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What Primary Care Clinicians Need to Know about MASLD and MASH

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What Primary Care Clinicians Need to Know about MASLD and MASH

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Disclosures

- **Scott Springer, PA-C,** has disclosed that he is an advisor and speaker for Abbvie and Gilead.

- **Austin Ulrich, PharmD,** medical writer, and **Michael Hanak**, MD, CME Reviewer, have no disclosures to report.

- All relevant financial relationships have been mitigated.

Learning Objectives

Participants in this presentation should be able to…
Apply evidence-based strategies for identifying and stratifying risk in patients at high risk for MASH.
Formulate strategies for diagnosing, staging, and monitoring MASLD/MASH with non-invasive tests and biomarkers.
Implement current treatment guidelines and care pathways in managing MASLD/MASH and underlying metabolic diseases.
Initiate referrals to specialists for patients with high-risk disease, including MASH as appropriate.

Introduction to MASLD and MASH

What are MASLD and MASH?

- Relatively new terms, converted from[1]:
  - NAFLD (nonalcoholic fatty liver disease)
  - NASH (nonalcoholic steatohepatitis)
- Rationale:
  - NAFLD and NASH were exclusionary terms, indicating diagnosis of exclusion
  - “Nonalcoholic” does not reflect the underpinnings of the disease
  - Steatohepatitis is a very important aspect of the disease and its main driver

MASLD = metabolic dysfunction-associated steatotic liver disease

MASH = metabolic dysfunction-associated steatohepatitis

1. Rinella ME. *Gastroenterol Hepatol (N Y)*. 2023;19(11):697-699.

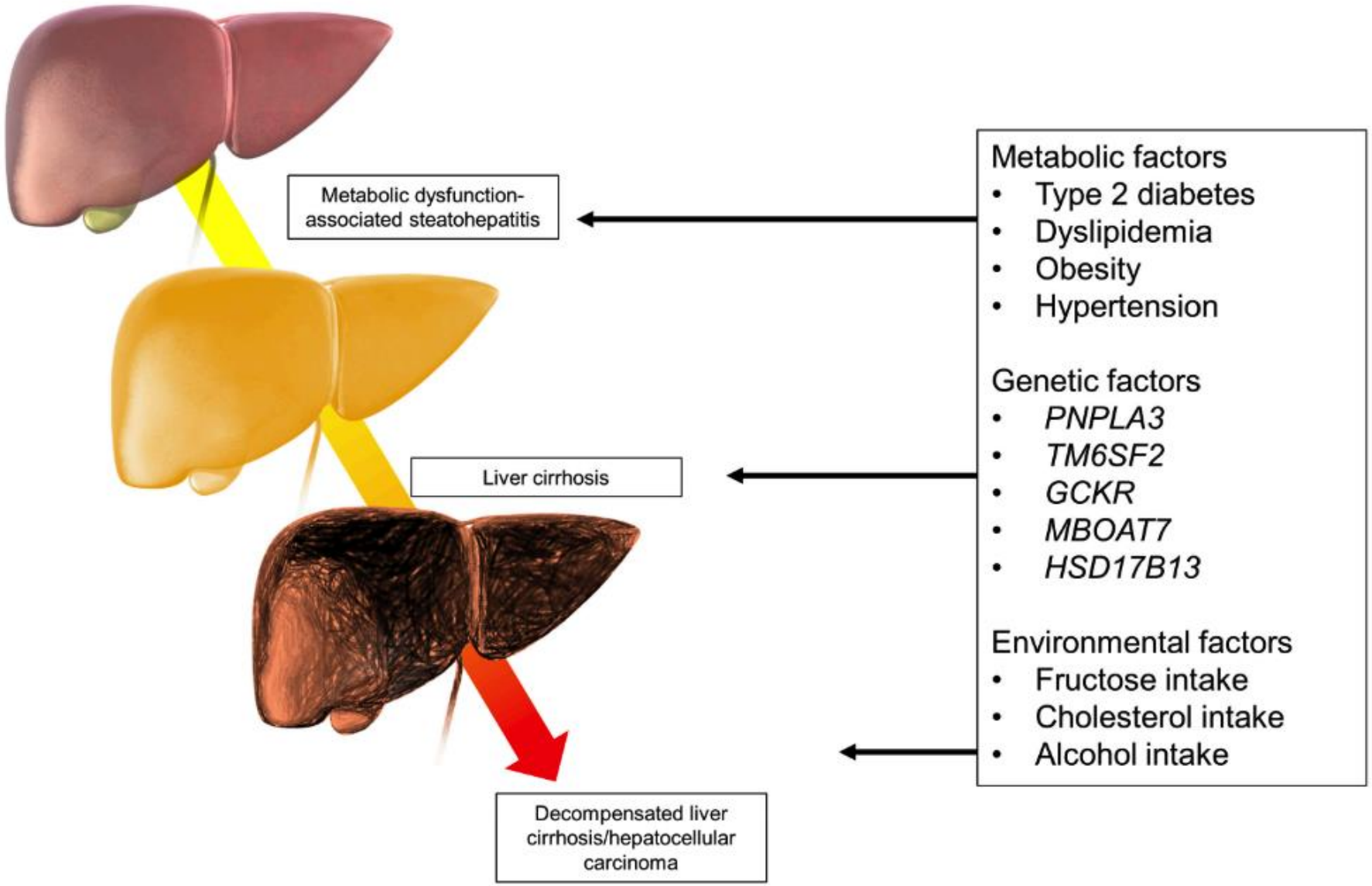
Prevalence

- MASLD is estimated to affect 30% of the adult population worldwide[1] and 41% of US adults by 2050[2]
- Globally, the prevalence of MASLD increased from 22% to 37% from 1991 to 2019[3]
- The burden of MASLD and its complications is expected to continue increasing in the coming years[4]
- Increasing MASLD prevalence parallels increases in obesity and obesity-related diseases[4]
- MASH has been found in up to 63% of patients with MASLD undergoing liver biopsy[5]
- MASLD and MASH burden is predicted to rise substantially by 2050 in the absence of effective treatments[2]

US, United States

1. Le MH, et al. *Clin Gastroenterol Hepatol.* 2022;20:2809-2817. 2. Le P, et al. *JAMA Netw Open*. 2025;8(1):e2454707. 3. Huh Y, et al. *J Obes Metab Syndr*. 2022;31:17-27. 4. Chan WK, et al. *J Obes Metab Syndr*. 2023;32(3):197-213. 5. Chan WK, et al. *Aliment Pharmacol Ther*. 2018;47:816-825.

Development and Progression of MASLD



Nagai K, et al. Frontiers of Collaboration between Primary Care and Specialists in the Management of Metabolic Dysfunction-Associated Steatotic Liver Disease: A Review. *Life (Basel)*. 2023;13(11):2144. Figure licensed under Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution, and reproduction. https://creativecommons.org/licenses/by/4.0/legalcode.

Clinical Burden of MASLD and MASH

Associated with severe complications such as CVD and end-stage liver disease

- CVD is the leading cause of mortality in patients with MASLD[1]

Widely underdiagnosed[2]

- Asymptomatic presentation until cirrhosis or hepatic decompensation is present

Earlier identification and diagnosis can help reduce burden

- Earlier intervention to reduce progression of liver disease
- Address contributing comorbidities

CVD, cardiovascular disease

1. Chan WK, et al. *J Obes Metab Syndr*. 2023;32(3):197-213. 2. Shieh C, et al. *JGH Open*. 2020;4(5):1002-1006.

Fibrosis - 4

- Fibrosis-4 (FIB-4) is a clinical marker used to evaluate the degree of **liver fibrosis (the higher the score, the greater the likelihood of significant liver fibrosis).**

- The formula for determining FIB-4 includes the patient's age, levels of two liver enzymes (AST and ALT) and the platelet count.

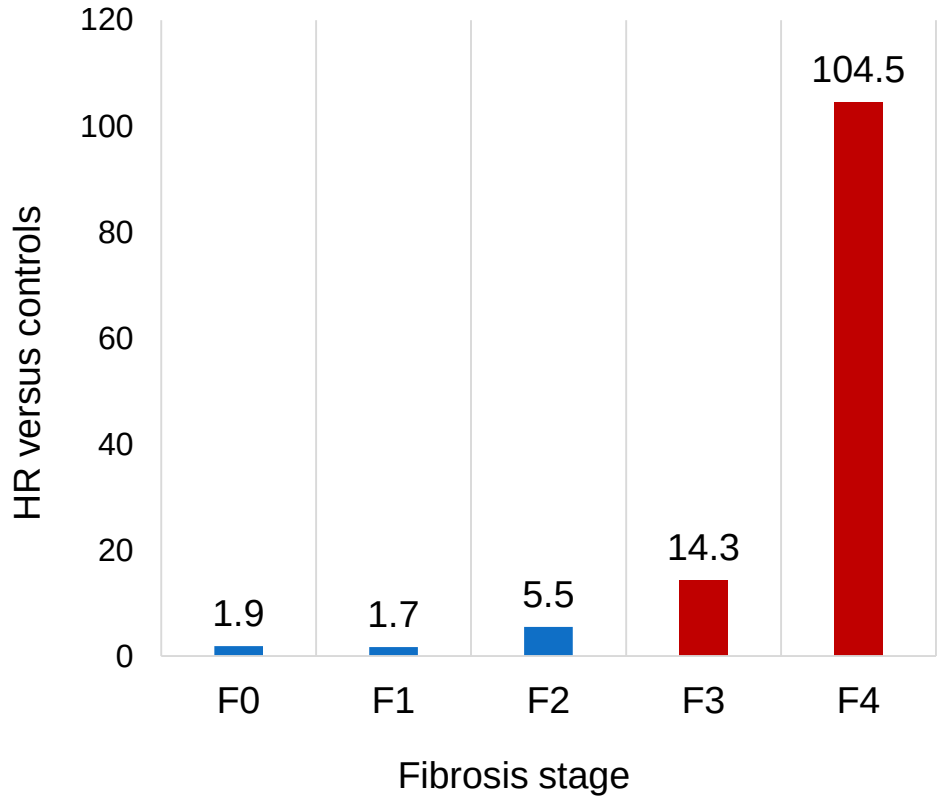
- **FIB-4 Score = (Age* x AST) / (Platelets x √ (ALT))***
- *Use with caution in patients <35 or >65 years old, as the score has been shown to be less reliable in these patients.

AST= Aspartate transaminase (AST): 8–33 U/L
ALT= Alanine transaminase (ALT): 4–36 U/L

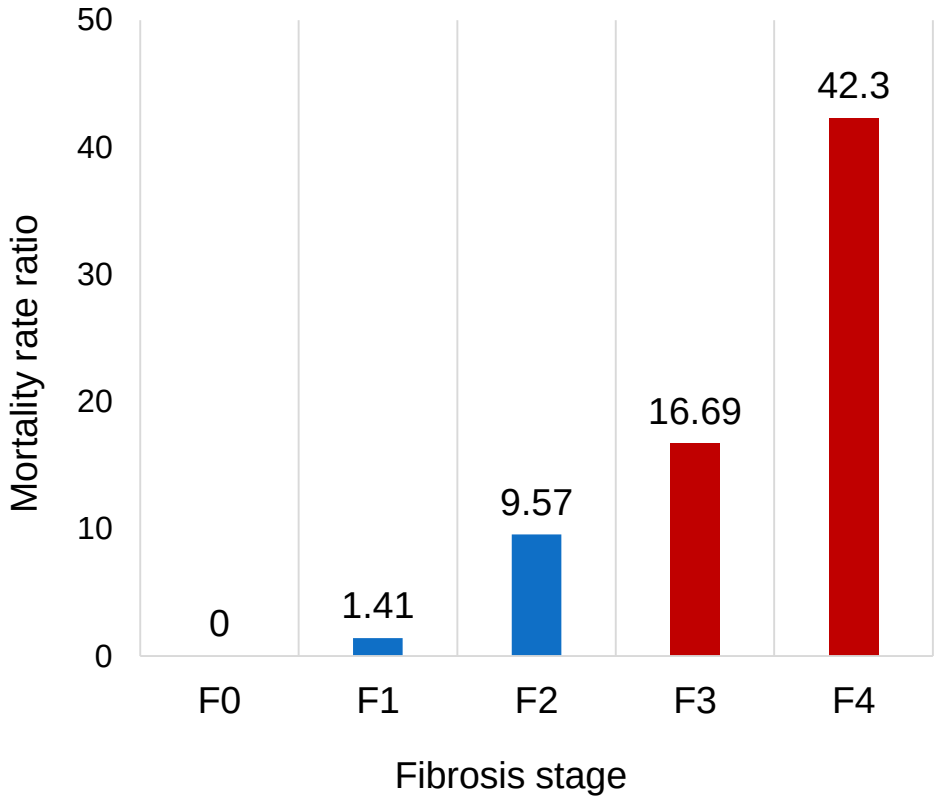
The Fatty Liver Foundation, FIB-4 Index, https://www.fattyliverfoundation.org/fib_4_index#gsc.tab=0. Accessed October 3, 2024.

Clinical Burden: Liver-Related Outcomes

Risk of severe liver disease[1]



Liver-related mortality[2]



MASLD increases risk of severe liver disease and liver-related mortality, particularly in advanced stages (F3-F4) of fibrosis and cirrhosis

1. Hagström H, et al. *J Hepatol*. 2017;67(6):1265-1273. 2. Dulai PS, et al. *Hepatology.* 2017;65(5):1557-1565.

Clinical Burden: Patient Perspectives

- MASLD and MASH may be perceived by some as asymptomatic conditions
- Multiple studies have shown that patients with MASH have poor quality of life[1,2]
- Patients may experience non-specific symptoms like fatigue or abdominal pain.[3]
- MASH is often accompanied by comorbidities such as dyslipidemia, hypertension, and T2D.[3]

Approximately 89% of patients with MASH report that their comorbidities have an impact on the severity of disease[3]

About 40% of patients feel that successful management of MASH would improve their symptoms[3]

T2D, type 2 diabetes

1. Younossi M, et al. *Am J Gastroenterol*. 2019;114(10):1636-1641. 2. McSweeny L, et al. *JHEP Rep*. 2020;2(3):100099. 3. Nadolsky K, et al. *Ann Med*. 2023;55(1):2211349.

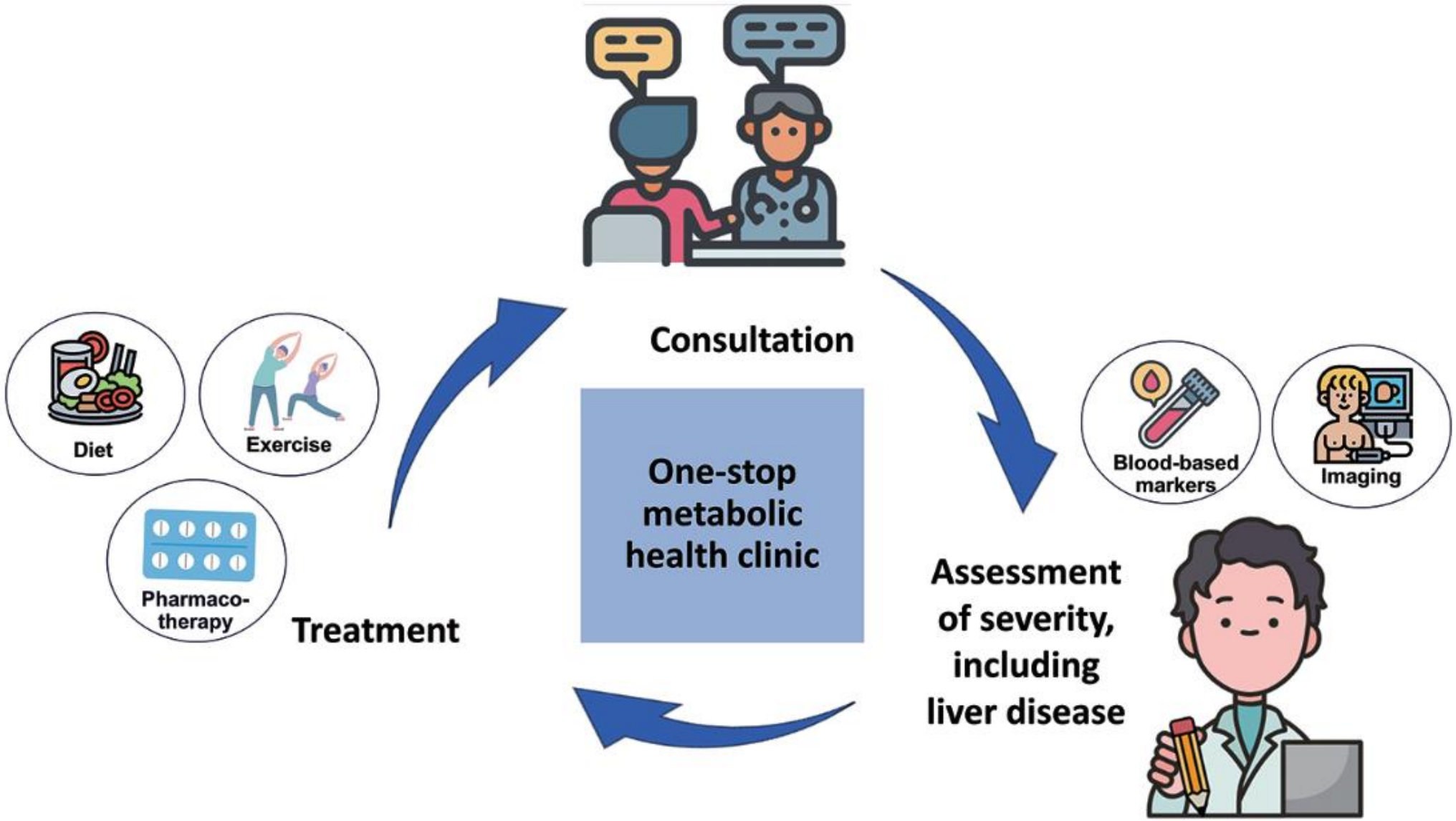
Multidisciplinary Care for MASLD and MASH

"A collaborative approach to MASH and liver disease care has the potential to positively affect MASH progression and the deleterious complications it can impart to patients and their families." [1]

Sujit V. Janardhan, MD, PhD, Dipl ABOM
Medical Director of Liver Transplant
Director of the Weight Intervention in Liver Disease Clinical Program
Assistant Professor, Rush University Medical Center

1. Janardhan S. MASLD requires multidisciplinary care to 'improve global metabolic, liver health.' Published February 19, 2024. Accessed March 18, 2024. https://www.healio.com/news/gastroenterology/20240214/masld-requires-multidisciplinary-care-to-improve-global-metabolic-liver-health

Example model of an integrated multidisciplinary clinic for MASLD and MASH



The Primary Care Clinician's (PCC's) Role

Non-hepatology clinicians are needed to handle the anticipated burden of MASH-related advanced liver disease expected to flood the health care system[1]

Patients with less severe MASLD are best managed in primary care[2]

Potential Roles of PCCs for Identification and Management of MASLD/MASH
Screening, diagnosis, risk stratification
Treatment of less-severe disease
Referral to specialists

1. Janardhan S. MASLD requires multidisciplinary care to 'improve global metabolic, liver health.' Published February 19, 2024. Accessed March 18, 2024. https://www.healio.com/news/gastroenterology/20240214/masld-requires-multidisciplinary-care-to-improve-global-metabolic-liver-health 2. Chan WK, et al. *J Obes Metab Syndr*. 2023;32(3):197-213.

Patient and PCC Survey on MASLD/MASH

Cross-sectional survey on diagnosis and treatment of MASLD/MASH in primary care[1]:

- 72% of patients had initial discussions about their symptoms with a PCC
  - Only 30% received a diagnosis of MASH
- Patients saw an average of 1.7 healthcare professionals for their symptoms
  - Most (65%) saw a PCC for MASLD/MASH
- In the survey, PCCs noted that they personally diagnose most patients with MASH in the primary care setting
  - About one-third of patients are referred to other healthcare professionals for diagnosis

1. Nadolsky K, et al. *Ann Med*. 2023;55(1):2211349.

Patient Case Scenario

A 57-year-old woman with T2D and obesity presents to establish care at a new primary care clinic. She notes that she is concerned about “dying from heart disease” because that’s what happened to her parents. She consumes 5-6 alcoholic beverages per week.

- Medical history: T2D (12 years), obesity, hypothyroidism, osteoporosis, hypertension
- Labs: HbA1c 8.7%, fasting triglycerides 200 mg/dL, fasting glucose 140 mg/dL
- Medications: metformin, glipizide, insulin glargine, lisinopril, hydrochlorothiazide, levothyroxine, alendronate

What indicates the patient should be screened for MASLD/MASH?

What needs to be addressed for her related comorbidities?

Patient Case Scenario (cont)

A 57-year-old woman with T2D and obesity presents to establish care at a new primary care clinic. She notes that she is concerned about “dying from heart disease” because that’s what happened to her parents. She consumes 5-6 alcoholic beverages per week.

- Medical history: T2D (12 years), obesity, hypothyroidism, osteoporosis, hypertension, ASCVD
- Labs: HbA1c 8.7%, fasting triglycerides 200 mg/dL, fasting glucose 140 mg/dL
- Medications: metformin, glipizide, insulin glargine, lisinopril, hydrochlorothiazide, levothyroxine, alendronate

The patient has risk factors for MASLD: T2D, obesity, hypertension, likely insulin resistance, elevated triglycerides, and alcohol intake

- **She needs to be screened, then diagnosed and risk stratified if steatotic liver disease is found**

She is not currently receiving optimal treatment for her metabolic comorbidities

- **Needs high intensity statin**
- **If MASLD/MASH are diagnosed, treatment should also address liver issues**

Screening, Diagnosis, and Risk Stratification

Identify Patients at Risk

Patients at greatest risk who would benefit most from screening[1-3]:

Patients who have overweight or obesity
Patients with T2D or prediabetes
Patients with one or more features of metabolic dysregulation: • Central adiposity • Insulin resistance • Obstructive sleep apnea • Triglycerides > 150 mg/dL • HDL cholesterol < 50 mg/dL (men) or < 40mg/dL (women) • Blood pressure ≥ 130/85 mmHg
Patients with a family history of MASLD

HDL, high-density lipoprotein

1. Kanwal F, et al. *Gastroenterology*. 2021;161(5):1657-1669. 2. Rinella ME, et al. *Hepatology*. 2023;78(6):1966-1986. 3. Rinella ME, et al. *Hepatology*;77(5):1797-1835.

MASLD Diagnostic Criteria

Positive diagnostic criteria for MASLD[1,2]

Hepatic steatosis detected by imaging or biopsy, plus at least 1 of 5 characteristics:

1. BMI ≥ 25 kg/m^2 (≥ 23 kg/m^2 in Asians) or waist circumference > 94 cm in men, > 80 cm in women, or ethnicity adjusted
2. Fasting serum glucose ≥ 100 mg/dL or 2-hour post-load glucose level ≥ 140 mg/dL or HbA1c ≥ 5.7% or receiving antihyperglycemic drug treatment for
3. Blood pressure ≥ 130/85 mmHg or specific drug treatment for hypertension
4. Plasma triglycerides ≥ 150 mg/dL or specific drug treatment
5. Plasma HDL cholesterol < 40 mg/dL for men and < 50 mg/dL for women or specific drug treatment

BMI, body mass index

1. Rinella ME, et al. *Hepatology*. 2023;78(6):1966-1986. 2. Chan WK, et al. *J Obes Metab Syndr*. 2023;32(3):197-213.

Noninvasive Testing

Liver biopsy is the gold standard to diagnose and stage severity of liver fibrosis[1]

- Invasive, not feasible to use for initial screening or detection

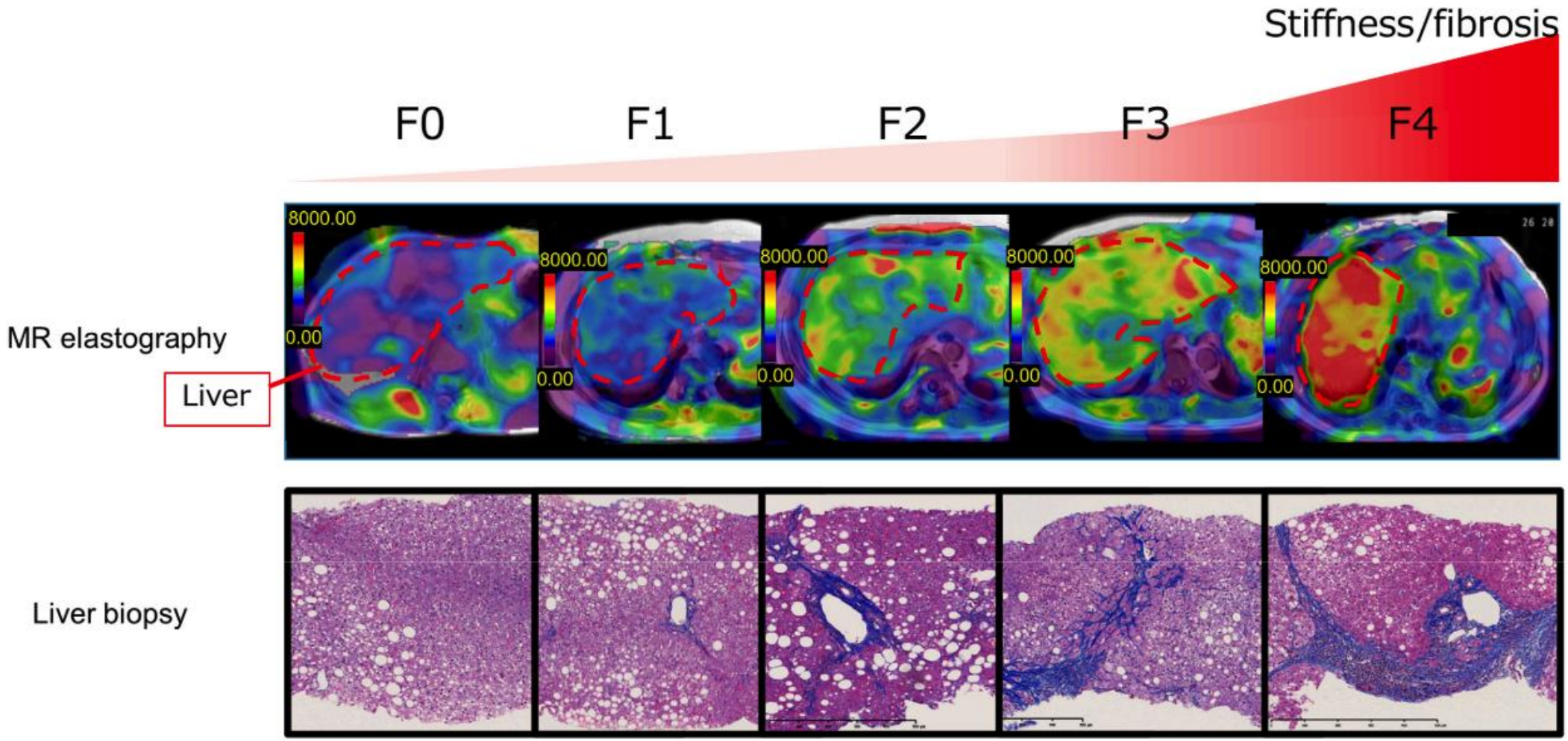
Validated noninvasive testing can detect disease and stratify risk[2]

- Fibrosis 4 Index (FIB-4) score < 1.3 may be useful for excluding advanced hepatic fibrosis in patients with MASLD
  - Magnetic resonance imaging (MRI)-AST (MAST) and FibroScan-AST (FAST) may perform better than FIB-4 for identifying patients with or at risk for MASH[3]
- Additional testing (liver stiffness, biomarkers) for risk stratification if FIB-4 score is > 1.3
- Patients with results suggesting advanced liver fibrosis or cirrhosis should be monitored with elastography

Clinical practice guidelines recommend stratifying risk in patients with MASLD using noninvasive testing, limiting patients who are referred to specialists to those with high risk for advanced liver disease[4,5]

1. Chan WK, et al. *J Obes Metab Syndr*. 2023;32(3):197-213. 2. Wattacheril JJ, et al. *Gastroenterology*. 2023;165(4):1080-1088. 3. Qi S, et al. *J Gastroenterol Hepatol*. 2024;39(8):1565-1662. 4. Kanwal F, et al. *Gastroenterology*. 2021;161(5):1657-1669. 5. Cusi K, et al. *Endocr Pract*. 2022;28(5):528-562.

Correlation of Fibrosis/Stiffness with MR Elastography and Biopsy



MR, magnetic resonance

Risk Stratification

Fibrosis 4 index is useful as an initial test to screen for advanced liver fibrosis[1]

- High negative predictive value - reliable at excluding advanced fibrosis if score is < 1.3
- Suboptimal positive predictive value[2]

Patients with an elevated Fibrosis 4 score should undergo liver stiffness measurement (LSM)[1]

- **Risk stratification**
- Can help identify compensated advanced chronic liver disease (cACLD) and clinically significant portal hypertension (CSPH)

Liver biopsy or elastography considered for patients with indeterminate or discordant noninvasive test results

Based on risk, monitor with noninvasive testing, referral for elastography or liver biopsy, or referral to a specialist for further workup and management

1. Chan WK, et al. *J Obes Metab Syndr*. 2023;32(3):197-213. 2. Chan WK, et al. *Clin Gastroenterol Hepatol*. 2019;17:2570-2580.

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Patients with an elev…ement (LSM)[1]

- **Risk stratification**
- Can help identify co…ant portal hypertension (CSPH)

Noninvasive tests can be used for risk stratification in the diagnostic evaluation of MASLD

Liver biopsy or elastography considered for patients with indeterminate or discordant noninvasive test results

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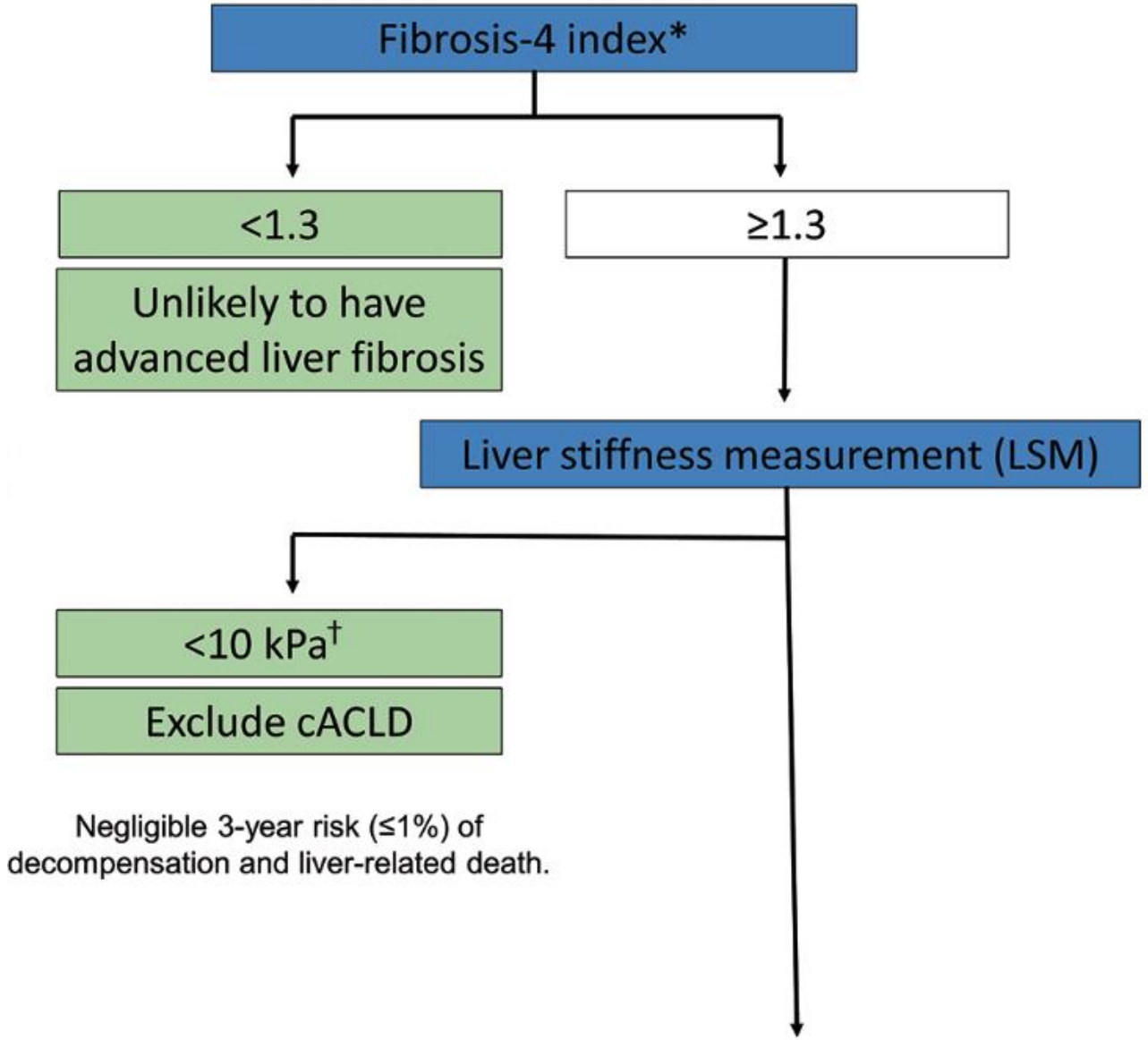
1. Chan WK, et al. *J Obes Metab Syndr*. 2023;32(3):197-213. 2. Chan WK, et al. *Clin Gastroenterol Hepatol*. 2019;17:2570-2580.

Example algorithm for noninvasive testing of MASLD and MASH



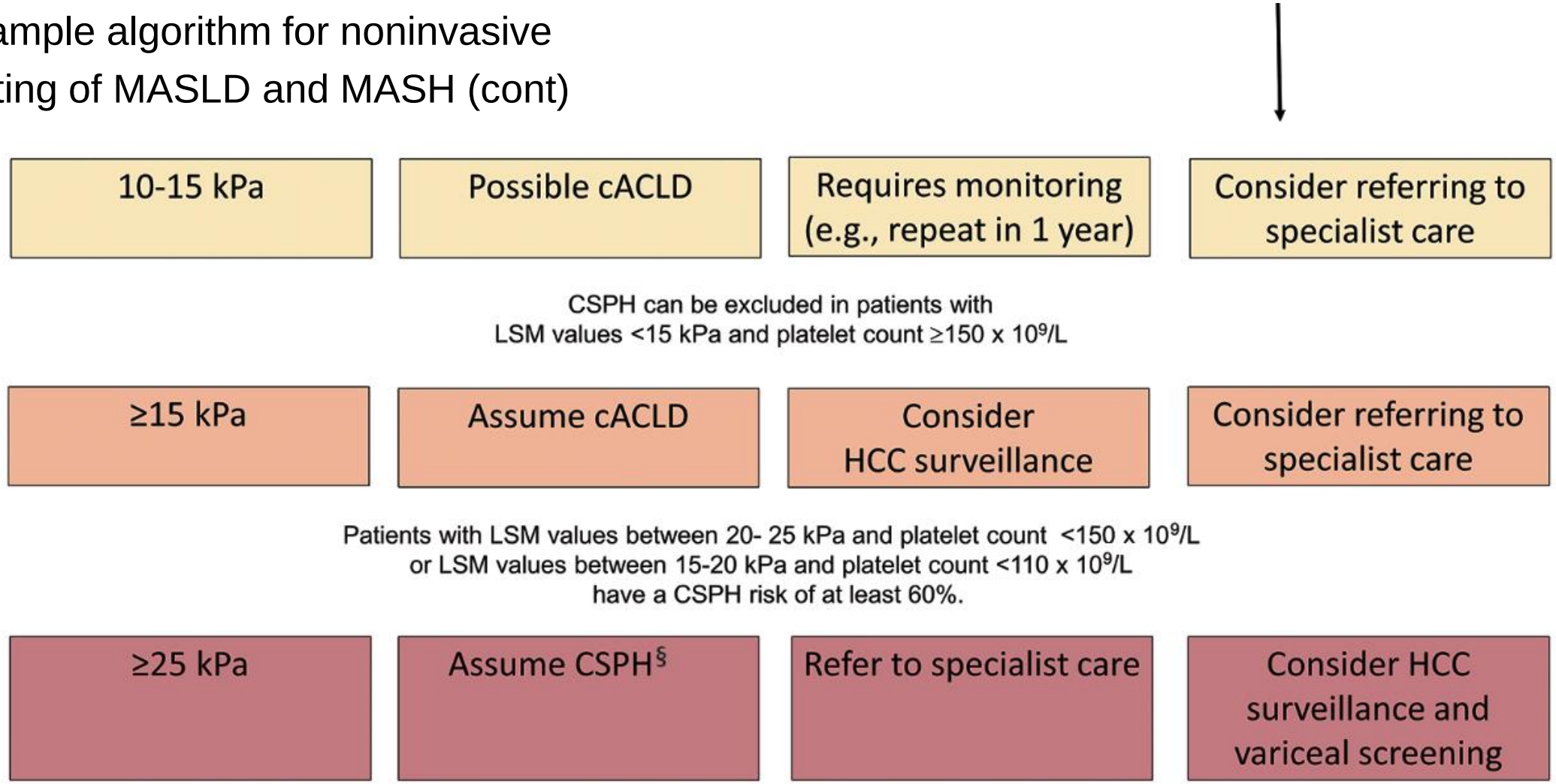
*For patients ≥65 years old, fibrosis-4 index cut-off 2.0 (instead of 1.3) may be used to improve specificity

† Sensitivity and negative predictive value > 90%

cACLD, compensated advanced chronic liver disease

Chan WK et al. Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD): A State-of-the-Art Review. *J Obes Metab Syndr*. 2023;32(3):197-213.

Example algorithm for noninvasive testing of MASLD and MASH (cont)



§ Specificity and positive predictive value >90%

CSPH, clinically significant portal hypertension; HCC, hepatocellular carcinoma

Treatment of MASLD, MASH, and Metabolic Comorbidities in Primary Care

Guidelines Review: AGA

The AGA Clinical Care Pathway emphasizes several steps for identifying, diagnosing, and managing MASLD[1]

1. Identify patients at risk
2. Obtain history and laboratory tests
3. Conduct noninvasive testing (Fibrosis 4 Index score)
4. Conduct LSM (if Fibrosis 4 score is 1.3 to 2.67)
5. Initiate treatment or referral based on risk
   - Low risk: repeat noninvasive tests in 2-3 years unless clinical circumstances change
   - Indeterminate risk: refer to hepatology for liver biopsy or MR elastography or monitor with re-evaluation in 2-3 years
   - High risk: refer to hepatologist

AGA, American Gastroenterological Association

1. Kanwal F, et al. *Gastroenterology*. 2021;161(5):1657-1669.

Guidelines Review: AASLD/AACE

AASLD/AACE key guidance statements for treatment[1]

- "Patients with [MASLD] who are overweight or obese should be prescribed a **diet that leads to a caloric deficit** … diets with limited carbohydrates and saturated fat and enriched with high fiber and unsaturated fats"
- "Patients with [MASLD] should be strongly encouraged to **increase their activity level** to the extent possible"
- "**Bariatric surgery should be considered as a therapeutic option** in patients who meet criteria for metabolic weight loss surgery"
- "… **drugs approved to treat associated comorbidities** with potential benefit in [MASLD] **may be considered** in the appropriate clinical setting"
- "**Semaglutide can be considered** for its approved indications ([T2D]/obesity) in patients with [MASH], as it confers a cardiovascular benefit and improves [MASH]"
- "**Pioglitazone** improves [MASH] and can be considered for patients with [MASH] in the context of patients with [T2D]"

AASLD, American Association for the Study of Liver Diseases; AACE, American Association of Clinical Endocrinology

1. Rinella ME, et al. *Hepatology.* 2023;77(5):1797-1835.

Guidelines Review: EASL-EASD-EASO

Published June 2024; key guidance statements for treatment[1]

- "… dietary and **behavioral therapy-induced weight loss should be recommended** to improve liver injury"
- "In adults with MASLD and overweight, weight loss should aim at a sustained reduction of **≥5% to reduce liver fat, 7%-10% to improve liver inflammation, and ≥10% to improve fibrosis**"
- "Adults with non-cirrhotic MASH with significant liver fibrosis (stage ≥2) should be considered for **treatment with resmetirom as a MASH-targeted therapy** …"
- Treatment with **resmetirom may be considered for individuals with MASLD** without cirrhosis who have advanced fibrosis, at-risk steatohepatitis with significant fibrosis, or risk of adverse liver-related outcomes
- **GLP-1 RAs, pioglitazone, are safe to use in MASH** and should be used for their indications
- **SGLT-2 inhibitors, and metformin are safe to use in MASLD** and should be used for their indications
- In adults with non-cirrhotic MASLD who have an approved indication, **bariatric surgery should be considered**

EASL, European Association for the Study of the Liver; EASD, European Association for the Study of Diabetes; EASO, European Association for the Study of Obesity; GLP-1 RAs, glucagon-like peptide-1 receptor agonists; SGLT-2, sodium-glucose cotransporter-2

1. European Association for the Study of the Liver (EASL), European Association for the Study of Diabetes (EASD), European Association for the Study of Obesity (EASO). *J Hepatol*. 2024;S0168-8278(24)00329-5. doi:10.1016/j.jhep.2024.04.031

Lifestyle Interventions

Lifestyle intervention is a cornerstone in management of MASLD and MASH[1]

- Emphasize at all levels of care with the aim to improve liver and cardiometabolic health
- Can lead to weight loss, which may result in resolution of MASH and improvement in liver fibrosis

Physical activity recommendations:

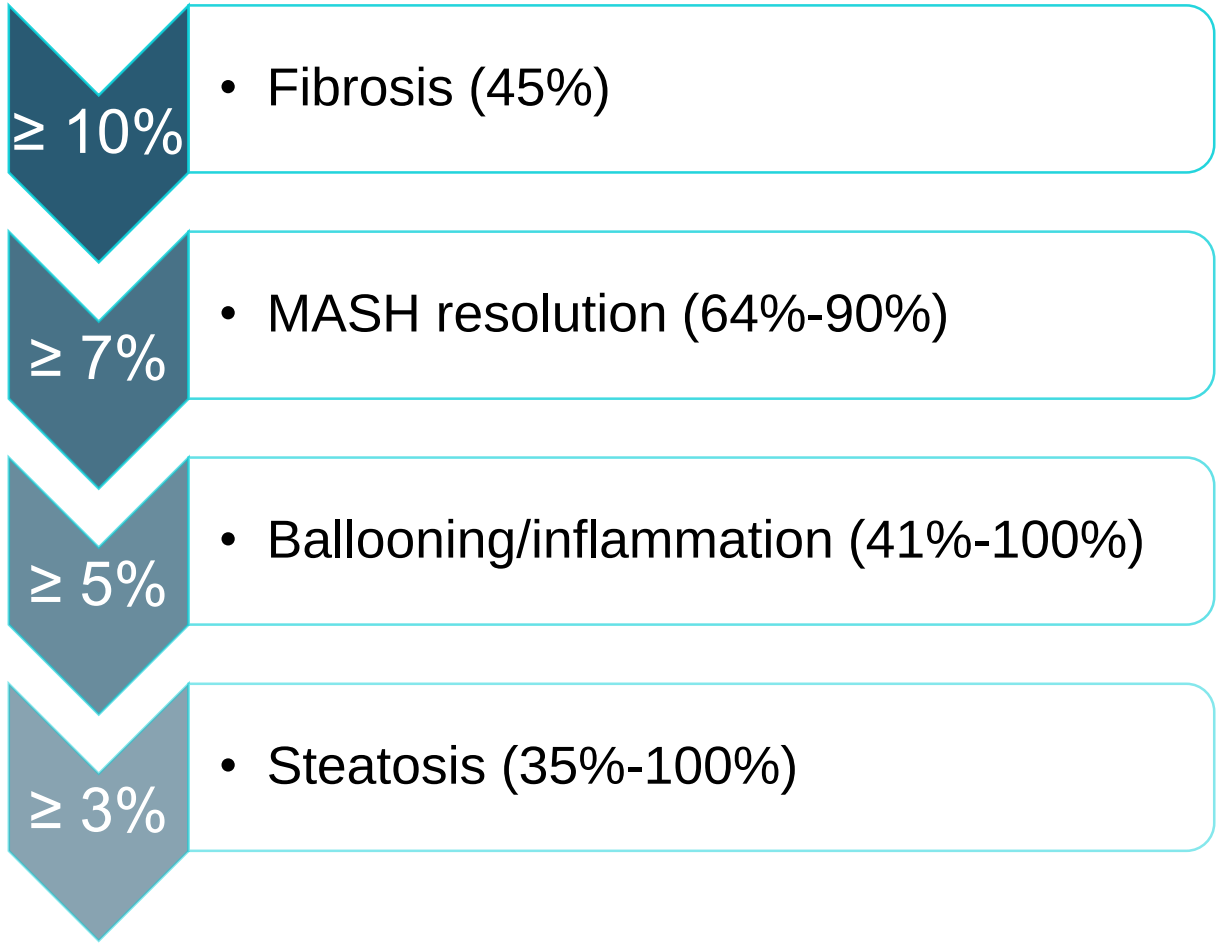
- 30 minutes per day of moderate intensity exercise for at least 150 minutes per week
- 20 minutes per day of vigorous intensity exercise for at least 75 minutes per week

1. Chan WK, et al. *J Obes Metab Syndr*. 2023;32(3):197-213.

Weight Loss Impact on MASLD and MASH

Weight reduction is associated with improvements in MASLD/MASH[1]

Greater weight loss yields greater benefits on liver symptoms[1]



1. Hannah WN, Harrison SA. *Clin Liver Dis*. 2016;20(2):339-350.

Pharmacotherapy Considerations

Historically, there were no approved MASLD/MASH pharmacotherapeutic agents for many years[1]

- Pioglitazone and GLP-1 RAs (liraglutide, semaglutide) have demonstrated efficacy in reversing MASH
- SGLT-2 inhibitors have also been recommended as adjunctive agents

Resmetirom is currently the only pharmacologic agent approved for treating either MASLD or MASH (FDA approval March 2024)

- Phase 3 study: MAESTRO-NASH[2]
  - Patients with biopsy-confirmed MASH and fibrosis stage F1B, F2, or F3
  - Those taking resmetirom experienced improved liver outcomes compared to those who received placebo
    - Significantly higher rates of MASH resolution
    - Improvement in liver fibrosis by at least one stage

GLP-1 RAs, glucagon-like peptide-1 receptor agonists; SGLT-2, sodium-glucose cotransporter-2

1. Chan WK, et al. *J Obes Metab Syndr*. 2023;32(3):197-213. 2. Harrison SA, et al. *N Engl J Med*. 2024;390(6):497-509.

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- Phase 3 study: MA
  - Patients with biop
  - Those taking resmetirom experienced improved liver outcomes compared to those who received placebo
    - Significantly higher rates of MASH resolution
    - Improvement in liver fibrosis by at least one stage

Pioglitazone, GLP-1 RAs, SGLT-2 inhibitors, and metformin are not currently approved for treating MASH

GLP-1 RAs, glucagon-like peptide-1 receptor agonists; SGLT-2, sodium-glucose cotransporter-2

1. Chan WK, et al. *J Obes Metab Syndr*. 2023;32(3):197-213. 2. Harrison SA, et al. *N Engl J Med*. 2024;390(6):497-509.

Many Agents Have Been Studied for MASLD/MASH

Class	Agent(s)	Mechanism of Action
Incretins	Semaglutide*, liraglutide*	GLP-1 RA
	Tirzepatide*	GLP-1 and GIP receptor agonist
	Survodutide	Glucagon and GLP-1 receptor agonist
Farnesoid X receptor (FXR) agonists	Obeticholic acid*, tropifexor	FXR agonist
Peroxisome proliferator-activated receptor (PPAR) agonists	Pioglitazone*	PPARγ agonist
	Saroglitazar	PPARα/γ agonist
	Elafibranor	PPARα/δ agonist
Fibroblast growth factor (FGF) analogues	Pegbelfermin, efruxifermin	FGF21 analogue
	Aldafermin	FGF19 analogue
Other	Aramchol	Inhibits de novo lipid synthesis
	Cenicriviroc	Chemokine receptors 2 and 5 agonist
	Selonsertib	ASK1 inhibitor

ASK, Apoptosis signal-regulating kinase; GIP, glucose-dependent insulinotropic polypeptide

*FDA-approved for another indication

1. Branković M, et al. *Diagnostics (Basel)*. 2024;14(2):229.

MASLD/MASH Data for Agents Approved in Other Conditions

Agent	Study	Patients	Results
Semaglutide	Phase 2 study[1]	MASH with F1, F2, or F3 fibrosis	Significantly higher percentage of MASH resolution
	10-year retrospective study[2]	MASH without cirrhosis	Improvement in transaminases and MASH scores (NFS, FIB4, APRI)
Liraglutide	LEAN[3]	Overweight and clinical evidence of MASH	Significantly higher percentage of MASH resolution
Tirzepatide	Phase 2 T2D study[4]	T2D	Significant decrease in MASH biomarkers and increase in adiponectin
Obeticholic acid	REGENERATE[5]	MASH with F2 or F3 fibrosis, or F1 with comorbidities	Significant improvement in fibrosis and reduction in disease activity
	FLINT[6]	MASH without cirrhosis	Significant histological improvement, but not significant improvement in MASH resolution
Pioglitazone	Meta-analysis[7]	Patients with MASH across 8 randomized trials	Improvement in advanced fibrosis and overall fibrosis stages, resolution of MASH

1. Newsome PN, et al. *N Engl J Med*. 2021;384(12):1113-1124. 2. Shah P, et al. *JGH Open*. 2024;8(2):e13037. 3. Armstrong MJ, et al. *Lancet*. 2016;387(10019):679-690. 4. Hartman ML, et al. *Diabetes Care.* 2020;43(6):1352-1355. *5*. Ratziu V, et al. *Contemp Clin Trials.* 2019;84:105803. 6. Neuschwanter-Tetri BA, et al. *Lancet*. 2015;385(9972):956-965. 7. Musso G, et al. *JAMA Intern Med*. 2017;177(5):633-640.

Managing Comorbidities

Treatment recommendations for patients with metabolic comorbidities and MASLD/MASH are focused on addressing[1]:

1. Cardiometabolic risk factors (glycemia, BP, lipids, body weight)
2. Steatohepatitis, especially with clinically significant fibrosis (stage F2-F4)

Initiating pharmacologic therapy to address comorbidities and MASLD/MASH can be based on noninvasive testing[1]:

1. Elevated Fibrosis 4 score (>1.3)
2. Elevated serum aminotransferase level
3. Imaging (transient elastography, MR elastography)
4. Plasma biomarkers for liver fibrosis

1. Chan WK, et al. *J Obes Metab Syndr*. 2023;32(3):197-213.

Pharmacotherapy for MASLD/MASH-Associated Comorbidities

Comorbidity	Recommended target	Preferred therapy
Hypercholesterolemia	• Moderate or intermediate risk (diabetes alone): < 100 mg/dL • Higher risk (diabetes+multiple other ASCVD risk factors): < 70 mg/dL • High risk (established ASCVD): < 55 mg/dL	• First line: Statin at appropriate dose/intensity for risk category • Second line: add non-statin agent if target not achieved on maximum tolerated statin dose
Hypertriglyceridemia	<150 mg/dL	Intensify lifestyle modification and optimize glycemic control; statin therapy can reduce triglycerides
Hypertension	• Treat if BP ≥ 140/90 mmHg in all patients • Treat if BP ≥ 130/80 mmHg in diabetes or ASCVD risk ≥ 10% • Aim for BP 120–129/70–79 mmHg	RAS blockade preferred if albuminuria present or patient has ischemic heart disease or heart failure

ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; RAS, renin-angiotensin system

1. Chan WK, et al. *J Obes Metab Syndr*. 2023;32(3):197-213.

Pharmacotherapy for MASLD/MASH-Associated Comorbidities (cont)

Comorbidity	Recommended target	Preferred therapy
Obesity	• Ethnicity- and gender-specific targets • BMI: < 23 kg/m^2 for Asians and < 25 kg/m^2 for Caucasians • Weight loss ≥ 5%	• Lifestyle modification • Adjunctive GLP-1 RA or incretin-based agent with proven cardiovascular benefit if BMI ≥ 27 kg/m^2 with comorbidities or BMI ≥ 30 kg/m^2 without comorbidities
T2D	HbA1c <6.5%	• SGLT-2 inhibitor preferred in patients with CVD/heart failure/CKD • GLP-1 RA preferred in patients with CVD/albuminuria

CKD, chronic kidney disease

1. Chan WK, et al. *J Obes Metab Syndr*. 2023;32(3):197-213.

Surgical Considerations

- Bariatric surgery is an important tool to assist in meeting weight loss goals[1,2]
  - Should be considered for appropriate candidates sigh significant fibrosis, obesity, and other comorbidities

- Patients should be offered the option of bariatric surgery based on BMI and comorbidities[1,2]:
  - BMI ≥ 35 kg/m^2
  - BMI 30-34.9 kg/m^2 with metabolic comorbidities

- Studies have demonstrated improvement in MASLD/MASH histology after bariatric surgery

1. Kanwal F, et al. *Gastroenterology*. 2021;161(5):1657-1669. 2. Chalasani N, et al. *Gastroenterology*. 2012;142:1592-1609. 3. Lassailly G, et al. *Gastroenterology*. 2020;159:1290-1301. 4. Verrastro O, et al. *Lancet.* 2023;401:1786-1797.

Patient Case Scenario (revisited)

A 57-year-old woman with T2D and obesity presents to establish care at a new primary care clinic. She notes that she is concerned about “dying from heart disease” because that’s what happened to her parents.

- Medical history: T2D, obesity, hypothyroidism, osteoporosis, hypertension, ASCVD
- Labs: HbA1c 8.7%, fasting triglycerides 200 mg/dL, fasting glucose 140 mg/dL
- Medications: metformin, glipizide, insulin glargine, lisinopril, hydrochlorothiazide, levothyroxine, alendronate, simvastatin
- Fibrosis 4 score: 1.5, LSM 17 kPa. Liver biopsy positive for steatosis.

What interventions could you make to her treatment regimen to better address comorbidities and potentially MASLD/MASH?

Patient Case Scenario (revisited, cont)

A 57-year-old woman with T2D and obesity presents to establish care at a new primary care clinic. She notes that she is concerned about “dying from heart disease” because that’s what happened to her parents.

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- **Emphasize lifestyle interventions**
- **Adjust antihyperglycemic medication to agents with benefit in MASLD/MASH**
  - **GLP-1 RA, pioglitazone**
- **Adjust medications to promote weight loss**
  - **Discontinue glipizide, possibly insulin depending on response to new therapy**
- **Increase statin to high intensity**

Additional Resource: AGA App for MASLD/MASH

The American Gastroenterological Association (AGA) has initiated a multidisciplinary effort to align clinicians, including PCCs, to improve diagnosis and management of MASLD/MASH.

The free AGA NASH App contains a clinical care pathway that can be a useful and practical resource for clinicians managing patients with MASLD/MASH.

AGA NASH App 17+

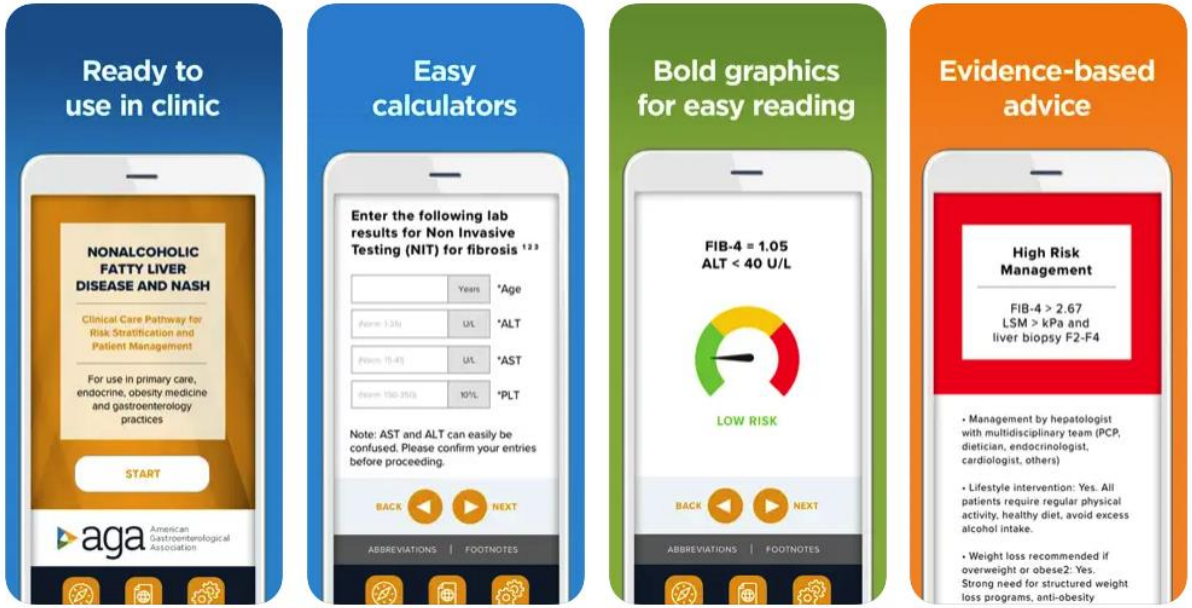
American Gastroenterological Association

★★★★★ 5.0 • 1 Rating

Free

https://nash.gastro.org/

iPhone Screenshots



Key Takeaways

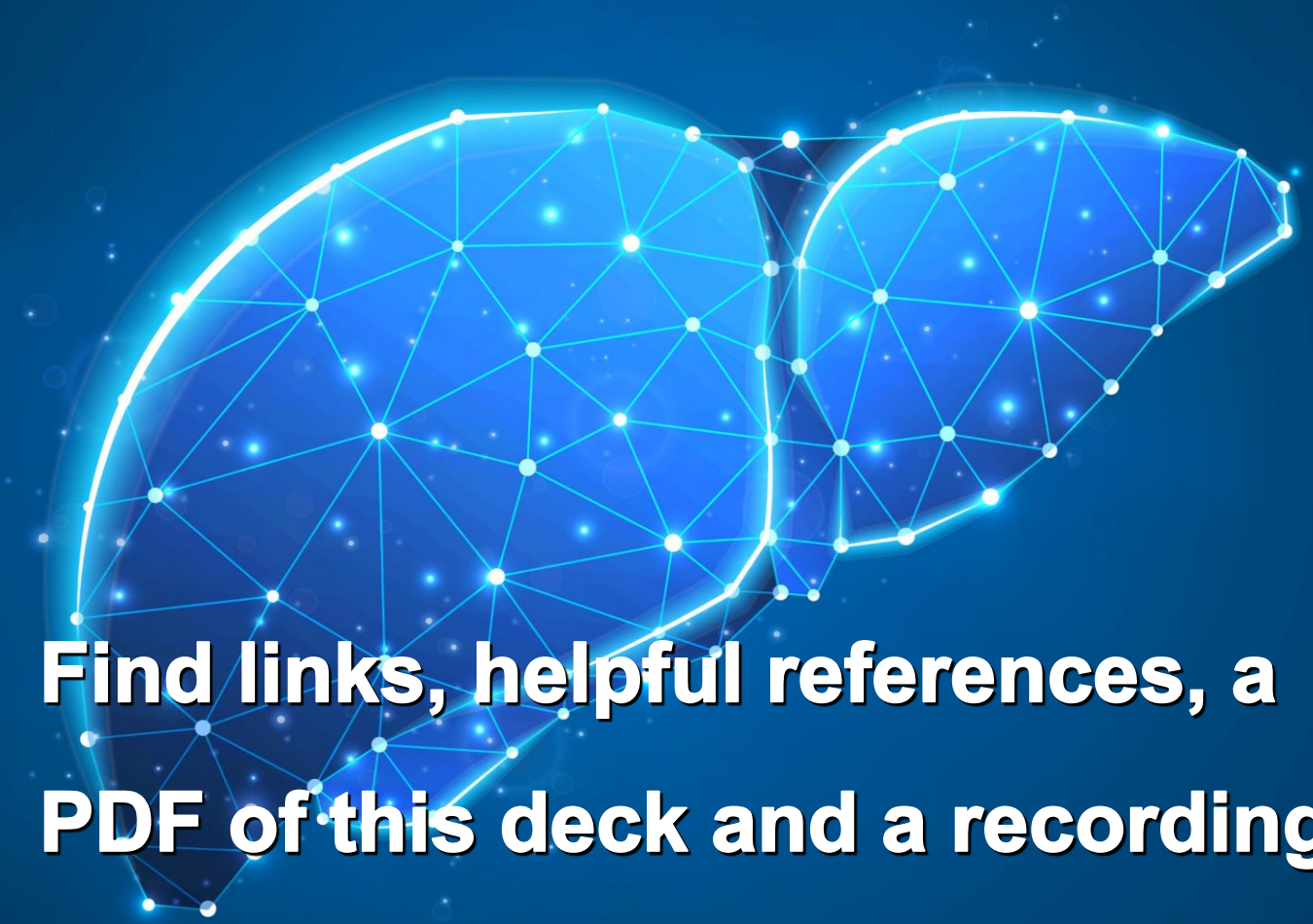
- MASLD and MASH are common diseases with significant clinical consequences and patient burden
- Collaborative, multidisciplinary approaches to managing MASLD and MASH is ideal, when possible
- In primary care settings, PCCs can successfully screen for, diagnose, and stratify risk for patients with MASLD/MASH; they can also treat less-severe disease and refer to a specialist
- Screening for MASLD involves identifying patients at risk, obtaining relevant patient history and laboratory tests, conducting noninvasive liver testing and LSM to stratify risk
- Treatment of MASLD and MASH involves improving liver and cardiometabolic health
- Weight loss, resmetirom, GLP-1 RAs, and other treatments can help improve liver complications

QR Code for

Resource Toolkit

https://www.pcmg-us.org/toolkit/MASH

Resource Toolkit



Find links, helpful references, a PDF of this deck and a recording of this presentation.

Let’s review what we’ve covered…

Participants in this presentation should be able to…
Apply evidence-based strategies for identifying and stratifying risk in patients at high risk for MASH.
Formulate strategies for diagnosing, staging, and monitoring MASLD/MASH with non-invasive tests and biomarkers.
Implement current treatment guidelines and care pathways in managing MASLD/MASH and underlying metabolic diseases.
Initiate referrals to specialists for patients with high-risk disease, including MASH as appropriate.

Please take the post-survey using the QR Code or URL below.

https://www.pcmg-us.org/survey/post/mash4

What Primary Care Clinicians Need to Know about MASLD and MASH

Thank you!