Consensus Building Discussions Around Priority Recommendations: Treatment

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Why MASH Requires a Systems-Level Approach

- MASH is the progressive, fibrotic form of MASLD
- Highly prevalent in **T2D, obesity, and cardiometabolic disease**
- Cardiovascular disease remains the leading cause of death
- Progression risk: F2–F3 fibrosis → cirrhosis, HCC, transplantation
- Now a treatable disease (resmetirom, semaglutide) → **care delivery must evolve**
- **Key Question:** Who should manage MASH in the era of disease-modifying therapy?

Who Owns MASH? A Shared Disease Model

MASH sits at the intersection of:

- **Endocrinology** – T2D, obesity, insulin resistance
- **Hepatology/GI** – fibrosis staging, cirrhosis, HCC risk
- **Cardiology** – ASCVD risk, heart failure
- **Primary Care** – early detection and longitudinal care
- No single specialty captures the full risk spectrum.
- **Conclusion:** MASH should not be siloed within hepatology.

Proposed Care Model by Fibrosis Stage

Primary Care

- Case finding in high-risk populations (T2D, obesity)
- FIB-4–based initial risk stratification
- Management of metabolic drivers

Endocrinology

- Case finding in high-risk populations (T2D, obesity)
- FIB-4–based initial risk stratification
- Management of metabolic drivers
- **Indeterminate/high NITs**
- **F2–F3 fibrosis (treatment candidates)**

Hepatology

Indeterminate/high NITs

- F2–F3 fibrosis (treatment candidates)
- Suspected cirrhosis or portal hypertension

Advanced Disease

- Multidisciplinary cirrhosis management
- HCC surveillance
- Transplant referral when appropriate

Care should be risk-stratified, not specialty-restricted.

Risk Stratification Drives Management

Stepwise approach:

1. **FIB-4** in high-risk populations
2. Secondary testing:
   - VCTE
   - ELF
   - MRE when needed
- Referral triggers:
  - FIB-4 > 2.67
  - Elevated VCTE/ELF
  - Persistent ALT elevation
- Goal: Identify **“at-risk” MASH (≥F2 fibrosis)** early.

Lifestyle: Still Foundational

- Weight loss targets:
  - ≥5% → reduce steatosis
  - 7–10% → improve inflammation
  - ≥10% → fibrosis improvement
- Multidisciplinary support improves durability:
  - Dietitians
  - Behavioral therapy
  - Exercise physiology
- Lifestyle alone is insufficient for many patients → pharmacotherapy integration is essential.

Metabolic Pharmacotherapy as Liver Therapy

- For T2D/obesity:
  - **GLP-1 receptor agonists / dual GIP-GLP-1 agents**
  - **Pioglitazone**
  - **SGLT2 inhibitors** (cardiorenal benefit)
- Benefits:
  - Weight reduction
  - MASH resolution (semaglutide data)
  - Cardiovascular risk reduction
- Endocrinologists are central in early-stage and metabolic-driven disease.

Liver-Directed Therapy

- **Resmetirom**
  - Approved for non-cirrhotic MASH with F2–F3 fibrosis
  - Targets thyroid hormone receptor-β
  - Improves steatohepatitis and fibrosis
- **Semaglutide 2.4 mg**
  - Approved for MASH with moderate–advanced fibrosis
  - Histologic improvement in phase 3 data
- Not recommended in decompensated cirrhosis.
- Treatment selection should consider:
- Fibrosis stage
- Cardiometabolic profile
- Cirrhosis exclusion

Management of Cirrhosis

- In compensated cirrhosis:
  - Careful metabolic pharmacotherapy
  - Portal hypertension assessment
  - HCC surveillance
- In decompensated cirrhosis:
  - Avoid MASH-targeted therapy
  - Insulin for diabetes management
  - Transplant evaluation
- Advanced disease must be hepatology-led but metabolically co-managed.

Why Multidisciplinary Care Fails Today

Barriers:

- Low screening rates in T2D/obesity
- Over-reliance on ALT
- Limited NIT familiarity among non-hepatologists
- Referral bottlenecks
- Siloed reimbursement models

Result: Most F2–F3 patients remain undiagnosed until cirrhosis.

Building a High-Functioning MASH Program

1. Standardized Risk Algorithms

- Embed FIB-4 in EMR for T2D/obesity
- Automatic VCTE referral pathways

2. Defined Role Allocation

- PCP: case finding
- Endocrine: metabolic optimization
- Hepatology: fibrosis management
- Cardiology: ASCVD integration

3. Shared Metrics

- Fibrosis regression
- Weight loss durability
- Cardiovascular event reduction

4. Institutional Support

- Administrative buy-in
- Nurse navigators
- Centralized NIT access

The Future of MASH Care

- MASH is not a liver disease alone. It is a **cardiometabolic–hepatic syndrome**.
- Optimal management requires:
  - Early identification
  - Risk-based referral
  - Combined metabolic + liver-directed therapy
  - True multidisciplinary infrastructure
- The question is no longer *whether* we treat MASH. The question is *how we redesign care to do it effectively*.