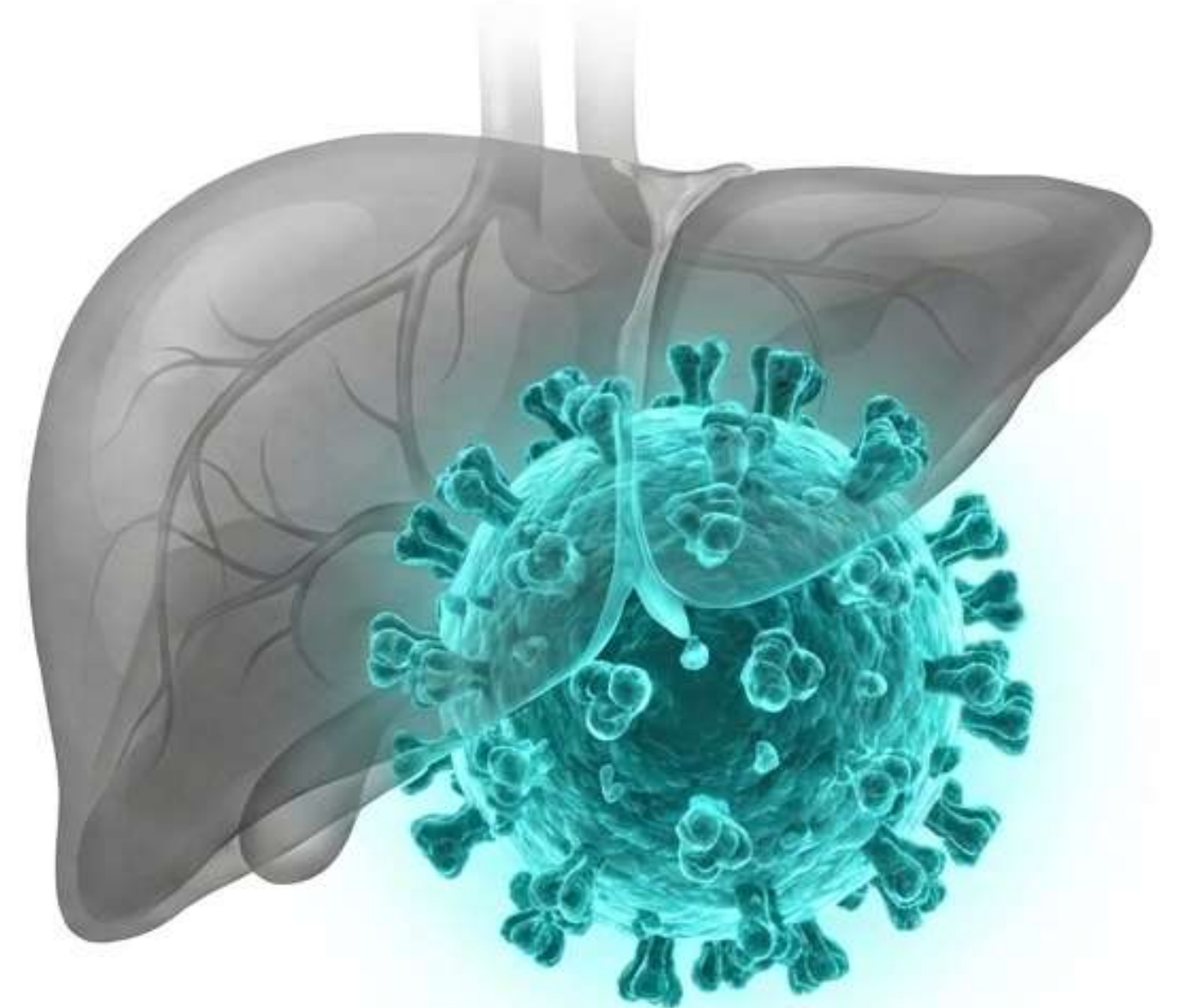


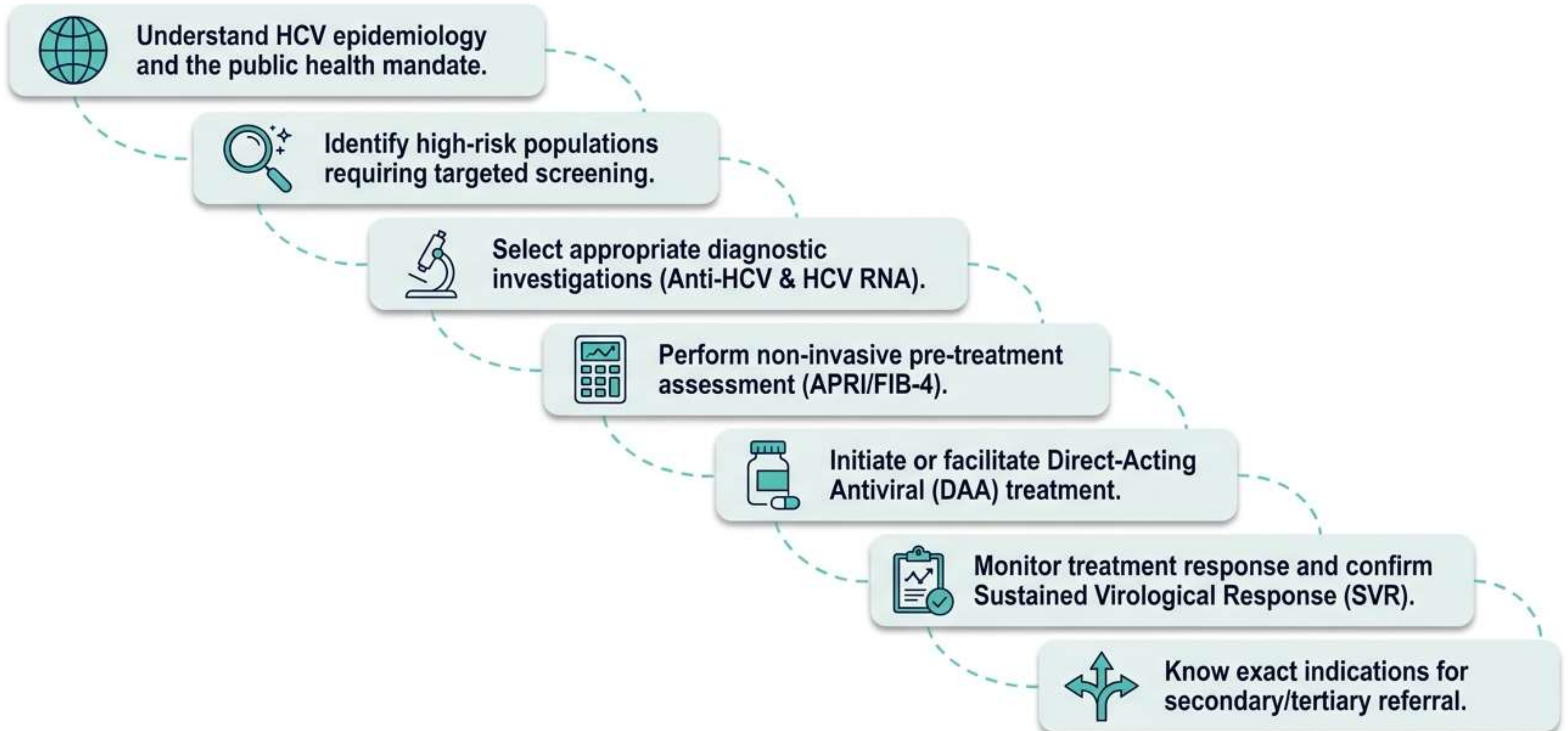
Hepatitis C: Identifying High-Risk Groups for Timely Testing and Treatment

From Screening to Cure in Primary Care

Dr. Mohd Hazizul bin Ab Samad
Family Medicine Specialist
Klinik Kesihatan Jalan Mengkibol
27 July 2026



Learning Objectives

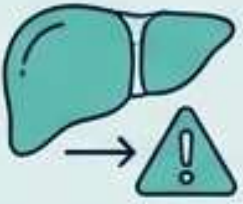


Introduction to Hepatitis C



The Pathogen

RNA virus of the Flaviviridae family.
Blood-borne transmission.



The Disease

Often transitions from acute to persistent chronic infection.
A major global driver of cirrhosis and Hepatocellular Carcinoma (HCC).



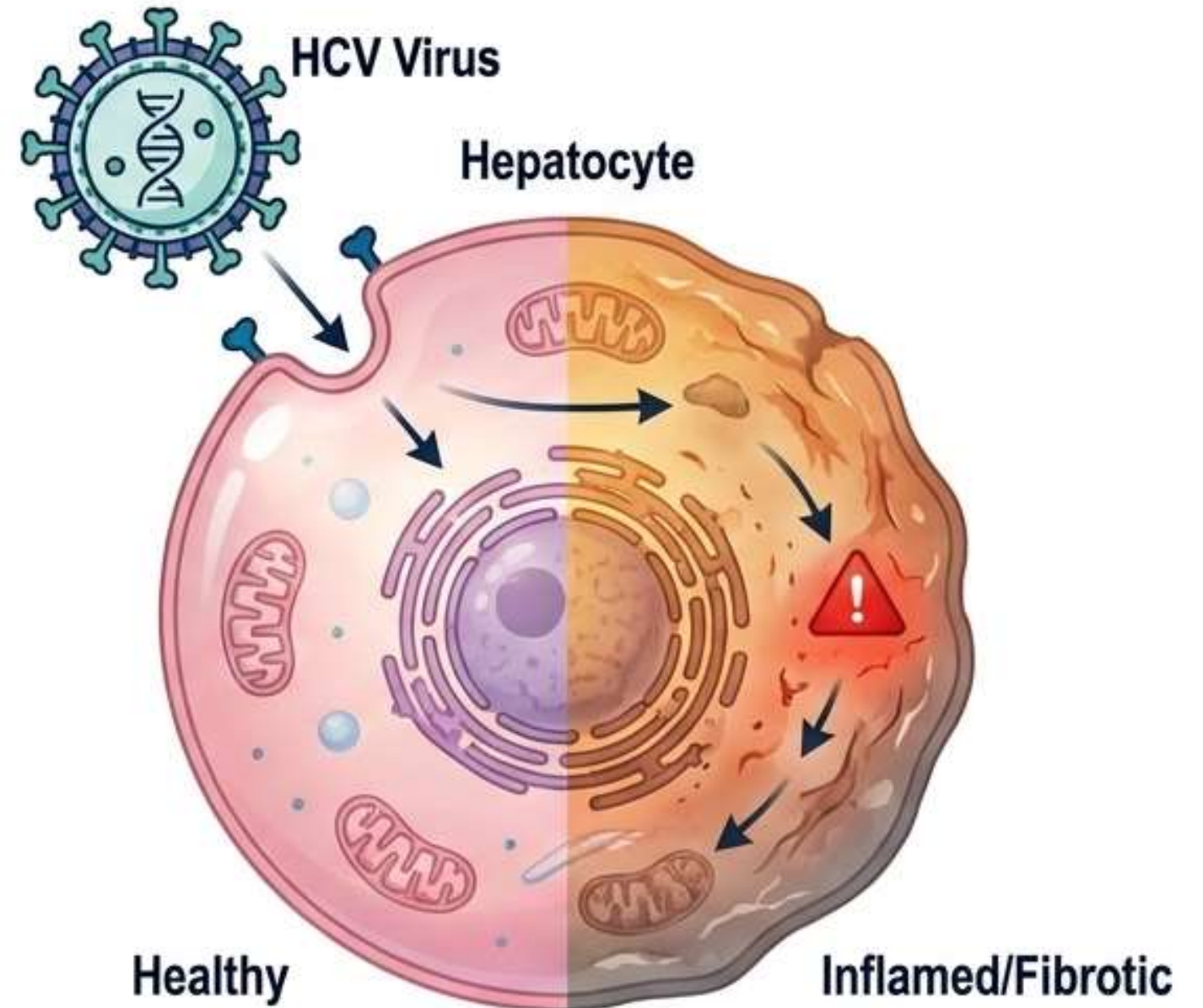
The Paradigm Shift

Fully curable disease. Direct-Acting Antivirals (DAAs) offer short durations (12–24 weeks) with exceptional efficacy and tolerability.



The Global Mandate

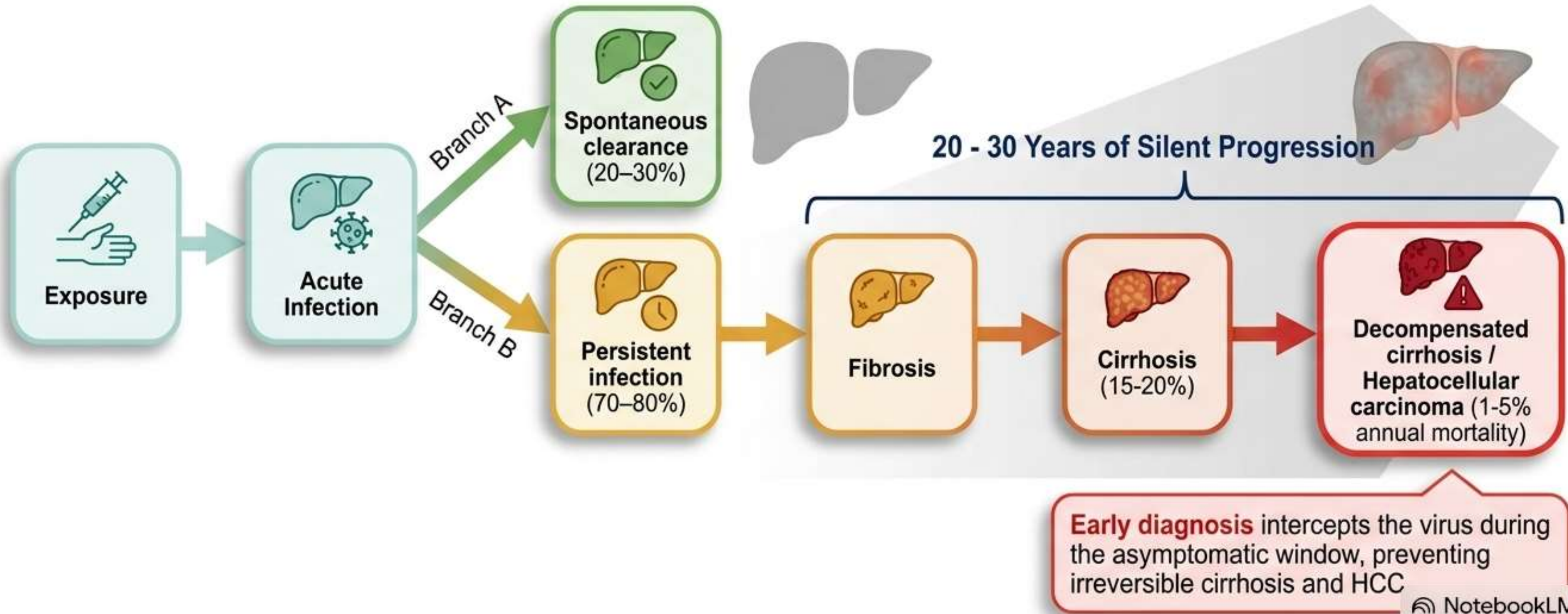
WHO target to eliminate viral hepatitis as a public health threat by 2030.



Key Insight: HCV is no longer a lifelong chronic condition to be managed; it is a short-term infection to be cured.

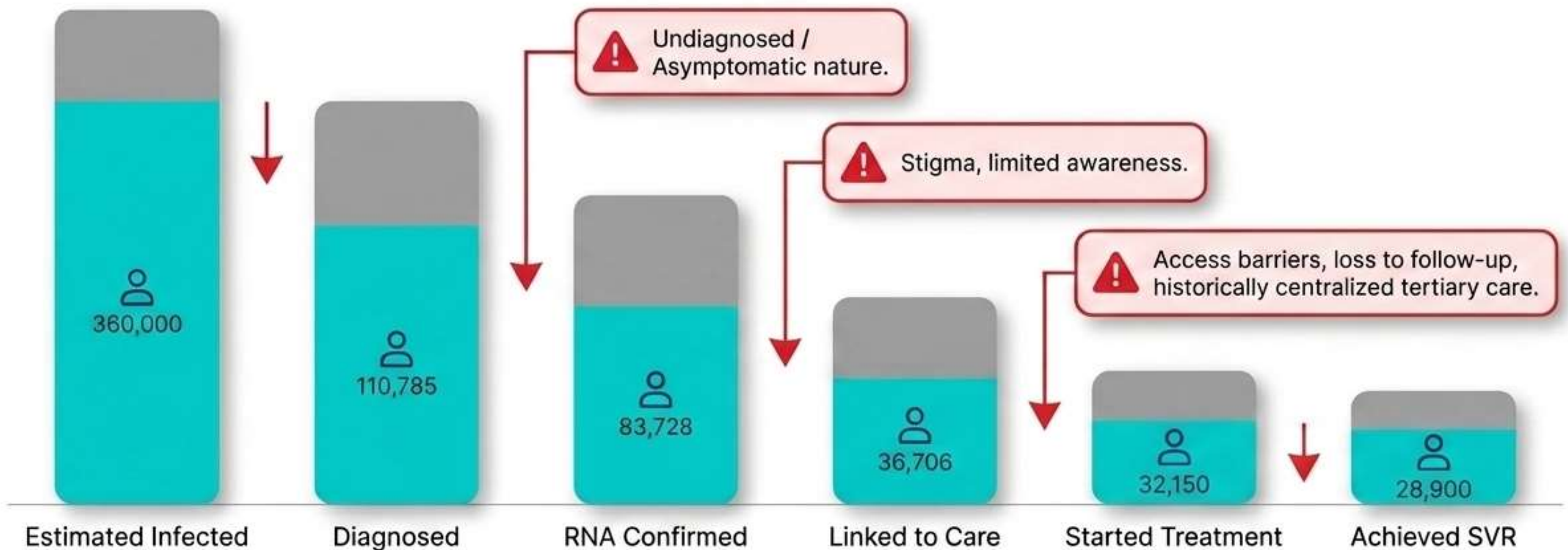
Natural History of HCV: The Decades of Silence

Disease progression is remarkably slow and silent. Most patients remain completely asymptomatic for years, making early diagnosis critical to prevent irreversible architectural liver damage.



Gaps Along the Hepatitis C Care Continuum

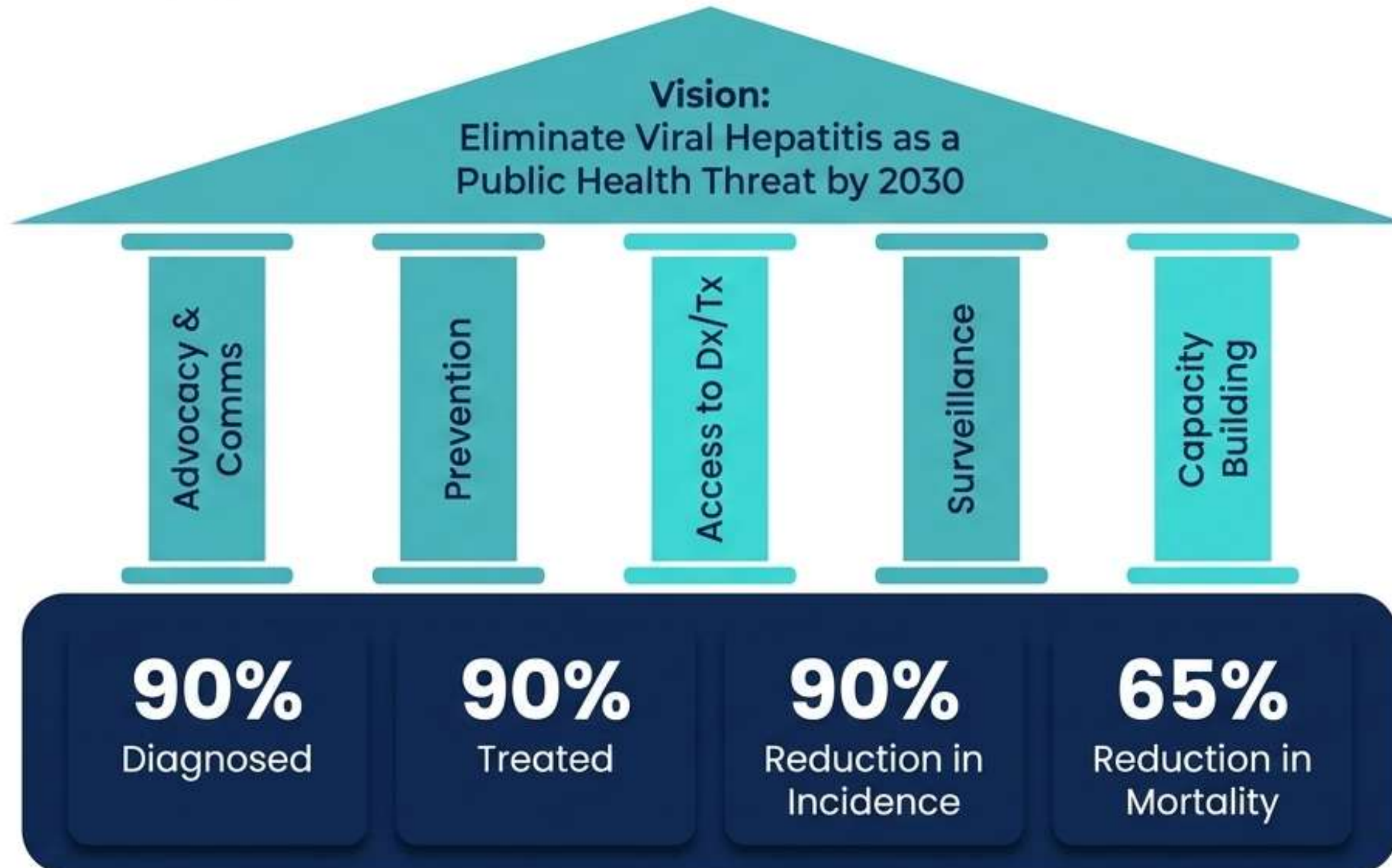
Despite highly effective treatments, millions of patients fall through the cracks of the healthcare system. Our goal is to **plug these leaks at the primary care level**.



The failure to cure HCV is systemic, not biological.
Decentralizing care directly addresses access and linkage barriers.

National Strategic Plan for Viral Hepatitis (2019–2023)

Malaysia's comprehensive strategy aligns with the WHO vision to eliminate viral hepatitis as a public health threat by 2030.



Global Epidemiology: A Worldwide Threat

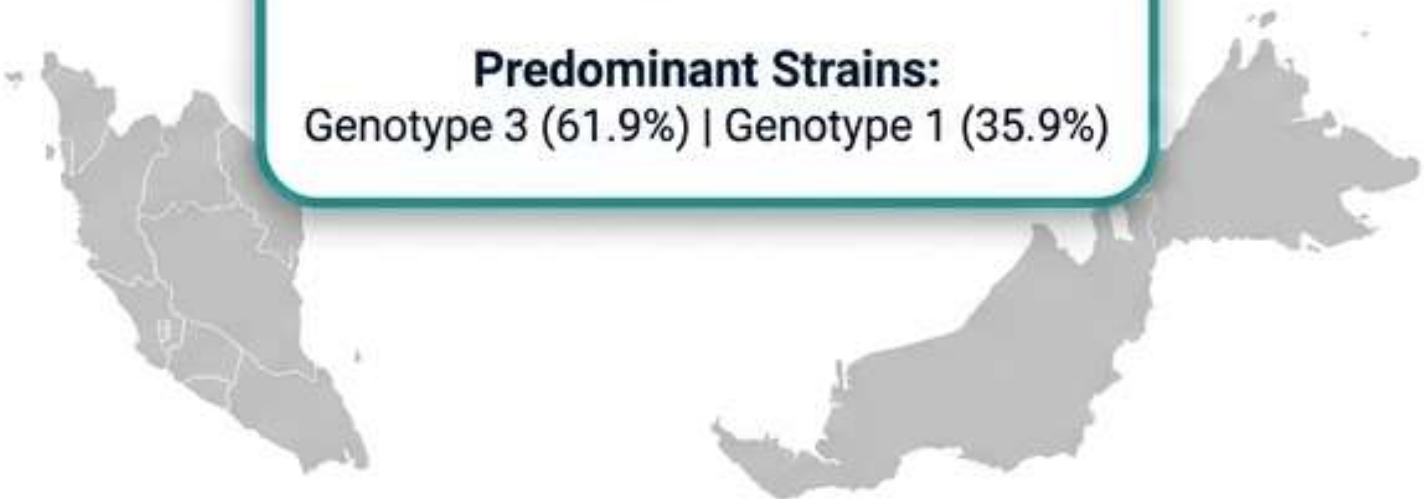
Hepatitis C remains a leading cause of preventable liver-related death globally, historically hampered by the high cost of treatment and lack of systematic screening.



We possess the biological cure, but lack the global screening infrastructure.

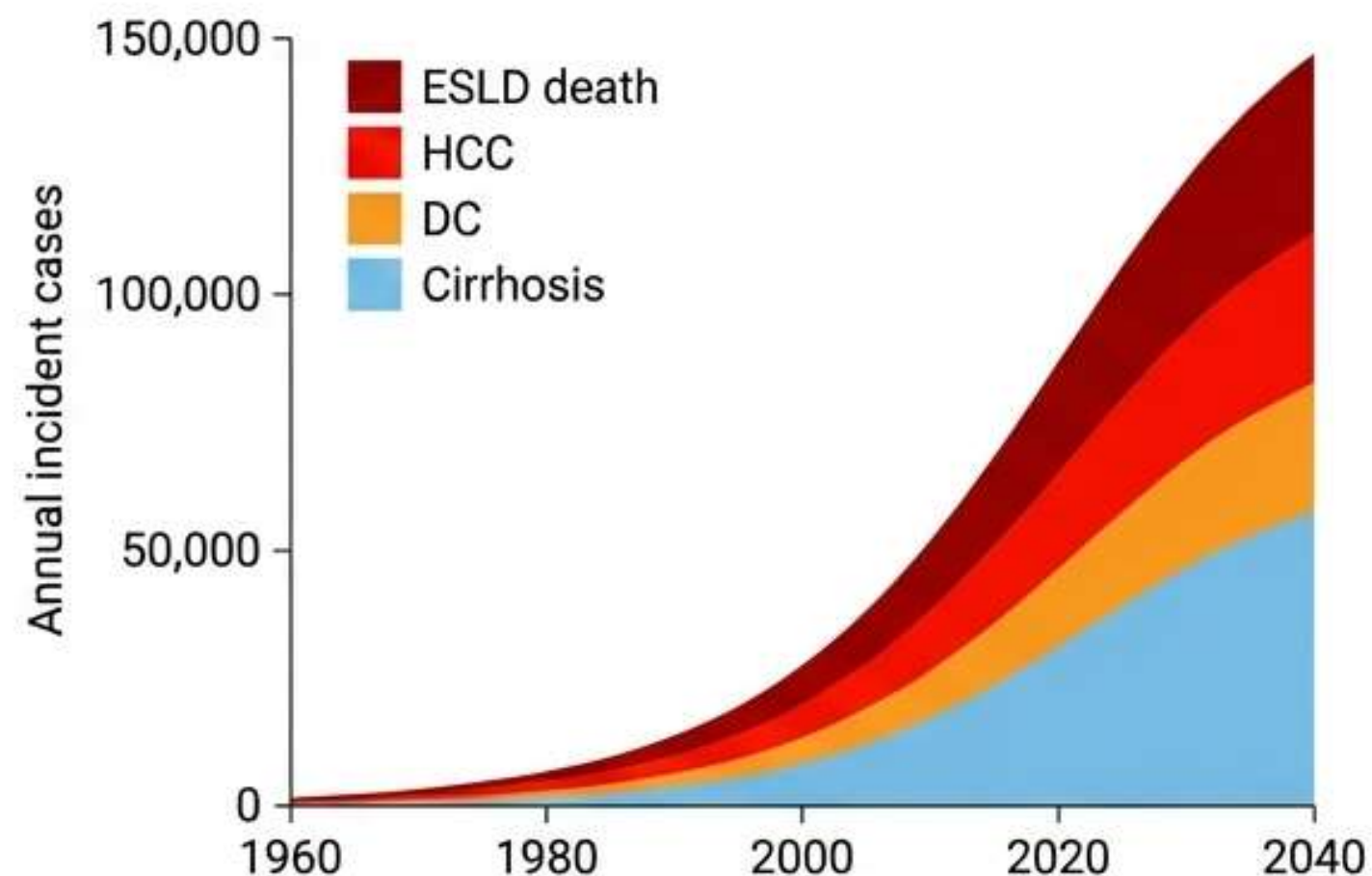
Epidemiology in Malaysia: The Cost of Inaction

Malaysia faces a severe and rising HCV burden. Projections indicate exponential growth in End-Stage Liver Disease (ESLD) and HCC if radical decentralization and screening are not implemented.



453,700 estimated anti-HCV positive individuals (2.5% prevalence in ages 15-64).

Predominant Strains:
Genotype 3 (61.9%) | Genotype 1 (35.9%)



Over 380,000 Malaysians remain completely undiagnosed.
The tertiary system alone cannot handle the impending wave of ESLD.

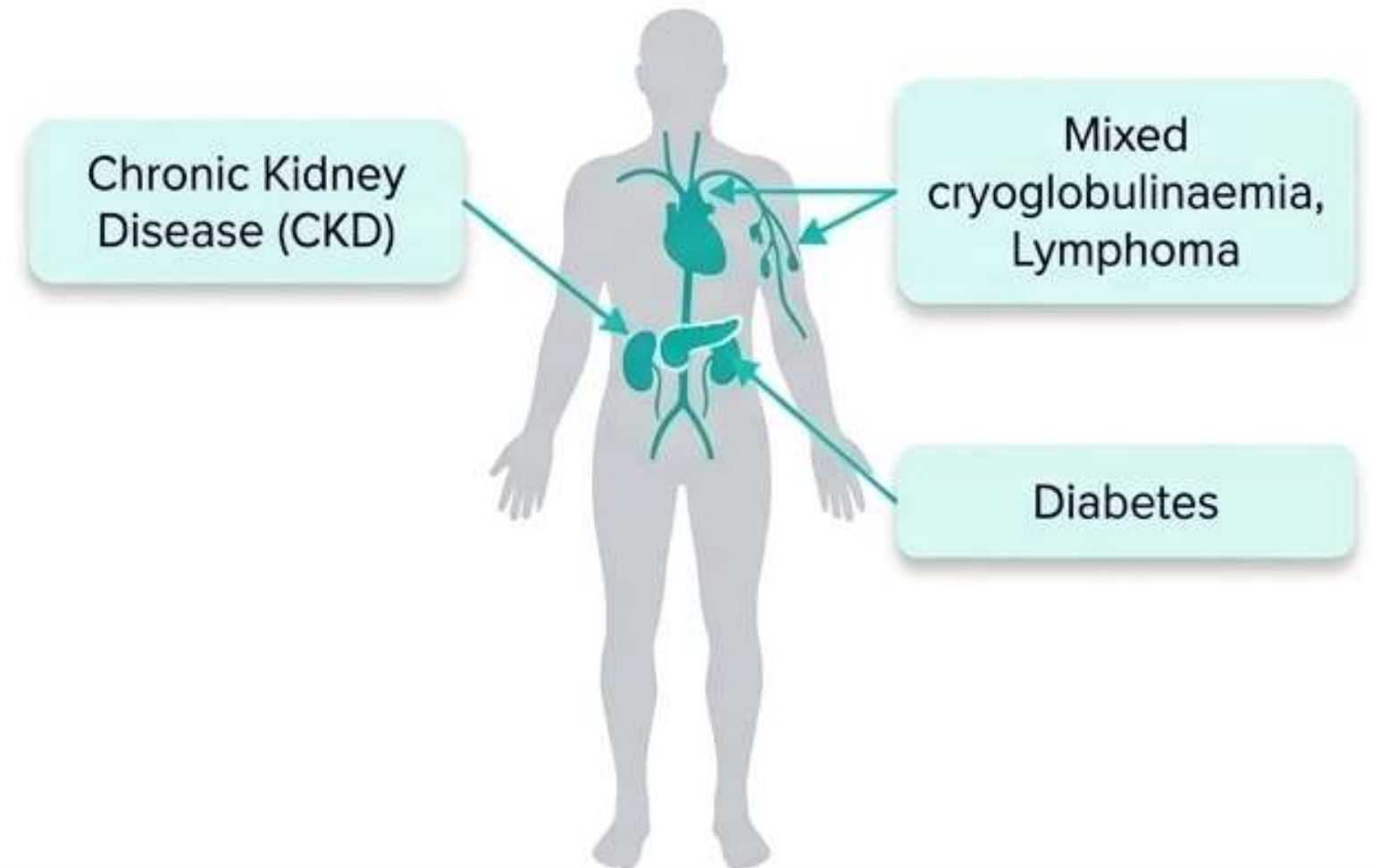
Clinical Manifestations: The Invisible Epidemic

Hepatitis C is a systemic viral infection, not just a liver disease. Because the hepatic presentation is overwhelmingly silent, waiting for symptoms ensures late-stage diagnosis.

Clinical Spectrum Matrix

Acute	 Usually asymptomatic. Rarely jaundice, malaise, nausea.
Chronic	 Often asymptomatic. Mild fatigue, arthralgia.
Late Disease	 Ascites, variceal bleeding, encephalopathy.

Anatomical Mapping



The disease is invisible. The timeline is slow. Therefore, primary care must proactively screen based on patient risk factors, not clinical symptoms.

Sources of Hepatitis C Infection

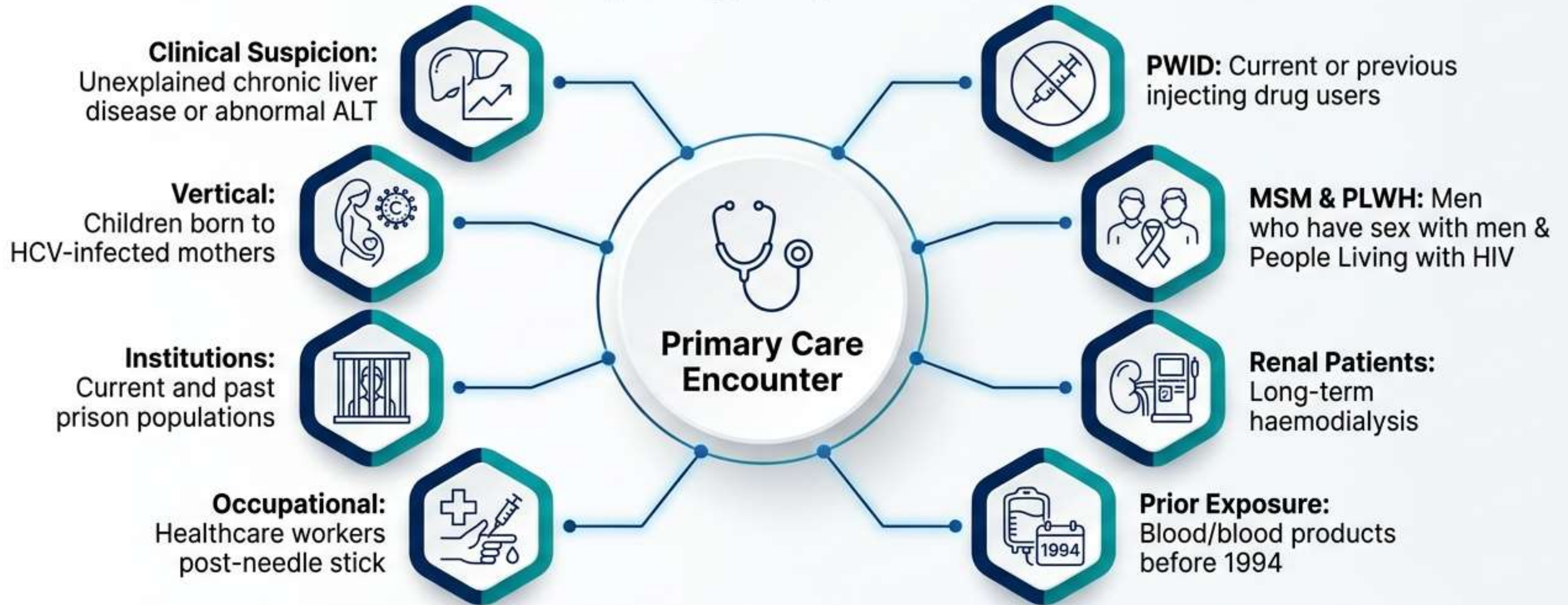
Learning Objective: Accurately identify and communicate confirmed transmission vectors while dispelling common myths.

Transmission Matrix					
	Primary Blood Exposure		Less Common		Not Transmitted
	Injecting drug use (PWID)		Sexual transmission (High risk in MSM or HIV/STI co-infection)		Food
	Blood transfusion or products (Prior to 1994)				Water
	Unsafe medical procedures		Vertical transmission (Mother-to-child)		Casual contact (Hugging, sharing utensils)
	Tattooing				
	Needle sharing				

High-Yield Key Message: HCV is primarily a blood-borne pathogen. In Malaysia, a critical screening trigger is any history of receiving blood products prior to 1994

Targeted Case Finding: Who Should Be Screened?

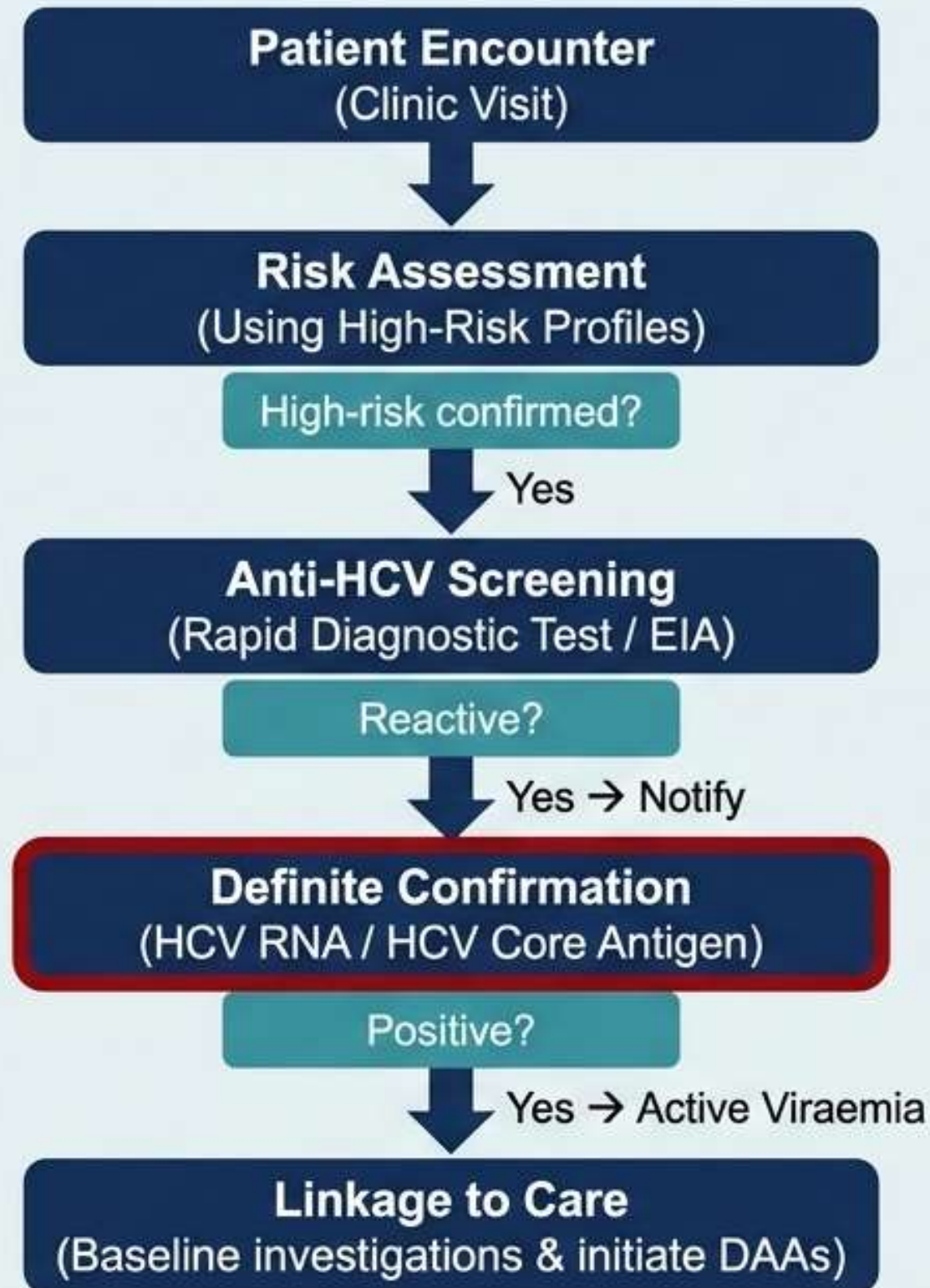
Learning Objective: Recognize specific patient demographic profiles requiring proactive HCV screening during primary care encounters.



High-Yield Key Message: Malaysia utilizes a targeted, risk-based screening strategy. Proactive case-finding in primary care is the cornerstone of the WHO strategy to eliminate hepatitis C by 2030.

Risk-Based Screening Algorithm

Learning Objective: Apply the step-by-step clinical pathway from risk identification to confirmatory testing.

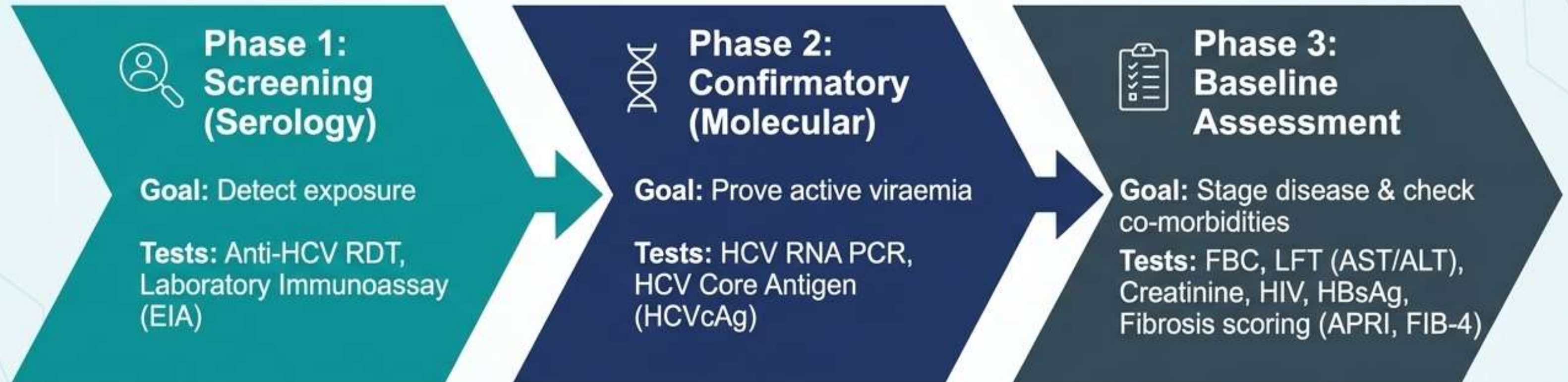


High-Yield Key Message:

A reactive Anti-HCV screening test must **ALWAYS** be followed by a confirmatory molecular test (HCV RNA or Core Antigen) before diagnosing active infection.

Investigations: The Diagnostic Roadmap

Learning Objective: Differentiate the three distinct phases of laboratory investigations required for HCV management.



High-Yield Key Message: Do not initiate **Phase 3** (baseline staging) until **Phase 2** (confirmatory active viraemia) is conclusively proven.

Serological Assays: The First Line

Learning Objective: Understand the performance characteristics and limitations of initial Anti-HCV testing.

High Sensitivity Screening
(Captures all potential cases)



Specific Confirmation Required

Anti-HCV RDT (Rapid Diagnostic Test)

- 📋 Point-of-care, fast turnaround
- 📋 Excellent for outreach & primary care clinics
- 📋 High sensitivity

ELISA / EIA

- 📋 Laboratory-based, automated
- 📋 Highly reliable

Interpretation Note: Both detect IgG antibodies.
Detectable ~4-10 weeks post-exposure.

High-Yield Key Message: Anti-HCV tests have excellent sensitivity (ruling OUT disease if negative), but cannot differentiate between an active infection and a past, spontaneously resolved infection.

Molecular Assays: Definitive Confirmation

Learning Objective: Compare and select appropriate confirmatory tests to establish active chronic HCV infection.

		HCV RNA PCR	HCV Core Antigen (HCVcAg)
1	Target Detected	Viral Nucleic Acid	Viral Protein
2	Result Type	Quantitative (Viral load in IU/mL) and/or Qualitative	Quantitative / Qualitative (Highly specific alternative to RNA)
3	Clinical Utility in MoH	Gold standard for confirming viraemia & assessing Sustained Virological Response (SVR12)	Cost-effective, faster alternative for confirming active infection
4	Genotyping	Genotyping is done at the physician's discretion if determining specific DAA regimens (mostly GT 3 and 1 locally).	

High-Yield Key Message: HCV Core Antigen (HCVcAg) is officially endorsed by the Malaysian CPG as a valid, operational alternative to HCV RNA for confirming active viraemia.

Synthesis: Interpretation of Laboratory Results

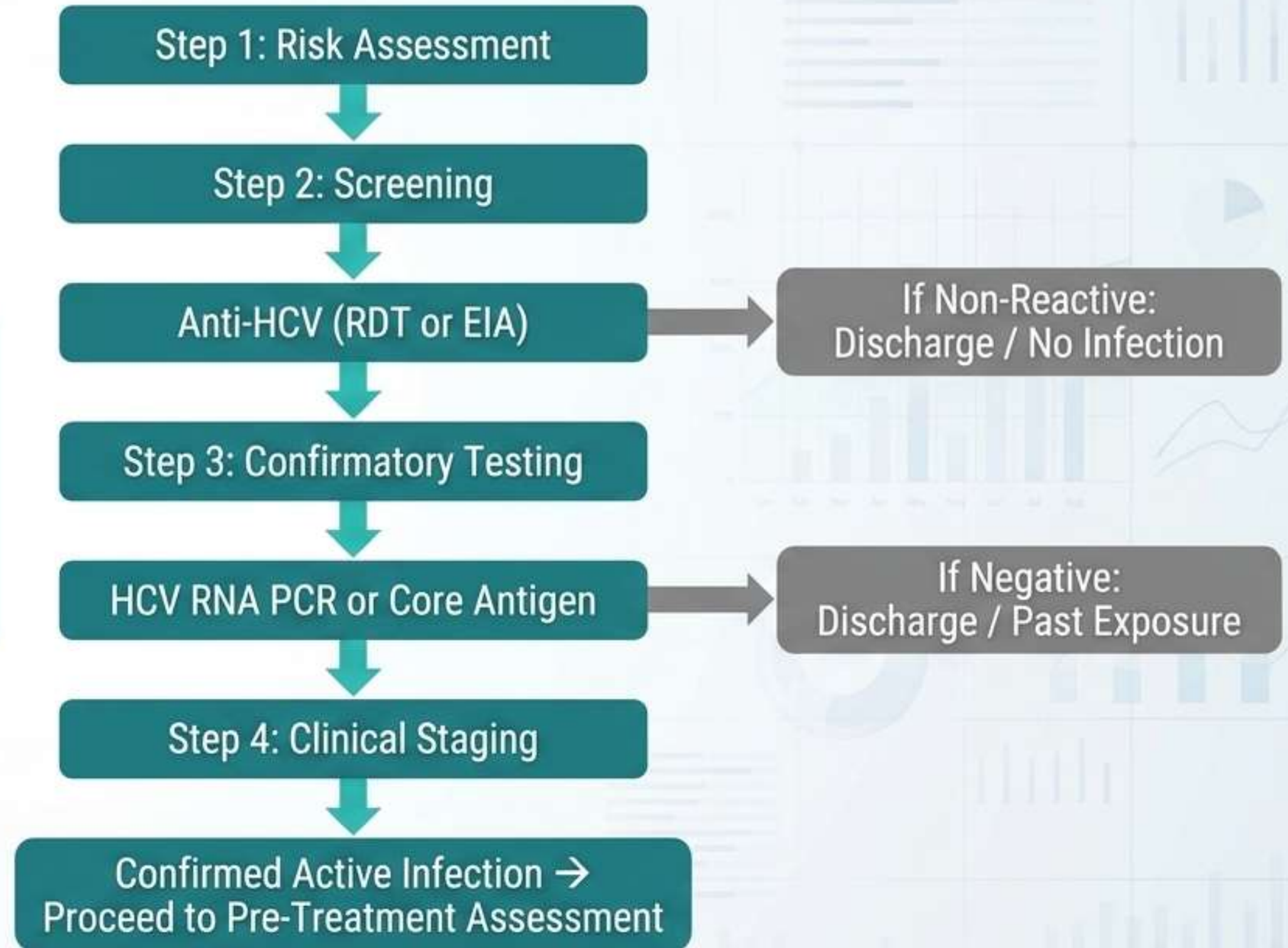
Learning Objective: Synthesize Anti-HCV and RNA/Core Antigen results into definitive clinical diagnoses and actions.

Anti-HCV	RNA / Core Ag	Diagnosis	Action
Non-Reactive (-)	Not Indicated	No HCV Infection	Discharge. (Yearly screening if ongoing risk)
Reactive (+)	Not Detected (-)	Resolved infection (past clearance) OR False positive	No active infection. Discharge if no reinfection risk.
Reactive (+)	Detected (+)	Active Chronic HCV Infection	Mandatory Notification. Proceed to baseline staging & initiate DAAs.

High-Yield Key Message: A Reactive Anti-HCV + Detected RNA/Core Ag = Active Infection.
Notify the case and initiate the DAA treatment pathway immediately.

Diagnostic Laboratory Workflow

 **Crucial Triage:**
Antibodies (Anti-HCV) only
prove exposure.
Active viremia (HCV RNA or Core
Antigen) must be confirmed
prior to treatment.



Mandatory Notification Protocol (Act 342)



**Hepatitis C is
Notifiable within
7 Days
of Diagnosis.**

Applies to BOTH Probable (Anti-HCV+) and Confirmed (HCV RNA/Ag+) cases.



Comprehensive Pre-Treatment Dashboard



Clinical Evaluation

Q1

- Assess symptoms
- Co-morbidities (HTN, DM)
- Ongoing alcohol/drug abuse
- Comprehensive medication review



Baseline Laboratory

Q2

- CBC (focus on platelets for fibrosis scoring)
- LFT (AST/ALT)
- Renal Profile (Creatinine/eGFR)
- INR (mandatory for cirrhotics)



Virology Screen

Q3

- HBV (HBsAg) co-infection
- HIV co-infection



Special Risks

Q4

- Pregnancy status (counseling required for both partners)
- Severe Drug-Drug Interaction (DDI) assessment

Undiagnosed co-infections (HIV/HBV) or drug interactions can severely alter Direct-Acting Antiviral (DAA) efficacy.

Mapping the Liver: Fibrosis Assessment Modalities

Modality	Advantages	Limitations
Blood-Based (APRI / FIB-4)	Cheap, instantly calculated from routine baseline labs (AST, ALT, Plt). Highly accessible in primary care.	Lower specificity for intermediate fibrosis stages.
Imaging (Transient Elastography / FibroScan)	Highly accurate, preferred non-invasive gold standard.	High equipment cost, limited availability in standard primary care clinics.
Imaging (Ultrasound)	Essential for Hepatocellular Carcinoma (HCC) screening.	Poor sensitivity for early-stage fibrosis detection.
Invasive (Liver Biopsy)	Historical gold standard.	Invasive, risk of morbidity. Rarely used in the DAA era.

While Transient Elastography is the preferred imaging modality, APRI and FIB-4 are the validated, accessible workhorses of decentralized primary care

First-Line Triage: The APRI Score

Calculator Card

$$[(\text{AST} / \text{AST Upper Limit of Normal}) / \text{Platelet Count}] \times 100$$

< 1.5
(Non-
Cirrhotic)



≥ 1.5
(Advanced
Fibrosis /
Cirrhosis)

✓ APRI is the primary triage tool in Malaysian primary care due to the universal availability of AST and Platelet labs. A score ≥ 1.5 triggers mandatory HCC surveillance.

Factoring Age & ALT: The FIB-4 Score

Calculator Card

$$(\text{Age} \times \text{AST}) / (\text{Platelet Count} \times \sqrt{\text{ALT}})$$

< 3.25
(Non-
Cirrhotic)

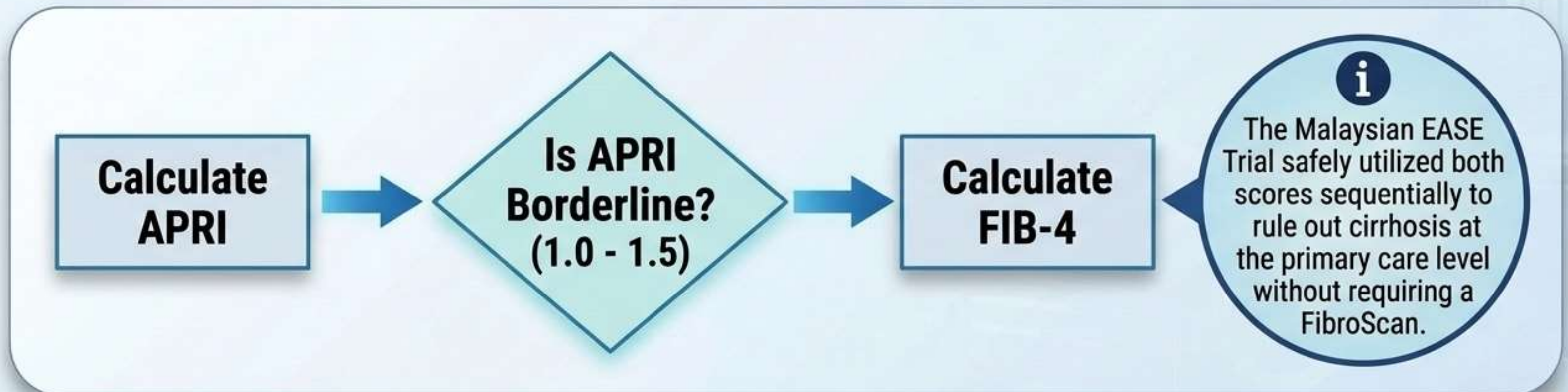


≥ 3.25
(Cirrhosis)

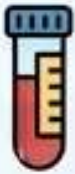
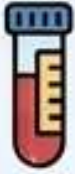
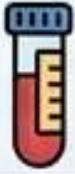
i FIB-4 is highly sensitive for severe fibrosis but is heavily influenced by the patient's age. Older patients naturally trend toward higher scores.

Head-to-Head: APRI versus FIB-4

APRI (First-Line)	FIB-4 (Secondary Validation)
• Variables: 🍷 AST, Platelets • Cirrhosis Cut-off: 1.5 • Limitations: Lower specificity	• Variables: 🩸 Age, AST, ALT, Platelets • Cirrhosis Cut-off: 3.25 • Limitations: Heavily skewed by Age



Grading Severity: Child-Pugh Classification

Clinical Parameter		1 Point	2 Points	3 Points
Encephalopathy		None	Mild	Marked
Ascites		None	Mild	Moderate/severe
Bilirubin ($\mu\text{mol/L}$)		< 34	34 - 50	> 50
Albumin (g/L)		> 35	28 - 35	< 28
INR		< 1.7	1.7 - 2.2	> 2.2

Class A (5-6 points):
Well-compensated

Class B (7-9 points):
Significant functional compromise

Class C (10-15 points):
Decompensated

The Clinical Decision Matrix: Care Pathways

COMPENSATED CIRRHOSIS

- **Profile:** Child-Pugh Class A. Asymptomatic. Normal synthetic function.
- **Primary Care Action:** TREAT. Initiate Direct Acting Antivirals (DAA) within a year.
- **Ongoing Care:** Mandatory 6-monthly Ultrasound for HCC screening & variceal surveillance.



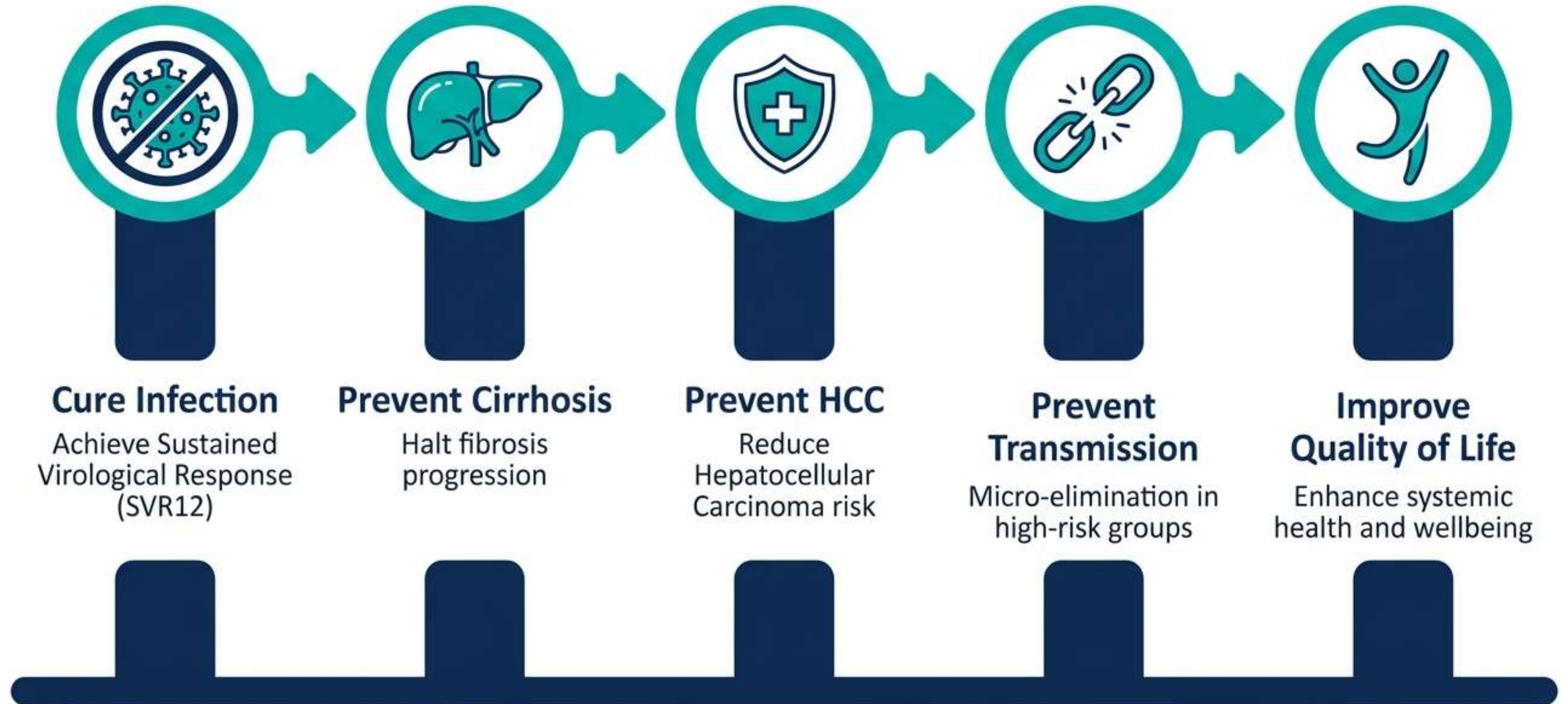
DECOMPENSATED CIRRHOSIS

- **Profile:** Child-Pugh Class B or C. Presence of Jaundice, Ascites, or Encephalopathy.
- **Primary Care Action:** REFER. Urgent referral to Secondary/Tertiary Hepatology center.
- **Clinical Risk:** High risk of mortality and severe complications. Requires specialist DAA dosing.

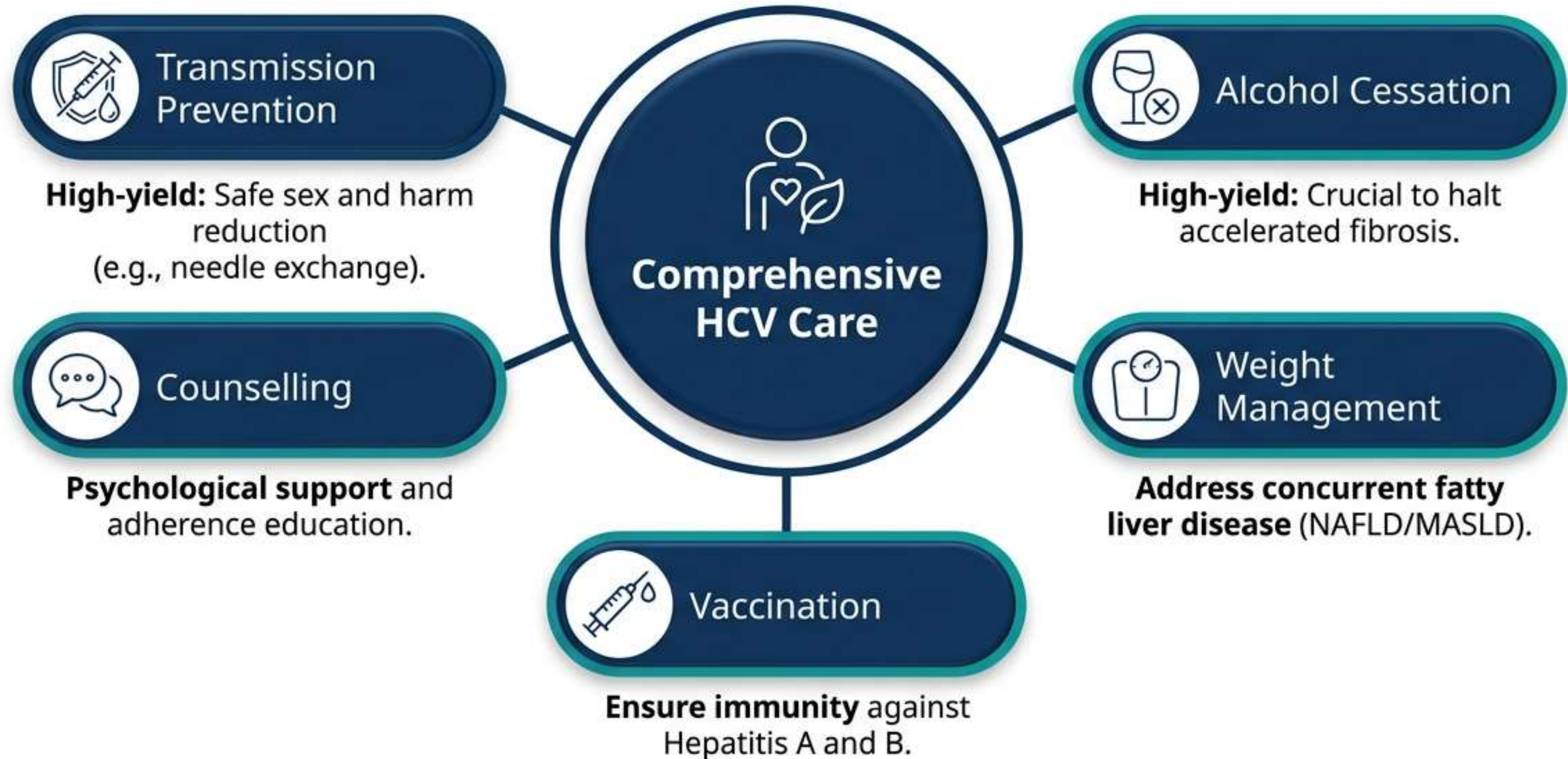


**Primary care safely manages non-cirrhotics and compensated cirrhotics.
Any sign of decompensation mandates immediate tertiary referral.**

Clinical Goals of Hepatitis C Therapy



Establishing the Baseline: Non-Pharmacological Management



Pharmacological Safety: Drug-Drug Interaction Assessment

1. Inventory

Compile all prescribed, OTC, and herbal medications.



2. Check

Process regimen through the Liverpool Hep Drug Interaction Checker



3. Act

Adjust, switch, or proceed based on interaction color coding.



RED: Stop / Contraindicated

Certain statins, specific anticonvulsants, St. John's Wort.



AMBER: Caution / Monitor

Acid-reducing agents (PPIs), specific Antiretroviral Therapy (ART).



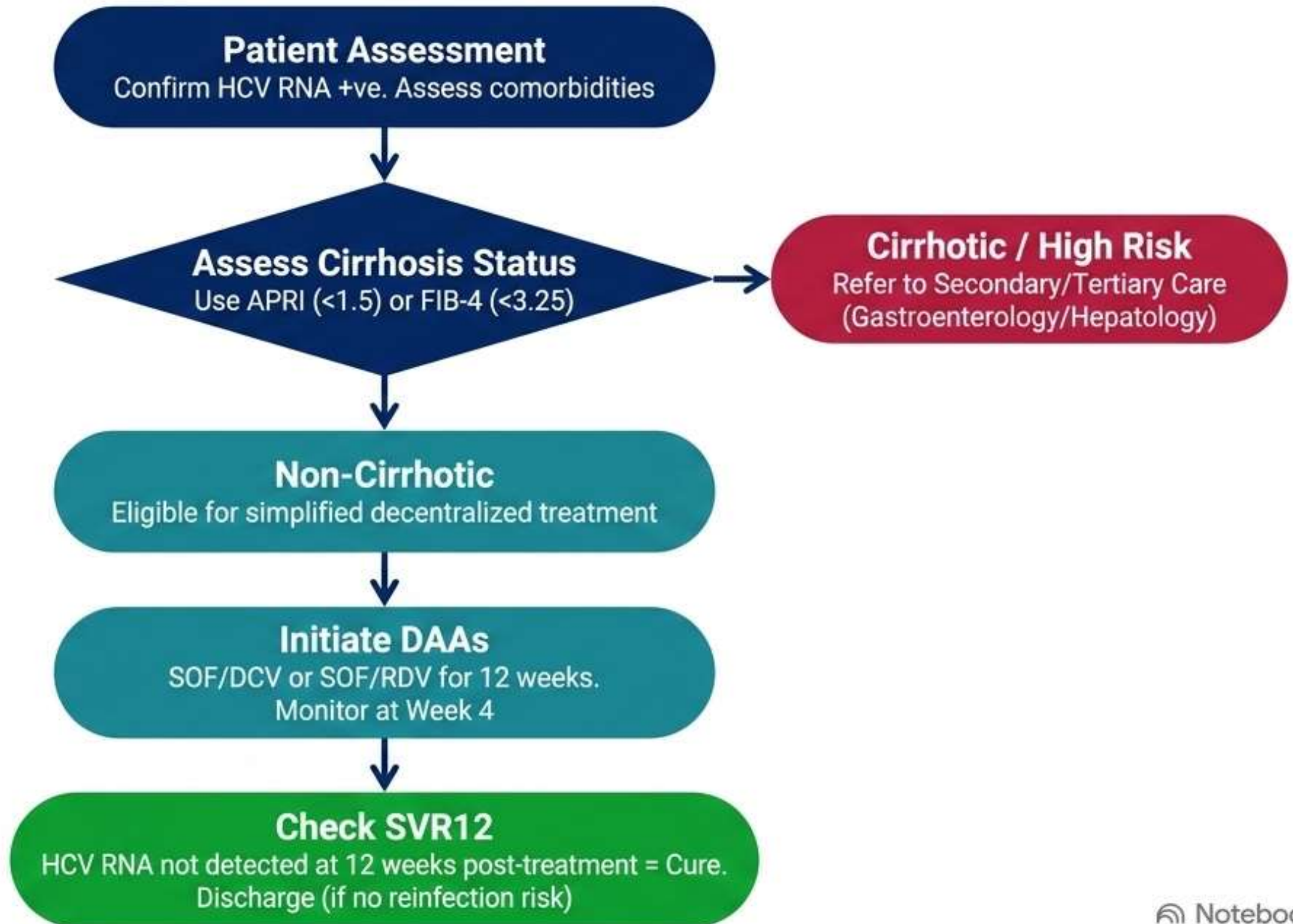
GREEN: Safe / Go

Most anti-hypertensives, standard analgesics.

Direct-Acting Antivirals (DAAs) Available in Malaysia

Regimen	Mechanism & Duration	Indications	Advantages
Sofosbuvir / Daclatasvir (SOF/DCV)	NS5B + NS5A Inhibitor 12 weeks	Pan-genotypic Non-cirrhotic / Compensated Cirrhosis	Well-tolerated, widely accessible in primary care.
Sofosbuvir / Ravidasvir (SOF/RDV)	NS5B + NS5A Inhibitor 12 weeks	Pan-genotypic	Extremely high efficacy for Genotype 3, excellent in HIV co- infection.
Other Regimens	Ledipasvir (LDV), Velpatasvir (VEL), Glecaprevir/Pibrentasvir (GLE/PIB)	Specialist Referral Required	Primarily reserved for specific specialist scenarios or specific comorbidities.

The Blueprint: Simplified Primary Care Treatment Pathway



Local Evidence, Global Standard: The STORM-C Trial



Clinical Implication for FMS: Validates the safety and extreme efficacy of prescribing DAAs at the primary care level.

Future Horizons: The EASE Trial (2026)

Key Finding: 8-week SOF/RDV is non-inferior to 12-week therapy in non-cirrhotic patients.

8-Week Regimen

- SOF/RDV
- ~93-94% SVR12
- Excellent safety profile



12-Week Regimen

- SOF/RDV
- ~93-94% SVR12
- Excellent safety profile

Clinical Implications

- **Supports Treatment Simplification:** Shorter duration equals higher patient adherence.
- **Facilitates Decentralized Care:** Lowers per-patient treatment costs, allowing scale-up in primary care clinics.
- **Policy Horizon:** Potential future incorporation into Malaysian national pathways following guideline reviews.

Direct-Acting Antiviral (DAA) Regimens for Chronic Hepatitis C

Sofosbuvir + Daclatasvir (SOF/DCV) vs. Sofosbuvir + Ravidasvir (SOF/RDV)



NS5B Polymerase Inhibition (SOF) + NS5A Replication Inhibition (DCV/RDV)

Sofosbuvir + Daclatasvir (SOF/DCV)

- **Drug Class:** NS5B + NS5A Inhibitor
- **Standard Dose:** SOF 400 mg / DCV 60 mg Once Daily
- **Duration:** 12 weeks (Non-cirrhotic / Compensated); 24 weeks (Decompensated)
- **Target Population:** Pangenotypic (GT 1–6); eligible for primary care scale-up.
- **Efficacy:** Highly reliable standard of care achieving 96–100% SVR12 globally.

Crucial Dose Adjustments in HIV Co-infection:
CYP3A4 Inducers (e.g., Efavirenz, Nevirapine):
Increase DCV to 90 mg.
CYP3A4 Inhibitors (e.g., Ritonavir-boosted Atazanavir): Decrease DCV to 30 mg.

Sofosbuvir + Ravidasvir (SOF/RDV)

- **Drug Class:** NS5B + NS5A Inhibitor
- **Standard Dose:** SOF 400 mg / RDV 200 mg Once Daily
- **Treatment Duration:** 12 weeks standard. **Emerging Evidence:** 8-week regimen.
- **STORM-C Trial Evidence:** 97% overall SVR12. Demonstrated 96% cure rate in difficult-to-treat Genotype 3 cirrhosis without the use of teratogenic ribavirin.
- **EASE Trial (2026) Evidence:** Groundbreaking data proving non-inferiority of an 8-week regimen (93.4% SVR12) versus 12-week regimen (93.5% SVR12) in non-cirrhotics. Enables better adherence and 33% lower programmatic costs.

Favorable HIV ART Profile: No dose adjustment required when co-administered with Efavirenz or Tenofovir Disoproxil Fumarate.

Special Populations: HIV Co-Infection

Screening

All HIV patients must be screened for HCV; all HCV patients must be screened for HIV.



ART Interactions

Critical priority. Check DAA interactions with existing **Antiretroviral Therapy** (e.g., Efavirenz, Nevirapine) using Liverpool tool.

Cure Rates

Highly encouraging. Cure rates (SVR12) with DAAs are identical to mono-infected HCV patients.

Treatment Timing

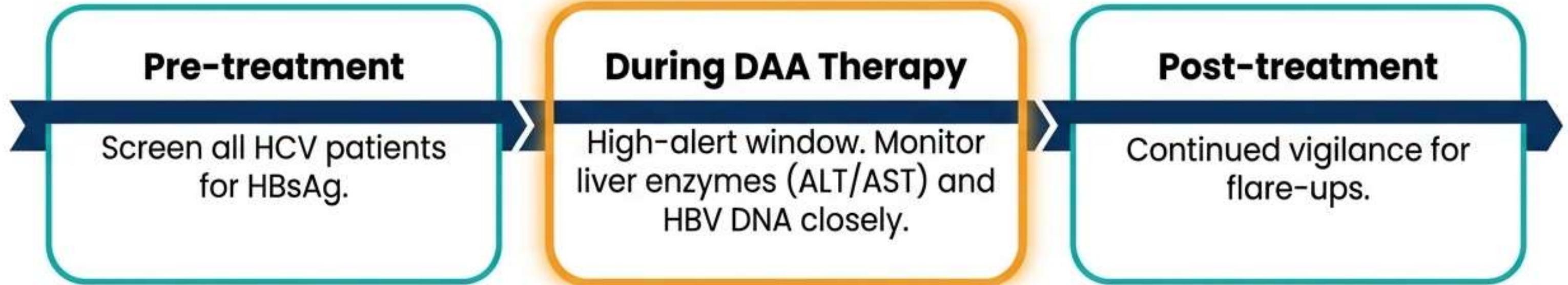
Usually, establish HIV viral suppression **first**, then initiate HCV treatment. **Do not** delay HCV treatment unnecessarily once stable.



Special Populations: Hepatitis B Co-Infection



The Clinical Risk: Clearing HCV rapidly removes viral interference, posing a high risk of life-threatening Hepatitis B (HBV) reactivation.



Management Protocol

- Patients positive for HBsAg should be assessed for concurrent HBV antiviral prophylaxis (e.g., Tenofovir/Entecavir).
- **Mandatory Referral:** Co-infected patients must be referred to Gastroenterology/Hepatology.

Special Populations: Advanced CKD & ESRF



Baseline screening required: Serum creatinine and eGFR must be recorded prior to DAA initiation.

Primary Care Management

Mild to Moderate CKD (Stages 1-3)

Standard DAA regimens (SOF-based) are generally safe. Proceed with standard simplified protocol.

Specialist Referral

Severe CKD & ESRF (Stages 4-5 / Dialysis)

Action: Mandatory Tertiary Referral.

- **Clinical Rationale:** Sofosbuvir has historical warnings in severe renal impairment (eGFR <30).
- **Choice of DAA:** Specialists will utilize renally safe, non-sofosbuvir regimens (e.g., Glecaprevir/Pibrentasvir) and coordinate with hemodialysis schedules.

Special Populations: Pregnancy & Family Planning

Pre-Pregnancy

Strongly counsel female patients (and male partners of female patients) to avoid pregnancy during DAA treatment and for 6 months after completion.

During Pregnancy (Defer Treatment)

Current Recommendation: DAAs are not approved for use during pregnancy.

Risk: Discuss the risk of vertical transmission (mother-to-child) which is approximately 5%, higher if HIV co-infected.

Post-Partum (Defer until weaning)

Breastfeeding: No safety data exists regarding DAAs and human milk. Defer treatment until breastfeeding is complete.

Timing: Initiate HCV workup and DAA therapy post-weaning.

Special Populations: Children & Adolescents



WHO to Screen?

Children born to HCV-positive mothers.

Adolescents with high-risk behaviors (e.g., early IVDU).



WHAT is Approved?

DAA approvals are age and weight-dependent (e.g., specific DAAs approved for >3 years or >12 years globally).

Efficacy firmly matches adult cohorts.



WHERE to Manage?

Pediatric HCV management requires highly specialized weight-based dosing formulations not kept in primary care.

Mandatory Tertiary Referral Pathway: All positive cases under 18 must be referred directly to Paediatric Gastroenterology.

Monitoring During DAA Therapy Requires Minimal Routine Testing



Before Treatment (Baseline)

- Assess comorbidities & drug-drug interactions.
- Calculate APRI / FIB-4.
- **Labs:** FBC, Creatinine, ALT, AST, HIV, HBsAg.
- **Counseling:** Avoid pregnancy (patient/partner).



Week 4

- Assess adherence and side effects.
- **Labs:** Minimal routine labs. FBC only required if patient is on Ribavirin.



End of Treatment (Week 12 or 24)

- Complete DAA course.
- Reinforce counseling on reinfection prevention.



12 Weeks Post-Treatment

- HCV RNA testing to confirm Sustained Virological Response (Cure).
- **Alternative:** HCVcAg at 24 weeks if RNA unavailable.

DAA's represent a paradigm shift: routine laboratory monitoring is significantly reduced compared to historical interferon-based therapies.

Managing Treatment Interruptions and Virological Failure

Missed Doses

Trigger:

Patient reports missed DAA doses.



Action:

Counsel immediately on strict adherence. High SVR depends on completion.



Rule:

Do not double-dose to make up for missed doses.

Restarting Therapy

Trigger:

Prolonged interruption of treatment.



Action:

Assess duration of missed therapy and risk of viral rebound.



Pathway:

Consult with specialist/hepatologist before bridging or restarting a prolonged interrupted course.

Treatment Failure & Retreatment

Trigger:

HCV RNA Detected at 12 weeks post-treatment (SVR12 not achieved).



Action:

Do NOT attempt retreatment in primary care.

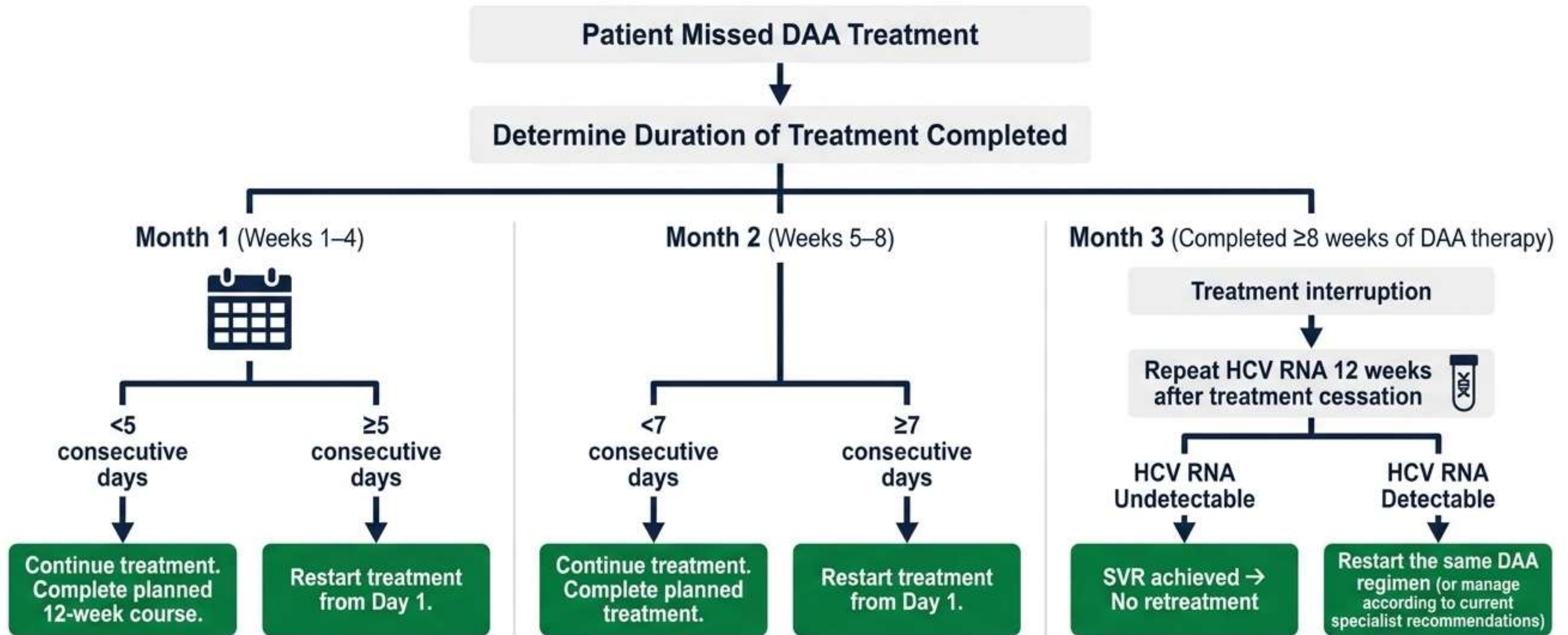


Pathway:

Mandatory referral to Secondary/Tertiary centre for specialized retreatment regimens and resistance genotyping.

**Treatment failure requires escalation, not primary care retreatment.
Strict adherence counseling at Baseline and Week 4 is your best preventive tool.**

Management of Treatment Interruption



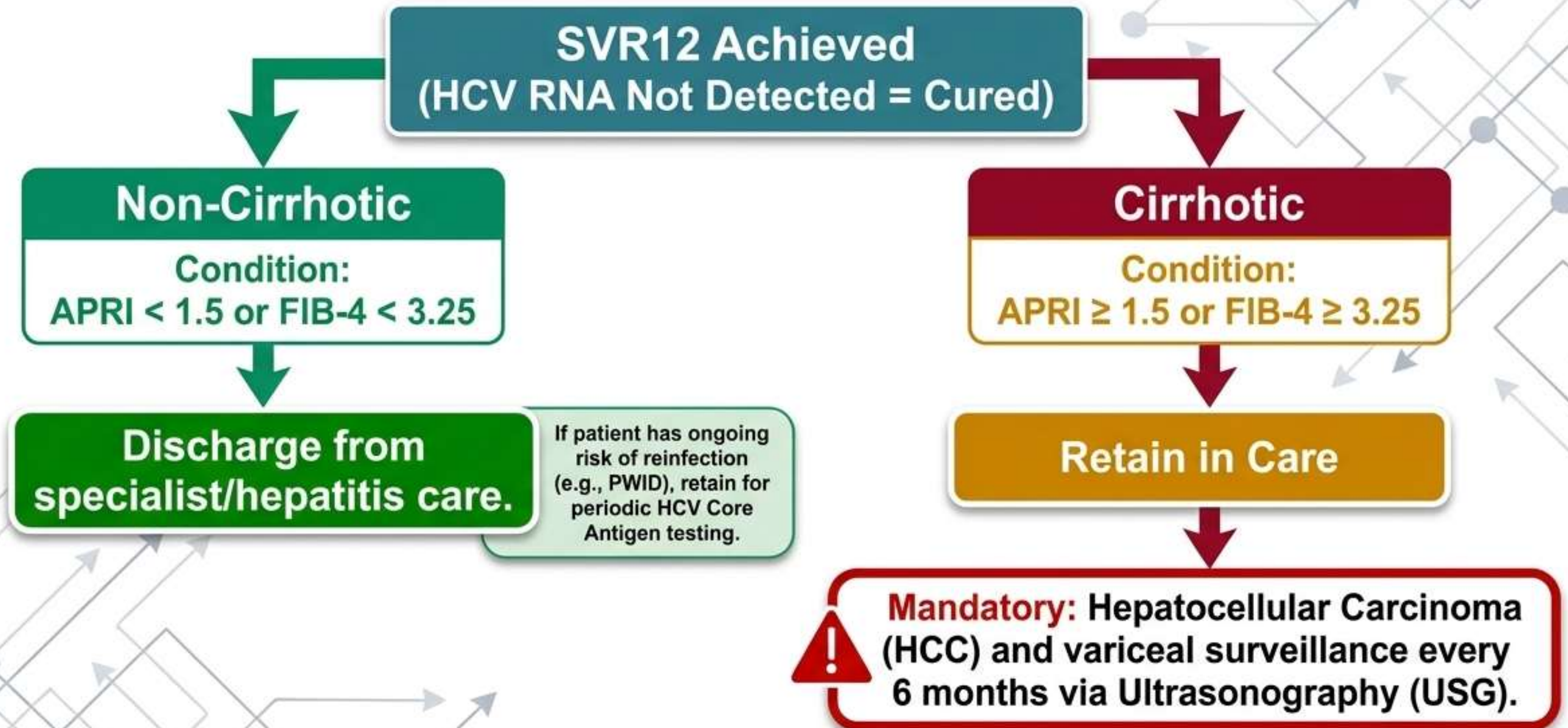
- Counsel adherence at every visit.

- Avoid treatment interruption whenever possible.

- Restart decisions should be based on the duration of interruption and cumulative treatment completed.

- Refer complicated cases to hepatology.

Post-Treatment Pathways Diverge Based on Cirrhosis Status



CRITICAL PITFALL: SVR is a cure for the virus, but cirrhosis is permanent. Discharging a cirrhotic patient post-SVR is a fatal error due to ongoing HCC risk.

Establishing the Safety Net: Clinical Referral Criteria



Immediate Referral

- Decompensated Cirrhosis (e.g., ascites, jaundice, encephalopathy)
- Liver Failure
- Hepatocellular Carcinoma (HCC) or suspicious liver nodules
- Complex, unresolvable Drug-Drug Interactions



Specialist Co-Management

- Treatment Failure (No SVR12 achieved)
- Pregnancy (DAA safety not established; avoid pregnancy during and 6 months post-treatment)
- Children and Adolescents
- Severe Chronic Kidney Disease (Stage 4 and 5)
- HBV or HIV co-infection requiring specialized care

Primary care is the engine of the HCV elimination programme.
Specialists serve as your safety net for complex and decompensated cases.

The Six Pillars of Malaysia's Hepatitis C Elimination Strategy



Hepatitis C is Curable

Direct-acting antivirals (DAAs) achieve >95% cure rates across most populations (supported by local STORM-C & EASE trials).



Targeted Screening

Do not wait for symptoms. Actively screen individuals at increased risk (e.g., PWID) using RDTs.



Confirm Viraemia First

Antibodies indicate exposure; always confirm active infection with HCV RNA or HCV Core Antigen before initiating treatment.



Assess Fibrosis Early

Utilize simple, non-invasive calculators (APRI / FIB-4) at baseline to identify cirrhosis and determine post-SVR pathways.



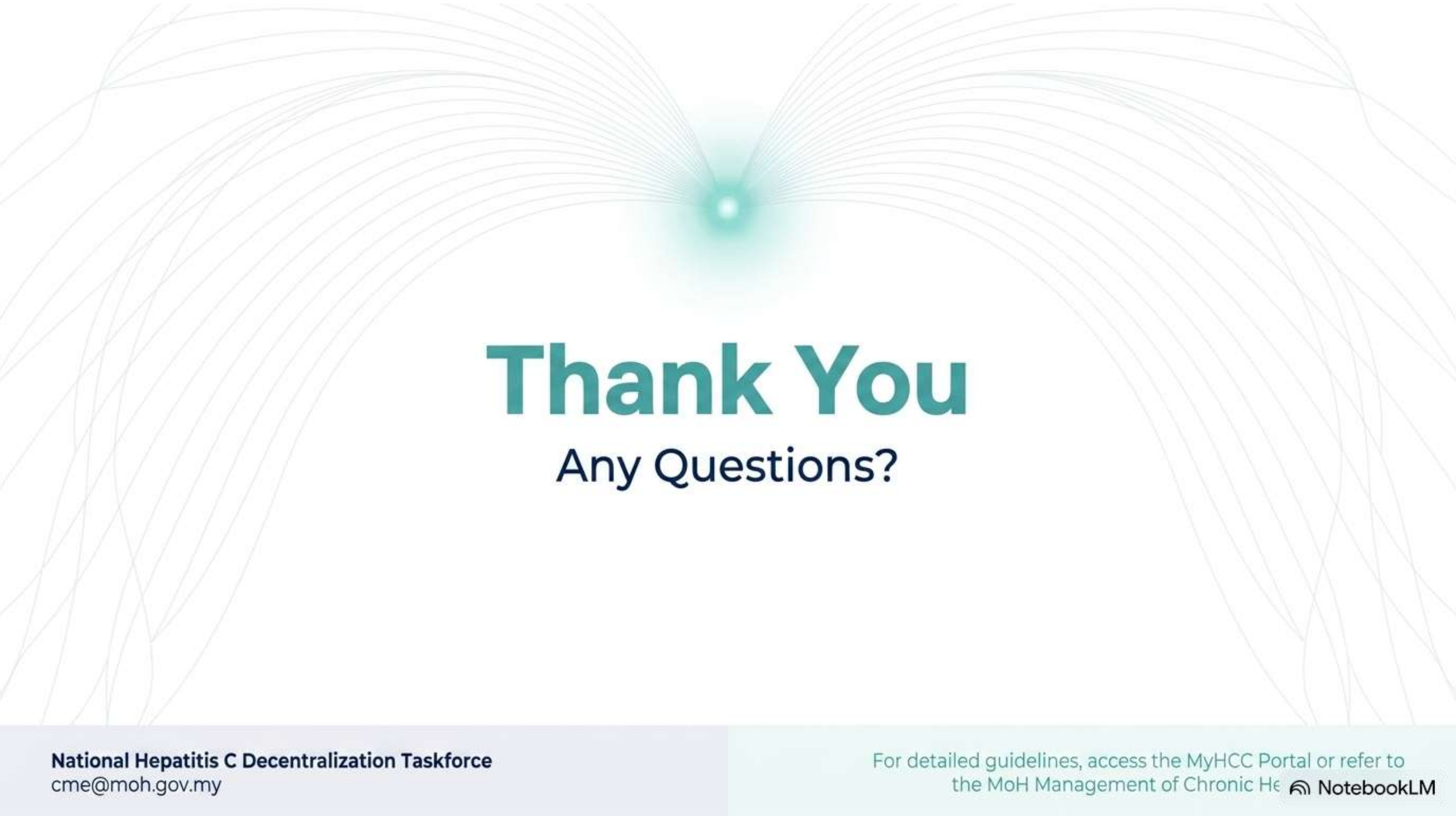
Simplified Treatment Regimens

Modern treatments are short in duration, highly effective, and require minimal routine lab monitoring.



Primary Care is the Engine

Decentralization to Klinik Kesihatan is the cornerstone of Malaysia achieving the WHO 2030 elimination targets.



Thank You

Any Questions?