Editorials

Detecting liver disease in primary care:

are we ready for change?

Liver disease is the third commonest cause of premature death in the UK, with an estimated 61 000 years of working life lost per year.[1] Liver disease is often diagnosed late, when intervention is less effective. Reports from the All Party Parliamentary Hepatology Group (APPHG)[2] and *Lancet* Liver Commission in 2014[3] both highlighted primary care as a setting where detection and management of liver disease require urgent improvement. The Royal College of General Practitioners (RCGP) has made liver disease a clinical priority area from April 2016 for 3 years. The liver champion's mandate is to support primary care to work towards better identification of patients at risk of, or in the early stages of, liver disease. The goal is for GPs to intervene before liver disease becomes established.

WHAT HAS CHANGED?

Recommendations from the *Lancet* commission and new National Institute for Health and Care Excellence (NICE) guidelines on cirrhosis and non-alcoholic fatty liver disease (NAFLD) signal a shift in focus around detection of liver disease.[3–5] A risk factor-based approach is recommended, particularly for NAFLD and alcohol-related liver disease (ALD). It is acknowledged that normal blood tests do not exclude significant disease, and there is little mention of complex algorithms to interpret liver function tests (LFTs). The guidelines do emphasise the importance of ruling out less common, and often easily treated, causes early in the diagnostic pathway. Clinicians are advised to tailor diagnostic tests according to clinical suspicion, and refer early for viral, autoimmune, and metabolic causes of liver disease.

NICE now recommends that all persistently heavy drinkers have a liver fibrosis assessment, independent of derangements in LFTs. This translates as all *'men who drink >50 units of alcohol per week and women who drink >35 units of alcohol per week and have done so for several months'* being offered transient elastography (fibroscan).[4] The guidelines advise fibroscan as the first-line investigation in hazardous drinkers, rather than serum markers or scoring systems, to estimate fibrosis. If the fibroscan excludes cirrhosis, this should be repeated every 2 years if heavy alcohol consumption continues. Diagnosing NAFLD is more complicated.

> *"We have been failing to detect large numbers of patients with liver disease in our communities. We now have up-to-date guidelines to help us increase diagnosis rates. So what are we waiting for?"*

It is estimated that between 20–30% of the adult population have NAFLD.[6] This number is far higher than experience and evidence suggest we are currently diagnosing in primary care.[7] NICE falls short of recommending any formal diagnostic testing for those at high risk of NAFLD due to concerns around the specificity of the most cost-effective and accurate test — the fatty liver index (FLI). This is seen as a priority area for further research by the guideline development group. We are advised by NICE to *'be aware that NAFLD is more common in people who have type 2 diabetes or metabolic syndrome'*.[5] How this 'awareness' translates into any additional assessment in these patients is open to interpretation.

Although NAFLD is common, most cases will run a benign course. Only about 10% of those with NAFLD (2–3% of the total population) have non-alcoholic steatohepatitis (NASH) with risk of progressive fibrosis leading to cirrhosis.[6] Several non-invasive methods to identify those at risk have been compared. The NICE NAFLD guidelines advise considering the use of the enhanced liver fibrosis (ELF) blood test. This was based on high clinical accuracy and modelled cost-effectiveness. The ELF test combines three serum biomarkers, which have been shown to correlate with advanced fibrosis/cirrhosis as assessed by liver biopsy[8] (hyaluronic acid (HA), procollagen III amino terminal peptide (PIIINP), and tissue inhibitor of metalloproteinase 1 (TIMP-1)). It requires a single serum sample. Those with a score of less than 10.51 are unlikely to have advanced fibrosis and should be reassessed using the ELF test every 3 years (Figure 1).

BARRIERS TO IMPLEMENTING CHANGE

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Liver disease is not currently promoted as a priority area by clinical commissioning groups (CCGs). There are no incentives to keep registers of patients with chronic liver disease. There are no targets for detection based on estimated population prevalence. Patients at risk of NAFLD, who are often already under routine follow-up for other reasons, do not, generally, have a comprehensive assessment for liver disease. It is not standard practice to recall patients with NAFLD/ALD, who do not yet have advanced fibrosis, creating difficulties in reassessment if risk factors remain. If diagnosis rates are to increase, robust systems need to become embedded in routine practice and incentivised at national and local levels. With news that the Quality and Outcomes Framework (QOF) is being gradually phased out, new methods to ensure this happens will need to be devised.

The NICE recommendation that all persistently harmful drinkers should have a fibroscan to assess for cirrhosis, and that this should be repeated every 2 years, is currently unrealistic. Most GPs do not have access to fibroscan as a direct test and, unless this becomes available, secondary care will be swamped with referrals for cirrhosis assessments. Five per cent of males and 4% of adult females are estimated to be drinking at harmful levels of ≥50 and ≥35 units of alcohol per week respectively.[9] With an estimated adult UK population of about 50 million in 2014[10] this equates to 2.25 million people. To conduct around 1.125 million scans a year for this purpose alone would require about 250 scanners doing 20 scans a day, 5 days a week, all year. With the estimated cost (taking into account equipment and staff costs) being around £50 per scan[11] this would cost about £56 million per year. Consultations with hospital specialists would be in addition to this figure.

The NICE recommendation for the use of the ELF test in NAFLD poses similar challenges. ELF is currently unavailable in most NHS laboratories. If it was to become available, and used on even half

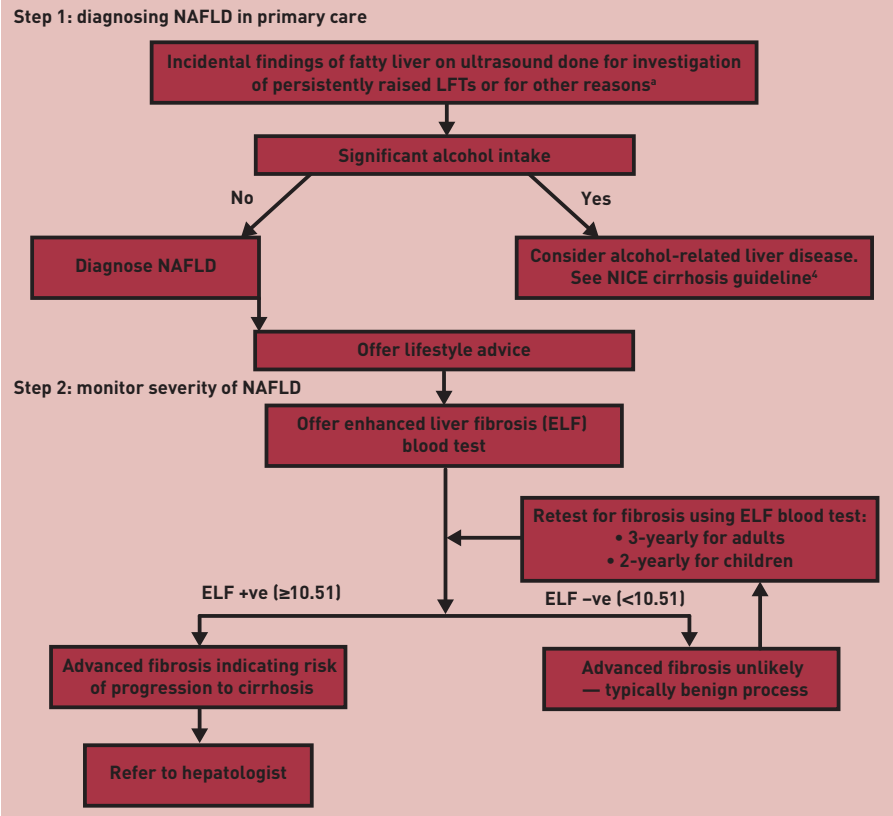

Figure 1. NICE pathway for diagnosing NAFLD in primary care. [a]Please note, abnormal LFTs are not diagnostic for NAFLD and may be normal or raised. LFT = liver function test. NAFLD = non-alcoholic fatty liver disease.

of the patients estimated to have NAFLD, this would mean 5 million tests conducted annually, the majority of which would need to be repeated on a 3-yearly basis. The ELF test costs around £108.[5] If 10% of these identified NAFLD patients have NASH, with a predicted incidence of advanced fibrosis of 7% per year among this group,[6] then 0.7% of NAFLD patients would have a score of >10.51. This could lead to 35 000 referrals annually to hepatology for NAFLD alone. These figures are all based on identifying NAFLD in 10% of the population. Actual prevalence of NAFLD may be up to three times higher. The use of alternatives such as the AST:ALT ratio or NAFLD fibrosis score recommended by the *Lancet* commission may also challenge current resources. AST (required for both scores) is not part of the standard LFT panel in many areas. Concern about the increased rates of referral if the AST:ALT ratio was to become a standard part of assessment have led at least one CCG to reject its introduction.[12]

CONCLUSION

Liver disease is at a crossroads. Its contribution to avoidable morbidity and mortality has been recognised. Our ability to detect disease early has improved and national recommendations are in place. There is also a move by the RCGP to promote liver disease as a priority area. What has not been addressed is the question of cost. Referrals to secondary care will increase dramatically unless there is a shift to more community-based care. Making fibroscans and the recommended blood tests more readily available to GPs are essential first steps, but this will increase costs in the short term. NHS England and CCGs have some difficult decisions to make about resource allocation. If we fail to adopt a public health approach to liver disease, and invest upstream, the long-term costs to the NHS may be catastrophic. With UK incidence and mortality rates rising,[13] the case for investing in prevention and early detection has never been stronger.

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