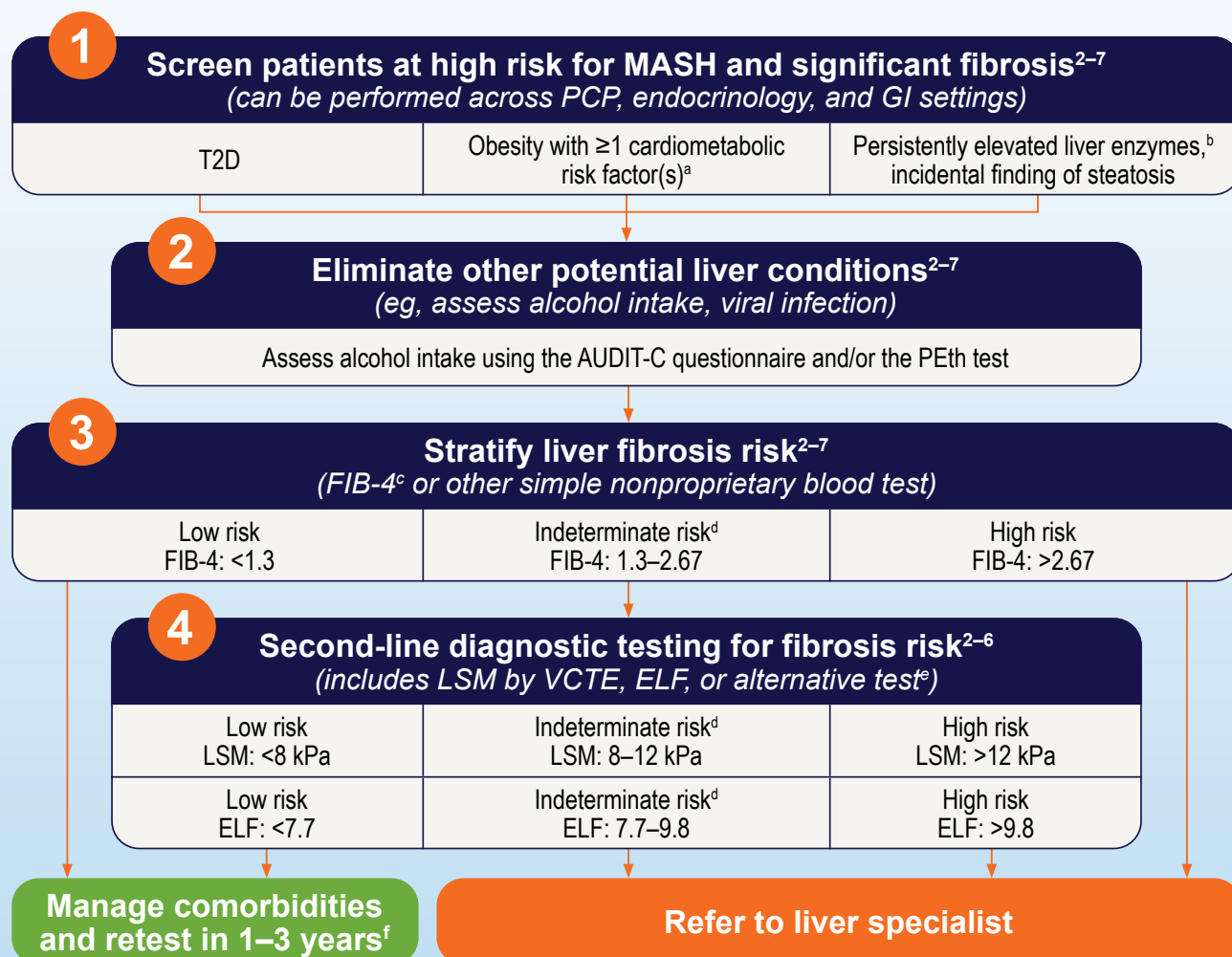


# Integrated Algorithm for Risk Stratification of Liver-related Outcomes in MASLD

People with type 2 diabetes are at an increased risk of MASLD and advanced liver fibrosis,\* often without symptoms.<sup>1</sup> Early identification can help prevent progression to cirrhosis and associated liver-related complications.<sup>1</sup>

## Integrated Algorithm for Non-invasive Risk Stratification of Advanced Liver Fibrosis\* and Liver-related Outcomes in MASLD

Adapted from AACE, AASLD, ADA, AGA, APP, and EASL-EASD-EASO guidance documents.



To learn more about MASH, sign up to Madrigal Connect  
[www.madrigalconnect.co.uk](http://www.madrigalconnect.co.uk)



\*Advanced liver fibrosis is a severe stage of liver scarring (typically stage F3 and F4), inclusive of cirrhosis.

<sup>a</sup>Examples: obesity, high triglycerides, low HDL cholesterol, hypertension, insulin resistance.

<sup>b</sup>Elevated liver enzymes alone do not indicate presence of MASH, as patients with MASH may present without elevated liver enzymes; conversely, the absence of elevated liver enzymes does not indicate absence of MASH.

<sup>c</sup>FIB-4 thresholds valid for age ≤65 years (for age >65 years: lower FIB-4 cutoff is 2.0).

<sup>d</sup>FIB-4 is a rule-out test; "indeterminate" is used in this intermediate group as the risk is not yet known and a second non-invasive test is required to guide next steps.

<sup>e</sup>Eg, MRE, SWE, ELF, with adapted thresholds.

<sup>f</sup>EASL-EASD-EASO, AACE/AASLD, AGA, and APP guidance documents provide 1- to 3-year retesting timeline.

AACE, American Association of Clinical Endocrinology; AASLD, American Association for the Study of Liver Diseases; ADA, American Diabetes Association; AGA, American Gastroenterological Association; APP, advanced practice provider; AUDIT-C, Alcohol Use Disorder Identification Test-Concise; EASD, European Association for the Study of Diabetes; EASL, European Association for the Study of the Liver; EASO, European Association for the Study of Obesity; ELF, enhanced liver fibrosis test; F, fibrosis score; FIB-4, fibrosis-4 index; GI, gastrointestinal; HDL, high-density lipoprotein; kPa, kilopascals; LSM, liver stiffness measurement; MASH, metabolic dysfunction-associated steatohepatitis; MASLD, metabolic dysfunction-associated steatotic liver disease; MRE, magnetic resonance elastography; PCP, primary care physician; PEth, phosphatidylethanol; SWE, shear wave elastography; T2D, type 2 diabetes; VCTE, vibration-controlled transient elastography.

1. Zoncapè M, Tsochatzis EA. *Diabetes Care*. 2025;48(6):871-873. 2. EASL-EASD-EASO. *J Hepatol*. 2024;81(3):492-542. 3. Rinella ME, et al. *Hepatology*. 2023;77(5):1797-1835. 4. Cusi K, et al. *Endocr Pract*. 2022;28(5):528-562. 5. Wattacheril JJ, et al. *Gastroenterology*. 2023;165(4):1080-1088. 6. Cusi K, et al. *Diabetes Care*. 2025;48:1057-1082. 7. Lam BP, et al. *J Clin Gastroenterol*. 2025;59(4):298-309.

# FIB-4 Index at a Glance

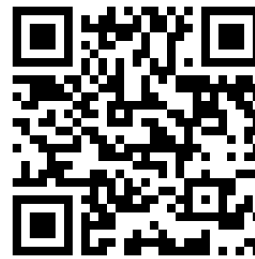
FIB-4 provides a simple, low cost, first-line test to identify patients needing further assessment.<sup>1,2</sup> Routine fibrosis screening fits naturally within diabetes reviews, using labs already collected in standard care (AST, ALT, platelets).<sup>3</sup>

## Why FIB-4 Testing Matters

- Accessible, guideline endorsed, with support from NICE CKS, BASL and BSG Quality Standards<sup>2,4–6</sup>
- FIB-4 could fit into the UK diabetes care pathways<sup>2,4,5</sup>
  - AST, ALT and platelet counts are routinely requested as part of standard diabetes reviews, enabling FIB-4 to be calculated easily from existing blood results<sup>3</sup>
  - Readily available calculators and potential EMR support make FIB-4 a simple and non-invasive tool for liver fibrosis risk stratification in diabetes care<sup>2,4</sup>
- Supports identification of patients with elevated risk<sup>2,4</sup>

### The FIB-4 Formula<sup>7</sup>

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST (U/L)}}{\text{Platelet count (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}}$$



The QR code will direct you to an external website ([www.mdcalc.com](http://www.mdcalc.com)).

Madrigal Pharmaceuticals UK Ltd. accepts no responsibility for the content of any external websites.

### Cutoffs for Risk of Advanced Fibrosis<sup>8,\*</sup>

|                                 | Age 36–65 years | Age >65 years |
|---------------------------------|-----------------|---------------|
| Low risk                        | <1.3            | <2.0          |
| Indeterminate risk <sup>†</sup> | 1.3–2.67        | 2.0–2.67      |
| High risk                       | >2.67           | >2.67         |

FIB-4 has not been validated in patients <35 years old.<sup>5</sup> Test specificity declines with age and cutoffs are adjusted for patients aged ≥65 years.<sup>8</sup>



**Liver fibrosis is common, silent, and progressive in type 2 diabetes.<sup>1,3</sup> Screening with FIB-4 may enable early and low-burden intervention.<sup>2,4</sup>**

\*Advanced liver fibrosis is a severe stage of liver scarring (typically stage F3 and F4), inclusive of cirrhosis. <sup>†</sup>FIB-4 is a rule-out test; “indeterminate” is used in this intermediate group as the risk is not yet known and a second non-invasive test is required to guide next steps.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BASL, British Association for the Study of the Liver; BSG, British Society of Gastroenterology; CKS, clinical knowledge summary; EMR, electronic medical record; F, fibrosis score; FIB-4, fibrosis-4 index; NICE, National Institute for Health and Care Excellence; U, unit.

1. Zoncapè M, Tsochatzis EA. *Diabetes Care*. 2025;48(6):871–873. 2. Rinella ME, et al. *Hepatology*. 2023;77(5):1797–1835. 3. EASL-EASD-EASO. *J Hepatol*. 2024;81(3):492–542. 4. Brown P. Diabetes distilled: Fib-4. Available at: <https://diabetesonthenet.com/diabetes-primary-care/diabetes-distilled-fib4/>. Accessed June 2026. 5. McPherson S, et al. *Lancet Gastroenterol Hepatol*. 2022;7(8):755–769. 6. NICE. Clinical Knowledge Summaries: Non-alcoholic fatty liver disease (NAFLD). Available at: <https://cks.nice.org.uk/topics/non-alcoholic-fatty-liver-disease-naflid/>. Accessed June 2026. 7. Sterling RK, et al. *Hepatology*. 2006;43(6):1317–1325. 8. McPherson S, et al. *Am J Gastroenterol*. 2017;112(5):740–51.