The Clinical Blueprint for NAFLD

Proactive Risk Stratification and Metabolic Management in Primary Care

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A visual synthesis of Australian clinical guidelines for Nonalcoholic Fatty Liver Disease (Med2Date, 2026).

The Epidemic

25–30%

Estimated prevalence of NAFLD in Australian adults. It is the nation's most common chronic liver condition, mirroring the rise of obesity and type 2 diabetes.

The Cost

$1 Billion+

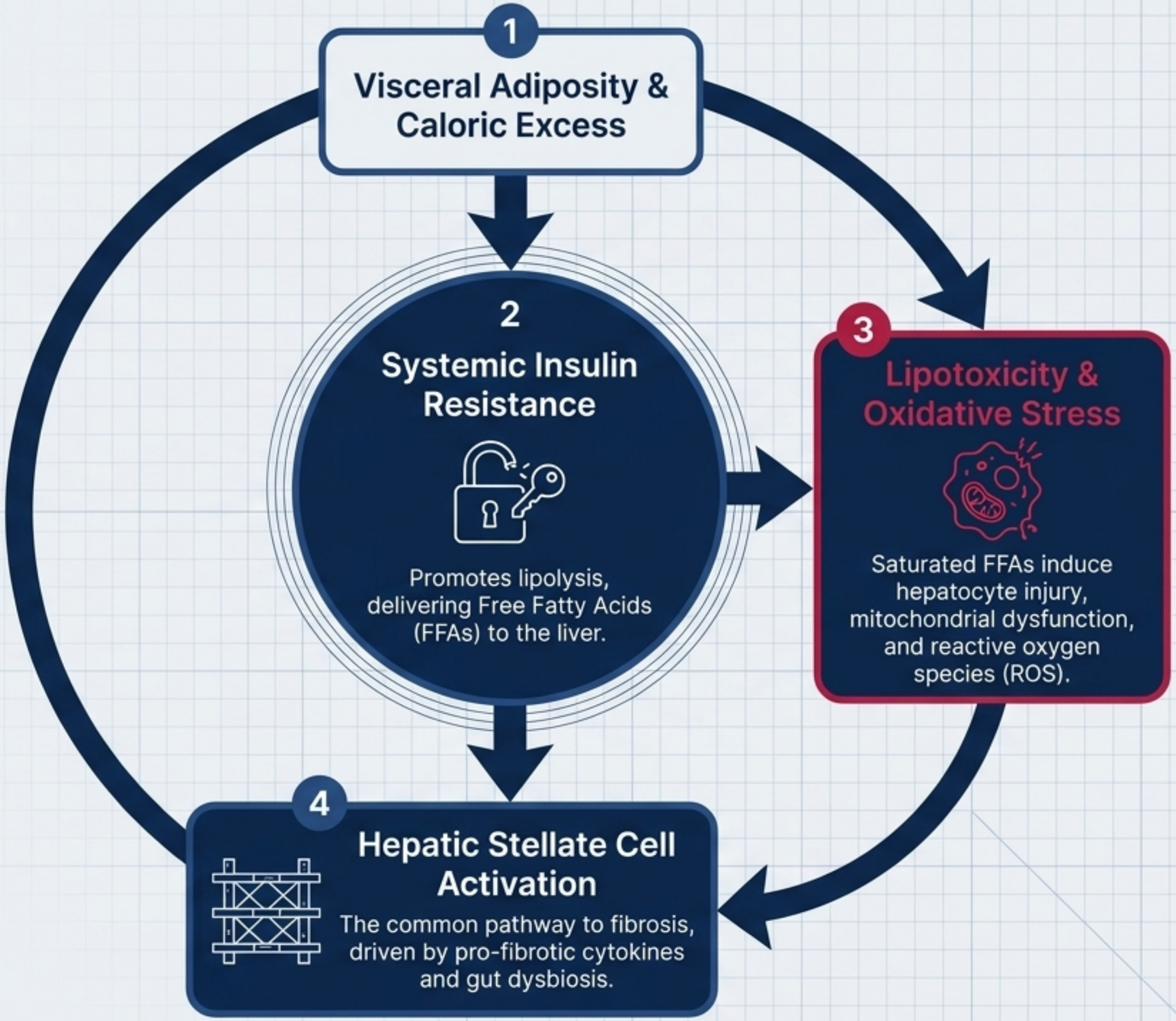
Annual healthcare burden in Australia, factoring direct medical costs, cirrhosis complications, and liver transplantation.

The Paradox

Cardiovascular disease—not liver-related mortality—is the leading cause of death in NAFLD patients.

Key Clinical Concern: Up to 70% of type 2 diabetics have hepatic steatosis, yet remain under-assessed in primary care.

Pathophysiology: The Multiple-Hit Model



Genetic Modifiers: PNPLA3 (I148M variant), TM6SF2, and MBOAT7 polymorphisms significantly influence susceptibility.

The Tiered Severity Model

Stage 1: Simple Steatosis (NAFL)

≥5% steatosis.

F0–F1 fibrosis.

No significant inflammation.

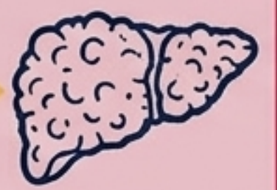
Benign prognosis (1–2% progression over 20 years).

Stage 2: NASH (Non-cirrhotic)

Steatosis + lobular inflammation + ballooning.

F1–F3 fibrosis.

Progressive. 20–30% of NAFLD patients have this inflammatory subtype.



Stage 3: NASH-Cirrhosis

F4 fibrosis.

Regenerative nodules.

Severe risk: Annual HCC risk 1–2%, decompensation 3–5%.

The clinical priority is identifying NASH and staging the fibrosis before irreversible architectural distortion occurs.

Identification: Who to Screen

High Alert 1

Type 2 Diabetes

Present in 50–70% of NAFLD cases; strongest independent predictor of advanced fibrosis.

High Alert 2

Obesity

BMI ≥30 kg/m² (or ≥25 in ATSI populations); central adiposity (>94cm M, >80cm F).

High Alert 3

Metabolic Syndrome

≥3 criteria (obesity, TG ≥1.7, HDL <1.0/1.3, BP ≥130/85, glucose ≥5.6).

Investigate 4

Incidental Steatosis

Found on ultrasound/CT/MRI for other indications.

Investigate 5

Persistently Elevated ALT

1–3x ULN.

⚠ **Warning:** ALT may be completely normal in up to 50% of advanced fibrosis cases.

Associated 6

OSA, PCOS, Hypothyroidism

Conditions sharing insulin resistance pathways.

Investigate: Primary Care Workup

Confirm Inclusion Criteria

Exclude significant alcohol intake (<20 g/day women, <30 g/day men).
Review medications (corticosteroids, amiodarone, tamoxifen).

Exclude Competing Aetiologies

- **Viral**: Hep B (HBsAg), Hep C (anti-HCV)
- **Genetic**: Iron studies (haemochromatosis), caeruloplasmin (if <40 yrs)
- **Autoimmune**: ANA, anti-smooth muscle, IgG.

Baseline Investigations

LFTs, FBC (crucial for platelets), HbA1c, Fasting lipids, TSH.

Proceed to Fibrosis Assessment

Calculate FIB-4.

Liver biopsy is NOT routine. It is reserved for diagnostic uncertainty or pre-pharmacotherapy grading.

Risk Stratification: The FIB-4 Algorithm

$$\text{FIB-4 Index} = \frac{(\text{Age} \times \text{AST})}{(\text{Platelets} \times \sqrt{\text{ALT}})}$$

Note: Use cutoff of 2.0 instead of 1.3 for patients >65 years.

Result: < 1.3

Low Risk

Action: Reassure. F0-F2 excluded. Repeat in 2-3 years if risk factors persist. Manage metabolically.

Result: 1.3 – 2.67

Indeterminate Risk

Action: Cannot exclude advanced fibrosis. Proceed immediately to Second-Line Testing (ELF, NFS, or FibroScan).

Result: ≥ 2.67

High Risk

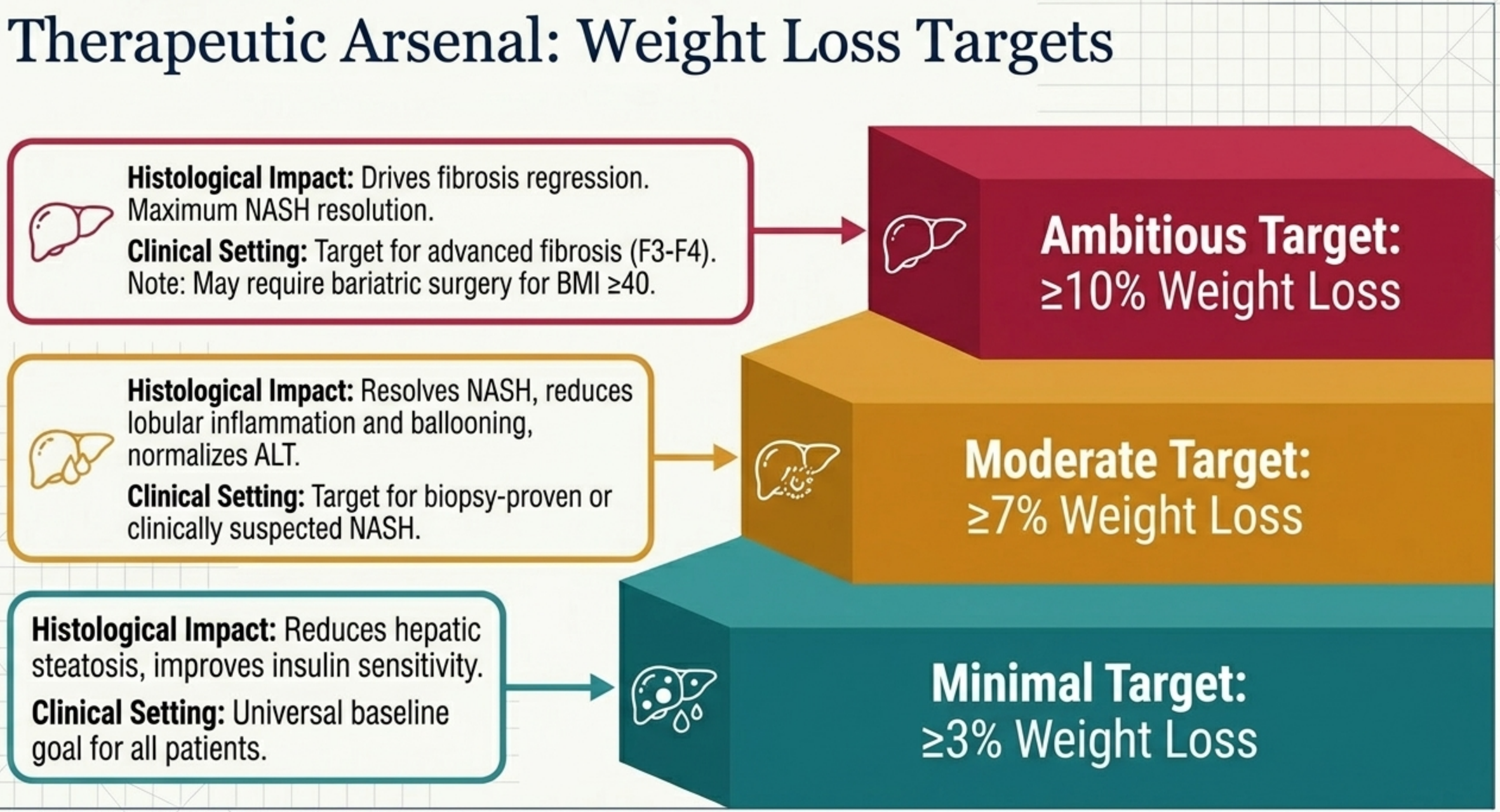
Action: High probability of F3-F4. Urgent hepatology referral.

Second-Line Non-Invasive Fibrosis Tools

For patients in the Indeterminate (1.3–2.67) FIB-4 zone.

NAFLD Fibrosis Score (NFS)	Enhanced Liver Fibrosis (ELF) Test	FibroScan (Transient Elastography)
Modality: Serum calculator (Age, BMI, glucose, AST/ALT, plt, albumin).	**Modality:** Direct serum biomarker panel (HA, TIMP-1, PIIINP). Available via major pathology providers.	**Modality:** Ultrasound-based liver stiffness measurement.
Thresholds: >0.676 (High risk), <-1.455 (Low risk).	**Thresholds:** ≥9.8 indicates advanced fibrosis.	**Stiffness Thresholds:** ● <7.0 kPa (F0-F1, Teal) ● 7.0-9.5 kPa (F2, Amber) ● 9.5-12.5 kPa (F3, Amber/Red) ● ≥12.5 kPa (F4 Cirrhosis, Crimson)

Therapeutic Arsenal: Weight Loss Targets



Therapeutic Arsenal: Lifestyle Foundations

Nutrition

- **The Standard:** Mediterranean-style diet (EVOO, legumes, fish, nuts).
- **The Eliminations:** Zero fructose/sugar-sweetened beverages (drives de novo lipogenesis). Minimize ultra-processed foods and alcohol.
- **The Addition:** 2-3 cups of coffee daily (associated with reduced fibrosis progression).

Action: Dietitian referral via MBS Item 10954.

Movement

- **Aerobic:** ≥150 min/week moderate or ≥75 min/week vigorous. Reduces steatosis independent of weight loss.
- **Resistance:** ≥2 sessions/week. Crucial for insulin sensitivity and preserving muscle mass.

Action: Exercise Physiologist referral via MBS Item 10953.

Pharmacotherapy Matrix

Medication	Primary Indication	Liver Impact	Key Cautions/Dose	PBS Status
Metformin	Glycaemic control.	None.	Up to 2.5-3g/day. Contraindicated eGFR <30.	✓
Pioglitazone (TZD)	Biopsy-proven NASH.	Strongest NASH resolution evidence.	15-30mg mane. Weight gain, fracture risk, fluid retention. Avoid in HF.	⚠ Authority Required
Semaglutide / Liraglutide (GLP-1)	T2DM + NAFLD.	High weight loss (10-15%), NASH resolution.	GI side effects, pancreatitis risk.	⚠ Authority Required
Vitamin E	Biopsy-proven NASH (Non-diabetic).	Improves lobular inflammation.	800 IU/day. Avoid in CVD or prostate cancer risk.	OTC

Managing Systemic Cardiovascular Risk

Shield 1: Lipids (Statins)

Statins are SAFE in NAFLD/NASH. Do not worsen liver disease.

Use Atorvastatin (20-80mg) or Rosuvastatin (10-40mg) aggressively for CVD risk reduction. Safe in Child-Pugh A cirrhosis.

Shield 2: Blood Pressure (ACEi/ARBs)

Preferred antihypertensives.

Agents like perindopril, telmisartan may have anti-fibrotic properties.

Shield 3: Renal/Metabolic (SGLT2i)

Empagliflozin/Dapagliflozin.

Emerging evidence for steatosis reduction.

Provides cardiovascular and renal benefits alongside 2-3kg weight loss.

Special Populations: ATSI Health

Aboriginal and Torres Strait Islander Considerations

Zone 1

The Burden

Disproportionate rates of metabolic syndrome and diabetes (often >20% in remote communities). High frequency of the PNPLA3 I148M genetic risk variant driving rapid fibrosis.

Zone 3

The Barriers

Limited access to fresh food (costs 2-3x higher in remote stores), lack of local FibroScan/specialist services, and co-existence of **harmful alcohol use** and **Hepatitis B.**

Zone 2

Adjusted Clinical Thresholds

Due to higher metabolic risk, use lower BMI thresholds:

- Overweight: ≥25 kg/m^2
- Obesity: ≥30 kg/m^2
- Waist circumference: >90 cm (M), >80 cm (F)

ATSI Health: Community Care Model

ACCHO Integration

Aboriginal Community Controlled Health Organisations are the Organisations are the primary setting.

Utilize Medicare Item 715 (Health Assessments) for early NAFLD screening.

Remote Diagnostics

Use Point-of-Care Testing (POCT) via QAAMS for HbA1c/LFTs. Calculate FIB-4 remotely.

Utilize Telehealth (MBS 99200–99215) for hepatology input without patient transfer.

Culturally Safe Lifestyle

Co-designed interventions (e.g., Deadly Liver Mob, Mai Wiru nutrition programs) led by Indigenous health workers.

Holistic Assessment

Address coexistent liver disease (alcohol, Hep B) concurrently with culturally appropriate counseling.

Special Populations: Pregnancy & Paediatrics

Pregnancy

- **Risk**: NAFLD rising with pre-existing obesity/GDM.
- **Medication Rules**: Metformin is safe. CEASE Pioglitazone, Statins, and GLP-1 RAs (Semaglutide ≥2 months pre-conception).
- **Note**: AFLP/HELLP in 3rd trimester require urgent obstetric/hepatology input (distinct from NAFLD).

Paediatrics

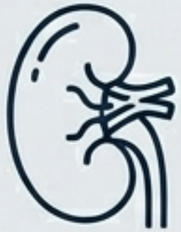
- **Epidemiology**: Affects 8-12% of children, up to 40% with obesity. Screen from age 10. Distinct periportal (zone 1) pattern.
- **Intervention**: Family-based lifestyle programs first. Vitamin E (400-800 IU/day) used off-label for NASH. Metformin for concurrent insulin resistance.

Special Populations: Systemic Impairment & Aging

The Elderly (≥65 years)

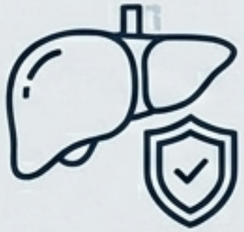
- **FIB-4 Adjustment:** Use 2.0 as the lower bound instead of 1.3.
- **Clinical Balance:** Avoid aggressive weight loss (>10%) which worsens sarcopenia.
- **Medication Caution:** Pioglitazone carries high fracture risk; DEXA recommended.

Renal Impairment (CKD)



- **Diagnostics:** Prefer FibroScan or ELF test over serum calculators (urea/creatinine distort scores).
- **Medications:** Metformin contraindicated if eGFR <30. SGLT2i provide renal protection but avoid if eGFR <20-30.

Hepatic / Immune Impaired



- **Cirrhosis:** Avoid Statins in Child-Pugh C. Avoid Pioglitazone in decompensation (fluid retention).
- **Immunocompromised:** Corticosteroids and Tacrolimus drive metabolic syndrome; minimize doses where possible.

Thresholds for Hepatology Escalation

Urgent Referrals (Action: Refer within 2-4 weeks)

- FIB-4 ≥ 2.67 (High probability of F3-F4).
- FibroScan ≥ 12.5 kPa (Probable cirrhosis).
- Clinical features of cirrhosis (splenomegaly, spider naevi, ascites, thrombocytopenia <150).

Prompt Referrals

- Indeterminate FIB-4 (1.3–2.67) WITH an elevated second-line test (ELF ≥9.8 or FibroScan ≥9.5).
- Diagnostic uncertainty (suspected autoimmune or iron overload).
- Persistently elevated ALT/AST >3x ULN.

Routine Referrals

- Pre-bariatric surgery assessment.
- Initiation of NASH-specific pharmacotherapy (e.g., Pioglitazone/Vit E).

F4 Cirrhosis: Surveillance Protocol

Core Checkpoint 1: HCC Surveillance

6-monthly abdominal ultrasound ± serum alpha-fetoprotein (AFP). MBS Items 55056 & 66507.

If obesity limits ultrasound, use contrast CT/MRI.

Core Checkpoint 2: Variceal Screening

Gastroscopy at diagnosis.

If negative, repeat every 2-3 years.

If small varices present, consider non-selective beta-blockers (carvedilol/propranolol).

Core Checkpoint 3: Decompensation Monitoring

Continual clinical assessment for ascites, hepatic encephalopathy, and jaundice.

Calculate Child-Pugh and MELD scores to guide transplant referral.

The Multidisciplinary Ecosystem

General Practitioner
Orchestrates care, calculates FIB-4, manages lipids/BP, prevents cardiovascular mortality.

Hepatologist
Stages advanced fibrosis, conducts HCC surveillance, manages decompensation.

Dietitian & EP
Drives the 7-10% weight loss target to reverse histological damage.

Endocrinologist
Optimizes glycaemic control, prescribes GLP-1/TZDs for NASH resolution.

Central Insight: Treating NAFLD is **not** about treating the liver in isolation; it is about aggressively optimizing systemic metabolic health to halt hepatic fibrosis and prevent cardiovascular mortality.