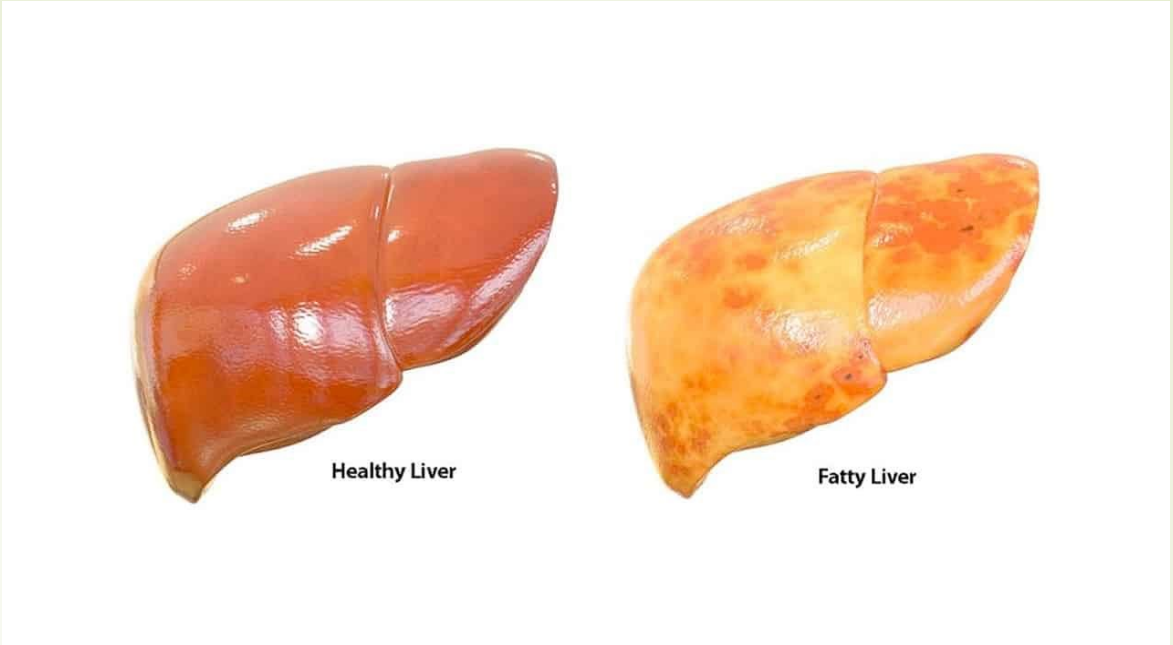

https://liverfoundation.org/liver-diseases/fatty-liver-disease/nonalcoholic-steatohepatitis-nash/mash-definition-prevalence/

Steatotic Liver Disease

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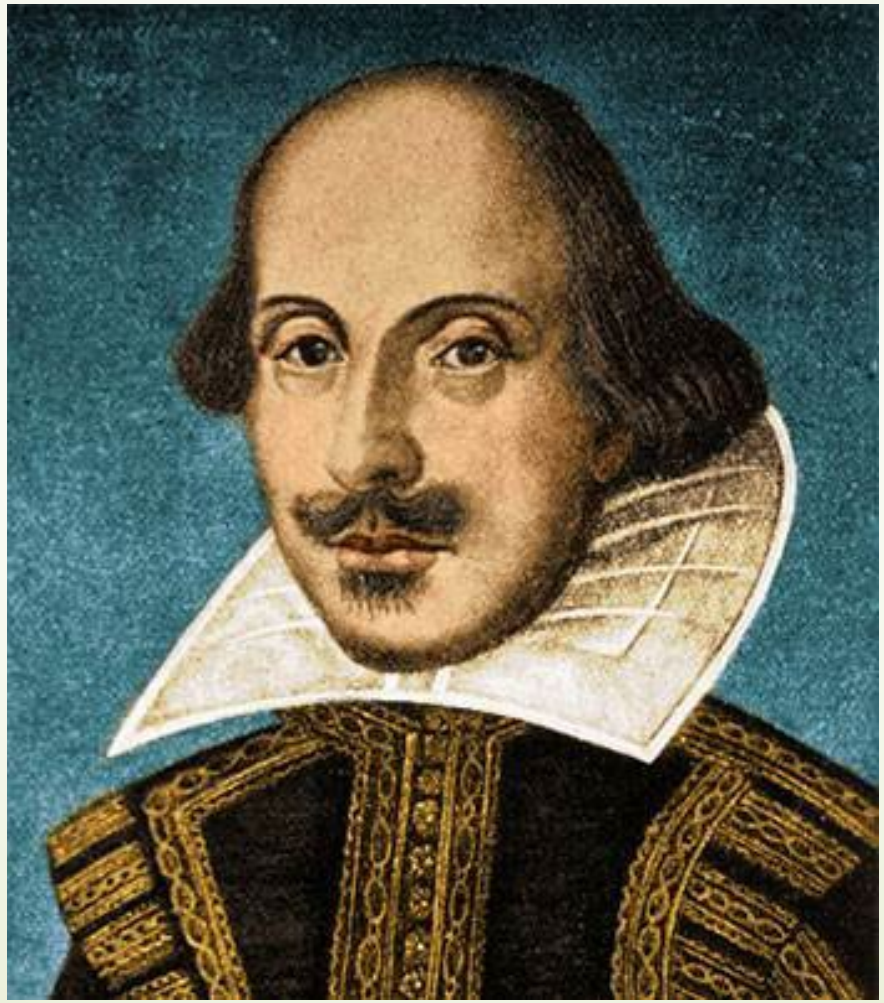
We have no conflicts of interest or financial disclosures to disclose.

OBJECTIVES

- Review new nomenclature for hepatic steatosis/ steatotic disease states
- Discuss Prevalence and Pathophysiology of steatotic liver disease
- Explore how to identify patients at risk for advanced disease and when it is appropriate to refer to hepatology
- Discuss pharmacological and non-pharmacological management of hepatic steatosis/ MASH

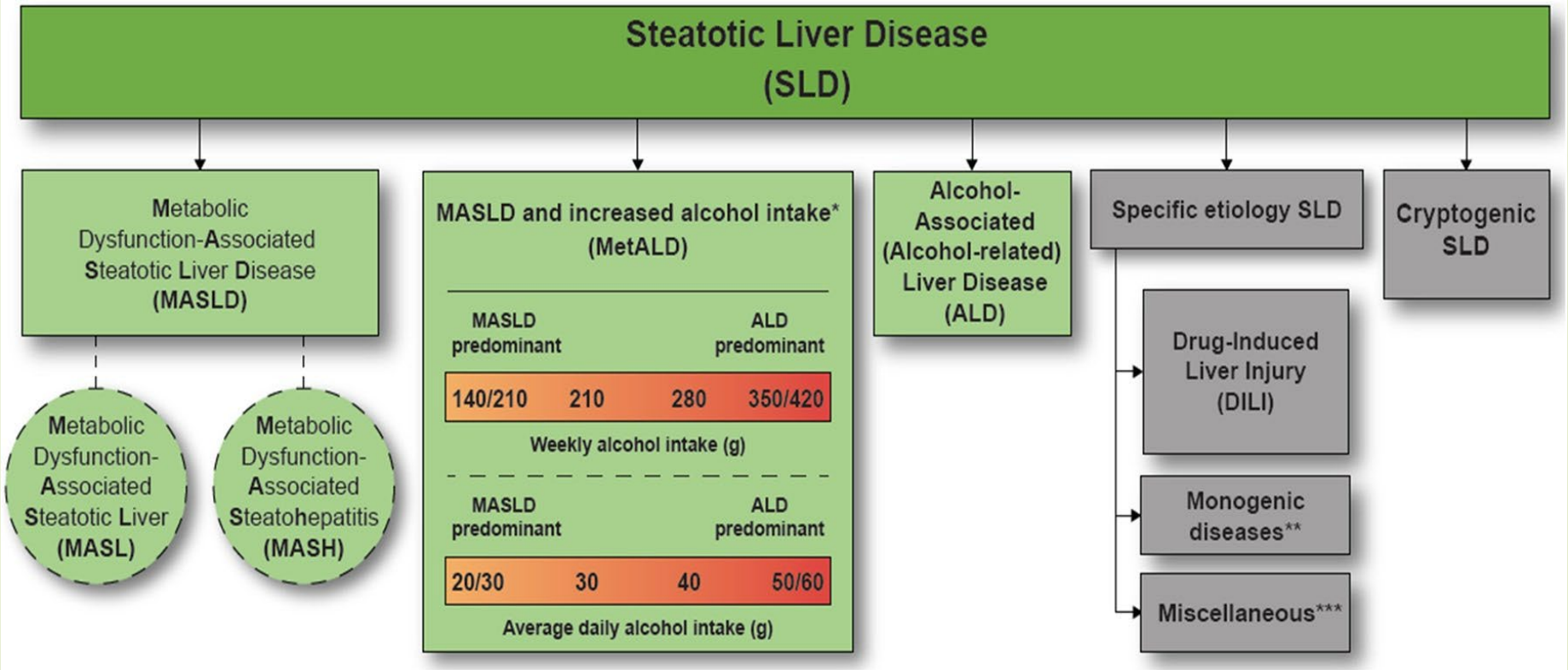
MASLD vs Fatty Liver Disease: What's in a Name?



How Comfortable Do You Feel You Understand The New Terminology?

Steatotic Liver Disease

- Overarching term for conditions related to hepatic steatosis



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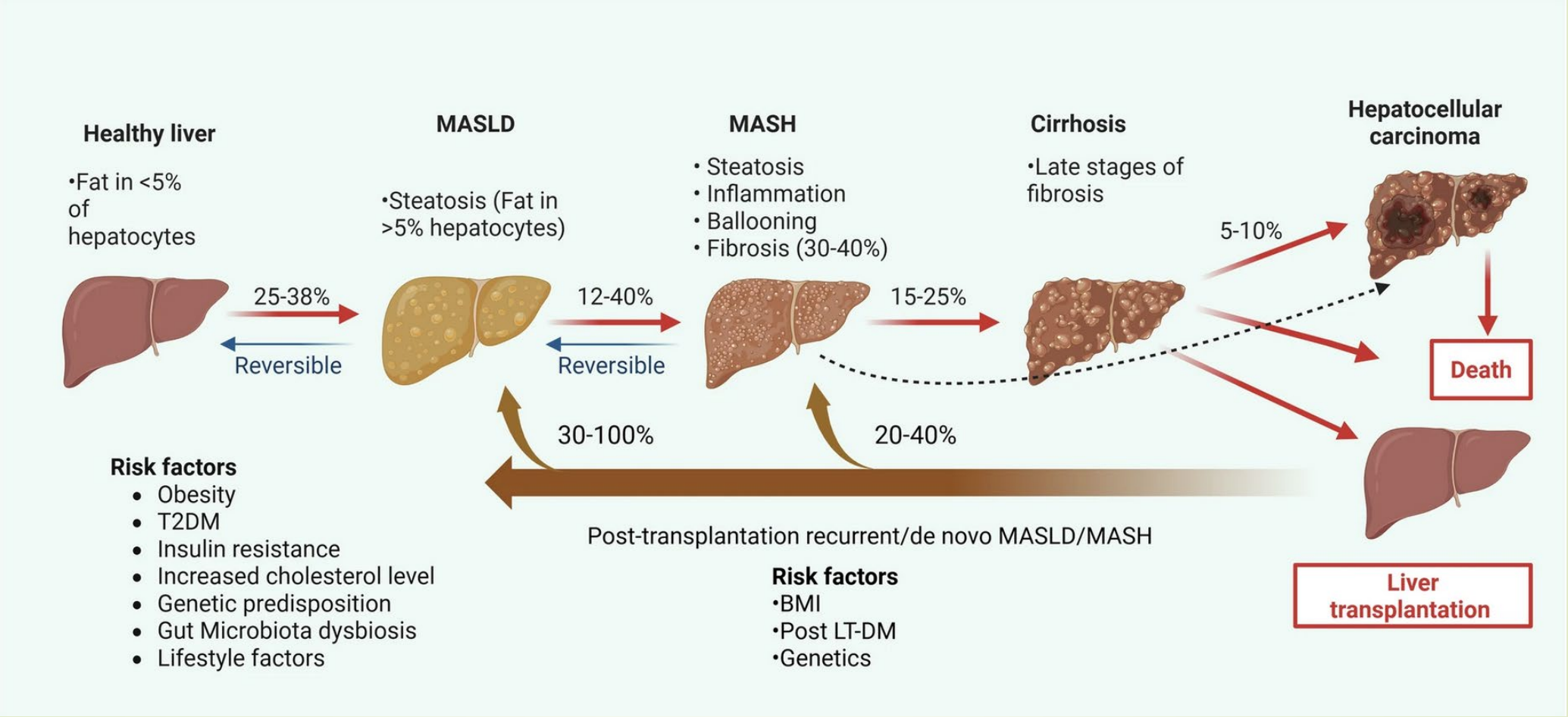
Prevalance of Steatotic Liver Disease

- AASLD 2023 guidelines estimated prevalence of NAFLD in general population as 25-30%
- Global Prevalence from recent Metanalysis released Dec 2025
  - SLD: 37.5%
  - MASLD: 33.6%
  - Met-ALD 4.1%
  - Notably higher in DM II and elevated BMI/ obesity
- Prevalence of MASLD in US projected to increase from 33.7% in 2020 to 41.4% by 2050
  - Would result in more than tripling decompensated cirrhosis, doubling liver cancer, and quadrupling liver transplant

Pathophysiology



Tantu, M.T., Farhana, F.Z., Haque, F. et al. Pathophysiology, noninvasive diagnostics and emerging personalized treatments for metabolic associated liver diseases. npj Gut Liver 2, 18 (2025). https://doi.org/10.1038/s44355-025-00030-2

MASLD

- Metabolic dysfunction- Associated Steatotic Liver Disease
- Effectively replaces NAFLD
- Presence of hepatic steatosis in conjunction with one cardiometabolic risk factor (CMRF) and no other discernible cause
- Excludes patients with consumption of > 20 g alcohol per day in women and >30 g per day in men

Cardiometabolic Risk Factors (CMRFs)

- Diabetes
- Hypertension
- Hyperlipidemia
- Obesity

Adult Criteria

At least 1 out of 5:

- ☐ BMI ≥ 25 kg/m² [23 Asia] **OR** WC > 94 cm (M) 80 cm (F) **OR** ethnicity adjusted equivalent
- ☐ Fasting serum glucose ≥ 5.6 mmol/L [100 mg/dL] **OR** 2-hour post-load glucose levels ≥ 7.8 mmol/L [≥140 mg/dL] **OR** HbA1c ≥ 5.7% [39 mmol/L] **OR** type 2 diabetes **OR** treatment for type 2 diabetes
- ☐ Blood pressure ≥ 130/85 mmHg **OR** specific antihypertensive drug treatment
- ☐ Plasma triglycerides ≥ 1.70 mmol/L [150 mg/dL] **OR** lipid lowering treatment
- ☐ Plasma HDL-cholesterol ≤ 1.0 mmol/L [40 mg/dL] (M) and ≤ 1.3 mmol/L [50 mg/dL] (F) **OR** lipid lowering treatment

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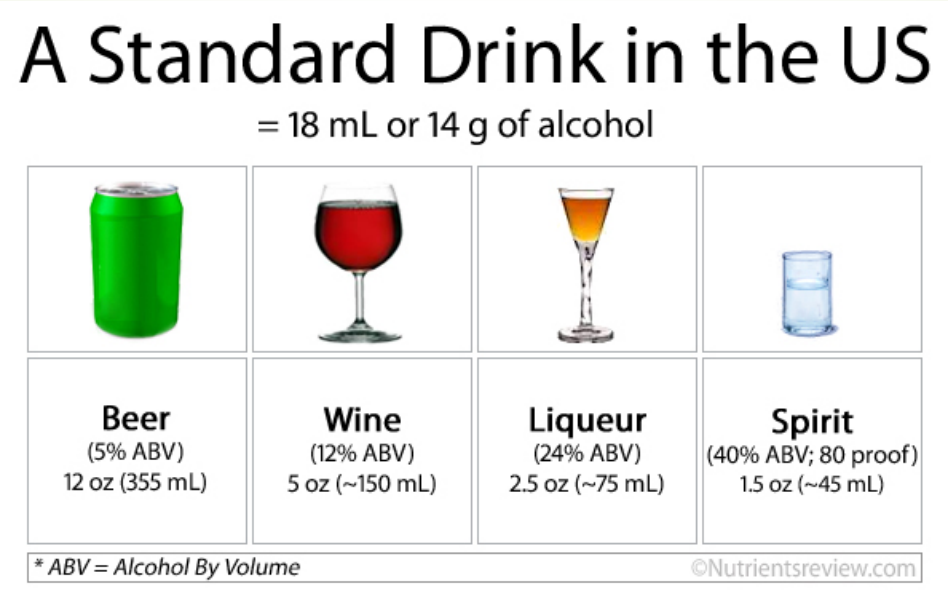
Met-ALD

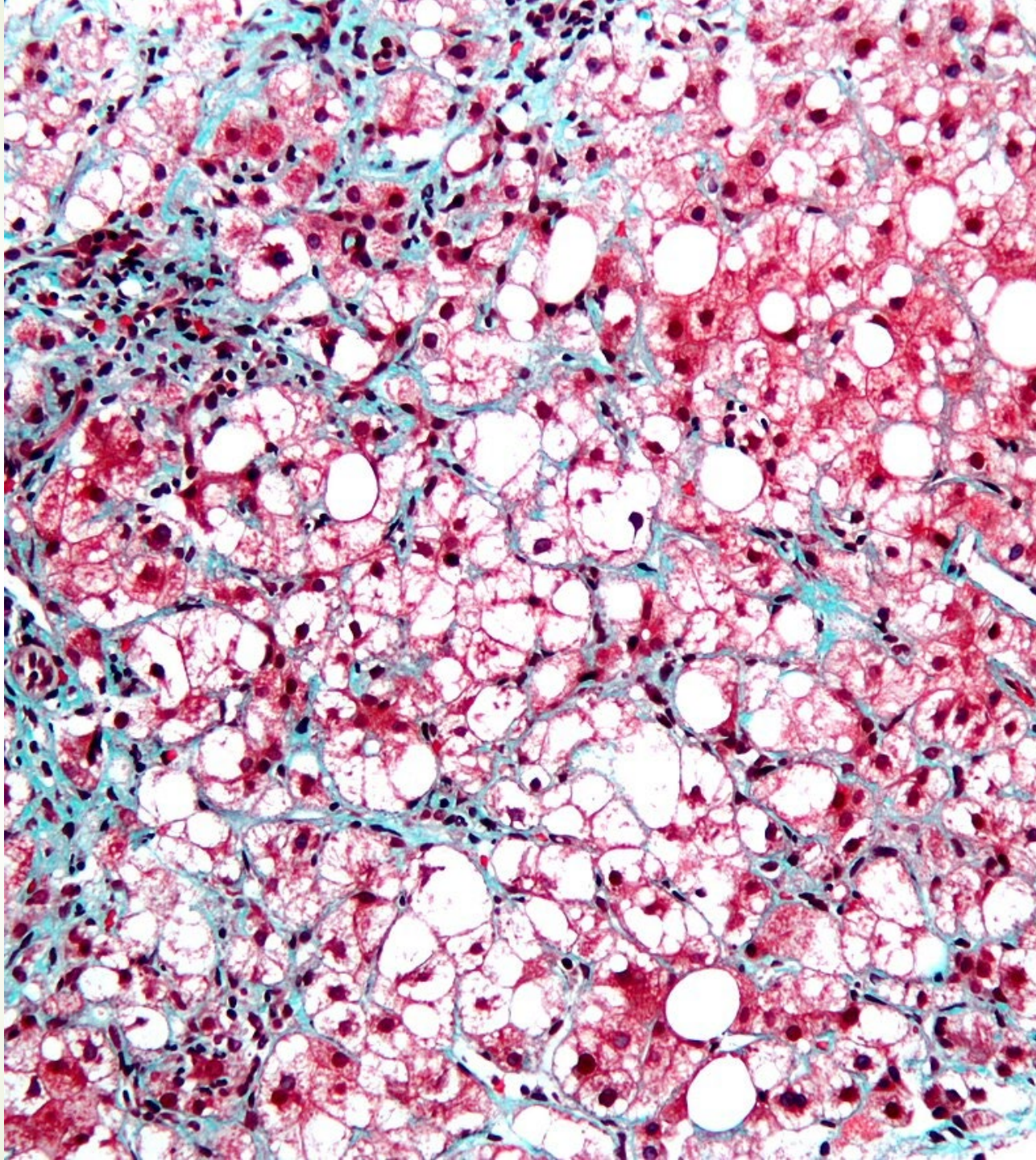
- Presence of hepatic steatosis, CMRF, and alcohol use
- Alcohol use classified as weekly intake of 140-350g in women and 210-420 g in men OR average of 20-50g daily in women and 30-50 g in men



- Works as continuum

MASH

- Metabolic Associated Steatohepatitis
- Presence of Steatohepatitis in persons with MASLD
- Can Consider Treatment with F2-F3 fibrosis



Specific Etiology SLD

- Absence of overt CMRFs
- Can include:
  - Drug-induced liver injury (DILI)
  - lysosomal acid lipase deficiency
  - Wilson's disease
  - hypobetalipoproteinemia, inborn errors of metabolism
  - HCV genotype 3 infection
  - Malnutrition
  - Celiac disease
  - HIV
  - Exposure to environmental agents associated with steatosis such as hydrocarbon inhalation

Medications to Consider

- Amiodarone
- 5-FU
- Irenotecan
- Tamoxifen
- Methotrexate
- Corticosteroids

Cryptogenic SLD

- No etiology is identified and no CMRFs are present
- Could also be considered MAFLD based on clinical judgement

How To Identify At Risk Patients

- Consideration of CMRFs and patient family history. Higher risk if having diabetes, family history of MASH cirrhosis
- Keep in mind that transaminases could still be higher than normal even if they appear to be in normal range.
- Do not necessarily need to refer to hepatology just because there is an ultrasound showing hepatic steatosis.

Serological Testing

- Helpful to rule out need for more non-invasive testing/ referral
- FIB-4
  - Calculated using ALT, AST, age, and platelet count
  - Low risk for fibrosis if <1.3
  - Not as accurate for age > 65. Still considered lower risk if < 2. Higher if greater than 2.67
  - Consider referral if >2.67
- ELF (Enhanced Liver Fibrosis Test)
  - Includes tissue inhibitor of matrix metalloproteinase-1 (TIMP-1), hyaluronic acid, and aminoterminal propeptide of type III procallagen (PIIINP)
  - Useful in predicting risk for progression of liver disease
  - Lower risk if <7.7. Intermediate up to 9.8
  - Low CD 4+ T-cell count and other factors such as cancer, bone fractures, or inflammation may affect accuracy

Ultrasound Elastography

- Vibration-controlled transient elastography (VCTE)
  - Include Fibroscan, I LivTouch, Liverscan
  - Can calculate CAP score to help identify degree of steatosis
- Two dimensional shear wave elastography (2D-SWE)
- Point-shear wave elastography (p-SWE)
- Patient factors can affect results such as high ALT (hepatic necroinflammation), hepatic congestion and extrahepatic cholestasis, ascites, or excessive alcohol intake
- BMI/ obesity can also cause inaccurate results
- Can consider treatment for MASH if shows F2-F3 fibrosis

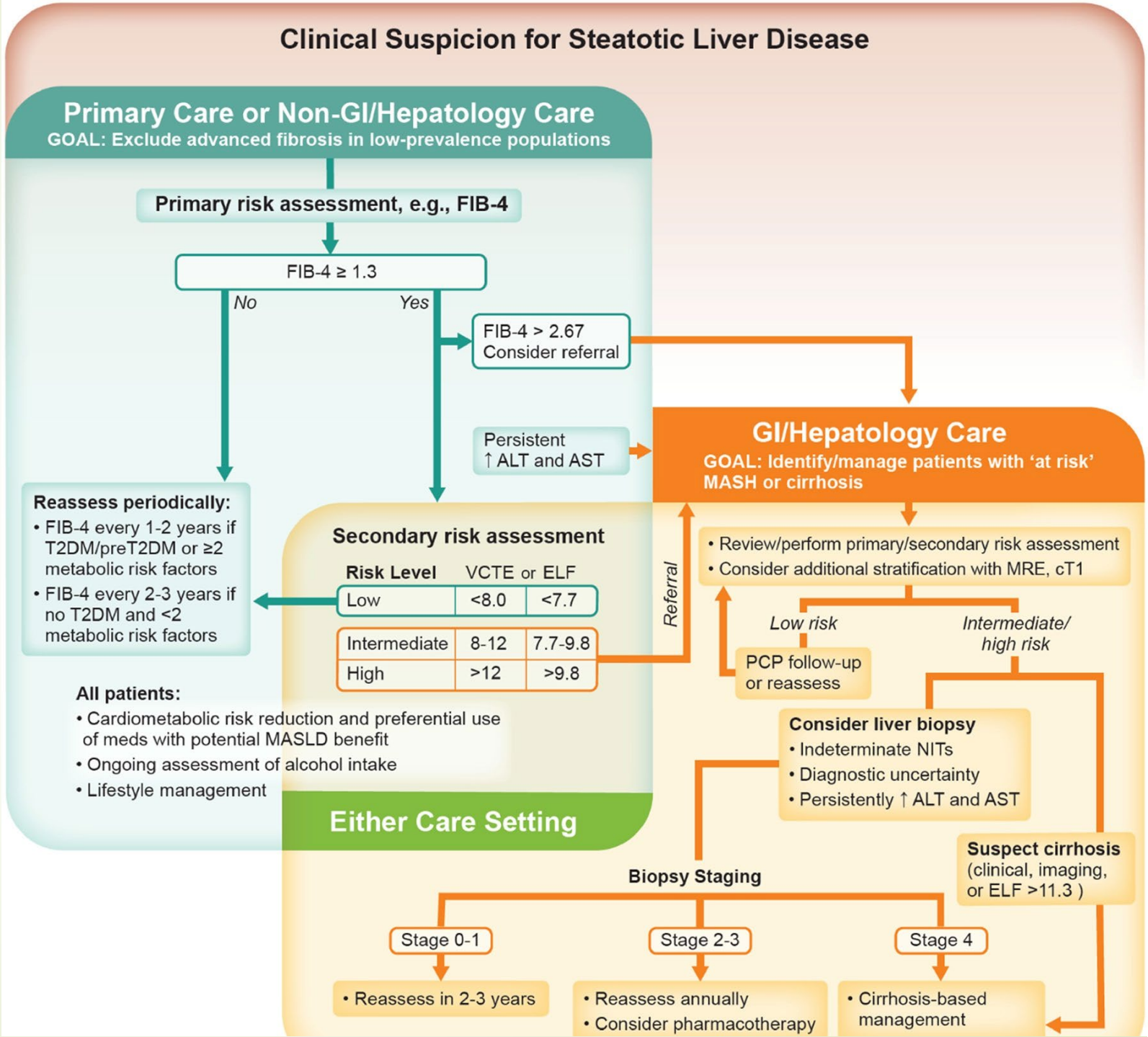
MRE

- Magnetic resonance elastography
- Whole liver is examined using mechanical wave propagation
- Most accurate NIT for liver fibrosis
- Drawbacks include cost, availability, and weight limit
- The only available MR elastography in our area is Sentara Norfolk General

Risk Evaluation

- Start with Fib 4
- Consider secondary assessment with ELF
- Assess risk factors

Kanwal, Fasiha[1,2,3]; Neuschwander-Tetri, Brent A.[4]; Loomba, Rohit[5]; Rinella, Mary E.[6]. Metabolic dysfunction–associated steatotic liver disease: Update and impact of new nomenclature on the American Association for the Study of Liver Diseases practice guidance on nonalcoholic fatty liver disease. Hepatology 79(5):p 1212-1219, May 2024. | DOI: 10.1097/HEP.0000000000000670



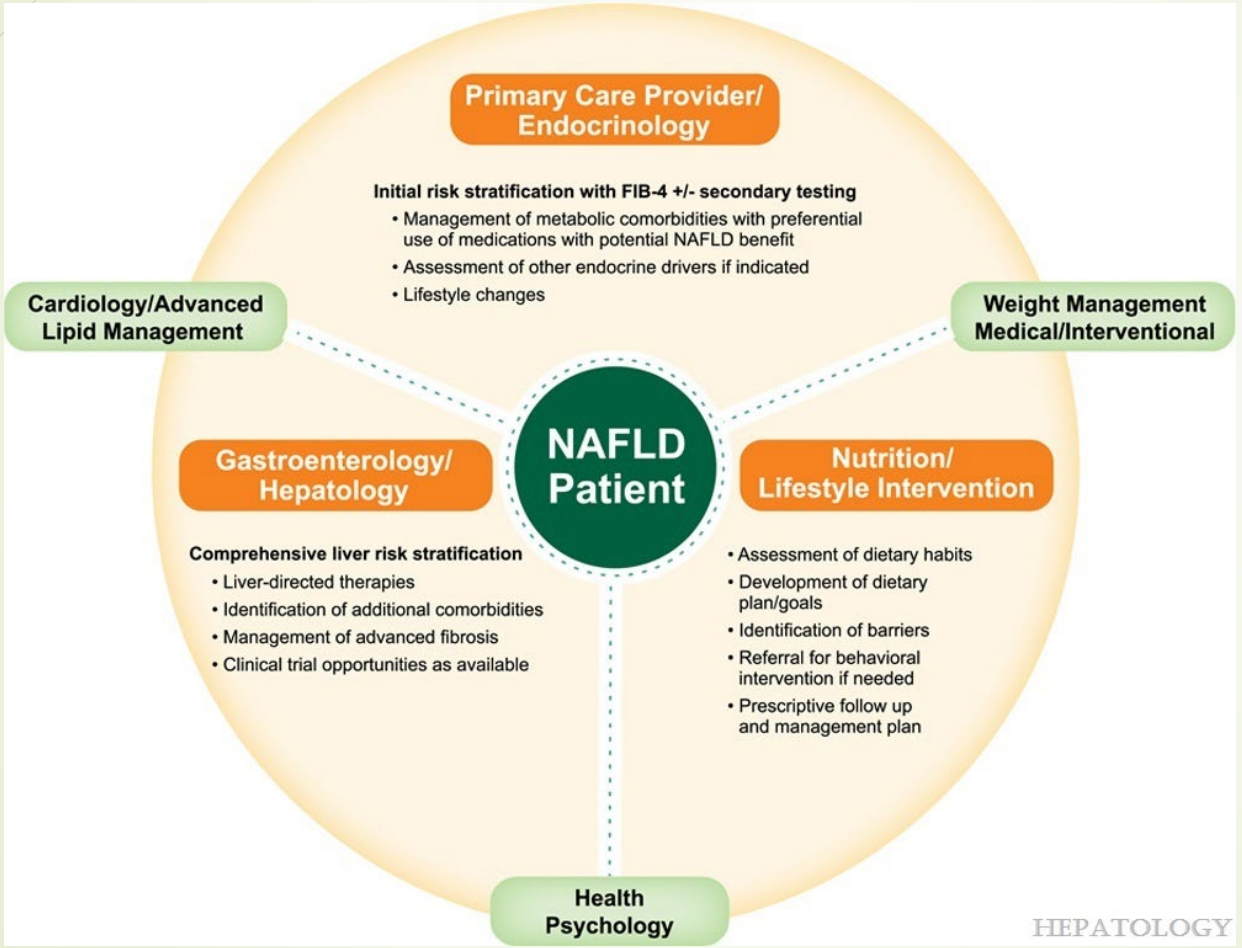
Now we have identified patients with MASL/ MASH…

How do we treat them?

Education

- It is important to have a detailed discussion about MASL/ MASH with our patients so that they know why it is important to take it seriously.
- MASL can lead to MASH which can lead to cirrhosis
- The mainstay of treatment is sustainable lifestyle change and optimization of other metabolic syndrome components.
- Adding any type of pharmacological strategy is used as an adjunct to lifestyle modifications, not instead of.

Multidisciplinary approach



AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease Hepatology77(5):1797-1835, May 2023.

Lifestyle modifications

- Optimization of metabolic comorbidities outside of weight (DM, HTN, HLD)
  - Statins can be used
- Weight loss: 3%-5% improves steatosis, >10% improves MASH and fibrosis.
  - Goal is to reach a calorie deficit
  - Low carb, moderate protein diet and mediterranean diets are particularly beneficial.
  - Individualize plan and consider cultural aspect of diet for greater sustainability.
  - Do not drink calories
  - Limit/ eliminate fructose
  - Coffee helps reduce risk of advanced fibrosis
  - Alcohol avoidance

Lifestyle continued

- Exercise
  - Regular exercise recommended for 30 minutes/ 5 days per week (150 minutes/ wk)
- Bariatric surgery

Lean MASH

- MASH in the setting of a BMI <25 or <23 in Asian individuals.
- Histological findings are typically milder than MASH involving obesity
- Though to be a genetic component to lean MASH

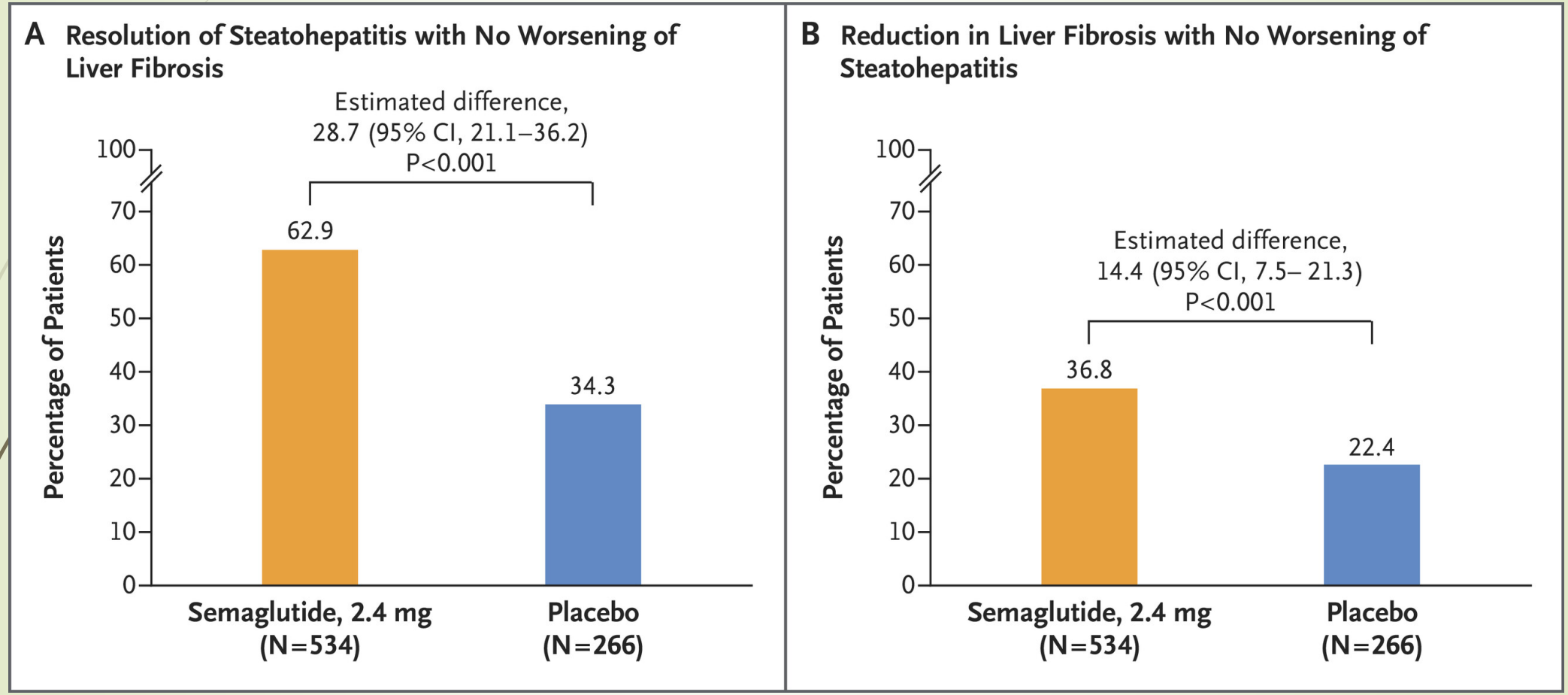
Pharmacological management

- Vitamin E
- Pioglitazone 30-45mg PO daily: can be considered in patients with MASH and T2DM
  - Risks: weight gain, heart failure exacerbation
- Milk thistle
  - Data remains inconclusive in terms of fibrosis improvement and thus is not recommended for the treatment of MASH.

Pharmacological management-GLP1 receptor agonists

- Liraglutide
  - Saxenda: approved for obesity management
  - Victoza: approved for T2DM
- Semaglutide
  - Ozempic: approved for T2DM. Using for weight management is considered "off label"
  - Wegovy: approved for weight management and in 8/2025 approved for MASH
- Tirzepitide
  - Mounjaro: approved for T2DM
  - Zepbound: approved for chronic weight management

ESSENCE trial data



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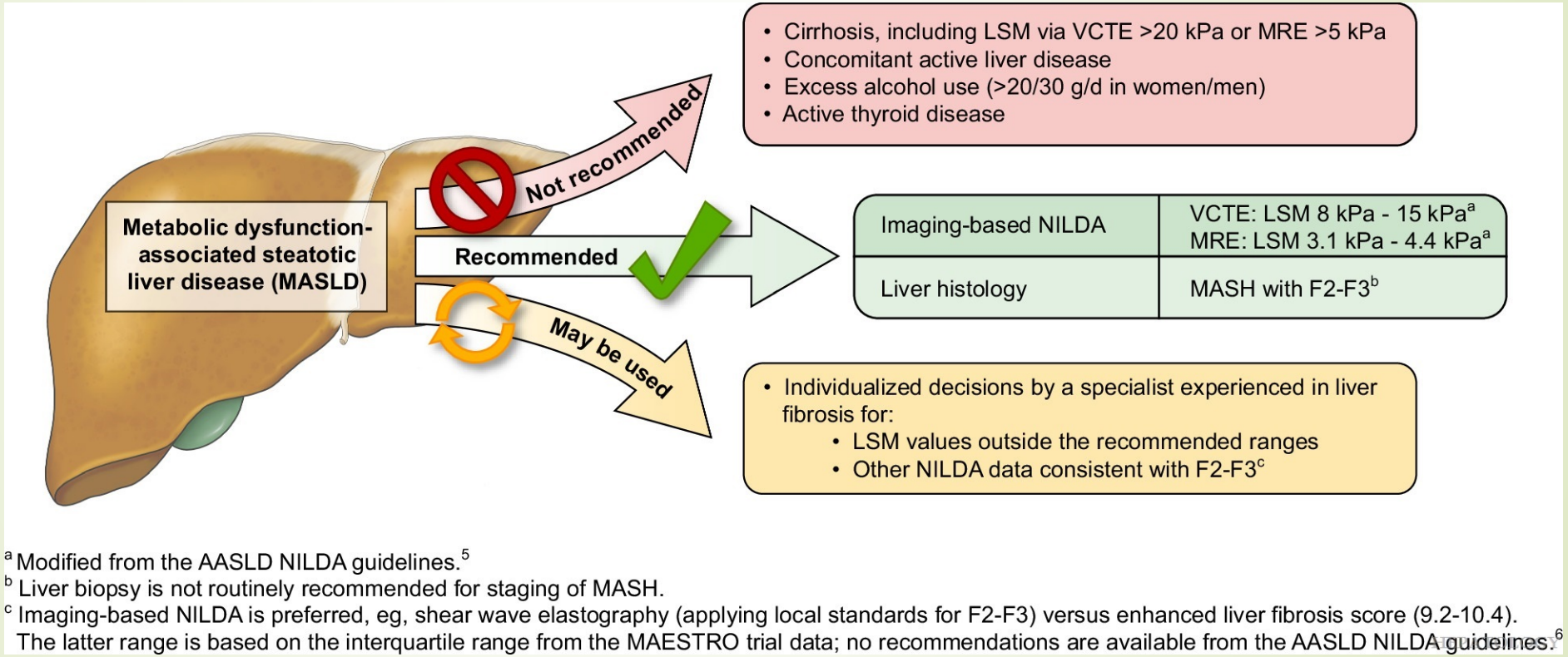
Resmetirom (Rezdiffra)

- Received accelerated approval from the FDA in 3/2024 for treatment of MASH with F2-F3 fibrosis.
- Approval based on results of MAESTRO-NASH trial
- MOA: Stimulates thyroid hormone receptor beta in the liver which improves lipid metabolism.
- Who to Treat: patients with MASH with F2-F3 fibrosis without other identified sources for liver disease including excess alcohol use (20g/day for women, 30g/day for men)
- Dosing: 100mg PO daily if > 100kg. 80mg PO daily if < 100kg.
  - Metabolized through CP450 2C8-need to dose reduce if on Plavix to 80mg if >100kg and 60mg if <100kg.

Resmetirom continued



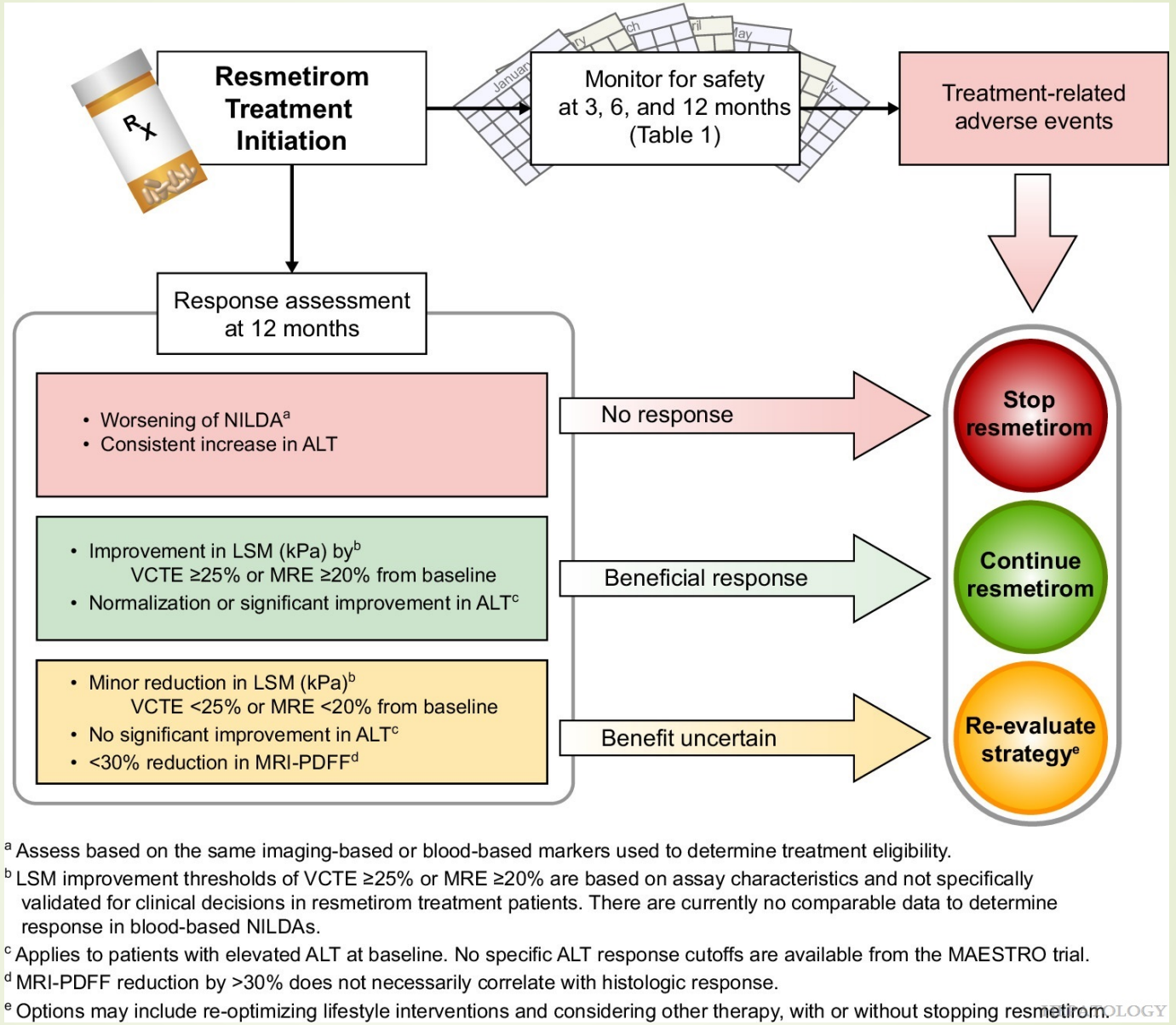
[a] Modified from the AASLD NILDA guidelines.[5]
[b] Liver biopsy is not routinely recommended for staging of MASH.
[c] Imaging-based NILDA is preferred, eg, shear wave elastography (applying local standards for F2-F3) versus enhanced liver fibrosis score (9.2-10.4). The latter range is based on the interquartile range from the MAESTRO trial data; no recommendations are available from the AASLD NILDA guidelines.[6]

Chen, Vincent L.1; Morgan, Timothy R.2,3; Rotman, Yaron4; Patton, Heather M.5,6; Cusi, Kenneth7; Kanwal, Fasiha8,9,10; Kim, W. Ray11. Resmetirom therapy for metabolic dysfunction-associated steatotic liver disease: October 2024 updates to AASLD Practice Guidance. Hepatology 81(1):p 312-320, January 2025. | DOI: 10.1097/HEP.0000000000001112

Resmetirom continued

- Monitoring:
  - Prior to treatment, 6, and 12 months: hepatic function panel, thyroid function, lipid panel
  - 3 mo: hepatic function panel
  - 12 months repeat non-invasive fibrosis testing

- Adverse effects:
  - Most common-diarrhea and nausea. Typically lasts < 4 weeks.
  - Increased risk for gallstone disease, although history of gallstones are not a contraindication to use.
  - Can increase risk for statin toxicity.
    - Max dose: rosuvastatin and simvastatin= 20mg/ day
    - Max dose: atorvastatin and pravastatin= 40mg/ day



[a] Assess based on the same imaging-based or blood-based markers used to determine treatment eligibility.

[b] LSM improvement thresholds of VCTE ≥25% or MRE ≥20% are based on assay characteristics and not specifically validated for clinical decisions in resmetirom treatment patients. There are currently no comparable data to determine response in blood-based NILDAs.

[c] Applies to patients with elevated ALT at baseline. No specific ALT response cutoffs are available from the MAESTRO trial.

[d] MRI-PDFF reduction by >30% does not necessarily correlate with histologic response.

[e] Options may include re-optimizing lifestyle interventions and considering other therapy, with or without stopping resmetirom.

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Patient Scenario Idea 1

- 65 year old female
- PMH: HLD, HTN, CVA, hypothyroidism, IBS-C
- Medications: hydrochlorothiazide, Plavix, atorvastatin 80 mg, Synthroid (thyroid levels controlled), Linzess 72 mcg (controls constipation)
- BMI 29, weight is below 100 kg (in 80 mg dosing range)
- Alcohol intake: about 2 beers or glasses of wine a month
- Fibroscan: CAP 268, e kPa 8.5 (S2 hepatic steatosis and F2 fibrosis)

Patient Scenario Idea 2

- 45 year old male
- PMH: DM II, HLD
- Medications: Metformin 500 mg daily, rosuvastatin 5 mg daily
- HgA1C 5.2 while on Metformin
- BMI: 32 (weight greater than 100 kg)
- Alcohol Intake: About a 12 pack of 16 oz beers on weekends and 1-2 mixed drinks
- No history of pancreatitis or gallbladder disease. No GI complaints. Interested in medications to help with weight loss.
- Fibroscan: CAP 301, e kPa 10.1 (S3 hepatic steatosis, F2-F3 fibrosis)

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Questions ?