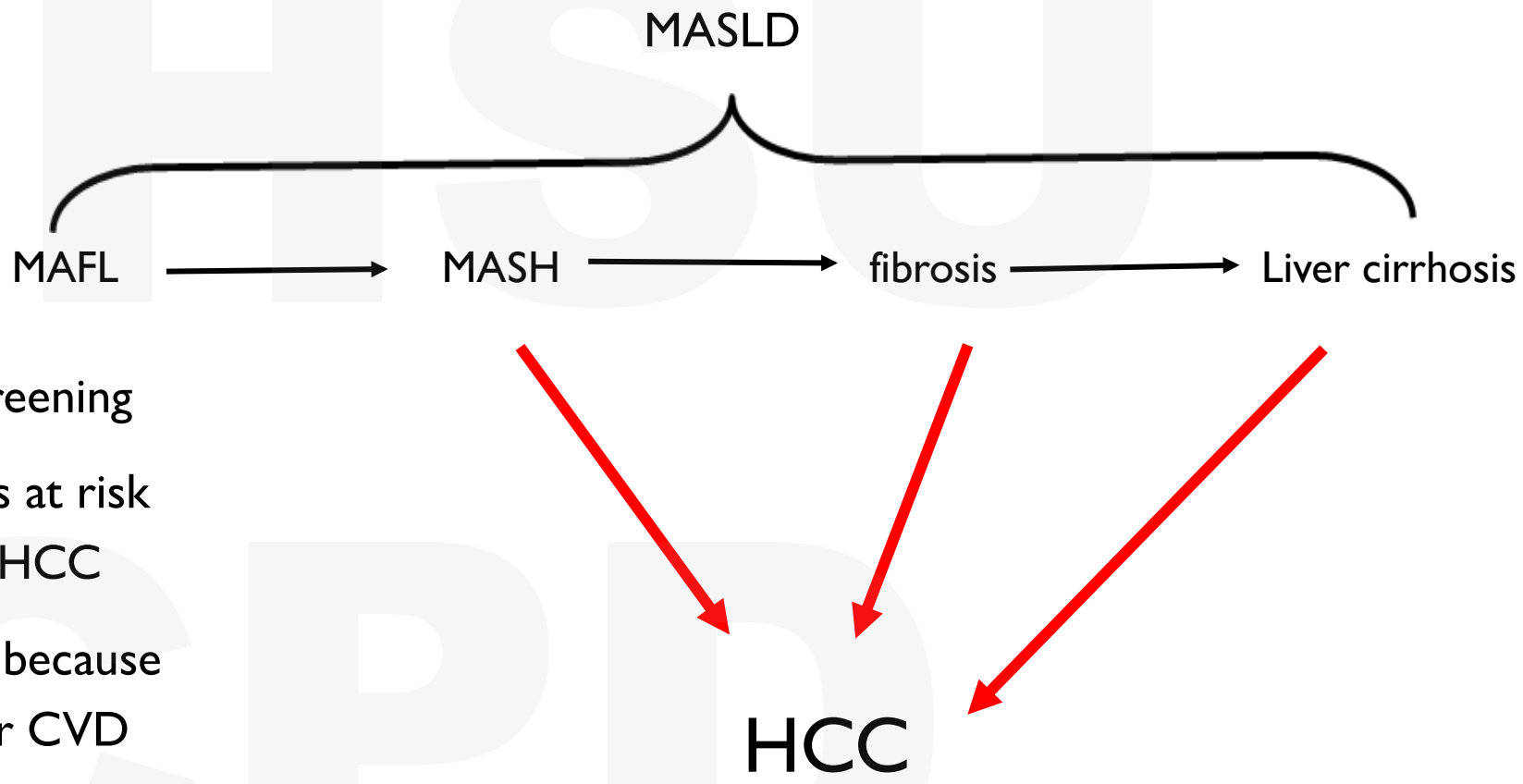
# SYMPTOMS OF MAFLD CONT'D

Metabolic Dysfunction-Associated Steatotic Liver Disease
Clark, J. M., Cryer, D. R. H., Morton, M., & Shubrook, J. H. (2023).

# 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

# 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

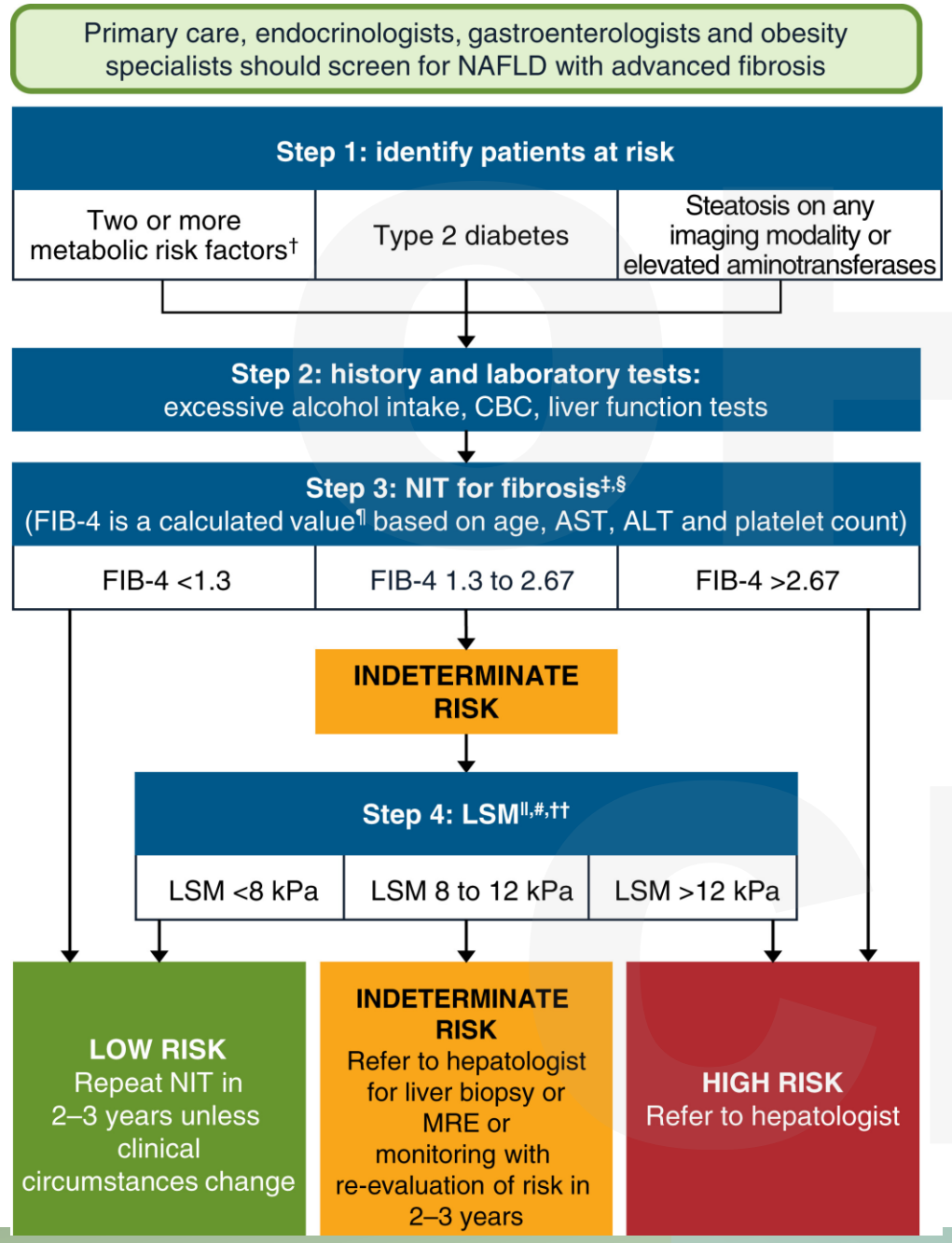
# DIAGNOSING LIVER DISEASE CTN'D

Unclear liver enzyme elevation

R value: (ALT/ULN ALT)/ (ALP/ULN ALP)
>5: hepatocellular
2-5: mixed
<2 cholestatic

MAFLD

| Fib4 | NFS |
|---|---|
| Age | Age |
| AST/ALT | AST/ALT |
| Platelet | Platelet |
| | Diabetes y/n |
| | Albumin |
| | BMI |




# 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<br>May benefit from structured weight loss programmes, antiobesity medications, bariatric surgery | Yes<br>Greater need for structured weight loss programmes, antiobesity medications, bariatric surgery | Yes<br>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) |

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

# 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: 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


1) Prevalence of alcohol-associated liver disease: a systematic review and meta-analysis, Hepatol Commun. 2023 May; 7(5): e0133. 2023 Apr
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,
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11) Health disparities in chronic liver disease Ani Kardashian,Hepatology. 2023 Apr

# THANK YOU FOR YOUR ATTENTION

OHSU

CPD