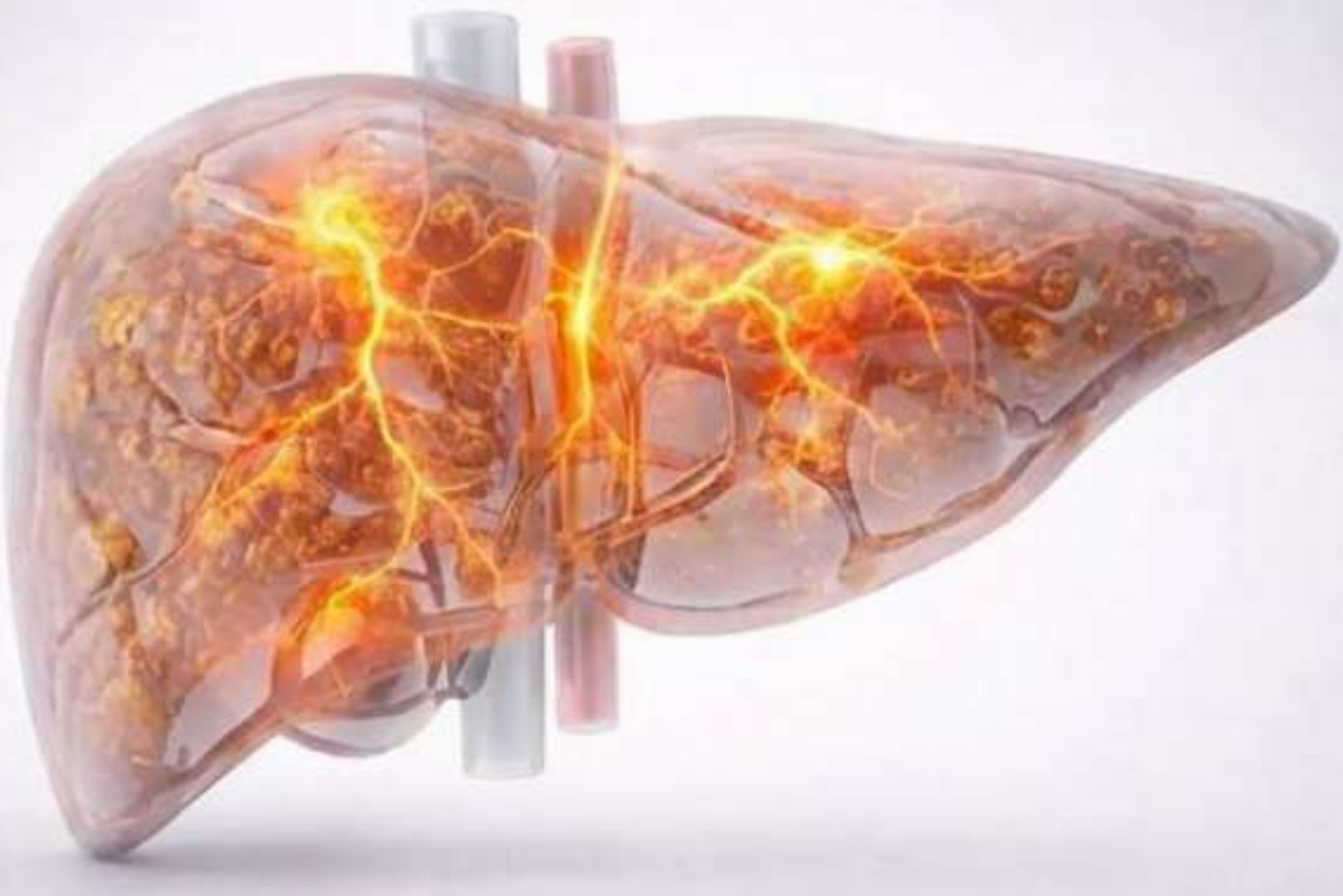
CHRONIC LIVER DISEASE

National Standard Treatment Guideline



Ministry of Health
Republic of Maldives

ADB

JFPR
Japan Fund for Prosperous and Resilient Asia and the Pacific

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World Health Organization
Maldives

National Standard Treatment Guidelines

- Acid Peptic Disease
- Acute Anxiety
- Acute Pancreatitis
- Acute Psychosis
- Acute kidney Injury
- Arrhythmia
- Chronic Liver Disease
- Chronic Pancreatitis
- Chronic kidney disease
- Congenital Heart Diseases
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- Interstitial Lung Disease
- Liver Failure
- Obesity
- Obstructive Sleep Apnoea
- Osteoarthritis
- Ovarian Cancer
- Pneumonia
- Stroke
- Upper Gastrointestinal bleed
- Unstable Angina

Version No	Version Date	Description of change
1	8 November 2025	Initial release

DOCUMENT NUMBER: MOH-QA/G/25/221-0

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Published by

Quality Assurance and Regulations Division
Ministry of Health, Male,
Republic of Maldives

GUIDELINES DEVELOPMENT METHODOLOGY

The development of the Maldives Standard Treatment Guidelines (STGs) followed a structured, evidence-informed, and consensus-driven methodology adapted from internationally accepted guideline-development standards and the Delhi Society for Promotion of Rational Use of Drugs (DSPRUD) model. The process combined systematic evidence retrieval, critical appraisal, contextual adaptation, and multidisciplinary expert review to ensure feasibility, clinical relevance, and national ownership.

1. Determining Scope and Priority Conditions

Priority clinical conditions were identified through consultation with national programme managers, specialty clinicians, and health-system stakeholders. Selection criteria included: (i) major causes of morbidity and mortality, (ii) observed variation in clinical practice or prescribing patterns, (iii) potential to improve patient outcomes, and (iv) the feasibility of implementation across health-facility levels in Maldives. The final list of diseases reflected national epidemiology, service-delivery capacity, and essential-medicine availability.

2. Identification of Existing Evidence and Source Guidelines

A targeted search strategy was used to identify high-quality existing clinical guidelines. Searches were conducted across international guideline repositories (e.g., WHO, NICE, SIGN and other intergovernmental bodies, international and national guideline repositories, specialty societies and professional associations.

3. Quality Appraisal of Source Guidelines

Retrieved guidelines were screened for transparency of development, methodological rigour, clarity of recommendations, applicability to health-system reality, editorial independence. Guidelines were included if they met the Institute of Medicine (IOM) definition of a clinical guideline and addressed treatment or management of priority conditions. Guidelines that did not meet minimum quality standards, review articles, diagnostic criteria, or technical standards were excluded.

4. Adoption, Adaptation, and Contextualization

The guideline-development team employed an adopt–adapt–contextualize model:

- **Adoption**: High-quality recommendations that aligned with Maldivian health-system realities were retained without modification.
- **Adaptation**: Recommendations were modified when local considerations such as diagnostic capacity, medicine availability, workforce skills, referral pathways, or cost constraints affected feasibility.

- **Contextualization**: Where evidence was absent or inconclusive, conditional recommendations were formulated based on expert consensus, with explicit consideration of pragmatism, safety, and local workflows.
  Medicines were selected in alignment with the Maldives National Essential Medicines List (NEML), based on suitability, efficacy, safety, and availability.

5. Expert Consensus and Multidisciplinary Input

Draft recommendations were initially prepared by experts from the DSPRUD, India, providing a strong methodological foundation for the process. Building on this, a collaborative and participatory process brought together clinicians from internal medicine, paediatrics, obstetrics-gynaecology, surgery, emergency medicine, endocrinology, cardiology, general practitioners, and public health representing different levels of healthcare. Consensus was achieved through moderated discussions, iterative revisions, and resolution of divergent views. For topics lacking strong evidence, recommendations were derived from expert clinical judgment grounded in extensive practice experience.

6. Drafting, Peer Review, and Validation

Each guideline section was organized in a standard format including key clinical features, essential investigations, non-pharmacological management, pharmacological therapy (with step-up/step-down options where relevant), referral criteria, paediatric considerations, and follow-up requirements. Drafts were peer-reviewed by senior clinicians and national experts. Reviewer comments were systematically integrated to strengthen clarity, accuracy, and applicability.

7. Addressing Conflicts of Interest

All contributors declared the absence of conflicts of interest. Individuals with potential or perceived conflicts were excluded from authorship or decision-making roles.

8. Updating and Future Revisions

The STGs were conceptualized as a living document. Future updates will incorporate new scientific evidence, changes in essential-medicine availability, national programme priorities, and user feedback from clinicians. Periodic review cycles will ensure the continued relevance and reliability of recommendations.

9. Distinctive Features of the Guidelines

Developed through a collaborative process involving a large group of multidisciplinary experts from different levels of healthcare, the guidelines incorporate the following distinctive features:

- **Diagnostic Assumption and Confirmation**: While assuming that an initial diagnosis has been established by the healthcare provider, the guidelines provide essential information for confirming diagnoses. This includes a comprehensive overview of major signs and symptoms, descriptions of confirmatory tests, and clear guidance on practices that are prohibited, discouraged, or unreliable—promoting evidence-based medicine supported by relevant references.
- **Comprehensive Treatment Approach**: The guidelines offer a systematic, up-to-date framework for managing medical conditions across the continuum of care. They begin at the primary care level and extend to secondary and tertiary care, incorporating protocols for treatment response assessment and referral criteria as integral components.
- **Diverse Treatment Modalities**: Recommendations encompass both non-pharmacological and pharmacological interventions and surgical intervention where applicable, providing flexibility for individualized treatment plans. Cautionary notes are included where necessary to ensure safe and effective use of therapies.
- **Assessment and Referral Criteria**: Clear criteria and goals for evaluating patient response to treatment are provided, along with guidance on when referral to higher levels of care is warranted ensuring continuity and comprehensiveness in patient management.

ACKNOWLEDGEMENTS

The Government of the Republic of Maldives is committed to ensuring universal access to quality health services for all citizens. The Constitution of Maldives mandates the progressive realization of rights, including the right to good standards of health care for the population. In line with this national commitment, standardized quality health services are regarded as the foundation of a strong and equitable healthcare system.

This important work would not have been possible without the cooperation and support of many individuals and institutions. We express our sincere appreciation to the Honourable Minister of Health, Abdullah Nazim Ibrahim, for his leadership, commitment, and continuous guidance throughout the development process. We are grateful to WHO and ADB for their significant contribution, support, and technical assistance.

Our heartfelt gratitude is extended to the technical lead and editor, Dr. Sangeeta Sharma, Professor, Neuropsychopharmacology, IHBAS and President, Delhi Society for Promotion of Rational Use of Drugs (DSPRUD), and her team. We express our deepest appreciation to the Maldivian and DSPRUD experts and contributors who played a pivotal role in this process. Their technical expertise and dedication to adapt the standards to the Maldivian context have been instrumental in the development and finalization of these guidelines. The time, experience, generous sharing of knowledge and insights contributed by all parties have not only enriched the work but also have been invaluable in making these standards practical, locally acceptable, and aligned with the needs of the resident population.

It is important to acknowledge the immense efforts, involvement, timely coordination, collaboration, and dedication of the Quality Assurance and Regulation Division team who made it possible for these Clinical Treatment Guidelines to come into existence.

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CHRONIC LIVER DISEASE

QUICK REFERENCE GUIDE

Chronic liver disease (CLD): Structural and/or functional liver abnormality persisting ≥6 months, with or without cirrhosis. Cirrhosis is defined as advanced fibrosis with regenerative nodules; compensated (no decompensation) vs decompensated (ascites, variceal bleed, jaundice, or hepatic encephalopathy).Common etiologies include alcohol-associated liver disease, viral hepatitis B/C, metabolic dysfunction-associated steatotic liver disease (MASLD; previously NAFLD), autoimmune hepatitis, cholestatic diseases (primary biliary cholangitis, primary sclerosing cholangitis), genetic (hemochromatosis, Wilson disease, alpha-1 antitrypsin deficiency), drug-induced liver injury (DILI), vascular (Budd-Chiari, congestive hepatopathy).

Causes, Risk factors & Triggers

- Causes as above
- Risk factors: Hazardous alcohol use, obesity, type 2 diabetes, dyslipidemia, viral exposure (perinatal, sexual, needle), family history (hemochromatosis/ Wilson), autoimmune conditions, chronic heart failure.
- Triggers of decompensation: Alcohol binge, infections (esp. spontaneous bacterial peritonitis), gastrointestinal bleeding, high-salt intake, nephrotoxic drugs (non-steroidal anti-inflammatory drugs [NSAIDs], aminoglycosides), sedatives, constipation, dehydration, surgery, contrast load.

Evaluation for Diagnosis

- **Clinical features:** Fatigue, pruritus, right upper quadrant discomfort, anorexia, weight/muscle loss; signs: jaundice, spider nevi, palmar erythema, ascites, splenomegaly, edema, asterixis.
- **Physical examination:** Vital signs, body mass index and sarcopenia, stigmata of chronic liver disease, encephalopathy grade, ascites/edema, signs of infection or bleeding.
- **Laboratory investigations:** Complete blood count (thrombocytopenia), liver panel (alanine aminotransferase [ALT], aspartate aminotransferase [AST], alkaline phosphatase [ALP], gamma-glutamyl transferase [GGT], bilirubin, albumin), prothrombin time/international normalized ratio (PT/INR), renal panel (creatinine, sodium), fasting glucose/ HbA1c, lipid profile.
- **Etiology workup:** hepatitis B surface antigen (HBsAg), hepatitis B e-antigen (HBeAg)/DNA, anti-hepatitis C virus (anti-HCV)/HCV RNA, autoimmune markers (antinuclear antibody [ANA], anti-smooth muscle antibody [ASMA], antimitochondrial antibody [AMA]), iron studies and transferrin saturation, serum ferritin, ceruloplasmin and 24-h urinary copper (<40 years), alpha-1 antitrypsin level/phenotype.
- **Infection screen** if decompensated: blood/urine cultures, ascitic fluid cell count and culture.

Imaging & non-invasive fibrosis

- Abdominal ultrasound (liver morphology, portal vein, spleen, ascites).
- Transient elastography (liver stiffness), fibrosis scores (Fibrosis-4 [FIB-4], AST-to-platelet ratio index [APRI]).
- Endoscopy for varices if clinically significant portal hypertension is suspected.

Confirmation of diagnosis

- Compatible clinical/imaging features; liver biopsy if etiology or stage unclear or to confirm autoimmune/overlap syndromes.

Staging/severity assessment criteria

- Clinical: Stage 1 compensated no varices; Stage 2 compensated with varices; Stage 3 decompensated with ascites; Stage 4 decompensated variceal bleed; Compensated vs decompensated drives surveillance and referrals
- Child-Turcotte-Pugh (CTP) class A/B/C (encephalopathy, ascites, bilirubin, albumin, INR); guides prognosis/drug dosing
- Model for End-Stage Liver Disease-sodium (MELD-Na) for prognosis and transplant prioritization; guides transplant priority
- Hepatic encephalopathy (HE): West Haven grades 0-4.Grades 1-2 = mild/ moderate; Grades 3-4 = severe, need urgent intensive management.
- Portal Hypertension: No portal hypertension to Subclinical to Clinically significant portal hypertension (CSPH) [if HVPG ≥10 mmHg or surrogate: platelets <150k with splenomegaly or liver stiffness >20 kPa] to Decompensation; predicts the risk of varies/decompensation
- Acute kidney injury (AKI) in cirrhosis: International Club of Ascites (ICA) criteria.
- Ascites: Uncomplicated vs refractory (diuretic-resistant or diuretic-intractable)
- Acute-on-Chronic Liver Failure (ACLF): various definitions and grading systems; high short-term mortality; signals acute deterioration and transplant need.
- Trigger urgent transfer if variceal bleed, HRS-AKI, grade 3-4 HE, sepsis, or ACLF
- HCC surveillance in all cirrhotics every 6 months regardless of stage

Differential Diagnosis

- Acute liver failure, congestive hepatopathy/right-sided heart failure, extrahepatic biliary obstruction, infiltrative disease, hemolysis/Gilbert syndrome (isolated unconjugated hyperbilirubinemia), drug-induced cholestasis, malignancy (metastatic disease).

Management Goals & principles

- Identify and treat the cause.
- Prevent and manage decompensation and complications.
- Optimize nutrition, vaccination, and lifestyle.
- Screen for hepatocellular carcinoma (HCC) and varices.
- Avoid hepatotoxic and nephrotoxic drugs.
- Evaluate timely for liver transplantation.

Approach to management

1. Establish etiology; start disease-specific therapy (e.g., antivirals for hepatitis B/C, immunosuppression for autoimmune hepatitis, abstinence counseling for alcohol, weight loss for MASLD).
2. Stage disease (CTP, MELD-Na) and screen for varices/HCC.
3. Compensation vs decompensation:
    - Compensated: risk reduction, surveillance, lifestyle, etiology control.

- Decompensated: treat precipitant, manage ascites/HE/bleeding/AKI, consider transplant referral.

4. Structured follow-up with labs, nutrition checks, and surveillance.

Non-Pharmacological interventions

- Alcohol abstinence: brief intervention; refer to de-addiction.
- Nutrition: 30-35 kcal/kg/day; protein 1.2-1.5 g/kg/day; late-evening snack; small frequent meals; correct micronutrients (vitamin D, zinc, thiamine).
- Sodium restriction: ≤2 g sodium/day (~5 g salt/day) for ascites.
- Fluid restriction only if severe hyponatremia (serum sodium <125 mmol/L).
- Exercise: gradual aerobic + resistance to reduce sarcopenia.
- Vaccines: hepatitis A and B, influenza, pneumococcal, COVID-19, tetanus boosters.
- Medication safety: avoid NSAIDs; use acetaminophen/paracetamol ≤2 g/day if needed; review sedatives.

Pharmacological therapy

Always individualize; check renal function, electrolytes, blood pressure, pregnancy status, and drug interactions.

Portal hypertension/ primary prophylaxis/secondary prophylaxis

- **Primary prophylaxis: Non-selective beta-blockers (NSBB):**
  - Carvedilol 6.25 mg once daily followed by 6.25 mg twice daily as tolerated (target heart rate 55-60/min; avoid if systolic blood pressure <90 mmHg, refractory ascites with hypotension, severe AKI).
  - Propranolol 20-40 mg twice daily; titrate to heart rate 55-60/min.
  - **Endoscopic variceal ligation (EVL) if intolerance to NSBB**
- **Secondary prophylaxis; EVL + NSBBs.**

Ascites

- Spironolactone 100 mg + furosemide 40 mg daily (maintain 100:40 ratio; titrate every 3-5 days; max commonly 400:160 mg/day).
- Large-volume paracentesis (LVP): give albumin 6-8 g per liter of ascites removed when ≥5 L.
- Avoid NSAIDs, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers in tense ascites/AKI.

Spontaneous bacterial peritonitis (SBP)

- Empiric therapy: Cefotaxime 2 g IV every 8 h or ceftriaxone 1-2 g IV daily (tailor to local resistance).
- Albumin 1.5 g/kg IV day 1 + 1 g/kg day 3 (reduces renal failure) [albumin infusion to be volume status guided to avoid overload]
- Secondary prophylaxis: Norfloxacin 400 mg orally daily; alternatives ciprofloxacin 500 mg daily or co-trimoxazole double-strength daily per local availability.

Hepatic encephalopathy (HE)

- Lactulose 15-30 mL orally every 8-12 h; titrate to 2-3 soft stools/day (or 25 mL rectal enema in acute episodes).

- Rifaximin 550 mg orally twice daily as add-on for recurrent HE.
- Treat precipitants: infection, constipation, gastrointestinal bleed, electrolyte issues.

Acute variceal bleeding (initial management)

- Airway/IV access, restrictive transfusion (hemoglobin target ~7-8 g/dL).
- Vasoactive agent: Terlipressin 1 mg IV every 6 h (titrate; monitor ischemia) or octreotide 50 mcg IV bolus then 50 mcg/h infusion for 2-5 days.
- Antibiotic prophylaxis: Ceftriaxone 1 g IV daily for ~7 days.
- Urgent endoscopy with EVL. Consider early TIPS (transjugular intrahepatic portosystemic shunt) in high-risk. (For details see guidelines on Upper GI Bleed)

Hepatorenal syndrome-AKI (HRS-AKI)

- Terlipressin continuous/bolus + albumin (e.g., 1 g/kg day 1 up to 100 g; then 20-40 g/day). Alternatives where terlipressin unavailable: midodrine + octreotide + albumin. Stop diuretics; avoid nephrotoxins.

Cholestatic pruritus

- Cholestyramine 4 g orally once-twice daily (separate from other drugs by ≥4 h).
- Add-on: rifampicin 150-300 mg twice daily (monitor liver tests), naltrexone 25-50 mg daily, sertraline 50-100 mg daily if needed.

Disease-specific management

- Hepatitis B virus (HBV): Tenofovir disoproxil fumarate 300 mg daily or entecavir 0.5-1 mg daily per indications (high viral load, active hepatitis, cirrhosis).
- Hepatitis C virus (HCV): Direct-acting antiviral (DAA) regimens per genotype/cirrhosis status (e.g., sofosbuvir/velpatasvir 400/100 mg daily for 12 weeks in many scenarios; avoid sofosbuvir if eGFR <30 mL/min/1.73 m²; specialist protocols apply).
- Autoimmune hepatitis: Prednisolone 30-40 mg/day taper + azathioprine 1-2 mg/kg/day (monitor blood counts, TPMT if available).
- Primary biliary cholangitis: Ursodeoxycholic acid 13-15 mg/kg/day; add obeticholic acid per specialist guidance (contraindicated in decompensated cirrhosis).

Cautions: Monitor potassium and creatinine with diuretics; watch hypotension with NSBB; dose-adjust renally cleared drugs; check pregnancy/teratogenicity; drug-drug interactions with antivirals.

Assessment of response, review, and treatment adjustment

- Every 3-6 months (compensated): symptoms, weight/mid-arm circumference, alcohol abstinence, labs (complete blood count, liver panel, PT/INR, creatinine, sodium), review meds, vaccine status.
- Decompensated: closer follow-up (2-8 weeks) with electrolytes, renal function, diuretic response, HE control, infection surveillance.
- HCC surveillance: ultrasound ± alpha-fetoprotein (AFP) every 6 months.
- Variceal follow-up: per endoscopy findings; after EVL, repeat until eradication, then 6-12 months.
- When to step-up: If refractory ascites, recurrent HE, recurrent SBP, progressive MELD-Na, hyponatremia, sarcopenia - consider TIPS (for refractory ascites) / transplant evaluation.

- When to step-down: resolution of precipitant, stable labs, no ascites/HE, intolerance to drugs.

Referral to specialist/tertiary care

- Immediate/urgent: acute variceal bleeding, suspected SBP, HRS-AKI, severe HE (grade ≥3), sepsis, acute-on-chronic liver failure.
- Early referral: MELD-Na ≥15-18, CTP-C, refractory/recurrent ascites or HE, recurrent bleeds, HCC suspicion, unclear etiology, pregnancy with cirrhosis, need for TIPS or transplant assessment.
- **Tiered approach:**
  - Primary care: screening, vaccinations, lifestyle, basic labs, lactulose titration, diuretic initiation, referral triggers recognized.
  - Secondary care: endoscopy, paracentesis with albumin, IV antibiotics, non-invasive fibrosis workup.
  - Tertiary center: TIPS, transplant workup, complex DAA/HBV rescue, refractory complications.

Complications

- Portal hypertensive bleeding, ascites and spontaneous bacterial peritonitis, hepatic encephalopathy, hepatorenal syndrome, hyponatremia, portal vein thrombosis, infections/sepsis, malnutrition and sarcopenia, osteodystrophy/osteoporosis, HCC.

Objectives of patient education & instructions to patient/caregiver

- Know the cause of your liver disease and the plan to treat it.
- No alcohol at all. Avoid NSAIDs; keep a current medication list; discuss any herbal/over-the-counter products first.
- Diet: adequate protein and calories; keep salt low if ascites; don't skip the late-evening snack.
- Lactulose use: aim for 2-3 soft stools/day; adjust dose, don't stop abruptly.
- Warning signs: increasing abdominal girth, black stools or vomiting blood, confusion/sleepiness, fever, severe muscle cramps, reduced urine—seek care promptly.
- Vaccinations are part of treatment—stay updated.
- Follow surveillance: ultrasound every 6 months; endoscopy as advised; keep appointments.
- Infection prevention: hand hygiene, safe food/water, early care for fever.
- Family & caregiver role: help monitor medications, stools, diet, and mental status; bring the patient for urgent care when red flags appear.

CHRONIC LIVER DISEASE

INTRODUCTION

Chronic Liver Disease (CLD) refers to progressive deterioration of liver function over months or years due to sustained hepatic injury. It includes cirrhosis, chronic hepatitis, and metabolic dysfunction-associated steatotic liver disease (MASLD). CLD is a major global health burden due to its silent onset, late detection, and risk of life-threatening complications.

More than 1.5 billion people are affected worldwide, with CLD contributing to nearly 4% of global deaths annually. The burden is especially high in Southeast Asia due to hepatitis B and C, alcohol misuse, and the rising prevalence of metabolic disorders. The Asia-Pacific region accounts for almost half of CLD-related deaths. In the Maldives, hepatitis infections, alcohol use, and increasing obesity are key drivers, though comprehensive data remain limited. A national guideline for hepatitis C management was launched in 2021 to address these concerns.

While some forms of CLD, such as hepatitis C, are curable with direct-acting antivirals, others including alcoholic liver disease, MASLD, metabolic dysfunction-associated steatohepatitis (MASH), and autoimmune hepatitis can be managed with lifestyle interventions and pharmacotherapy. This highlights the importance of standardized clinical approaches that ensure early diagnosis, uniform treatment, and timely referrals. Such standardization reduces complications and costs while strengthening training, policymaking, and resource planning.

SCOPE OF THIS GUIDELINE

This guideline provides a structured clinical framework for the comprehensive management of Chronic Liver Disease (CLD). It focuses on early identification, accurate diagnosis, and recognition of underlying causes, followed by tailored therapeutic strategies and supportive measures to improve outcomes. It also highlights the importance of ongoing monitoring, timely referral, and complication prevention.While it offers a broad management approach, detailed treatment protocols for specific etiologies are beyond its present scope.

Intended users

The guideline is designed for general physicians, specialists, nurses, and other healthcare professionals involved in the care of patients with CLD. It also serves as a reference for policymakers, program managers, and educators supporting health-system strengthening.

Applicability

The recommendations apply across all levels of healthcare from primary health centers and community clinics to secondary hospitals and tertiary referral facilities ensuring uniformity in practice and continuity of care.

- **Primary care -** early detection and prevention.

- **Secondary care-** diagnostic confirmation and initial complication management.
- **Tertiary care-** advanced diagnostics, specialized treatment, and transplantation.

DEFINITION

Chronic Liver Disease (CLD) refers to persistent or progressive liver injury (structural and/or functional) lasting at least six months, characterized by inflammation, fibrosis, and/or impaired synthetic, detoxification, or excretory functions of the liver. CLD may present with or without cirrhosis and can progress to decompensated disease or hepatocellular carcinoma.

As per AASLD and the joint EASL-EASD-EASO 2024

- **Steatotic Liver Disease (SLD)** is the umbrella term covering all liver conditions with excess fat (hepatic steatosis) irrespective of cause, including MASLD, MetALD, ALD, cryptogenic and other etiologies.
- **Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)** replaces the former term NAFLD. The criteria include:
  - Presence of hepatic steatosis (≥5% of hepatocytes on imaging or histology)
  - At least one cardiometabolic risk factor (e.g. obesity, type 2 diabetes, dyslipidaemia, hypertension, etc.)
  - Exclusion of other known causes of steatosis (significant alcohol, drugs, other diseases) where relevant and defined.
- **Metabolic Dysfunction-Associated Steatohepatitis (MASH)** replaces the former term NASH. It's a subtype of MASLD characterised by steatosis plus evidence of hepatocellular inflammation and injury (e.g. ballooning), with or without fibrosis.
- **MetALD** is a category for those who fulfill MASLD criteria but also have moderate alcohol consumption (above MASLD's low alcohol threshold but not heavy enough to be ALD).
- **Chronic Hepatitis B (CHB)** is established by persistence of hepatitis B surface antigen (HBsAg) for at least 6 months. This indicates hepatitis B virus (HBV) infection that has not cleared. The disease has different phases based on viral antigen (e.g. HBeAg), HBV DNA levels, ALT levels, and liver histology (or non-invasive fibrosis markers).
- **Chronic Hepatitis C (CHC)** is when hepatitis C virus (HCV) infection remains beyond six months (i.e. the virus is not cleared spontaneously in the acute phase). Chronic infection can lead to variable degrees of liver inflammation, fibrosis, cirrhosis, hepatocellular carcinoma. EASL's recommendations (2020) emphasise diagnosis (antibodies + HCV RNA), disease staging and treatment with direct-acting antivirals to achieve viral cure.

CAUSES, RISK FACTORS & DECOMPENSATION TRIGGERS

Category	Examples	Acute Decompensation Triggers
Viral	Hepatitis B, Hepatitis C, Hepatitis D	Viral reactivation or superinfection
Metabolic	MASLD / MAFLD (prev. NAFLD), diabetes, obesity	Worsening insulin resistance, poor glycemic control
Alcohol	Chronic alcohol consumption	Alcohol binges leading to acute alcoholic hepatitis
Autoimmune	Autoimmune hepatitis	Flare due to poor adherence, drug withdrawal
Genetic	Wilson's disease, Hemochromatosis	Decompensation due to missed chelation / iron overload
Drug-induced	Methotrexate, Isoniazid, herbal supplements	Hepatotoxic drug exposure (e.g., NSAIDs, paracetamol overdose)
Environmental	Aflatoxins, industrial toxins	Acute exposure leading to rapid worsening
Systemic / Vascular	-	Portal vein thrombosis (PVT)
Complications	-	GI bleed, spontaneous bacterial peritonitis (SBP), pneumonia, urinary tract infection

EVALUATION FOR DIAGNOSIS

Domain	Key Features / Examples
Clinical Features	■ Early: fatigue, loss of appetite, unintended weight loss ■ Progressive: jaundice, pruritus ■ Advanced: ascites, pedal edema, hepatic encephalopathy ■ Systemic: bleeding tendencies, palmar erythema, spider angiomas, gynecomastia, hepatomegaly
Duration of Injury	Evidence of hepatic injury or dysfunction persisting >6 months distinguishes CLD from acute liver disease
Clinical History	Alcohol intake, medication use (including traditional/herbal remedies), metabolic conditions (diabetes, obesity), viral exposures (HBV, HCV), family history of genetic/ metabolic liver diseases
Physical Examination	Signs suggesting chronicity: jaundice, ascites, spider angiomas, palmar erythema, gynecomastia, hepatomegaly

Laboratory Tests	■ Persistently abnormal liver enzymes: ALT, AST ■ Synthetic dysfunction: ↑ INR, ↓ albumin - Hyperbilirubinemia
Etiology Workup	■ Viral serology: HBsAg, Anti-HCV - Autoimmune markers: ANA, ASMA, LKM, AM/ ■ Metabolic panels: ferritin, transferrin saturation, ceruloplasmin, alpha-1 antitrypsin
Imaging Studies	Ultrasound (liver size, echotexture, ascites), FibroScan (elastography), CT/MRI (architecture, cirrhosis, focal lesions)
Exclusion of Other Conditions	Acute hepatitis, congestive hepatopathy, Budd-Chiari syndrome, biliary obstruction, non-progressive fatty liver
Liver Biopsy	Reserved for unclear cases, staging fibrosis, overlap syndromes; not mandatory in all patients

CONFIRMATION OF DIAGNOSIS

Diagnosis of CLD is established through a combination of persistent clinical and diagnostic findings. Abnormal liver function tests sustained for more than six months, along with imaging evidence of fibrosis or cirrhosis such as via ultrasound, FibroScan, or CTstrongly support the diagnosis. Serologic testing helps confirm the underlying etiology, whether viral, autoimmune, or metabolic. In select cases, liver biopsy may be performed to clarify unclear diagnoses, assess disease stage, or guide therapeutic decisions.

STAGING & SEVERITY ASSESSMENT

1. **Natural History Staging (Clinical Course)**

- Stage 1: Compensated without varices, no esophageal varices, no ascites. Often asymptomatic.
- Stage 2: Compensated with varices, presence of esophageal/gastric varices but no history of bleeding or ascites..
- Stage 3: Decompensated with ascites (± varices), first clinical decompensation often occurs with ascites.
- Stage 4: Decompensated with variceal bleed, life-threatening complication; higher mortality.

(Median survival: Stage 1/2 = >12 years; Stage 3 = ~2 years; Stage 4 = ~1 year without transplant).

2. Child-Turcotte-Pugh (CTP) Classification

Assesses severity and prognosis in cirrhosis using 5 parameters: Encephalopathy, Ascites, Bilirubin, Albumin, Prothrombin time/International normalized ratio (PT/INR)

Scoring

- Class A (5-6 points): Well-compensated
- Class B (7-9 points): Significant functional compromise
- Class C (10-15 points): Decompensated; poor prognosis

3. Model for End-Stage Liver Disease (MELD / MELD-Na)

- Uses bilirubin, creatinine, INR, sodium.
- Ranges from 6 (least severe) to 40 (most severe).
- MELD-Na ≥15-18: referral for liver transplantation.
- Updated MELD 3.0 also considers albumin, female sex for better accuracy.

4. Portal Hypertension-Based Staging

- Clinically Significant Portal Hypertension (CSPH): Defined as hepatic venous pressure gradient (HVPG) ≥10 mmHg or surrogate markers (platelets <150,000 + splenomegaly/ stiffness >20 kPa).
- Progression: no portal hypertension to subclinical to CSPH progressing to decompensation.

5. Acute-on-Chronic Liver Failure (ACLF) (EASL-CLIF Criteria/APASL criteria)

- EASL/CLIFF: Acute decompensation (ascites, HE, GI bleed, infection) + organ failure(s). Graded 1-3 by number/type of organ failures (liver, kidney, brain, coagulation, circulation, respiration). High short-term mortality requires transplant consideration.
- Under the APASL criteria, ACLF defined as acute hepatic insult manifesting as jaundice (bilirubin ≥5 mg/dL) and coagulopathy(INR≥1.5), complicated within 4 weeks by ascites and or encephalopathy in a patient with previously diagnosed or undiagnosed chronic liver disease with high short-term mortality.
- The EASL-CLIF definition restricts ACLF to those with established cirrhosis and defines organ failures using CLIF-SOFA scores.

In practice:

- Use clinical stage (compensated vs decompensated) to guide surveillance.
- Apply CTP for bedside prognosis and drug dosing.
- Use MELD-Na for transplant prioritization.
- Assess ACLF if acute deterioration occurs.

Assessment of Disease Severity

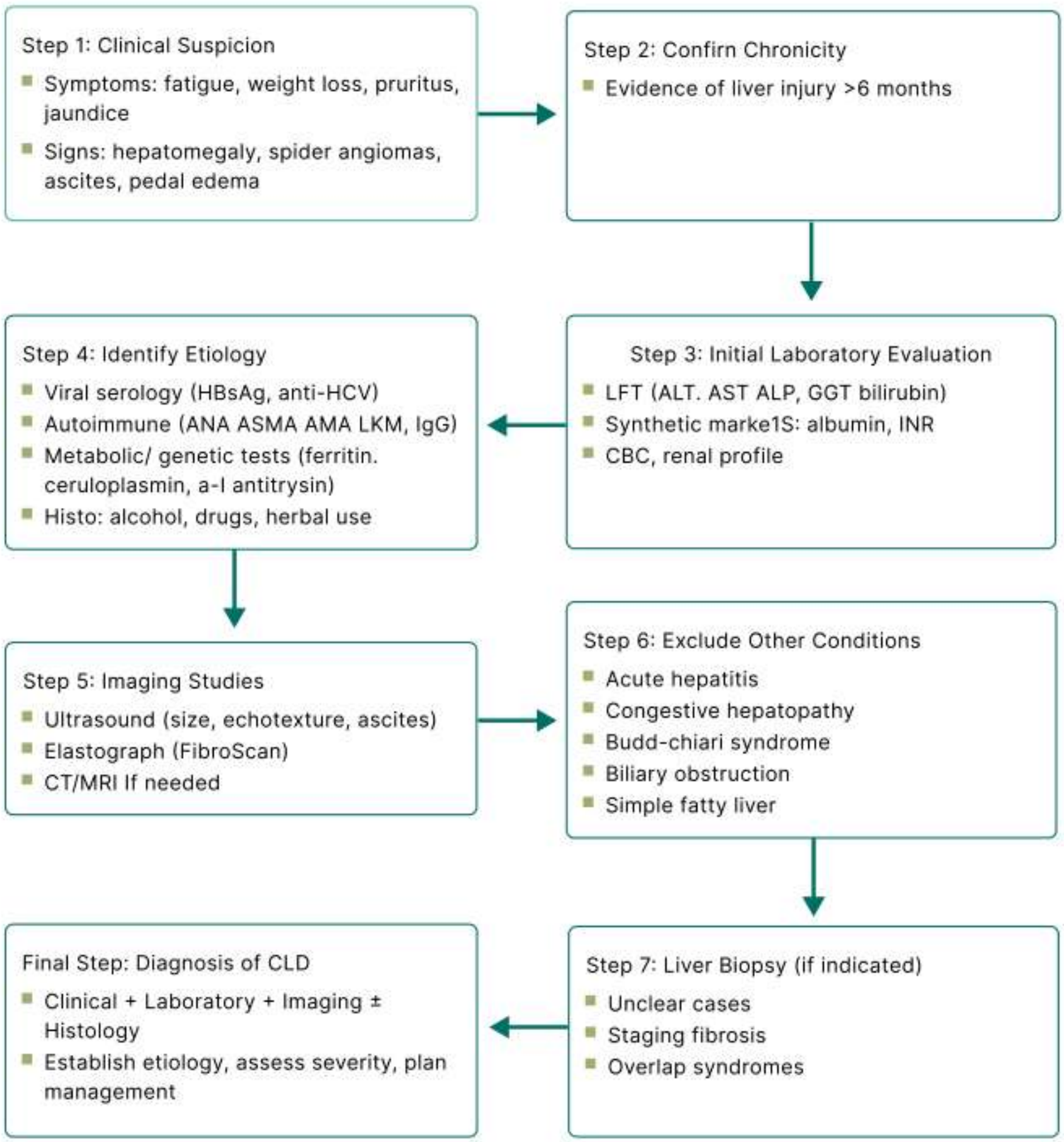
- Determine presence of clinically significant portal hypertension (CSPH).
- Hepatic venous pressure gradient (HVPG) is gold standard but invasive and not widely available.
- Elastography (LSM by transient elastography [TE]) is a practical alternative:
  - <10 kPa: rules out compensated advanced chronic liver disease (cACLD).
  - 10-15 kPa: suggestive of cACLD.
  - 15 kPa: highly suggestive of cACLD.
- LSM ≤15 kPa plus platelet count ≥150×10⁹/L rules out CSPH (NPV >90%).
- Baveno VII/EASL 2022: variceal surveillance can be avoided if LSM <20 kPa and PLT >150×10⁹/L.
- Patients with cACLD should be referred to a liver disease specialist.

DIFFERENTIAL DIAGNOSIS

Condition	How It Mimics CLD	Distinguishing Features / Key Tests
Acute Hepatitis (viral, drug-induced, ischemic)	Jaundice, elevated transaminases, malaise	Sudden onset, short duration (<6 months), markedly high ALT/AST (>10× ULN), negative fibrosis markers
Congestive Hepatopathy (Right heart failure, constrictive pericarditis)	Hepatomegaly, ascites, elevated liver enzymes	Cardiac history, elevated JVP, pulsatile hepatomegaly, echocardiography
Budd-Chiari Syndrome	Ascites, hepatomegaly, abdominal pain (can look like cirrhosis)	Acute/subacute onset, hepatic vein obstruction on Doppler/CT
Non-progressive Fatty Liver (simple steatosis without fibrosis)	Steatosis on imaging	No fibrosis on elastography/biopsy, absence of portal hypertension signs
Biliary Obstruction (choledocholithiasis, strictures, cholangiocarcinoma)	Jaundice, pruritus, cholestatic LFTs	Dilated bile ducts on ultrasound/MRCP, relief after obstruction removed
Infiltrative Diseases (lymphoma, leukemia, metastases)	Hepatomegaly, abnormal LFTs	Systemic features (weight loss, lymphadenopathy), focal lesions on imaging, biopsy confirms

Granulomatous Liver Disease (Sarcoidosis, TB)	Chronic hepatomegaly, abnormal liver enzymes	Systemic signs (lung, lymph nodes), biopsy with granulomas
Amyloidosis	Hepatomegaly, cholestasis, mild ascites	Systemic amyloid involvement, Congo red staining on biopsy
Non-hepatic Hyperbilirubinemia (Gilbert's syndrome, hemolysis)	Jaundice	Isolated unconjugated hyperbilirubinemia, normal liver enzymes, no fibrosis
Parasitic Liver Disease (Schistosomiasis, Echinococcosis)	Hepatomegaly, portal hypertension, splenomegaly	Travel/residence in endemic area, serology, characteristic imaging findings

DIAGNOSTIC ALGORITHM



MANAGEMENT GOALS

The goals are to remove the cause, slow fibrosis, prevent complications, detect cancer early, support the patient's wellbeing, and plan timely transplantation when needed.

Management Principles

- **Identify and treat underlying cause:** antiviral therapy for viral hepatitis, alcohol cessation, metabolic control for MASLD/MAFLD, immunosuppression for autoimmune disease.
- **Slow disease progression:** lifestyle modification (alcohol abstinence, weight control, healthy diet), appropriate drug therapy, comorbidity management (e.g., diabetes, dyslipidemia).
- **Prevent complications:** regular surveillance and timely management of varices, ascites, encephalopathy, and infections.
- **Hepatocellular carcinoma (HCC) surveillance:** abdominal ultrasound (± AFP) every 6 months; AFP should not be used alone.
- **Vaccination:** hepatitis A and B, influenza, pneumococcal, and others as indicated.
- **Medication review:** avoid hepatotoxic agents (NSAIDs, certain herbs, high-dose paracetamol).
- **Supportive Care and Quality of Life**
  - Nutritional support with adequate protein and energy intake.
  - Symptom control (e.g., pruritus, fatigue, pain).
  - Psychosocial support, including addiction services when needed.
- **Advanced Disease Management**
  - Evaluate for liver transplantation in patients with decompensation or advanced disease.
  - Early referral ensures continuity of care and optimizes survival outcomes.

PHARMACOLOGICAL THERAPY

Condition	Indication	Drug	Dose & Route	Duration	Cautions
Hepatitis B	Chronic Hepatitis B with active replication	Tenofovir Disoproxil Fumarate (TDF) / Tenofovir alafenamide (TAF)/Entecavir	Oral, once daily	Long-term or lifelong	Renal monitoring, Bone health
Hepatitis C	Chronic Hepatitis C (all genotypes)	All oral pangenomic DAA recommended (for details see below)	Oral, once daily	12 weeks	Genotype-based; avoid in pregnancy
Autoimmune Hepatitis	Confirmed autoimmune hepatitis	Prednisolone ± Azathioprine	Oral, tapering doses	Maintenance after induction	Monitor CBC, LFTs
Alcoholic Liver Disease	Alcohol use disorder, risk of Wernicke's	Thiamine, Hepatotoxic so avoid in dCLD. Acamprosate is safer.	Oral/IV	Ongoing with abstinence	Avoid hepatotoxic drugs
MASLD/MAFLD (NASH)	NASH or Significant fibrosis	Vitamin E(only in patients who are non diabetic and biopsy proven MASLD), Resmetirom, GLP-1 (semaglutide)	Oral/ S/C	Long-term (monitored)	Use cautiously in diabetics (Vit E)
Ascites	Moderate to severe ascites	Spironolactone (100mg) + Furosemide (40 mg daily)	Oral, titrate	As long as fluid overload persists	Monitor electrolytes, renal function
Encephalopathy	Hepatic encephalopathy	Lactulose (15-30 mL orally every 8-12 h; Rifaximin550 mg orally twice daily in recurrent HE	Oral	Ongoing if recurrent	Adjust dose to stool frequency
Variceal Bleeding	Primary or secondary prophylaxis	Propranolol, carvedilol	Oral	Long-term (beta-blockers)	Monitor BP, HR
HCC	Advanced hepatocellular carcinoma	Sorafenib, Lenvatinib, immunotherapy	Oral/IV	As per oncology protocol	Requires oncology referral

HEPATITIS C: DAA REGIMENS BY CLINICAL SCENARIO

Pretreatment Evaluation

- Confirm HCV RNA
- Fibrosis staging (FibroScan/APRI)
- HBV & HIV screening
- Baseline labs (CBC, LFTs, INR, eGFR)
- Pregnancy test if ribavirin
- Check drug interactions

Regimen Choice

- Non-cirrhotic: SOF/VEL 12w or GLE/PIB 8w
- Compensated cirrhosis: SOF/VEL or GLE/PIB 12w
- Decompensated cirrhosis: SOF/VEL ± Ribavirin 12-24w (avoid protease inhibitors)
- Renal impairment: GLE/PIB 8-12w
- HIV co-infection: same regimens, check ART interactions
- Post-transplant: SOF/VEL or GLE/PIB 12w

On-Treatment Monitoring

- Assess adherence & side effects
- CBC, LFTs, eGFR (if ribavirin)
- Check drug interactions
- Manage comorbidities

Post-Treatment Assessment

- HCV RNA at end of therapy (optional)
- HCV RNA at 12 weeks post-treatment (SVR12)
- SVR12 = cure

Long-Term Follow-Up

- Non-cirrhotic, cured: usually discharge
- Cirrhosis: continue HCC surveillance (US ± AFP every 6 months)
- Counsel on reinfection risk & prevention

Non-Pharmacological Interventions

Non-pharmacological interventions complement pharmacological therapy and improve long-term outcomes:

1. **Lifestyle Modification**
   - Alcohol Abstinence: Absolute avoidance of alcohol is the single most important step in all causes of CLD, particularly in alcohol-related disease and MASLD/MAFLD.
   - Dietary Adjustments:
   - Low-sodium diet (<2 g/day) for ascites and fluid retention.
   - Adequate protein intake (1.2-1.5 g/kg/day) to prevent sarcopenia, unless contraindicated.
   - Balanced calorie intake to maintain healthy body weight.
   - Limit processed foods, sugary drinks, and high-fat meals in MASLD/MAFLD.
   - Weight Management: Gradual weight loss (7-10% of body weight) improves steatosis and insulin resistance.
2. **Exercise and Physical Activity**
   - Regular aerobic and resistance training (≥150 minutes/week of moderate exercise).
   - Helps prevent sarcopenia, improves insulin sensitivity, and enhances quality of life.
   - Exercise prescriptions should be tailored to patient tolerance and cirrhosis severity.
3. **Infection Prevention**
   - **Vaccination:** Hepatitis A, Hepatitis B, influenza, pneumococcal, and other age/region-appropriate vaccines.
   - **Safe Food Practices:** Avoid raw seafood and unpasteurized foods to reduce infection risk.
   - **Hygiene:** Handwashing and safe food handling to minimize bacterial or parasitic infections.
4. **Patient Education and Counseling**
   - Educate patients about disease progression, warning signs (jaundice, GI bleed, confusion), and when to seek urgent care.
   - Lifestyle counseling (alcohol cessation programs, weight management, diabetes control).
   - Encourage caregiver involvement and psychosocial support, especially in advanced disease.

5. **Avoidance of Hepatotoxic Substances**
   - Avoid NSAIDs, high-dose acetaminophen, unnecessary supplements, and unregulated herbal remedies.
   - Medication review at each visit to reduce risk of drug-induced liver injury.

6. **Monitoring and Surveillance**
   - HCC Surveillance: Ultrasound ± AFP every 6 months.
   - Variceal Surveillance: Endoscopy as per Baveno VII criteria.
   - Symptom Monitoring: Maintain symptom diaries (e.g., encephalopathy, ascites, fatigue).

7. **Psychosocial and Nutritional Support**
   - Counseling and support for alcohol and substance cessation.
   - Nutritional counseling to optimize energy and protein intake.
   - Involve dietitians, physiotherapists, and mental health professionals as part of multidisciplinary care.

ASSESSMENT OF RESPONSE

Monitoring response to treatment in CLD involves both clinical and objective parameters.

Domain	Parameters	Indicators of Response
Clinical	Symptoms	Improvement in fatigue, appetite, jaundice, ascites; resolution of complications (e.g., encephalopathy, variceal bleed)
Biochemical	Liver function tests	Declining ALT, AST, bilirubin, increase in Albumin, Stable/normal INR
Diseasespecific	Viral hepatitis	HBV DNA or HCV RNA suppression/undetectable levels
	Autoimmune hepatitis	Normalization of LFTs, reduction in IgG
	MASLD/MAFLD	Improved glycemic control (HbA1c), improved lipid profile, weight reduction
Imaging	Ultrasound, elastography, CT/MRI	Regression or stabilization of fibrosis, absence of new focal lesions, surveillance for hepatocellular carcinoma (HCC)
Prognostic Scoring	MELD (Model for End-Stage Liver Disease)	Stable or improving MELD score indicates favorable prognosis Mortality risk: MELD <10 = 2% at 3 months; MELD >40 = 71-100% at 3 months without transplant
Transplant Assessment	Allocation systems	MELD score used by UNOS (United Network for Organ Sharing) and other transplant networks to prioritize organ allocation fairly
Global Outcomes	Overall disease course	Absence of decompensation episodes, maintained quality of life, stabilization of complications

REVIEW, FOLLOW-UP & ADJUSTMENT

- Patients with chronic liver disease should be reviewed every 3 to 6 months with liver function tests (LFTs), abdominal imaging, and alpha-fetoprotein (AFP) levels to monitor disease status and screen for hepatocellular carcinoma.

- Therapy should be adjusted based on drug side effects, evidence of disease progression, and patient compliance.

- Regular follow-up ensures timely identification of complications and allows for personalized treatment modifications.

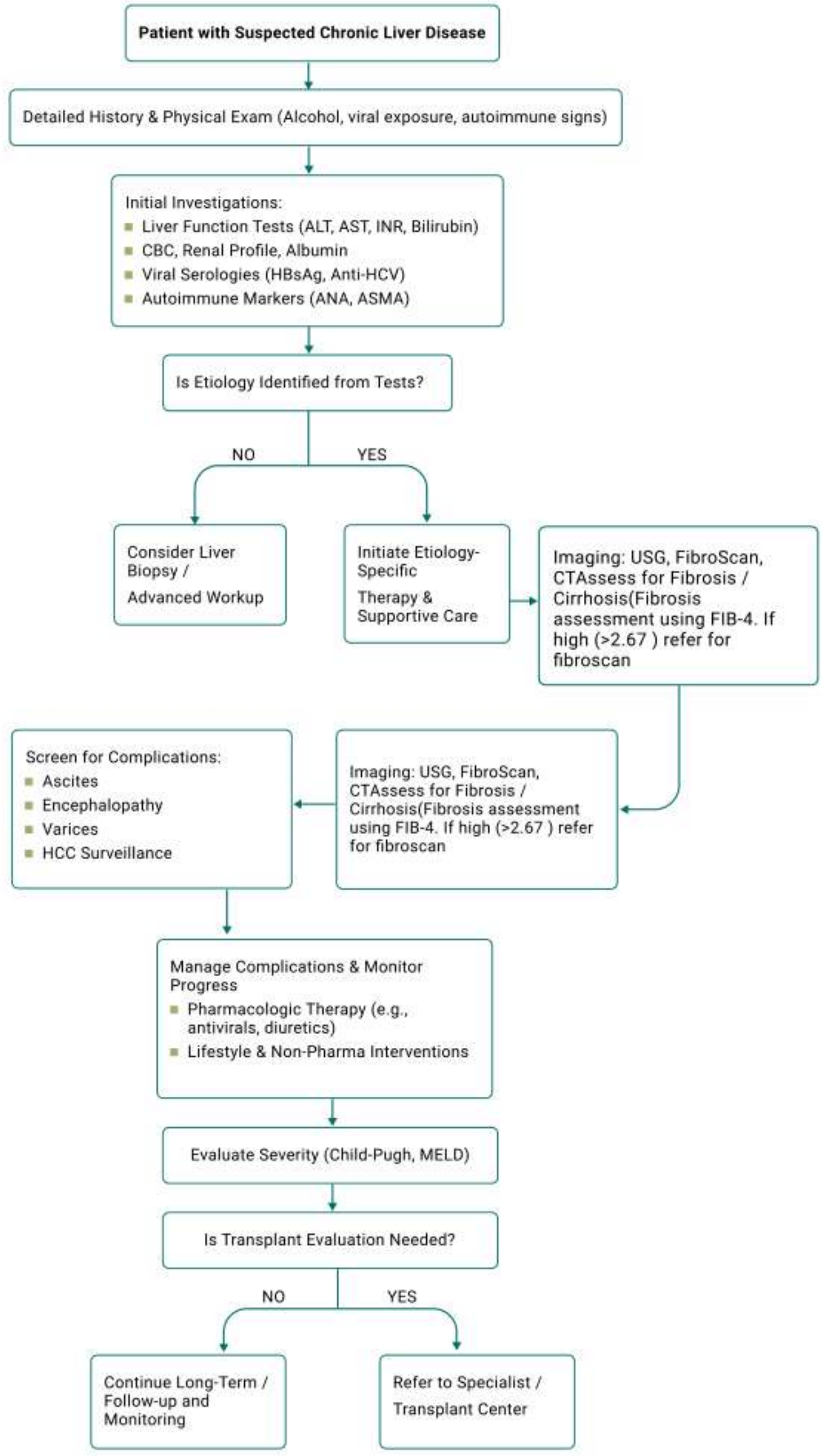
- Nutritional and sarcopenia assessment should be done every 6 monthly and managed accordingly

STEP-UP / STEP-DOWN CONSIDERATIONS

- Treatment intensity in chronic liver disease may need adjustment based on patient status. A step-up approach is warranted when symptoms worsen, complications arise, or response to current therapy is inadequate. This may involve adding medications, increasing doses, or referring for transplant evaluation.

- Conversely, a step-down approach is considered in patients with stable disease, significant side effects, or sustained remission, allowing dose reduction or withdrawal under close monitoring. This balance helps minimize toxicity while maintaining control over disease progression.

Diagnostic & Management Flowchart for Chronic Liver Disease



COMPLICATIONS

CLD can give rise to a range of serious complications that significantly impact prognosis and quality of life.

Complication	Underlying Mechanism	Clinical Features	Key Management / Surveillance
Ascites	Portal hypertension, hypoalbuminemia	Abdominal distension, shifting dullness, respiratory discomfort	Salt restriction, diuretics (spironolactone ± furosemide), large-volume paracentesis, albumin infusion, SBP prophylaxis
Variceal Bleeding	Dilated gastroesophageal varices due to portal hypertension	Hematemesis, melena, hematochezia, shock in severe cases	Non-selective beta-blockers (propranolol, carvedilol), endoscopic variceal ligation (EVL), vasoactive drugs (terlipressin), TIPS if refractory (For details see UGIB guidelines)
Spontaneous Bacterial Peritonitis (SBP)	Infection of ascitic fluid without obvious source	Fever, abdominal pain, encephalopathy, worsening ascites	Diagnostic paracentesis (PMN ≥250/μL), empirical antibiotics (3rd-gen cephalosporins), secondary prophylaxis
Hepatic Encephalopathy (HE)	Accumulation of toxins (ammonia, others) due to impaired detoxification	Confusion, asterixis, altered consciousness	Lactulose, rifaximin, dietary protein optimization, correction of precipitating factors
Hepatorenal Syndrome (HRS)	Renal vasoconstriction due to severe portal hypertension and splanchnic vasodilation	Progressive renal failure, oliguria, rising creatinine	Albumin, vasoconstrictors (terlipressin, norepinephrine), avoidance of nephrotoxins, liver transplantation
Hepatocellular Carcinoma (HCC)	Malignant transformation in cirrhotic liver	Often asymptomatic; detected on surveillance imaging	Regular surveillance with ultrasound ± AFP every 6 months; surgical resection, ablation, TACE, systemic therapy, or liver transplantation depending on stage

Referral for Specialist Consultation

- **Primary Care Level to Secondary Care**
  - Any patient with suspected CLD (persistent abnormal LFTs >6 months, stigmata of liver disease).
  - Patients with unexplained hepatomegaly, jaundice, or ascites requiring further evaluation.
  - Positive screening for HBsAg, anti-HCV, or autoimmune/metabolic markers.
  - Early or mild complications (ascites, mild encephalopathy) needing diagnostic confirmation.

- **Secondary Care to Tertiary Care (Hepatology / Liver Unit)**
  - Decompensated cirrhosis: ascites, variceal bleeding, recurrent encephalopathy.
  - Refractory or recurrent ascites despite optimal diuretic therapy.
  - Suspected HCC on ultrasound or elevated AFP.
  - Portal vein thrombosis or other vascular complications.
  - Acute-on-chronic liver failure or rapidly progressive liver dysfunction.
  - Complex autoimmune or metabolic liver disease not controlled with standard therapy.
  - Requirement of specialized procedures: endoscopic variceal ligation, TIPS, or liver biopsy.

- **Tertiary Care to Transplant Center**
  - Advanced cirrhosis with poor prognosis (high MELD or Child-Pugh C).
  - Treatment-refractory complications (ascites, variceal bleeding, hepatic encephalopathy, hepatorenal syndrome).
  - Confirmed or high suspicion of HCC within transplant criteria.
  - Progressive metabolic/genetic liver diseases (e.g., Wilson's disease, hemochromatosis) not responding to therapy.
  - Candidates for liver transplantation: evaluation and listing through recognized transplant networks (e.g., UNOS - United Network for Organ Sharing).

Prognosis

Natural History: CLD progresses from chronic inflammation to fibrosis to cirrhosis to complications (decompensated cirrhosis, hepatocellular carcinoma).Rate of progression varies by etiology, comorbidities, and lifestyle factors.

Favorable Prognostic Factors: Early diagnosis and treatment of underlying cause (e.g., HBV/HCV cure, alcohol abstinence, metabolic control).Absence of portal hypertension or complications. Good nutritional status and preserved muscle mass (avoiding sarcopenia).

Poor Prognostic Indicators:

- Decompensated cirrhosis (ascites, variceal bleeding, hepatic encephalopathy, jaundice).
- Development of hepatocellular carcinoma (HCC).
- Clinically significant portal hypertension (HVPG ≥10 mmHg or surrogate markers).
- Persistent alcohol use, obesity, uncontrolled diabetes.
- Recurrent or severe infections (esp. SBP, sepsis).

Prognostic Scoring Systems:

- Child-Pugh Score: estimates severity and survival; useful for clinical decision-making.
- MELD Score (Model for End-Stage Liver Disease): predicts 3-month mortality; used for liver transplant allocation (higher MELD = worse prognosis).
  - MELD <10: 2% 3-month mortality.
  - MELD >40: >70% 3-month mortality without transplant.

Progression Risks by Etiology:

- Hepatitis B/C: Risk of cirrhosis and HCC if untreated.
- MASLD/MAFLD: Accelerated by obesity, diabetes, and alcohol use.
- Alcohol-related disease: Risk worsens with ongoing alcohol intake.
- Autoimmune/Metabolic conditions: Variable course; can be slowed with early targeted therapy.

Overall Outlook:

- **Compensated cirrhosis:** Median survival >10 years.
- **Decompensated cirrhosis:** Median survival 2-4 years without transplant.
- **Liver transplantation:** Dramatically improves survival and quality of life in eligible patients.

PREVENTION AND PROMOTION OF HEALTH

- Primary prevention focuses on reducing risk factors through universal hepatitis B vaccination (including birth dose), targeted HBV/HCV screening, safe blood and injection practices, and public education. Alcohol harm reduction is essential despite legal restrictions, and rising metabolic liver disease calls for promoting healthy diets and physical activity. Food safety measures include aflatoxin monitoring and enforcement of standards.

- Secondary prevention emphasizes early detection via national screening protocols for high-risk groups, integration of elastography and ultrasound at hospitals, training of primary care providers, and family screening with vaccination.

- Tertiary prevention aims to reduce complications by standardizing cirrhosis management, establishing referral pathways to tertiary centers, enhancing HCC surveillance, expanding access to antiviral therapies, and initiating a liver transplant referral program.

- Health promotion includes culturally sensitive public awareness campaigns, workforce training, and policy integration with NCD programs. Collaboration with WHO and regional partners supports system strengthening.

- Key priorities are sustaining high HBV vaccination coverage, scaling HCV treatment, addressing obesity and diabetes, building diagnostic capacity, and developing cross-border transplant linkages.

PATIENT EDUCATION

Educating patients with CLD improves adherence, prevents complications, and supports active self-care. Patients should understand the nature of the disease, its progression, and risks such as cirrhosis, encephalopathy, and liver cancer. Preventive care, lifestyle changes, and early recognition of warning signs are central to long-term outcomes.

Instructions to the caregivers

Do's	Don'ts
Take medications exactly as prescribed; keep a regular schedule.	Don't drink alcohol—even small amounts are unsafe.
Attend follow-up visits every 3-6 months for blood tests, imaging, and cancer surveillance.	Don't stop or adjust medicines on your own; consult your doctor first.
Completely stop alcohol; seek counseling or support programs if needed.	Don't use NSAIDs (ibuprofen, naproxen) unless approved by your doctor.
Screen family members for hepatitis B/C and ensure vaccination if eligible.	Don't take over-the-counter or herbal supplements without medical advice.
Follow a healthy diet: low sodium, balanced nutrition, adequate protein (unless restricted by your doctor).	Don't eat raw seafood or unpasteurized foods, which increase infection risk.
Maintain healthy weight and control diabetes, blood pressure, and cholesterol.	Don't skip follow-up appointments or cancer screening.
Exercise regularly: ≥150 minutes/week of moderate aerobic activity + resistance training to prevent sarcopenia.	
Get vaccinated for hepatitis A and B, influenza, and pneumococcal infections.	
Keep a symptom diary and involve caregivers if possible.	
Report warning signs immediately: jaundice, confusion, abdominal swelling, bleeding, or black stools.	

REFERENCES

1. Sarin SK, Kumar M, Lau GK, Abbas Z, Chan HLY, Chen CJ, et al. Asia-Pacific clinical practice guidelines on the management of hepatitis B: A 2015 update. Hepatol Int. 2016;10(1):1-98.

2. Omata M, Kanda T, Wei L, Chuang WL, Pyrsopoulos NT, Hanna GJ, et al. APASL consensus statements and recommendations for hepatitis C prevention, epidemiology, and laboratory testing. Hepatol Int. 2016;10(5):869-986.

3. You H, Cheng X, Song J, et al. Guidelines for the Prevention and Treatment of Chronic Hepatitis B, China 2022. (East Asia expert opinion) GlobalHep. 2023.

4. WHO. WHO publishes new guidelines on chronic hepatitis B prevention, diagnosis and treatment. WHO; 2024 Mar 29 [cited 2025 Sep 22]. Available from: https://www.who.int/news/item/29-03-2024-who-publishes-updated-guidelines-on-hepatitis-b

5. Sandhu HS, Roesel S, Sharifuzzaman M, Chunsuttiwat S, Tohme R. Progress Toward Hepatitis B Control — South-East Asia Region, 2016-2019. MMWR Morb Mortal Wkly Rep. 2020;69(30):988-992. CDC

6. Ramasamy S, Khatri R, Shukla S, et al. Eliminating Viral Hepatitis from India and Southeast Asia: Opportunities and Challenges. PM&R. 2024;16(1):xx-xx.

7. American Association for the Study of Liver Diseases. New MASLD nomenclature [Internet]. Washington (DC): AASLD; 2023 [cited 2025 Sep 22]. Available from: https://easl.eu/news/new_fatty_liver_disease_nomenclature-2/

8. European Association for the Study of the Liver. New fatty liver disease nomenclature announced [Internet]. Geneva: EASL; 2023 [cited 2025 Sep 22]. Available from: https://easl.eu/news/new_fatty_liver_disease_nomenclature-2/

9. Rinella ME, Lazarus JV, Ratziu V, Francque SM, Sanyal AJ, Kanwal F, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. J Hepatol. 2023;79(4):745-59.

10. EASL-EASD-EASO Clinical Practice Guidelines on metabolic dysfunction-associated steatotic liver disease (MASLD). J Hepatol. 2024;81(1):1-36.

11. Rinella ME, Lazarus JV, Ratziu V, Kanwal F, Sanyal AJ, Francque S, et al. Updating nomenclature for fatty liver disease: consensus-driven proposal. Hepatol Commun. 2023;7(10):e10824973.

12. European Association for the Study of the Liver. EASL Clinical Practice Guidelines on the management of hepatitis B virus infection. J Hepatol. 2025;83(2):502-583.

13. European Association for the Study of the Liver. EASL Recommendations on Treatment of Hepatitis C: Final update of the series. J Hepatol. 2020;73(5):1170-1218.

14. American Association for the Study of Liver Diseases. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 Hepatitis B guidance. Hepatology. 2018;67(4):1560-1599.

15. European Association for the Study of the Liver. EASL Recommendations on Treatment of Hepatitis C 2020. J Hepatol. 2020 Nov;73(5):1170-1218.