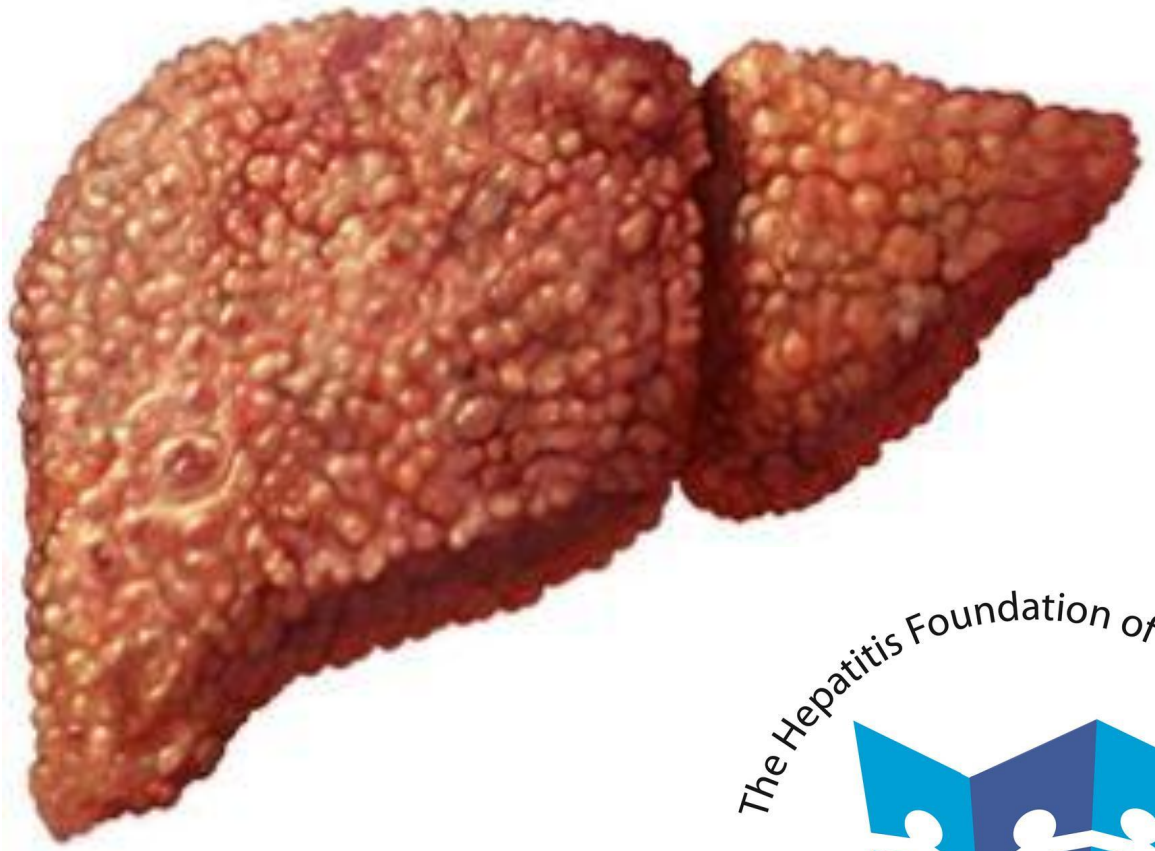
NON-ALCOHOLIC FATTY LIVER DISEASE



The Hepatitis Foundation of New Zealand

www.hepatitisfoundation.org.nz

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Learning objectives

- Gain an understanding of non-alcoholic fatty liver disease (NAFLD)
- Learn how to assess and manage patients with the condition in primary care
- Build knowledge of possible outcomes of non-alcoholic fatty liver disease.

Non-alcoholic fatty liver disease (NAFLD)

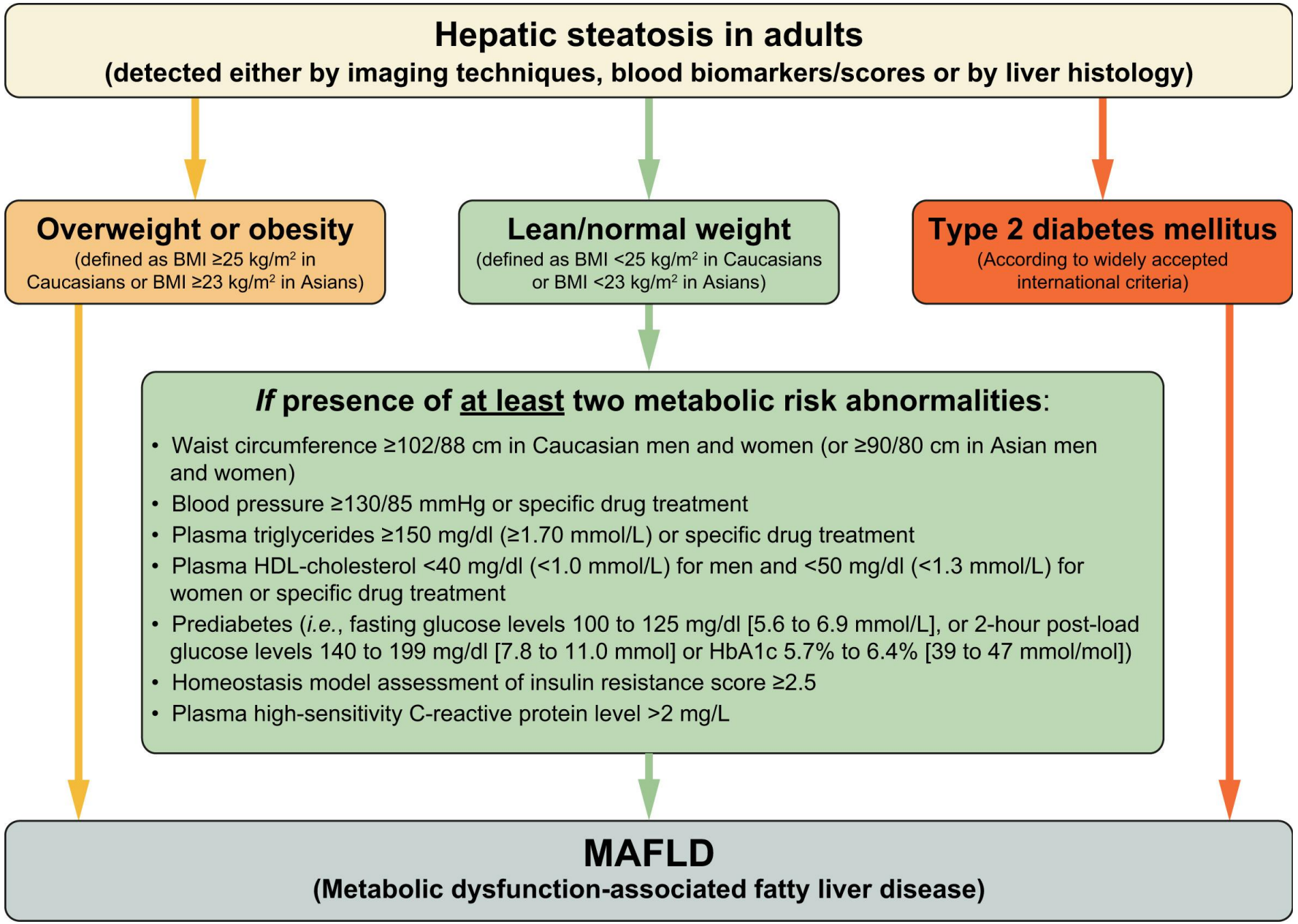
Non-alcoholic fatty liver disease is the most common liver condition in the western world. Lifestyle factors can contribute to its onset, such as:

- A high-calorie diet
- Consumption of excess saturated fats, refined carbohydrates and sugar-sweetened drinks
- A high fructose intake

Risk factors: male, obesity, increasing age, presence of hypertension and diabetes.

Definitions and prevalence

- Other names: Fatty liver, metabolic-associated fatty liver disease (MAFLD)
- Definition: Presence of hepatic steatosis (fat in the hepatocytes) and obesity (BMI >25) or diabetes
- Other factors can contribute steatosis (i.e alcohol, hepatitis C, Wilson's disease)
- Non-alcoholic steatohepatitis (NASH): is a histological diagnosis where a biopsy shows fat and the presence of inflammatory cells
- In the general population, prevalence varies between 13–32 percent globally. NAFLD affects 60–80 percent of people with type two diabetes.



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Symptoms and diagnosis

In general, people with fatty liver disease have **no** symptoms. Some people report discomfort in the abdomen around the liver, fatigue, feeling of being unwell and vague discomfort.

Fatty liver disease is usually suspected in people with body mass index (BMI) >25 or diabetes

An ultrasound of the liver will often show the presence of a fatty liver.

History

- The patient's weight now and history of weight gain
- Risk factors for liver disease
- FHx of liver disease, diabetes, IHD, CVA
- Lifestyle: Diet and exercise patterns.

Examination

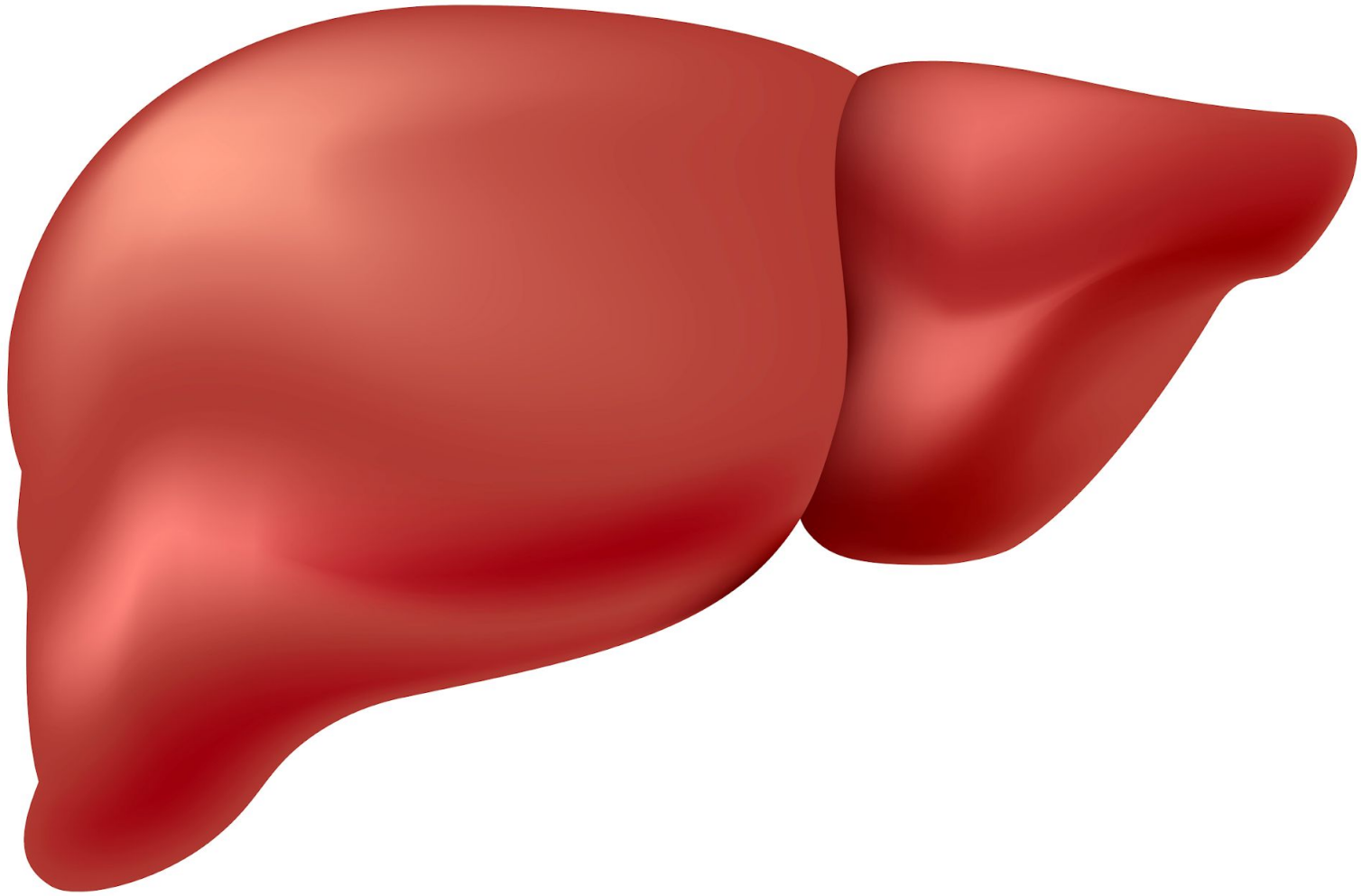
- Height, weight, BMI and waist circumference
- Blood pressure
- Peripheral stigmata of chronic liver disease.

Investigations

- LFTs + AST
- Iron studies + ferritin
- Lipid profile
- HbA1c
- UEC
- FBC.

Liver function test results

- The most common pattern is normal LFTs
- Elevated GGT
- Elevated GGT + ALT (+ AST).



Liver screening tests for deranged LFTs

Alcohol

Viral

- Hepatitis B and C

Metabolic

- Diabetes, iron studies + ferritin and lipid profile

Autoimmune

- ANA, AMA, anti-smooth muscle Ab, coeliac serology, immunoglobulins and TFT

Genetic

- Copper and ceruloplasmin and alpha-1-antitrypsin.

NAFLD outcomes

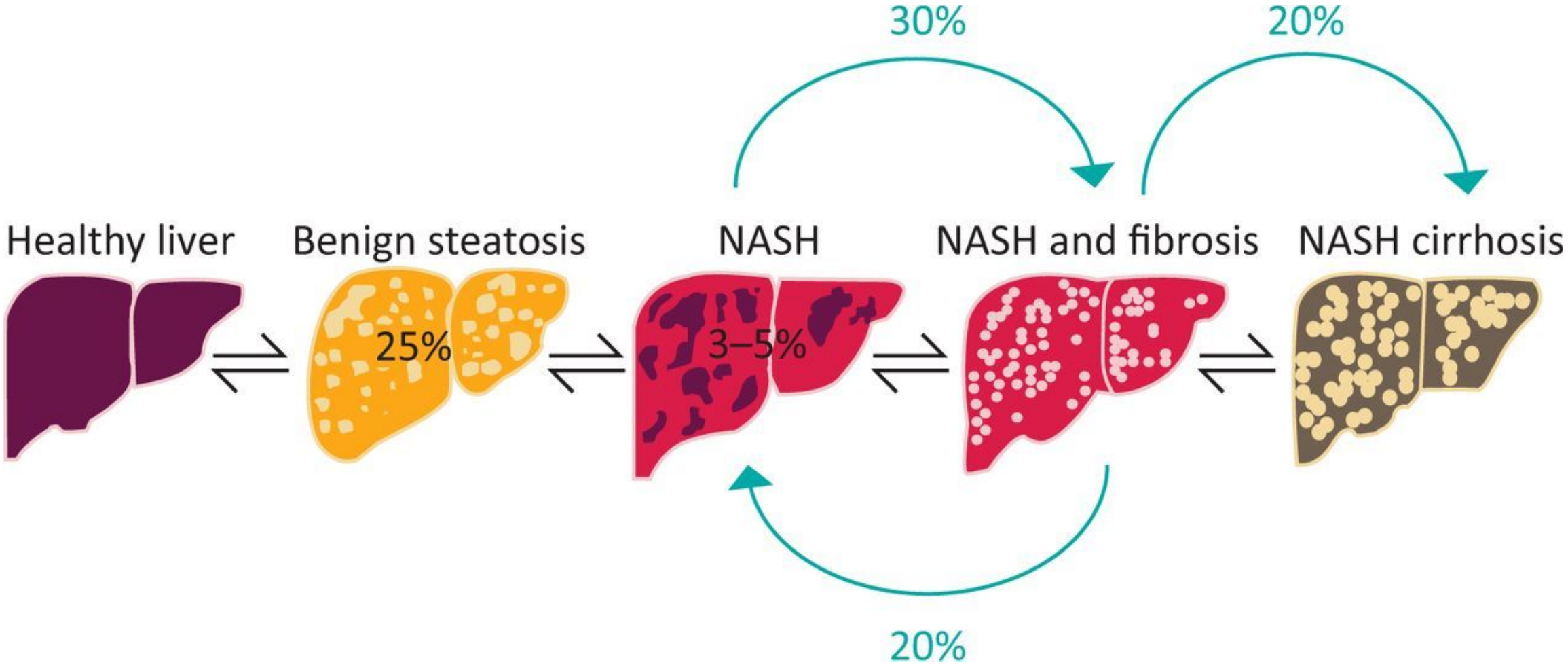
Mortality: increased compared to unaffected population

- Cardiovascular disease
- Cancer
- Decompensated liver disease
- The risk of liver cancer is 2-13 percent over eight years.

Predictors of worse outcomes

- Presence of advanced liver fibrosis
- Presence of diabetes
- Central obesity
- Male
- Cardiovascular disease
- Renal impairment
- Any alcohol consumption.

The NAFLD spectrum



Clin Med September 2020
https://doi.org/10.7861/clinmed.2020-0696

NAFLD - screening

People should only be screened for conditions if:

- They cause preventable harm
- There is an easy diagnostic test (low-cost, high-sensitivity and- specificity)
- Treatment can be put in place to reduce future harm.

All three criteria must be cost-effective for the population being screened.

NAFLD - screening

Screening should be done for:

- Select patients at high risk of progressive fibrosis and cirrhosis
- People aged over 50
- Anyone with T2DM or other features of the metabolic syndrome.

First step: Diagnose fatty liver disease. Ultrasound to look for steatosis. If unable to request US from primary care, it is recommended GPs use the fatty liver index (MD Calc: BMI, waist circumference, GGT, trig) to estimate the likelihood of fatty liver disease.

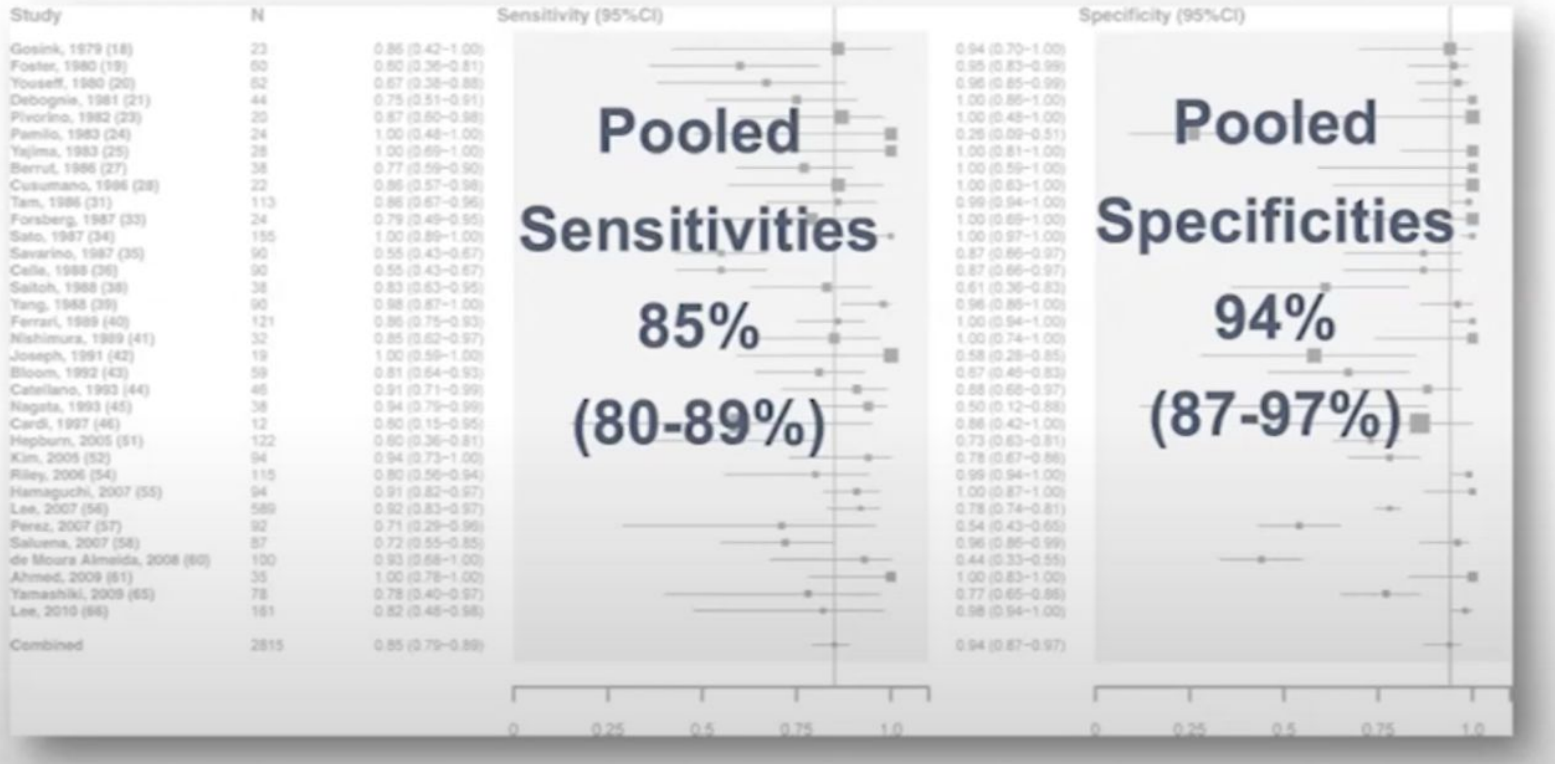
Second step: estimate degree of fibrosis biomarker scores: FIB-4, NFS.

LFTs are a poor indicator of NAFLD as the majority:

>80 percent of people with NAFLD have normal ALT.

NAFLD: Diagnosis of steatosis

US performance for detecting steatosis



Meta-analysis; 49 studies (N= 4720 subjects)

(limited sensitivity, not reliable if <20 percent steatosis or BMI >40)

Haernez R et al. Hepatology 2011; 54: 1082-90

Assessment of liver fibrosis

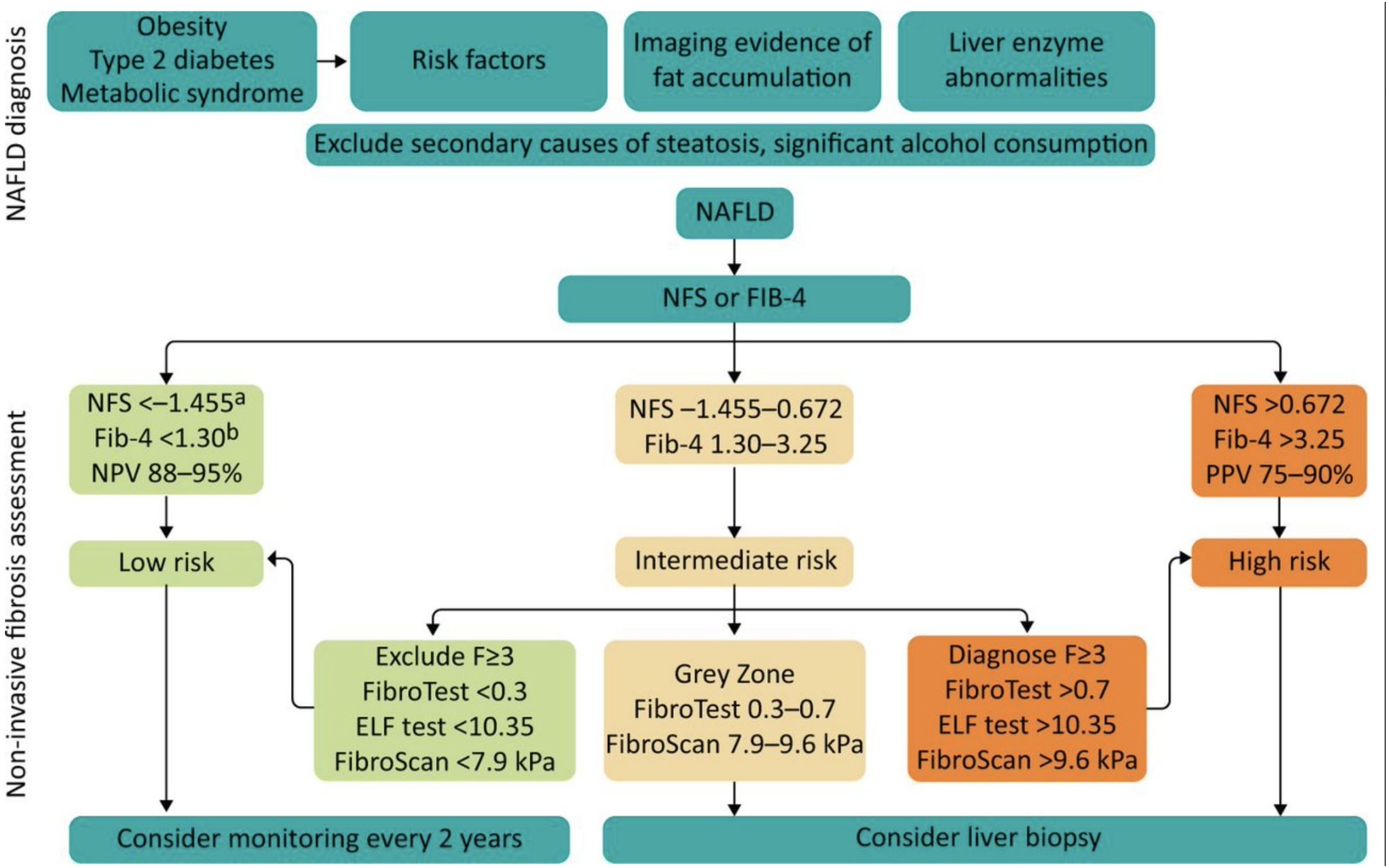
- USS and fibroscan
- Liver biopsy
- Only a small proportion of people with NAFLD (3-5 percent) will have progressive liver fibrosis and liver-specific complications.
- Blood test scores:
    - Fibrosis-4 (FIB-4, index for liver fibrosis)
    - NAFLD fibrosis score (NFS)
- Fibrosis stage predicts overall survival and disease-specific mortality.

Non-invasive tests in NAFLD: FIB-4 and NFS

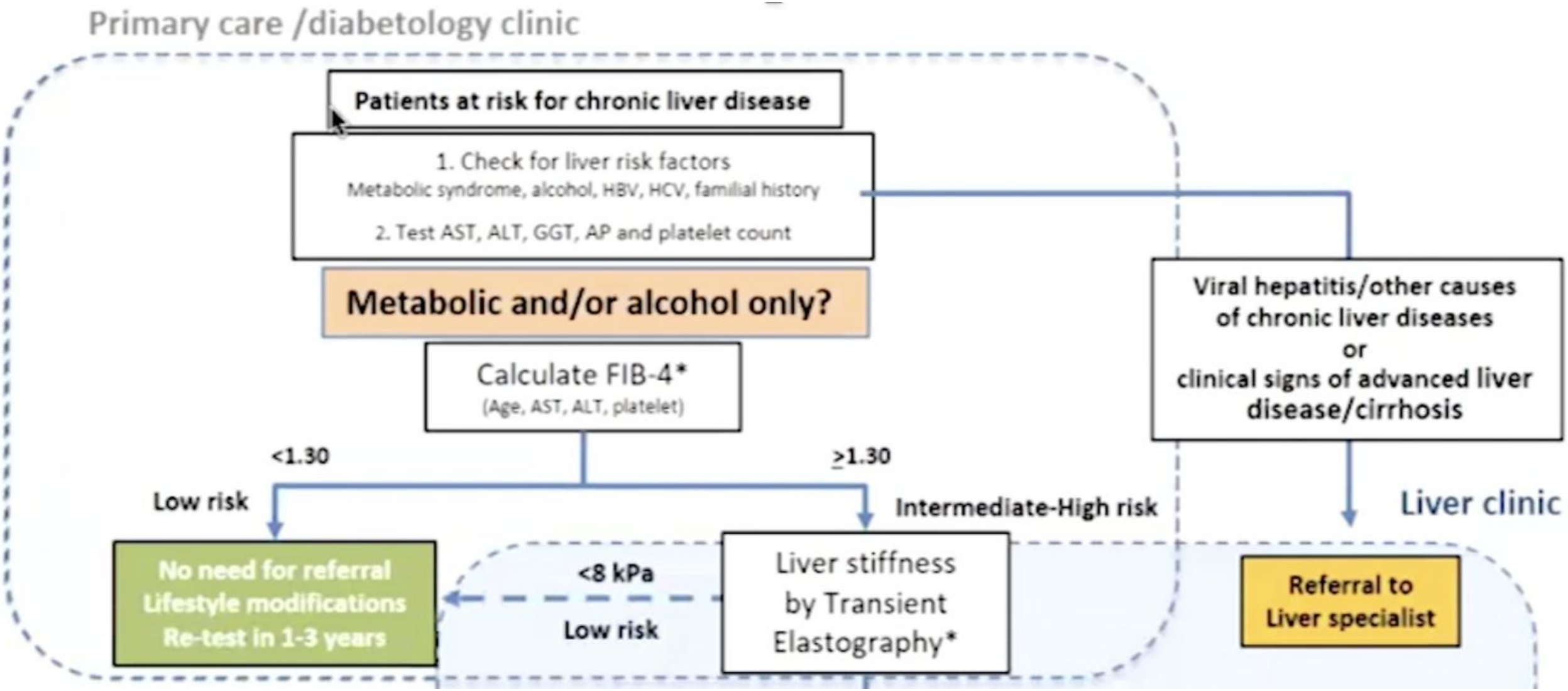
Most experts would recommend a two-tier approach with FIB-4 or NFS ruling out patients very unlikely to have significant fibrosis, followed by a second test for those with indeterminate or high-risk scores

- FIB-4 calculator: https://www.mdcalc.com/fibrosis-4-fib-4-index-liver-fibrosis#use-cases

- NFS calculator: https://www.mdcalc.com/nafld-non-alcoholic-fatty-liver-disease-fibrosis-score


NAFLD diagnosis
Obesity
Type 2 diabetes
Metabolic syndrome
Risk factors
Imaging evidence of fat accumulation
Liver enzyme abnormalities
Exclude secondary causes of steatosis, significant alcohol consumption
NAFLD
NFS or FIB-4
Non-invasive fibrosis assessment
NFS <–1.455[a]
Fib-4 <1.30[b]
NPV 88–95%
NFS –1.455–0.672
Fib-4 1.30–3.25
NFS >0.672
Fib-4 >3.25
PPV 75–90%
Low risk
Intermediate risk
High risk
Exclude F≥3
FibroTest <0.3
ELF test <10.35
FibroScan <7.9 kPa
Grey Zone
FibroTest 0.3–0.7
FibroScan 7.9–9.6 kPa
Diagnose F≥3
FibroTest >0.7
ELF test >10.35
FibroScan >9.6 kPa
Consider monitoring every 2 years
Consider liver biopsy

Proposed assessment in primary care



Management

Cardiovascular risk assessment

Complete abstinence from alcohol

Diet

- Hypocaloric diet. The best diet is unknown
- The specific macronutrient composition of diet long-term appears to be less relevant than the end result of sustained weight loss.

Exercise

- Improves LFTs and fibrosis, even in the absence of weight loss.

Management of comorbidities in NAFLD

Type 2 Diabetes	Yearly HbA1c and fasting glucose Assess historical risk factors: • Family history of T2DM/ History of Gestational DM
Cardiovascular Diseases	Yearly fasting lipid profile and blood pressure screening Assess historical ASCVD risk factors: • Smoking history/ Diabetes history • Family history of premature CVD (males<50, females<60) Calculate 10-year and lifetime ASCVD risk using AHA/ACC risk calculator • If age 40-79 and 10-year risk > 7.5%, consider statin for primary prevention Heightened clinical awareness for CVD signs/symptoms, additional testing/referral to cardiologists
Chronic Kidney Disease	Yearly urine microalbumin and urinary albumin/creatinine ratio Yearly eGFR
Extrahepatic cancers	Assess and document standard risk factors Heightened clinical awareness for cancer risk > GI tract, screening according to guidelines

THE INTERN LIVER CONGRESS

Modified from VanWagner et al Curr Hepatol Rep 2016

Learning activity one

Answer the following questions to demonstrate your understanding of fatty liver and the metabolic syndrome:

- How can you diagnose fatty liver disease?
- What factors contribute to its onset?
- How would you determine whether a patient should be referred to secondary care?
- What dietary and/or lifestyle changes would you recommend for a patient with fatty liver disease?
- What conditions should be screened for in people with deranged LFT results?

Note: Your response will not be assessed but if you would like feedback please contact a Hepatitis Foundation of NZ clinician. Phone 0800 33 20 10 or email hepteam@hfnz.nz

Learning activity two

Read the case study on the following slide and consider how you would manage the patient.

What tests would you recommend and why?

Include sound reasoning for your decisions and your expected outcomes.

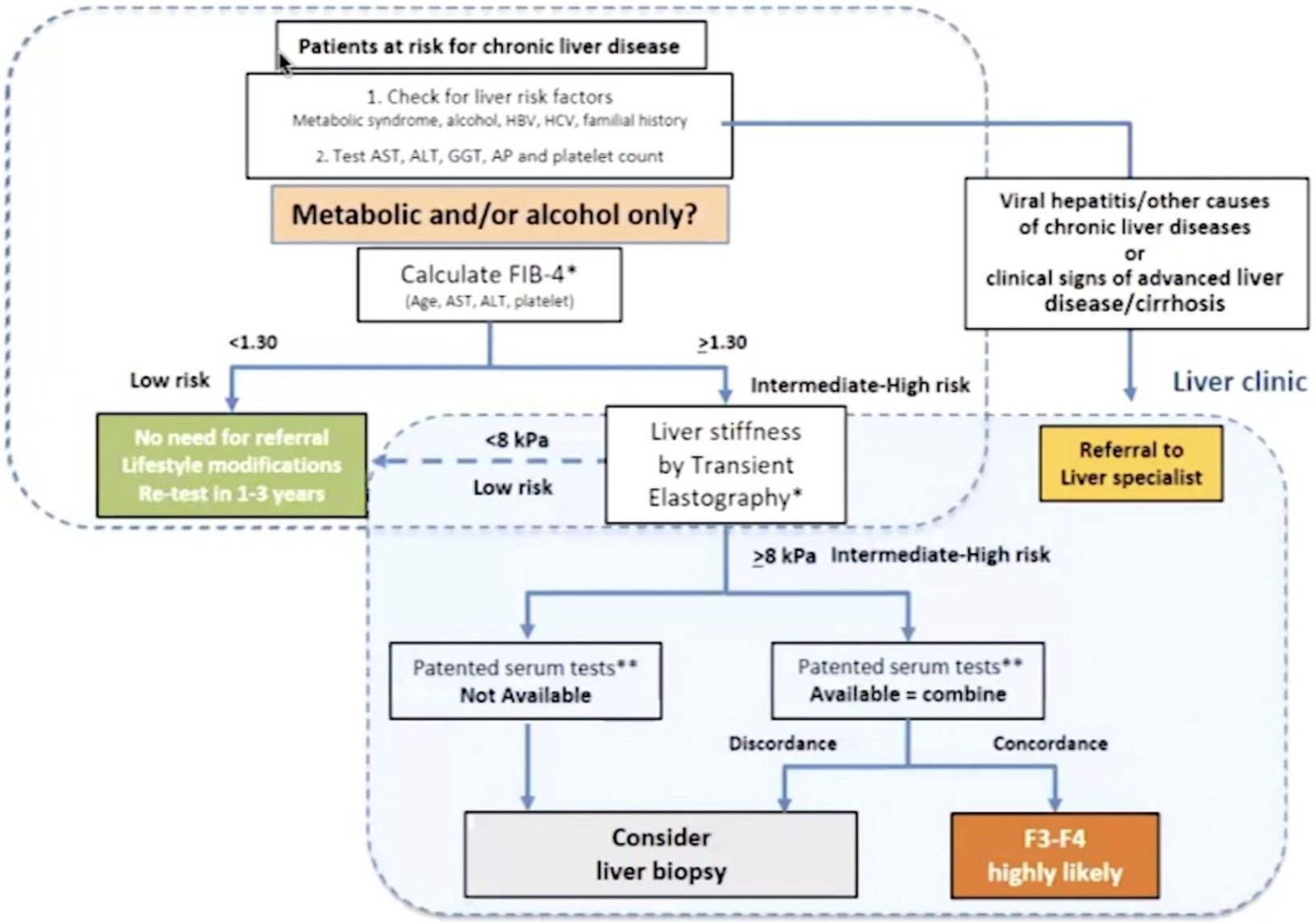
Note: Your response will not be assessed but if you would like feedback please contact a Hepatitis Foundation of NZ clinician. Phone 0800 33 20 10 or email hepteam@hfnz.nz.

* Please see slide 26 for case study management advice

Case study

- 50-year-old man
- BMI 35
- Type two diabetes managed with metformin
- Hypertension managed with ACEi
- Dyslipemia on statin
- Alcohol intake 15 units a week
- Bloods: ALT 47, AST 56, platelets 180
- Abdominal US: Fatty liver.

Primary care/ diabetology clinic



* Transient elastography or FIB-4 may be performed before or after referral to liver specialist according to local availability and pathways

** Cut-offs to use : ELF 9.8 kPa (NAFLD/ALD); FibroMeter 0.45 (NAFLD), Fibrotest 0.48 (NAFLD)

NAFLD for patients: useful websites

https://www.healthnavigator.org.nz/health-a-z/f/fatty-liver-disease/

https://www.liver.ca/patients-caregivers/liver-diseases/fatty-liver-disease/

https://britishlivertrust.org.uk/information-and-support%20/living-with-a-liver-condition/liver-conditions/non-%20alcohol-related-fatty-liver-disease/

Case study: Assessment and management advice

- Diagnosis of NAFLD or MAFLD (obesity and diabetes and steatosis on USS)
- Consider excluding other causes of chronic liver disease
- Advice against any alcohol intake
- Advice weight loss through healthy diet and physical exercise
- Optimise management of metabolic risk factors.

Calculate FIB-4, 2.27 points

https://www.mdcalc.com/fibrosis-4-fib-4-index-liver-fibrosis#use-cases

FIB-4 intermediate-high risk. Refer to secondary care for consideration for fibroscan.

Thank you for completing this NAFLD course. Any questions or feedback about the content should be directed to Justine McLeary, Hepatitis Foundation of NZ communications manager, phone 027 650 2605 or email justine.mcleary@hfnz.nz

Hepatitis B help, care and support

Hepatitis B āwhina tiaki me te tautoko