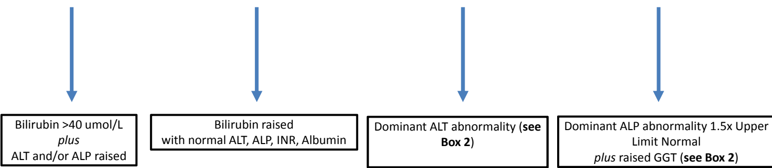
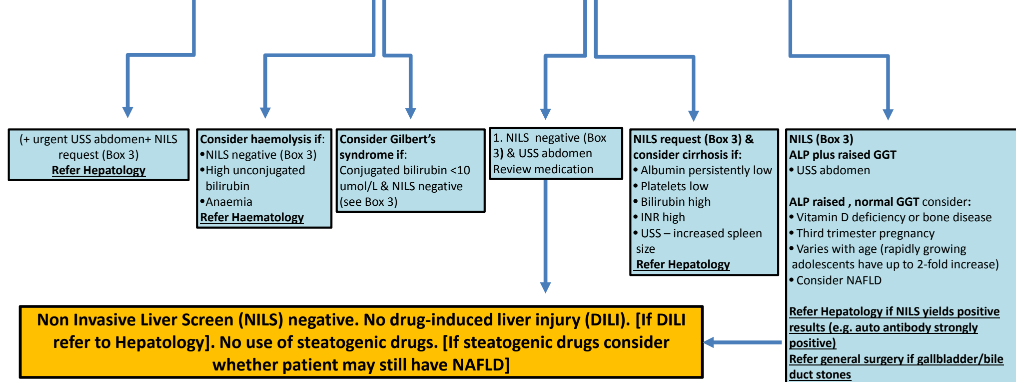
Asymptomatic patient with abnormal LFTs (or unsuspected hepatic steatosis detected on imaging) and weekly alcohol consumption within recommended guidelines

History & Examination RED FLAGS (see Box 1)





Bilirubin >40 umol/L
plus
ALT and/or ALP raised

(+ urgent USS abdomen+ NILS request (Box 3)
Refer Hepatology

Bilirubin raised
with normal ALT, ALP, INR, Albumin

Consider haemolysis if:
- NILS negative (Box 3)
- High unconjugated bilirubin
- Anaemia

Refer Haematology

Consider Gilbert's syndrome if:
Conjugated bilirubin <10 umol/L & NILS negative (see Box 3)

Dominant ALT abnormality (**see Box 2**)

1. NILS negative (Box 3) & USS abdomen
Review medication

NILS request (Box 3) & consider cirrhosis if:
- Albumin persistently low
- Platelets low
- Bilirubin high
- INR high
- USS – increased spleen size

Refer Hepatology

Dominant ALP abnormality 1.5x Upper Limit Normal
plus raised GGT (**see Box 2**)

NILS (Box 3)
ALP plus raised GGT
- USS abdomen

ALP raised , normal GGT consider:
- Vitamin D deficiency or bone disease
- Third trimester pregnancy
- Varies with age (rapidly growing adolescents have up to 2-fold increase)
- Consider NAFLD

Refer Hepatology if NILS yields positive results (e.g. auto antibody strongly positive)
Refer general surgery if gallbladder/bile duct stones

Non Invasive Liver Screen (NILS) negative. No drug-induced liver injury (DILI). [If DILI refer to Hepatology]. No use of steatogenic drugs. [If steatogenic drugs consider whether patient may still have NAFLD]

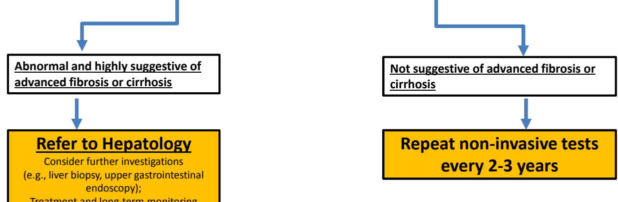
USS abdomen – Confirm the presence of hepatic steatosis and rule out other liver pathology (e.g. biliary disease)

(Suspected) NAFLD with or without _coexistent_ type 2 diabetes mellitus
or
obesity (BMI ≥30 kg/m^2)
or
metabolic syndrome (≥3 cardiometabolic risk factors)

- **Lifestyle advice**
- **Weight loss and increase in physical activity (if appropriate)**
- **Control of all coexisting cardiometabolic risk factors**
- **Cardiovascular risk assessment annual monitoring**
- **Consider the use of pioglitazone or vitamin E in patients with biopsy-proven NASH (if not contraindicated)**

Strategy recommended by the European and American guidelines for ruling out presence of advanced fibrosis

Rule out presence of advanced fibrosis using either non-invasive markers of hepatic fibrosis as first-line tests (e.g., the FIB4 score and the NAFLD fibrosis score) or the commercially available ELF blood test (if available) *
plus
transient elastography (FibroScan) or other imaging techniques for hepatic fibrosis as second-line tests



Abnormal and highly suggestive of advanced fibrosis or cirrhosis

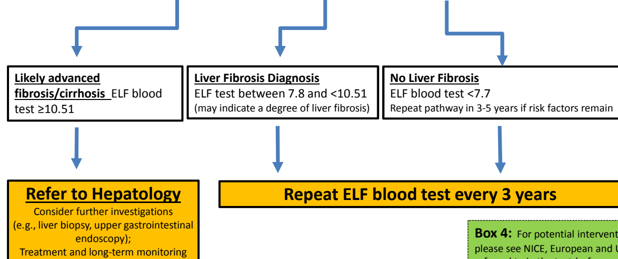
Refer to Hepatology
Consider further investigations
(e.g., liver biopsy, upper gastrointestinal endoscopy);
Treatment and long-term monitoring

Not suggestive of advanced fibrosis or cirrhosis

Repeat non-invasive tests every 2-3 years

Strategy recommended by the NICE guidelines for ruling out presence of advanced fibrosis

*** Enhanced Liver Fibrosis (ELF) blood test**
(see Non-alcoholic fatty liver disease (NAFLD): assessment and management (2016) NICE NG49)
(offer retesting for advanced fibrosis for people with an ELF blood test <10.51 every 3 years)



Likely advanced fibrosis/cirrhosis ELF blood test ≥10.51

Refer to Hepatology
Consider further investigations
(e.g., liver biopsy, upper gastrointestinal endoscopy);
Treatment and long-term monitoring

Liver Fibrosis Diagnosis
ELF test between 7.8 and <10.51
(may indicate a degree of liver fibrosis)

No Liver Fibrosis
ELF blood test <7.7
Repeat pathway in 3-5 years if risk factors remain

Repeat ELF blood test every 3 years

Useful information
Non-alcoholic fatty liver disease (NAFLD): assessment and management (2016) NICE NG49

Box 1: Red Flags – consider admission or urgent referral
- Suspected malignancy
- Jaundice
- Ascites
- Encephalopathy
- Sepsis
- Haematemesis
- ALT or ALP very high (i.e.5x upper limit of normal)
- Persistently low albumin or platelets.
- Evidence of disordered clotting
- Rapid deterioration

Box 2: LFTs results within the normal range do not exclude NAFLD. N.B. As disease severity progresses transaminase levels may decrease over time due to cell death.

Serum GGT levels should be interpreted alongside other LFTs (NILS is needed – **see Box 3**)

A serum GGT measurement might be requested if the ALP is raised to confirm a liver origin to the increased ALP concentration

Isolated GGT (consider alcohol abuse (sensitivity of elevated GGT for detecting alcohol ingestion ranges from 50-95%)

Box 3: Non Invasive Liver Screen (NILS)

Refer to Hepatology if NILS yields positive results for:
- Hepatitis B and C
- Autoimmune liver screen (Primary biliary cholangitis)
- Immunoglobulins raised
- High ferritin and high transferrin saturation
- Low caeruloplasmin
- Low alpha 1 anti-trypsin protein

Consider non-hepatic causes for raised ALT:
- Thyroid diseases
- Muscle diseases, e.g. polymyositis, heavy exercise
- Coeliac disease

Box 4: For potential interventions and treatments please see NICE, European and US Guidelines referred to in the text (references 1, 12 and 17). N.B. Statins are safe in patients with confirmed NAFLD.