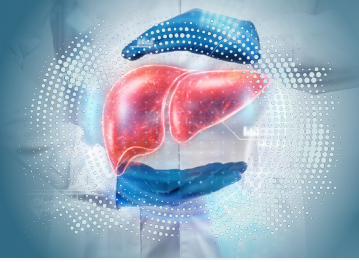

REDEFINING MASLD/MASH CARE:

Personalized Strategies for Assessment, Diagnosis and Management

in partnership with GLI GLOBAL LIVER INSTITUTE

Treatment Approaches

When the FIB-4 score is <1.3, patients are at low risk to have advanced fibrosis and can be managed in the endocrinology (or primary care) setting

A Multidisciplinary Approach is Key:

- To see sustained benefits, in particular for weight loss
- To address social, economic, and psychological challenges
- Behavioral medicine specialists, dieticians, nutritionists, health psychologists should be involved in care

Non Liver-Directed Use of Medications

- 1 FDA-approved medication for MASH for those with Fibrosis 2 or 3
- No FDA-approved drugs for treatment of MASLD; other medications have shown benefit, including incretins such as liraglutide, semaglutide, and tirzepatide, which have been included in the updated ADA & AASLD Practice Guidelines
  - » Non-liver related improvement in insulin sensitivity, weight

Treatment approaches for patients at low and indeterminant risk for advanced fibrosis may include:

Lifestyle intervention	Weight loss	CVD risk reduction		Diabetes care
Foundation of treatment for majority of patients	3-5% weight loss can improve steatosis	Including use of statins	Low Risk	Standard of care
Improved diet composition and exercise have benefits when weight loss not needed	10% weight loss can improve MASH and fibrosis		Ind Risk	Prefer medications with efficacy in MASH (pioglitazone, GLP-1RA)

FIB-4; fibrosis-4 index; MASH, metabolic dysfunction-associated steatohepatitis; MASLD, Metabolic dysfunction-associated steatotic liver disease; T2D, Type 2 Diabetes;

Clark JM, Cryer DRH, Morton M, Shubrook JH. Nonalcoholic fatty liver disease from a primary care perspective. Diabetes Obes Metab. 2023;25(6):1421-1433. doi:10.1111/dom.15016; ElSayed NA, Aleppo G, Aroda VR, et al., American Diabetes Association. 4. Comprehensive medical evaluation and assessment of comorbidities: Standards of Care in Diabetes—2023. Diabetes Care 2023;46(Suppl. 1): S49–S67.2; Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, et al. AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. Hepatology. 2023;77(5):1797-1835. doi:10.1097/HEP.0000000000000323

Treatment Approaches

When FIB-4 scores are >2.67 and VCTE scores are >8 or ELF scores are >7.7 , patients should be referred to GI/ Hepatology care

Further risk stratification in gastroenterology & hepatology care to identify patients with "at-risk" MASH or advanced fibrosis

- Patients may require further assessment & benefit from targeted interventions

Multidisciplinary Approach

- While management of MASLD/MASH is by a GI specialist or hepatologist, a multidisciplinary team is recommended due to complexity of care to manage hepatic manifestations & metabolic comorbidities & CV risk
- Behavioral medicine specialists, dieticians, nutritionists, health psychologists

Use of Medications

- 1 FDA-approved medication for MASH; no FDA-approved drugs for treatment of MASLD
- Other medications have shown benefit, including incretins such as liraglutide, semaglutide, and tirzepatide have been included in the updated ADA & AASLD Practice Guidelines

Treatment approaches for patients at high risk for advanced fibrosis may include:

Lifestyle intervention	Weight loss	CVD risk reduction	Diabetes care	Pharmacotherapy for MASH
Foundation of treatment for majority of patients	3-5% weight loss can improve steatosis	Prefer medications with efficacy in MASH	Prefer medications with efficacy in MASH (pioglitazone, GLP-1RA)	THR-beta agonist was recently approved in conjunction with diet and exercise for treatment of MASH
Improved diet composition and exercise have benefits when weight loss not needed	10% weight loss can improve MASH and fibrosis			Some GLP-1RAs have shown liver histological benefit in MASH

FIB-4; fibrosis-4 index; MASH, metabolic dysfunction-associated steatohepatitis; MASLD, Metabolic dysfunction-associated steatotic liver disease; T2D, Type 2 Diabetes;

Clark JM, Cryer DRH, Morton M, Shubrook JH. Nonalcoholic fatty liver disease from a primary care perspective. Diabetes Obes Metab. 2023;25(6):1421-1433. doi:10.1111/dom.15016; ElSayed NA, Aleppo G, Aroda VR, et al., American Diabetes Association. 4. Comprehensive medical evaluation and assessment of comorbidities: Standards of Care in Diabetes—2023. Diabetes Care 2023;46(Suppl. 1): S49–S67.2; Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, et al. AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. Hepatology. 2023;77(5):1797-1835. doi:10.1097/HEP.0000000000000323

Treatment Approaches

Pharmacologic Management of MASLD/MASH: Potential Impact of Available Medications

Medication	Indication	MOA	Effect	How taken	Weight Loss	MASLD clinical benefits	Cardiac benefit
Resmetirom	NASH with moderate to advanced liver fibrosis with diet and exercise	THR-β agonist	↓ Intrahepatic triglycerides	PO, once daily	NA	Liver related: improves steatosis, improves fibrosis	Unknown
Vitamin E	NA	Unknown	Improved aminotransferases	PO, once daily	NA	Liver related: improves steatosis, MASH resolution? No proven benefit on fibrosis	Unknown
Pioglitazone	T2D	PPAR	↑ Glucose utilization	PO, once daily	NA	Liver related: improves steatosis, activity and MASH resolution, fibrosis improvement? Nonliver related: improves insulin sensitivity, prevention of diabetes, CV risk reduction and stroke prevention	Yes
SGLT-2i	Chronic T2D; Mitigate CV risk	SGLT-2i	↑ Glucose excretion	PO, once daily	NA	Liver related: reduction in steatosis by imaging Nonliver related: may improve insulin sensitivity, improves CV and renal outcomes; benefit in heart failure, modest weight loss	Yes
Liraglutide	Chronic Obesity Management	GLP-1 RA	↓ Appetite	SQ, once daily	~5-7%	Liver: improves steatosis, no proven impact on fibrosis Nonliver related: improvement in insulin sensitivity, weight loss, CV risk reduction, may slow progression of renal disease	Yes
Semaglutide	Chronic Obesity Management/ Mitigate CV risk; Chronic T2D/ Mitigate CV risk	GLP-1 RA	↓ Appetite	SQ, once weekly	~10-16%	Liver related: improves steatosis, activity, and MASH resolution, no proven benefit on fibrosis, but may slow fibrosis progression Nonliver related: improvement in insulin sensitivity, weight loss, improves CV and renal outcomes, stroke prevention	Yes
Tirzepatide	Chronic T2D Treatment w/ Weight Loss; Chronic Obesity Management	Dual GIP/ GLP-1 RA	↓ Appetite	SQ, once weekly	~15-23%	Liver related: reduces steatosis on imaging Nonliver related: improvement in insulin sensitivity, significant weight loss	Unknown

GLP-1, glucagon-like peptide-1; PPAR, peroxisome proliferator-activated receptor; PO, oral; SQ, subcutaneous injection.

Blonde L, et al. Endocr Pract. 2022; Grunvald E, et al. Gastroenterology. 2022; Clark JM, Cryer DRH, Morton M, Shubrook JH. Nonalcoholic fatty liver disease from a primary care perspective. Diabetes Obes Metab. 2023;25(6):1421-1433. doi:10.1111/dom.15016; FDA Prescribing Information; Jastreboff AM, et al. N Engl J Med. 2022; Enright C, et al. J Endocr Soc. 2023; Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, et al. AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. Hepatology. 2023;77(5):1797-1835. doi:10.1097/HEP.0000000000000323; Wadden TA, et al. Nat Med. 2023.