Investigation of adult patients with abnormal LFT in Primary Care

This guideline is directed towards an LFT that is raised, but an urgent referral is not appropriate.
(Criteria for urgent referral decompensated cirrhosis (cirrhosis with ascites +/- encephalopathy +/- coagulopathy), ALT >500 u/L, bilirubin >100 umol/L or imaging suggestive of hepato-pancreatic-biliary malignancy)

LFT Panel

Initial investigation of LFT for potential liver disease will include the following tests bilirubin, Alkaline Phosphatase (ALP); Alanine aminotransferase (ALT) and albumin. Gamma-glutamyltransfease (GGT) and conjugated bilirubin may be requested in addition. A full blood count should also be considered if not performed within the last 12 months.

General Advice

Abnormal LFT blood test results should be interpreted after review of the previous results, past medical history and current medical condition. The extent of LFT abnormalities is not necessarily a guide to clinical significance. This is determined by the specific analyte which is abnormal and the clinical context. Patients with abnormal LFT should be considered for investigation with a NILS screen irrespective of level or duration of the abnormality. It should be remembered that normal LFT do not rule out liver disease and further investigation of patients with appropriate risk factors may still be appropriate.

The rising burden of liver disease is mainly a reflection of the three most common causes: alcohol-related liver disease, non-alcoholic fatty liver disease (NAFLD) and viral hepatitis although autoimmune liver disease is also a significant contributor. LFTs are frequently checked in an attempt to exclude liver disease, for the monitoring of potential adverse effects of drugs and the investigation of the generally unwell patient. They often produce an abnormal result the significance of which is unclear. Thus used in isolation LFT are neither specific diagnostic tools nor specific exclusion tools.

When should LFT be checked?

- Non-specific symptoms

Liver disease tends to develop silently with no signs or symptoms and there is evidence that the majority of people with late stage liver disease are undiagnosed.

So the presence of non-specific symptoms would be an indication to check LFT accepting there are many other causes for those symptoms

- Evidence of chronic liver disease

Patients with symptoms/signs of cirrhosis, portal hypertension or liver failure including ascites, peripheral oedema, spider naevi and hepatosplenomegaly

- Conditions which are associated with a high risk of developing liver disease

Patients with pre-existing autoimmune disease, inflammatory bowel disease (including ulcerative colitis and Crohn's disease)

- Use of hepatotoxic drugs

A wide variety of drugs are associated with liver disease and a requirement for monitoring of LFT may be documented.
For patients on statins do not routinely exclude therapy from patients that are raised but less than 3 times the upper limit of normal. For methotrexate and other DMARDs less than 2 times upper limit of normal but may be higher. In each case local guidance should be consulted for a detailed protocol
https://remedy.bnssgccg.nhs.uk/formulary-adult/scps/scps/

- Family history of liver disease

Investigating relatives of patients with familial disease including hemochromatosis and Wilson's would be an indication for specific tests

- Viral hepatitis

May be associated with non-specific symptoms but many or identified on risk factors such as country of origin or parental exposure. While LFT can detect liver inflammation viral serology in high risk groups such as injecting drug users, migrants from high risk areas and prisoners is important

- Presence of lifestyle risk factors associated with the development of NAFLD

NAFLD risk factors include obesity, diabetes, hypertension, HDL cholesterol <1 mmol/L or triglyceride >1.7 mmol/L

Does the extent and duration of abnormal LFT determine subsequent investigation?

Many guidelines have previously stipulated minimum criteria for further investigation but these do not take into account the fact that over 50% of patients with end-stage liver disease with-out a previous diagnosis were noted to have had previously abnormal results. This put a significant burden of GP practices and decisions will be based around the context of the investigation and the extent of the abnormality. It should also be noted that the extent of the abnormality does not fully reflect the prognosis and the assumption that abnormal LFT may be transient and incidental and will normalise thus precluding any significant liver disease may not be true. It

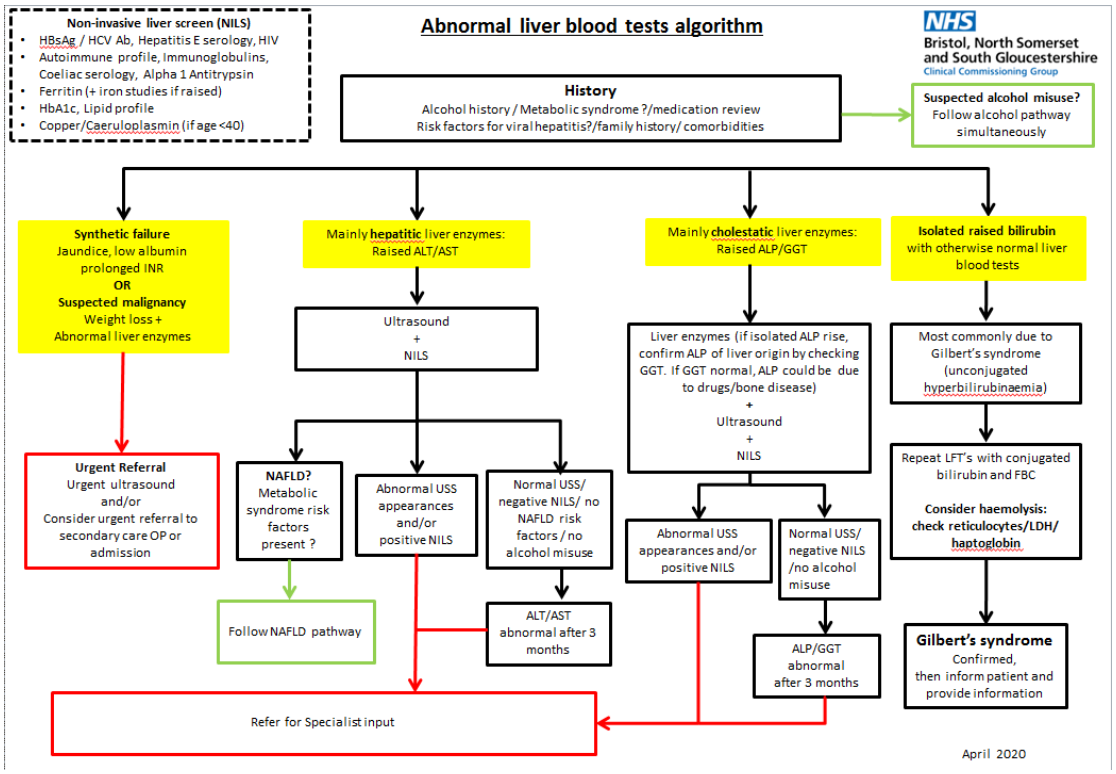
may be true of some acute liver disease but is less likely in chronic liver disease. The first abnormality may trigger a NILS screen.

Clinical pattern recognition for LFT
There are three common patterns of abnormal LFT results whose recognition can aid diagnosis.

1. Isolated raised bilirubin—most commonly caused by Gilbert's syndrome (affects 5–8% of the population.) Bilirubin levels are typically persistently increased but less than 80 umol/L. For patients with higher levels or previously normal bilirubin consider other causes. Haemolysis in patients with anaemia. Repeat liver blood tests on a fasting sample with a full blood count and a direct and indirect bilirubin; the total bilirubin should rise further, owing to the indirect component, and there should be no evidence of anaemia. If the patient is anaemic, haemolysis needs to be excluded.

2. Cholestatic— predominantly raised ALP and GGT indicate cholestasis. Common causes include primary biliary cholangitis, PSC, biliary obstruction (stones, strictures, neoplasia etc), hepatic congestion and drug-induced liver injury. The presence of a concomitantly elevated GGT can help confirm the cause of liver disease.

3. Hepatitic—predominantly raised ALT and AST indicate hepatocellular liver injury (hepatitis). Common causes include viral hepatitis, NAFLD, ARLD, AIH and drug induced liver injury.



Abnormal LFT blood test algorithm

Non-invasive liver screen (NILS)

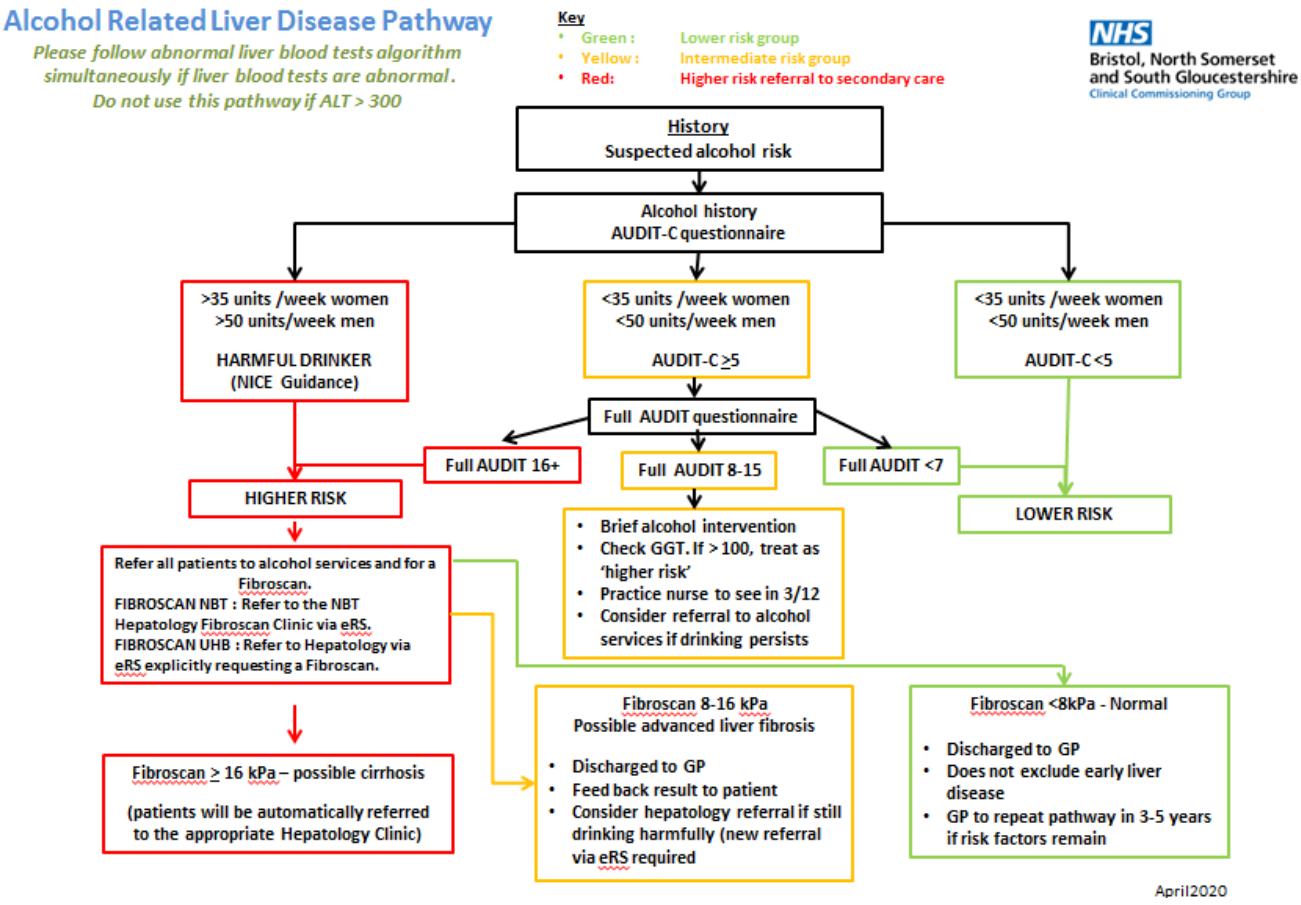
NILS screen is available in ICE

ALL PATIENTS
HbA1c
Fasting lipid profile
Coeliac screen
Ferritin (+ Iron studies if ferritin raised)
Autoimmune profile
Immunoglobulins
Hepatitis B & C serology
HIV
Hepatitis E serology
Caeruloplasmin & Copper (under 45 year olds)

Approaches to common conditions; alcohol related liver disease

This pathway should be considered for all patients drinking over 14 units of alcohol per week.

- Patients may have normal LFTs but still be at risk.
- Please follow the Abnormal liver blood test algorithm simultaneously if liver blood tests are abnormal.
- Do not use this pathway if ALT > 300



Approaches to common conditions; NAFLD

NAFLD may be suspected in those with metabolic risk factors obesity, diabetes, hypertension, HDL cholesterol <1 mmol/L or triglyceride >1.7 mmol/L and does not require liver function tests to be abnormal.

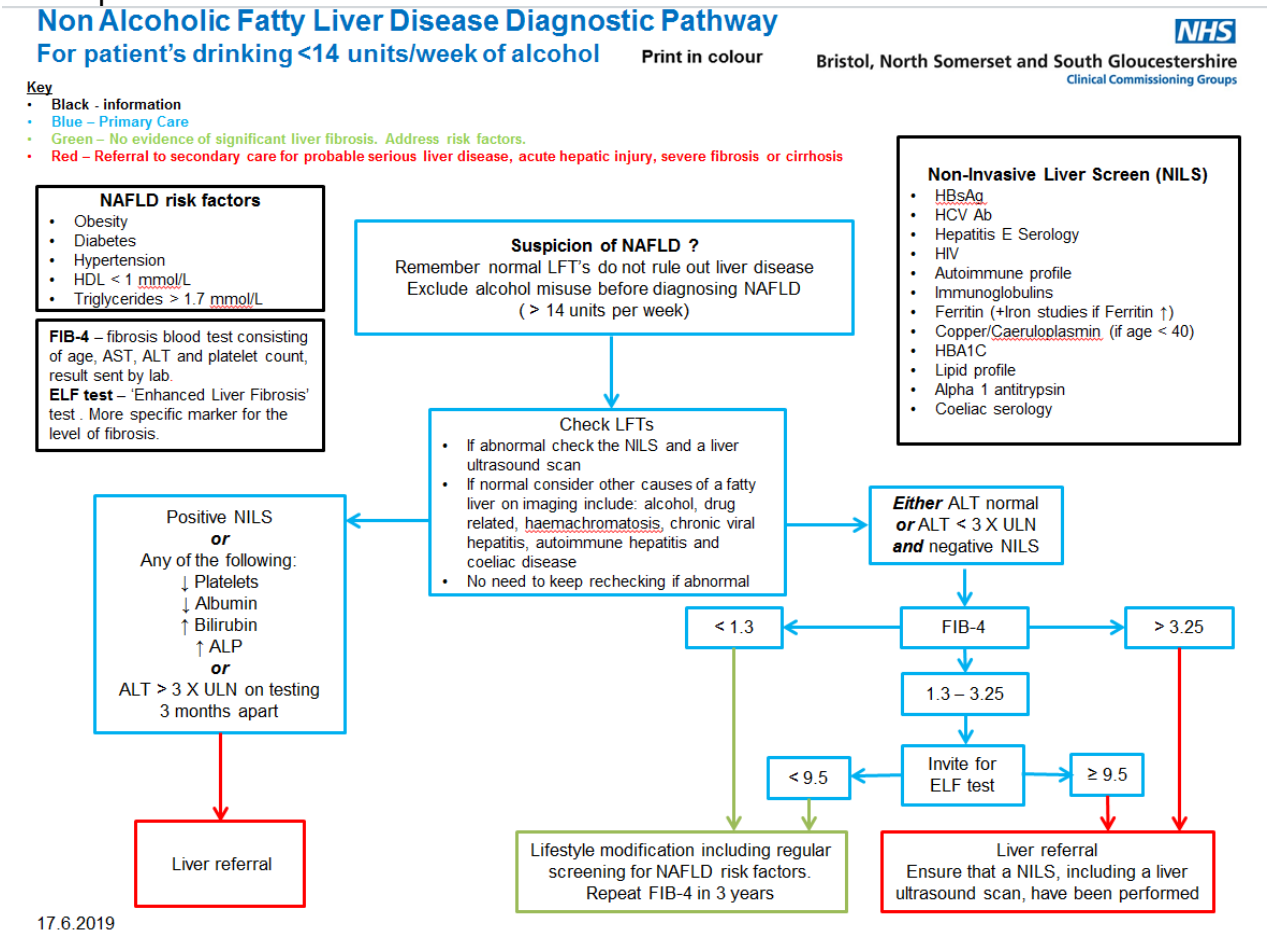
NAFLD is increasingly common with 20% of the population estimated to have NAFLD and up to 70% of the obese and diabetic population. It is not always a benign disease. Up to 5% have steatohepatitis and can progress to liver fibrosis. Therefore, it is essential to actively manage these patients even when they do not meet the threshold to refer to secondary care. Basic assessment is by Fibrosis 4 test (FIB-4). Low FIB-4 results in regular review of NAFLD risk factors and a repeat in 3 years, intermediate level results in enhanced liver fibrosis test (ELF) and high level direct referral to hepatology. It is also important to refer to the appropriate department if there are difficulties in managing any of the metabolic features such as the diabetes or lipid clinics.

<u>General measures</u>

- Weight loss by a combination of moderate calorie restriction and increased exercise aiming to lose 10% of body weight. More rapid weight loss may exacerbate liver damage.

Diet should consist of a low saturated fat, "heart healthy" diet or standard diabetic diet if indicated.

- Smoking cessation
- Current recommended "sensible" alcohol limits (Men and women up to 14 units weekly)
- In Type 2 diabetic patients tight glycaemic control with metformin is recommended since this has been shown to reduce the risk of diabetes-related microvascular complications and death and all-cause mortality. Treatment with metformin may also be beneficial to the liver.
- Use statins for conventional indications including Type 2 diabetes and cardiovascular risk >20% over 10 years. There is no evidence that patients with NAFLD are at greater risk from statin-induced hepatotoxicity
  Consider using a fibrate first line if isolated raised triglycerides 5-10 mmol/l.
  Refer Lipid Clinic if triglycerides > 10mmol/l.
- Look for and treat hypertension particularly in patients with type 2 DM.
  Consider ACE Inhibitors or A2RA's as first line therapies for hypertensive patients with NAFLD.



References

Advice based on
Guidelines on the management of abnormal liver blood test. Newsome P et al. Gut 2017

(Clinical services and standards committee of the British Society of Gastroenterology)