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Metabolic Dysfunction-Associated Steatotic Liver Disease in General Medicine: From Incidental Fatty Liver to Cardiometabolic Risk Stratification

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Abstract

Context: Metabolic dysfunction-associated steatotic liver disease (MASLD) has replaced non-alcoholic fatty liver disease in contemporary nomenclature and reframes hepatic steatosis as a multisystem cardiometabolic condition. In general medicine, the usual presentation is incidental steatosis on imaging or mildly abnormal aminotransferases in a patient with obesity, diabetes, hypertension, dyslipidemia, or cardiovascular risk.

Evidence Acquisition: This narrative review was updated through June 2026 using PubMed/MEDLINE, major society guidance, clinical care pathways, systematic reviews, randomized trials, and regulatory sources relevant to adult primary care, internal medicine, endocrinology, obesity medicine, cardiology, and hepatology.

Results: Current evidence supports a pragmatic shift from detecting steatosis alone to identifying clinically significant fibrosis and cardiometabolic risk. MASLD is diagnosed when hepatic steatosis coexists with at least one cardiometabolic risk factor after assessment of alcohol intake and alternative causes of steatosis. Clear separation of MASLD, MetALD, and alcohol-related liver disease is clinically important because alcohol exposure modifies prognosis, counseling, surveillance, and referral needs. Stepwise non-invasive testing, usually beginning with the fibrosis-4 index followed by transient elastography or serum fibrosis testing when indicated, can identify patients who need hepatology referral. Resmetirom and semaglutide have expanded the treatment landscape for selected adults with non-cirrhotic MASH and moderate-to-advanced fibrosis in the jurisdictions where they are approved, but long-term clinical outcome data remain incomplete.

Conclusion: MASLD should be approached as a cardiometabolic risk signal with liver-fibrosis implications. A structured pathway for incidental steatosis can reduce missed advanced fibrosis while improving diabetes, obesity, lipid, blood pressure, cardiovascular, and lifestyle care.

Keywords: metabolic dysfunction-associated steatotic liver disease; metabolic dysfunction-associated steatohepatitis; liver fibrosis; cardiovascular risk; non-invasive testing; primary care.

1. Context

This review addresses how general physicians should translate incidental hepatic steatosis into actionable liver and cardiometabolic risk stratification. MASLD is now the preferred term for steatotic liver disease associated with metabolic dysfunction after a global multisociety Delphi process that aimed to remove stigmatizing terminology and better reflect disease biology (1).

The terminology sits within the broader category of steatotic liver disease (SLD). This umbrella includes MASLD, MASLD with moderate alcohol intake (MetALD), alcohol-related liver disease, specific causes of SLD such as drug-induced or monogenic disorders, and cryptogenic SLD (1,2). For general medicine, the nomenclature is useful only if it changes clinical behavior: steatosis should prompt fibrosis

assessment, cardiometabolic risk reduction, and careful alcohol assessment rather than passive documentation.

Most patients with MASLD are first encountered in general medicine, primary care, diabetes, obesity, or cardiovascular clinics rather than hepatology clinics. The incidental report of fatty liver on ultrasonography, computed tomography, or magnetic resonance imaging, or a mildly elevated alanine aminotransferase (ALT), is often under-acted upon. Yet the same patient may already have type 2 diabetes, hypertension, dyslipidemia, visceral obesity, chronic kidney disease, obstructive sleep apnea, or atherosclerotic cardiovascular disease (2-4).

The practical challenge is that steatosis is common and often asymptomatic, whereas advanced fibrosis is less common but drives liver-related outcomes. A generalist pathway must avoid both extremes: ignoring fatty liver because liver enzymes are normal and over-referring all steatosis without fibrosis triage. The contemporary approach is to identify high-risk individuals, calculate a simple fibrosis score, confirm risk with second-line non-invasive testing when needed, manage cardiometabolic disease aggressively, and refer patients with suspected advanced fibrosis, cirrhosis, diagnostic uncertainty, or eligibility for MASH-specific therapy (2-5).

2. Evidence Acquisition

This article was prepared as a narrative review rather than a systematic review or meta-analysis. PubMed/MEDLINE, major professional society websites, clinical care pathways, and regulatory sources were searched for English-language adult studies and guidance published between January 2015 and June 2026.

Search terms included MASLD, metabolic dysfunction-associated steatotic liver disease, NAFLD, MASH, NASH, incidental fatty liver, MetALD, alcohol-related liver disease, FIB-4, transient elastography, non-invasive tests, cardiovascular risk, type 2 diabetes, obesity, resmetirom, semaglutide, tirzepatide, primary care, internal medicine, and clinical care pathway.

Priority was given to multisociety nomenclature statements, international clinical practice guidelines, AASLD guidance, EASL-EASD-EASO guidance, AACE guidance, AGA clinical care pathways, systematic reviews, meta-analyses, randomized controlled trials, and regulatory approvals. The review focused on adult general medicine practice. Pediatric-only studies, preclinical studies, highly specialized hepatology techniques without direct general-medicine applicability, and opinion pieces without clinical implementation relevance were not prioritized.

3. Results

3.1. Terminology and Diagnostic Framing

MASLD is defined by hepatic steatosis in association with at least one cardiometabolic risk factor after assessment of alcohol intake and other dominant causes of steatosis (1,2). MASH replaces non-alcoholic steatohepatitis and denotes steatosis with hepatocellular injury and inflammation, with or without fibrosis. The renaming does not invalidate the large evidence base generated under the NAFLD/NASH terminology because cohort reclassification studies show substantial overlap between NAFLD and MASLD populations, especially in patients with metabolic risk factors (1,2).

The clinically important distinction is alcohol exposure. Patients with steatosis, metabolic dysfunction, and alcohol intake below the MetALD range are generally classified as MASLD. MetALD describes patients who meet MASLD criteria but also have moderate alcohol intake, commonly 20-50 g/day in women or 30-60 g/day in men. Alcohol-related liver disease is favored when alcohol intake is higher than this range or is the dominant driver of liver injury (1,2).

This separation matters because metabolic dysfunction and alcohol can act synergistically. MetALD should not be treated as simple MASLD with a minor label change. It requires explicit alcohol quantification, brief intervention, reassessment over time, and lower thresholds for specialist input when fibrosis markers, liver enzymes, or clinical features are concerning. Patients may also move between categories if alcohol exposure changes, so the classification should be revisited during follow-up (1,2).

For the general physician, the first step is not to prove MASH histologically in every patient. Instead, the priority is to confirm steatosis, document the metabolic context, quantify alcohol exposure, review medications and secondary causes, and determine whether clinically significant fibrosis is likely. Liver biopsy is reserved for selected cases, such as diagnostic uncertainty, discordant non-invasive tests, suspected competing liver disease, or therapeutic decision-making in specialist care(2,3).

3.2. Epidemiology and Why Incidental Steatosis Matters

MASLD is one of the most prevalent chronic liver diseases worldwide. In a large systematic review and meta-analysis using the NAFLD terminology, global adult prevalence was estimated at approximately one-third of the population and increased over time (6). The epidemiology mirrors the global rise in obesity, type 2 diabetes, sedentary behavior, and cardiometabolic multimorbidity. This makes MASLD a routine general-

medicine problem rather than a niche hepatology diagnosis.

Prevalence alone should not determine urgency. The major clinical distinction is between steatosis without significant fibrosis and steatotic liver disease with advanced fibrosis or cirrhosis. Fibrosis stage is consistently associated with all-cause mortality, liver-related events, and liver-related mortality, whereas aminotransferase levels and steatohepatitis alone are less reliable risk markers(7,8).

The importance of MASLD extends beyond liver outcomes. Cardiovascular disease is a leading cause of morbidity and mortality in patients with fatty liver disease, and NAFLD/MASLD is associated with a higher long-term risk of cardiovascular events, particularly when fibrosis or metabolic comorbidities are present (9,10) Therefore, a fatty liver report can function as a visible marker of hidden cardiometabolic risk.

3.3. Initial Evaluation in General Medicine

A practical first visit for suspected MASLD should confirm the source of steatosis, assess cardiometabolic risk factors, quantify alcohol intake, review medications, exclude common alternative liver diseases when clinically indicated, and begin fibrosis triage. The history should include alcohol quantity and pattern, steatogenic medications, viral hepatitis risk, family history of cirrhosis or liver cancer, prior bariatric surgery, sleep apnea symptoms, and features of decompensated liver disease.

Baseline investigations should generally include complete blood count, ALT, aspartate aminotransferase (AST), alkaline phosphatase, bilirubin, albumin, international normalized ratio when advanced disease is suspected, fasting lipids, hemoglobin A1c or fasting glucose, renal function, urine albumin-creatinine ratio when diabetes or hypertension is present, and hepatitis B and C testing when not previously documented. Platelet count, AST, ALT, and age are sufficient to calculate the fibrosis-4 index (FIB-4), making it attractive for routine practice (2-5).

Normal aminotransferases do not exclude advanced fibrosis. Conversely, mildly elevated ALT does not prove MASH or advanced disease. Patients with cholestatic enzymes, marked aminotransferase elevation, low platelets, impaired synthetic function, splenomegaly, ascites, hepatic encephalopathy, gastrointestinal bleeding, or suspicious liver lesions require specialist assessment independent of FIB-4. Table 1 summarizes a practical general-medicine pathway for the common situation of incidental hepatic steatosis or suspected MASLD.

3.4. Fibrosis Risk Stratification: The Central General-Medicine Task

Contemporary guidance supports a stepwise non-invasive approach. FIB-4 is recommended as a first-line test because it is inexpensive, uses routinely available variables, and has good negative predictive value for advanced fibrosis in lower-prevalence settings (2-5,11). In adults younger than 65 years, a FIB-4 value below 1.3 generally identifies low risk for advanced fibrosis, whereas values of 1.3 or higher should prompt second-line assessment such as vibration-controlled transient elastography (VCTE), enhanced liver fibrosis testing where available, magnetic resonance elastography in selected settings, or referral depending on local resources. FIB-4 greater than 2.67 increases concern for advanced fibrosis. In adults older than 65 years, higher cutoffs, commonly around 2.0, should be considered because age can increase false-positive results (2,3,5).

FIB-4 also has limitations. It performs poorly in very young adults, can be falsely high during acute illness or active hepatitis, and can be distorted by thrombocytopenia from non-hepatic causes. Indeterminate results are common in older or metabolically complex patients. Second-line testing with VCTE provides liver stiffness measurement and controlled attenuation parameter, which help estimate fibrosis and steatosis, although obesity, congestion, inflammation, and operator factors can influence results (11,12).

The purpose of this pathway is not to label every patient precisely as F0, F1, F2, F3, or F4 in general medicine. The purpose is to separate patients who can be managed with periodic monitoring and cardiometabolic treatment from patients who require specialist evaluation for advanced fibrosis, cirrhosis surveillance, portal hypertension assessment, liver cancer surveillance, or MASH-targeted treatment.

Table 1. Practical general-medicine pathway for incidental hepatic steatosis or suspected MASLD.

Step	Action	Interpretation	General-medicine response
1. Identify trigger	Incidental steatosis on imaging, unexplained ALT/AST elevation, obesity, type 2 diabetes, metabolic syndrome, or dyslipidemia.	MASLD is likely when steatosis coexists with cardiometabolic risk factors.	Do not ignore normal liver enzymes; proceed to risk assessment.
2. Exclude obvious competing causes	Alcohol history, viral hepatitis status when indicated, medication review, and autoimmune/cholestatic work-up if the biochemical pattern suggests it.	Coexisting causes can change the diagnosis to MetALD, alcohol-related liver disease, viral hepatitis, drug-induced liver injury, or mixed disease.	Address alcohol and reversible causes; refer when diagnosis is uncertain.
3. Assess metabolic context	BMI/waist circumference, blood pressure, HbA1c, lipids, kidney function, cardiovascular history, and sleep apnea symptoms.	MASLD is a cardiometabolic risk marker, not only a liver imaging finding.	Optimize diabetes, weight, blood pressure, lipids, kidney, and cardiovascular prevention.
4. Calculate FIB-4	Use age, AST, ALT, and platelet count.	<1.3 usually low risk in adults <65 years; >=1.3 needs second-line testing; >2.67 increases concern for advanced fibrosis. In adults >65 years, interpret cautiously and consider a higher cutoff.	Repeat periodically if low risk; arrange VCTE/ELF or referral if indeterminate/high risk.
5. Confirm fibrosis risk	VCTE, ELF test, MR elastography, or hepatology review depending on availability.	High liver stiffness or discordant tests indicate increased risk.	Refer for advanced fibrosis, cirrhosis features, discordance, or treatment eligibility.
6. Longitudinal follow-up	Repeat fibrosis score and metabolic review every 1-3 years based on risk; sooner if diabetes, multiple risk factors, or worsening labs.	Risk can evolve with weight gain, diabetes progression, alcohol exposure, or aging.	Use MASLD as a chronic disease prompt within routine general medicine.

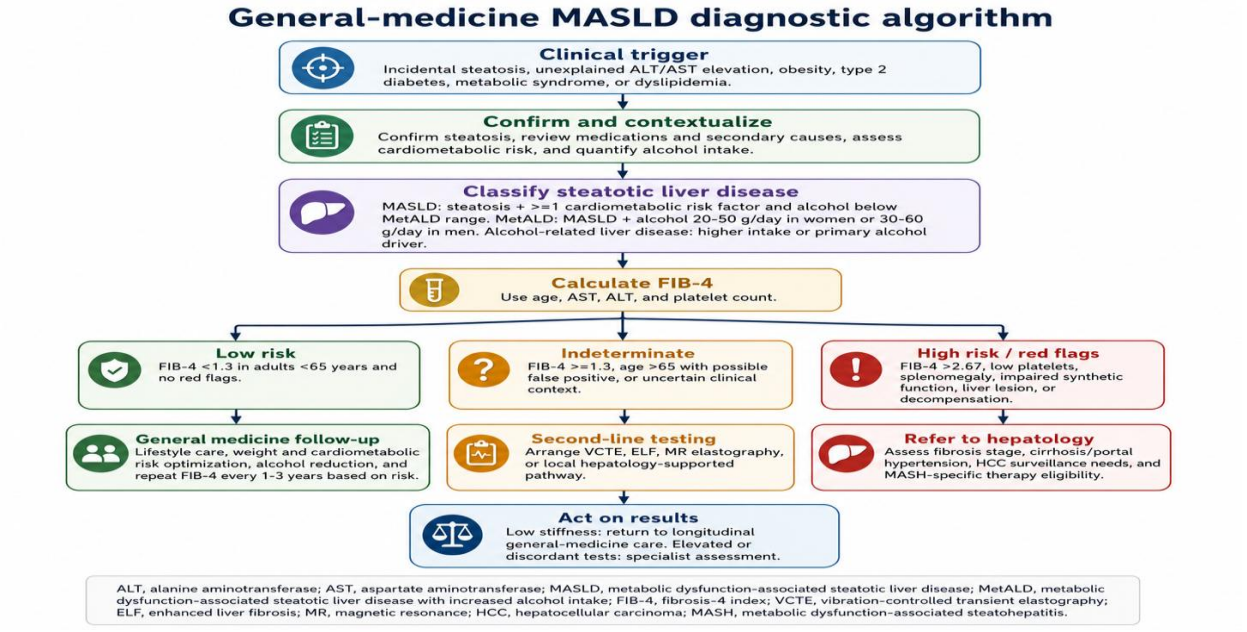

Figure 1. Concise diagnostic algorithm for incidental hepatic steatosis or suspected MASLD in general medicine.

3.5. Cardiometabolic Risk Stratification

The generalist should treat MASLD as a warning signal for cardiometabolic disease. Assessment should include global atherosclerotic cardiovascular disease risk, diabetes status, lipid profile, blood pressure, kidney disease, smoking, physical inactivity, and obesity complications. Statins should not be withheld solely because of MASLD; guidance supports statin use for cardiovascular indications in patients with fatty liver disease, including compensated chronic liver disease, with standard clinical monitoring [2,3,9,10].

Diabetes and MASLD amplify risk in both directions. Type 2 diabetes increases the likelihood of MASH and advanced fibrosis, while MASLD is associated with incident diabetes and more complex cardiometabolic disease. Therefore, patients with type 2 diabetes, prediabetes, obesity with additional metabolic risk factors, or imaging-detected steatosis should not be followed with liver enzymes alone. They should undergo fibrosis risk stratification and metabolic optimization in the same care cycle (2-5).

The cardiometabolic visit should also address alcohol, sleep, diet quality, sedentary time, sarcopenia risk, and medications. Even alcohol below traditional harmful thresholds may worsen steatotic liver disease in some patients, particularly when metabolic risk is high. Clinicians should use validated screening tools such as AUDIT-C when available and provide brief intervention or referral when alcohol use disorder is suspected (1,2).

3.6. Management: From Lifestyle to Emerging Pharmacotherapy

Lifestyle intervention remains the foundation of MASLD management. Weight loss through dietary change and physical activity improves steatosis and can improve steatohepatitis and fibrosis in a dose-response manner. Histologic studies suggest that greater weight loss is associated with greater probability of NASH resolution and fibrosis improvement, with approximately 7%-10% or more total body-weight loss commonly used as a practical target for patients with MASH or fibrosis risk [13,14]. Dietary advice should be individualized but can emphasize reduced energy intake, Mediterranean-style dietary patterns, high-fiber foods, reduced sugar-sweetened beverages, reduced refined carbohydrates, adequate protein, and avoidance of excessive alcohol. Exercise should include both aerobic and resistance activity where possible, because cardiorespiratory fitness, insulin sensitivity, muscle mass, and weight maintenance are relevant even when weight loss is modest. Bariatric surgery or endoscopic obesity interventions may be appropriate for selected patients with severe obesity after multidisciplinary evaluation and can improve MASH and fibrosis in many patients (15).

Pharmacotherapy is evolving rapidly, but patient selection remains central. Older options such as vitamin E in selected non-diabetic adults with biopsy-proven NASH and pioglitazone in selected patients, especially with diabetes, have evidence but require individualized risk-benefit discussion (16). Resmetirom, a thyroid hormone receptor-beta agonist, demonstrated histologic benefits in a phase 3 trial and received US accelerated approval for adults with non-cirrhotic NASH/MASH with moderate-to-advanced fibrosis in conjunction with diet and exercise (17-20). Semaglutide 2.4 mg showed histologic benefit in phase 2 and phase 3 MASH trials, and the US Food and Drug Administration granted accelerated approval in August 2025 for adults with non-cirrhotic MASH with moderate-to-advanced fibrosis, in conjunction with reduced-calorie diet and increased physical activity (21-23). Tirzepatide also showed promising phase 2 results for MASH resolution without worsening fibrosis, but as of this review update it should be considered investigational for MASH unless approved in the relevant jurisdiction (24).

These therapies do not remove the need for lifestyle and cardiometabolic management. They also require appropriate patient selection, exclusion of cirrhosis when the label does not cover cirrhosis, attention to drug interactions and contraindications, monitoring, and coordination with hepatology or experienced metabolic-liver clinics. In general medicine, the immediate priority is to identify patients with probable F2-F3 fibrosis who may benefit from referral for treatment consideration.

3.7. Referral, Follow-up, and Systems of Care

Referral should be based on risk rather than the mere presence of steatosis. Patients should be referred to hepatology or a metabolic-liver clinic when FIB-4 is high, second-line testing suggests significant or advanced fibrosis, liver stiffness is elevated, there are signs of cirrhosis or portal hypertension, aminotransferases remain persistently elevated without explanation, autoimmune/cholestatic/viral disease is suspected, or MASH-specific pharmacotherapy is being considered (2-5,20,23).

Low-risk patients still need follow-up. In patients with diabetes, obesity, or multiple metabolic risk factors, fibrosis scores should be repeated periodically because risk can progress. Follow-up should be linked to routine chronic disease care: HbA1c, blood pressure, lipids, renal function, smoking status, weight trajectory, alcohol exposure, and medication adherence. Embedding FIB-4 calculation into

electronic health records may improve case-finding, but clinicians must still interpret results in context.

A systems-based model is important because MASLD crosses traditional specialty boundaries. The highest-yield intervention may be a pathway that enables the radiology report or abnormal laboratory result to trigger metabolic assessment, FIB-4 calculation, and second-line fibrosis testing rather than an isolated fatty liver comment. Such pathways can reduce missed advanced fibrosis and avoid overwhelming hepatology services with low-risk steatosis.

Table 2. General-medicine management priorities by MASLD risk category.

Risk category	Typical findings	Management priorities	Referral/monitoring
Low fibrosis risk	FIB-4 below rule-out threshold; no features of chronic liver disease; stable platelets and liver tests.	Lifestyle counseling, weight reduction when indicated, diabetes/lipid/BP optimization, statin when indicated, alcohol reduction, and vaccination review.	Repeat FIB-4 every 1-3 years depending on diabetes and metabolic burden.
Indeterminate fibrosis risk	FIB-4 >=1.3 or difficult interpretation due to age/comorbidity; no overt cirrhosis.	Second-line test with VCTE/ELF if available; intensify metabolic management while awaiting results.	Refer if second-line testing suggests significant fibrosis or results are discordant.
High fibrosis risk	FIB-4 >2.67, high liver stiffness, falling platelets, splenomegaly, or persistent ALT/AST elevation with risk factors.	Assess for advanced fibrosis/cirrhosis, avoid hepatotoxic risks, and optimize cardiovascular and diabetes therapy.	Hepatology referral; consider MASH-targeted therapy eligibility if non-cirrhotic F2-F3 fibrosis.
Possible cirrhosis/decompensation	Low platelets, low albumin, high INR, nodular liver, ascites, varices, encephalopathy, jaundice, or liver lesion.	Do not manage as simple fatty liver; assess urgently for complications and medication safety.	Urgent hepatology referral; HCC/variceal surveillance and portal hypertension management.
High cardiometabolic risk regardless of fibrosis	Type 2 diabetes, established ASCVD, CKD, obesity complications, hypertension, or dyslipidemia.	Cardiovascular risk score, statin, BP control, diabetes agents with metabolic benefit, smoking cessation, and sleep apnea evaluation.	Shared care with primary care, endocrinology, cardiology, obesity medicine, and hepatology as indicated.

3.8. Practical Pitfalls, Controversies, and Knowledge Gaps

Several pitfalls are common in general medicine. Liver enzymes may be normal in advanced fibrosis, so ALT alone is not a screening tool for risk. Ultrasound-detected steatosis is not equivalent to low-risk disease and cannot stage fibrosis. FIB-4 is useful for triage but not definitive, especially in younger adults, older adults, acute illness, thrombocytopenia, or mixed liver disease. MASLD should not lead to undertreatment of dyslipidemia; cardiovascular prevention remains central.

Terminology also creates practical controversies. MASLD is more biologically accurate and less stigmatizing than NAFLD, but some patients fall into overlapping zones of metabolic dysfunction, alcohol exposure, viral hepatitis, medication-related steatosis, and genetic susceptibility. MetALD is particularly important because alcohol thresholds are imperfect, intake is often under-reported, and the interaction between alcohol and metabolic risk is probably continuous rather than binary (1,2).

Pharmacologic therapy raises additional unanswered questions. Trials have generally enrolled selected patients with non-cirrhotic MASH and F2-F3 fibrosis, so results should not be extrapolated to low-risk steatosis, decompensated cirrhosis, or unclassified mixed liver disease. Long-term clinical outcomes,

durability after discontinuation, safety in multimorbidity, use in older adults, combination therapy, sequencing, and equitable access remain unresolved. More real-world data are also needed to determine whether these therapies reduce cardiovascular events, liver decompensation, transplantation, and mortality rather than only improving histologic endpoints.

Implementation remains another gap. Optimal screening frequency, thresholds for older adults, cost-effectiveness of elastography in primary care, and region-specific pathways require further study. More evidence is needed in populations in the Middle East and North Africa, where obesity, diabetes, and cardiometabolic disease are highly prevalent and where alcohol reporting, health-system pathways, and access to elastography or newer therapies may differ from trial settings.

4. Conclusion

MASLD is now a central general-medicine condition because it links incidental liver steatosis with systemic cardiometabolic risk and potentially progressive liver fibrosis. The most important clinical shift is from passively documenting fatty liver to actively stratifying fibrosis and cardiovascular risk. A practical pathway begins with recognition of steatosis or metabolic risk, assessment of alcohol and competing causes, calculation of FIB-4, second-line non-invasive testing when indicated, and referral for high-risk or uncertain cases.

For clinicians, the immediate message is simple: incidental fatty liver should not be dismissed, but neither should every patient be referred without triage. Most low-risk patients can be managed in general medicine with lifestyle intervention, weight and diabetes management, cardiovascular prevention, alcohol reduction, and periodic reassessment. Patients with suspected significant fibrosis, advanced fibrosis, cirrhosis, or potential eligibility for MASH-directed treatment should be identified early and linked to hepatology care. This integrated approach can transform MASLD from an incidental imaging finding into a structured opportunity for prevention.

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Ethical Considerations and Compliance with Ethical Guidelines

This article is a narrative review with no human or animal sample and no patient-level data. Therefore, institutional ethical approval and informed consent were not required.

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Conflict of interest

The authors declare no conflict of interest

AI Using Declaration

AI-assisted tools were used to support language editing, grammar checking, readability improvement, and formatting. The authors reviewed and verified all scientific content, clinical interpretation, and references and take full responsibility for the integrity and accuracy of the work.

Authors' contributions

All authors equally contributed to the preparation of this article.

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