CMEO Snack

Welcome to the Glow-Up* Era of MASH Management

*Modern term meaning “dramatic, positive change"

Supported by an educational grant from Novo Nordisk Inc.

CMEO Snack 3

What's Hot: Mastering MASH-Specific Therapies That Deliver

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Falls Church, VA

CMEO Snack

LEARNING OBJECTIVE

Identify available MASH-specific therapies appropriate for timely management in concordance with treatment guidelines and care pathways

Patient Case: Mr. B

Mr. B is a 61-year-old utilities field crew chief

- Presents for a routine follow-up visit
- Feels well and has no specific complaints
- Denies fatigue, abdominal pain, pruritus, or jaundice

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History

- T2D, dyslipidemia, hypertension
- Overweight with a BMI of 29.1 kg/m^2
- Drinks an occasional glass of wine with dinner
- Current medications: metformin, valsartan, hydrochlorothiazide

- Physical exam is unremarkable

BMI = body mass index; T2D = type 2 diabetes.

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Lab Findings

- AST: 28 U/L
- ALT: 36 U/L (ALT > AST, both normal)
- ALP: 100 U/L
- Total bilirubin: 1.0 mg/dL
- Albumin: 4.0 g/dL
- Platelets: 110,000/µL
- LDL: 130 mg/dL
- HDL: 36 mg/dL
- TG: 235 mg/dL
- A1C: 7.1%

ALP = alkaline phosphatase; ALT = alanine transaminase; AST = aspartate transaminase; HDL = high-density lipoprotein; LDL = low-density lipoprotein; TG = triglycerides.

Fibrosis-4 (FIB-4) Score and Abdominal Ultrasound

FIB-4

- Predicts advanced fibrosis in the liver
  - Age (years)
  - ALT (U/L)
  - AST (U/L)
  - Platelet count (x10^9/L)

Mr. B's FIB-4 score = 2.59

Understanding the FIB-4 Score		
Score <1.3 Rules out advanced fibrosis Sn: 74% Sp: 71%	Indeterminate	**Score >2.67** Predicts advanced fibrosis Sn: 33% Sp: 98%

Shah AG, et al. *Clin Gastroenterol Hepatol.* 2009;7:1104-1112. Angulo P, et al. *Hepatology.* 2007;45:846-854.

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- **Abdominal ultrasound:** hepatic steatosis without focal hepatic lesions, biliary ductal dilation, or ascites
- **VCTE (FibroScan):** 9 kPa (↑ IQR)
- **MRE:** 4.2 kPa
- **ELF score:** 10.2

ELF = enhanced liver fibrosis; IQR = interquartile range; kPa = kilopascals; MRE = magnetic resonance elastography; VCTE = vibration-controlled transient elastography.

Shah AG, et al. *Clin Gastroenterol Hepatol.* 2009;7:1104-1112. Angulo P, et al. *Hepatology.* 2007;45:846-854.

Audience Response

How would you treat Mr. B?

A. Lifestyle intervention only (nutrition/exercise)
B. Resmetirom
C. Semaglutide
D. Resmetirom + semaglutide
E. I’m not sure

Faculty Discussion

Mr. B: Management Considerations

- 3 components of the metabolic syndrome:
  - Dyslipidemia, diabetes, hypertension
- Normal liver function tests, but platelet count is low

Suspect advanced fibrosis

Younossi ZM, et al. *Clin Mol Hepatol*. 2025;31(Suppl):S32-S50.

Mr. B: Management Considerations

- 3 components of the metabolic syndrome:
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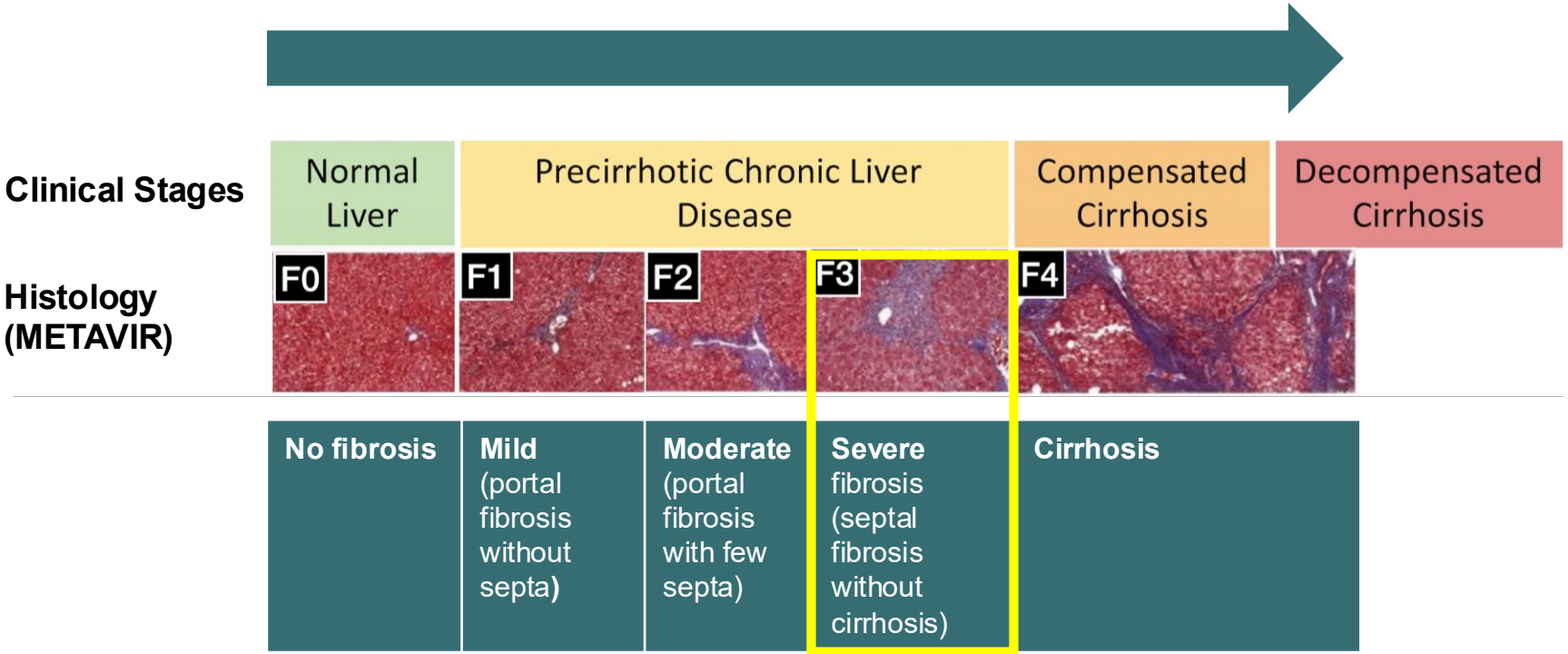
Suspect advanced fibrosis

- Secondary non-invasive tests (NITs) important to *rule out cirrhosis*
  - Approved drugs for MASH should **not** be used in patients with cirrhosis
  - Mr. B's additional NITs after FIB-4: VCTE, MRE, ELF
  - F3 fibrosis suspected

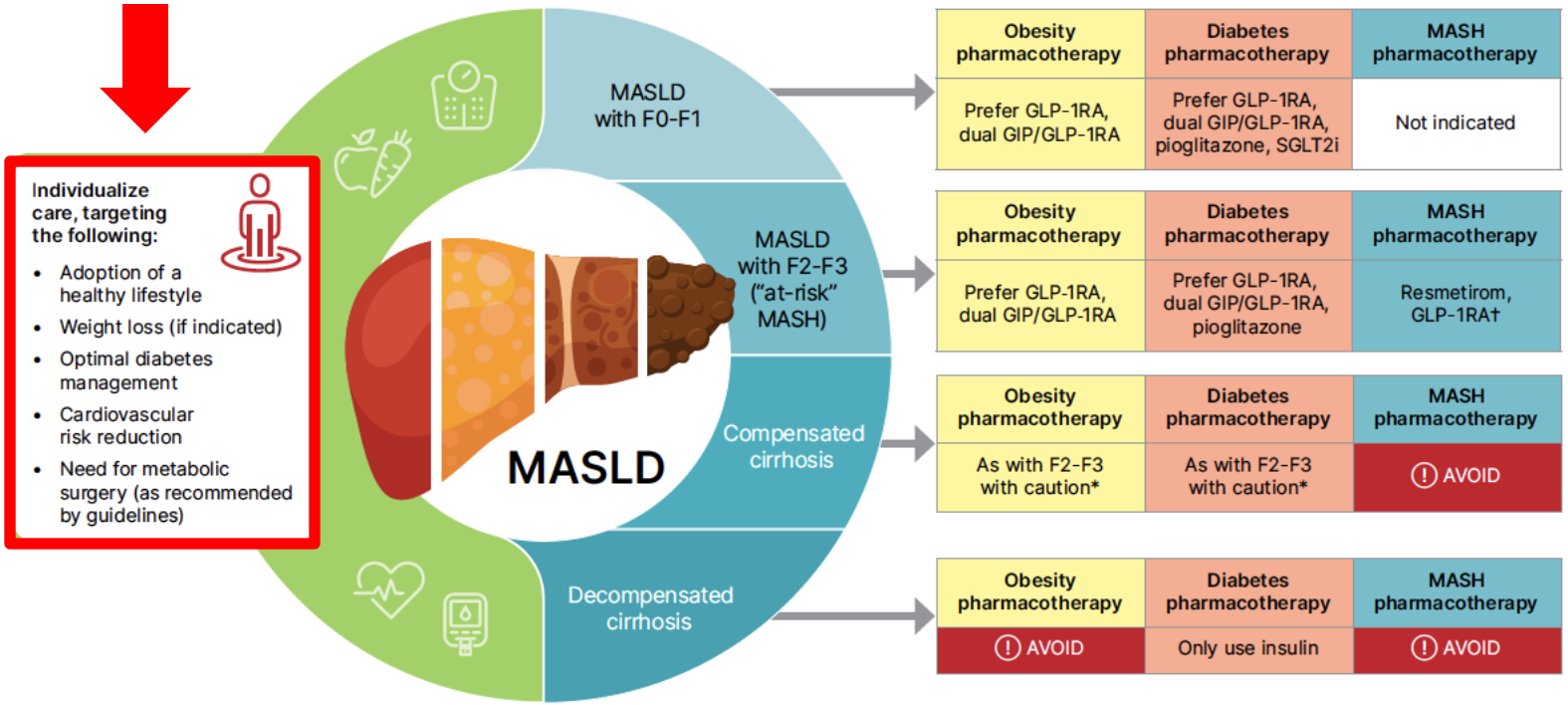
Younossi ZM, et al. *Clin Mol Hepatol*. 2025;31(Suppl):S32-S50.

Stages of Liver Fibrosis (METAVIR System)



METAVIR Cooperative Study Group. *Hepatology*.1994;20(1):15-20.

MASLD Treatment Algorithm for Individuals with Prediabetes or Diabetes



F0 = no fibrosis; F1 = mild fibrosis; F2 = moderate fibrosis; F3 = advanced/severe fibrosis; GLP-1 RA = glucagon-like peptide-1 receptor agonist;
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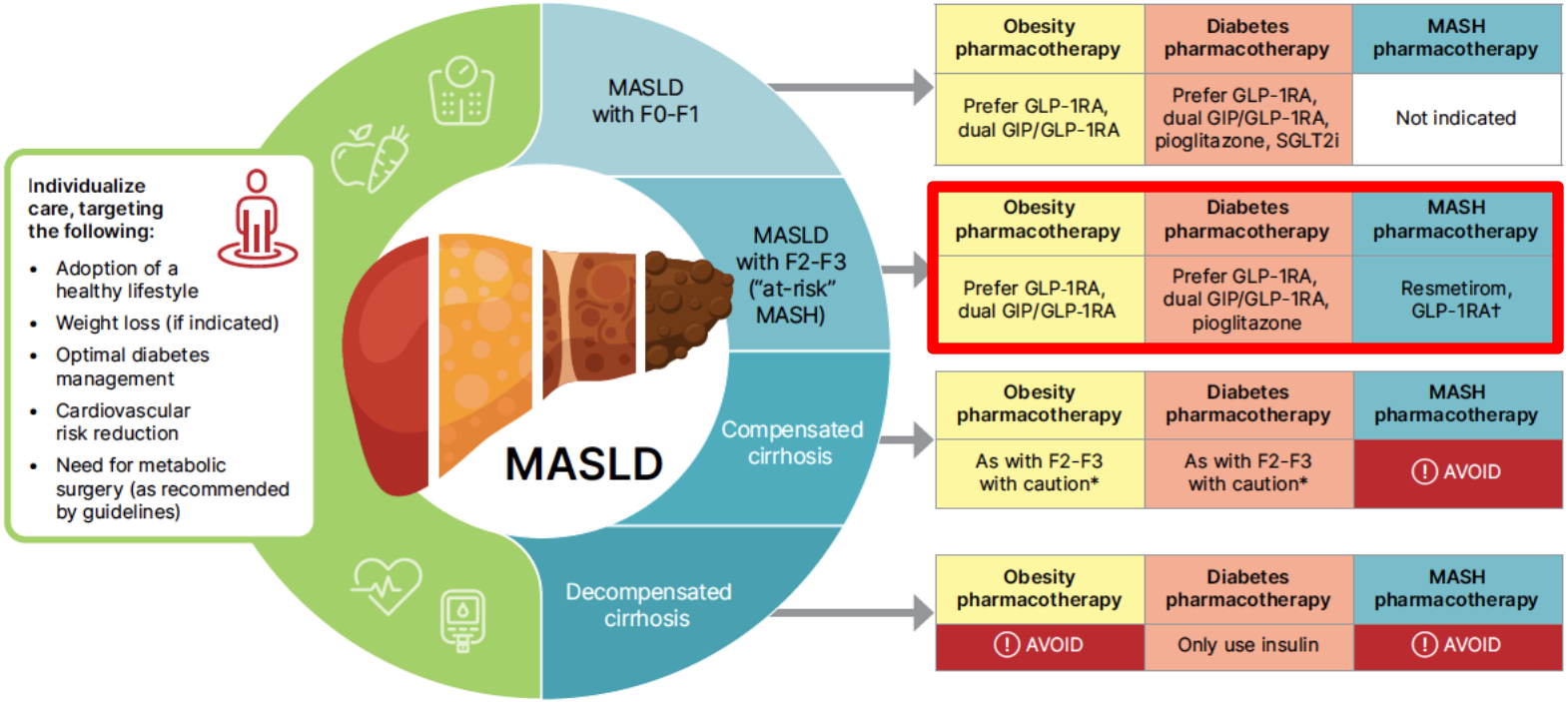

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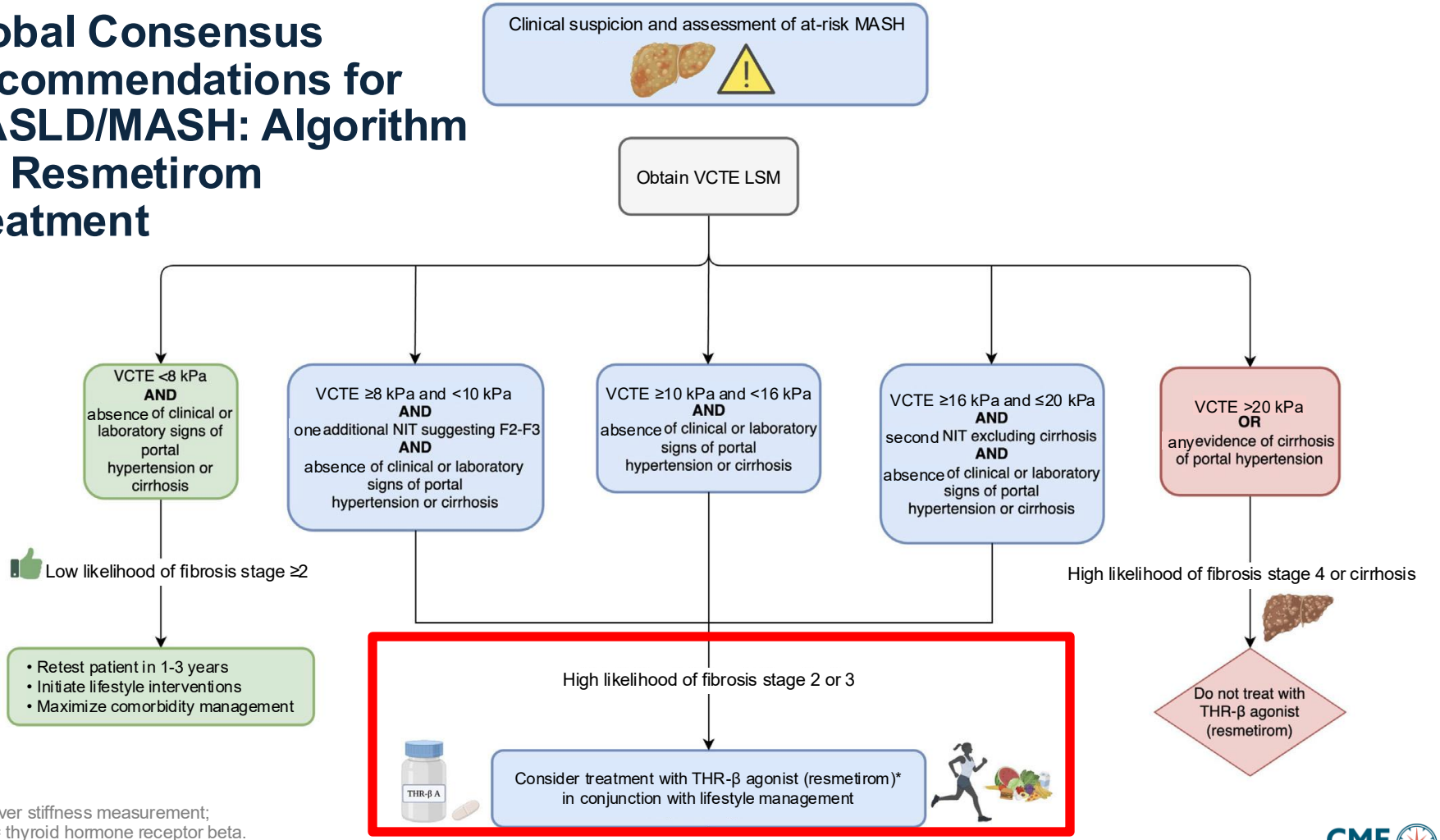
Global Consensus Recommendations for MASLD/MASH: Algorithm for Resmetirom Treatment



LSM = liver stiffness measurement;
THR-β = thyroid hormone receptor beta.
Younossi ZM, et al. *Gastroenterology.* 2025;169:1017-1032.

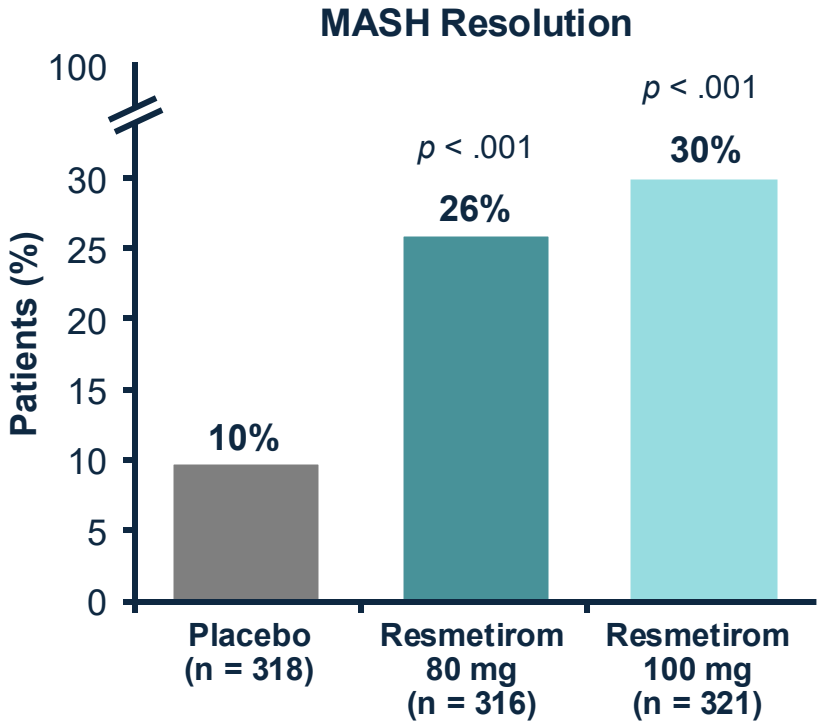
Approved Treatments for MASH (U.S.)

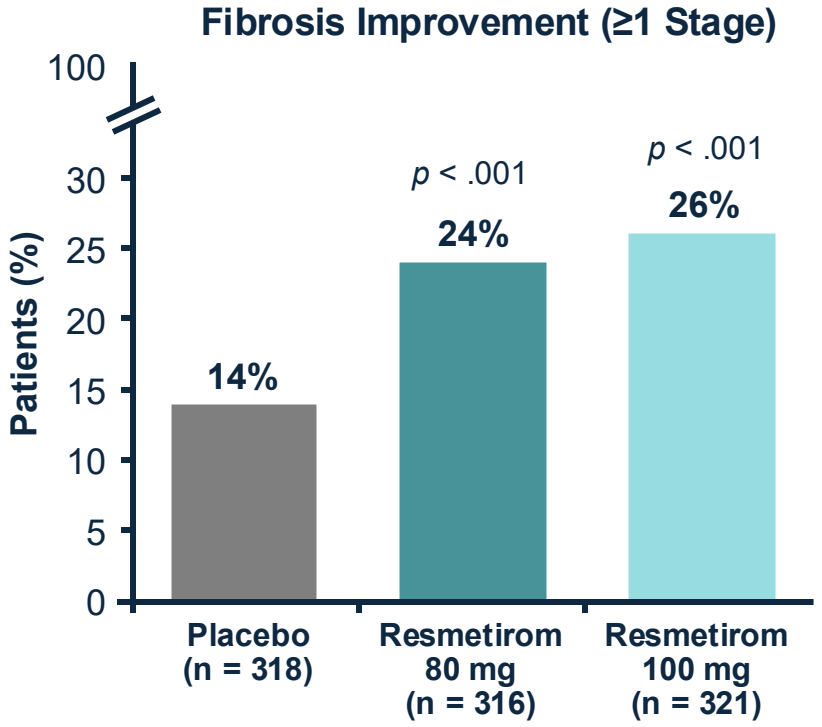
Resmetirom

- FDA approval March 14, 2024
- Indicated for treatment of adults with MASLD/MASH with moderate to advanced liver scarring (fibrosis); to be used in conjunction with diet and exercise
- MAESTRO-NASH Phase III
  - Higher rates of MASH resolution with no worsening of fibrosis
  - Greater rates of ≥1-stage fibrosis improvement with no worsening MASLD activity score (vs placebo)

Resmetirom [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/217785s000lbl.pdf.

Resmetirom: Phase III (MAESTRO-NASH) Trial Results





Harrison SA, et al. *N Engl J Med*. 2024;390(6):497-509.

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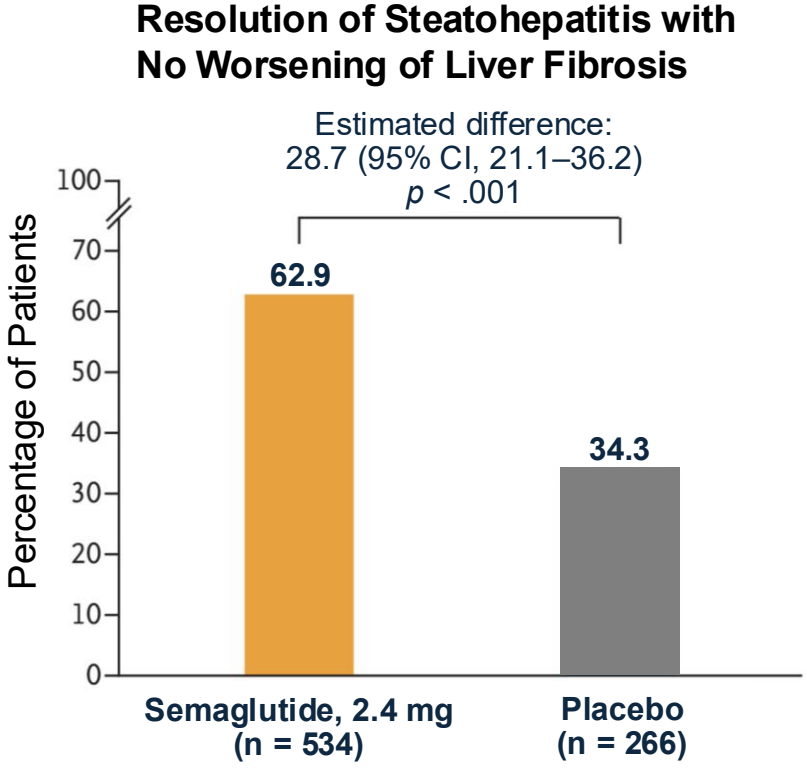
- MAESTRO-NASH Phase III
  - Higher rates of MASH resolution with no worsening of fibrosis
  - Greater rates of ≥1-stage fibrosis improvement with no worsening MASLD activity score (vs placebo)

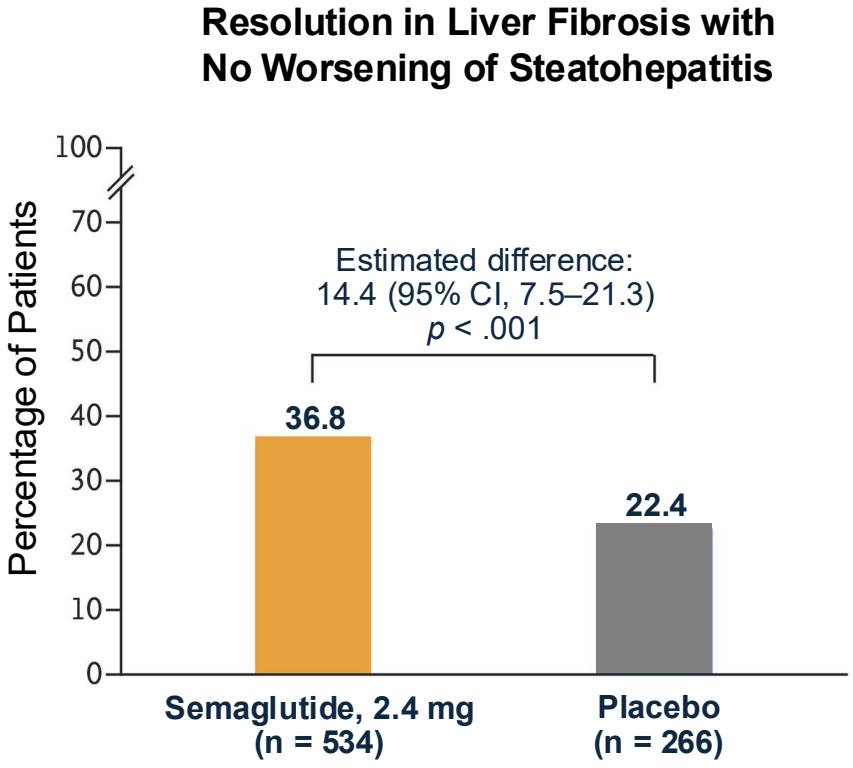
Semaglutide

- FDA approved August 15, 2025
- Indicated for adults with non-cirrhotic MASH with moderate to advanced liver fibrosis (administered with diet and exercise)
- ESSENCE Phase III
  - Greater proportion achieved reduction in liver fibrosis with no worsening of steatohepatitis (vs placebo)

Resmetirom [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/217785s000lbl.pdf.
Semaglutide [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209637lbl.pdf.

Semaglutide: Phase III (ESSENCE) Trial Results





Sanyal AJ, et al. *N Engl J Med*. 2025;392:2089-2099.

Liver and Cardiorenal Effects of Glucose-Lowering Medications

Medication	Effect in MASLD and MASH*				Cardiovascular, Renal, and Other Relevant Clinical Effects			
	Hepatic Steatosis	Steatohepatitis	Fibrosis Regression	Reduction of Fibrosis Progression	ASCVD*	CKD*	HF*	Hypoglycemia‡
Semaglutide**	Beneficial	Beneficial	Beneficial	Potential benefit	Beneficial	Beneficial	Beneficial	Low risk
Tirzepatide***†	Potential benefit	Potential benefit	Potential benefit	Potential benefit	?	?	Beneficial	Low risk
Pioglitazone†	Potential benefit	Potential benefit	Potential benefit	Potential benefit	Beneficial	Neutral	Not recommended in HF stage B/C/D	Low risk
SGLT2 inhibitors	Potential benefit	?	?	?	Beneficial	Beneficial	Beneficial	Low risk
Metformin‡	Neutral	Neutral	Neutral	Neutral	Potential benefit?	Neutral	Neutral	Low risk
DPP-4 inhibitors‡	Neutral	?	?	?	Neutral	Neutral	Neutral (except saxagliptin, alogliptin?)	High risk
Insulin‡	Potential benefit	?	?	?	Neutral	Neutral	Neutral	High risk
Sulfonylureas‡	Neutral	?	?	?	Neutral	Neutral	Neutral	High risk

*Includes people with and without type 2 diabetes.
**Only semaglutide among GLP-1RAs has been reported to be of benefit in a Phase II RCT with improvement in steatohepatitis and more recently in a Phase III RCT with histological outcomes in MASH, including improvements in steatohepatitis and fibrosis. Liraglutide may offer potential benefit, based on results of a Phase II RCT. Other GLP-1RAs have not been tested in RCTs with liver histological outcomes.
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ASCVD = atherosclerotic cardiovascular disease; CKD = chronic kidney disease; DPP-4 = dipeptidyl peptidase-4; HF = heart failure.
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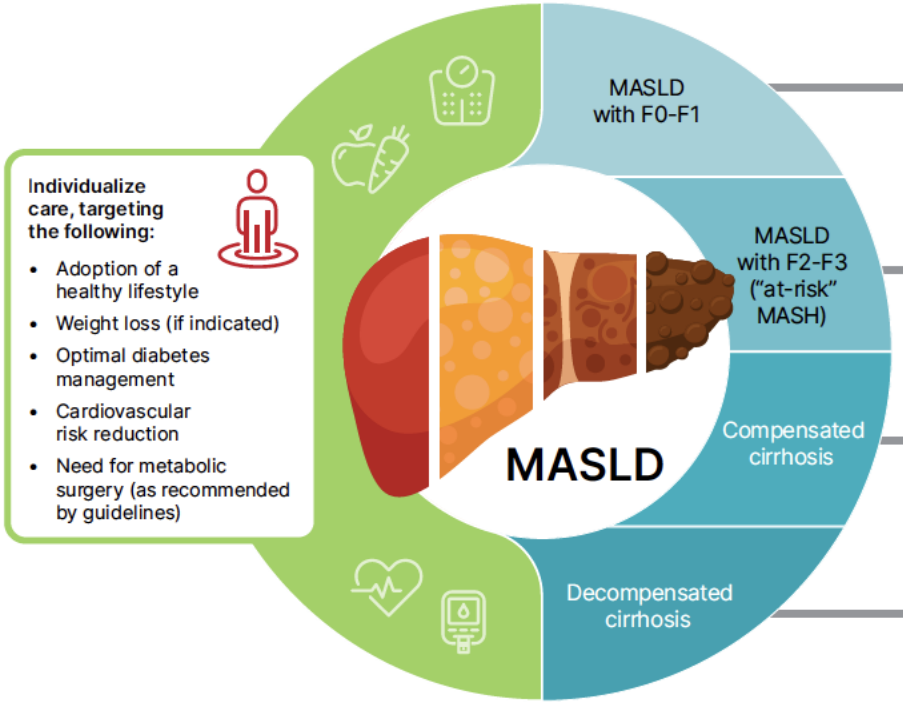

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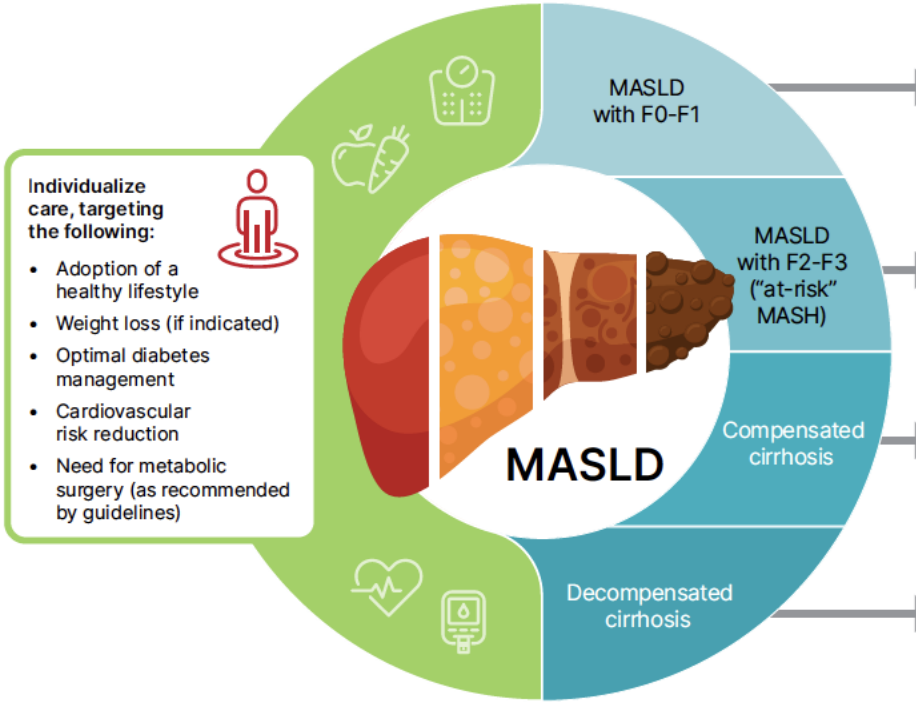

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Insulin‡	Potential benefit	?	?	?	Neutral	Neutral	Neutral	High risk
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*Includes people with and without type 2 diabetes.
**Only semaglutide among GLP-1RAs has been reported to be of benefit in a Phase II RCT with improvement in steatohepatitis and more recently in a Phase III RCT with histological outcomes in MASH, including improvements in steatohepatitis and fibrosis. Liraglutide may offer potential benefit, based on results of a Phase II RCT. Other GLP-1RAs have not been tested in RCTs with liver histological outcomes.
***Tirzepatide is the only dual glucose-dependent insulinotropic polypeptide (GIP)/GLP-1RA available and tested with histological outcomes in a Phase II RCT in MASH.
†Tirzepatide and pioglitazone are considered of potential benefit, based on Phase II trials.
‡Only in people with type 2 diabetes.

Cusi K, et al. *Diabetes Care*. 2025;48(7):1057-1082.

Liver and Cardiorenal Effects of Glucose-Lowering Medications

Medication	Effect in MASLD and MASH*				Cardiovascular, Renal, and Other Relevant Clinical Effects			
	Hepatic Steatosis	Steatohepatitis	Fibrosis Regression	Reduction of Fibrosis Progression	ASCVD*	CKD*	HF*	Hypoglycemia‡
Semaglutide**	Beneficial	Beneficial	Beneficial	Potential benefit	Beneficial	Beneficial	Beneficial	Low risk
Tirzepatide***†	Potential benefit	Potential benefit	Potential benefit	Potential benefit	?	?	Beneficial	Low risk
Pioglitazone†	Potential benefit	Potential benefit	Potential benefit	Potential benefit	Beneficial	Neutral	Not recommended in HF stage B/C/D	Low risk
SGLT2 inhibitors	Potential benefit	?	?	?	Beneficial	Beneficial	Beneficial	Low risk
Metformin‡	Neutral	Neutral	Neutral	Neutral	Potential benefit?	Neutral	Neutral	Low risk
DPP-4 inhibitors‡	Neutral	?	?	?	Neutral	Neutral	Neutral (except saxagliptin, alogliptin?)	High risk
Insulin‡	Potential benefit	?	?	?	Neutral	Neutral	Neutral	High risk
Sulfonylureas‡	Neutral	?	?	?	Neutral	Neutral	Neutral	High risk

*Includes people with and without type 2 diabetes.
**Only semaglutide among GLP-1RAs has been reported to be of benefit in a Phase II RCT with improvement in steatohepatitis and more recently in a Phase III RCT with histological outcomes in MASH, including improvements in steatohepatitis and fibrosis. Liraglutide may offer potential benefit, based on results of a Phase II RCT. Other GLP-1RAs have not been tested in RCTs with liver histological outcomes.
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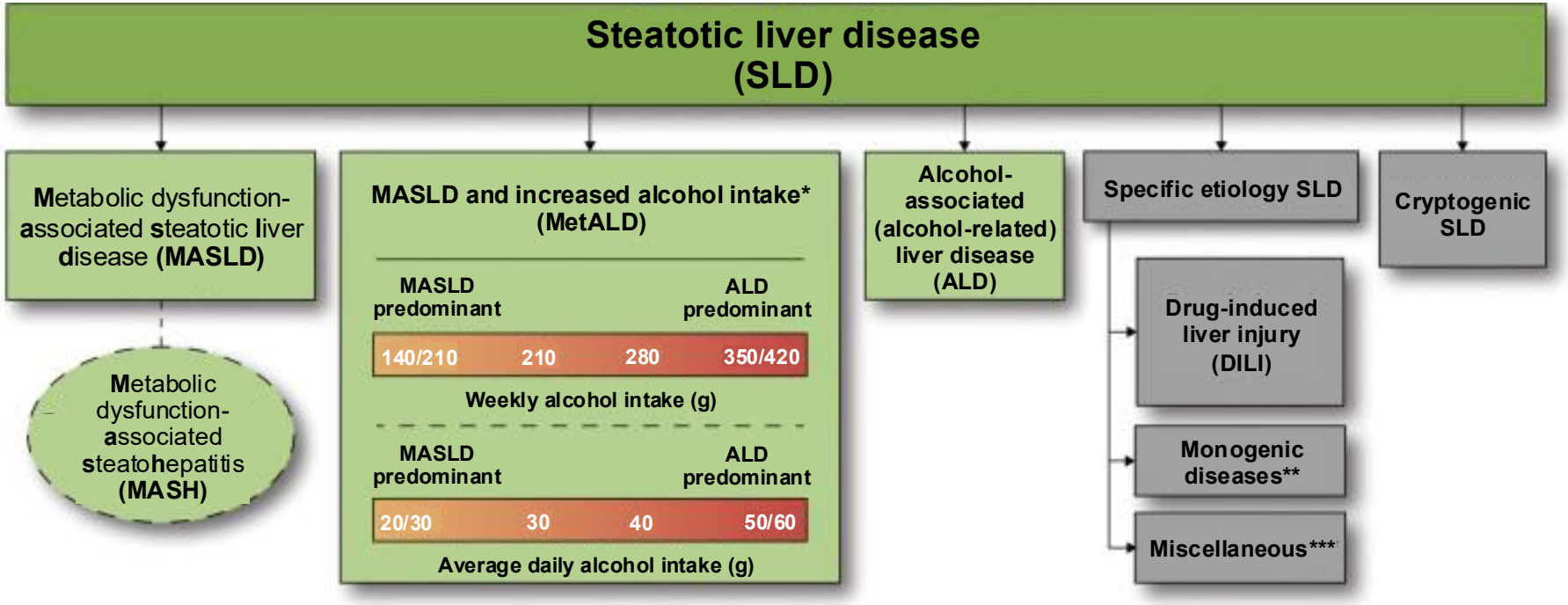
Cusi K, et al. *Diabetes Care*. 2025;48(7):1057-1082.

Faculty Discussion

Dynamic Spectrum of Steatotic Liver Disease



Rinella ME, et al. *Hepatology*. 2023;78(6):1966-1986.

Lifestyle Recommendations for People with MASLD

Weight goals

People with MASLD and overweight/obesity

- Reduction of ≥5% of total body weight to reduce liver fat
- Reduction of 7%-10% to improve liver inflammation
- Reduction of ≥10% to improve fibrosis

Consider bariatric procedures for people with obesity class II or III

People with MASLD and normal weight

Reduction of 3%-5% of total body weight to reduce liver fat

Lifestyle

Diet

- Follow the Mediterranean dietary pattern or similar plant-based diet
- Increase consumption of fruits, vegetables, lentils, nuts, olive oil, and unprocessed poultry and fish

- Limit the consumption of ultra-processed food and saturated fats
- Avoid sugar-sweetened beverages

Exercise

- Increase daily physical activity
- Increase exercise (aim: 150-300 min/week of moderate intensity or 75-150 min/week of vigorous intensity)
- Decrease sedentary time

Other

- Avoid smoking
- Avoid alcohol consumption (especially in advanced disease)

Younossi ZM, et al. *Gastroenterology.* 2025;169:1017-1032.

Interprofessional Teams, Management, and Liver Monitoring

MASLD with no fibrosis (F0) or early fibrosis (F1) stage

Care team
- Primary care physicians, physicians associates/assistants, and nurse practitioners
- Registered dietitian nutritionist, obesity management team
- Behavioral modification team, diabetes care and education specialist
- Metabolic surgery team, as per ADA Standards of Care

Management
- Lifestyle intervention, weight loss with pharmacotherapy or metabolic surgery, as per ADA Standards of Care
- Diabetes care, as per ADA Standards of Care; favor medications that reduce CVD and steatosis (GLP-1RA, SGLT2i, pioglitazone)
- CV risk reduction, as per ADA Standards of Care

Liver monitoring
- FIB-4 every 1-2 years. LSM by transient elastography (or ELF) if FIB-4 score is >1.3 (possible disease progression)

MASLD with fibrosis stage F2 F3 ("at-risk" MASH)

Care team
- Same as for MASLD with stage F0-F1, and consider referrals to:
  - Hepatologist or GI (with physician associates/assistants and nurse practitioners team)
  - Endocrinologist/diabetes specialist

Management
- Lifestyle intervention, weight loss same as for MASLD with stage F0-F1
- Diabetes care: prefer GLP-1, dual GIP/GLP-1RA, pioglitazone, or combination to treat MASH; consider resmetirom after treatment optimization of obesity and/or diabetes for at least 6-12 months
- CV risk reduction, same as for MASLD with stage F0-F1

Liver monitoring
- Consider annual imaging (LSM either by transient elastography or MRE) and measurement of blood-based liver fibrosis biomarkers

Cirrhosis

Care team
- Same as for MASLD with stage F2-F3, and consider referrals to:
  - Transplant team for decompensated cirrhosis
  - Social support team

Management
- Lifestyle intervention same as for MASLD with stage F0-F1, but decompensated cirrhosis requires tailored nutritional planning
- Diabetes care:
  - In compensated cirrhosis: same as for MASLD with stage F2-F3 but with caution
  - In decompensated cirrhosis: insulin only
- Avoid use of resmetirom in cirrhosis
- CV risk reduction, same as for MASLD with stage F0-F1; caution with lipid-lowering medications in decompensated cirrhosis

Liver monitoring
- Tailored to cirrhosis severity and presence of its complications.
- Screen for HCC

ADA = American Diabetes Association; LEF = enhanced liver fibrosis; GI = gastroenterologist; HCC = hepatocellular carcinoma.

Cusi K, et al. *Diabetes Care*. 2025;48(7):1057-1082.

Faculty Discussion

Patient Perspectives on the Metabolic Clinic Model

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Faculty Discussion

CMEO Snack 3

What's Hot: Mastering MASH-Specific Therapies That Deliver

Put information into action!

Takeaways from this program can be implemented into your practice to improve patient care.

Within the next 3 months:

- *Increase lifestyle counseling (nutrition, weight management, and physical activity) in combination with pharmacotherapy, when appropriate, for patients with or at risk for MASLD/MASH*
- *Implement FDA-approved therapies (resmetirom and/or semaglutide), when relevant, in appropriate patients with MASLD/MASH*

To Receive Credit

To receive CME/CE credit for this activity, participants must complete the post-test and evaluation online.

Participants will be able to download and print their certificate immediately upon completion.

CMEO Snack

Other programs in this series include:

Welcome to the Glow-Up Era of MASH Management

Spotting the Red Flags:
Screening and Risk Strat Like a Pro

Welcome to the Glow-Up Era of MASH Management

Ditch the Guesswork:
Non-Invasive Tools That Slay Diagnosis and Monitoring

Welcome to the Glow-Up Era of MASH Management

GLP-1s Got That Rizz:
The Future of MASH and Metabolic Syndrome Care

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