

Analysis

The pathway to better primary care for chronic liver disease

THE INCREASING HEALTH BURDEN OF LIVER DISEASE: A CASE FOR A CHANGE IN APPROACH

Liver disease, most commonly caused by alcohol or the metabolic syndrome (leading to non-alcohol related fatty liver disease [NAFLD]), is now a leading cause of premature death in the UK.¹ Morbidity and mortality due to liver disease have been rising in line with obesity, diabetes, and high levels of hazardous alcohol consumption. Liver disease caused by chronic viral hepatitis is an exception to this trend, with successful vaccination programmes for hepatitis B, along with very effective curative treatments for hepatitis C, leading to a reduction in end-stage liver disease as a result of these aetiologies in the UK.² Most patients with cirrhosis are diagnosed late, with up to 70% presenting with a complication of cirrhosis, such as variceal haemorrhage or ascites.³ Rising mortality rates due to liver disease are in sharp contrast to most other chronic diseases in the UK, where rates have been steadily falling with improved primary and secondary prevention, and better access to effective interventions.³ This has been partly driven by enhanced risk assessment and early intervention in primary care.⁴

Liver disease should now be considered as a preventable chronic disease. Risk factors are well known and easily identifiable, and access to diagnostic tests and evidence-based interventions has improved. But adoption of a preventive approach in primary care will require a major shift in the framing of liver disease. GPs are more familiar with reacting to abnormal blood results or a late-stage decompensated cirrhotic patient. In contrast with the preventive approach widely adopted for conditions such as heart disease, proactive assessment of the patient with risk factors for liver disease has not yet been widely accepted. There are no Quality and Outcomes Framework (QoF) incentives or widely followed guidelines in UK general practice to prompt change, although evidence is mounting that this would be a clinical and cost-effective response to rising levels of disease and death.

RESPONDING TO THIS INCREASED DISEASE BURDEN: POLICY INITIATIVES, GUIDELINES, AND RESEARCH

The rising burden of liver disease and the obvious disparity between liver disease and

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other chronic disease outcomes has led to a number of recent policy initiatives. A *Lancet* commission addressing liver disease in the UK was established in 2014 inviting a broad range of clinical, public health, and policy experts to establish a blueprint for improving liver disease outcomes.³ Initial recommendations and subsequent updates have all focused on improving the detection of liver disease in primary care as a priority goal.⁵ The Royal College of General Practitioners (RCGP), in collaboration with the British Liver Trust, made liver disease a priority area from 2016–2019. In addition to developing online clinical management resources,⁶ the partnership led to the publication of commissioning recommendations. This recognised that a policy approach was required to change individual practice.⁷ Lobbying by these groups has led to a recent change in the NHS Health Check best-practice guidelines, with a clinical assessment for liver damage now recommended for individuals reporting a history of hazardous alcohol consumption.⁸ These policy initiatives could have gone further with a more proactive approach to liver assessments for people with NAFLD risk factors, but the evidence base fell short of being able to support this. The latest National Institute for Health and Care Excellence (NICE) guidelines on NAFLD and liver cirrhosis were both published in 2016^{9,10} and already need updating with the rapid expansion of relevant research in the area.

Much recent research has focused on the clinical utility and cost-effectiveness of novel approaches to finding liver disease in the community, using primary care pathways. Three important areas have been identified: a structured or automated approach to the interpretation of liver blood tests; a more proactive approach to identifying who may be at high risk of significant liver disease; and improved community access to better diagnostic tests. It is likely that

a comprehensive strategy to tackle early liver disease would have to incorporate all three of these approaches, and much of the published work in this area now recognises this.

THE INTERPRETATION OF LIVER BLOOD TESTS: MOVING TOWARDS TARGETED TESTING AND AUTOMATION

Large numbers of liver blood tests are requested every day in primary care, as part of diagnostic work-up and treatment monitoring. A high proportion of these tests report at least one liver blood test abnormality and many of the abnormal tests are never investigated any further.^{11,12} A large UK study concluded that the majority of people in primary care with abnormal liver blood tests, but no clinical suspicion of liver disease, did not have diagnosed liver disease when actively investigated.¹³ This highlights the importance of the initial decision to request these tests, which should be based on clinical suspicion arising from knowledge of risk factors, or for specific drug monitoring, with agreed thresholds for drug discontinuation. How to respond to a mildly abnormal test outside of these contexts is the more difficult question. Targeted initial testing will reduce the proportion of ‘unexpected’ abnormal results and allow time and resources to focus on people at higher risk of clinically significant liver disease.

In part because of the reasons outlined above, GPs find the area of interpretation of liver blood tests challenging and many of the published algorithms are complex.¹⁴ In recognition of this, the British Society of Gastroenterology, in collaboration with a wide panel of stakeholders, developed a comprehensive guide to the management of abnormal liver blood tests, which advocates for early decision making around risk factors and likely aetiology, to avoid repeat testing.¹⁵ Creation of an ‘intelligent’ liver blood test requesting and

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reporting system takes these guidelines a step further, and has been developed and implemented in Tayside, Scotland.¹⁶ Using existing IT pathology systems, the requestor inputs some basic information about the patient including alcohol intake, metabolic risk profile, and test reason. The test is then processed by the lab in the context of this information with additional further second-line tests being analysed automatically according to initial results. Rather than isolated results being fed back, a complete results panel is produced with a suggested likely cause for the abnormality and advice on further management. This has led to a significant reduction in the number of abnormal liver tests that have not been appropriately investigated and managed.¹⁶

NOVEL PATHWAYS FOR MANAGING COMMON CAUSES OF CHRONIC LIVER DISEASE IN THE COMMUNITY

As the commonest reasons for liver blood abnormalities in primary care are alcohol-related liver disease (ARLD) and NAFLD, several collaborative groups have developed referral pathways for these conditions. The pathways aim to identify the minority who are at a high risk of developing liver cirrhosis, to refer them on for specialist management. The majority are directed to community-based management, with a focus on lifestyle modification and addressing risk factors in the context of multimorbidity and holistic care. The Camden and Islington Pathway is a recently published example of this approach, which focuses on liver fibrosis assessment for people presumed to have NAFLD.¹⁷ A clinical commissioning group (CCG)-wide approach was studied, where individuals with abnormal liver blood tests from presumed NAFLD had liver fibrosis staging using a two-step process in primary care. An initial assessment of the likelihood of significant liver disease was carried out using a Fib-4 score, which uses a combination of routinely available blood tests in an algorithm giving a likelihood score for advanced liver fibrosis. Patients identified as low risk of progressive liver disease using the Fib-4 score could then be confidently managed by primary care with guidance to recheck the Fib-4 score

every 3 years. If this test showed patients to be in an ‘indeterminate category’ this was followed by the NICE-recommended enhanced liver fibrosis (ELF) test (a direct liver fibrosis serum marker) before a referral decision was made. Direct referral was recommended in those with a high-risk Fib-4 score. This more structured approach with increased test availability led to a three-fold increase in cirrhosis detection, and reduced unnecessary referrals (where no liver fibrosis was detected) by 80%.¹⁷ Other CCGs have commissioned similar pathways. The inclusion of patients with ARLD and the addition of GP direct access to transient elastography (FibroScan) have led to large increases in the detection of advanced fibrosis/cirrhosis in these published examples.¹⁸

Reliance on abnormal liver blood tests alone to enter a detection pathway will miss a significant proportion of individuals with advanced liver disease. Liver blood tests are insensitive for the detection of advanced liver disease secondary to NAFLD and ARLD. In order to increase the early detection of significant liver disease, alternative approaches using liver disease risk factors to trigger an assessment have been studied. A good example of this approach is the Nottingham Scarred Liver Project, which has become a regionally commissioned pathway following a successful pilot project.¹⁹ In this pathway, individuals with risk factors including type 2 diabetes, obesity (BMI >30), the metabolic syndrome, or harmful alcohol use are triaged directly to have transient elastography conducted regardless of any abnormality in liver enzymes. This risk-based approach found that 6% of those with these risk factors who underwent transient elastography had cirrhosis. If these patients had been triaged using abnormal liver

blood tests alone, 39% of these cirrhosis cases would have been missed.¹⁹ Both the Scarred Liver Project and Camden/Islington approach have been shown to be highly cost-effective as compared with standard care.^{20,21}

WHAT NEXT FOR CHRONIC LIVER DISEASE MANAGEMENT IN PRIMARY CARE?

Comprehensive uptake of a standardised approach to chronic liver disease management in UK primary care remains elusive. This is despite the existence of recently updated guidelines and commissioning recommendations, more automated approaches, and better access to improved diagnostic tests and pathways. There are many potential reasons for this, including a historical lack of emphasis on liver disease in the GP training curriculum contributing to low confidence in this area of practice.¹⁴ As part of the RCGP liver disease priority work from 2016–2019 the curriculum has now been updated to reflect the importance of increasing liver disease morbidity and mortality as an emerging issue.²² Liver disease outcomes have been consistently absent from the QoF and it is hoped that the introduction of new quality improvement (QI) modules as part of the QoF may provide a long overdue opportunity to prioritise improvements in liver disease outcomes at a primary care level. There is still a pervasive attitude that diagnosing liver fibrosis and cirrhosis is futile, as therapeutic options are limited to ‘only lifestyle interventions’. As well as mounting evidence for the effectiveness of these lifestyle interventions in both ARLD and NAFLD,^{23,24} there are also now a number of drugs in late-stage clinical trials shown to be effective in slowing liver fibrosis/progression to cirrhosis.²⁵ Finally, there remains an absence of implementation research into liver disease pathways and how these may fit into the many competing priorities within high primary care workloads.

Tackling the challenges of implementing new chronic disease management pathways in primary care, and how liver disease

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fits into established ways of working, is key to improving usability and therefore effectiveness. An inclusive approach to pathway development is crucial to maximise clinical impact, while minimising any additional workload. Primary care professionals and service users will need to be at the core of any change. GPs are already working at more than full capacity and approaches that are funded and dovetail with established and related management pathways (for example, diabetes and obesity management) are most likely to be implementable outside of a research environment. Any future research into this area must consider real-world implementation throughout the research process, as well as further defining the best clinical approach incorporating risk assessment, optimal use of diagnostic modalities, and referral criteria/intersectional working.

The pathway to better primary care for chronic liver disease is becoming clearer: if primary care is serious about improving outcomes for patients with liver disease, now is the time to implement change.

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