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Hepatic Steatosis in Primary Care

Targeted Literature Review in Support of Primary Care Practice

Authors (alphabetical order):
Samuel Boudreault, M.D., M.Sc., FCFP
Emma Glaser, M.D., M.Sc., CCFP
Julie Laurence, M.Sc., ACNP
Guylène Thériault, M.D., Dip Sc, MEd, CCFP
Marc-Antoine Turgeon, M.D., MBA, CCFP
René Wittmer, M.D., CCFP

Reviewers:
Marie Brien, B.Sc., M.Sc., NP-Primary care
Isabelle Carrière, M.D. Émilie Tulk, M.D.

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References have been formatted in NMA style by ChatGPT (free version).

Context

Screening and routine investigations that lead to incidental findings pose a significant challenge for primary care clinicians.

For instance, hepatic steatosis is detected by ultrasound in approximately 21% of adults (1). Elevated liver enzymes (ALT or AST) occur in about 10% of the population, with most cases attributable to non-alcoholic fatty liver disease (2).

When faced with such results, clinicians often encounter uncertainty: Should further investigations be pursued? Should follow-up be arranged? Are there patients who require specific management?

Several guidelines address these questions. Unfortunately, many are not supported by strong evidence demonstrating a meaningful impact on patient-important outcomes. Moreover, applying these recommendations in primary care is challenging, as they potentially target a substantial proportion of patients—between one-quarter and one-third of the population. Some guidelines also present notable methodological shortcomings, such as recommendations not backed by a systematic review or supported by a review that is not publicly available. Additionally, several authors disclose financial conflicts of interest without clear mitigating measures.

Our goal here is to provide a pragmatic tool for clinicians managing hepatic steatosis. We aim to present current scientific evidence in a transparent and accessible way, while acknowledging areas of uncertainty and clinical equipoise. To achieve this, we conducted a rapid narrative review structured around specific clinical PICO questions (Population, Intervention, Comparison, Outcome). We sought to capture the most relevant literature, though we did not perform a full systematic review. If you believe we have overlooked important studies, we welcome your input. This tool is designed with the realities of primary care in mind—where decisions must be relevant, efficient, and mindful of responsible resource use.

Finally, given the high prevalence of metabolic risk factors such as obesity and diabetes, we must consider the workload implications of implementing recommendations. Even relatively brief interventions can impose a substantial opportunity cost when applied to large patient populations. We should therefore prioritise interventions with demonstrated benefits on outcomes that matter to patients.

> **“There is a massive mismatch between the expectations of healthcare personnel and the time that healthcare personnel have to give the care that is expected. This massive mismatch contributes to ineffective care, because we don’t spend time on interventions with the greatest benefit. It also contributes to unequal care, because we don’t spend our time with the patients with the greatest care needs. It also leads to moral stress, injury, and burnout amongst clinicians”.**
>
> **— Dr. Minna Johansson, family physician and founder of the Cochrane Sustainable Healthcare initiative**

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01 Definitions

Hepatic steatosis (1964)
Term referring to the accumulation of fat in the liver; still often used by primary care clinicians despite its low specificity.

Non-alcoholic steatohepatitis (NASH) (1980)
Histological term describing steatohepatitis occurring in patients who do not abuse alcohol. It cannot be distinguished histologically from alcoholic steatohepatitis.

Non-alcoholic fatty liver disease (NAFLD) (1986)
Term introducing the concept of a "disease."

Metabolic-dysfunction associated fatty liver disease (MAFLD) (2020)
This term replaces "non-alcoholic" with "metabolic dysfunction." It clarifies that we are referring to steatotic liver disease arising from metabolic problems such as diabetes and obesity. However, in English it still retains the word "fatty."

Metabolic-dysfunction associated steatotic liver disease (MASLD) (2023)
A less stigmatizing term that refers neither to fat nor to alcohol. It allows MASLD to be distinguished from other subtypes of steatotic liver disease (e.g., secondary to hemochromatosis).

Metabolic associated steatohepatitis (MASH)
MASLD with histologically proven tissue inflammation.

The term "hepatic steatosis" is used occasionally in this document because it is frequently used and not stigmatizing. However, we recognize the importance of clearly defining the condition being discussed here, which is in fact metabolic dysfunction-associated steatotic liver disease (MASLD).

02 Key Findings from Our Literature Review

No evidence supports screening for MASLD

Studies comparing screening with no screening are needed to assess potential benefits and harms before recommending this practice. Whether in patients without risk factors or those living with obesity or diabetes, there is no evidence that screening with ultrasound or blood tests has any impact on patient-important outcomes (e.g., reducing mortality or morbidity).

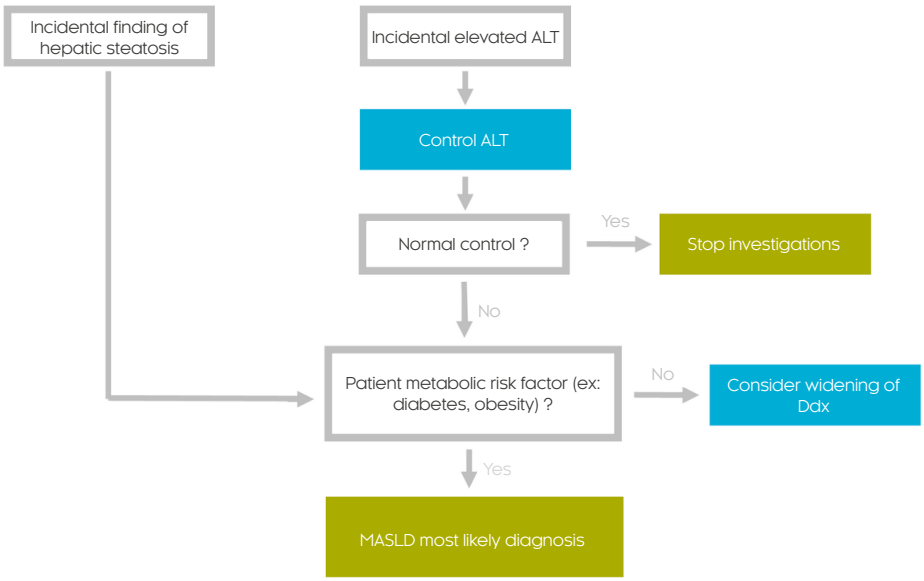
A diagnosis of MASLD does not help patients change their lifestyle habits

We found no evidence suggesting that a diagnosis of hepatic steatosis leads to positive changes in lifestyle habits or to sustained weight loss.

Extensive investigation is rarely justified

When metabolic risk factors or conditions are present, further investigations are not routinely suggested—except those needed to elucidate comorbidities often associated with steatosis, such as diabetes (if not already diagnosed), hypertension, and cardiovascular risk.

If the patient has no metabolic risk factors, it is reasonable to broaden investigations to look for secondary causes. Clinical assessment and physician judgment should guide whether to proceed with more extensive testing.



*These recommendations do not apply to individuals whose ALT values are 2–3 times above the upper limit of normal.

Lifestyle interventions remain the cornerstone of treatment

Lifestyle interventions have demonstrated benefits and can be offered regardless of the degree of fibrosis. Alcohol cessation, adopting healthy eating habits, and increasing physical activity should be the foundation of MASLD management. Hepatitis A and B vaccination should be considered to prevent further liver damage (see the Quebec Immunization Program). Beyond cardiovascular risk management, high-quality data are limited regarding patient-important clinical outcomes. GLP-1 receptor agonists and other antidiabetic medications appear to be promising avenues for treatment.

No evidence shows that fibrosis risk assessment changes clinical outcomes

No high-quality study has shown that stratifying advanced fibrosis risk in MASLD patients affects patient-important outcomes.

03 Screening for MASLD

Clinical Question 1

What are the benefits and harms associated with screening for metabolic dysfunction-associated steatotic liver disease (MASLD)?

Key Point

Whether in the general patient population or in those living with obesity or diabetes, there is no evidence that screening with ultrasound or blood tests has any impact on patient-important outcomes (e.g., reducing mortality or morbidity).

Context and Literature Review

For screening to be effective, it must first detect a disease at an early, asymptomatic stage. Furthermore, the proposed test (followed by management of any detected abnormalities) must also be able to change the course of the disease—that is, for at least some of the participants, clinical outcomes should improve, and these potential benefits should outweigh potential harms.

We conducted a rapid search in PubMed, Google Scholar, Trip Database, DynaMed, and Elicit using the terms “steatosis”, “hepatic steatosis”, “NASH”, “NAFLD”, “fatty liver”, “MASLD”, and “screening”, applying the filters systematic review and randomized controlled trial.

We found seven articles addressing MASLD screening (one from 2024, two from 2023, two from 2022, and one from 2021). Below is a summary of these articles as well as a summary of the most recent guideline on the subject, published in 2024.

Summary of Studies and Guidelines

Huang and al. (2024) (1)

This article cites studies with varying methodologies (retrospective, cohort, epidemiological) showing that a percentage of MAFLD cases have normal liver enzymes (ALT). The authors discuss potential screening strategies using scores such as FIB-4. However, they cite no study that shows whether systematic implementation of such scoring can meaningfully change patient-important outcomes.

Ciardullo and al. (2023) (2)

This article examines screening in diabetics, a population at higher risk of MASLD and its complications. The authors describe potential screening tests, assessing their ability to detect fibrosis and other intermediate outcomes (fat quantity, histologic inflammation, fibrosis score). They do not include studies examining patient outcomes after screening.

Kjaergaard and al. (2023) (3)

This is a diagnostic study comparing various scores to indicate presence or absence PROJECT of liver fibrosis. The gold-standard test (biopsy) was not performed on all participants for safety reasons, but no alternative reference test was used.

Binet and al. (2022) (4)

This is a narrative review of different non-invasive tests. The authors recommend measuring BMI, waist circumference, and routine blood tests (AST, ALT, albumin, triglycerides, platelets) in diabetic patients. They do not include any studies that identify potential benefits or harms of performing these tests.

Pal and Mendez-Sanchez (2022) (5)

This is a narrative review noting that various guidelines suggest screening, but controversy persists. The authors discuss different screening tests, but do not mention any comparative studies for these screening tests.

Eskridge et al. (2021) (6)

This study investigates a population-based screening initiative using liver stiffness measurement and a risk score. There is no comparison group. The study solely reports prevalence of different fibrosis stages. It is thus impossible to assess benefits and harms of screening.

Dietrich et al. (2021) (7)

This is a narrative review describing prerequisites before introducing screening. They discuss a cross sectional study performed in Spain that shows a a 9% MASLD prevalence in asymptomatic patients. The authors underscore the risk of overdiagnosis and overtreatment. They suggest screening diabetics and obese individuals based on higher prevalence and higher chances of developing complications, yet again with no studies to support screening benefits on patient important outcomes.

Most Recent Guidelines: EASL–EASD–EASO Clinical Practice Guideline (June 2024) (8)

This guideline suggests screening for MASLD in people with diabetes or obese individuals with a cardiovascular risk factor (low HDL, high TG, or BP > 130/85). Despite being labelled a "strong" recommendation, it is based on expert consensus. The stated evidence level is "3" (cohort studies with a control group), but no studies are cited. The authors acknowledge that there are no randomized controlled trials.

Despite this lack of evidence, the authors argue that monitoring for hepatocellular carcinoma and oesophageal varices in individuals with cirrhosis supports screening, even if cirrhosis is diagnosed in only a minority of those for whom screening is suggested. This recommendation does not consider opportunity costs or the impact of potentially unnecessary interventions.

They argue that screening, fibrosis risk stratification, and follow-up could reduce progression to cirrhosis by aggressively managing traditional risk factors (obesity and diabetes management) , but no specific approach is defined. Some promising medications for histologic regression of MASLD are discussed, but none have demonstrated clinical impact. Many target only fibrosis progression, not cardiovascular mortality—the main cause of death for MASLD patients.

Thus, in many cases, MASLD screening does not change management, treatment, or outcomes—but may greatly increase follow-up burden and add low-value investigations.

Why Screening Is Hard to Recommend

It is hard to recommend a screening test when there is no proof it yields more benefits than harms. MASLD is found in ~30% of adults (9) and 65% of people with diabetes (10). Prevalence increases as obesity increases. Abnormal transaminases affect 10–20% of outpatients (11). Therefore, screening—even limited to those with diabetes or obesity—will generate many incidental findings. Studies are needed to weigh potential benefits and harms before recommending this practice.

Jungner & Wilson Screening Criteria (12)

- **The condition should be an important health problem:**
  MASLD can lead to cirrhosis. While common, cirrhosis is rarer (0.84% in Canada, 2016) (13). MASLD accounts for just over half of cirrhosis cases in Canada (52.7%) (14).
- **The natural history should be well understood:**
  While we know the factors that influence MASLD progression it is still difficult to predict who will progress to cirrhosis.
- **The condition should be detectable at a pre-clinical phase:**
  Fibrosis stage can be estimated with liver stiffness measurement and confirmed by biopsy (stages F0–F3 before cirrhosis at F4).
- **A valid screening test exists:**
  No study has examined the impact of systematic blood, ultrasound, or liver stiffness screening. FIB-4 score validation focuses on predicting fibrosis presence, with many false positives (15).
- **An acceptable test exists:**
  Ultrasound, liver stiffness measurement, and blood tests are generally acceptable to patients.
- **An effective treatment exists:**
  Lifestyle changes can be effective. No medication has been proven to reduce liver related morbidity or mortality in high-quality RCTs.
- **Test and treatment costs must be acceptable:**
  Without evidence that screening changes outcomes, the clinical time required to implement these recommendations is disproportionate.

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04 Impact of Diagnosis on Lifestyle Habits

Clinical Question 2

Does a MASLD diagnosis help patients change their lifestyle habits?

Key Point

We found no evidence suggesting that a MASLD diagnosis has positive effects on patients' lifestyle changes.

Context and Literature Review

We found only one study relevant to our clinical question — the BALLETS study (1). In this prospective cohort study, an abnormal liver function test result or an incidental finding of hepatic steatosis was associated with a temporary increase in anxiety, but no lasting improvement in lifestyle habits and no sustained weight loss over time.

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05 Evaluation of Elevated Liver Enzymes or Incidental Hepatic Steatosis on Ultrasound

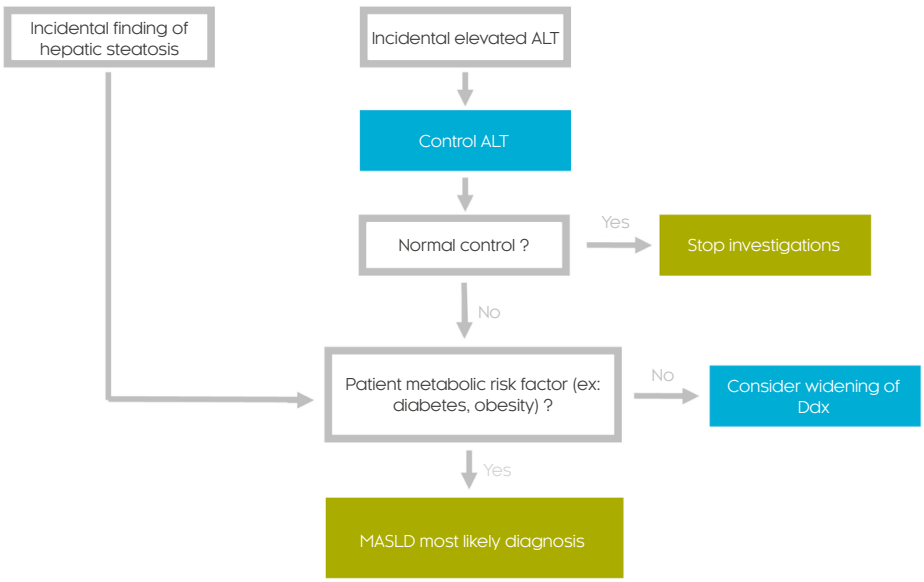
Clinical Question 3

How should patients be evaluated when there is an incidental fi nding of imaging showing hepatic steatosis or incidental elevated liver enzymes?

Key Point

In this diagnostic approach, it is reasonable to consider population prevalence, symptoms, and risk factors such as family history. Rather than ordering a broad panel of tests blindly, a stepwise approach is preferred—starting with the most likely causes or those suggested by history and physical.

If metabolic risk factors are present (BMI ≥ 25, diabetes) and no other cause is suspected (e.g., alcohol, viral hepatitis), this confirms the diagnosis of MASLD (4).



*These recommendations do not apply to individuals whose ALT is 2–3x the upper limit of normal.

Workup Recommended by a Recent European Guideline (1) in Case of Steatosis Found on Abdominal Ultrasound

When MASLD is diagnosed, further investigations are not suggested except those needed to assess comorbidities often associated with it, such as diabetes (if not already known), hypertension, or a lipid profile indicating high cardiovascular risk.

- The guideline (1) also suggests assessing for chronic kidney disease, sleep apnea, and polycystic ovary syndrome—without explaining how this would change clinical outcomes.
  - Without supporting evidence, we do not think creatinine measurement, Epworth score calculation, or PCOS workup should be performed without clinical suspicion.
- No follow-up ultrasound is needed to monitor steatosis. For fibrosis assessment, see the following dedicated section.

Approach Recommended by the Quebec CRDS (Centralized Referral System) for Elevated Liver Enzymes

Referral criteria: ALT ≥ 40 U/L for 6 months or ≥ 91 U/L at presentation. Priority is based on bilirubin and INR results.

BASELINE WORKUP FOR ALL:

- Ultrasound
- AST, ALT, alkaline phosphatase, bilirubin, INR
- HBsAg, anti-HCV
- TSH
- Ferritin and transferrin saturation (to investigate hemochromatosis)

ADDITIONAL CONSIDERATIONS:

- Hypothyroidism is associated with increased MASLD risk independently of diabetes or obesity (2). This association is consistent across most cross-sectional and retrospective cohort studies. Two studies show that thyroid hormone replacement can improve steatosis and cause regression in a significant proportion of patients (3, 4).
- Hemochromatosis prevalence varies by ethnicity (5):
  - 0.44% (1/277) in Caucasians, especially of Northern European descent.
  - 0.11% (1/909) in Indigenous peoples.
  - 0.014% (1/7,142) in Black populations.
  - 0.000039% (1/2.5+ million) in people of Asian origin. A family history of hemochromatosis increases risk.

While CRDS-recommended tests are mandatory for referral, physicians should think carefully before ordering them in all patients—especially those not meeting CRDS criteria (e.g., mildly elevated ALT for < 6 months).

Searching for Metabolic Causes

- Consider a lipid panel if not done in the past 10 years, to assess cardiovascular risk and manage associated factors. Reminder: target-based lipid approaches are not evidence-based; in primary prevention, discuss cardiovascular risk with patients using shared decision-making tools (6).
- Order HbA1C if the patient is not diabetic and it has not been recently verified.

Steatosis caused by metabolic syndrome (MASLD) is the most common form of hepatic steatosis. In North America, chronic alcohol use and hepatitis C are the other leading causes of steatosis. (7).

When a likely etiology is identified, it is reasonable to limit further investigations. Evaluating and excluding rarer secondary causes may be considered depending on the clincal context.

Counseling and Basic Risk Assessment

- Counsel all patients about alcohol.
- Check for hepatotoxic medications.
- Assess risk factors for hepatitis.
- Consider metabolic risk factors.

Expanding the Differential Diagnosis

If imaging shows steatosis in a patient with BMI < 25 and no diabetes, it is reasonable to sequentially investigate secondary causes, starting with the most common. The following tests are not needed for all patients. Each test has an inherent risk of false positives and incidental findings. False positives can often make up most positive results — especially in low-prevalence settings.

ADDITIONAL INVESTIGATIONS — ONLY IF WARRANTED BY CLINICAL SUSPICION:

Test	Condition Investigated	Considerations	Prevalence
Anti-transglutaminase antibodies	Celiac disease	In patients with diarrhea, abdominal pain, or malabsorption. Consider if unexplained elevated liver enzymes with normal BMI. **NOTE** Celiac disease is found more often (2–3%) in MASLD patients than in the general population (9). **However** no evidence shows that detecting it in asymptomatic individuals changes mortality, morbidity, or quality of life (10).	1:100 in Canada (8)
Alpha-1 antitrypsin level	Alpha-1 antitrypsin defi ciency	Consider if coexisting lung disease	1:3,000–1:5,000 in North America (11)
ANA, anti–smooth muscle Ab, anti-LKM, immunoglobulin levels	Autoimmune hepatitis	More common in women	1:3,500 in high-income countries (12)
Ceruloplasmin	Wilson's disease	Mostly in younger patients (< 30–40) with neuropsychiatric symptoms	1:30,000–1:40,000 (13)
Anti-mitochondrial antibodies (not CRDS-suggested)	Primary biliary cholangitis	In patients with cholestatic profile; rare before 25, usually diagnosed after 40; women affected 10:1 vs men	1:4,500 in North America (14)

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06 Assessment of Fibrosis Stage

Clinical Question 4

Does evaluating the risk of advanced fibrosis in patients diagnosed with MASLD improve clinical outcomes?

Key Point

No high-quality study has shown that assessing advanced fibrosis risk in MASLD patients affects patient-important outcomes.

Context and Literature Review

IS IT USEFUL?

Several practice guidelines suggest estimating advanced fibrosis risk using non-invasive tests (serologic tests, liver elastography). Our search found no high-quality evidence that such risk stratification changes clinical outcomes—such as reducing progression to decompensated liver disease or mortality.

Non-invasive monitoring (fibrosis risk stratification) is therefore not based on strong evidence. Treatment remains the same—managing cardiometabolic risk factors—regardless of fibrosis stage (see Treatments section). Thus, for many patients, clinicians can recommend lifestyle changes and other effective interventions without first performing fibrosis risk stratification.

Risk stratification may still be considered if:

- Results would change management or access to treatment (e.g., pre-bariatric surgery evaluation)
- It is part of a diagnostic process where cirrhosis is clinically suspected

If compensated cirrhosis is detected during stratification, additional exams and monitoring can be offered. However, no treatment exists to reverse MASLD at the cirrhosis stage. In these cases, hepatocellular carcinoma and esophageal varices screening can be done — but high-quality data on these interventions are lacking:

- A 2019 narrative review on varices surveillance in cirrhosis found no randomized studies showing benefits (1). It mentions clinical criteria to reduce endoscopy frequency in lower-risk patients (based on blood tests and fibrosis measurement).
- A 2022 systematic review on hepatocellular carcinoma surveillance in cirrhosis found no randomized trials; it reported lower overall mortality with surveillance, but only 12 studies adjusted for lead-time bias, and none accounted for prognostic selection bias or overdiagnosis (2).

Who Is at Higher Risk of Advanced Fibrosis?

Conditions associated with higher prevalence of advanced fibrosis (3):

- Type 2 diabetes
- Obesity with metabolic complications
- MASLD plus at least moderate alcohol consumption
- First-degree relative with MASH-related cirrhosis

Montreal CRDS notes higher risk in patients with: (4)

- Long-standing diabetes or metabolic syndrome
- BMI > 40, or > 35 since adolescence with weight gain despite ≥ 2 years of counselling and follow-up
- Splenomegaly or thrombocytopenia on imaging
- Nodular or dysmorphic liver on imaging

Time to Develop Severe Liver Disease

One observational study (7) followed patients by fibrosis stage for ~20 years:

Fibrosis Stage	Avg. time to hepatic decompensation
F0-1	22–26 years
F2	9.3 years
F3	2.3 years
F4	0.9 years

At earlier stages, patients can be followed for decades before the first sign of decompensation.

If We Stratify Risk — Which Test to Use?

Fibrosis progresses from F0 (none) to F3–F4 (advanced). F4 = cirrhosis. Common non-invasive tools: NAFLD score, FIB-4, APRI, elastography, MRI, ELF test. Recent guidelines and Quebec experts prefer FIB-4 and elastography (FibroScan®) (4, 8, 9).

Important !

- Ultrasound often detects steatosis but is not sensitive for fibrosis detection (10). Follow-up ultrasounds for steatosis grading have no clinical utility for fibrosis. These ultrasounds waste resources.
- Liver enzymes alone are not reliable for fibrosis stage estimation (11).

Test Accuracy

Studies report sensitivity and specificity compared to biopsy:

FIB-4 in diabetics (12):		
Cut-off	**Sensitivity**	**Specificity**
> 1.3–1.67	74 %	62 %
> 2.67–3.25	33 %	92 %

Guidelines recommend a low cut-off (≥ 1.3) to avoid missing advanced fibrosis (8, 9). Evidence is lacking for patients < 35 and > 65 years; in > 65, a higher cut-off (> 2) is suggested, but based only on expert opinion (9).

FibroScan® (14):		
Probe / threshold	**Sensitivity**	**Specificity**
M probe (< 9.6 kPa)	80.1 %	89.9 %
XL probe (5.7–9.3 kPa)	75.3 %	74 %

Because FIB-4 yields many false positives, guidelines recommend confirming with FibroScan® for scores 1.3–2.67 or > 2.67 (9). In Quebec, limited access to FibroScan® means some regions of CRDS advise referring only if FIB-4 > 3.25 when FibroScan® is unavailable (4).

Combining FIB-4 + FibroScan® (15):		
Criteria	**Sensitivity**	**Specificity**
FIB-4 > 1.3 + FibroScan® > 8 kPa	84.7 %	94.7 %

These results are better in high-risk populations (prevalence of cirrhosis 13.4% in the study vs 1.48% in Canadian MASLD cases) (5, 15). No high-quality evidence exists for general primary care use.

How Often to Repeat?

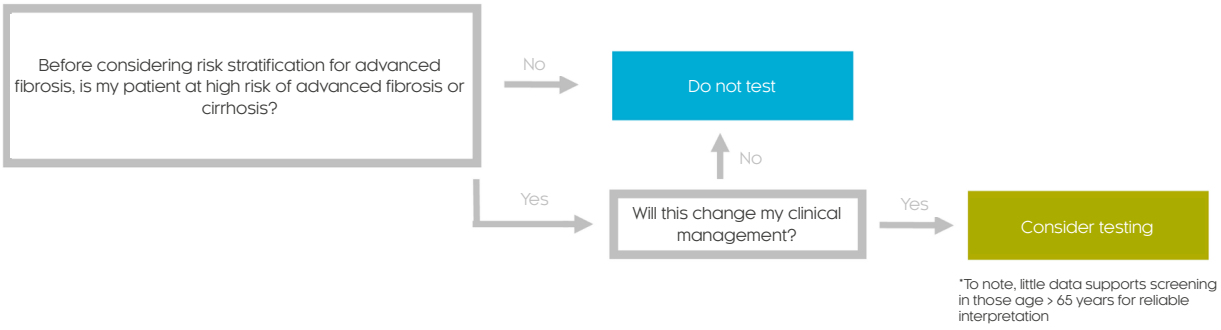
No clear consensus. No evidence guides optimal repeat interval. American guidelines suggest FIB-4 every 2–3 years in low-risk, yearly in intermediate, and automatic referral in high-risk patients (9). Montreal CRDS advises yearly for intermediate risk; otherwise, no guidance is offered (4).

Given the natural history of fibrosis progression, we esteem that a 5–10 year recheck is more appropriate when advanced fibrosis is excluded.

Our Algorithm (if risk stratification is considered useful)

The authors of this document question whether these tests, that are more sensitive than they are specific, are worth the cost of clinician and patient time, in money and resources.

Especially, considering that management will remain unchanged, and that no well done study has supported their use outside of specialty clinics. We recommend the following algorithm to guide your clinical management with regards to fibrosis risk stratification:



***Risk factors:**

- Age > 50 with:
  - Long-standing type 2 diabetes
  - Obesity with complications
  - Obesity since adolescence with major weight gain despite ≥ 2 years of lifestyle habits counselling
- First-degree relative with MASH cirrhosis
- Additional: moderate/high alcohol use, chronic HCV infection

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07 Potential Treatments

Clinical Question 5

Which treatments improve patient-important clinical outcomes in MASLD?

Key Point

Lifestyle interventions of MASLD management are effective and can (and should) be offered regardless of fibrosis stage. Alcohol cessation, healthy eating patterns, and increased physical activity are the cornerstone of care. Hepatitis A and B vaccination should be considered to avoid further liver injury (see the Quebec Immunization Program). Beyond cardiovascular risk management, high-quality data remain limited for interventions improving patient-important clinical outcomes in MASLD. GLP-1 receptor agonists and other antidiabetic agents appear to be a promising avenue. Yet, RCTs on clinically important outcomes have yet to be performed.

Context

It's important to remember that recommendations for interventions should be based on patient important outcomes (clinical morbidity and/or mortality), not only secondary outcomes (histological variation or variation on biochemical tests such as liver enzymes). Randomized controlled trials should be prioritised for these questions, because they have less bias than observational studies.

Note that the majority of studies examining interventions on steatosis, included biopsy confirmed steatosis. These patients were not diagnosed using FIB-4 and/or elastography.

Interventions Recommended for All

Unhealthy lifestyle habits, such as malnutrition, sedentary lifestyle, and alcohol consumption are well known contributors to poor health in general, including liver health. Clinicians can propose brief interventions, without adverse effects, and potential benefits for patients with hepatic steatosis. Here is a quick review of interventions to be encouraged in all contexts:

- Conduct medication review and consider deprescribing or replacing medications that are hepatotoxic(1).
- Support weight loss : even modest weight loss may engender a regression in hepatic inflammation and fibrosis (2).
- Encourage Mediterranean diet : rich in untransformed foods, good fats and polyphenols (3).
- Encourage physical activity (4).
- Encourage alcohol cessation or reduction.
- Verify vaccine status against hepatitis A & B : vaccinate if necessary (see PIQ).
- Screen and manage cardiovascular risk factors such as hypertension, diabetes. These risk factors are what contribute to morbidity and mortality for these patients.

Data concerning lifestyle habits are mainly from observational studies, and studies that regard secondary outcomes, or risk of developing MASLD. Since lifestyle habit interventions have been associated with other benefits, notably cardiovascular risk reduction, it appears to be reasonable to offer these interventions to all patients, even in the absence of randomized controlled trials showing improvement on specifically liver related patient oriented outcomes.

Pharmacological Interventions

The limited data surrounding pharmacological interventions is presented in the following section :

AGLP-1

- aGLP-1 have been demonstrated to have cardiovascular benefits for people with diabetes (5) and for non diabetic people with obesity and cardiovascular disease (6). In these populations, aGLP-1 are often already considered and offered.
  - Even if at this time no direct study has shown cardiovascular benefits for obese and non diabetic patients without cardiovascular disease, certain benefits seem still plausible. However these benefits are likely to be less pronounced given that baseline risk is less elevated (7). Weight loss in general seems likely to confer benefits.
- Two systematic reviews on observational studies were published in 2025. The first (8) showed a decrease in major liver related patient important outcomes (1,82% vs 2,48%) (composite score that included cirrhosis development, liver transplant, incidence of hepatic carcinoma, or mortality of hepatic related cause). This study did not show a reduced risk in carcinoma or liver related mortality when analyzed separately. The second review (9) showed a reduction in hepatic cancers in people living with diabetes, a report that did not include absolute risk reductions. A reduction in hepatic decompensation was present in both these studies (reduction of 0,26%; from 1,75% to 1,49% in the first review, unable to calculate in the second).
- Randomized controlled trials conducted in the context of MASLD show impacts solely on biological markers, such as hepatic enzymes, weight, glucose, or fatty liver cells. No data has been reported on clinical issues (10), including a recent study published in April 2025 (11). In this last study, like in others, patients had a biopsy confirmed diagnosis. Patients were not fortuitously discovered or screened with FIB-4 and elastography.
- It would be relevant to see if future randomized controlled trials would be performed in populations that resemble those seen in primary care, and whether these interventions would confer benefits on patient important outcomes.

Potential Treatments

RESMETIROM

- Resmetirom is a β receptor agonist of thyroid hormone. It links to this receptor and activates metabolic cascades related to fat cells and inflammation in liver cells.
- Three studies have shown histological regression of fibrosis 25% vs 15% with placebo, a reduction in fat cell content in the liver, a reduction in steatohepatitis(27,6% vs 10,6% with placebo), and a reduction in liver enzymes (reduction in AST 6 U/L and decreased ALT of 12U/L) (12). Once again, there are still no data showing changes in patient oriented outcomes. All three studies have the same first author, who has declared financial links with pharmaceutical companies. Furthermore, one of the studies is in fact an interimary report of an ongoing study (13).
- There is no clear data showing the impact of Resmetirom when patients are concomitantly on aGLP-1. One study was published before the common use of aGLP-1 (14). The most recent study (10) did not report how many patients were on aGLP-1 and the last (15) where information was collected, did not do a separate analysis of those on and off these medications in order to evaluate whether this modified the impact of Resmetirom.

ISGLT2

- Many studies, including some randomized controlled trials, suggest that iSGLT2 could have benefit for patients with MASLD (16,17). In a systematic review (13) which included observational studies as well as randomized trials in diabetic patients, 19 out of 25 studies reported improvement on hepatic enzymes. Two studies showed histological regression. More studies used non-invasive measures of fibrosis compared to studies with aGLP-1.
- A randomized study published in June 2025, with more than half of patients non diabetic, confirmed histological regression of fibrosis using dapafliglozine (45% vs 20% with placebo) and regression of (23% vs 8% with placebo) at 48 months (18).
- No study to date with iSGLT2 shows improvement for patient oriented outcomes

OTHER MEDICATIONS

- Other pharmacological options, including antidiabetic medications, have been studied. Available data is limited and contradictory, and is once again focused on secondary outcomes (16, 17).
- Statins may have benefits for fibrosis. Studies are lacking to recommend them to all patients. When they are indicated, and in absence of important anomalies of hepatic enzymes, they seem to confer benefits for hepatic outcomes as well as their known cardiovascular effect (19).

Surgical Interventions

BARIATRIC SURGERY

- Bariatric surgery is the most effective treatment for resolution of MASH, surpassing lifestyle and pharmacological interventions (20).
- In an RCT with 288 adults with MASH confirmed by biopsy, the histological resolution of MASH without deteriorating fibrosis was obtained in 50% of operated patients, compared to 16% in the lifestyle treatment group (20).
- Meta-analyses of retrospective cohort studies (21,22) show similar results. Improvement of steatosis over time, reduced inflammation and fibrosis, and decreased hepatic related complications, including reduced progression toward cirrhosis (23).
- Still, no randomized control trial has reproduced these clinically important outcomes.
- It must be noted that bariatric surgery is an invasive intervention, and should always be considered in the context of potential benefits and harms. It has been shown to have cardiovascular benefits.

Summary Table — Interventions with Evidence in MASLD

Intervention	Evidence for Histological Improvement	Evidence for Improved Patient-Important Outcomes
Weight loss ≥ 7–10%	Yes	Observational only
Mediterranean diet	Yes	No
Aerobic or resistance exercise	Yes	No
GLP-1 RAs (liraglutide, semaglutide)	Yes	No
Pioglitazone	Yes	No
Vitamin E (non-diabetics)	Yes	No
Bariatric surgery	Yes	Observational only

As is shown in this table, up until now, few interventions have been shown using rigorous scientific studies to have significant clinical benefit for patients. Given this context, before recommending a treatment specific to steatosis, it is essential to have better data on patient oriented outcomes.

This being said, some data suggests that there are likely hepatic benefits for certain treatments, like iSGLT2 or GLP-1 agonists, or bariatric surgery. Given that most patients with advanced fibrosis already have an indication for these medications. In these cases, it is relevant to consider these treatments, in the light of their principal indications, all while recognizing their potential added benefits for the liver.

Because generally, treatments will be guided by comorbidities rather than steatosis alone, screening doesn't have a major impact on management. It would be prudent to pause before recommending large scale screening in this context.

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08 Time Needed to Treat

Clinical Question 6

How much time do clinicians need to screen for and monitor MASLD according to clinical practice guidelines?

Key Point

We found no literature on the impact of MASLD screening and monitoring on clinician time. Our modelling suggests that, annually, this represents just over 30 hours for a patient panel of 1,000 patients. Over 25 years of practice, calculating FIB-4 annually for patients targeted by the guidelines would take a clinician more than 800 hours — the equivalent of 20 weeks of full-time work.

Given that there is no evidence showing that screening changes clinical outcomes, is this a good use of our time?

Context

TNT (Time Needed to Treat) represents the time required for clinicians to implement a recommendation. Here we explain how we estimated the time needed to treat for the following recommendation (1):

> "Investigate MASLD in patients with diabetes, obesity plus a cardiovascular risk factor (low HDL, high triglycerides, or BP >130/85), or in cases of incidental findings of abnormal liver enzymes or hepatic steatosis on ultrasound."
> — Guidelines of the European Association for the Study of the Liver (EASLD)

We made our estimates for a panel of 1,000 adult patients followed over 25 years. We used available data to estimate the prevalence of abnormal bloodwork results (2)(3)(4) and the prevalence of diabetes and other metabolic risk factors (5)(6)(7).

Number of Patients With Diabetes, Obesity, or Metabolic Syndrome

- Obesity prevalence in Quebec (2024): 29%
- Metabolic syndrome prevalence (2012):
  - 13% among 18–39 years
  - 25% among 40–59 years
  - 39% among 60–79 years
- Patients already followed by a family physician are likely at higher risk of obesity and metabolic syndrome, but many of these individuals are probably also known to have diabetes.

Given the prevalence of hypertension, diabetes, obesity, and other cardiovascular risk factors, we used a conservative estimate that 30% of the patient panel could be eligible for screening as recommended in some guidelines.

Estimated Discovery of Abnormal Bloodwork Results

- Prevalence of abnormal liver enzymes in asymptomatic individuals: ~10–20%. We used a conservative estimate of 10%.
- Prevalence of CBC abnormalities (needed to calculate a FIB-4): 15%.

We conducted a survey (8) to estimate the time required for each step potentially needed to implement advanced fibrosis screening. The survey was distributed to practising family physicians in Quebec, obtaining 58 responses (1 excluded as the respondent was not a family physician).

Physicians were recruited via virtual communities of practice hosted on Facebook over 10 days (August 22 to September 1, 2024).

Time Estimates From Respondents

Step	Average time required
Discuss ultrasound result showing hepatic steatosis	8 min
Discuss abnormal liver enzyme result	7 min
Order blood tests	3 min
File normal blood test result	2 min
Manage abnormal blood test result	9 min
Order ultrasound	3 min
File normal ultrasound result	2 min
Manage abnormal ultrasound result	9 min
Request hepatic elastography (FibroScan®)	6 min
Complete specialty referral request	5 min

Applying The Screening Recommendation (per clinician)

To look for advanced fibrosis in at-risk patients, most guidelines recommend using the FIB-4.

These recommendations also suggest repeating the process every 1–3 years (see section on this topic).

Using our survey results and the prevalence data above, for a panel of 1,000 patients — 300 of whom would be considered at risk — the estimated clinician time is:

- Monthly hours: 3 h
- Annual hours: 34 h
- 25-year total if screening every 3 years: 281 h
- 25-year total if screening annually: 844 h

Additional time for follow-up interventions

- FibroScan request (396/1,000 patients screened):
  - 396 × 6 min = 2,376 min ≈ 40 h
- Gastroenterology referral (46/1,000 patients screened):
  - 46 × 5 min = 230 min ≈ 4 h
- Rheumatology referral (15/1,000 patients screened) (11):
  - 15 × 5 min = 75 min ≈ 1 h

These three downstream interventions from screening would add ~45 hours of clinician time at least once. It is difficult to model how often these would recur over years (e.g., a patient referred to gastroenterology would not be referred annually).

Applying the Recommendation to the Quebec Population

We also attempted to estimate TNT for the entire Quebec population with diabetes or metabolic risk factors:

- 540,000 adults with diabetes in Quebec (2019)
- Removing type 1 diabetes (~10%), leaves 500,000 with type 2 diabetes.

Annual FIB-4 screening for all Quebec adults with diabetes would require at least 56,250 hours per year — the equivalent of 29 full-time clinicians (assuming 40-hour weeks and 48 working weeks/year) — not counting time for referrals and follow-up tests arising from screening.

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Conclusion

This document provides an overview of current knowledge on hepatic steatosis. There is no simple answer to the many questions raised by MASLD. By combining various resources and studies on the topic, we hope to encourage critical reflection on this subject. Family physicians and other primary care practitioners must apply critical thinking in many areas. We hope this document will help foster reflection on MASLD.

We will make every effort to keep this document up to date. Please refer to the date shown on the first page when consulting it. Do not hesitate to contact us if we have missed any studies you feel should be brought to our attention.

Disclosure of Conflicts of Interest

Samuel Boudreault reports no affiliations with industry. He states that he has received presenter fees for various continuing professional development events, and has never received honoraria from industry. He is a full-time faculty member in the Department of Family Medicine and Emergency Medicine at Université Laval, a member of the steering committee for the Choosing Wisely Québec campaign, chair of the scientific committee for the Practising Wisely training program, and a member of the Best Practices Working Group at the Québec College of Family Physicians.

Emma Glaser reports no affiliations with industry. She states that she has received presenter fees for various continuing professional development events, and has never received honoraria from industry. She is an editor for two knowledge translation platforms: TopMF and Réseau-1 Québec.

Julie Laurence reports no affiliations with industry. She states that she has received presenter fees for one continuing professional development event, not linked to industry.

Guylène Thériault reports no affiliations with the pharmaceutical or diagnostic industries. She states that she has received presenter fees and expense reimbursements for various continuing professional development events and her role as member and chair of the Canadian Task Force on Preventive Healthcare. She receives honoraria in her role as co-lead for primary care at Choosing Wisely Canada and serves as vice-president of Choosing Wisely Québec. She is involved as a member of the scientific committee for Practising Wisely and TopMF. She is also a member of the Best Practices Working Group at the Québec College of Family Physicians.

Marc-Antoine Turgeon reports no affiliations with industry. He states that he has received presenter fees for various continuing professional development events and has never received honoraria from industry. He is a full-time faculty member in the Department of Family Medicine and Emergency Medicine at Université Laval, a member of the steering committee for the Choosing Wisely Québec campaign, a member of the scientific committee for the Practising Wisely training program, and a member of the scientific review committee for Le Médecin du Québec.

René Wittmer reports no affiliations with pharmaceutical or diagnostic industry. He states that he has received presenter fees and expense reimbursements for various continuing professional development events and has never received payments from industry. He is president of the Choosing Wisely Québec campaign and chair of the Best Practices Working Group at the Québec College of Family Physicians.

Appendix

Modelling of the cascade of interventions generated by a screening test for a patient population of 1000, who meet critera for fibrosis screening in primary care, as recommended in the AASLD guideline.

Quantification of Investigations and Findings in 1000 People		
	396 FIB 4 > 1.3	396 who need Fibroscan
	46 Fibroscan > 8 kPa	46 consultations in Gastroenterology (priority E)
	27 advanced fibroses found	9 cirrhoses F4 18 fibroses F3
	16 advanced fibroses missed	6 cirrhoses F4 10 fibroses F3
	250 abnormal results CBC, AST, ALT	150 abnormal CBC to follow 100 AST, ALT increased*
	15 abnormal ANA results	15 consultations in Rheumatology (priority E)
	< 1 rare cause of advanced fibrosis found	

*We consider that for 100 increased AST, ALT, clinicials may feel compelled to investigate other rare causes of hepatic diseases (auto-immunem, a-1 antitrypsine deficiency, Wilson's, etc.), which would genereate asking for ANA tests.

Summary of Potential Harms Related to the Intervention		
Total population screened	1000 patients may be anxious regarding their risk of developing cirrhosis.	< 3 % of people with advanced firbosis will develop complications of cirrhosis in the next 20 years (8). This corresponds to 1-2 patients on 1000 followed for 20 ans.
	396 people may have to miss a half day of work to get their Fibroscan. Wait times to access Fibroscan may contribute to increasing anxiety.	Fibroscans are not accessible in all regions of Quebec, some patients may have to travel in order to receive their test. This increase in patients may prolong wait times where the test is offered.
	46 patients will miss a half day of work in order to consult the GI specialist. Wait times for seeing the specialist may increase anxiety.	Wait times to see GI are some of the longest in Quebec. Many wait over a year before being seen.
	9 people will receive a cirrhosis diagnosis. 18 will received an advanced fibrosis diagnosis.	People with cirrhosis will eventually be seen in specialist clinics with periodic tests to evaluate progression. People with advanced fibrosis will be urged to work harder on lifestyle management and weight loss. Certain medications can be proposed to diminish fibrosis progression, according to eligibility. Until this date, no supplementary resource is available in Quebec for an aggressive weight loss management program. No medication has a fibrosis code or reimbursement related to fibrosis.
	16 people will be falsely reassured to not have fibrosis, including 6 with cirrhosis.	
	250 people will have to come back for supplementary testing, because of incidental findings. This can create increased anxiety.	Many patients will have anemia or increased or decreased white blood cells. Clinical relevance of these incidental findings is difficult to estimate.
	15 people will miss a half day of work to see a Rheumatologist. Anxiety of potentially having an auto-immune disorder may disturb patients' perception of their health and further other intervention cascades.	A Rheumatology referral will be priority E, and wait times may be over a year. Wait lists could worsen.
	< 1 patient will have advanced fibrosis due to a rare cause.	

Summary of Potential Benefits Associated With the Intervention:

Benefits to systematic screening of MASLD remain uncertain, especially in the absence of studies directly evaluating screening. Many hypothetical benefits to this day have not been quantified or demonstrated.

- **Motivational effect to improve lifestyle habits :** Many people assume that abnormal liver findings will motivate patients to change their lifestyle habits. However, no available evidence supports this hypothesis. On the contrary, some data shows no effect on behaviour change.
- **Improving management of metabolic risk factors :** Screening could improve management of metabolic risk factors, including introduction of statins and other pharmacological options. Clinical benefits of this approach are nto well defined and may be accompanied by adverse effects.
- **Potetnail reduction in cirrhosis and its complications :** The interventions put in place may reduce cirrhosis incidence. Rapid detection of cirrhosis may offer appropriate treatments (treating portal hypertension, oesophageal varice ligature) which could theoretically prevent cirrhosis complications. These potential benefits have not been shown in studies evaluating the effect of screening.

Parameters and Sources Used for Modelization

Considering that screening is proposed to 1000 people, we calcuated investigations assuming CBC, ALT, AST would be performed in 1000 people in order to stadify risk for advanced fibrosis.

Parameters Used for Calculation	
Initial prevalence of advanced fibrosis (1)	4.27%
Initial prevalence of cirrhosis (2)	1.48%
FIB4 > 1.3-1.67 (2) - Sensitivity - Specificity	 74% 62%
FIB 4 > 1.3 and Fibroscan > 8 kPa (3) - Sensitivity - Specificity	 84.7% 94.7%
Prevalence of elevated hepatic enzymes (4)	10%
Prevalence of abnormal CBC (5)	10-20% (15%)
Prevalence of positive ANA (≥ 1 :160) (6)	15%
Prevalence of rare causes of advanced fibrosis (auto-immune hepatitis, a-1 antitrypsine deficit, Wilson's, primary biliary cirrhosis, etc.) (7)	< 1 : 1000

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