

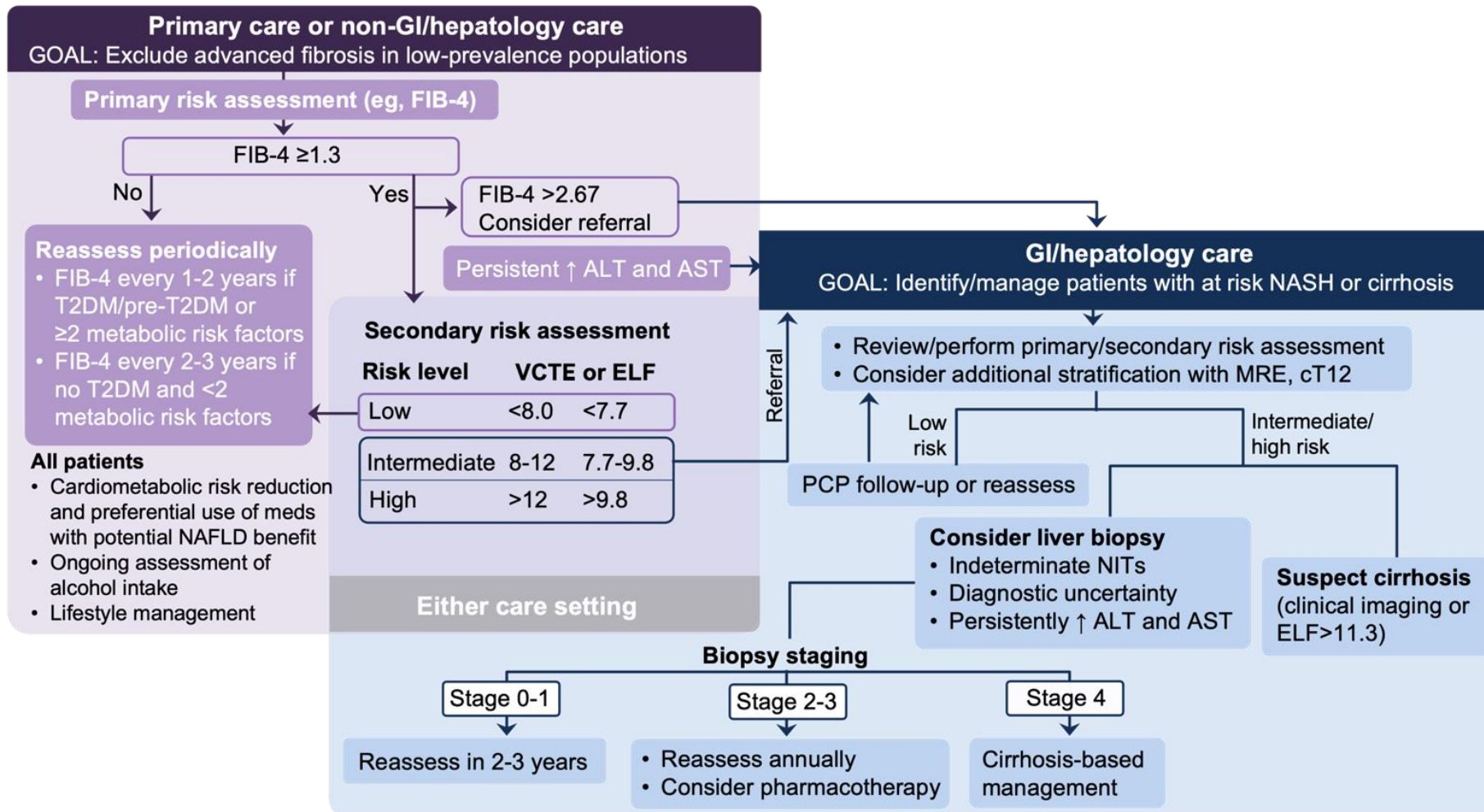
# Primary Care's Important Role in the Management of MASH

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Texas Liver Institute  
San Antonio

# Patient ABC

- 51-year-old, Hispanic male seen by you for annual physical
  - BMI 40, hypertension, hyperlipidemia, T2DM, hypothyroidism
  - Family history: Cirrhosis, CAD
  - Conmeds: Lisinopril, atorvastatin, semaglutide, baby aspirin, levothyroxine
  - Labs:
    - AST 34, ALT 59
    - Normal TB, ALP, GGT
    - Platelets 185
  - Ultrasound: Liver mildly enlarged with diffuse increased echogenicity
- 
- All aligned with MASLD. Need to stage fibrosis.
  - What would you order?

# AASLD Practice Guidance Recommends the Use of Non-Invasive tests (NITs) for Staging



**AASLD recommends FIB-4 followed by ELF or VCTE**

Note: Liver biopsy should be considered if there is diagnostic uncertainty.  
Rinella ME et al. *Hepatology*. 2023;77:1797-1835.

# Staging Fibrosis with NITs

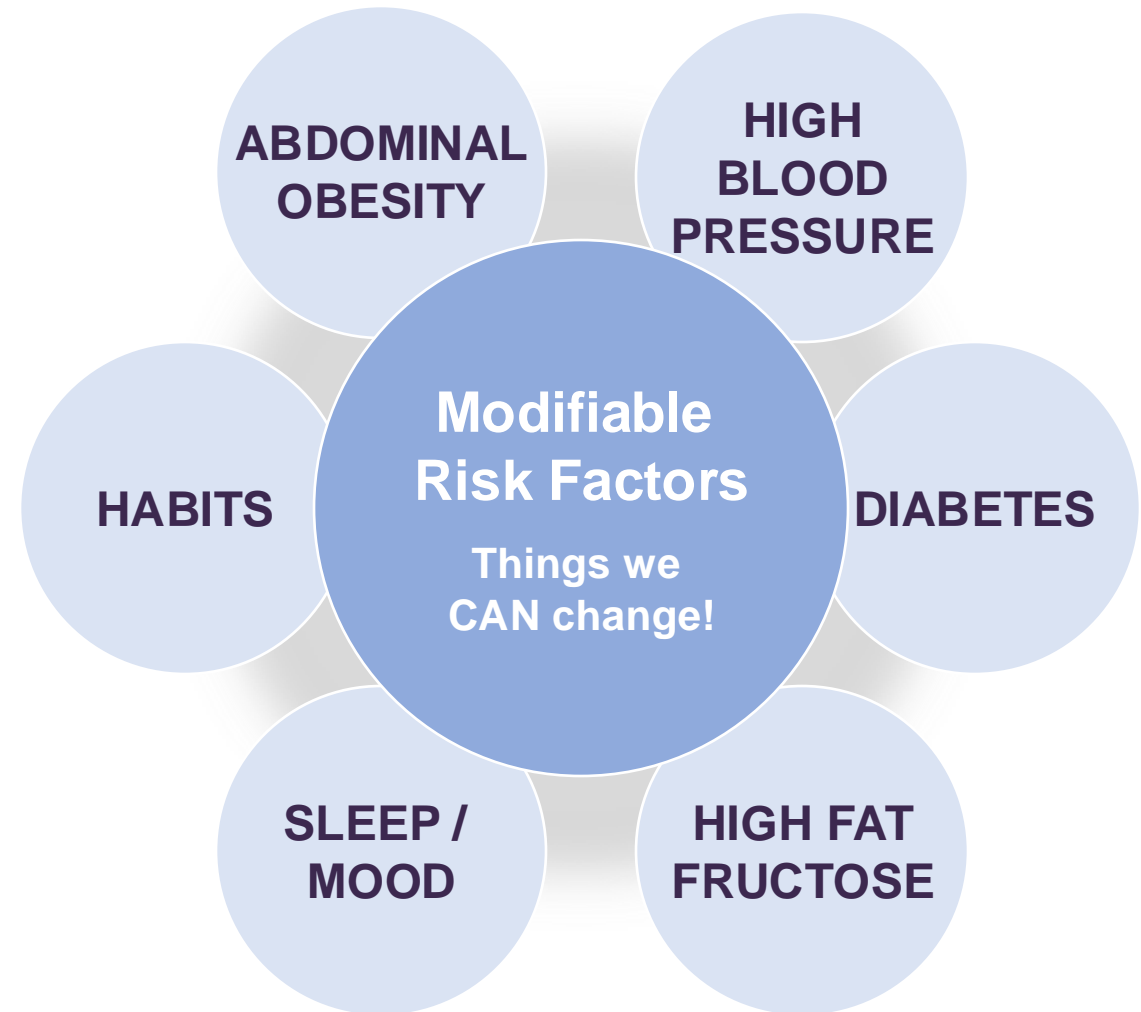
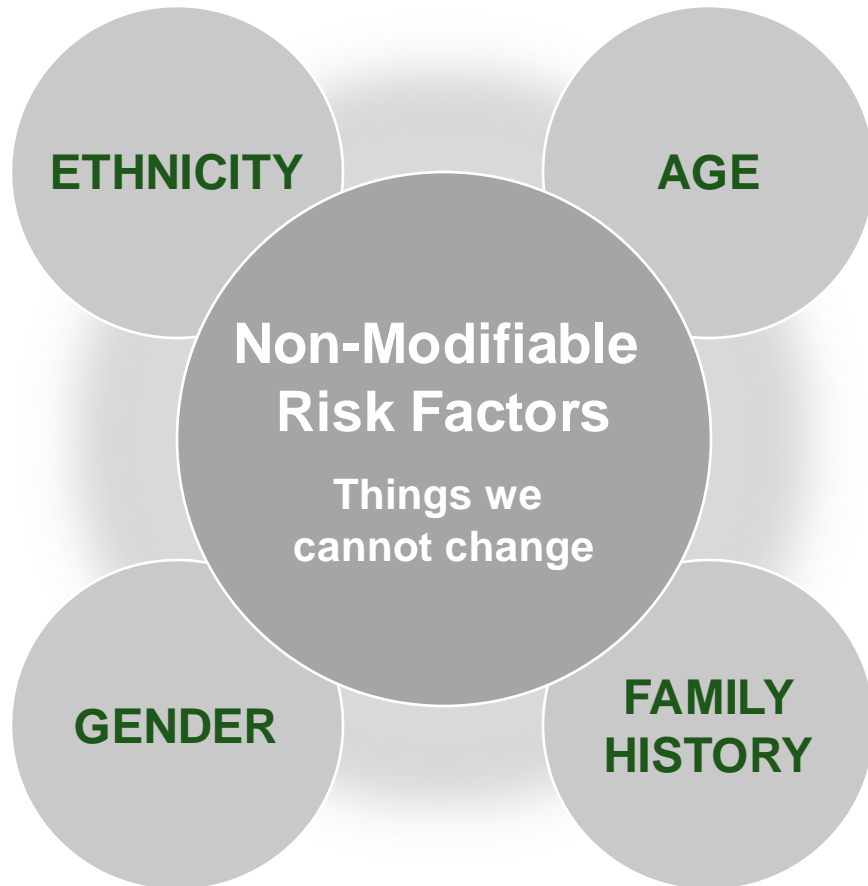
- You calculate FIB-4 from most recent labs.
  - FIB-4 = 1.22
  - Deemed low risk
  - Recalculate FIB-4 annually since patient remains at risk for progression
- What more can you do to decrease his risk of progression?

# Clinical Care Pathways for the Risk Stratification and Management of Patients With MASLD

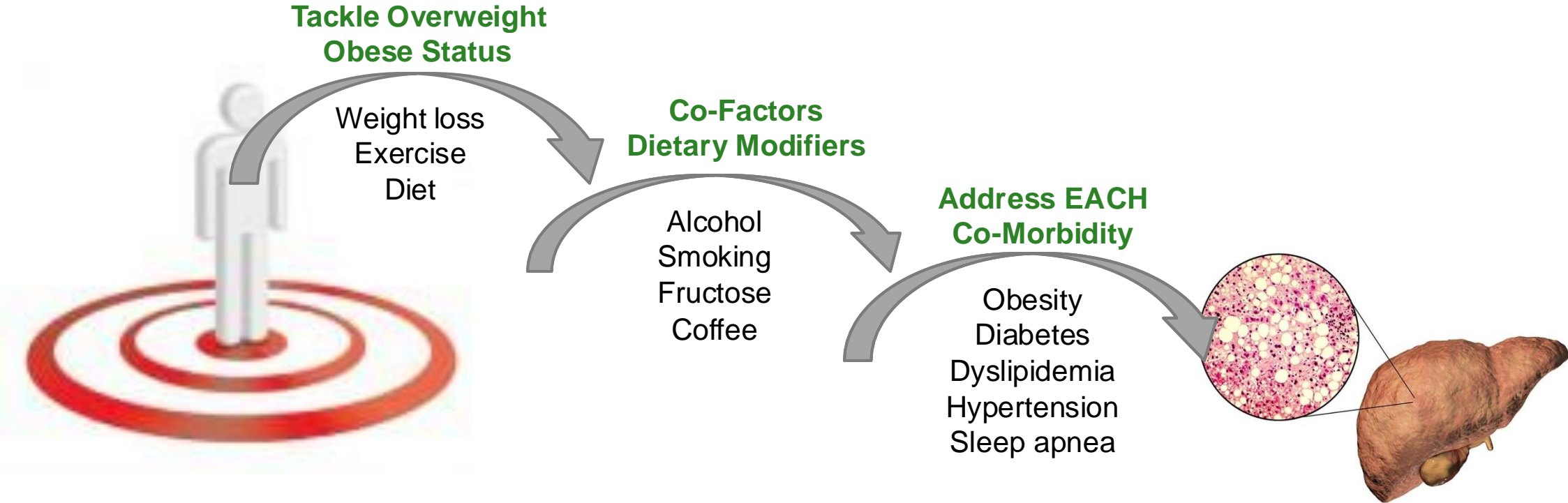
	<b>LOW RISK</b> FIB-4 <1.3 or LSM <8kPa or ELF <7.7 or Liver biopsy F0-F1	<b>INTERMEDIATE RISK</b> FIB-4 1.3-2.67 and/or LSM 8-12kPa and Liver biopsy not available	<b>HIGH RISK</b> FIB-4 >2.67 or LSM >12kPa or Liver biopsy F2-F4
	Management by PCP, dietician, endocrinologist, cardiologist, others	Management by hepatologist with multidisciplinary team (PCP, dietician, endocrinologist, cardiologist, other)	
Lifestyle intervention	Yes	Yes	Yes
Weight loss recommended if overweight or obese	Yes May benefit from structured weight loss programs, anti-obesity medications, bariatric surgery	Yes Greater need for structured weight loss programs, anti-obesity medications, bariatric surgery	Yes Strong need for structured weight loss programs, anti-obesity medications, bariatric surgery
Pharmacotherapy for MASH	Not recommended	Yes	Yes
CVD risk reduction	Yes	Yes	Yes
Diabetes care	Standard of care	Prefer medications with efficacy in NASH (pioglitazone, GLP-1 RA)	Prefer medications with efficacy in NASH (pioglitazone, GLP-1 RA)

# Managing the Low Risk MASLD Patient in Your Office

# Identify All **Modifiable** Risk Factors

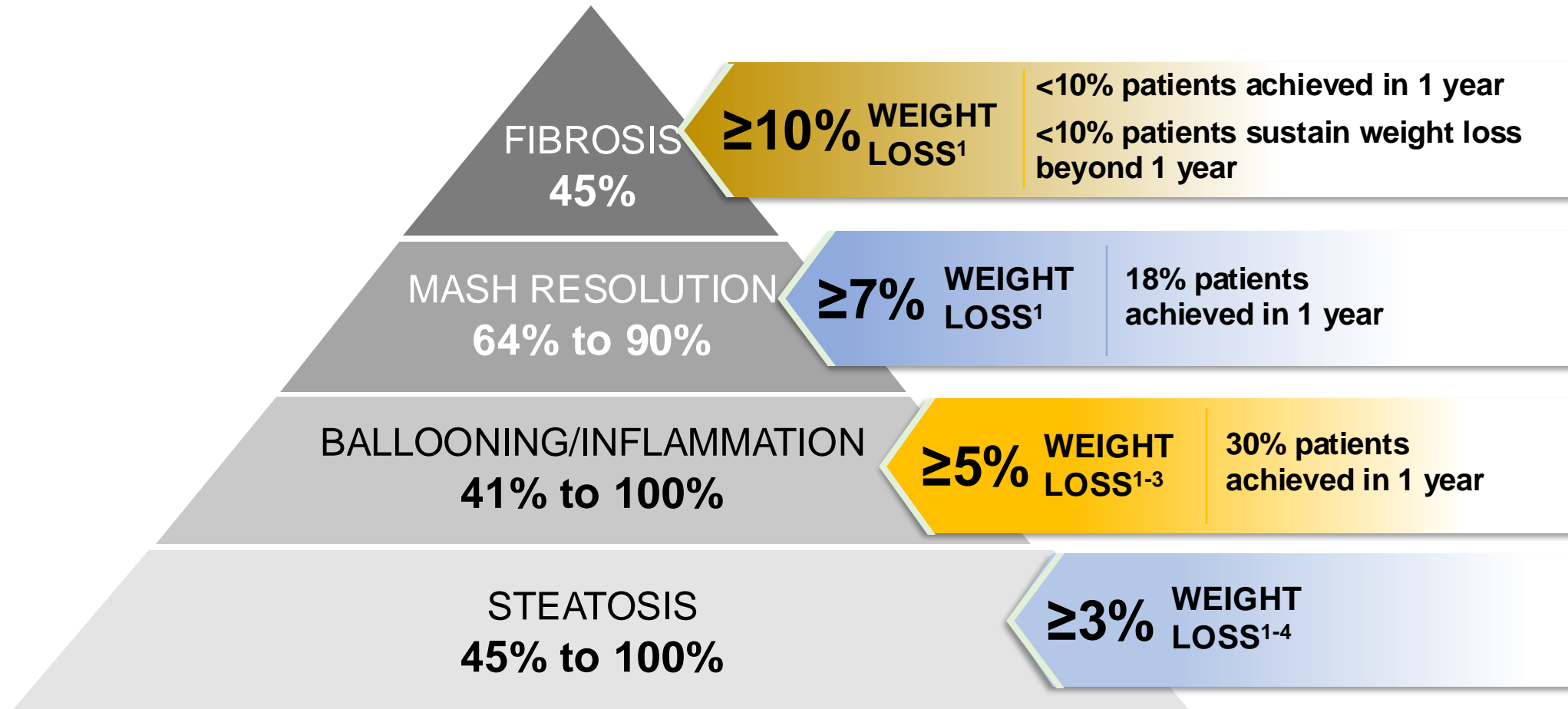


# Current Treatment of Low-Risk MASH is Patient Centered-Individualized Therapy





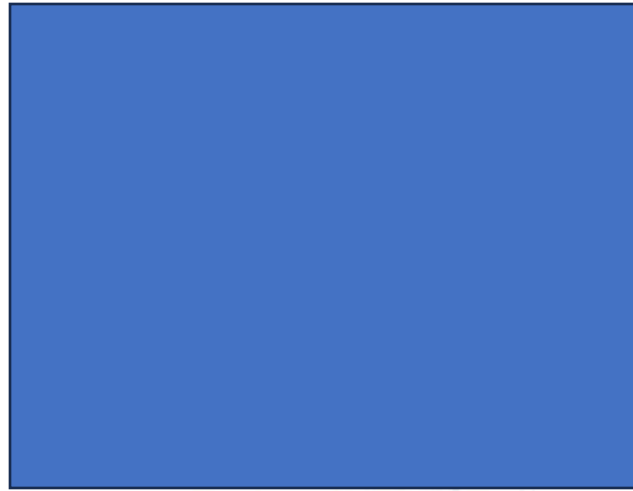
# Weight Loss Works...but Can Be Difficult



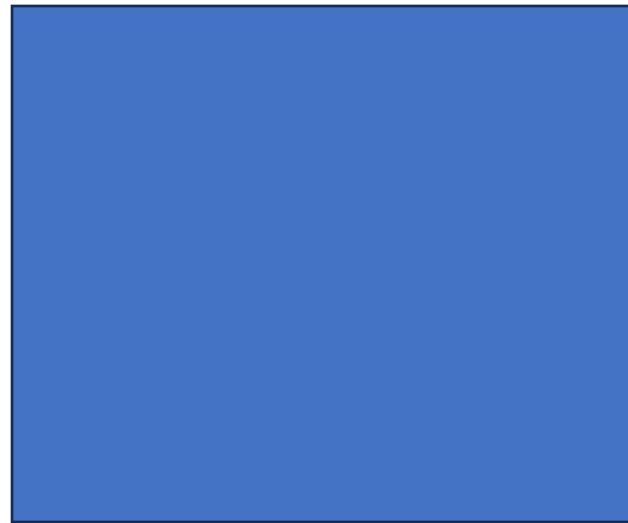
Data from paired liver biopsies in 261 patients with NASH who underwent 52 weeks of lifestyle modification.

1. Vilar-Gomez E et al. *Gastroenterology*. 2015;149:367-378; 2. Promrat K et al. *Hepatology*. 2010;51(1):121-129; 3. Harrison SA et al. *Hepatology*. 2009;49:80-86; 4. Wong VW et al. *J Hepatol*. 2013;59(3):536-542.

# Diet Matters!!



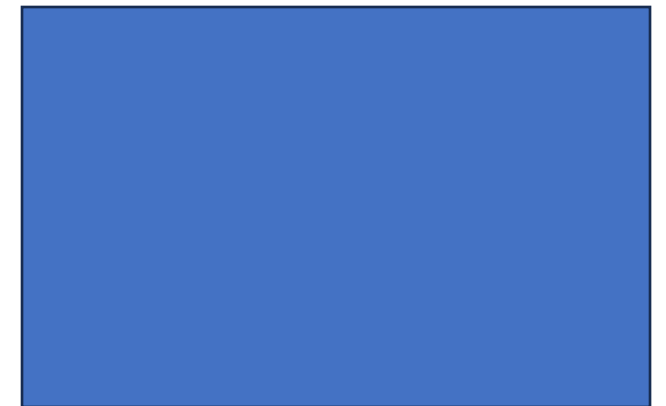
Excess calories  
Excess carbohydrates  
Saturated fats  
High cholesterol  
High meat intake  
Low fiber  
Low PUFAs



**Increased fructose consumption  
associated with liver injury and fibrosis**



Modest alcohol



Coffee is good

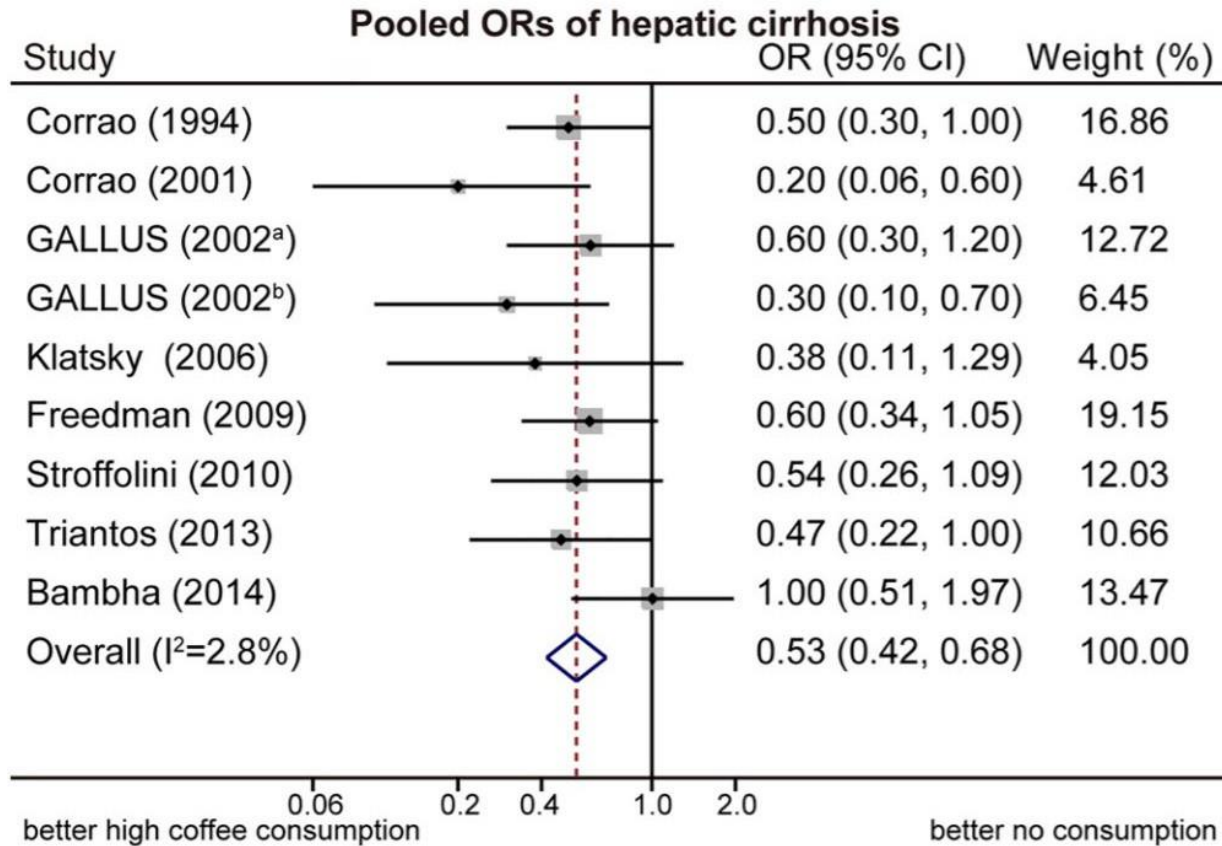
# Effects of Mediterranean Diet in MASLD

Meta-analysis of studies<sup>a</sup> comparing Mediterranean diet and no intervention or other diets on hepatic endpoints

Endpoint	No. of studies	SMD <sup>b</sup> between Mediterranean diet and no intervention or other diets (95% CI)	P-value
Liver stiffness	2	-0.67 (-1.70 to 0.36)	0.04
HOMA-IR	5	-0.34 (-0.65 to -0.03)	0.03
Fatty Liver Index	3	-1.06 (-1.95 to -0.17)	0.02

<sup>a</sup>Study durations ranged from 6 weeks to 6 months; <sup>b</sup>Estimates derived from random effects model.  
Kawaguchi T. *Sem Liver Dis.* 2021;41(3):225-234..

# Coffee Consumption Decreases Risk for Hepatic Fibrosis and Cirrhosis



Caffeine is inversely associated with:

- MASLD
- MASH
- Hepatic fibrosis

Steatosis vs MASH (P=0.005) MASH  
F0-1 vs MASH F2-4 (P=0.005)

# Weight Loss Beyond Lifestyle Modifications

Orlistat

Phentermine

Naltrexone/bupropion

Liraglutide

Semaglutide

Tirzepatide

**Drugs**

Gastric balloon

Sleeve gastropasty-  
overstitch

DMR

**Endoscopy**

Gastric bypass

Sleeve gastropasty

**Surgery**

**NOTE: None of the strategies listed are approved for the treatment of MASH.**

DMR, duodenal mucosal resurfacing.

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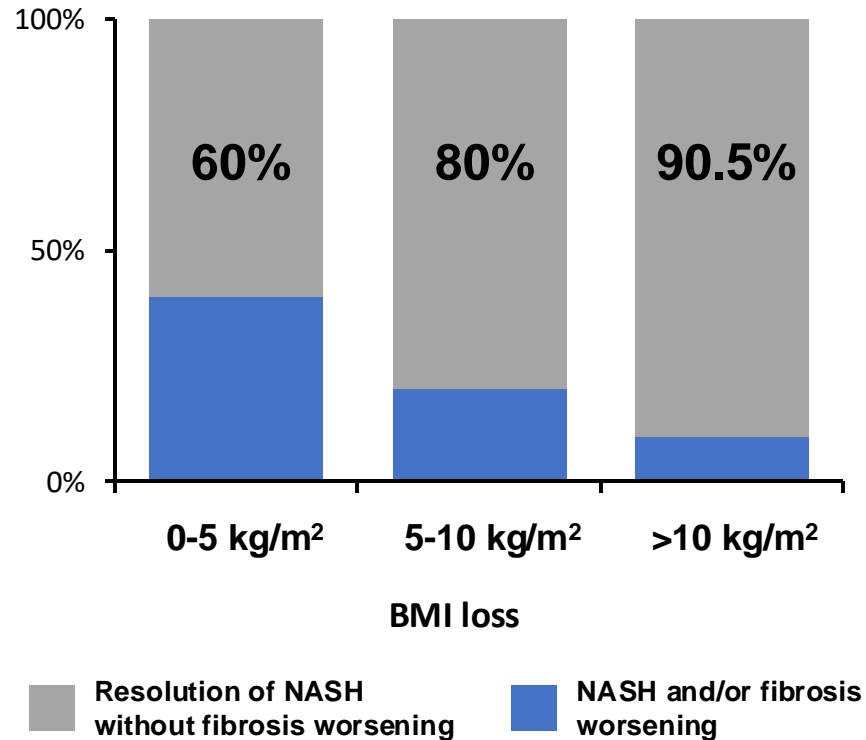
# Recommendations for Physical Activity

- Tailor to the patient
- Aim for >150 min/week of moderate intensity or 75 min/week of vigorous intensity physical activity
- Minimize sedentary time



# MASH Resolution With Bariatric Surgery

**Resolution of NASH according to weight loss**



Characteristic	Before Surgery	After Surgery	P-value
BMI (kg/m <sup>2</sup> )	48 ± 6.9	36.1 ± 7.8	<0.001
HDL-C (mmol/L)	1.1 (0.9-1.3)	1.3 (1.2-1.5)	<0.001
Triglycerides	1.6 (1.3-2.4)	1.1 (0.7-1.6)	<0.001
AST (IU/L)	36 (27-50)	21 (18-26)	<0.001
ALT (IU/L)	47 (36-50)	19 (13-30)	<0.001
GGT (IU/L)	50 (38-77)	20 (13-39)	<0.001
Fasting glucose (mg/dL)	132 (92-192)	103 (89-103)	<0.001
HbA1c (%)	7.5 (6-8.8)	5.9 (5.5-6.5)	<0.001
R index (1/QUICKI)	3.4 (3.3-3.6)	2.9 (2.7-3.1)	<0.001

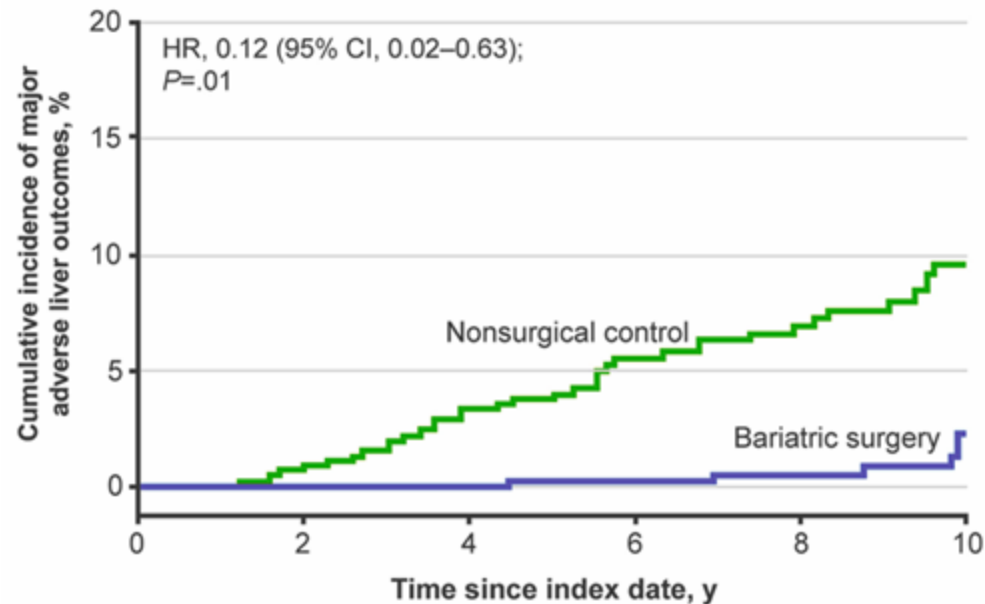
Data presented as mean ± SD or median (IQR)

# Bariatric Surgery for Patients With Obesity and MASH

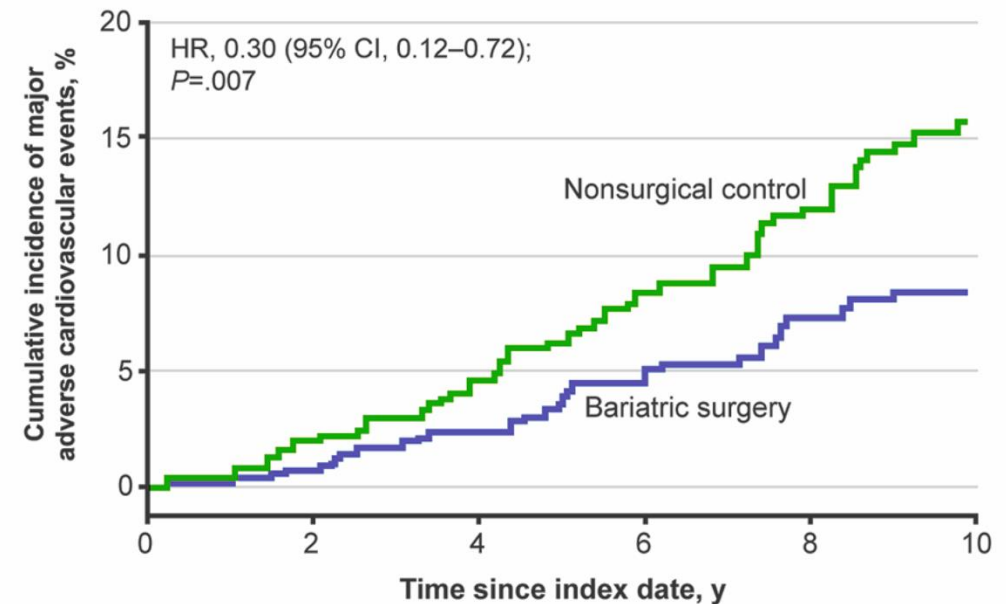
## Major adverse outcomes

(N=1158 adults with obesity and confirmed histological diagnosis of NASH and presence of liver fibrosis)

### Liver outcomes<sup>a</sup>



### CV events<sup>b</sup>



<sup>a</sup>Composite end point that was defined as the first occurrence of progression to clinical or histological cirrhosis, development of hepatocellular carcinoma, liver transplantation, or liver-related mortality after the index date; <sup>b</sup>Composite end point that was defined as the first occurrence of coronary artery events, cerebrovascular events, heart failure, or cardiovascular mortality after the index date; Aminian A et al. *JAMA*. 2021;326(20): 2031–2042.



# Medical Society Guidelines for Lifestyle Modifications in Patients With MASLD

AASLD  
2023

EASL-EASD-  
EASO 2024

AACE/  
AASLD 2022



## Weight loss goals (TBW %)

- Steatosis:  $\geq 5\%$
- MASH & Fibrosis:  $\geq 10\%$

- Steatosis: 3–5%
- MASH & Fibrosis:  $> 10\%$

- Steatosis and MASH: 7–10%
- Fibrosis:  $> 10\%$



## Diet

- Restrict saturated fat, starch, and added sugar
- Healthier eating patterns, **Mediterranean diet**

- Improve diet quality (**Mediterranean diet**)
- Limit ultra-processed food and avoid sugar-sweetened beverages

- **Mediterranean diet**



## Physical activity

- Participate in structured exercise program, when possible, tailored to the patient's lifestyle and preferences

- Increase activity level to the extent possible
- Individualized prescriptive exercise

- Exercise to reduce hepatic fat content
- No data on efficacy in improving necroinflammation



## Coffee

- Not addressed

- $\geq 3$  cups of coffee (caffeinated or not) daily is associated with less advanced liver disease

- Coffee consumption, more likely to benefit
- Largest risk reduction at 3-4 cups a day

# Drugs: Optimizing Cardio-Metabolic Risks and MASH-Targeted Therapy

Preferred pharmacological options for treating comorbidities

## T2DM

### GLP1RA

(e.g. semaglutide, liraglutide, dulaglutide) and **co-agonists**  
(e.g. tirzepatide)

### SGLT2 inhibitors

(e.g. empagliflozin, dapagliflozin)

### Metformin\*

### Insulin

(in case of decompensated cirrhosis)

## Dyslipidemia

### Statins

## Obesity

### GLP1RA

(e.g. semaglutide, liraglutide) and **co-agonists**  
(e.g. tirzepatide)

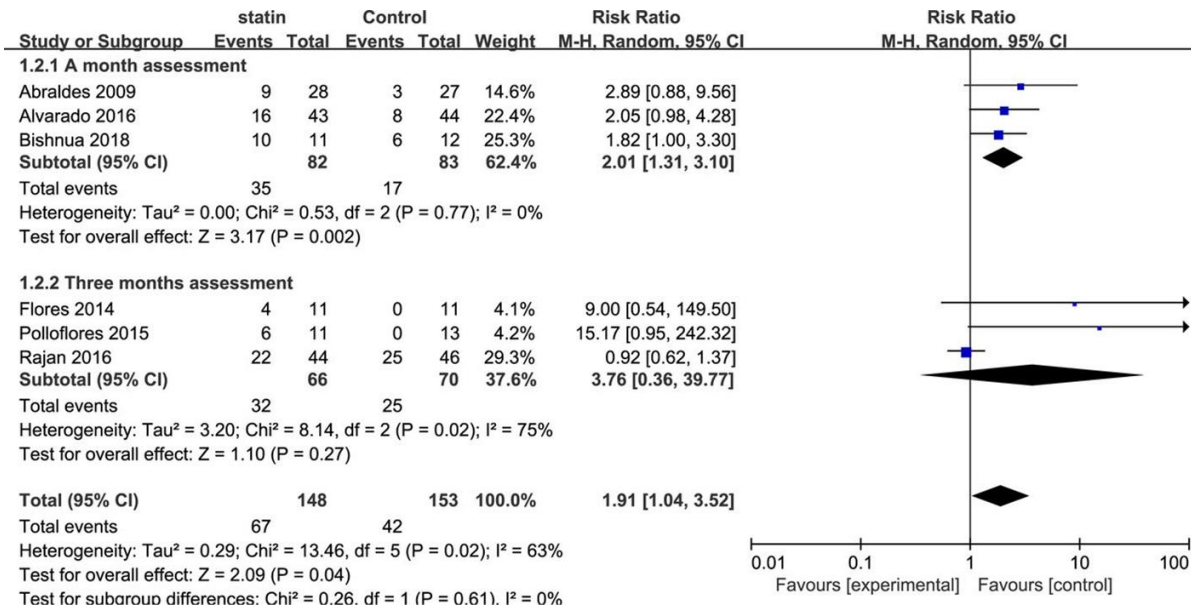
### Bariatric interventions

(special caution in case of compensated cirrhosis)

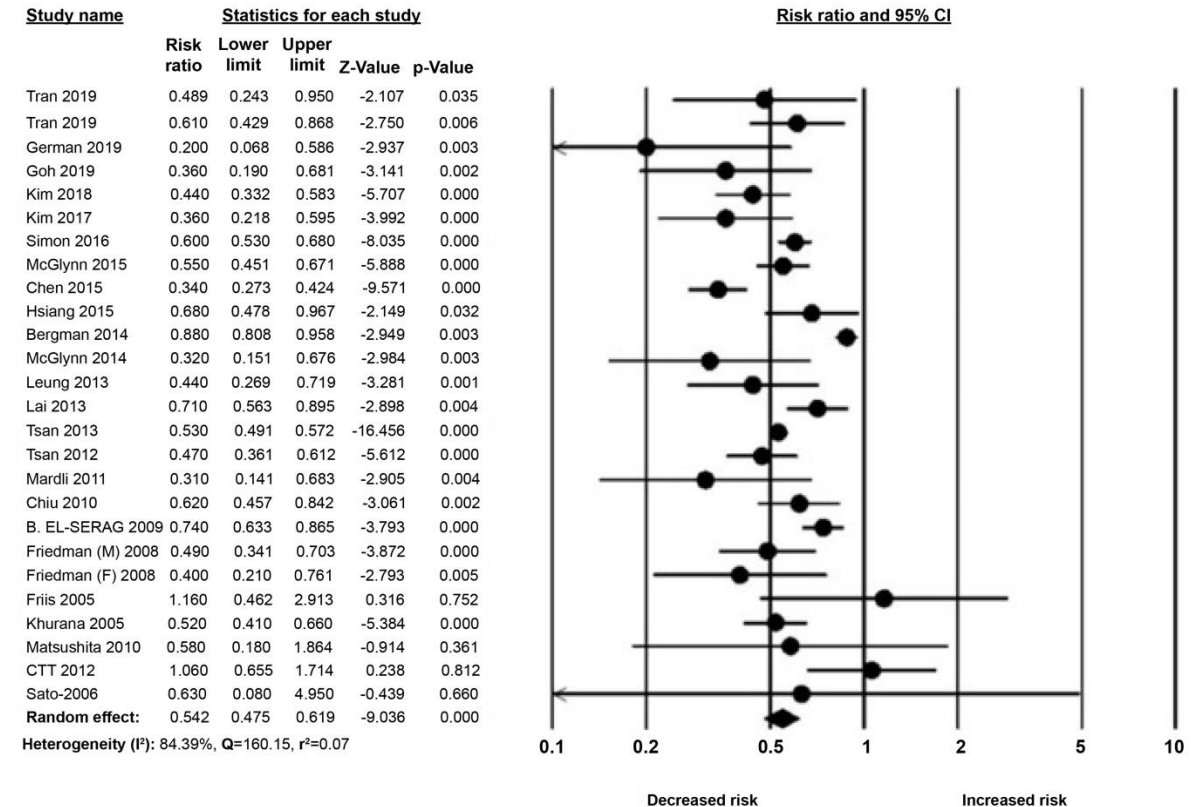
\*If glomerular filtration rate > 30 ml/min

# Statins Lower Portal HTN and HCC Risk

## Decreased Risk of Portal Hypertension<sup>1</sup>



## Decreased Risk for HCC<sup>2</sup>



<sup>1</sup>Wan et al. *BMJ Open*. 2019; <sup>2</sup>Islam et al. *Cancers*. 2020.

# Statins in Patients With MASLD

- Meta-analysis of Studies of Use of Statins in Patients with MASLD (n=12 publications)<sup>2</sup>
- Statins are indicated for CVD risk reduction in all patients<sup>3</sup>
- Statins can improve LDL cholesterol and liver function
- Statins are safe in patients with MASLD
- Consistent histologic data to support use of statins for the indication of MASLD/MASH are still pending

Open label pilot study of patients with biopsy proven MASH (n=20) rosuvastatin (10 mg /day x 52 weeks) improved liver enzymes (p<0.001) and resolved NASH in 19/20 (95%)<sup>1</sup>

**Statins are not approved for the treatment of MASLD/MASH.**

CVD, cardiovascular disease; LDL, low-density lipoprotein.

1. Kargiotios et al. *World J Gastroenterol*. 2015;21:7860–8; 2. Sigler et al. *Clin Med Insights Gastroenterol*. 2018;11:1–9; 3. Chalasani et al. *Hepatology*. 2018;67:328–57.

# Summary/Conclusions

- Calculate FIB-4 on patients at risk for MASLD/MASH. You only need age, AST, ALT and PLT.
- Order secondary risk assessment if FIB-4 >1.3.
  - Refer patients with intermediate or high-risk scores to liver specialist.
  - Manage patients deemed low risk (FIB-4 <1.3) in primary care.
    - Discuss lifestyle modifications to reduce weight.
    - Continue to manage comorbidities.
    - Recalculate FIB-4 every 1-2 years if T2DM/pre-T2DM or  $\geq 2$  metabolic risk factors (every 2-3 years if no T2DM and <2 metabolic risk factors).
- Coffee is good for the liver.
- Statins are safe in patients with MASLD.