



Update on the Management of T2D and MASLD in NB

April 24, 2026

Keillor Steeves, MD, FRCPC,
Assistant Professor (Dalhousie)



**NB Internal
Medicine Update**

Disclosures

Relationships With Financial Sponsors

SPEAKERS BUREAU/ HONORARIA:	<u>Diabetes/Obesity</u> : CPD Network Association, Eli Lilly, Novo Nordisk, Dexcom, Abbott (FreeStyle Libre) <u>Lipids</u> : Ultragenyx
GRANTS/RESEARCH SUPPORT/PATENTS:	<u>Diabetes</u> : Novo Nordisk
CONSULTING FEES:	<u>Diabetes</u> : Abbott (FreeStyle Libre), Dexcom
OTHER:	Assistant Professor in Medicine (Dalhousie)

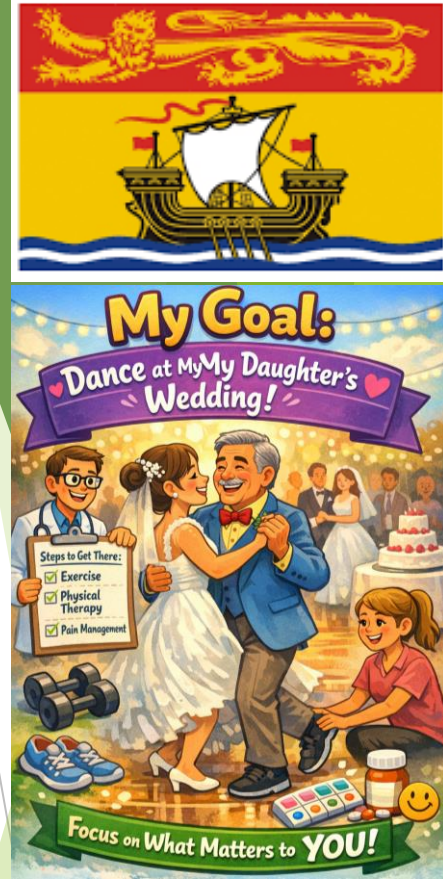


Image generated using Microsoft Copilot 2026.

- ▶ Mitigation of potential bias: not applicable
- ▶ I do not intend to make therapeutic recommendations for medications that have not received regulatory approval.
- ▶ I will be using AI-generated images (not content).

Objectives

- ▶ At the conclusion of this activity, participants will be able to
 1. Describe the impact of MASLD on patients in New Brunswick living with diabetes.
 2. Explain non-pharmacologic options for the prevention & management of MASLD in T2D.
 3. Compare pharmacologic options to reduce steatohepatitis & progression of fibrosis of MASLD in T2D.



Ultimate Goal:
Design patient-centred
care plan to manage
MASLD (integrating
lifestyle modification &
pharmacotherapy)

MASLD - Guidelines

- ▶ Today, I've drawn mainly upon:
 - 2025 Diabetes Canada Clinical Practice Guideline
- ▶ I've also included some material from:
 - 2025 Obesity Canada Clinical Practice Guideline
 - 2025 ADA Consensus
 - 2024 EASL–EASD–EASO Clinical Practice Guidelines



MASLD = metabolic dysfunction-associated steatotic liver disease; ADA = American Diabetes Association; EASL = European Association for the Study of the Liver; EASD = European Association for the Study of Diabetes; EASO = European Association for the Study of Obesity

¹Kim et al. 2025, ²Pedersen et al. 2025, ³Cusi et al. 2025, ⁴EASL 2024

Case - John (1)

- ▶ 56M with T2D, hypertension, dyslipidemia, obesity, obstructive sleep apnea
- ▶ Metformin 1000mg BID, atorvastatin 20mg, perindopril 8mg, amlodipine 5mg
- ▶ Do I have fatty liver?

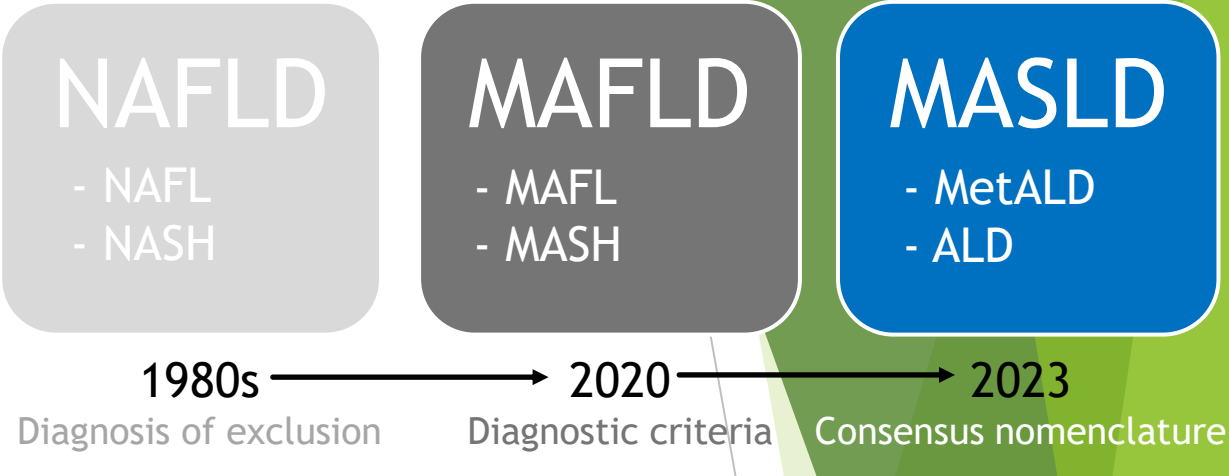
Metabolic syndrome

- BMI 32 kg/m³
- WC 102 cm
- BP 134/78 mmHg
- A1C 6.7
- LDL 1.9 mmol/L
- nHDL 2.3 mmol/L
- eGFR 54 mL/min
- ALT 35 U/L
- AST 32 U/L
- Plt 165 x E9/L



MASLD - Definition (1)

- ▶ “Nonalcoholic” = inaccurate
- ▶ “Fatty” = stigmatising



Prior	New	Nomenclature	Definition
NAFLD	<u>MASLD</u>	Metabolic dysfunction-associated steatotic liver disease	“Fatty liver” (imaging/biopsy) + ≥ 1 metabolic risk factor w/o *alcohol
▪NAFL	▪ <u>MASL</u>	Metabolic dysfunction-associated steatotic liver	Non-progressive subtype
▪NASH	▪ <u>MASH</u>	Metabolic dysfunction-associated steatohepatitis	Progressive subtype
▪ At-risk		MASH + ≥ stage 2 fibrosis	
-	<u>MetALD</u>	MASLD + increased EtOH intake	MASLD + *alcohol ♀20-50/♂30-60 g/day
ALD	ALD	Alcohol-associated liver disease	*Alcohol ♀>50/♂>60 g/day

NAFLD = non-alcoholic fatty liver disease; NAFL = non-alcoholic fatty liver; NASH = non-alcoholic steatohepatitis

¹Kim et al. 2025, ³Cusi et al. 2025, ⁴EASL 2024, ⁵Chopra 2025, ⁶Bae 2024

MASLD - Definition (2)



Steatotic liver disease (SLD)

Metabolic dysfunction-associated steatotic liver disease (MASLD)

Metabolic dysfunction-associated steatohepatitis (MASH)

MASLD and increased alcohol intake* (MetALD)

MASLD predominant ALD predominant

140/210 210 280 350/420

Weekly alcohol intake (g)

MASLD predominant ALD predominant

20/30 30 40 50/60

Average daily alcohol intake (g)

Alcohol-associated (alcohol-related) liver disease (ALD)

Others



MASLD - Progression (1)

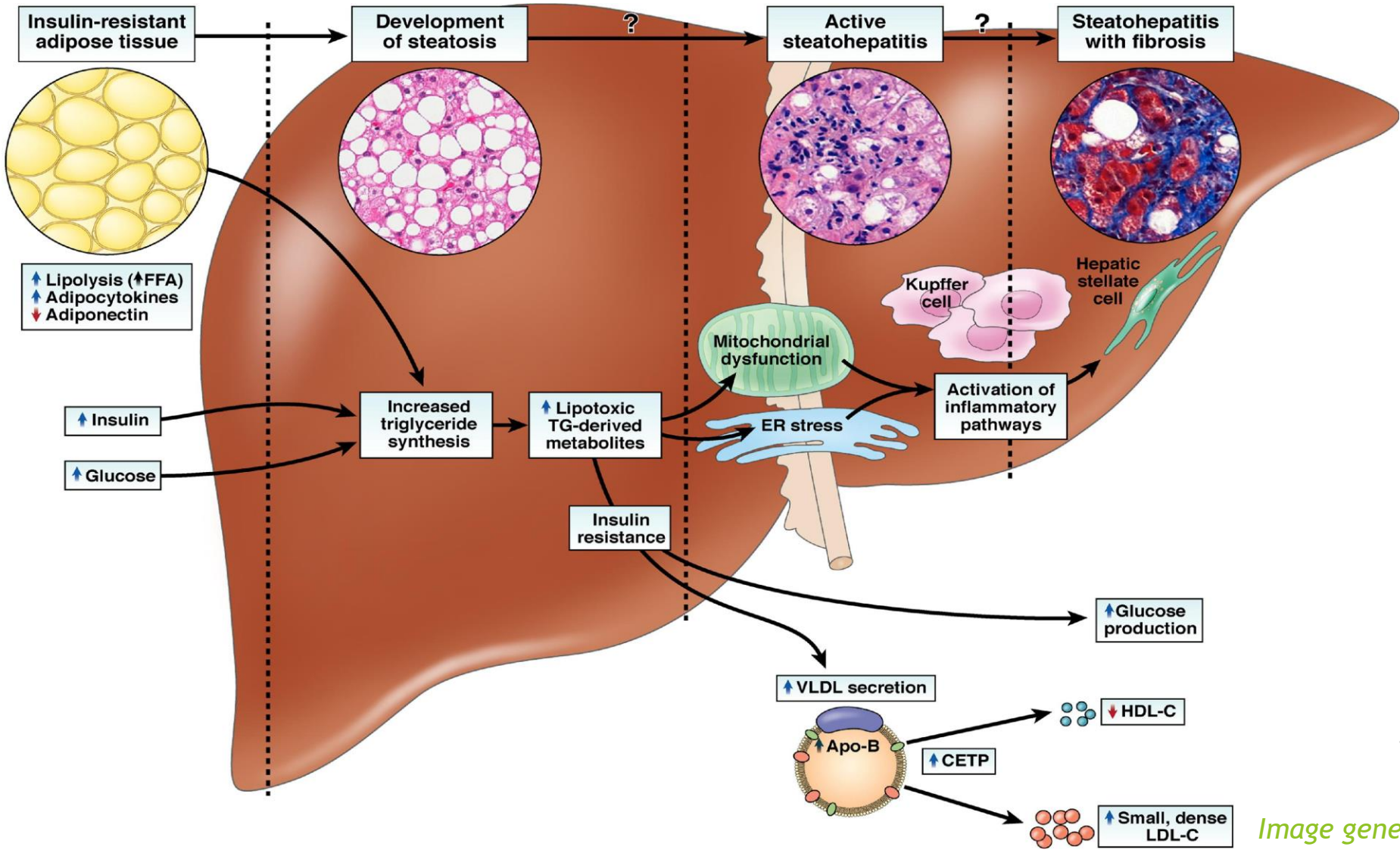
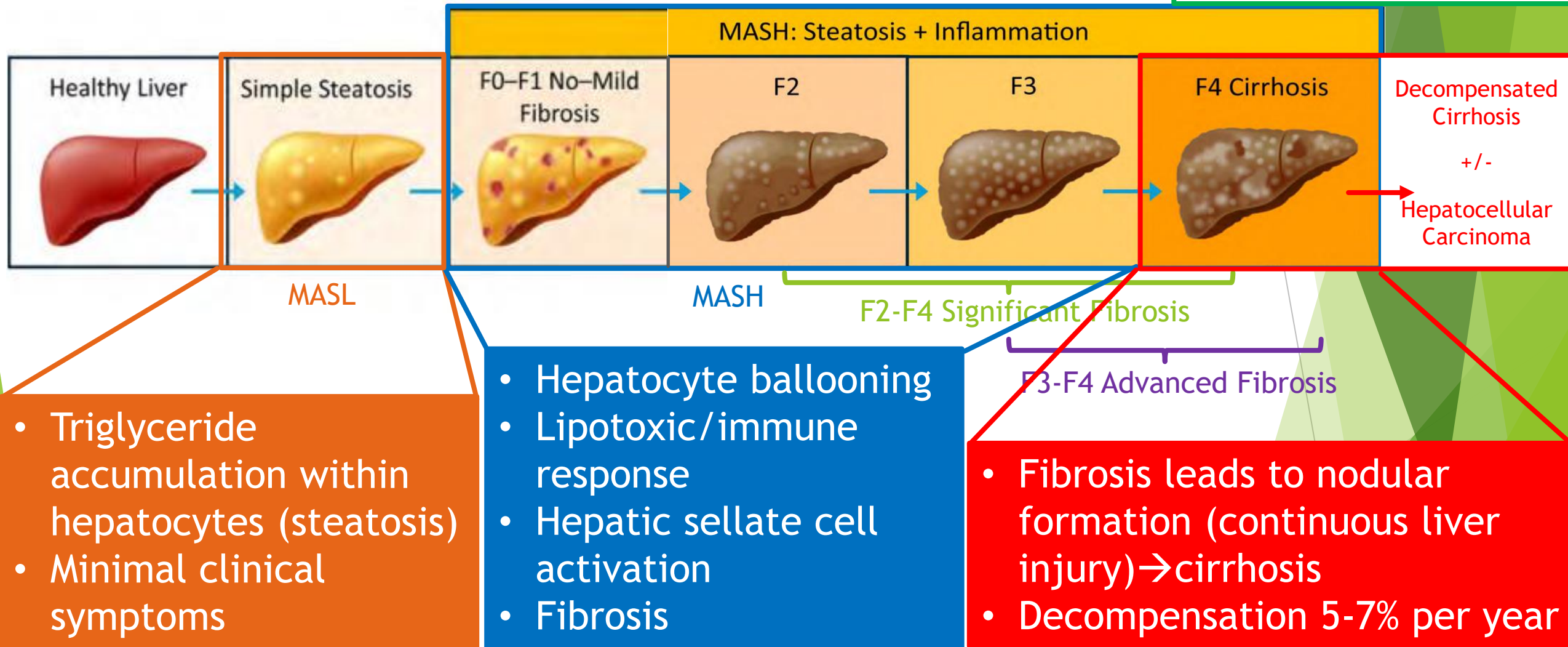


Image generated using Microsoft Copilot 2026.

MASLD = metabolic dysfunction-associated steatotic liver disease; FFA = free fatty acids; ER = endoplasmic reticulum; HDL = high density lipoprotein; VLDL = very-low density lipoprotein; LDL = low density lipoprotein; CETP = Cholesteryl ester transfer protein; ¹Kim et al 2025, ⁹Cusi 2012

MASLD - Progression (2)



Key Point # 1 - Impact

MASLD = common in NB (and under-explored)

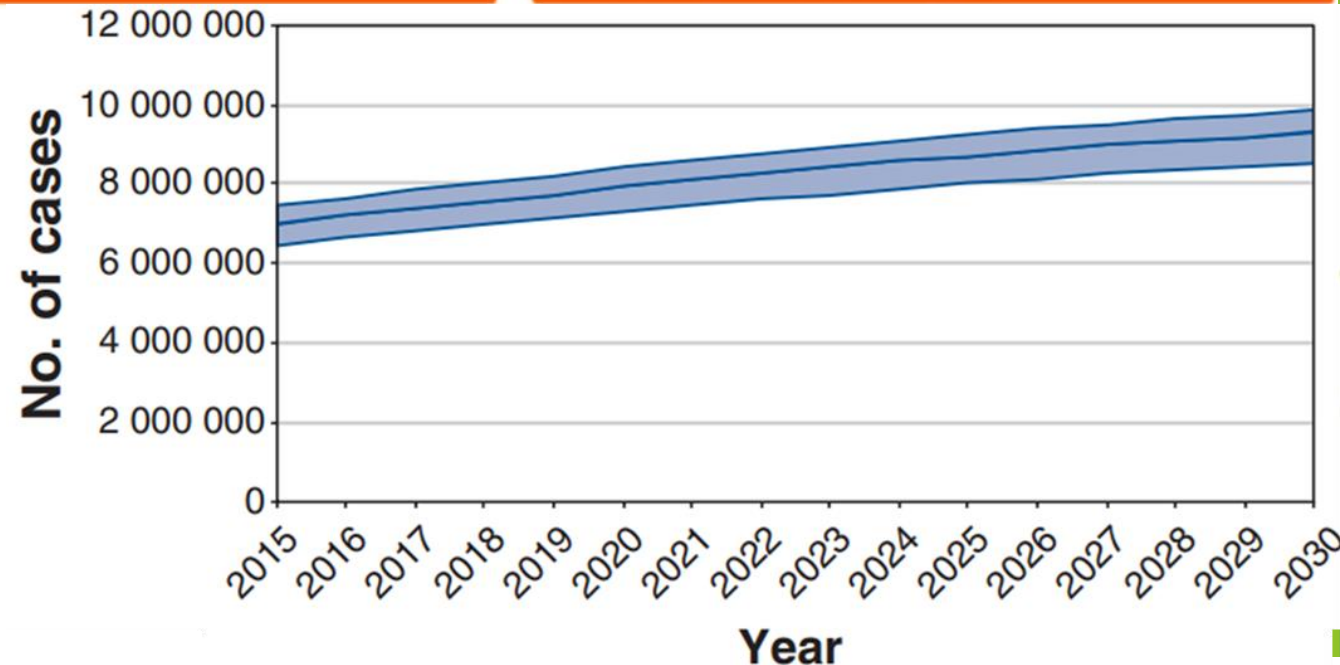
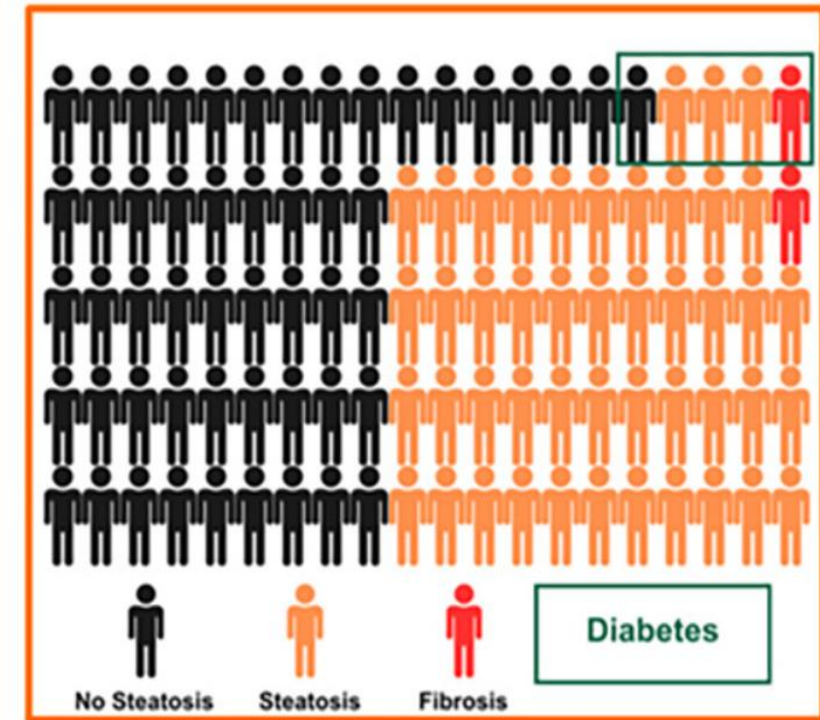
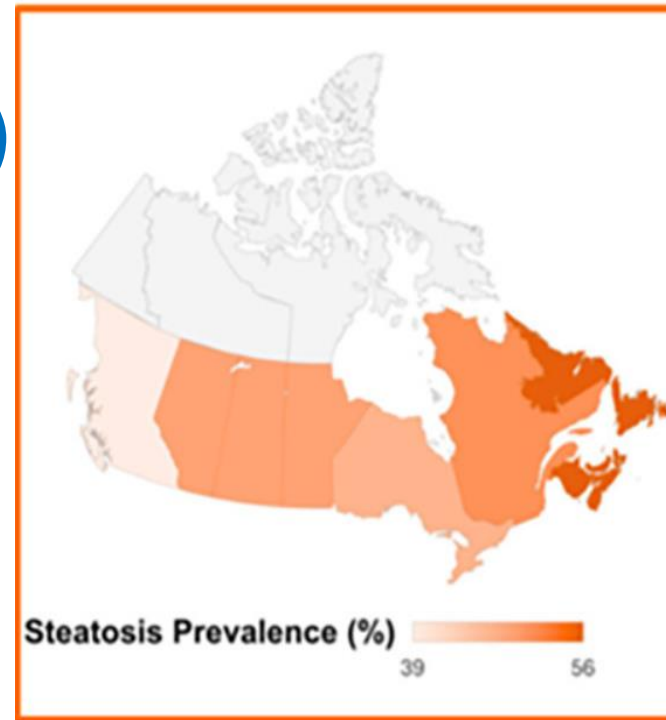


Image generated using Microsoft Copilot 2026.

MASLD = metabolic dysfunction-associated steatotic liver disease

MASLD - Impact (1)

- ▶ Steatosis in 33-50% of Canadian adults
- ▶ Steatosis more common in T2D
 - Progresses faster
- ▶ MASLD prevalence projected to increase



MASLD - Impact (2)

Local data (Moncton):

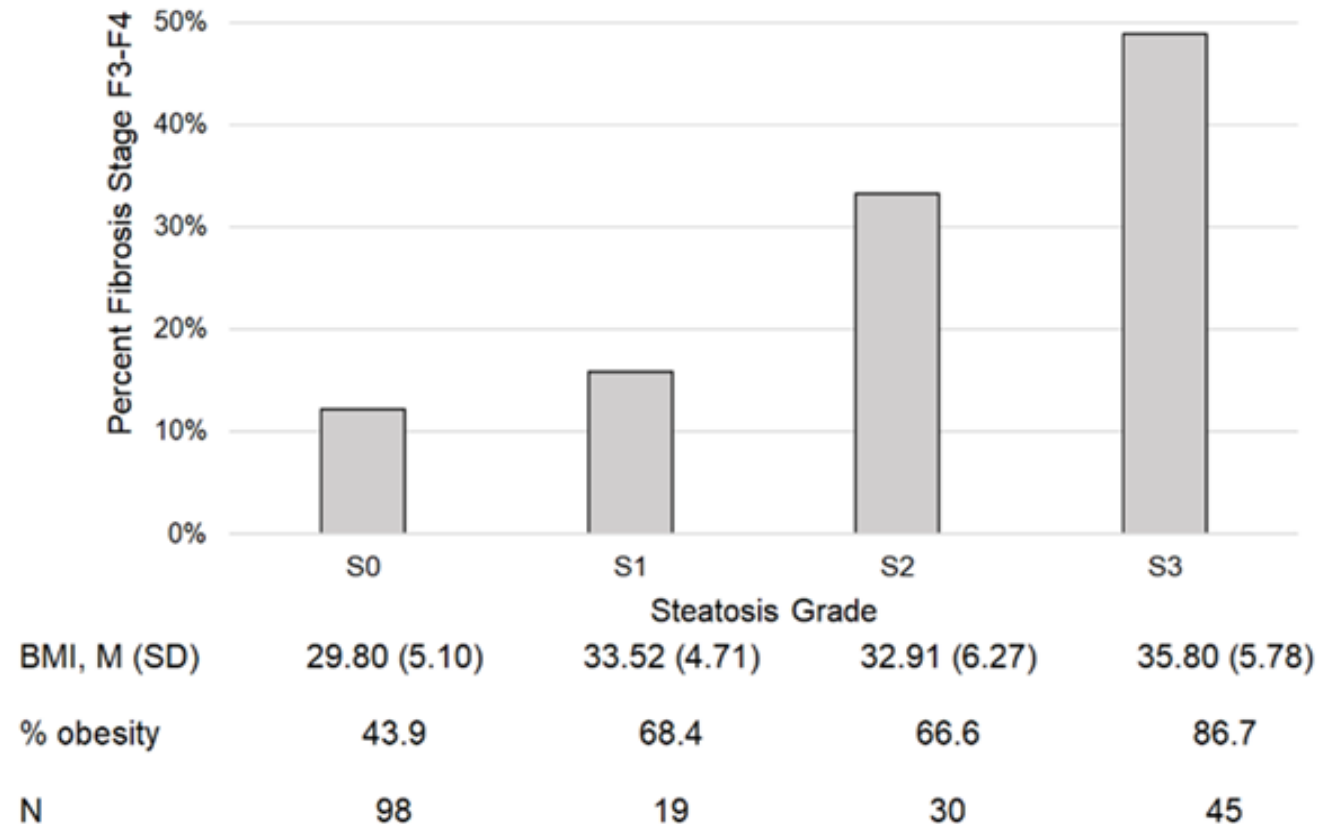
► **2064** patients 35-74 y with diabetes (elevated A1C) for FIB-4

- 402 (19.5%) FIB-4 **>1.3**
 - 192 (47.8%) had Fibroscan
 - 60.4% obesity
 - 49.0% **hepatic steatosis**
 - 24.5% **advanced fibrosis**

Prevalence of Metabolic Dysfunction-Associated Steatotic Liver Disease in patients with diabetes at a Regional Hospital in New Brunswick

John Igoe MD, FRCPC^a, Anissa Belkaid PhD^b, Valerie Dery DSS^c,
Muhammad Rasul MD, FRCPC^d, Donaldo D. Canales, PhD^e,
Louis-Jacques Cartier MD, PhD^f

Figure 2: Advanced Liver Fibrosis (F3F4) in Relation to Steatosis Grade in Patients with Diabetes



MASLD - Impact (3)

Patients	Primary Care Providers
➤ Often asymptomatic ▪ <u>96%</u> unaware of MASLD ▪ Often seen as “benign” disease ➤ Often unrecognized until end stage ▪ <u><20%</u> of MASLD undiagnosed ▪ Most with MASH/significant fibrosis go undiagnosed ➤ Formal education enhances knowledge/following care plan	➤ Early diagnosis can help minimize <u>progression</u> ➤ <u>95%</u> of high-risk patients seen in primary care (*pre-covid) ➤ >40% of PCPs unfamiliar with MASLD screening ▪ Tend to screen <u>low-risk</u> patients (c.f. hepatologists)

MASLD = metabolic dysfunction-associated steatotic liver disease; MASH = metabolic dysfunction-associated steatohepatitis

¹¹Allen et al. 2024, ¹²Golabi et al. 2023; ¹³Blais et al 2015; ¹⁴Forlano et al. 2023; ¹⁵Sebastiani et al. 2023

MASLD - Screening (1)

Guideline differences in recommendations

Diabetes Canada	ADA	AACE	EASL-EASD-EASO
Consider for MASLD-related fibrosis in <u>prediabetes</u> and <u>T2D</u>	<u>T2D</u> or <u>prediabetes</u> (esp. with cardio-metabolic risk factors or CVD)	<u>Prediabetes</u> or <u>T2D</u> - Obesity ± ≥2 cardiometabolic risk factors - Hepatic steatosis on imaging - AST or ALT >30 IU/L	<u>T2D</u> - Obesity + 1 cardiometabolic risk factor - Persistently elevated liver enzymes

All guidelines recommend screening in T2D



MASLD = metabolic dysfunction-associated steatotic liver disease; ADA = American Diabetes Association; AACE = American Association of Clinical Endocrinology; EASL = European Association for the Study of the Liver; EASD = European Association for the Study of Diabetes; EASO = European Association for the Study of Obesity; CVD = cardiovascular disease; ALT / AST = alanine / aspartate aminotransferase

¹Kim et al. 2025, ³Cusi et al. 2025, ¹⁶Cusi et al. 2022, ⁴EASL 2024

MASLD - Screening (2)

Comorbidities in (or at risk of) MASLD:



Prediabetes / T2D



Strong
drivers

Overweight / Obesity



Hypertension / DLD



CKD



CVD



OSA



PCOS



MASLD - Risk Factors (1)

Red Flags/High-risk:

► Strong predictors MASH/fibrosis

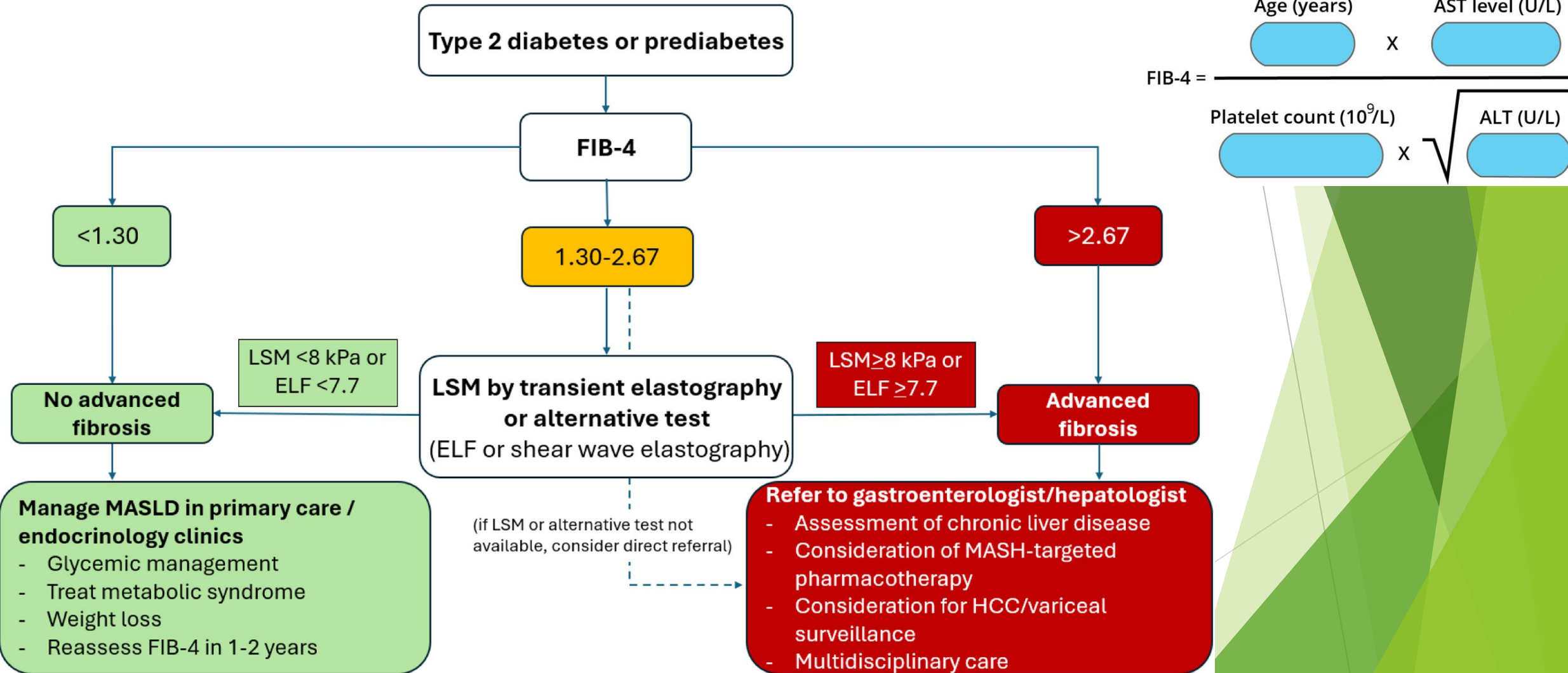
- Older adults
- T2D
- 1st-degree relative
(MASLD/MASH cirrhosis)

► Important risk factors

- Sedentary
- High fructose diet
- Overweight/obesity
- Metabolic syndrome
- Atherogenic DLD
- PCOS
- OSA
- Endocrinopathies
 - e.g. panhypopituitarism

MASLD - Screening (3)

Figure 6. Overview of screening for advanced liver fibrosis and MASLD management



MASLD = metabolic dysfunction-associated steatotic liver disease; LSM = liver stiffness measurement; ELF = enhanced liver fibrosis test
ALT / AST = alanine / aspartate aminotransferase ¹Kim et al 2025

MASLD - Screening (4)

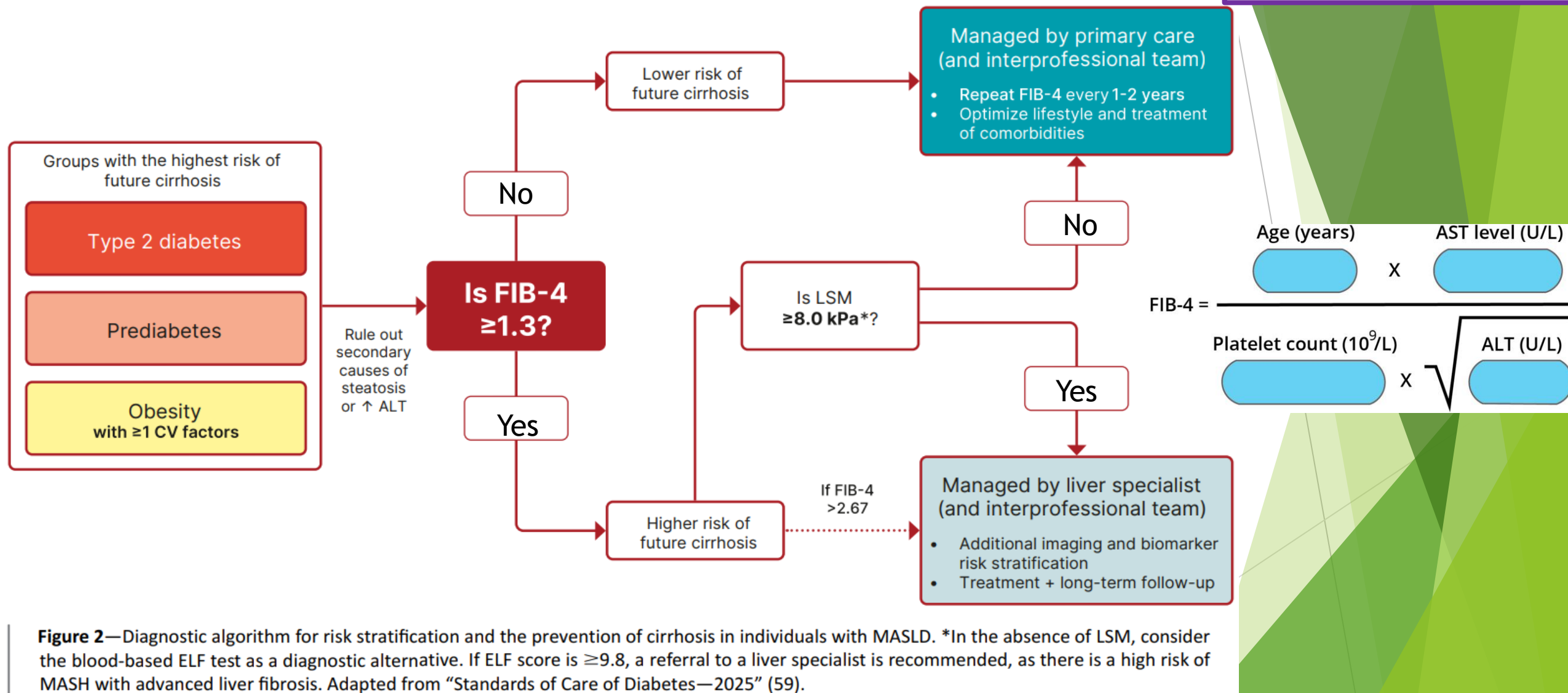


Figure 2—Diagnostic algorithm for risk stratification and the prevention of cirrhosis in individuals with MASLD. *In the absence of LSM, consider the blood-based ELF test as a diagnostic alternative. If ELF score is ≥ 9.8 , a referral to a liver specialist is recommended, as there is a high risk of MASH with advanced liver fibrosis. Adapted from “Standards of Care of Diabetes—2025” (59).

MASLD = metabolic dysfunction-associated steatotic liver disease; LSM = liver stiffness measurement; ELF = enhanced liver fibrosis test
ALT / AST = alanine / aspartate aminotransferase; CV = cardiovascular ³Cusi et al. 2025

Case - John (2)

- ▶ 56M with T2D, hypertension, dyslipidemia, obesity, obstructive sleep apnea
- ▶ Metformin 1000mg BID, atorvastatin 20mg, perindopril 8mg, amlodipine 5mg
- ▶ Do I have fatty liver?

MASLD?

Metabolic syndrome

- ▶ BMI 32 kg/m³
- ▶ WC 102 cm
- ▶ BP 134/78 mmHg
- ▶ A1C 6.7
- ▶ LDL 1.9 mmol/L
- ▶ nHDL 2.3 mmol/L
- ▶ eGFR 54 mL/min
- ▶ ALT 35 U/L
- ▶ AST 32 U/L
- ▶ Plt 165 x E9/L



Next steps:
FIB-4 2.3
LSM = 7.2 kPa

T2D = type 2 diabetes; BMI = body mass index; WC = waist circumference; BP = blood pressure; A1C = glycated hemoglobin; LDL = low-density lipoprotein; eGFR = estimated glomerular filtration rate; ALT / AST = alanine / aspartate aminotransferase; plt = platelets
LSM = liver stiffness measurement; MASLD = metabolic dysfunction-associated steatotic liver disease

Key Point # 1 - Summary

MASLD = common in NB (and under-explored)

- ▶ Most patients with MASLD/MASH are unaware
- ▶ Rates in NB are high, especially with T2D
- ▶ Use Fib-4 to screen high-risk patients



MASLD - Management (1)

Goals:

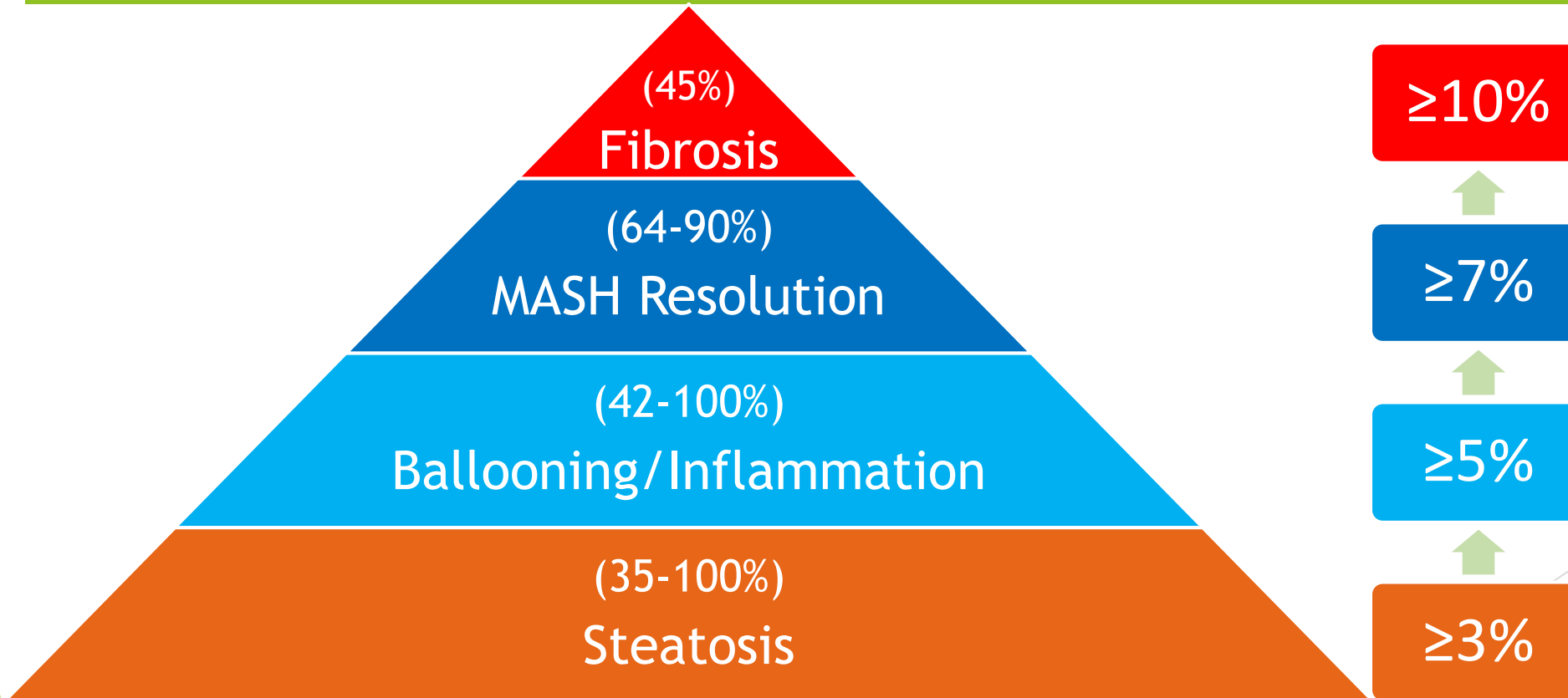
1. Cardiovascular protection
2. Optimize comorbidities
 - ▶ T2D, obesity, HTN, DLD, OSA, CKD
3. Resolve/stabilize MASH ± fibrosis
4. Prevent progression/complications
 - ▶ Cirrhosis, HCC, liver-related death



Key Point # 2 - Weight Loss



Weight loss = effective MASLD prevention & treatment



MASLD = metabolic dysfunction-associated steatotic liver disease; MASH = metabolic dysfunction-associated steatohepatitis

¹⁸Hannah et al. 2016, ⁴EASL 2024

Weight Loss (1)



► 1st-line treatment for MASLD

3. Individuals with T2D and MASLD-related liver fibrosis should aim for sustained reductions in body weight of 5% to 10% to improve glycemia and insulin sensitivity and decrease hepatic steatosis. A weight loss of $\geq 10\%$ is recommended to increase the chance to reverse fibrosis [Grade B, Level 2].

► Reduces steatosis, inflammation/steatohepatitis, fibrosis

- Sustained loss can reverse MASH or slow progression
 - Histologic improvement associated with degree of weight loss

► Lifestyle: possible

- Difficult to sustain to reverse steatohepatitis/fibrosis

► Most require medication AND/OR bariatric surgery



Currently approved
for weight loss:

Contrave
(wellbutrin/
naltrexone),
Saxenda
(liraglutide),
Wegovy
(semaglutide),
Xenical (orlistat),
Zepbound
(tirzepatide)

MASLD = metabolic dysfunction-associated steatotic liver disease; MASH = metabolic dysfunction-associated steatohepatitis

¹Kim et al 2025, ²Pedersen et al. 2025, ³Cusi et al. 2025

Medical Nutrition Therapy (MNT)

MNT is used in managing chronic diseases and focuses on nutrition assessment, diagnostics, therapy and counselling. MNT should:

- a. be personalized and meet individual values, preferences and treatment goals to promote long term adherence
- b. be administered by a registered dietitian to improve weight-related and health outcomes

Physical Activity

30-60 mins of aerobic activity on most days of the week, at moderate to vigorous intensity, can result in:

- a. small amount of weight and fat loss
- b. improvements in cardiometabolic parameters
- c. weight maintenance after weight loss



① Remember nutrition and physical activity recommendations are important for all Canadians regardless of body size or composition.

The Three Pillars of Obesity Management that Support Nutrition and Activity

Psychological Intervention

- a. Implement multicomponent behaviour modification
- b. Manage sleep, time, and stress
- c. Cognitive behavioural therapy and/ or acceptance and commitment therapy should be provided for patients if appropriate

Pharmacological Therapy

- a. semaglutide
- b. liraglutide
- c. naltrexone/bupropion
(in a combination tablet)
- d. orlistat
- e. tirzepatide

criteria

BMI ≥ 30 kg/m² or

BMI ≥ 27 kg/m² with obesity (adiposity) related complications

Bariatric Surgery

① Procedure should be decided by surgeon in discussion with the patient.

- a. Sleeve gastrectomy
- b. Roux-en-Y gastric bypass
- c. Biliopancreatic diversion with/without duodenal switch

criteria

BMI ≥ 40 kg/m² or

BMI $\geq 35 - 40$ kg/m² with an obesity (adiposity) related complication or

BMI ≥ 30 kg/m² with poorly controlled type 2 diabetes

Treating the root causes of obesity is the foundation of obesity management refer to the 4m framework - **mechanical, metabolic, mental and social milieu** BMI = body mass index ²Pedersen et al. 2025

Weight Loss - Medications (1)



9. Pharmacotherapy may be offered, in conjunction with health behaviour changes, in treating people living with MASH, for weight loss and:

- Resolution of MASH without worsening of fibrosis:
 - [semaglutide](#) 2.4 mg weekly [Level 2a, Grade B]
 - liraglutide 1.8 mg daily (BMI ≥ 25 kg/m²) [Level 3, Grade C]
 - tirzepatide 5/10/15 mg weekly (BMI 27-50 kg/m²) [Level 3, Grade C]
- Improvement in fibrosis without worsening of MASH:
 - [semaglutide](#) 2.4 mg weekly [Level 2a, Grade B]
 - tirzepatide 5/10/15 mg weekly (BMI 27-50 kg/m²) [Level 3, Grade C]

Weight Loss - Medications (2)



**obesity
canada**

	Liraglutide	Naltrexone/ Bupropion	Orlistat	Semaglutide	Tirzepatide
Effect on type 2 diabetes (A1c, placebo subtracted)	-1.0% ²⁴	-0.5% ²⁵	-0.4% ²⁶	-1.2% ²²	-1.6% (10 mg) -1.6% (15 mg) ²³
Effect on MASH	Resolution of MASH without worsening of fibrosis (39% with liraglutide 1.8 mg vs. 9% with placebo) ²⁸	Not studied	No benefit ¹³⁸	Resolution of MASH without worsening of fibrosis (62.9% vs 34.3% with placebo) ²⁷ Improvement in fibrosis without worsening of steatohepatitis (36.8% vs 22.4% with placebo) ²⁷	Resolution of MASH without worsening of fibrosis: 44% (5mg) 56% (10mg) 62% (15 mg) 10% (placebo) ²⁹ Improvement in fibrosis without worsening of MASH: 55% (5 mg) 51% (10 mg) 51% (15 mg) 30% (placebo) ²⁹

MASH = metabolic dysfunction-associated steatohepatitis; A1C = glycated hemoglobin; BMI = body mass index ²Pedersen et al. 2025

Weight Loss - Bariatric Surgery

- ▶ Recommended for MASH in select patients
 - Substantial weight loss improves glucose regulation and reduces hepatic fat content within 1 year
- ▶ Improvement in liver histology reported in several studies
 - Improved steatosis in 70-80%
 - Resolved ballooning/inflammation in 50-75%
 - Resolved fibrosis in 30-40%
- ▶ Sleeve gastrectomy and Roux-en-Y similar
 - MASH resolution without worsening fibrosis (57% vs. 56%)
 - Improved fibrosis without worsening MASH (39% vs. 37%)
- ▶ Laparoscopic sleeve gastrectomy can be performed in patients with compensated cirrhosis at experienced centers (>100/yr)



Key Point # 2 - Summary

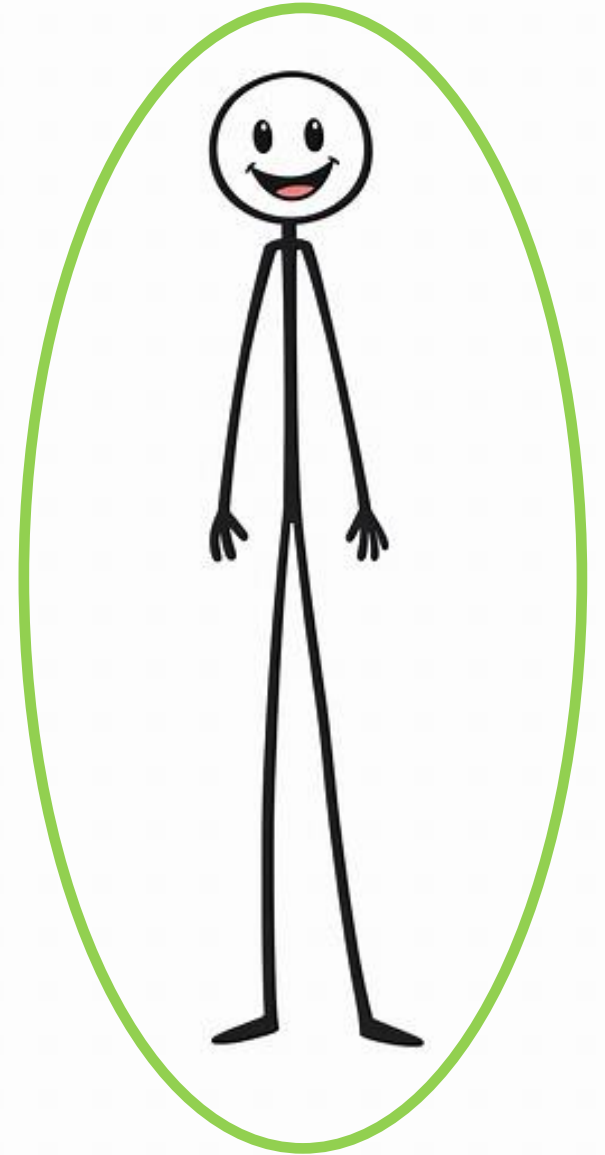
Weight loss = effective MASLD prevention and treatment

- ▶ Weight loss ≥3% can be impactful
- ▶ MASH / fibrosis resolution possible
- ▶ Most require medication and/or surgery

Lean MASLD

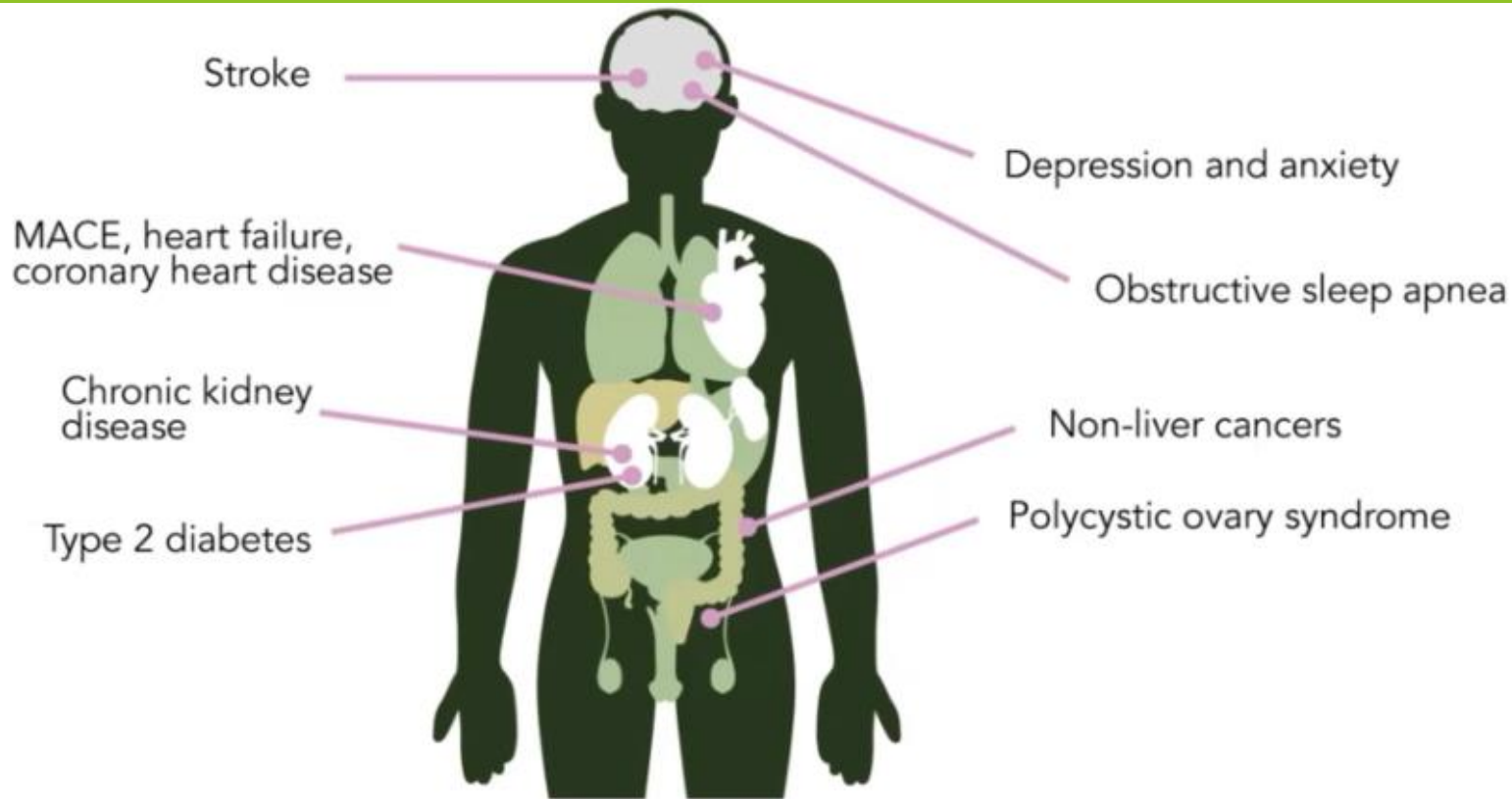
10-20% of patients have normal (or low) BMI

- ▶ Higher waist circumference (visceral adiposity)
- ▶ Higher-risk ethnicity
 - Hispanic, Indigenous Canadian, African, South Asian
- ▶ Higher genetic risk factors
- ▶ Pathogenesis similar, but less progression
 - Lower rates of inflammation, MASH, fibrosis



Key Point # 3 - Risk Factors

Managing MASLD risk factors = crucial support



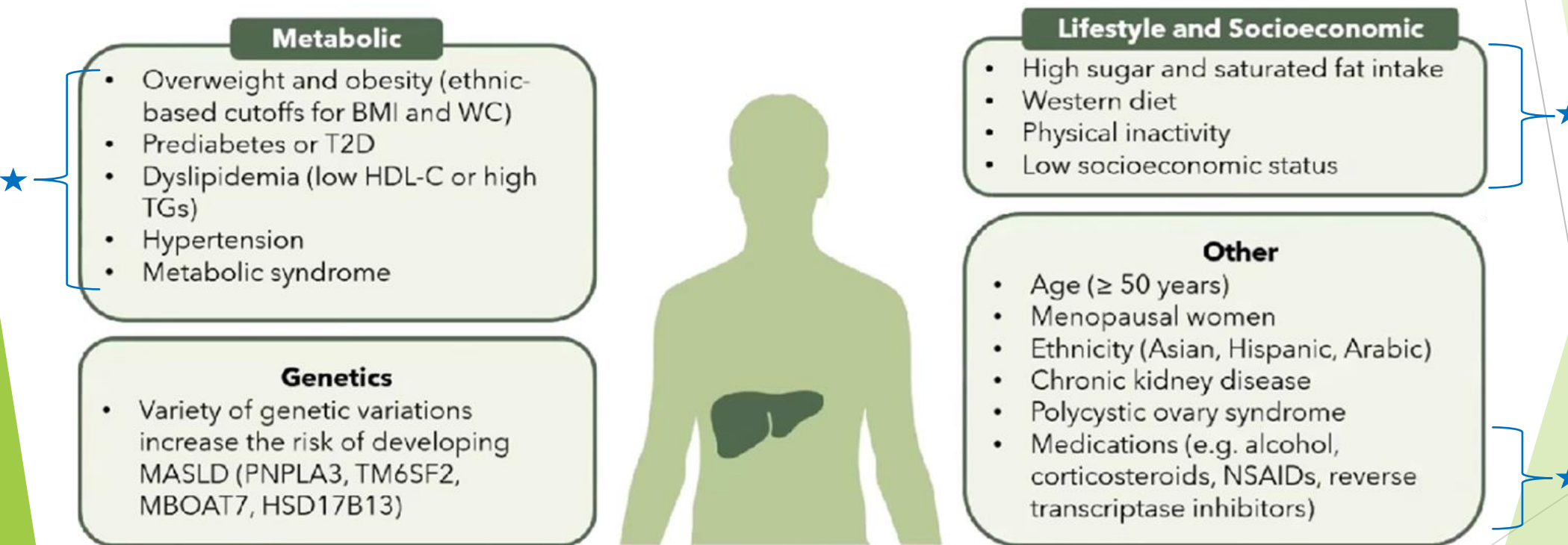
There is a bidirectional relationship between the incidence of MASLD and CKD, T2D, PCOS, etc.

MASLD = metabolic dysfunction-associated steatotic liver disease; CKD = chronic kidney disease; T2D = type 2 diabetes; PCOS = polycystic ovarian syndrome; MACE = major adverse cardiovascular events

MASLD - Risk Factors (2)



► Identify targets to modify risk



***Potentially modifiable**

MASLD - Risk Factors (3)



History

- ▶ Smoking, alcohol, diet, exercise, body weight
- ▶ HTN, DLD, T2D, hyperuricemia, OSA, PCOS
- ▶ Medications
- ▶ Family history: obesity, MASLD, T2D, CAD, stroke, cirrhosis



Exam

- ▶ Height, weight, waist circumference, blood pressure, insulin resistance (e.g. acanthosis nigricans)
- ▶ Advanced liver disease
 - Hepatomegaly, splenomegaly, abdominal veins, edema, jaundice



Labs

- ▶ General
 - ALT, AST, CBC (platelets), eGFR, albumin:creatinine, fasting glucose, A1C, lipids
- ▶ Consider
 - Hepatitis B / C

Lifestyle Interventions

Weight loss

- Encourage calorie deficit that promotes weight loss
- ~5% weight reduction to reduce steatosis
- ~7-10% to reverse steatohepatitis and liver fibrosis

Nutrition (healthy eating)

- Emphasize a high-fiber, whole foods eating pattern with personalized goals, that is low in saturated fat and added sugar
- Individuals should abstain from sugar-containing beverages and minimize consumption of ultraprocessed foods

DSMES

- Support behavior change to address factors complicating diabetes management
- Address lifestyle modification with medical nutrition therapy

Physical activity

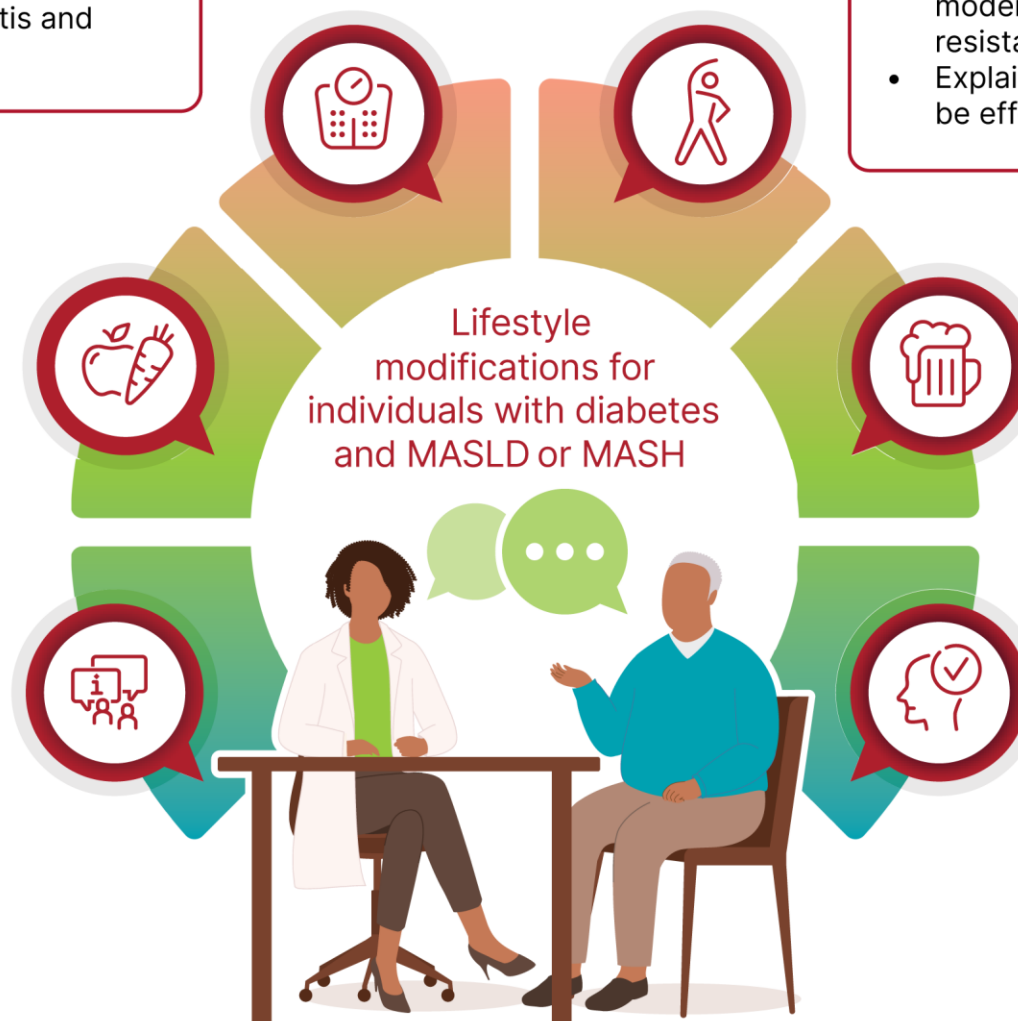
- Discuss goal of performing ≥ 150 min/week moderate-intensity aerobic activity and resistance activities 2-3 times/week
- Explain that brief sessions (~10 min) can be effective ways to reach goal

Alcohol

- Assess intake at every visit
- Recommend minimizing alcohol intake in MASLD
- Individuals should abstain if moderate fibrosis is present ($\geq F2$)

Behavioral health

- Promote stress reduction via positive health behaviors
- Screen for depression and anxiety at least annually and refer to behavioral health professionals when indicated
- Advise adequate sleep and quitting smoking



Lifestyle - Diet



Cornerstone of MASLD management

- ▶ Saturated fat/sugar increase MASH risk
- ▶ Fructose linked to fibrosis severity
 - Regardless of total caloric intake
- ▶ Optimal diets should be personalized, practical, sustainable
 - Mediterranean: strongest data on cardiometabolic/mortality benefit
 - Not adequately studied in MASLD
 - DASH, high-protein meal replacement, intermittent fasting

Choices to support MASLD

- ▶ Whole grains
- ▶ Health protein
 - Seafood, low-fat dairy, lean meat
- ▶ Reduce red/processed meats
 - Less saturated/trans fat, ultra-processed, added sugar
- ▶ Deeply coloured fruits/vegetables
- ▶ Liquid plant cooking oil



Lifestyle - Exercise

Liver benefits beyond weight loss:

- ▶ Increased insulin sensitivity
- ▶ Decreased AST / ALT
- ▶ Decreased steatosis
- ▶ Improved cardiovascular health

Exercise prescription:

- ▶ ≥150 min/week of moderate intensity
- ▶ ≥75min/week of vigorous intensity
- ▶ Resistance activity 2-3x/week

Lifestyle - Smoking

Tobacco significantly worsens MASLD outcomes

- ▶ Worsen progression to MASH/advanced fibrosis
- ▶ Increased risk of hepatocellular carcinoma
- ▶ Increased risk of cardiovascular disease

Abstinence is best



Image generated using Microsoft Copilot 2026.

Lifestyle - Alcohol

Even moderate alcohol use can accelerate MASLD

- ▶ Worsen steatosis
- ▶ Worsen fibrosis
- ▶ Increased risk of hepatocellular carcinoma
- ▶ Increased risk of cardiovascular disease

Abstinence is best

~~DIABETES~~
CANADA

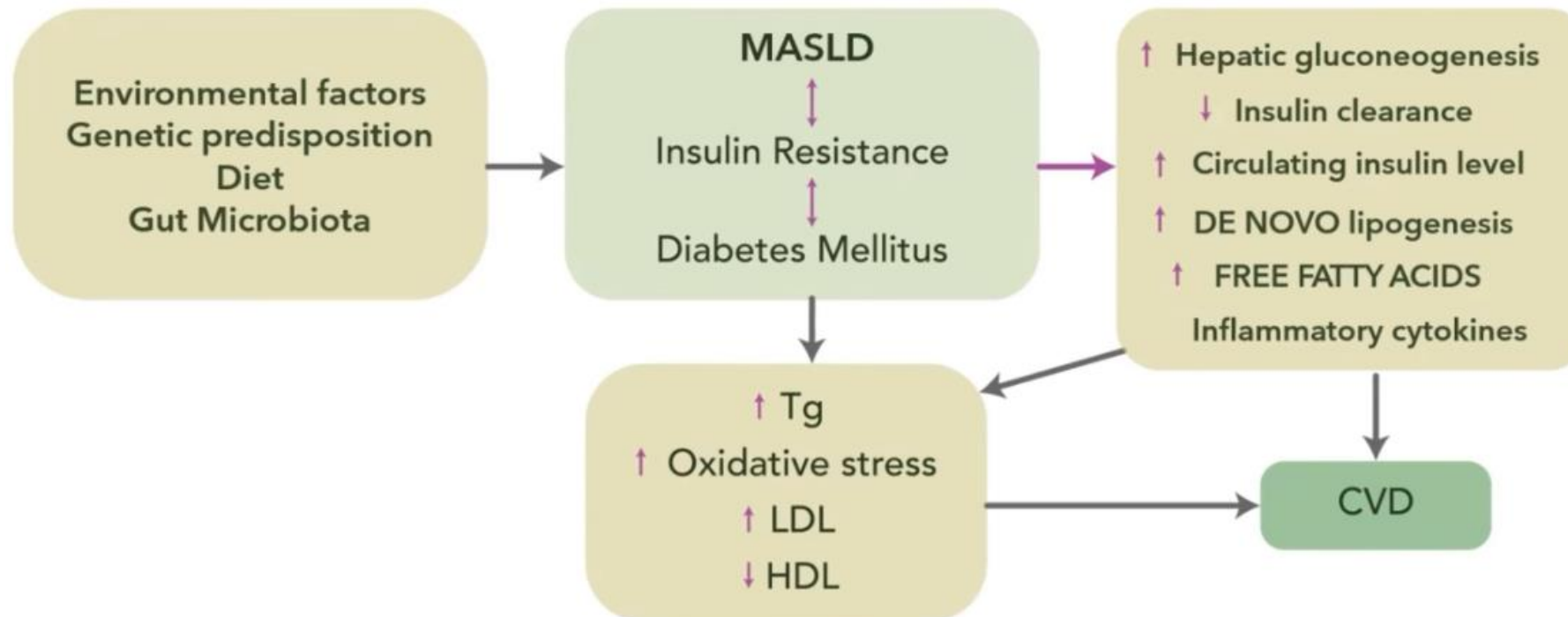
 American
Diabetes
Association®



Image generated using Microsoft Copilot 2026.

Diabetes (1)

- ▶ Bidirectional pathophysiological link between MASLD and T2D
- ▶ Fortunately, treatment can address both!



**DIABETES
CANADA**

Diabetes (2)



► Guidelines now recognize MASLD as an important factor in choosing T2D pharmacotherapy (2026)

If additional cardiovascular and kidney risk reduction, management of other metabolic comorbidities, and/or glycemic lowering is needed

+Mitigating risk of MASLD or MASH

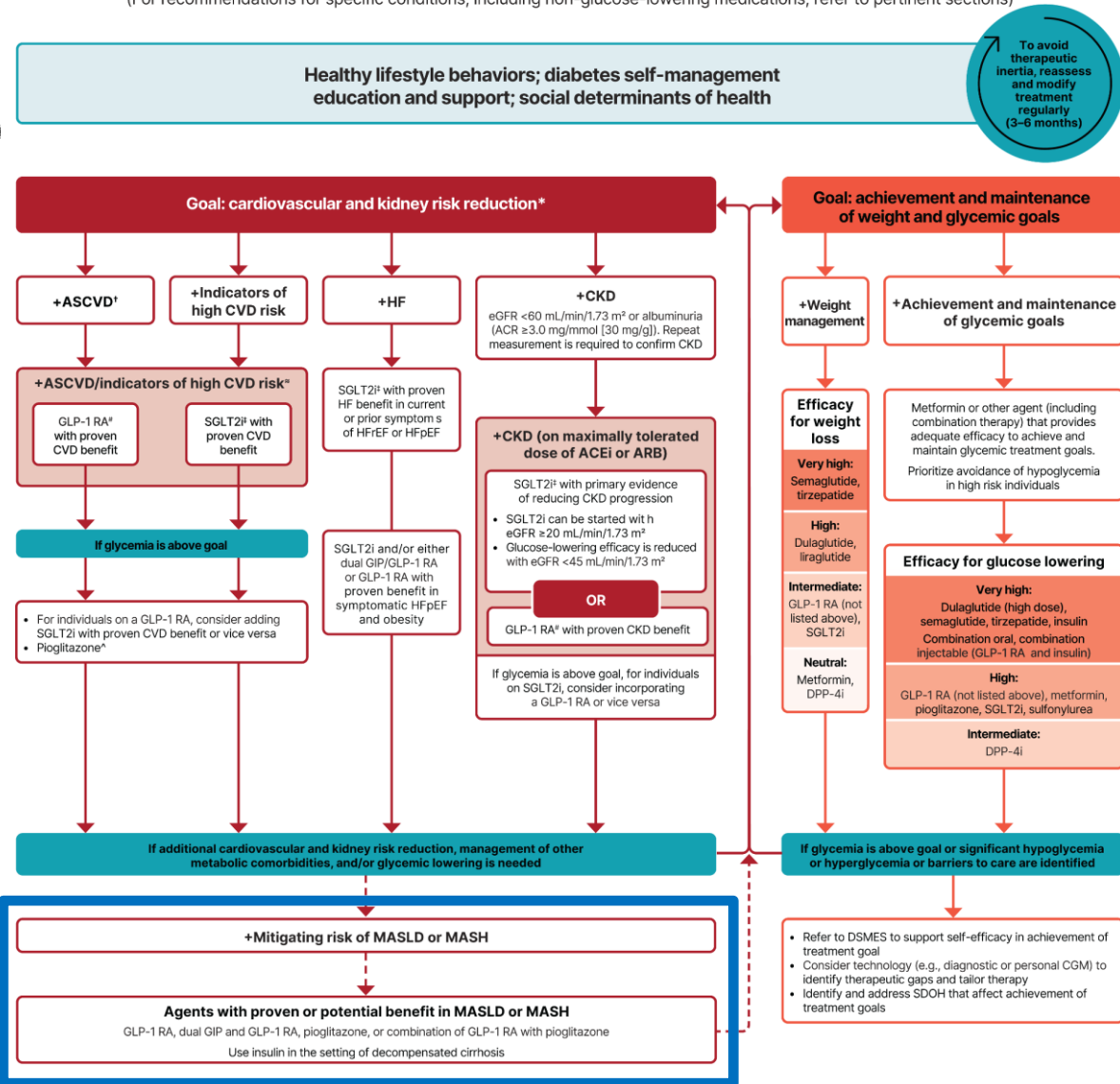
Agents with proven or potential benefit in MASLD or MASH

GLP-1 RA, dual GIP and GLP-1 RA, pioglitazone, or combination of GLP-1 RA with pioglitazone

Use insulin in the setting of decompensated cirrhosis

MASLD = metabolic dysfunction-associated steatotic liver disease;
MASH = metabolic dysfunction-associated steatohepatitis; T2 = type 2 diabetes
GLP-1 RA = glucagon-like peptide-1 receptor agonist; GIP = glucose-dependent insulinotropic polypeptide ²⁴Bajaj et al. 2026

Use of glucose-lowering medications in the management of type 2 diabetes
(For recommendations for specific conditions, including non-glucose-lowering medications, refer to pertinent sections)



* In people with HF, CKD, established CVD, or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be made irrespective of attainment of glycemic goal.

† ASCVD: Defined differently across CVOTs but all included individuals with established CVD (e.g., MI, stroke, and arterial revascularization procedure) and variably included conditions such as transient ischemic attack, unstable angina, amputation, and symptomatic or asymptomatic coronary artery disease. Indicators of high risk: While definitions vary, most comprise ≥55 years of age with two or more additional risk factors (including obesity, hypertension, smoking, dyslipidemia, or albuminuria).

‡ A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high risk CVD. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details.

For GLP-1 RAs, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and kidney end points in individuals with T2D with established or high risk of CVD. One kidney outcome trial demonstrated benefit in reducing persistent eGFR reduction and CV death for a GLP-1 RA in individuals with CKD and T2D.

‡ For SGLT2is, CV and kidney outcomes trials demonstrate their efficacy in reducing the risks of composite MACE, CV death, all-cause mortality, MI, HF, and kidney outcomes in individuals with T2D and established or high risk of CVD.

^ Low-dose pioglitazone may be better tolerated and similarly effective as higher doses.

Medication	Effect in MASLD and MASH*				Cardiovascular, renal, and other relevant clinical effects			
	Hepatic steatosis	Steatohepatitis	Fibrosis regression	Reduction of fibrosis progression	ASCVD*	CKD*	HF*	Hypoglycemia¶
Semaglutide**	Beneficial	Beneficial	Beneficial	Potential benefit	Beneficial	Beneficial	Beneficial	Low risk
Tirzepatide***†	Potential benefit	Potential benefit	Potential benefit	Potential benefit	?	?	Beneficial	Low risk
Pioglitazone†	Potential benefit	Potential benefit	Potential benefit	Potential benefit	Beneficial	Neutral	Not recommended in HF stage B, C, or D	Low risk
SGLT2 inhibitors	Potential benefit	?	?	?	Beneficial	Beneficial	Beneficial	Low risk
Metformin¶	Neutral	Neutral	Neutral	Neutral	Potential benefit?	Neutral	Neutral	Low risk
DPP-4 inhibitors¶	Neutral	?	?	?	Neutral	Neutral	Neutral (except saxagliptin, alogliptin?)	Low risk
Insulin¶	Potential benefit	?	?	?	Neutral	Neutral	Neutral	High risk
Sulfonylureas¶	Neutral	?	?	?	Neutral	Neutral	Neutral	High risk

ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; HF, heart failure. ? indicates unknown. *Includes people with and without type 2 diabetes. ¶Only in people with type 2 diabetes. **Only semaglutide among GLP-1RA has been reported to be of benefit in a phase 2 RCT (154) with improvement in steatohepatitis and more recently in a phase 3 RCT with histological outcomes in MASH, including improvements in steatohepatitis and fibrosis (11). Liraglutide may offer potential benefit, based on results of a phase 2 RCT (157). Other GLP-1RA have not been tested in RCTs with liver histological outcomes. ***Tirzepatide is the only dual GIP/GLP-1RA available and tested with histological outcomes in a phase 2 RCT in MASH (155). †Tirzepatide and pioglitazone are considered of potential benefit based on phase 2 trials.

MASLD = metabolic dysfunction-associated steatotic liver disease; MASH = metabolic dysfunction-associated steatohepatitis; RCT = randomized control trial; GLP-1 RA = glucagon-like peptide-1 receptor agonist; GIP = glucose-dependent insulinotropic polypeptide; SGLT2 = sodium-glucose co-transporter-2; DPP-4 = dipeptidyl peptidase-4 ³Cusi et al. 2025

Reducing Cardiovascular Risk



Medical therapy integral to manage MASLD risk

Statins	Antihypertensives	GLP1-RA	SGLT2i
▪ Safe for all MASLD • *Not <u>decompensated</u> cirrhosis ▪ Underused due to unfounded concerns ▪ Add on ezetimibe or PCSK9	▪ 1st line: <u>ACEi</u> or <u>ARB</u> ▪ May reduce liver inflammation/fibrosis ▪ BP target <130/80	▪ Indicated in <u>ASCVD</u> or <u>T2D</u> to reduce cardiovascular events and improve renal function	▪ Proven to reduce <u>ASCVD</u> and <u>CKD</u> progression with or without T2D ▪ Role in <u>CHF</u>

Significant overlap in co-management of risk among conditions

MASLD = metabolic dysfunction-associated steatotic liver disease; PCSK9i = Proprotein Convertase Subtilisin/Kexin type 9 inhibitor; GLP-1 RA = glucagon-like peptide-1 receptor agonist; SGLT2i = sodium-glucose co-transporter-2 inhibitor; ACEi = for Angiotensin-Converting Enzyme Inhibitors; ARB = Angiotensin II Receptor Blocker; T2D = type 2 diabetes; ASCVD = atherosclerotic cardiovascular disease; CKD = chronic kidney disease; CHF = congestive heart failure ¹Kim et al 2025, ³Cusi et al. 2025, ²¹Fan et al. 2024, ²³Michalopoulou et al. 2025

Key Point # 3 - Summary

Managing MASLD risk factors = crucial support

- ▶ Modifying risk factors can improve disease state
- ▶ Focus on reducing cardiovascular risk
- ▶ Significant overlap in MASLD and T2D

Key Point # 4 - Medication

~~Semaglutide = only currently indicated MASLD treatment*~~

► *Approved for MASH (with conditions)



Health
Canada

WEGOVY®, indicated for:

- the treatment of non-cirrhotic metabolic dysfunction-associated steatohepatitis (MASH) in adults with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis).

has been issued market authorization with conditions, pending the results of trials to verify its clinical benefit. Patients should be advised of the nature of the authorization. For further information for WEGOVY® please refer to Health Canada's [Notice of Compliance with conditions - drug products web site](#).

Pharmacology - Vitamin E

800 IU PO daily

- ▶ 2 RCTs (MASLD without T2D)
 - Improved steatohepatitis
 - Improved ALT/AST
 - Improved lobular inflammation
- ▶ Not recommended – not approved for MASH
 - No fibrosis benefit
 - Lack of Phase III data
 - Safety (hemorrhagic stroke, prostate cancer)



Pharmacology - Pioglitazone

30,45 mg PO daily (TZD, i.e. PPAR- γ agonist)

► Meta-analysis/systematic review (10 RCTs)

- Improved liver histology in MASH
- Improved liver enzymes

► Recommended over other T2D pharmacotherapy

- T2D and MASLD-related liver fibrosis (F2 or F3)
[Grade A, Level 1A] – not approved for MASH
- Safety (weight gain)



Health
Canada



TZD = thiazolidinedione; PPAR- γ = peroxisome proliferator-activated receptor gamma; MASLD = metabolic dysfunction-associated steatotic liver disease; T2D = type 2 diabetes; MASH = metabolic dysfunction-associated steatohepatitis RCT = randomized controlled trial

²⁵Sanyal et al. 2010, ¹Kim et al. 2025, ³Cusi et al. 2025, ⁴EASL 2024

Semaglutide



[Grade D, Level 4]

2.4mg SC weekly (GLP-1 receptor agonist)

► Multi-centre, double-blinded, placebo-controlled
Phase III RCT (ESSENCE): n = 1197 (MASH, F2/3)

- Included **T2D**

- Primary endpoint:

 - A. MASH resolution (no fibrosis)

 - B. Fibrosis improvement (without MASH worsening)

► **Significant** histological improvement

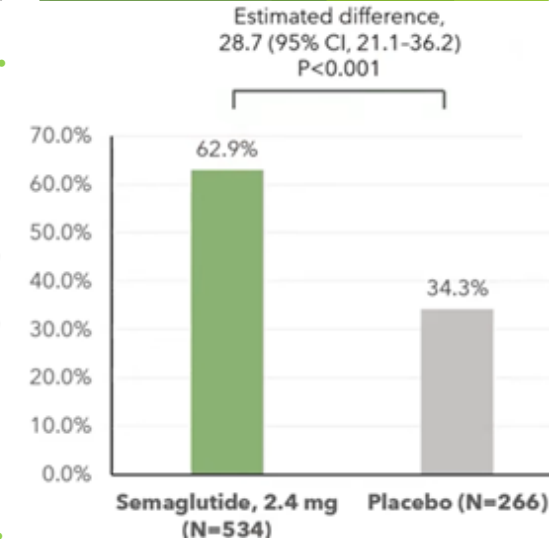
► Improved **cardiovascular** risk factors



Health
Canada

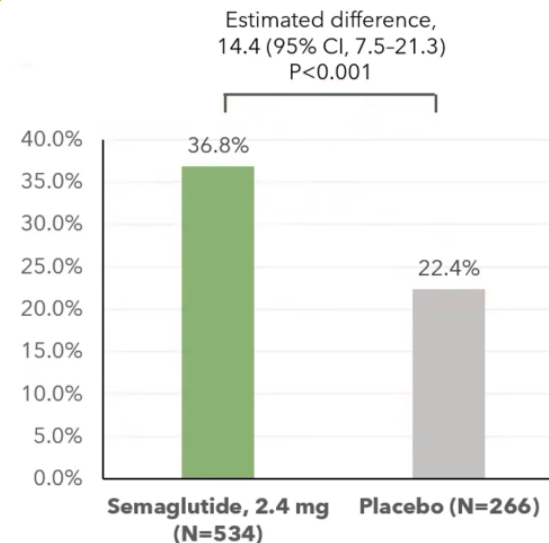
A.

Percentage of patients



B.

Percentage of patients



T2D = type 2 diabetes; MASH = metabolic dysfunction-associated steatohepatitis; T2D = type 2 diabetes; RCT = randomized controlled trial;
GLP-1 = glucagon-like peptide-1 ²⁶Sanyal et al. 2025, ¹Kim et al. 2025, ³Cusi et al. 2025, ⁴EASL 2024

Key Point # 4 - Summary

Semaglutide = only currently approved MASLD treatment*

- ▶ Approved with conditions (pending study results)
- ▶ Improved MASH, fibrosis, and CV risk factors
- ▶ Treats comorbidities



Key Point # 5 - Future

Newer MASLD medications = likely even more effective



Image generated using Microsoft Copilot 2026.

MASLD = metabolic dysfunction-associated steatotic liver disease; MASH = metabolic dysfunction-associated steatohepatitis; CV = cardiovascular

Pharmacology - Tirzepatide

5,10,15mg SC weekly (GLP-1/GIP receptor agonist)

► Multi-centre, double-blinded, placebo-controlled

Phase II RCT (SYNGERY-NASH):

n = 190 (BMI > 30, MASH, F2/3)

- Primary endpoint:

- A. MASH resolution (without worsening fibrosis)

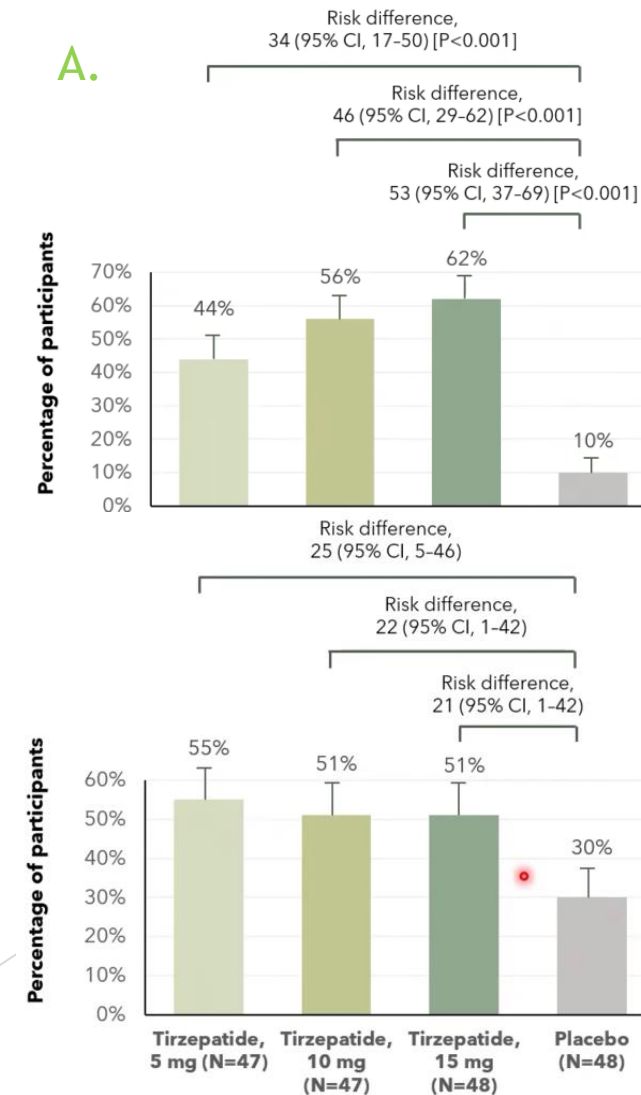
- Decrease in ≥ 1 F stage (without worsening MASH)

► Phase III pending (SYNERGY-Outcomes)

- Not approved for MASH



Health
Canada



MASLD = metabolic dysfunction-associated steatotic liver disease; MASH = metabolic dysfunction-associated steatohepatitis; RCT = randomized controlled trial; GLP-1 RA = glucagon-like peptide-1 GIP = glucose-dependent insulinotropic polypeptide ²⁷Loomba et al. 2024, ³Cusi et al. 2025

Pharmacology - Survodutide

2.4,4.8,6.0mg SC weekly (GLP-1/glucagon receptor agonist)

► Multi-centre, double-blinded, placebo-controlled parallel group Phase II RCT: n = 295 (MASH, F1-3)

- Primary endpoint:

- A. MASH reduction (without worsening fibrosis)

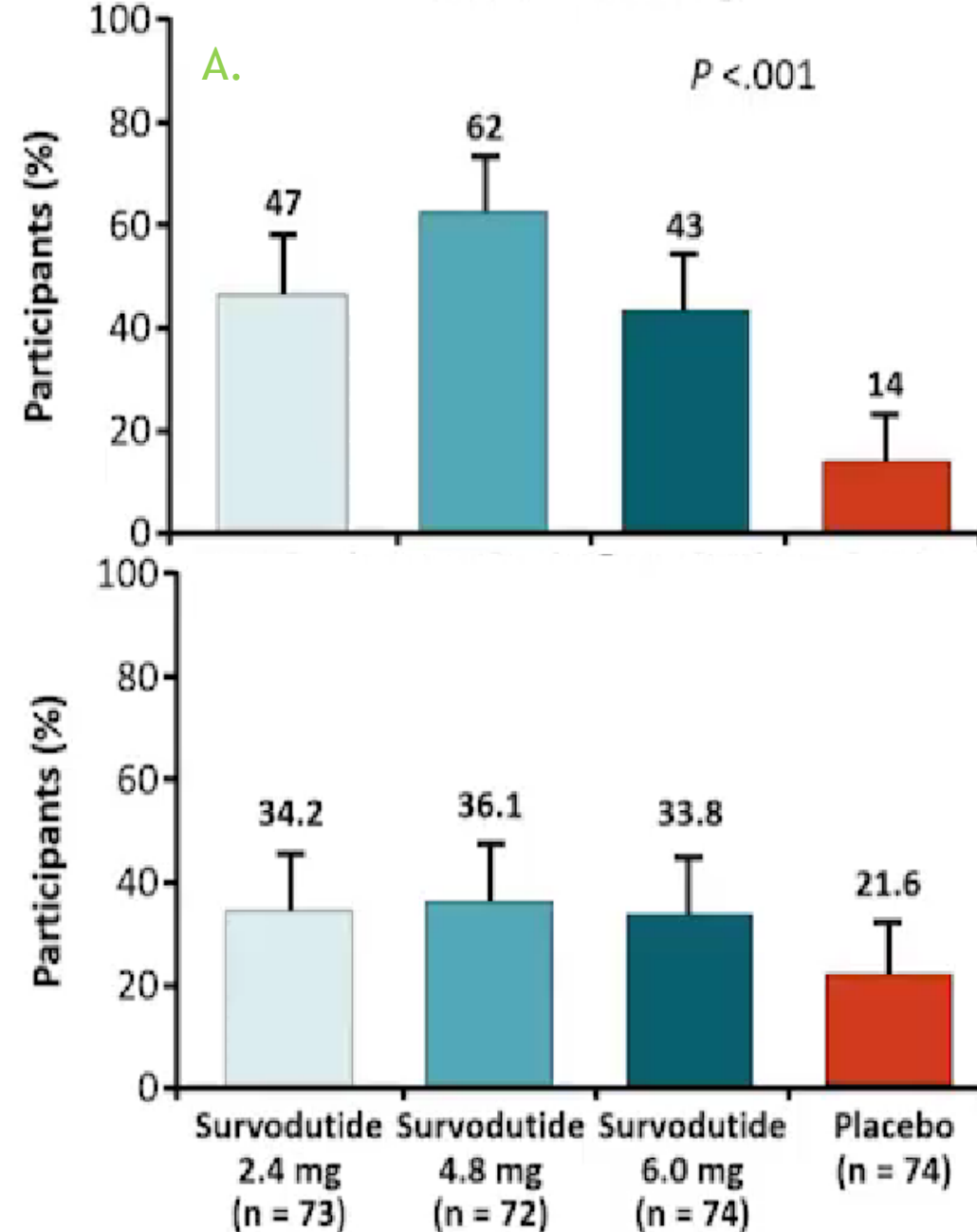
- Decrease in ≥ 1 F stage (without worsening MASH)

► Phase III pending (LIVERAGE / LIVERAGE CIRRHOSIS)

- Not approved for MASH



Health
Canada



Pharmacology - Resmetirom

80,100mg PO daily (THR- β agonist)

► Multi-centre, double-blinded, placebo-controlled Phase III RCT (MAESTRO-NASH):
n = 966 (MASH, F1-3)

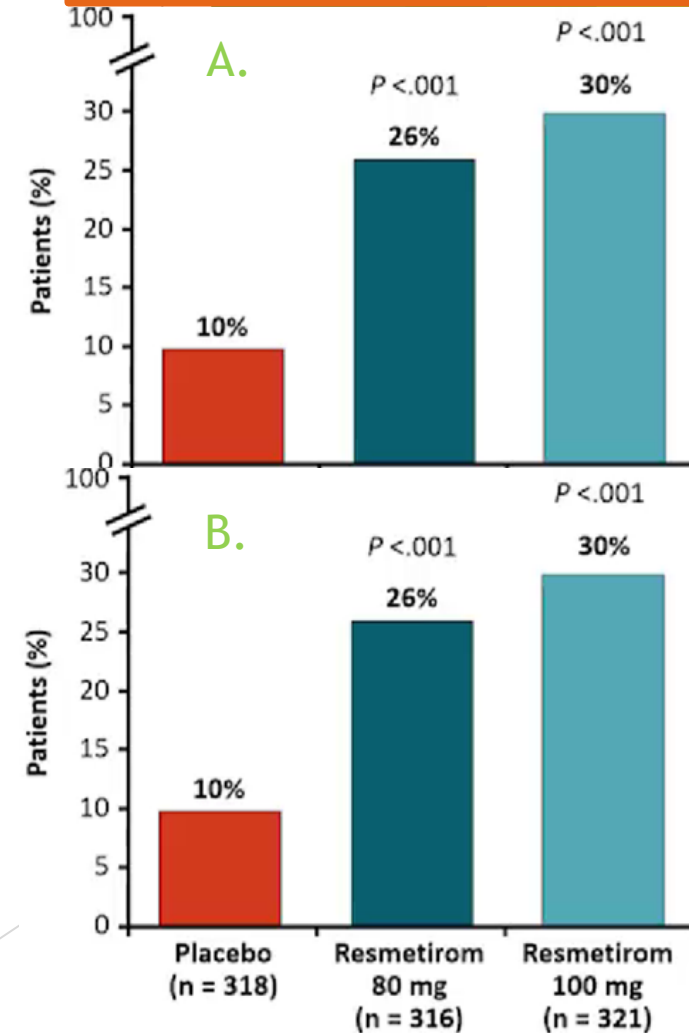
- Primary endpoint:

- A. MASH resolution (without worsening fibrosis)

- B. Decrease in ≥ 1 F stage (without worsening MASH)

► Not approved for MASH   Health Canada

- Approved in other countries



MASLD Pharmacology - Summary



Semaglutide	Vitamin E	Pioglitazone	Tirzepatide	Survodutide	Resmetirom
GLP-1	Anti-oxidant	PPAR- γ	GLP-1/GIP	GLP-1/ glucagon	THR- β
2.4mg SC weekly	800IU PO daily	30,40mg PO daily	5,10,15mg SC weekly	2.4,4.8,6mg SC weekly	80,100mg PO daily
Phase III	2 RCTs	10 RCTs	Phase II	Phase II	Phase III
Resolution	Reduction	Reduction	Resolution	Reduction	Resolution
Reduction	-	-	Reduction	Reduction	Reduction
Loss	-	Gain	Loss	Loss	Loss
GI	Prostate Ca?	Bladder Ca?	GI	GI	Diarrhea
✓	✋	✋	✋	✋	✋

MASH
Fibrosis
Weight

MASLD = metabolic dysfunction-associated steatotic liver disease; MASH = metabolic dysfunction-associated steatohepatitis; GLP-1 RA = glucagon-like peptide-1 GIP = glucose-dependent insulinotropic polypeptide; RCT = randomized controlled trial; PPAR- γ = peroxisome proliferator-activated receptor gamma; THR- β = thyroid hormone receptor-beta; GI = gastrointestinal; Ca = cancer ¹Kim et al. 2025, ³Cusi et al. 2025, ⁴EASL 2024

Key Point # 5 - Summary

Newer MASLD medications = likely even more effective

► Dual GLP-1 RA/GIP: [tirzepatide](#)



Health
Canada

► Dual GLP-1/glucagon: [survodutide](#)



Health
Canada

► THR- β : [resmetirom](#)



Health
Canada

No MASLD Management (2)

Guideline differences in recommendations

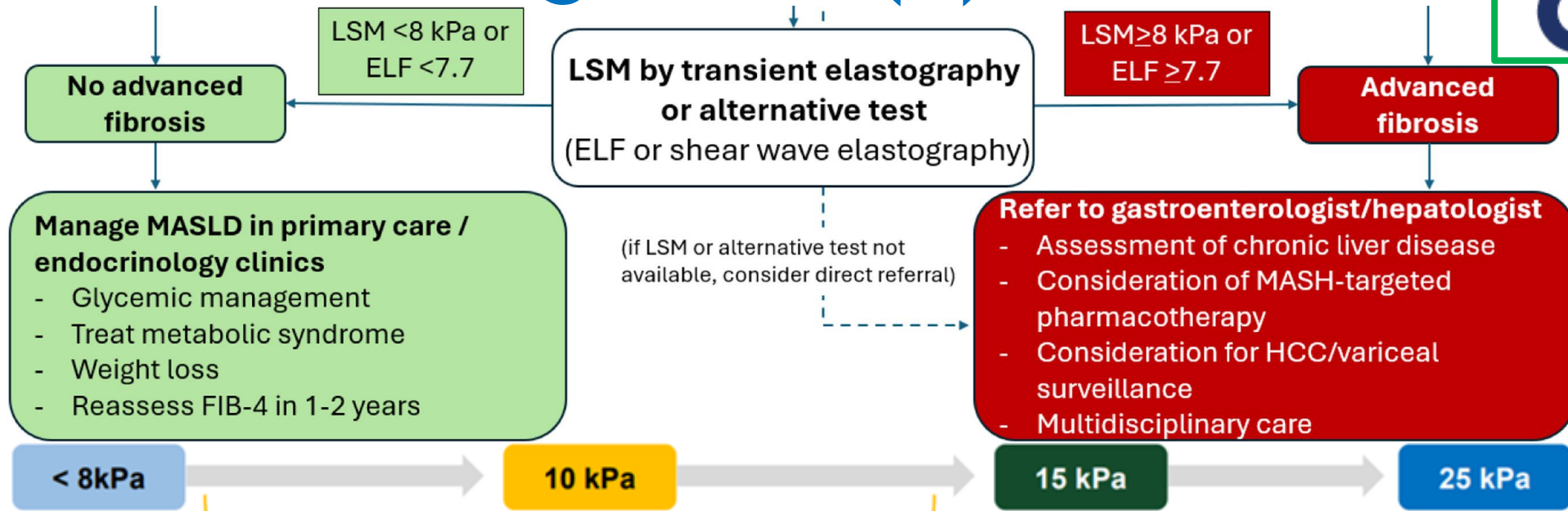
Diabetes Canada	ADA	AACE	EASL-EASD-EASO
- Nutrition (Medit.) - Exercise - Weight loss	- Nutrition (healthy) - Weight loss - Exercise - Minimize alcohol	- Nutrition (Medit.) - Weight loss	- Nutrition (Medit.) - Weight loss - Exercise - Smoking cessation - Avoid alcohol
- Pioglitazone - Semaglutide	- GLP-1 RA - GIP/GLP-1RA - Pioglitazone (or SGLT2i)	- Pioglitazone - Semaglutide - Vitamin E	- Resmetirom* - Vitamin E - GLP-1 RA - Pioglitazone
Optimize CV risk	Optimize	Manage (standard of care)	Manage



MASLD = metabolic dysfunction-associated steatotic liver disease; ADA = American Diabetes Association; AACE = American Association of Clinical Endocrinology; EASL = European Association for the Study of the Liver; EASD = European Association for the Study of Diabetes; EASO = European Association for the Study of Obesity; CVD = cardiovascular disease; ALT / AST = alanine / aspartate aminotransferase *not available in Canada

¹Kim et al. 2025, ³Cusi et al. 2025, ¹⁶Cusi et al. 2022, ⁴EASL 2024

MASLD Management (3)

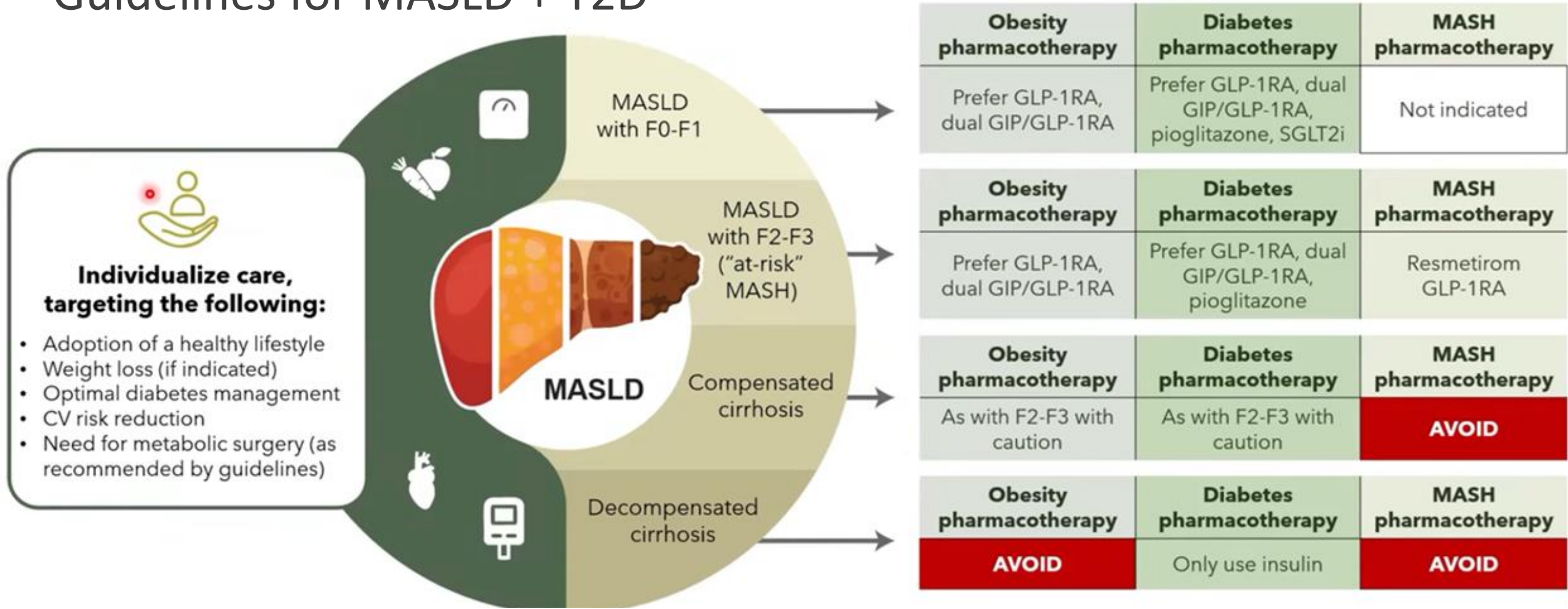


Low-risk	High-risk	Compensated	Portal HTN
- Obesity - T2D - HTN - Atherogenic DLD - Less alcohol - R/A q1-3 y	- MASH-directed therapy - AST/ALT reduction - LSM reduction - CAP reduction	HCC surveillance	Carvedilol

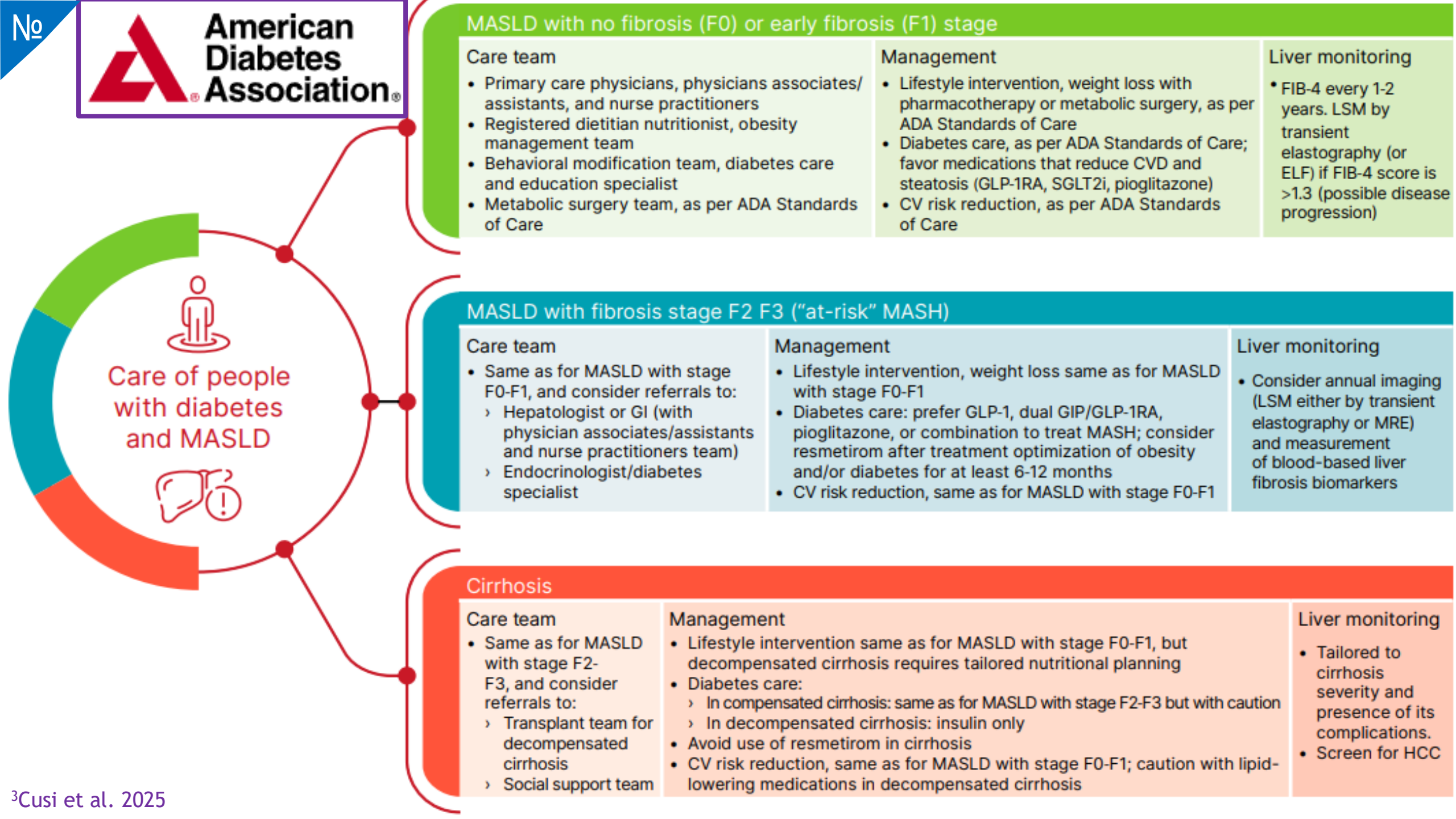
MASLD Management (4)



Guidelines for MASLD + T2D



MASLD = metabolic dysfunction-associated steatotic liver disease; MASH = metabolic dysfunction-associated steatohepatitis; GLP-1 RA = glucagon-like peptide-1 receptor agonist GIP = glucose-dependent insulintropic polypeptide ³Cusi et al. 2025



Case - John (3)

- ▶ 56M with T2D, hypertension, dyslipidemia, obesity, obstructive sleep apnea
- ▶ Metformin 1000mg BID, atorvastatin 20mg, perindopril 8mg, amlodipine 5mg
- ▶ Do I have fatty liver?

MASLD

Metabolic syndrome

- ▶ BMI 32 kg/m³
- ▶ WC 102 cm
- ▶ BP 134/78 mmHg
- ▶ A1C 6.7
- ▶ LDL 1.9 mmol/L
- ▶ nHDL 2.3 mmol/L
- ▶ eGFR 54 mL/min
- ▶ ALT 35 U/L
- ▶ AST 32 U/L
- ▶ Plt 165 x E9/L

FIB-4 2.3
Liver stiffness
measurement = 7.2 kPa

Abdominal US:
Hepatic steatosis

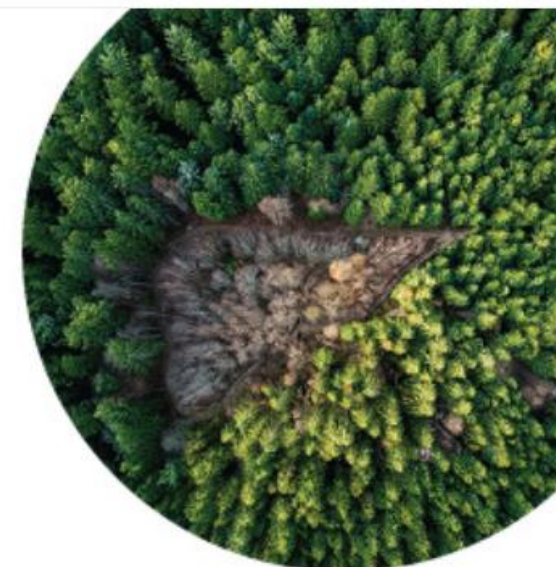
Medication:
Semaglutide 0.25mg SC
weekly x 4 weeks with
titration to 2.4mg SC
- Addresses BMI, WC, BP,
A1C, LDL, eGFR
and MASLD

T2D = type 2 diabetes; BMI = body mass index; WC = waist circumference; BP = blood pressure; A1C = glycated hemoglobin; LDL = low-density lipoprotein; eGFR = estimated glomerular filtration rate; ALT / AST = alanine / aspartate aminotransferase; plt = platelets; US = ultrasound
MASLD = metabolic dysfunction-associated steatotic liver disease

MASLD Masterclass



METABOLIC DYSFUNCTION-ASSOCIATED
STEATOTIC LIVER DISEASE



Log in

Sign up

Enhance your clinical practice with **MASLD MASTERCLASS**

An accredited self-learning program designed to deepen your understanding of MASLD through flexible, module-based education on disease awareness, diagnosis, and evolving management strategies.

MASLD = metabolic dysfunction-associated steatotic liver disease <https://masldmasterclass-elearning.ca/>

What Can I Do in Practice Today?

1. Start targeted [lifestyle](#) interventions
 - e.g. Mediterranean diet, exercise prescription, vices
2. Advise on benefits of [weight loss](#)
 - Start medication to assist patients in their journey
3. Address [cardiovascular](#) risk factors
 - e.g. HTN, DLD, tobacco/alcohol cessation
4. Start medication with [multiple](#) benefits
 - (e.g. GLP-1 RA)
5. Start medication approved for MASH ([semaglutide](#))



Health
Canada



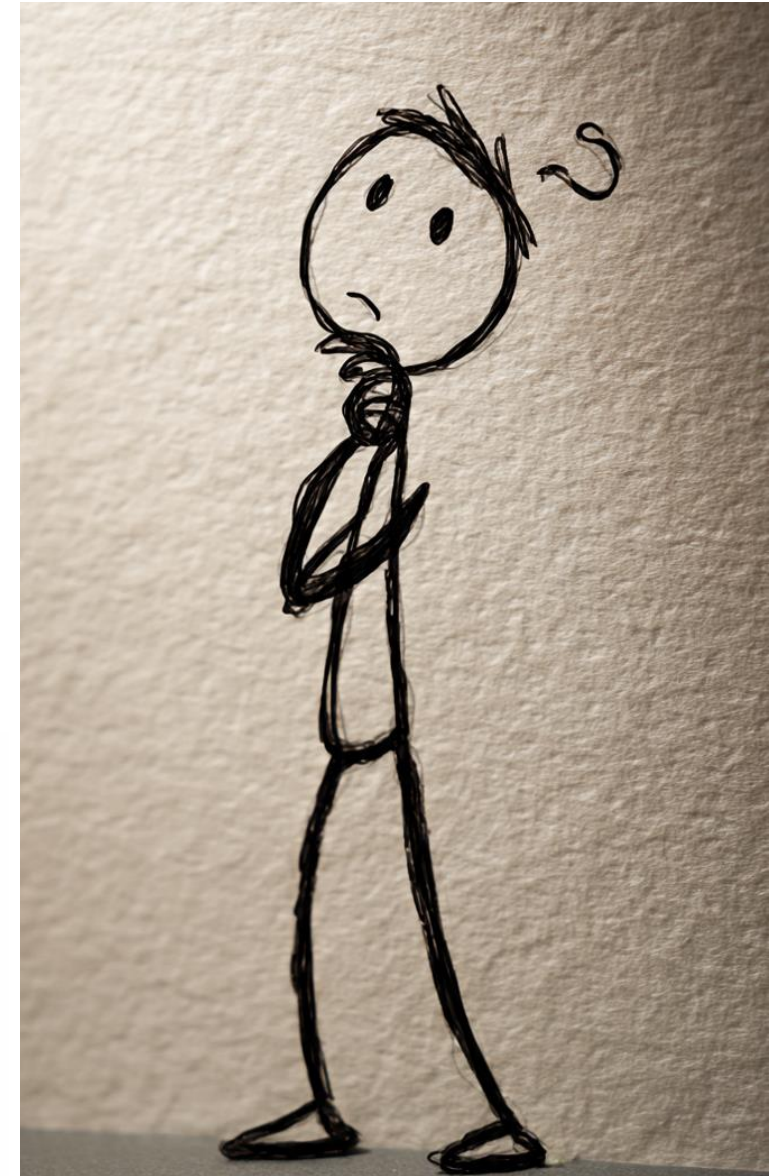
Questions?



Images generated using Microsoft Copilot 2026.



Image generated using Meta AI 2026.



References (1)

1. Kim, J., Bajaj, H. S., Ramji, A., Bemeur, C., & Sebastiani, G. (2025). Diabetes and Metabolic Dysfunction–associated Steatotic Liver Disease in Adults: A Clinical Practice Guideline. *Canadian Journal of Diabetes*, 49(4), 222-236.
2. Pedersen SD, Majoo P, Dash S, Jain A, Pearce N, Poddar M. Canadian Adult Obesity Clinical Practice Guideline: Pharmacotherapy for Obesity Management in Adults. Available from: obesitycanada.ca/healthcareprofessionals/adult-clinical-practice-guideline. Retrieved from Jan 30, 2026.
3. Cusi, K., Abdelmalek, M. F., Apovian, C. M., Balapattabi, K., Bannuru, R. R., Barb, D., ... & Bajaj, M. (2025). Metabolic Dysfunction–Associated Steatotic Liver Disease (MASLD) in People With Diabetes: The Need for Screening and Early Intervention. A Consensus Report of the American Diabetes Association. *Diabetes Care*, 48(7), 1057-1082.
4. European Association for the Study of the Liver, & European Association for the Study of Diabetes (EASD. (2024). EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). *Obesity Facts*, 17(4), 374-444.
5. Chopra, S., & Lai, M. Management of metabolic dysfunction-associated steatotic liver disease (nonalcoholic fatty liver disease) in adults. UptoDate. Retrieved from Jan 30, 2026.



References (2)

6. Bae, J. C. (2024). No more NAFLD: the term is now MASLD. *Endocrinology and Metabolism*, 39(1), 92-94.
7. Romano, J., Burnside, J., Sebastiani, G., Ramji, A., Patel, K., Swain, M., & Saeed, S. (2025). Examining the prevalence of hepatic steatosis and advanced fibrosis using non-invasive measures across Canada: A national estimate using the Canadian Health Measures Survey (CHMS) from 2009-2019. *Annals of Hepatology*, 30(1), 101757.
8. Swain, M. et al. (2020). Burden of nonalcoholic fatty liver disease in Canada, 2019–2030: a modelling study. *Canadian Medical Association Open Access Journal*, 8(2), E429-E436.
9. Cusi K. Role of obesity and lipotoxicity in the development of nonalcoholic steatohepatitis: Pathophysiology and clinical implications. *Gastroenterology* 2012;142:711e725.e6.
10. Igoe, J., Belkaid, A., Dery, V., Rasul, M., Canales, D.D., Cartier, J-L. (2026) Prevalence of Metabolic Dysfunction-Associated Steatotic Liver Disease in patients with diabetes at a Regional Hospital in New Brunswick. Unpublished manuscript.
11. Allen, A. M., Charlton, M., Cusi, K., Harrison, S. A., Kowdley, K. V., Nouredin, M., & Shubbrook, J. H. (2024). Guideline-based management of metabolic dysfunction-associated steatotic liver disease in the primary care setting. *Postgraduate medicine*, 136(3), 229-245.
12. Golabi, P., Isakov, V., & Younossi, Z. M. (2023). Nonalcoholic fatty liver disease: disease burden and disease awareness. *Clinics in liver disease*, 27(2), 173-186.

References (3)

13. Blais, P., Husain, N., Kramer, J. R., Kowalkowski, M., El-Serag, H., & Kanwal, F. (2015). Nonalcoholic fatty liver disease is underrecognized in the primary care setting. *Official journal of the American College of Gastroenterology ACG*, 110(1), 10-14.
14. Forlano, R., Sigon, G., Mullish, B. H., Yee, M., & Manousou, P. (2023). Screening for NAFLD—current knowledge and challenges. *Metabolites*, 13(4), 536.
15. Sebastiani, G., Ramji, A., Swain, M. G., & Patel, K. (2021). A Canadian survey on knowledge of non-alcoholic fatty liver disease among physicians. *Canadian Liver Journal*, 4(2), 82-92.
16. Cusi K, Isaacs S, Barb D, Basu R, Caprio S, Gavey WT, Kashysp et al. (2025). American Association of Clinical Endocrinology Clinical Practice Guideline for the Diagnosis and Management of Nonalcoholic Fatty Liver Disease in Primary Care and Endocrinology Clinical Settings. *Endocrine Practice*, 28, 528-562
17. Rinella, M. E. et al. (2023). AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. *Hepatology*, 77(5), 1797-1835.
18. Hannah, W. N., & Harrison, S. A. (2016). Effect of weight loss, diet, exercise, and bariatric surgery on nonalcoholic fatty liver disease. *Clinics in liver disease*, 20(2), 339-350.
19. Njei, B., Ameyaw, P., Al-Ajlouni, Y., Njei, L. P., & Boateng, S. (2024). Diagnosis and management of lean metabolic dysfunction-associated steatotic liver disease (MASLD): a systematic review. *Cureus*, 16(10).

References (4)

20. Wong, V (2024). Overview of Lean MASH and MASLD. *Gastroenterology & Hepatology*, 20(12), 745-7.
21. Fan, et al. (2024). Guideline for the prevention and treatment of metabolic dysfunction-associated fatty liver disease (version 2024). *Journal of Clinical and Translational Hepatology*, 12(11), 955.
22. Zeng XF et al. The role of dietary modification in the prevention and management of metabolic dysfunction-associated fatty liver disease: An international multidisciplinary expert consensus. *Metabolism*. 2024 Dec;161:156028
23. Michalopoulou, E., et al. (2025). The triad of risk: linking MASLD, cardiovascular disease and type 2 diabetes; from pathophysiology to treatment. *Journal of Clinical Medicine*, 14(2), 428.
24. Bajaj, M. et al. (2026). 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes—2026. *Diabetes Care*.
25. Sanyal, A. J et al. (2010). Pioglitazone, vitamin E, or placebo for nonalcoholic steatohepatitis. *New England Journal of Medicine*, 362(18), 1675-1685.
26. Sanyal, A. J. et al. (2025). Phase 3 trial of semaglutide in metabolic dysfunction-associated steatohepatitis. *New England Journal of Medicine*, 392(21), 2089-2099.
27. Loomba, R. et al. (2024). Tirzepatide for metabolic dysfunction–associated steatohepatitis with liver fibrosis. *New England Journal of Medicine*, 391(4), 299-310.
28. Sanyal, A. J. et al. (2024). A phase 2 randomized trial of survodutide in MASH and fibrosis. *New England Journal of Medicine*, 391(4), 311-319.
29. Harrison, S. A. et al. (2024). A phase 3, randomized, controlled trial of resmetirom in NASH with liver fibrosis. *New England Journal of Medicine*, 390, 497-509.