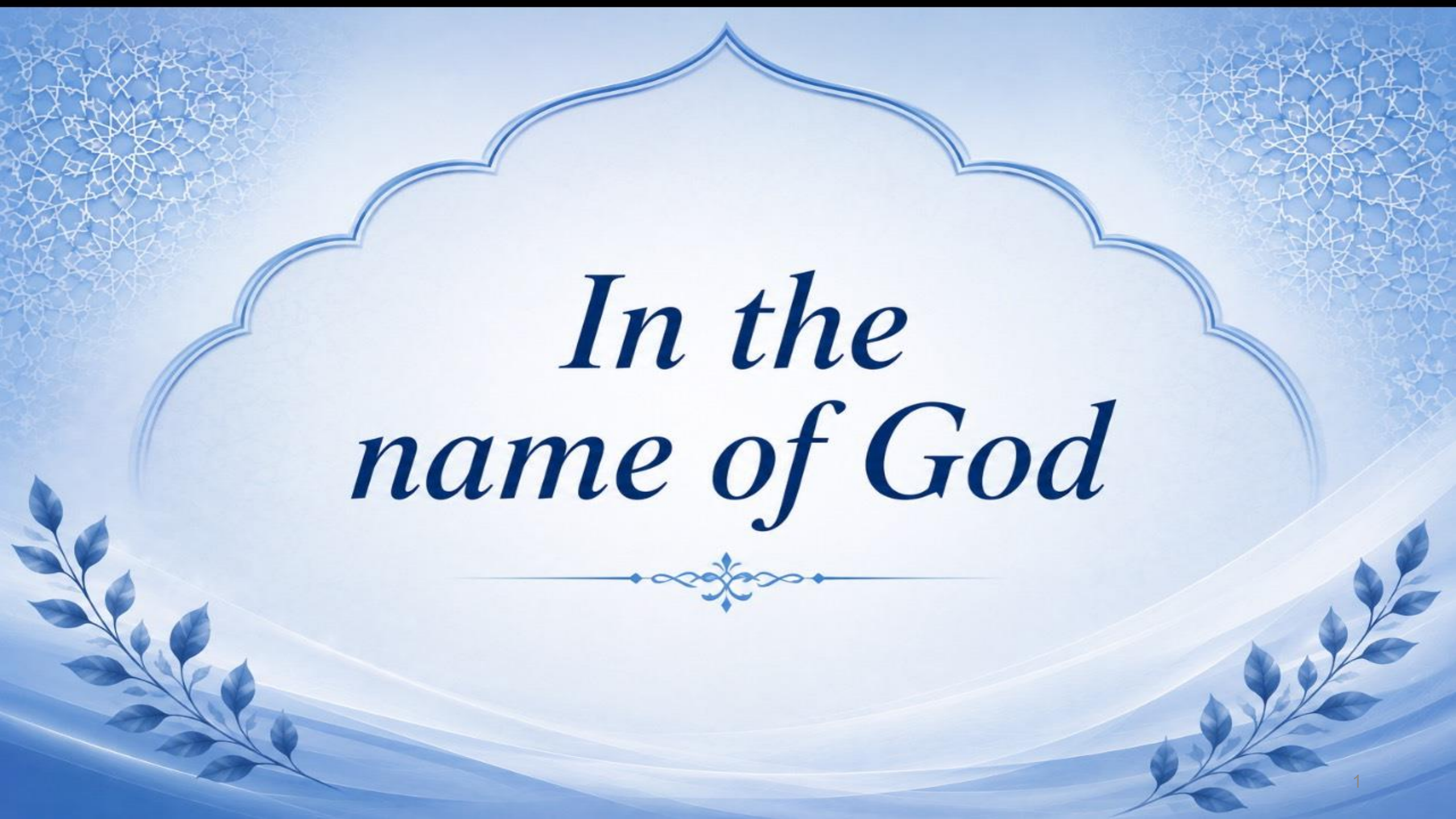




*In the
name of God*



Metabolic Dysfunction Associated Steatotic Liver Disease (MASLD)

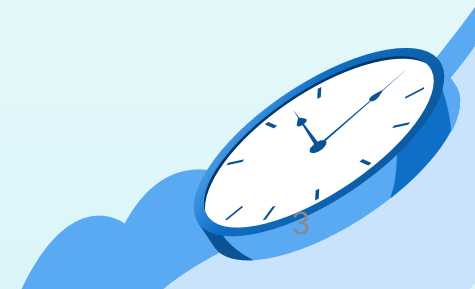
F.Imanzadeh

Professor of Pediatric
Gastroenterology and Hepatology

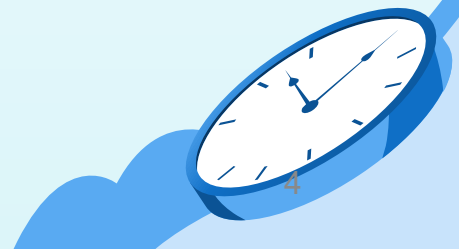


Why MASLD Matters?

- Most common chronic liver disease in children
- Closely linked to childhood obesity
- Progressive disease
- Leading cause of liver fibrosis
- Associated with cardiovascular disease
- Associated with Type 2 diabetes
- Increased mortality

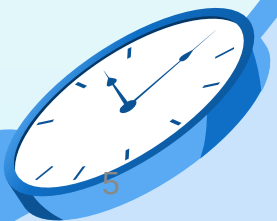


- New Nomenclature (2023)
- Old → New
- **NAFLD**(Non-alcoholic Fatty Liver Disease) → **MASLD**(Metabolic dysfunction-associated steatotic liver disease)
- **NASH**(Non-alcoholic Steatohepatitis) → **MASH**(Metabolic dysfunction-associated steatohepatitis)



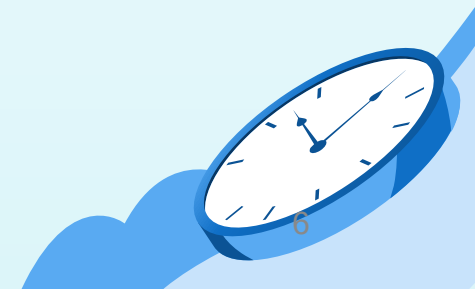
Definition of MASLD

- **Evidence of hepatic steatosis:** steatotic (fatty) liver as determined by imaging or biopsy (>5 percent hepatic steatosis)
- **At least one metabolic risk factor**



Risk Factors

1. Obesity
2. Overweight
3. Prediabetes
4. Diabetes
5. Dyslipidemia
6. Hypertension
7. Insulin resistance
8. Type 2 Diabetes
9. OSA (Obstructive sleep Apnea)
10. PCOS
11. Family history
12. PNPLA3 mutation



MASLD Classification

MASLD



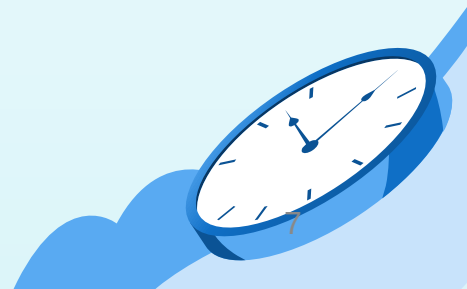
MASH



Fibrosis



Cirrhosis

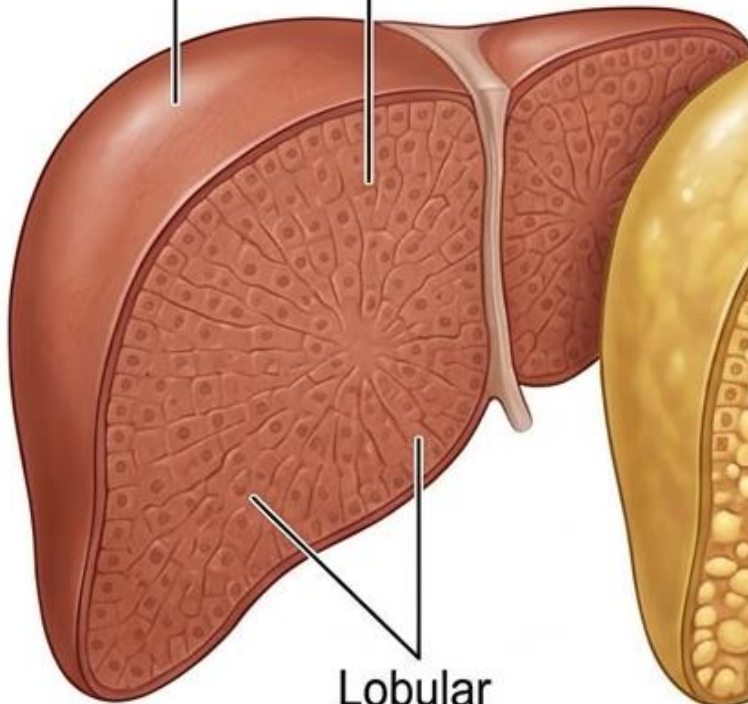


1. Healthy Liver

Smooth capsule

Normal parenchyma

Lobular structure



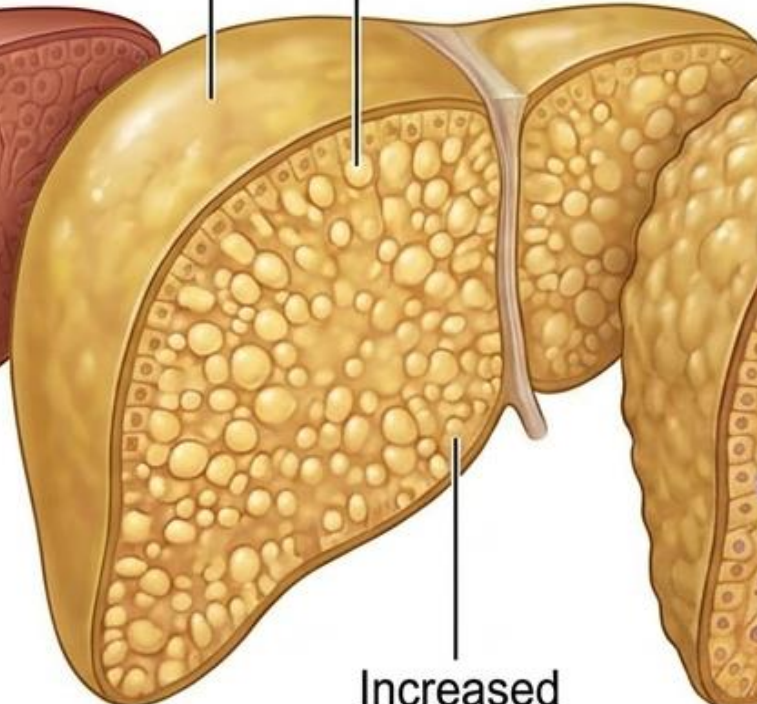
Lobular structure

2. Simple Steatosis

Yellow, greasy texture

Fat accumulation (steatosis)

Increased liver size



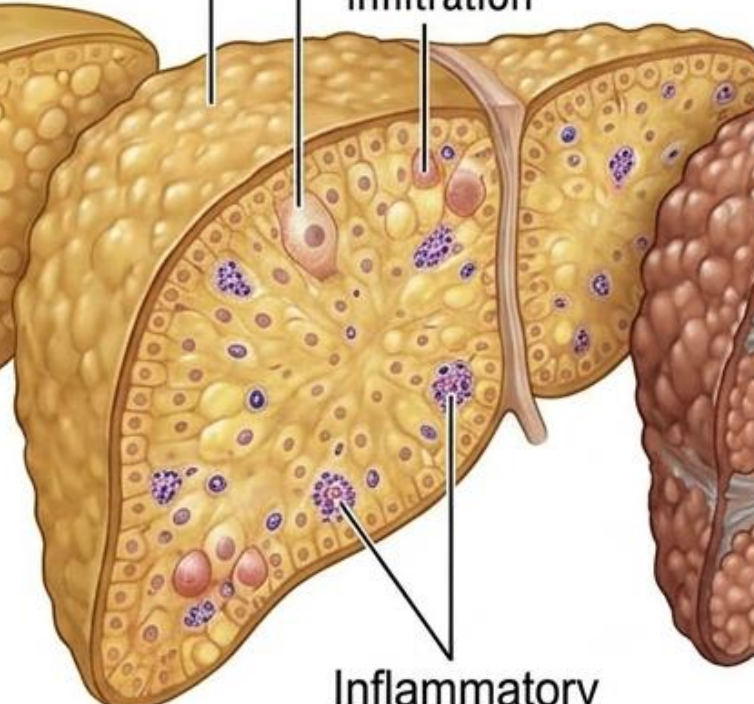
Increased liver size

3. MASH (Steatohepatitis)

Inflamed parenchyma

Hepatocyte injury/ballooning

Inflammatory cell infiltration



Inflammatory cell infiltration

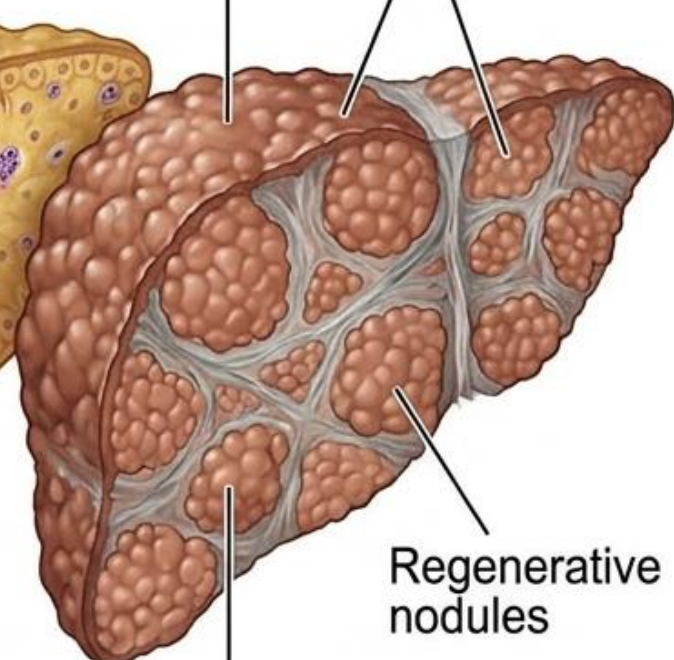
4. Fibrosis & Cirrhosis

Shrunken, nodular liver

Extensive fibrosis (scarring)

Regenerative nodules

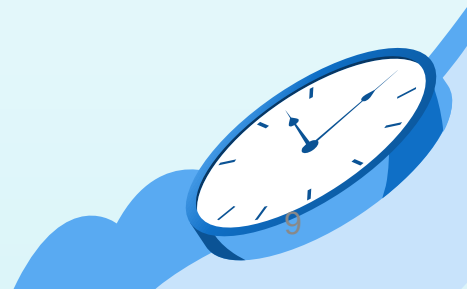
Disrupted architecture



Progression of Disease

Epidemiology

- General pediatric population
- 5–10%
- Obese children
- 30–40%
- Increasing worldwide
- Most common after age 10

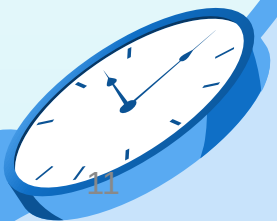




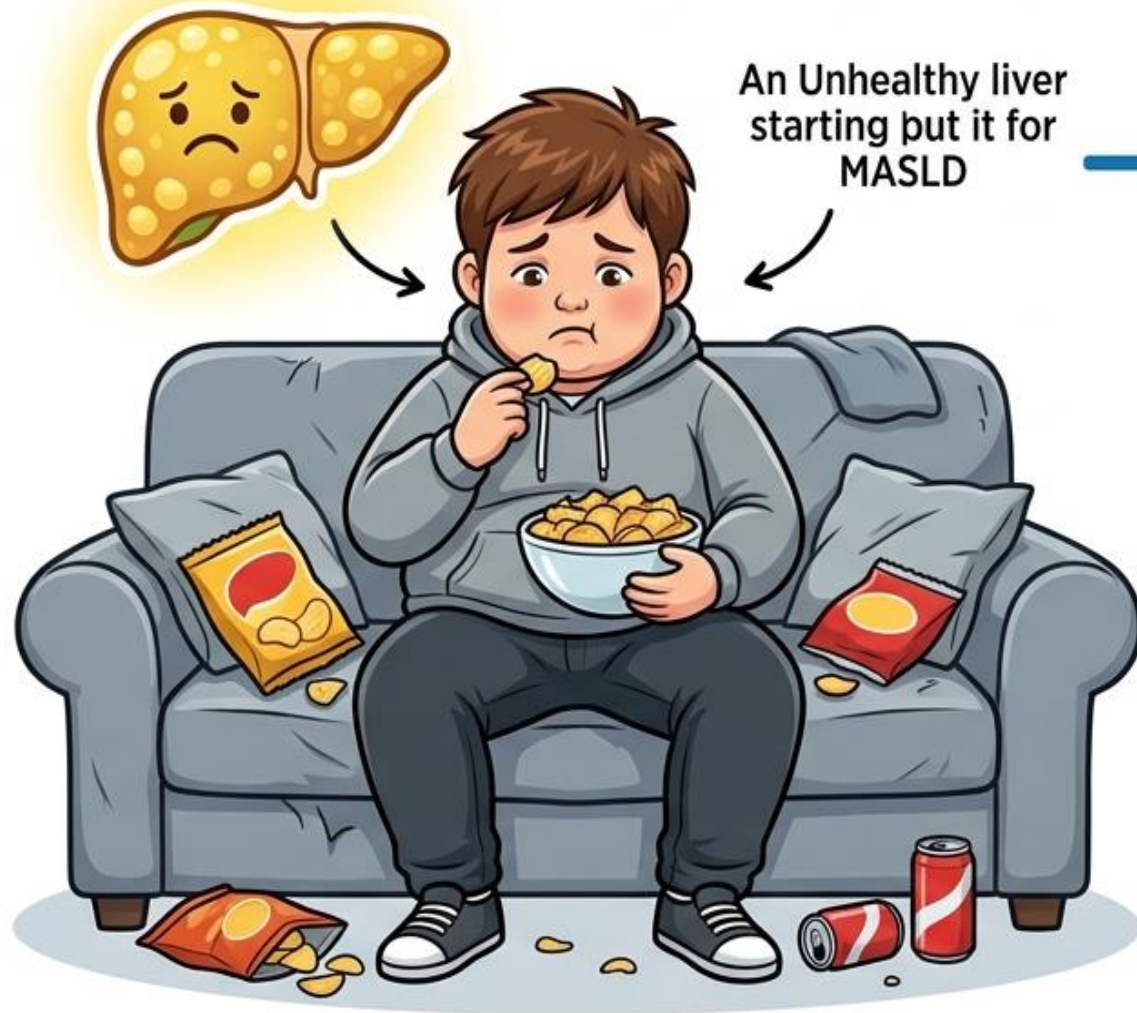
Clinical Presentation



- Usually asymptomatic
- Incidental elevated ALT
- Fatigue
- RUQ pain
- Acanthosis nigricans
- Hepatomegaly



UNHEALTHY START: MASLD RISK



An Unhealthy liver
starting put it for
MASLD

SAD, OVERWEIGHT CHILD:
Poor diet, lack of physical activity

HEALTHY TRANSITION: LIFESTYLE CHANGES



Healthy liver

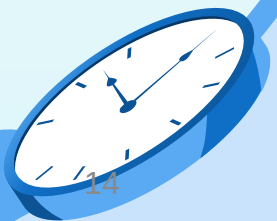
Regular exercise,
balanced nutrition
changes

HAPPY, ACTIVE CHILD: Regular exercise,
balanced nutrition with fruits & vegetables



Laboratory Findings

- ALT ↑
- AST ↑
- GGT ↑
- Normal ALT does NOT exclude MASLD

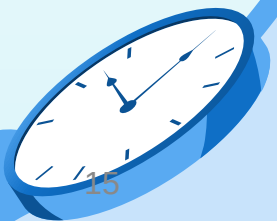


- **ALT Cut-off**

Girls: 22 U/L

Boys: 26 U/L

- Lower than laboratory references



Who Should Be Screened?

- Universal screening
- ✕ Not recommended



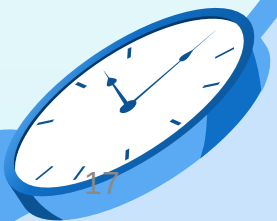
Who Should Be Screened?

- **All obese children**
- **Age ≥ 10 years**
- **Overweight children +Risk factors**

Family history

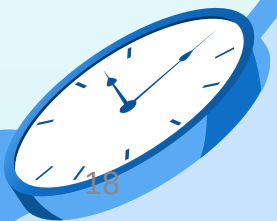
OSA(Obstructive sleep Apnea)

Diabetes



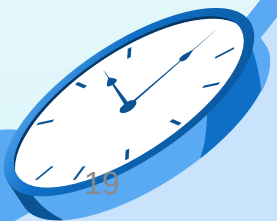
High-risk individuals

- ✓Type 2 diabetes
- ✓Obesity + cardiometabolic risk factors
- ✓Hepatic steatosis on imaging
- ✓Persistently elevated ALT/AST



- **Additional groups (selected guidelines):**

- Prediabetes
- HIV
- Family history of MASH cirrhosis
- Moderate alcohol intake



Obesity



ALT



Normal



Annual follow-up

Obesity



ALT



Elevated

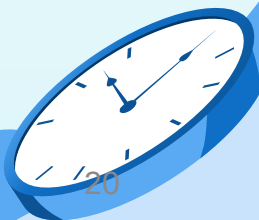


Repeat after 3 months

Persistent elevation



Full evaluation



First-Line Screening Test

- **Fibrosis 4 index (FIB-4)**

$$\text{Age} \times \text{AST} \div [\text{Platelet} \times \sqrt{\text{ALT}}]$$

- Advantages

1. Simple Inexpensive
2. Widely available
3. Suitable for primary care



FIB-4 <1.3	FIB-4 1.3–2.67	FIB-4 ≥2.67
Low risk	Moderate risk	Sever risk
Repeat assessment	FibroScan	Hepatology referral

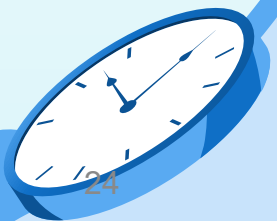


- **FibroScan**

- Steatosis
- Liver stiffness
- Fibrosis
- Needs pediatric validation

FibroScan

<8 KPa	≥8KPa
low risk	Refer to hepatologist



Ultrasound

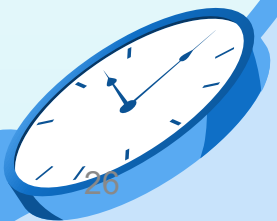
Not recommended for screening

- Useful :
- during evaluation
- Structural abnormalities
- Portal hypertension
- Gallstones



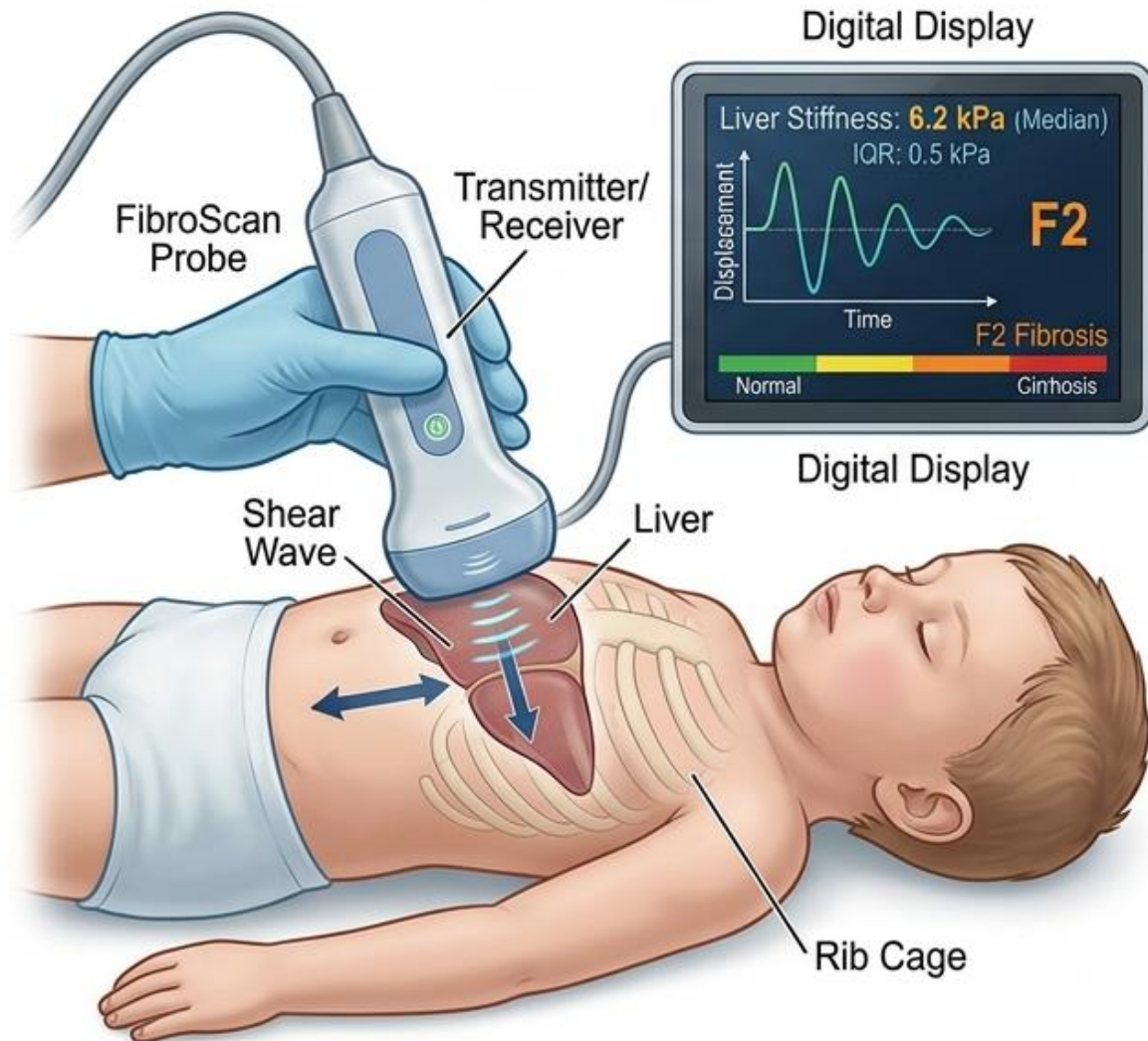
MRI-PDFF

- Magnetic Resonance Imaging- Proton Density Fat Fraction
- Most accurate : **Quantifies liver fat**
- Excellent research tool
- Limited availability



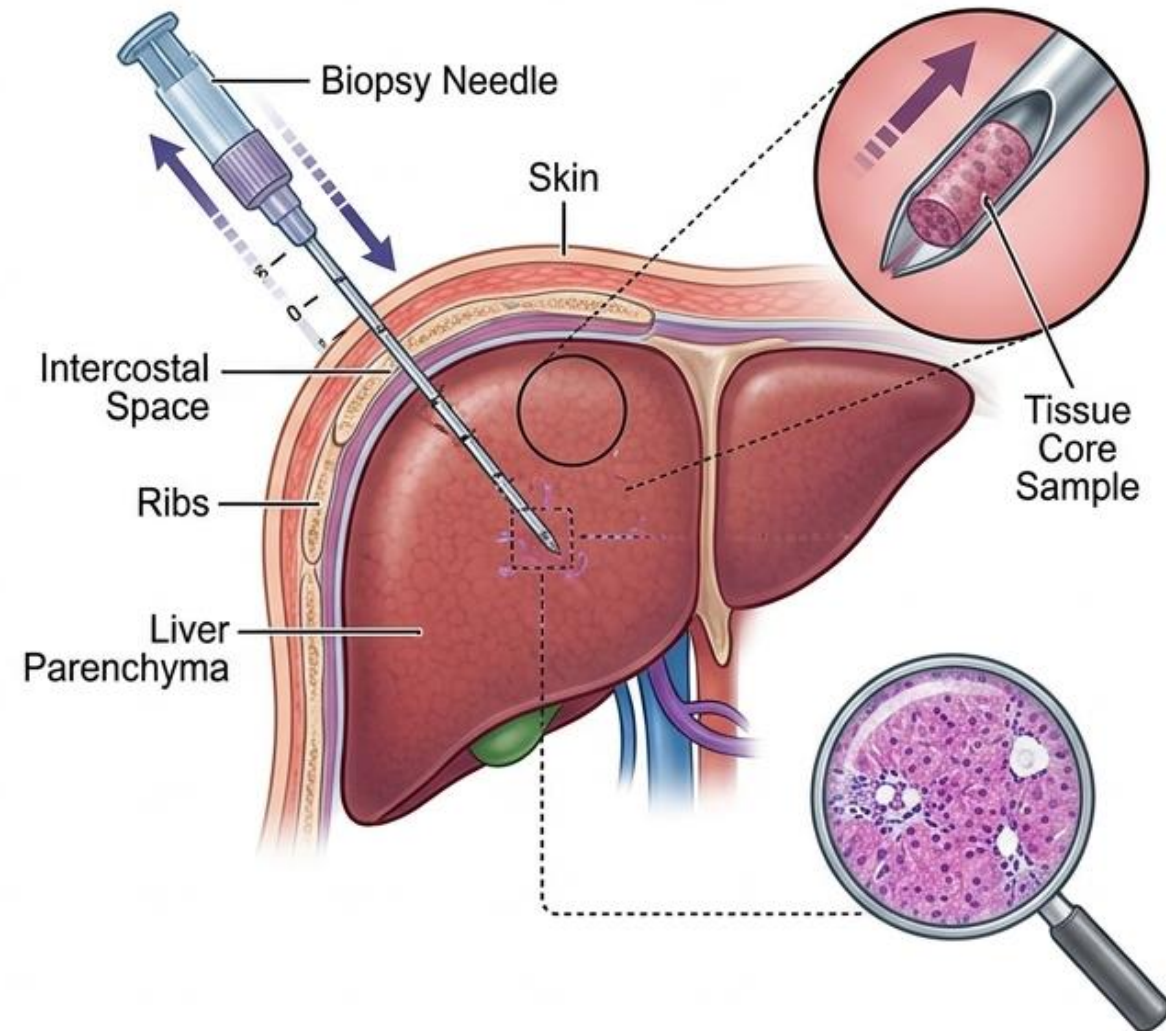
FIBROSCAN (Transient Elastography)

Non-Invasive Liver Stiffness Measurement



LIVER BIOPSY

Invasive Tissue Sampling for Histology

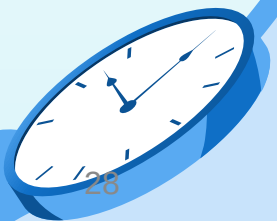


Liver Biopsy

- Gold Standard
- Confirms MASH
- Assesses fibrosis
- Excludes other diseases

-

Reference. AASLD Practice Guidance. Hepatology. 2025.



- ✓ Normal ALT does NOT exclude MASLD
- ✓ Ultrasound is NOT recommended for screening
- ✓ MRI-PDFF is best for steatosis
- ✓ FibroScan is useful for fibrosis assessment
- ✓ Liver biopsy remains the gold standard

- Reference: Wyllie R, et al. Pediatric Gastrointestinal and Liver Disease. 7th ed.
- UpToDate 2025.

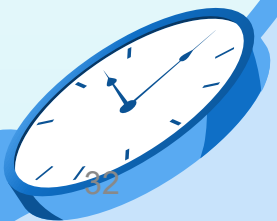






Differential Diagnosis

- Wilson disease
- Autoimmune hepatitis
- Alpha-1 antitrypsin deficiency
- Celiac disease
- Hypothyroidism
- Drug-induced liver injury
- Lysosomal Acid Lipase deficiency





Laboratory Evaluation

- **Initial Laboratory Tests**

ALT, AST, GGT, ALP

Total & Direct Bilirubin Albumin

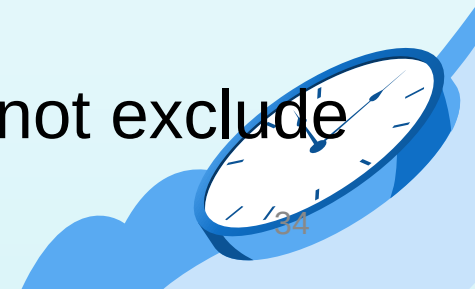
CBC PT/INR

- **Cardiometabolic Assessment**

HbA1c / Fasting glucose Lipid profile

Blood pressure BMI percentile

- ALT remains the preferred screening test, but normal ALT does not exclude MASLD.





Diagnosis of Pediatric MASLD

- **Diagnosis requires:**

- Evidence of hepatic steatosis (MRI, FibroScan or biopsy)
- ≥ 1 cardiometabolic risk factor Exclusion of other liver diseases
- Elevated ALT is not mandatory, Liver biopsy confirms MASH

Reference: UpToDate 2025.



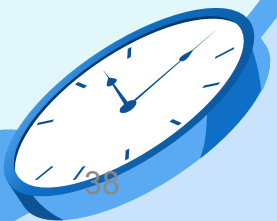
Treatment



- **Goals of Treatment**

- Prevent progression to MASH Prevent fibrosis
- Reduce cardiovascular risk Improve metabolic health
- Achieve sustainable weight reduction Improve quality of life

Reference:UpToDate 2025.



Lifestyle Modification

- First-line Therapy
- Healthy diet Reduce added sugars
- Avoid sugar-sweetened beverages Reduce ultra-processed foods
- Daily physical activity
- Family-centered intervention
- **Lifestyle modification remains the only universally recommended therapy.**

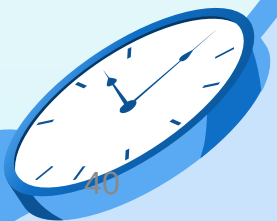
Reference:Wyllie 7th Edition.UpToDate 2025.



Weight Reduction

- Gradual weight loss is recommended.
- **Benefits include:**
 - ↓ ALT/AST
 - ↓ Liver fat Improved histology
 - Better insulin sensitivity
- **Rapid weight loss is NOT recommended.**

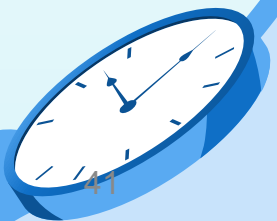
Reference:Wyllie. UpToDate 2026



Dietary Recommendations

❖ Recommended:

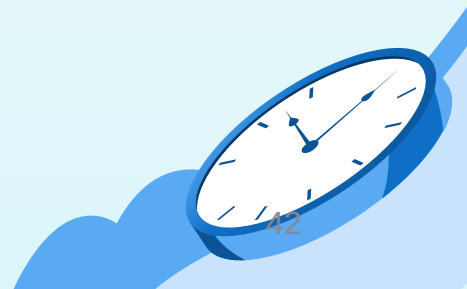
- Mediterranean-style diet Fruits & vegetables
- Whole grains Lean protein
- Low-sugar diet
- Reduce fructose intake
- Low glycemic index foods
- Unsaturated fats Omega-3-rich foods Fish



Dietary Recommendations

❖ Limit:

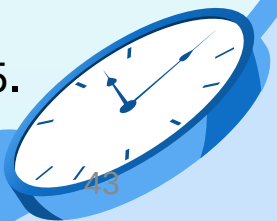
- Refined carbohydrates
- Saturated fat
- Soft drinks Fructose-rich beverages
- Fast foods* Processed snacks
- Avoid sugar-sweetened beverages



Physical Activity

- ≥ 60 minutes/day
- Moderate to vigorous exercise Reduce sedentary behavior
- Limit screen time Exercise benefits even without major weight loss

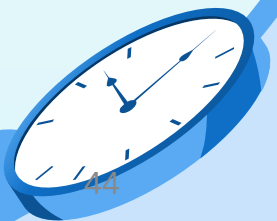
Reference: UpToDate 2025.



- **Additional Counseling**

- Avoid alcohol Avoid smoking
- Hepatitis A & B vaccination COVID vaccination
- Improve sleep quality Screen for OSA

Reference:AASLD Practice Guidance. 2025.



Pharmacologic Therapy

- Currently NO approved drug for pediatric MASLD

- Not recommended:

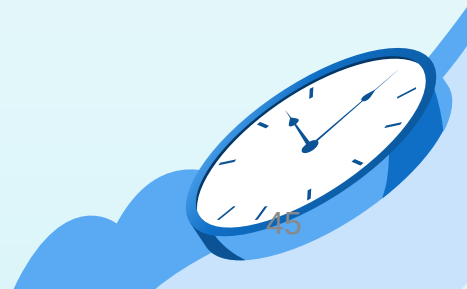
Vitamin E

Metformin

Ursodeoxycholic acid

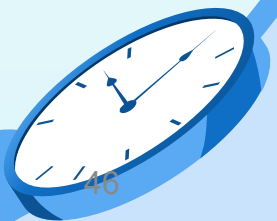
Omega-3

Probiotics



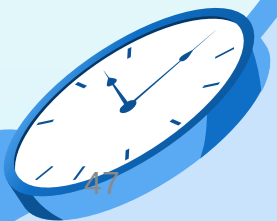
Pharmacologic Therapy

- Currently:
- **✗ No medication is routinely recommended for pediatric MASLD.**
- Lifestyle intervention remains first-line.



Vitamin E

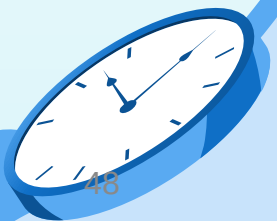
- Evidence:
- ✓ Some improvement in biopsy-proven NASH
- However:
- Benefit inconsistent
- Not routinely recommended Consider only selected biopsy-proven cases



Metformin

- Evidence:
- Improves diabetes Does NOT improve liver histology
- No routine role in pediatric MASLD
- Recommended only if diabetes is present.

Reference:UpToDate 2026



Other Drugs

- Insufficient evidence for routine use:

Cysteamine

UDCA

Losartan

Omega-3 supplements

Probiotics

- None are recommended routinely.



GLP-1 Receptor Agonists

- Examples:

1. Semaglutide

2. Tirzepatide

- **Adults:**

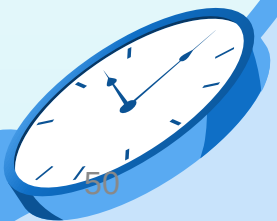
- ✓ Significant weight loss ✓ Histologic improvement

- **Children:**

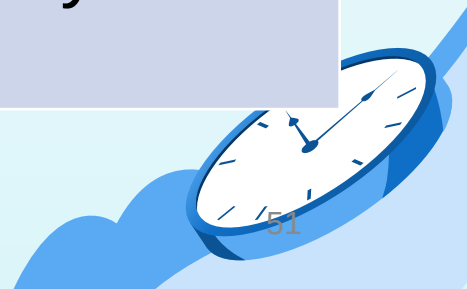
- Evidence limited.

- May be considered for obesity or T2DM—not routine MASLD treatment.

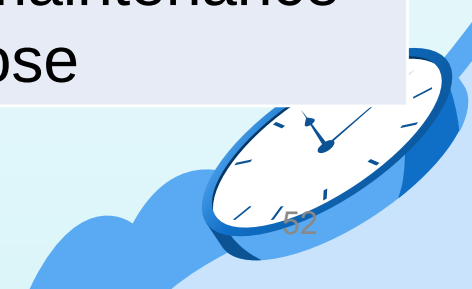
Reference: Diabetes Obesity Metabolism 2026 UpToDate 2026



week	Semaglutide dose (SC)
1-4	0.25 mg once weekly
5-8	0.5 mg once weekly
9-12	1 mg once weekly
13-16	1.7 mg once weekly
≥17	2.4 mg once weekly

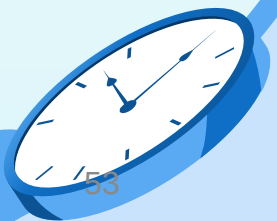


week	Tirzeptide dose (SC)	comment
1-4	0.25 mg once weekly	starting dose
5-8	0.5 mg once weekly	first therapeutic dose
9-12	7.5 mg once weekly	If additional effect is needed
13-16	10 mg once weekly	Dose escalation
17-20	12.5 mg once weekly	If tolerated
≥21	15 mg once weekly	Maximum maintenance dose



Resmetirom (Rezdiffra)

- First FDA-approved drug for adult MASH with fibrosis.
- Approved for adults only.
- No routine recommendation in children.



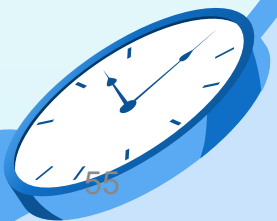
Resmetirom (Rezdiffra)

<100 kg	80 mg	daily
≥100 kg	100 mg	daily



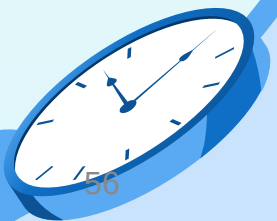
- **Obesity predominant**

- Semaglutide
- Tirzepatide
- Resmetirom



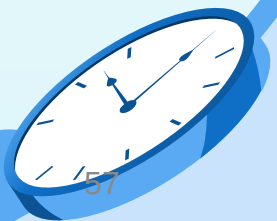
- **Diabetes predominant**

- Semaglutide
- Tirzepatide
- SGLT2 inhibitors
- Pioglitazone
- Resmetirom



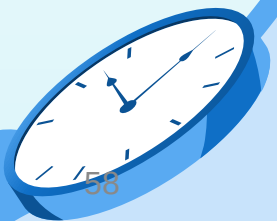
- **Lean phenotype**

- Resmetirom



Bariatric Surgery

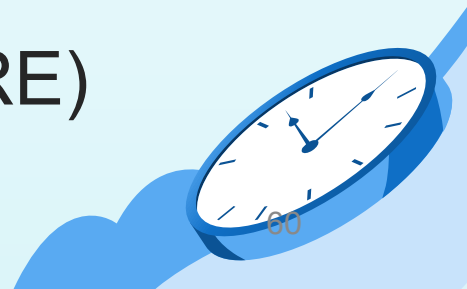
- **Consider in adolescents with:**
 - Severe obesity Failed lifestyle therapy
 - Significant comorbidities
- **Benefits:**
 - Weight reduction
 - Resolution of steatosis
 - Improvement of fibrosis



Monitoring Response



- Repeat assessment: after 12–18 months
- using:the same non-invasive test
- Meaningful response:
 - ≥25–30% reduction in Fibro Scan
 - ≥20% reduction in Magnetic Resonance Elastography (MRE)





Follow-up

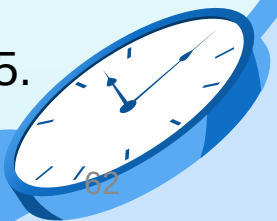
- **Every 3 months:**

- Weight
- BMI
- ALT
- Lifestyle adherence

- **Annually:**

- Lipid profile
- HbA1c Blood pressure
- Kidney function
- OSA screening

Reference:UpToDate 2025.





Prognosis

Progression may include:

- **Increased mortality:**

MASH

Fibrosis

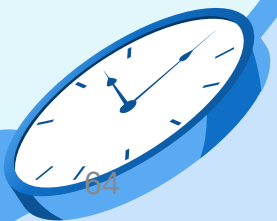
Cirrhosis

Type 2 diabetes

Cardiovascular disease

- Early diagnosis improves outcomes.

Reference: California Pediatric MASLD Cohort 2025.



Thank you for your attention



Fat accumulation
in the liver

Childhood NAFLD

A growing health concern