



Boston University Chobanian & Avedisian School of Medicine
Barry M. Manuel Center for Continuing Education



In Conversation with the Neighborhood Hepatologist: Practical Strategies for Improving Diagnosis & Risk Stratification of MASLD

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Faculty and Disclosures



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Dr. Mohanty has received grant research support from Gilead and Inventiva and has been a consultant for Novo Nordisk. She is also an investigator for Intercept, Inventiva, Novo Nordisk, Madrigal and Takeda.



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Dr. McDougal, planning committee member and speaker, has no relevant financial relationships to disclose.

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The AAFP has reviewed In Conversation with the Neighborhood Hepatologist: Practical Strategies for Improving Recognition and Risk Stratification of Metabolic Dysfunction Associated Steatotic Liver Disease (MASLD) and deemed it acceptable for up to 1.00 Live AAFP Prescribed credit(s). Term of Approval is from 06/25/2024 to 06/25/2024. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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What's in a name?

OLD

NonAlcoholic Fatty Liver Disease
(NAFLD)

NonAlcoholic SteatoHepatitis
(NASH)

NEW

Metabolic dysfunction-Associated Steatotic Liver Disease (MASLD)

Metabolic dysfunction-Associated SteatoHepatitis (MASH)



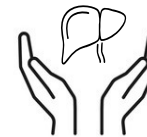
GOAL



Reduce
stigma



Reflects
disease etiology



Increases disease
awareness



Allows for
overlapping etiologies

Purpose and Scope

A MASLD/MASH primer for the busy clinician

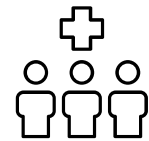


Understanding MASLD/ MASH

- Disease burden
- Patient perspectives



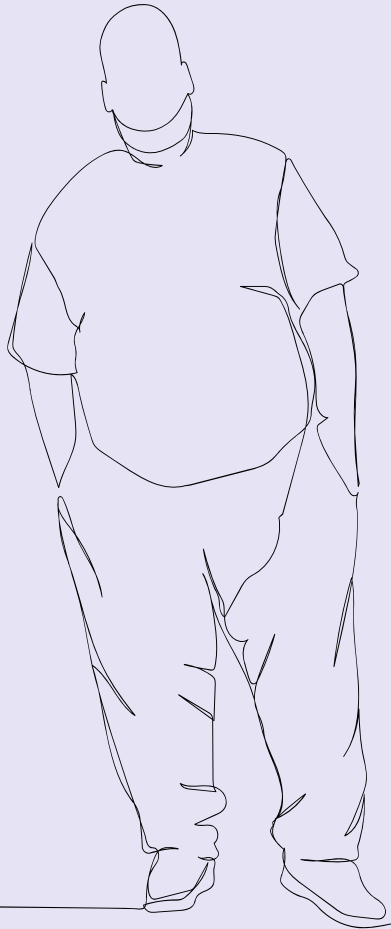
Diagnosis and risk stratification of MASLD/MASH



Management of patients with MASLD/ MASH in 2024

Provide contemporary insights into MASLD and tips to implement evidence – based guidance into your practice.

Clinical case: Carlos



30-year-old
Security guard
Recently had a cholecystectomy
Imaging had shown “echogenic liver”



Social alcohol use: enjoys drinks with friends on weekends



BMI 34 kg/m²

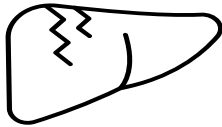


Prediabetes; HbA1C is 6.4%
Triglycerides are 200 mg/dL; HDL is 36 mg/dL
ALT is 65 U/L; AST is 70 U/L; Platelet count is 200 X 10⁹/L

Understanding MASLD/ MASH

Defining MASLD & MASH

MASLD



Presence of hepatic
steatosis



≥ 1
Cardiometabolic
criteria

International Diabetes Federation



Hypertension



Type 2 Diabetes Mellitus



Obesity



High triglycerides

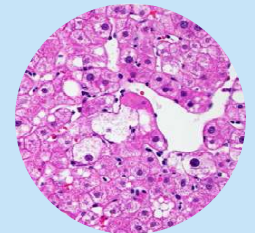
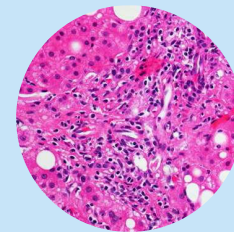


Low HDL

MASH

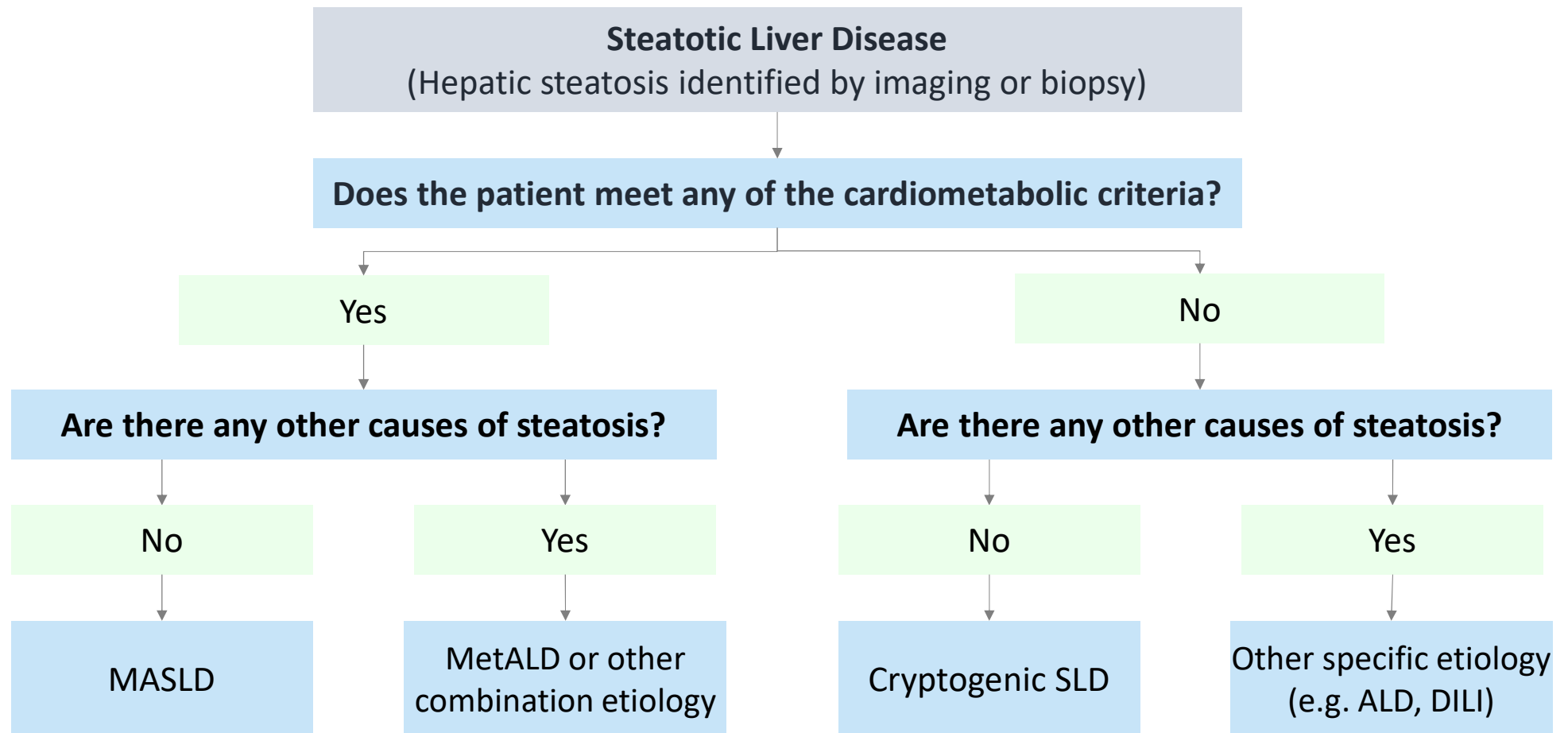


MASLD



Inflammation

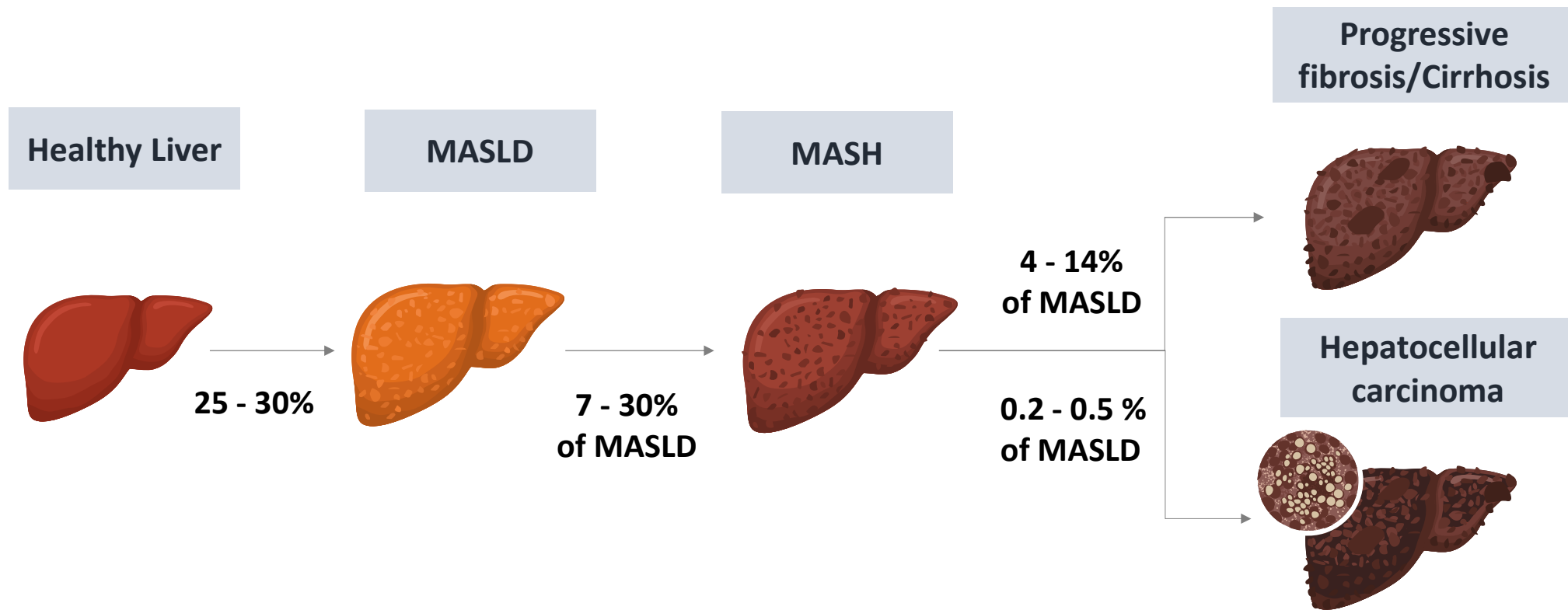
Clinical diagnostic algorithm



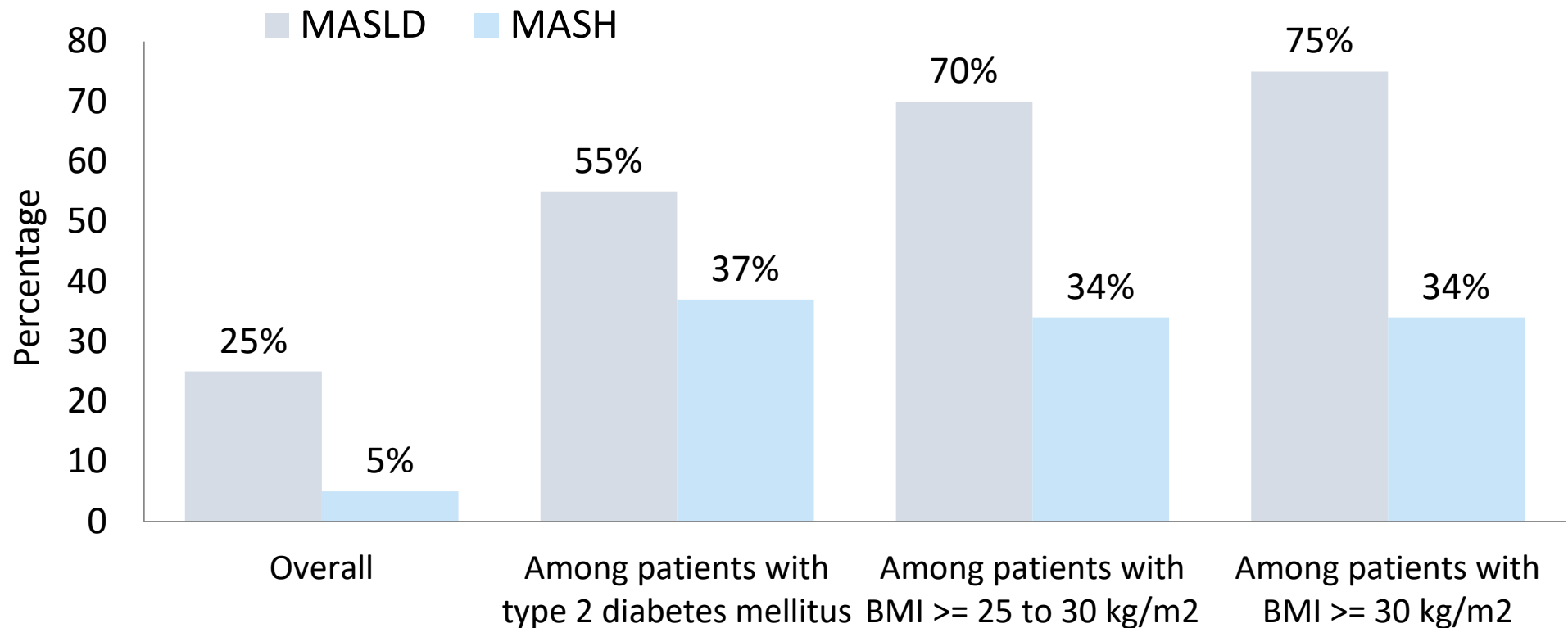
Carlos: His Diagnosis Story



Natural history of MASH



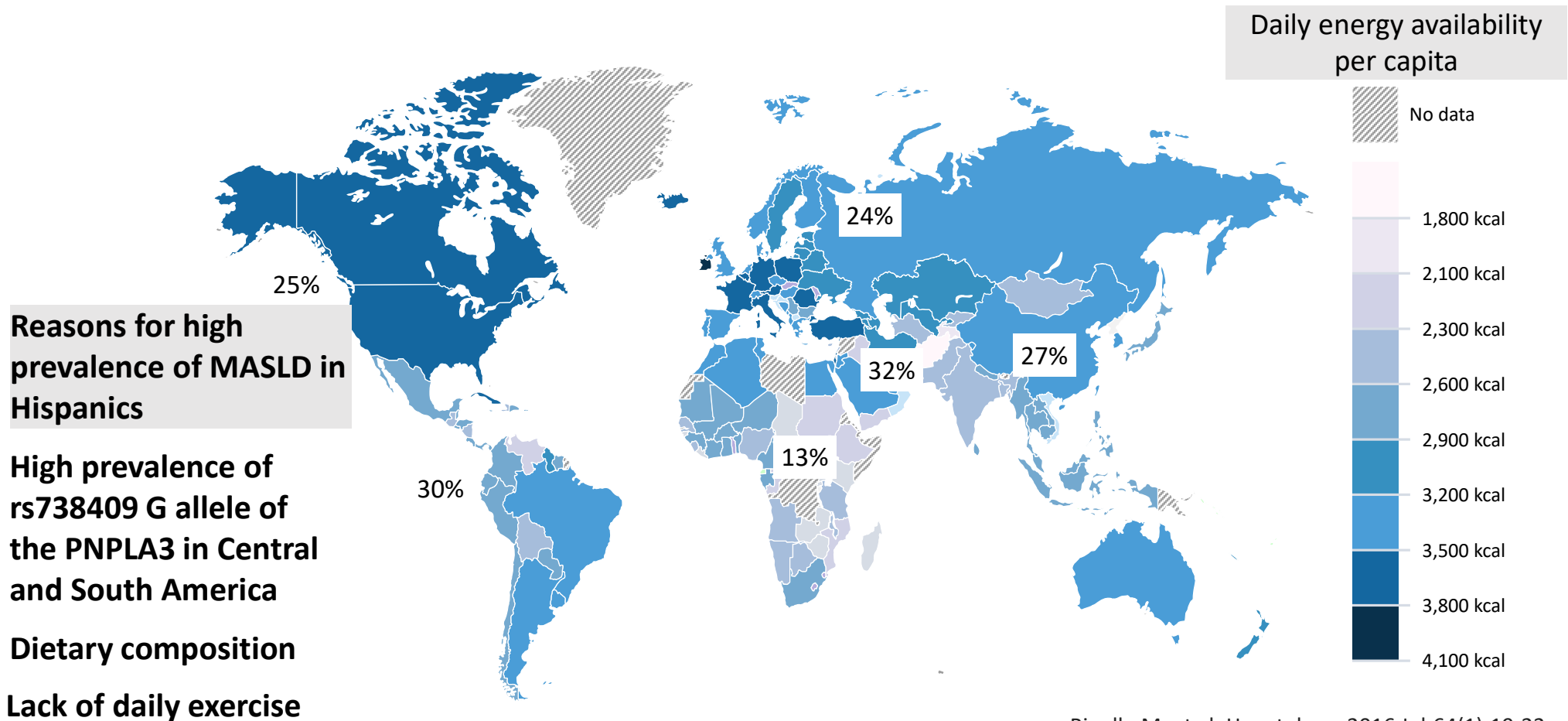
Global prevalence of MASLD and MASH



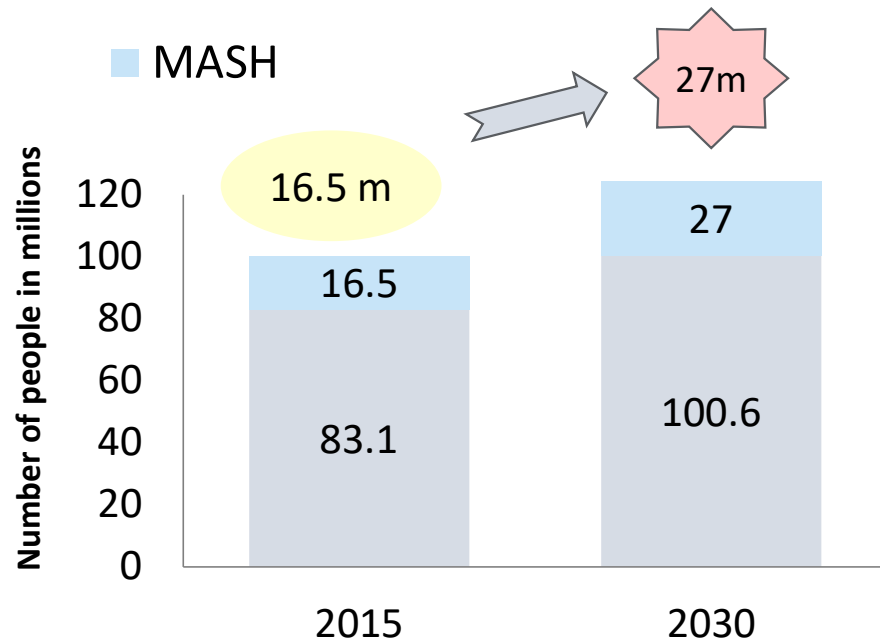
Younossi ZM et al. J Hepatol. 2019 Oct;71(4):793-801.

Quek J et al. Lancet Gastroenterol Hepatol. 2023 Jan;8(1):20-30.

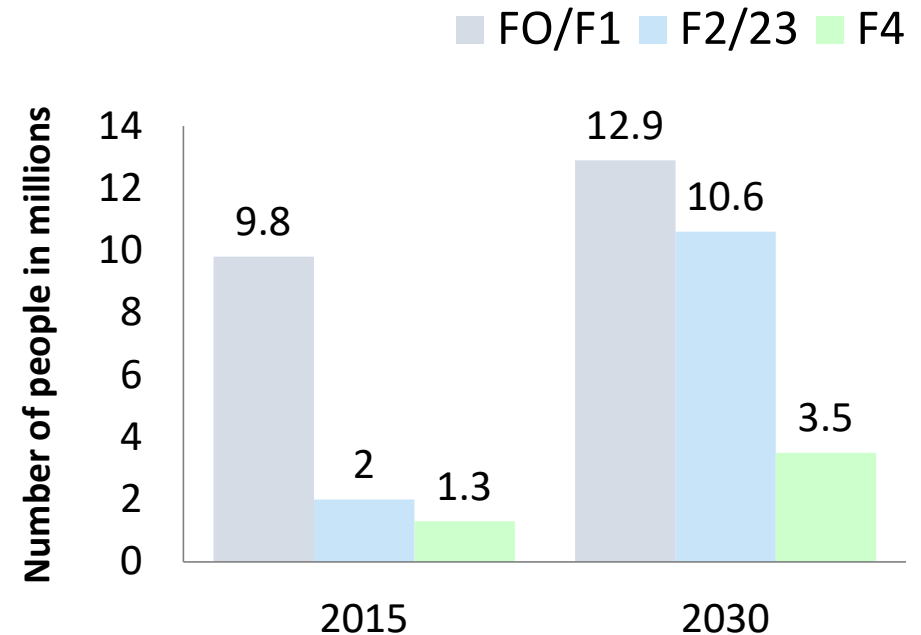
There is substantial geographic variation in the prevalence of MASLD



MASH is an epidemic on a relentless rise



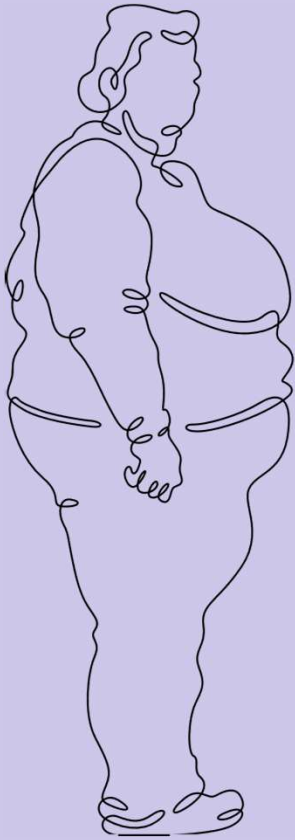
By 2030, 27% of all persons with MASLD are expected to have MASH = 27 millions Americans



By 2030, 50% with MASH are expected to have advanced fibrosis or cirrhosis

As primary clinicians, we will be seeing more advanced MASH in our clinic.

A person with MASH, has several co-morbidities



82% have obesity



72 % have dyslipidemia



68% have hypertension

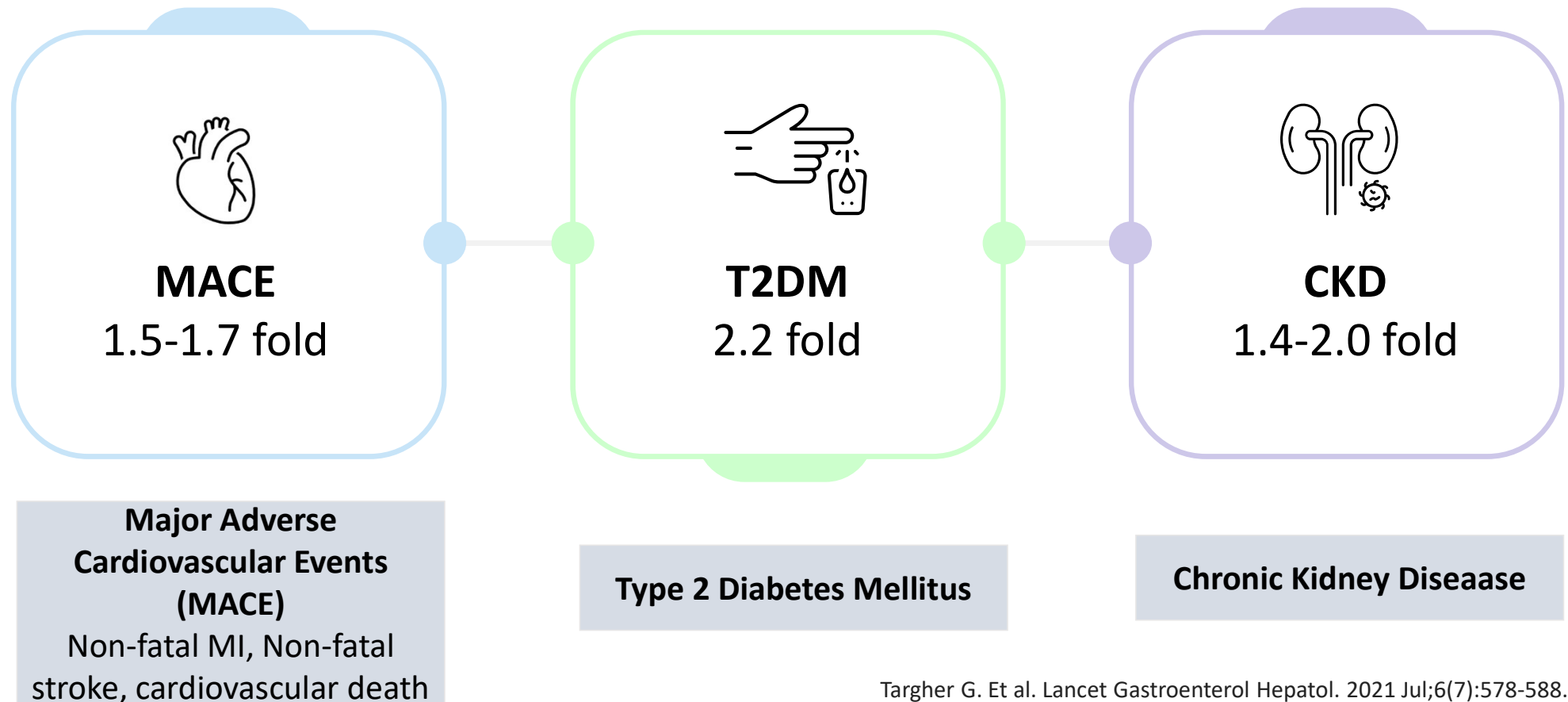


44 % have type 2 diabetes mellitus

Most patients are asymptomatic
They may not have an elevated ALT

A high index of suspicion needs to be
maintained while evaluating these patients

MASLD is associated with increased risk of incident comorbid conditions

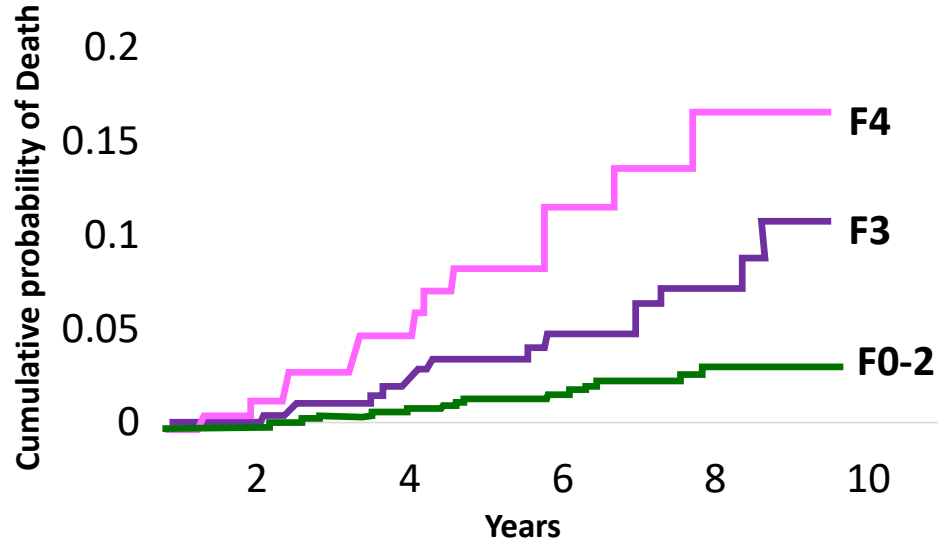


Targher G. Et al. Lancet Gastroenterol Hepatol. 2021 Jul;6(7):578-588.

Liver fibrosis is the most important predictor of poor outcomes in patients with MASH

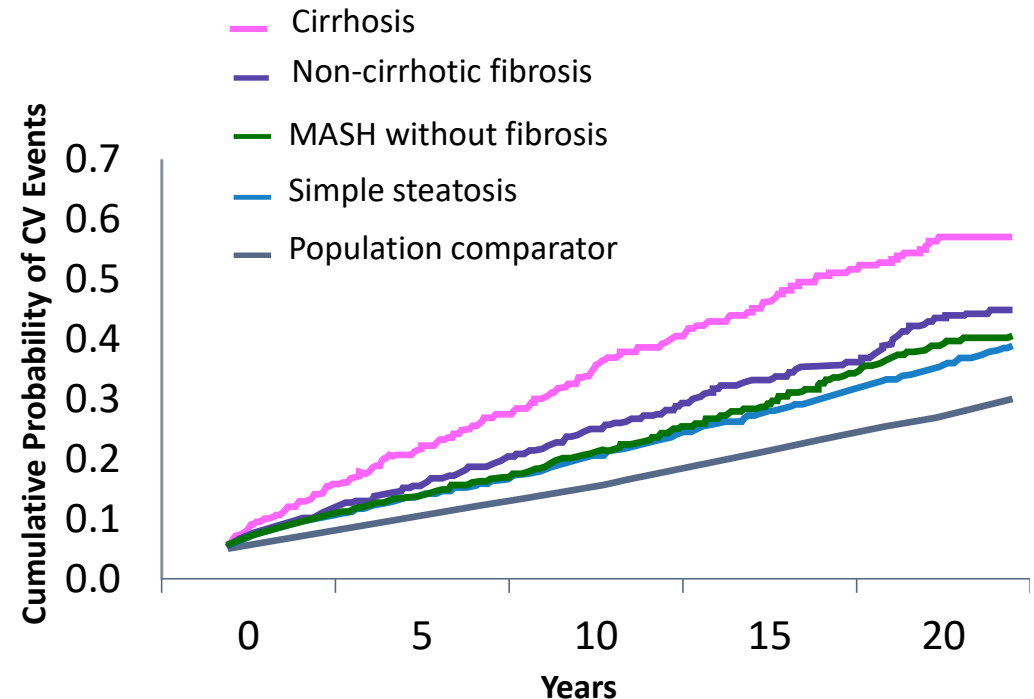
HR: F4 vs. F0-2
5.6 (95% CI, 2.8-11.5)

HR: F3 vs. F0-2
2.8 (95% CI, 1.4-5.4)



Higher stages of fibrosis are associated with increased risk of all-cause mortality

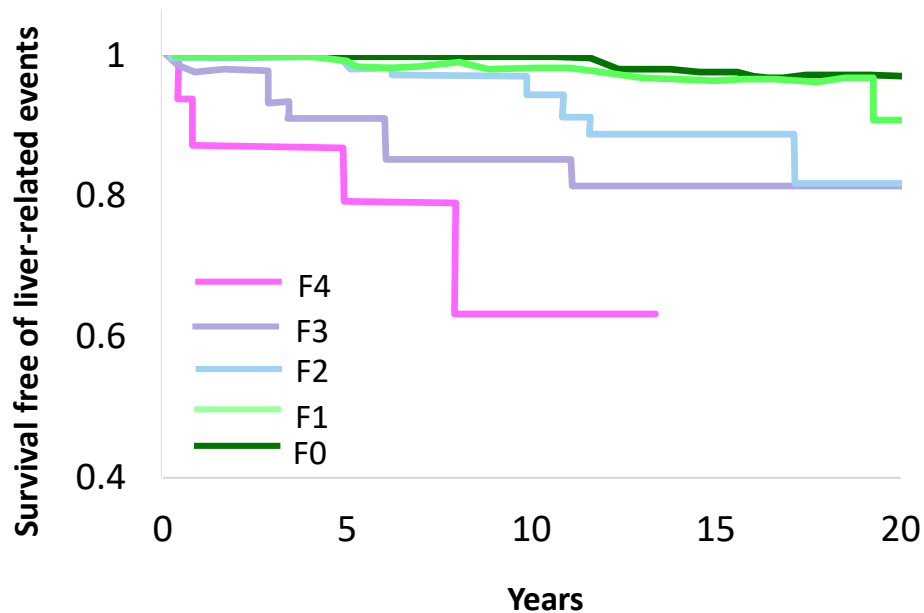
Sanyal AJ et al. NEJM, 2021 Oct 21;385(17):1559-1569.



The risk of major cardiovascular events is higher in MASH and increases with worsening fibrosis

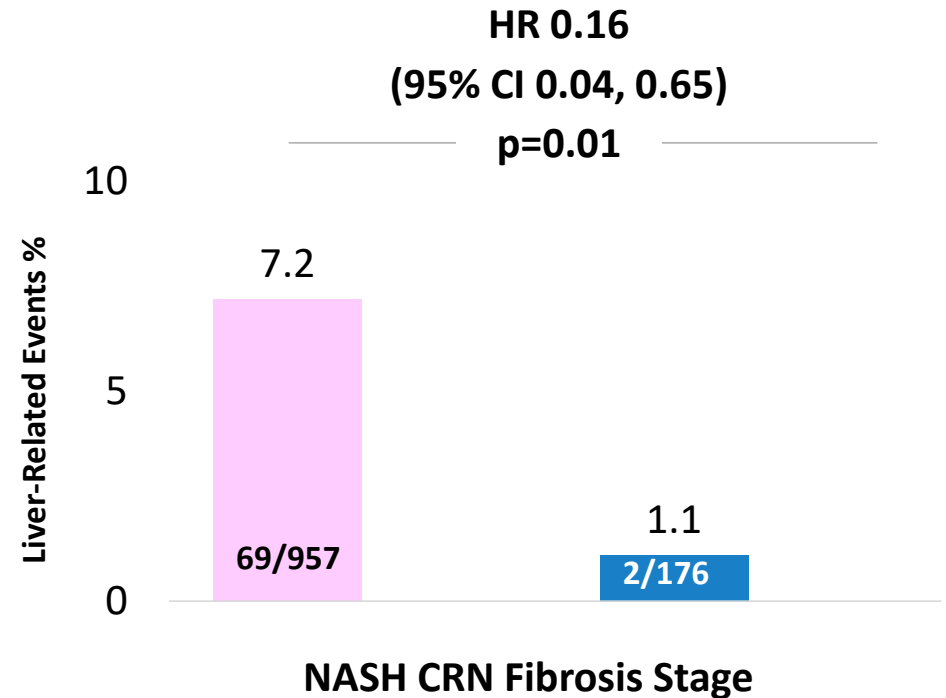
Simon TG et al. Gut. 2022 Sep;71(9):1867-1875.

Liver fibrosis is associated with liver related events and fibrosis regression can reduce the risk



Higher stages of fibrosis are associated with increased risk of liver related complications

Angulo P et al. Gastroenterology. 2015 Aug;149(2):389-97.e10.



Fibrosis regression is associated with reduction in liver related complications

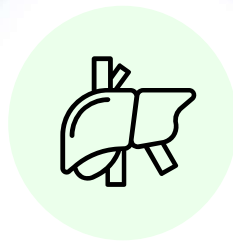
Sanyal AJ et al. Hepatology. 2022 May;75(5):1235-1246.

We need to identify and treat patients with MASH with significant fibrosis because...



Rising prevalence

The prevalence of significant fibrosis in MASLD is rising; yet many patients remain undiagnosed



Important predictor of adverse outcomes

Patients with significant fibrosis are at higher risk of developing major liver related and cardiovascular events



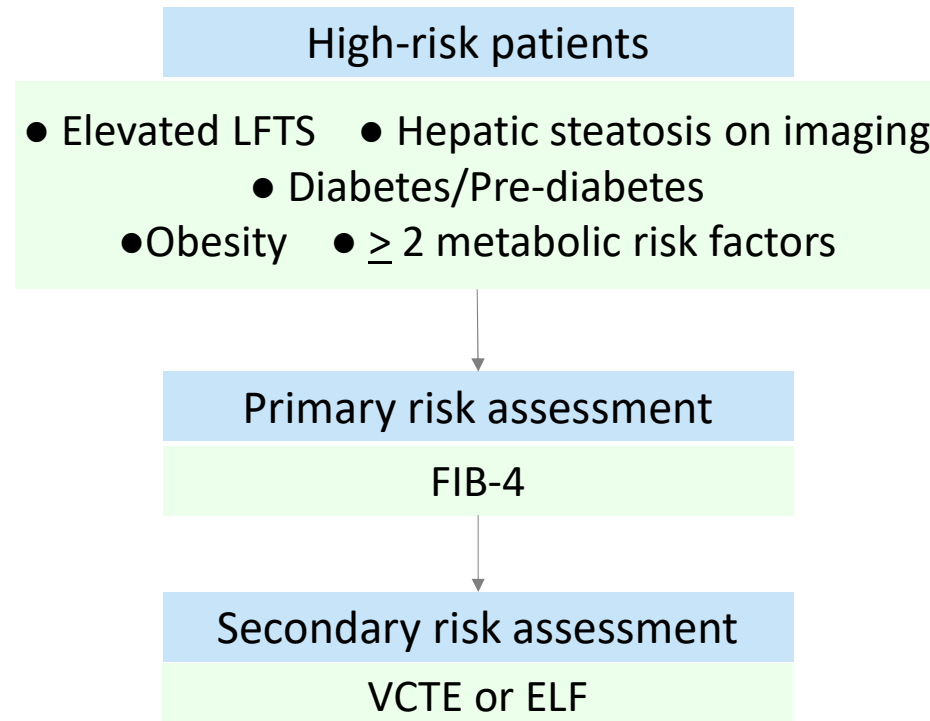
Treatment options increasing

Fibrosis regression is associated with reduced liver related events

Diagnosis and risk stratification of MASLD/ MASH

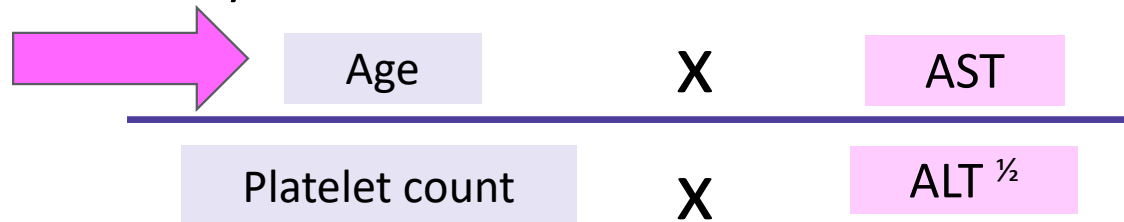
A proactive, tiered screening strategy is needed to recognize to identify patients with significant fibrosis

Primary care, endocrinology, weight management and gastroenterology/hepatology clinicians should screen for significant fibrosis

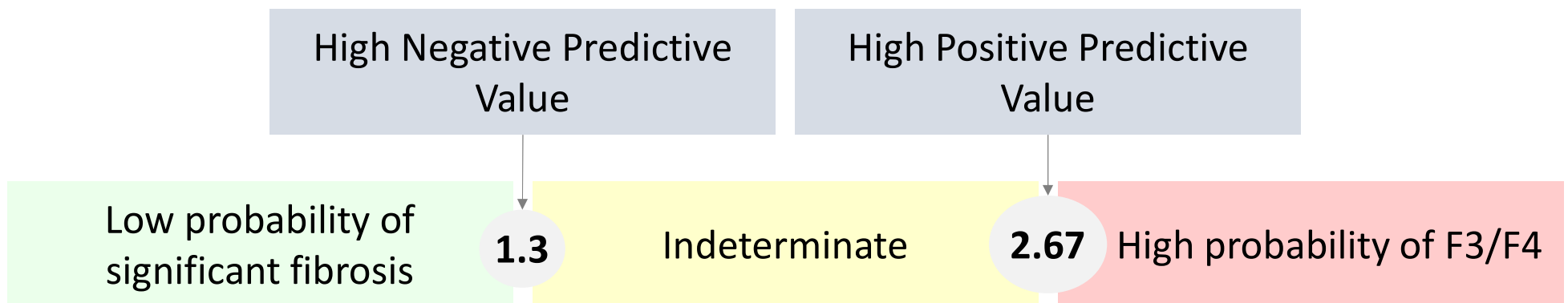


Noninvasive tests for risk stratification : FIB- 4

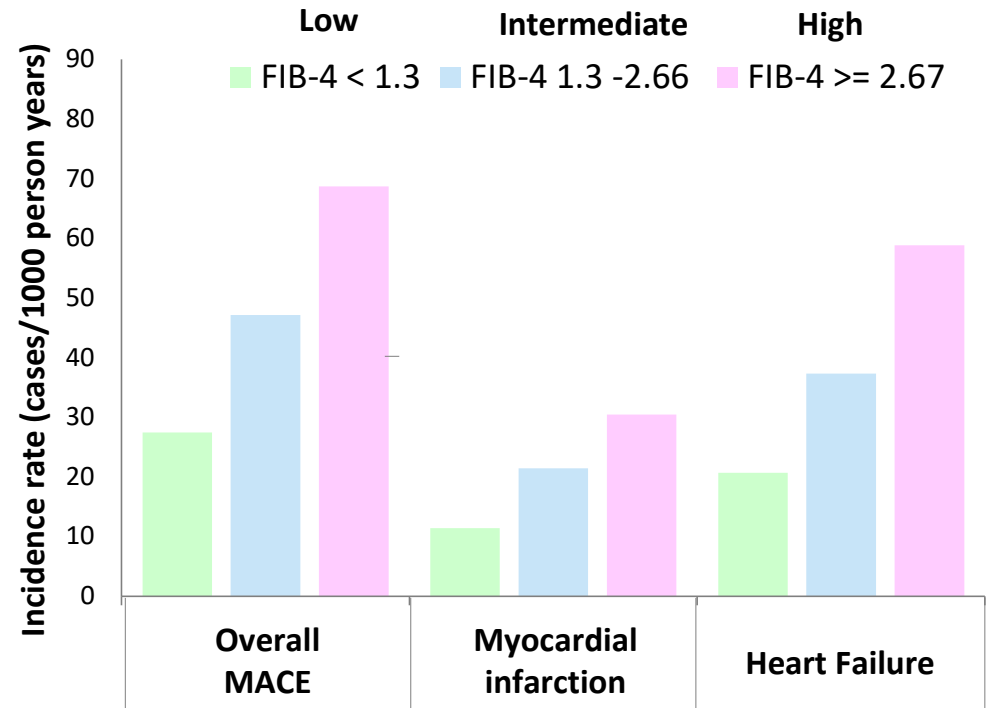
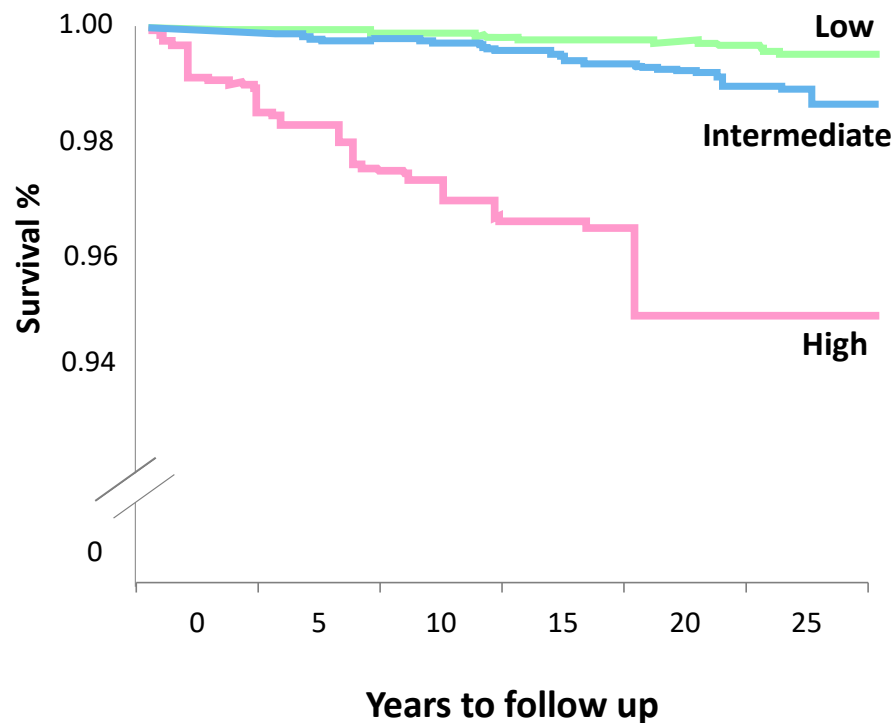
- Used commonly obtained blood tests



- Inexpensive; calculators widely available can be made into an Electronic Health Record phrase



FIB-4 can be used as a risk stratification tool

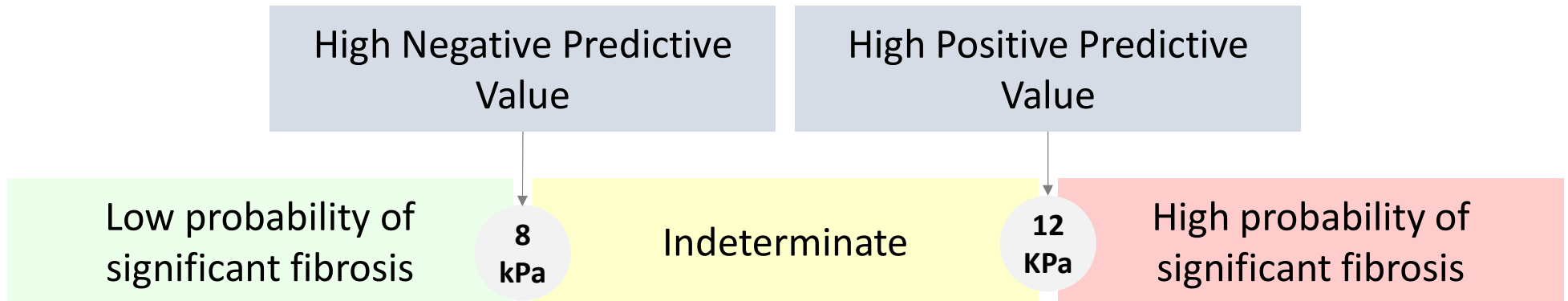
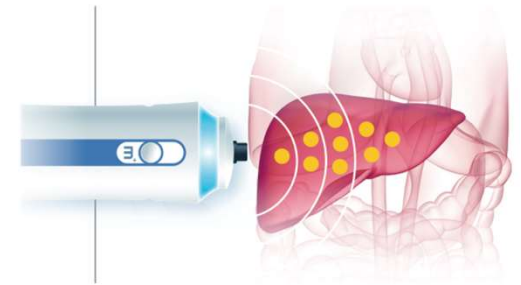


Higher FIB-4 scores are associated increased liver related mortality

Increase in FIB-4 predicts risk of cardiovascular events in patients with MASLD

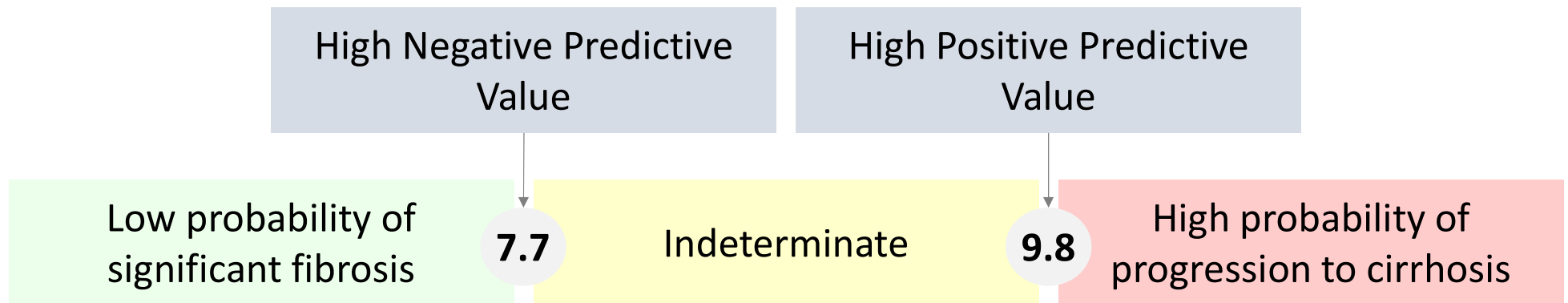
Noninvasive tests for risk stratification : VCTE/ Fibroscan (Vibration Controlled Transient Elastography)

- Ultrasound based
- Point-of-care test
- Marker of liver stiffness which is used as a surrogate for fibrosis
- Also measures Controlled Attenuation Parameter (CAP) that can detect >10% Steatosis
- Limited by BMI and significant ALT/ ALP elevation, hepatic congestion



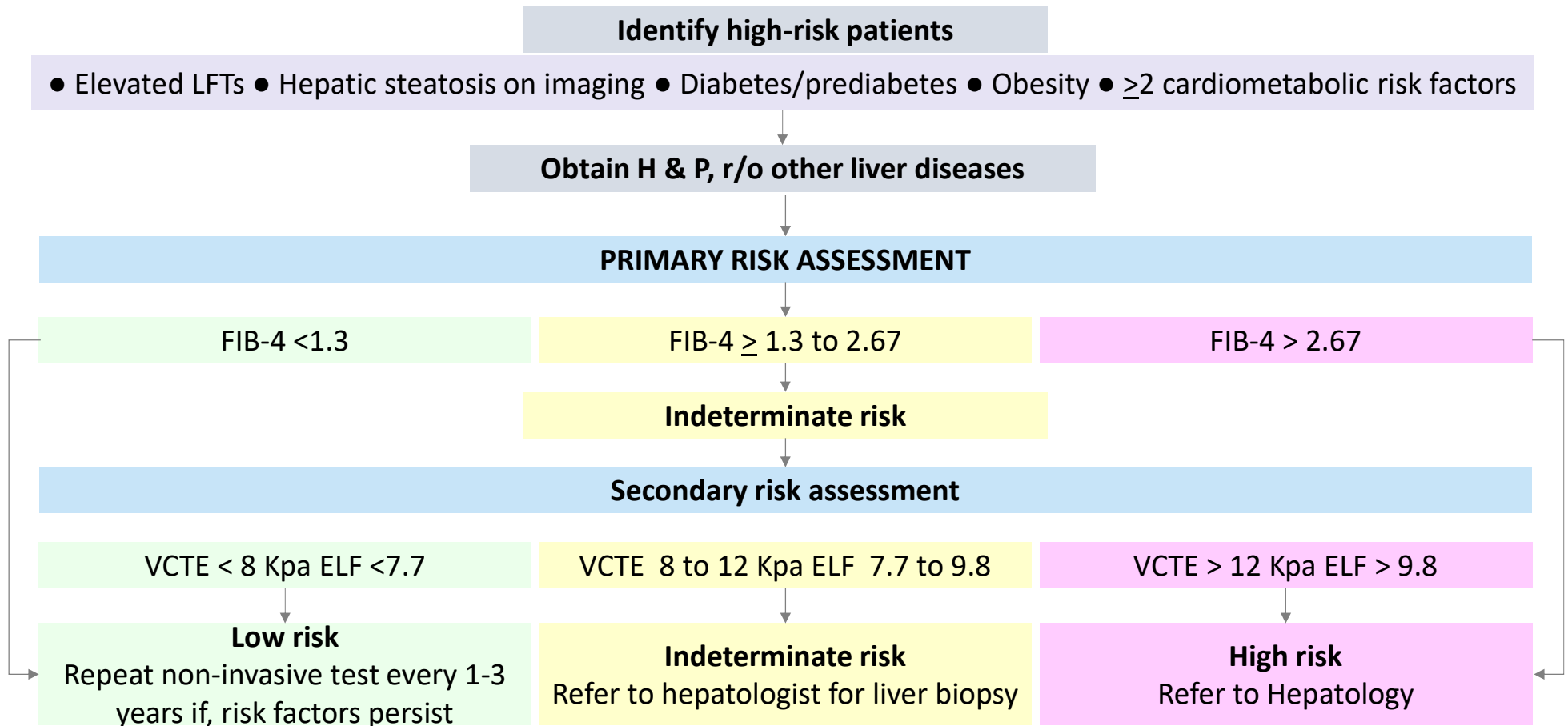
Noninvasive tests for risk stratification : Enhanced Liver Fibrosis (ELF) Test

- Proprietary blood test of 3 components involved in matrix turnover
 - Type III procollagen peptide (PIIINP)
 - Hyaluronic acid (HA)
 - Tissue inhibitor of metalloproteinase-1 (TIMP1)

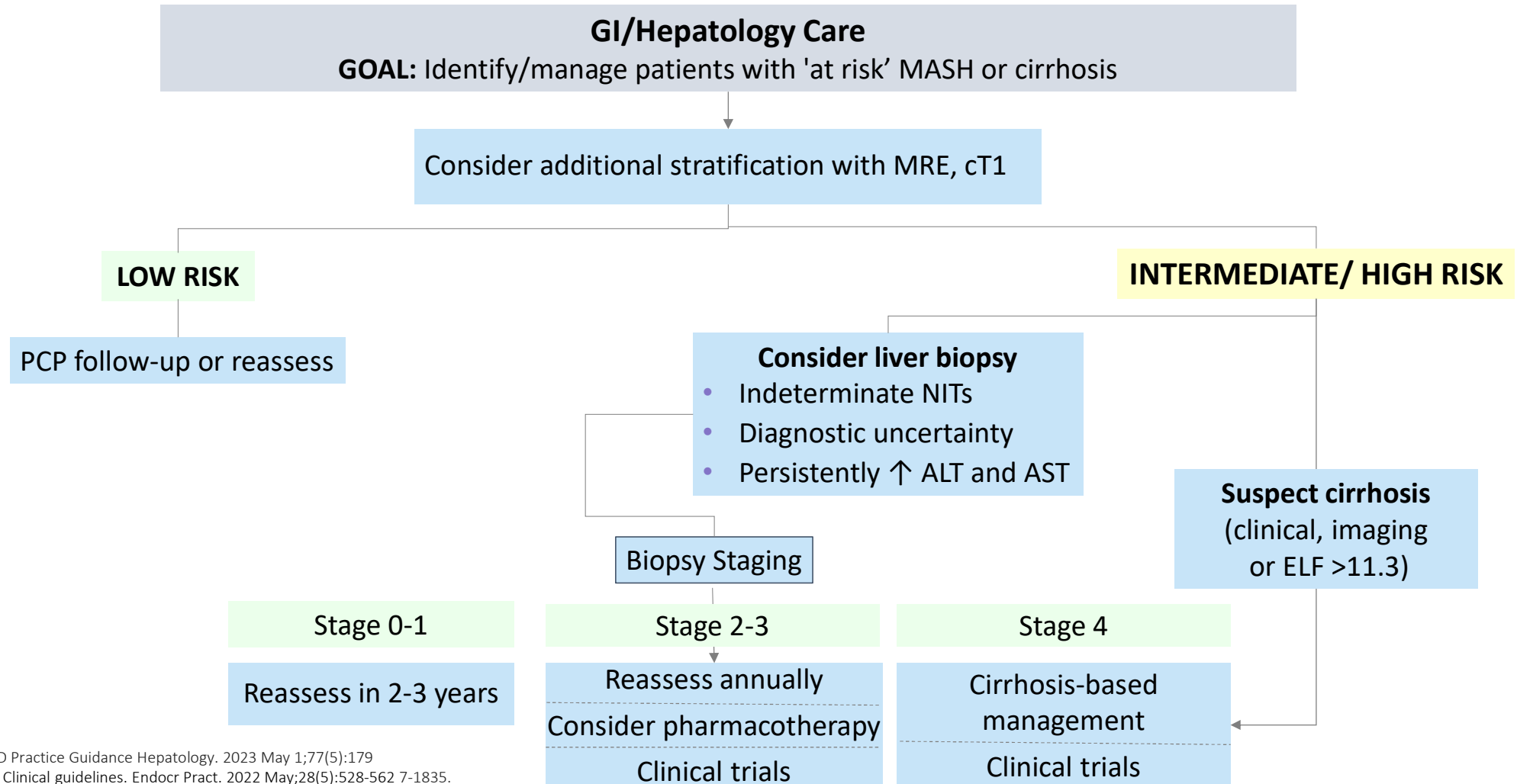


ELF test can be useful where elastography is not available

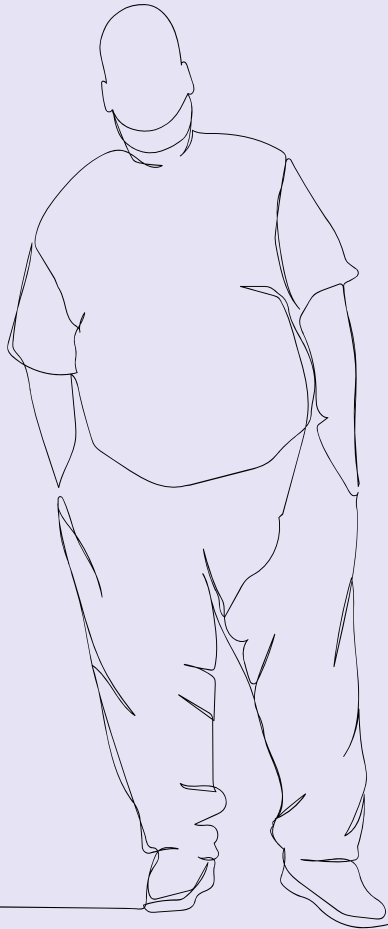
Tiered screening strategy for MASH with advanced fibrosis



New Clinical Practice Guidelines for Patients with Suspected NAFLD



Clinical case: Carlos



30-year-old

Imaging had shown “echogenic liver”

Several cardiometabolic criteria +



ALT is 65 U/L; AST is 70 U/L; Platelet count is $200 \times 10^9/L$
FIB 4 = 1.3



LSM (by TE) 9.4 kPa, CAP 310 dB/m



Liver biopsy showed steatohepatitis + F2 fibrosis

Carlos: Impact of Diagnosis

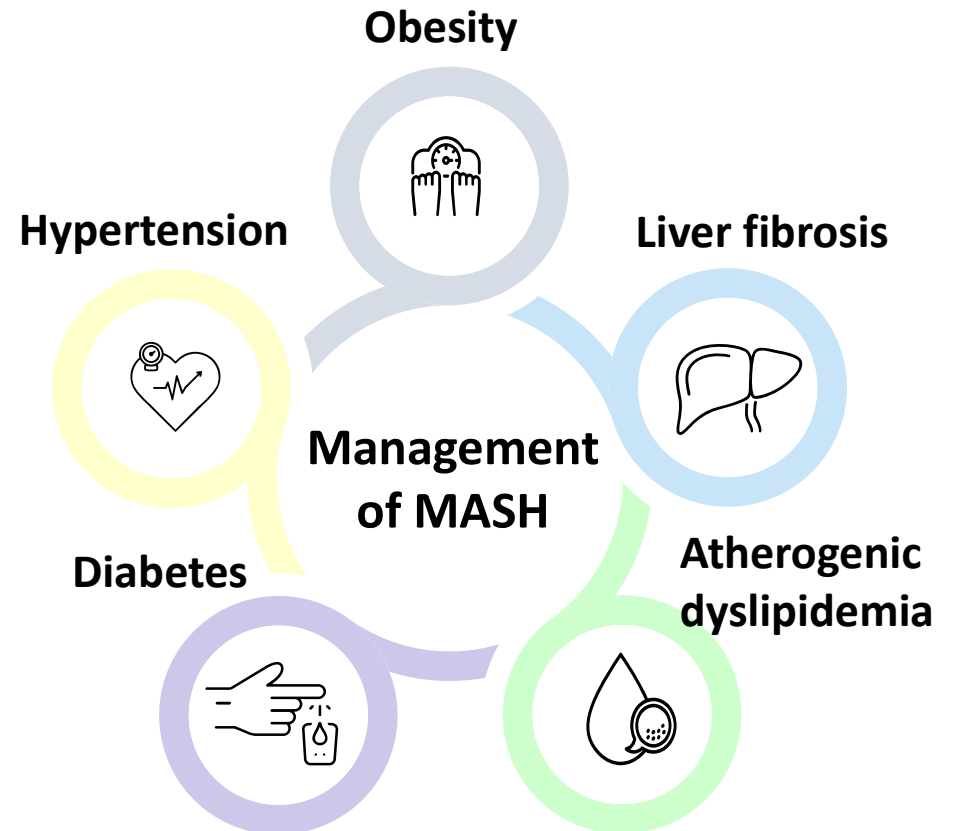


Management of MASLD/MASH in 2024

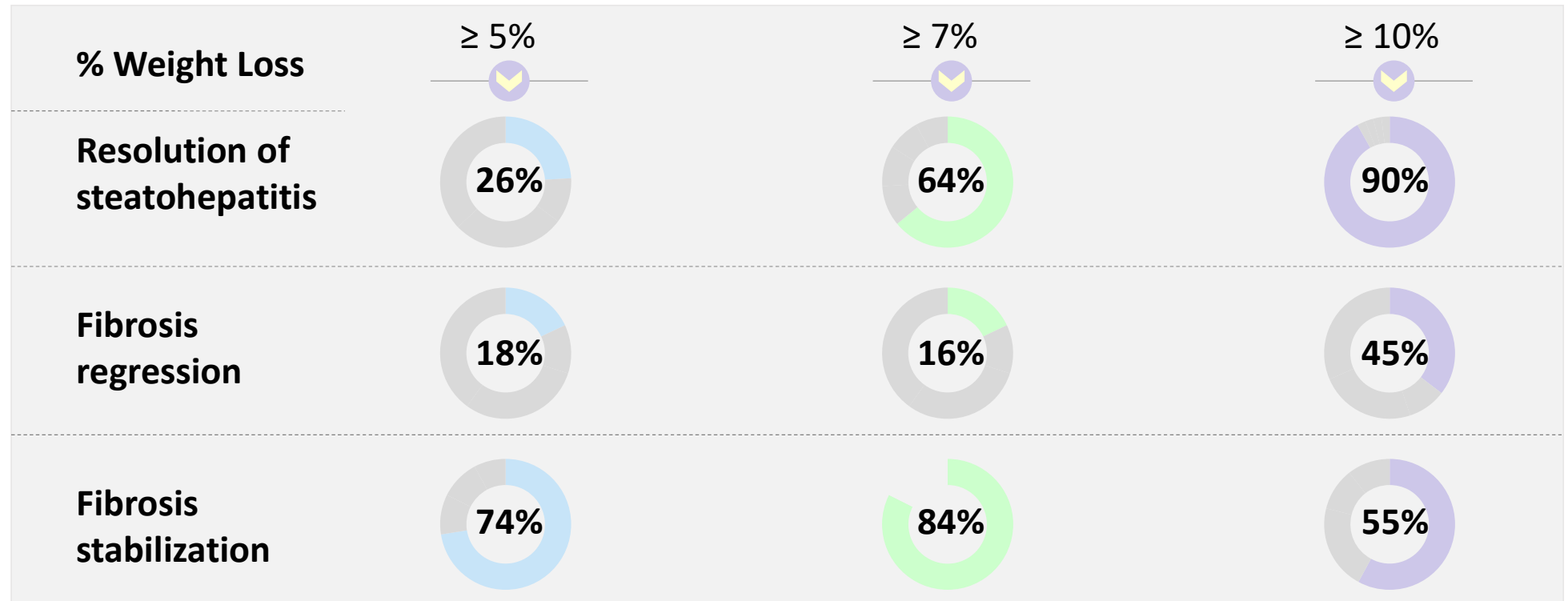
Goals of managing MASH

Prevention of cirrhosis and major adverse liver outcomes (MALOs)

Prevention of cardiovascular disease and major adverse cardiovascular events (MACEs)

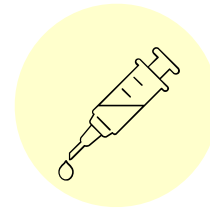
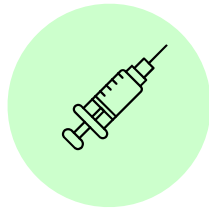
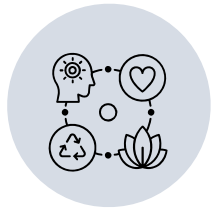


Weight loss through lifestyle modifications is associated with improvement of histological features of MASH



Hepatic fibrosis is dynamic and reversible

Weight loss with different options and approaches



**Lifestyle
intervention**

**Lifestyle
changes +
anti-obesity
medications
(Liraglutide)**

Semaglutide

**Endo-
bariatric**

Tirzepatide

**Bariatric
surgery**

2-5%

5-10%

15%

15-20%

20%

20-30%

Antidiabetic medications and MASH

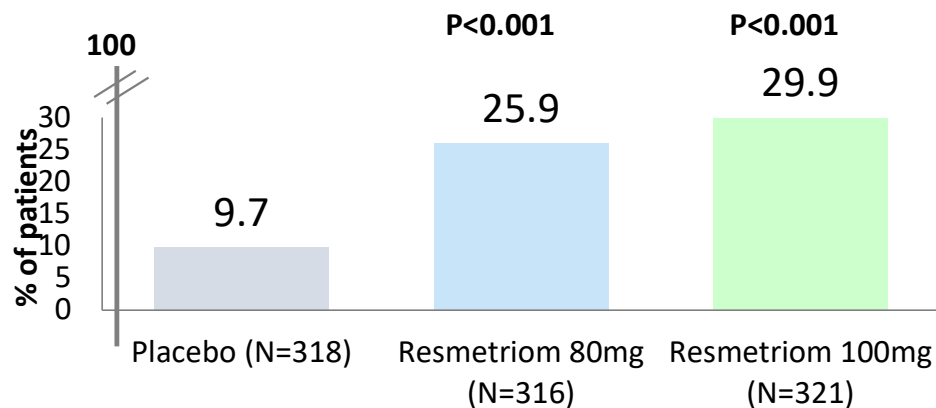
PIOGLITAZONE	LIRAGLUTIDE	SEMAGLUTIDE	TIRZEPATIDE
Thiazolidinedione	GLP-1 RA	GLP-1 RA	GLP-1/GIP RA
Type 2 DM, prediabetes MASLD	Type 2 DM Weight management	Type 2 DM Weight management	Type 2 DM Weight management
Improvement in steatosis Weight gain	Phase 2 (MASH) Resolution of MASH	Phase 2 (MASH F2/F3) Resolution of MASH without worsening of fibrosis	Phase 2 (MASH F2/F3) Resolution of MASH without worsening of fibrosis
Sanyal AJ N Engl J Med. 2010 May 6;362(18):1675-85.	Armstrong MJ et al. Lancet. 2016 Feb 13;387(10019):679-690.	Newsome PN et al N Engl J Med. 2021 Mar 25;384(12):1113-1124.	Loomba R et al. N Engl J Med. 2024 Jun 8

Pioglitazone or GLP-1 RA are recommended for persons with type 2 DM and biopsy proven MASH

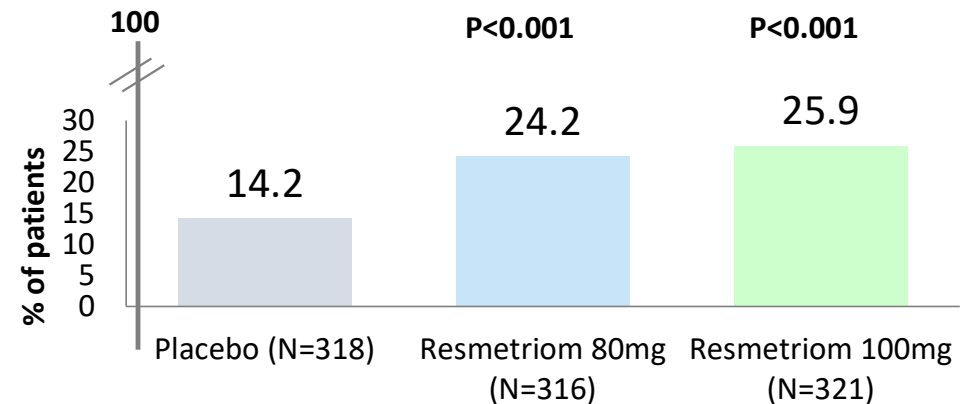
Clinicians should recommend the use of obesity pharmacotherapy as adjunctive therapy to lifestyle modification for individuals with obesity and MASLD or MASH

Resmetirom (THR- β receptor agonist): the first FDA approved drug for MASH

MASH resolution with no worsening of fibrosis



Fibrosis improvement by > 1 stage with no worsening of MASLD activity score

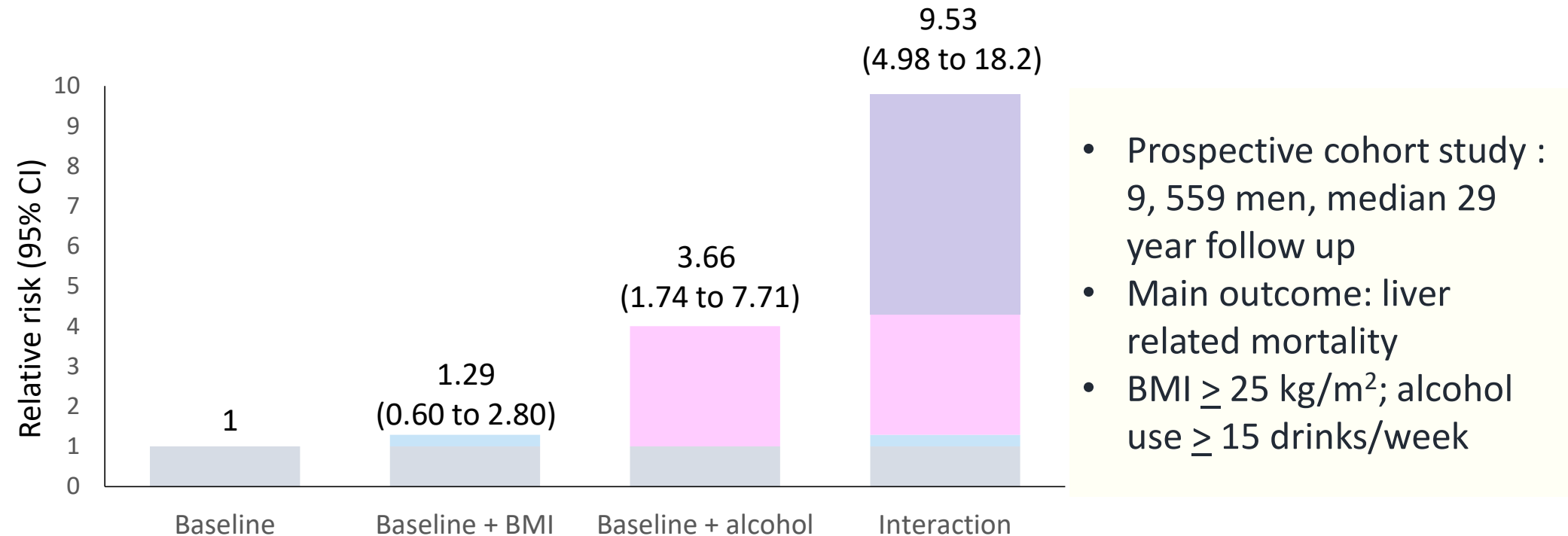


Phase 3, paired biopsies, intention-to-treat analysis at 52 weeks

Safety: generally safe; mild transient diarrhea and nausea

Eligible patients: Biopsy proven MASH (F2-F3) or LSM 10 – 15 kPa, CAP > 280 dB/m or ELF 9.2-10.4

The interaction of high BMI and alcohol is supra-additive

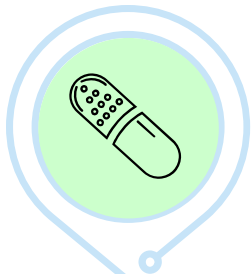


The combined effect of high BMI and alcohol is be greater than the simple additive effects of each factor separately

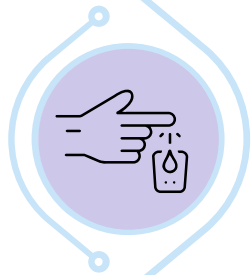
Carlos: Lifestyle changes with diagnosis



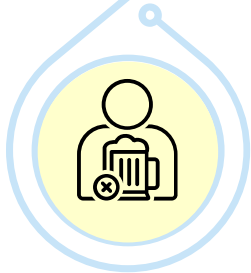
Other key take home points



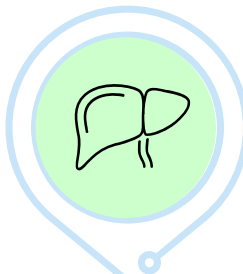
Statins are safe across the disease spectrum of MASH, including compensated cirrhosis



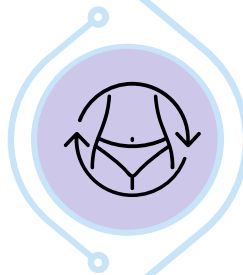
Patients with MASH should be screened for type 2 diabetes mellitus



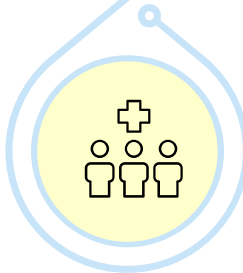
Effect of alcohol and MASH on the liver, is synergistic and supra-additive. In your patients with MASH, assess alcohol intake on a regular basis. Patients with MASH must abstain from alcohol.



AST/ALT levels are frequently normal in patients with advanced liver disease and should not be used in isolation to r/o significant fibrosis



Coffee consumption of at least 3 cups daily is associated with less advanced disease



Bariatric surgery can resolve MASH and should be considered as a therapeutic option in patients who meet criteria for weight loss surgery

Carlos: A Positive Outlook



Q&A Session