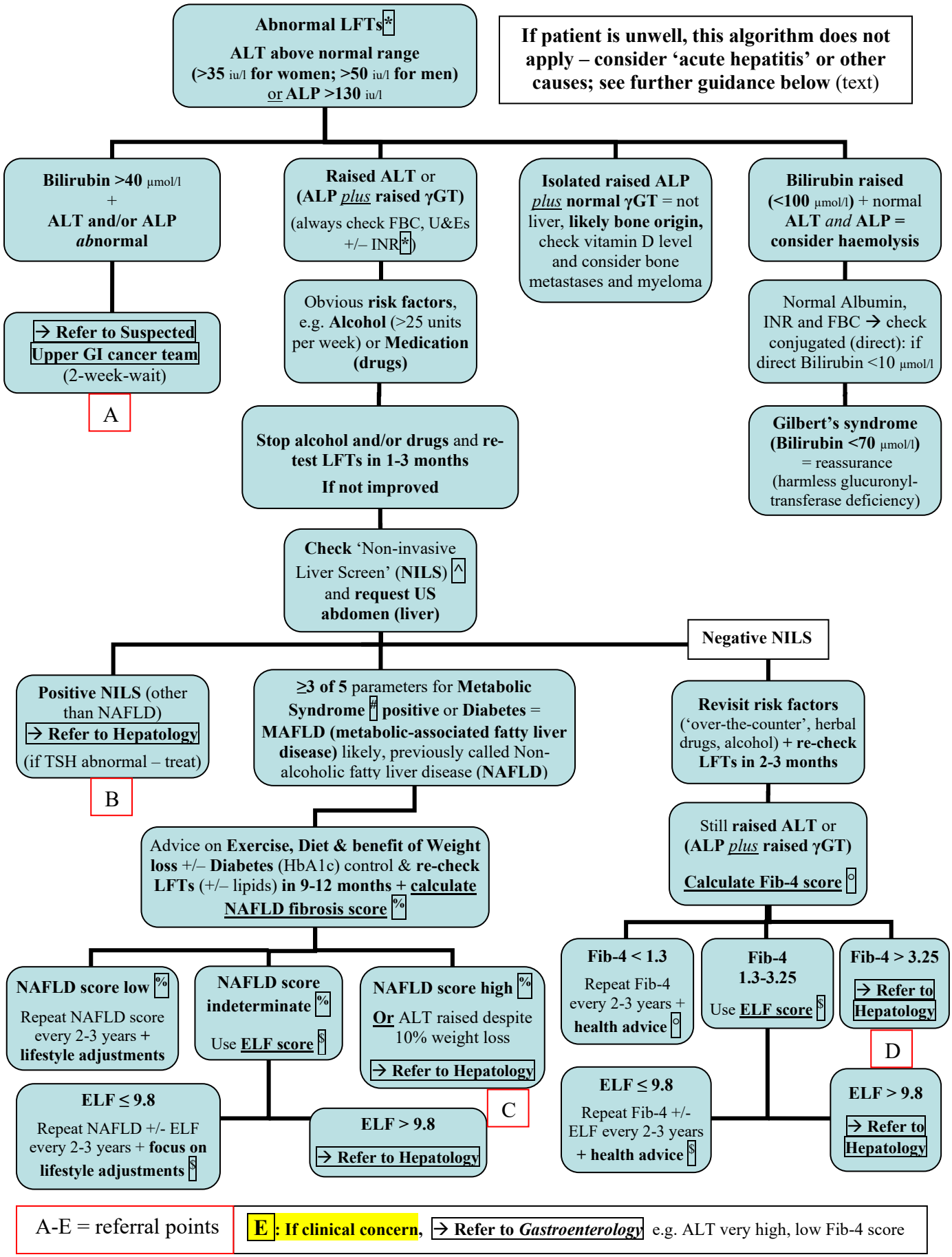
Abnormal Liver Function Tests (LFTs) in asymptomatic patient – Somerset Algorithm (2025)



A-E = referral points

E: If clinical concern, → Refer to *Gastroenterology* e.g. ALT very high, low Fib-4 score

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*: **Consider Liver Cirrhosis if albumin *low*, platelets *low* and/or bilirubin *high* (if also INR *high*, *decompensated* cirrhosis) –** if so, Refer to Hepatology

^: **Non-Invasive Liver Screen (NILS)** – blood tests (click here for **NILS form**)
- Hep B + C serology
- *Fasting* glucose, HDL, triglyceride (to investigate possible metabolic syndrome[#]), consider HbA1c
- Ferritin + transferrin saturation (fasting) if ferritin raised
- Autoimmune profile + immunoglobulins (IgG, IgA, IgM)
- α1-antitrypsin + TSH
- Coeliac screen (anti-TTG + IgA)
- AST (for Fib-4 and/or NAFLD fibrosis scores; also requires results for platelets +/- albumin and BMI)
- If age <40 years, NILS will also check serum caeruloplasmin and copper

[#]: **Metabolic Syndrome** (five parameters): Abnormal *fasting* glucose (e.g. >5.6 mmol/L; or diabetes mellitus), triglyceride (>1.7 mmol/L), HDL (<1.0♂/<1.3♀ mmol/L), high BMI (e.g. >30; or central obesity), blood pressure high (or on BP treatment) – if 3 out of 5 positive, **Non-Alcoholic Fatty Liver Disease** (**NAFLD**) is a probable (co)-diagnosis – **metabolic-associated fatty liver disease (MAFLD)** has become the preferred terminology. Further information is available in NICE guidance NG49 (July 2016): **www.nice.org.uk/guidance/NG49/**, incl. on treatment.

°: **Fib-4 score** provides a non-invasive estimate of liver fibrosis (scarring) (Tapper & Lok. NEJM 2017; 377(8):756). It requires results for AST, ALT, platelets and age to calculate, e.g. via **www.mdcalc.com/fibrosis-4-fib-4-index-liver-fibrosis**.
- Fib-4 score **low** (<1.3): it has a negative predictive value of approx. 90% for advanced fibrosis (F3 or F4, METAVIR) with approx. 80% sensitivity. Repeat every 2-3 years + lifestyle adjustments.
- Fib-4 score **intermediate** (1.3–3.25): use ELF score ([$]) + support lifestyle adjustments.
- Fib-4 score **high** (>3.25): → Refer to Hepatology with detailed drug history

[%]: **NAFLD fibrosis score** provides a "noninvasive system that identifies liver fibrosis in patients with NAFLD" (Angulo P *et al*. Hepatology 2007). It requires results for albumin, AST, ALT, platelets, diabetes/impaired fasting glucose, BMI and age to calculate, e.g. via **http://nafldscore.com/** (reliably predicts, with approx. 90% accuracy, which patients are unlikely to have cellular evidence of fibrosis on biopsy).

Age ≤ 65 years:
- NAFLD fibrosis score **low** (< -1.455): predictor of absence of significant fibrosis (F0-F2 fibrosis). Repeat every 2-3 years + focus on lifestyle adjustments.
- NAFLD fibrosis score **indeterminate** (≤ -1.455 to ≤ 0.675): use ELF score ([$]) + lifestyle adjustments

Age > 65 years:
- NAFLD fibrosis score **low** (< 0.12): predictor of absence of significant fibrosis (F0-F2 fibrosis). Repeat every 2-3 years + focus on lifestyle adjustments.
- NAFLD fibrosis score **indeterminate** (≤ 0.12 to ≤ 0.675): use ELF score ([$]) + lifestyle adjustments.

Any age:
- NAFLD fibrosis score **high** (> 0.675): predictor of presence of significant fibrosis (F3-F4 fibrosis): → Refer to Hepatology with detailed drug history

[$]: **ELF score** is a serum (blood) marker, testing Hyaluronic acid (HA), Procollagen III N-peptide (P3NP) and Tissue inhibitor of metalloproteinase 1 (TIMP-1); it provides a non-invasive estimate of liver fibrosis (scarring).
NICE guidance NG49 (July 2016) suggests ELF score ≤10.5 as cut-off for advanced fibrosis/cirrhosis assessment for patients with NAFLD (non-alcoholic fatty liver disease); **www.nice.org.uk/guidance/NG49/**.

The British Society for Gastroenterology (BSG) endorsed new guidance on the usage of **ELF test (Enhanced Liver Fibrosis)** in October 2024 which suggests a universal cut-off value of 9.8 – more information available via ELF test (Enhanced Liver Fibrosis) - Health Technology Wales (adapted in Somerset in February 2025).

Indeterminate NAFLD fibrosis score (between -1.455 and +0.675):
- ELF score ≥9.8: → Refer to Hepatology with detailed drug history
- ELF score <9.8: Focus on lifestyle adjustments (+/- medication to best manage metabolic syndrome, e.g. statins, BP therapy, metformin if diabetes); repeat NAFLD score every 2-3 years (+/- ELF score as per algorithm), for trend assessment. Give general well-being advice reg. positive effects of exercise and healthy diet (important).

For patients with negative NILS (and no metabolic syndrome):
Intermediate Fib-4 score (between 1.3 and 3.25):

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- ELF score ≥9.8: → Refer to Hepatology with detailed drug history
- ELF score <9.8: Monitor LFTs and keep reviewing alcohol, drugs (incl. over the counter, herbal remedies) and medications as possible explanations for raised ALT/ALP.
- Give general well-being advice reg. positive effects of exercise and healthy diet (important).
- Repeat Fib-4 score every 2-3 years (+/- ELF score as per algorithm), for trend assessment.

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If the **patient is unwell +/- pyrexia (e.g. sepsis)**, urgent clinical attention is required as some patient may benefit from acute admission into hospital (if working with sewage, consider leptospirosis).

For **patients with likely 'acute hepatitis'** (high ALT plus non-specific illness), check the following: Hep A, Hep B, EBV, CMV, +/- Hep E if other results negative ('acute hepatitis screen' on lab testing). Add Hep C if high-risk behaviour (e.g. intravenous drug use; men who have sex with men).

The British Society of Gastroenterology (BSG) has published its "**Guidelines on the management of abnormal liver blood tests**" in 2017 (Newsome PN, *et al.* Gut 2017), for more information.

- Mildly abnormal liver test results are a common and often incidental finding. In the absence of jaundice or symptoms suggestive of biliary or hepatic disease, mild to moderate elevation in the ALT (40–200) or the ALP (110–500) usually requires investigation, normally only on a routine basis. The ALT reflects hepatocellular injury, whilst the ALP often reflects biliary or obstructive liver disease. However, there is a considerable overlap in the degree of elevation of both these enzymes in both intrinsic and obstructive liver disease. An isolated raised ALP might not be of liver origin (e.g. bone, small intestine), particularly in the context of a normal gamma-GT (not liver-specific). *Functional* liver assessment is best done by looking at bilirubin (high), albumin (low) and INR (high), as well as platelet count (low); ALT and ALP reflect liver cell *injury*.
- In young patients with persistently abnormal LFTs check serum copper & caeruloplasmin, and in acute presentation consider Hep A, Hep B, Hep E, EBV, CMV serology (Hep C in patients with high-risk behaviour).
- The commonest causes of abnormal liver function tests (LFTs) are, in no particular order:
    - 'Fatty liver' (NAFLD, non-alcoholic fatty liver disease) – spectrum from echo-bright US abnormality over NASH (non-alcoholic steato-hepatitis) to NAFLD-related liver cirrhosis
    - Alcohol (alcohol-related liver disease, ARLD)
    - Drugs or medication (drug-induced liver injury = DILI)
    - Chronic viral hepatitis (B and/or C)
    - Obstructive biliary disease, e.g. gallstones or malignancy
    - Infiltrative diseases of the liver (e.g. neoplasia)
    - Autoimmune hepatitis (AIH), primary biliary cholangitis (PBC), primary sclerosing cholangitis (PSC)
- Non-invasive liver screen (NILS) investigations reveal a cause for liver test abnormalities in approximately 80–90% of patients. In this remaining 10 to 20% of patients, we then need to decide whether these patients should undergo further investigations like non-invasive fibrosis blood tests (e.g. Fib-4, NAFLD fibrosis, ELF score) or ultrasound-based elasticity assessment (e.g. FibroScan®, 'stiffness') or liver biopsy (histology). Many specialists will perform some of those investigations when there is persistent (more than six months) elevation of ALT levels. However, if there is strong reason to believe that the abnormal LFTs are due to alcohol or 'fatty liver' (NAFLD), patients should attempt a period of alcohol abstinence or weight loss (ideally, 5-10%) to assess whether there is any improvement in the LFT results before a more invasive investigation is performed. Previous studies have shown that in this group of patients the diagnoses made after liver biopsy tends to be as follows: approx. 1/3 non-alcoholic steato-hepatitis (NASH; i.e. risk of fibrosis progression), 1/3 simple 'fatty liver'; less than 1/10 had cryptogenic hepatitis (9%) and drug-related liver injury (8%); only 2% had autoimmune hepatitis (Skelly M, *et al*. J Hepatol. 2001; analysing 354 patients' liver biopsy specimens).