BMJ Open Gastroenterology

Enhanced liver fibrosis test facilitates stratification of people with alcohol use disorder in primary care

Alexander Hung ,[1,2] Charlotte Turner,[2] Freya Rhodes ,[1] Jennifer Ryan,[1] William M Rosenberg[1,2]

To cite: Hung A, Turner C, Rhodes F, *et al*. Enhanced liver fibrosis test facilitates stratification of people with alcohol use disorder in primary care. *BMJ Open Gastroenterol* 2025;**12**:e001905. doi:10.1136/bmjgast-2025-001905

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/bmjgast-2025-001905).

AH and CT contributed equally.

Received 13 May 2025
Accepted 9 July 2025

[1]Hepatology, Royal Free Hospital Sheila Sherlock Liver Centre, London, UK
[2]Institute for Liver and Digestive Health, Division of Medicine, UCL, London, UK

Correspondence to
Dr Alexander Hung;
alexander.hung1@nhs.net

ABSTRACT

Objective Alcohol-related liver disease (ArLD) is a leading cause of liver-related mortality, but affects a minority of people with alcohol use disorder (AUD). Of people with AUD, only those with ArLD require hepatologist input, necessitating case stratification. However, many are referred with established cirrhosis, when opportunities for intervention are limited. We report the evaluation of a novel primary care pathway using the enhanced liver fibrosis (ELF) test for early detection and stratification of ArLD patients.

Methods The ELF alcohol pathway (EAP) was established in January 2020 and evaluated in May 2023. General practitioner referrals to a single liver centre using the EAP were compared with standard care (SC) referrals. The presence of steatosis constituted an 'appropriate' referral. The prevalence of structural ArLD and each stage of fibrosis was assessed, with liver status ascertained through electronic patient records.

Results The EAP was followed by 121 patients. Unnecessary referral (ELF<9.8) was avoided for 24.8% (n=30), with the 91 remaining EAP referrals compared with 197 contemporaneous SC referrals. Most referrals were deemed appropriate (97.5% vs 92.3% for SC and EAP, respectively), but significantly more SC referrals had advanced fibrosis (OR 2.68 (1.50 to 4.93); p<0.001), cirrhosis (OR 6.58 (2.84 to 17.79); p<0.0001) or decompensated cirrhosis (10.7% vs 0%; p<0.001).

Conclusion Using the EAP facilitated earlier detection of ArLD, with 8% of EAP referrals having established cirrhosis versus 35.5% of SC referrals. Unnecessary specialist referral was avoided for one-quarter of those assessed on the EAP. Pathway uptake was impacted by poor dissemination during the COVID-19 pandemic. Better implementation is warranted.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Liver disease is often asymptomatic and can be hard to identify in the minority of the people with alcohol use disorder who develop liver damage. Consequently, severe liver disease is often diagnosed at a late stage, when cirrhosis has developed and liver damage may be irreversible. Furthermore, many individuals referred from primary care to specialist liver services for problematic drinking do not have liver damage and would be better served by community alcohol services focused on addressing their drinking habits.

WHAT THIS STUDY ADDS

⇒ This study demonstrates that the use of the enhanced liver fibrosis (ELF) test in primary care can facilitate the early diagnosis of liver damage among people with alcohol use disorder and reduce unnecessary referrals to specialist liver services.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study is likely to change practice in the assessment of people with alcohol use disorder in primary care, through the use of the ELF test to stratify people with liver damage according to need for specialist referral. This enables those without evidence of liver damage to receive care through community-based alcohol services, and for those with liver damage to undergo early assessment of fibrosis severity. Policy implications of this work relate to the use of measures that improve the early detection of reversible liver disease.

INTRODUCTION

Chronic liver disease (CLD) is a leading cause of death, accounting for approximately 2.4% of global mortality,[1] with deaths related to CLD continuing to rise even as deaths attributable to other common drivers of mortality are falling.[1] Following the emergence of highly effective treatments for viral hepatitis B and C, there has been an increasing focus on liver diseases driven by reversible aetiologies such as alcohol and metabolic risk factors.

Globally, alcohol-related liver disease (ArLD) accounts for approximately one-quarter of cirrhosis deaths and one-fifth of deaths from hepatocellular carcinoma,[2] with alcohol consumption responsible for approximately 60% of CLD cases in the UK.[3] Along with a 400% increase in mortality rates associated with ArLD since 1970,[4] annual alcohol-related hospital admission rates in the UK have risen by around 20% over the past

decade, with 350 000 such admissions in 2019.[5] These admissions confer a substantial financial burden, costing the National Health Service (NHS) approximately £3.5 billion per annum,[6] with the annual cost of alcohol-related harms estimated at £27.4 billion when factoring in productivity losses and costs to social and criminal justice services.[7]

Excessive alcohol intake entails 'hazardous' (>14 unit/week)[8] or 'harmful drinking' (>35 units/week for females or 50 units/week for males),[8] which may be accompanied by alcohol use disorder (AUD). AUD is defined as problematic alcohol use accompanied by significant functional impairment or psychosocial stress,[9] with alcohol excess perpetuated by an impaired ability to stop or control intake. While AUD is associated with a wide range of morbidities, including psychosocial, neurological and gastroenterological pathologies, only a third of hazardous or harmful drinkers develop liver damage.[10] In these individuals, chronic alcohol excess leads to alcohol-related liver damage (ie, ArLD) beginning with the accumulation of fat (steatosis), which is itself associated with increased mortality even in the absence of fibrosis.[11–13] Of those with steatosis, it is estimated that fibrosis will develop in up to 35%, with 10%–20% progressing to cirrhosis[14]; the likelihood of premature death increases commensurate with the degree of fibrosis. Notably, alcohol-related liver damage can occur in the absence of the behavioural changes reflective of AUD, thus assessment for the presence of ArLD is essential for all those with hazardous alcohol intake.

The rising incidence of CLD is placing increasing pressure on specialist liver services in secondary care, amplifying the need for optimisation of referral pathways. Recognition of this need has driven policy recommendations centred on shifting the focus of healthcare provision from illness to prevention, and from hospital settings to community and primary care.[15]

Effective and efficient provision of care for people with excessive alcohol intake heavily centres on differentiating those with ArLD (for whom specialist liver input is merited) from those who have hazardous or harmful drinking patterns without structural liver disease. Current practice among general practitioners (GPs) in England is highly variable, with some referrals to liver specialists based on patterns of alcohol use and others employing non-invasive tests to identify those most likely to have ArLD.[16] More effective approaches are required to differentiate patients with ArLD from those with isolated AUD.

Non-invasive tests of liver fibrosis include blood-based tests, which employ biomarkers of liver fibrosis, and elastography. Elastography requires operator expertise, specialised equipment and dedicated clinic time; furthermore, liver stiffness measurement (LSM) may be influenced by active alcohol excess.[14] Blood-based biomarker tests, meanwhile, lack the immediacy of elastography but can be readily performed in primary care for large numbers of patients efficiently. The most well-validated of these blood-based tests is the enhanced liver fibrosis (ELF) test, which integrates the automated measurement of three biomarkers of fibrosis—amino-terminal peptide of procollagen III, tissue inhibitor of matrix metalloproteinase-1 and hyaluronic acid—in an algorithm to generate a unitless composite score. Used at the recommended thresholds, ELF has lower specificity for the detection of advanced fibrosis in ArLD than elastography, but is highly sensitive with excellent negative predictive value.[17] The use of ELF has been validated as both a diagnostic and prognostic tool in patients with ArLD.[18 19]

In January 2020, the ELF alcohol pathway (EAP) was introduced as a referral pathway for primary care practices in Camden and Islington, North London.[20] An abridged flow diagram is shown in figure 1, with online supplemental figure 1 depicting the pathway in full; low-risk, hazardous and harmful drinking thresholds have been adapted from National Institute for Health and Care Excellence (NICE) guidance.[21] The pathway enables GPs to use the ELF test to guide the need for specialist referral in patients with AUD, with the recommendation that an ELF score >9.8 is an indication for referral (in line with evidence-based cut-offs for the prediction of advanced fibrosis).[22] In this longitudinal study, we sought to evaluate the impact of the pathway on referrals made over the subsequent 3-year period.

METHODS

This was a retrospective service evaluation of all alcohol-related referrals made from primary care to the Royal Free NHS Foundation Trust Hepatology service between January 2020 and January 2023. Alcohol-related referrals were defined as a referral made for the investigation and management of suspected liver disease in the context of alcohol excess or harmful alcohol intake. Referrals made during this period were extracted from a list of all hepatology outpatient clinics at the Royal Free London NHS Foundation Trust compiled by the data analytics team (filtered to identify first reviews for suspected ArLD), and cross-referenced with a list of ELF tests conducted by the central regional laboratory (Health Services Laboratories Pathology), see figure 2. Duplicate entries appearing in both lists were removed. Patients aged >75 years were excluded because the use of ELF has not been validated in this context in the elderly. Those referred for follow-up after a liver-related hospital admission were evaluated separately.

The final cohort was divided into two groups: patients referred using the EAP, and those referred using standard care (SC) who had not undergone community ELF testing. The number of patients assessed with ELF in primary care and appropriately not referred according to the EAP (based on an ELF score<9.8) was determined from the laboratory test lists.

This evaluation was reported in keeping with Strengthening the Reporting of Observational Studies in Epidemiology guidance for observational studies (checklist included as an online supplemental file 2).

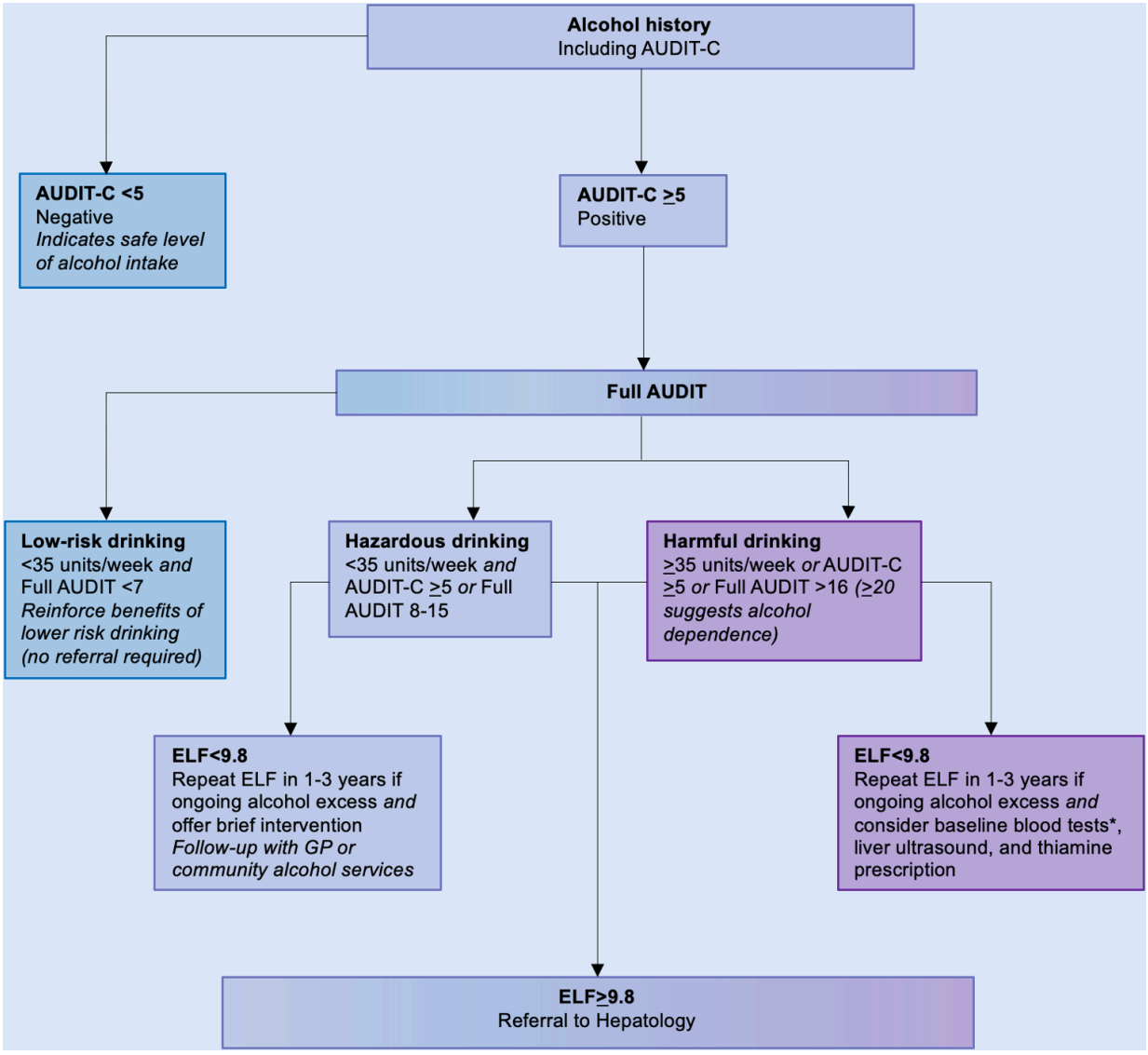

Figure 1 Abridged flow diagram depicting the referral process for alcohol use disorder patients with suspected alcohol-related liver disease (image adapted from the National Health Service Camden and Islington alcohol pathway). Simplified flow diagram depicting the ELF alcohol pathway (adapted from the NHS North Central London/Camden Clinical Commissioning Group Alcohol Pathway). Low-risk, hazardous and harmful drinking thresholds are adapted from National Institute for Health and Care Excellence guidance.[20] The North Central London Integrated Care Board pathway is shown in more detail in online supplemental data and can be viewed at https://gps.northcentrallondon.icb.nhs.uk/pathways/alcohol-1. *Blood tests should include: full blood count/liver function tests/coagulation profile±non-invasive liver screen. AUDIT, Alcohol Use Disorders Identification Test; AUDIT-C, Alcohol Use Disorders Identification Test Consumption; ELF, enhanced liver fibrosis; GP, general practitioner.

Patient and public involvement

The EAP was designed by the Camden and Islington Liver Working Group,[23] which includes patient and public members alongside representatives from local GPs, commissioners, public health and hepatology secondary care services.

Data extraction

Data were extracted from hospital electronic patient records with reference to primary care records where necessary. Information collected included results of haematology, biochemistry, imaging, elastography and (where available) liver histology tests. Fibrosis-4 Index (FIB-4) scores were calculated. Appropriate statistical tests for significance were performed to compare those patients referred using the EAP and SC (χ^2 for categorical variables, t-tests for parametric data and Mann-Whitney U for non-parametric data). A comparisonn was made between patients referred on the EAP or via SC, with ORs and 95% CIs calculated for each stage of CLD and significance values obtained using Fisher's exact test.

The performance of the two referral pathways was evaluated against a composite clinical judgement of liver fibrosis severity. After data extraction, the subject of each referral was assigned to a fibrosis category by

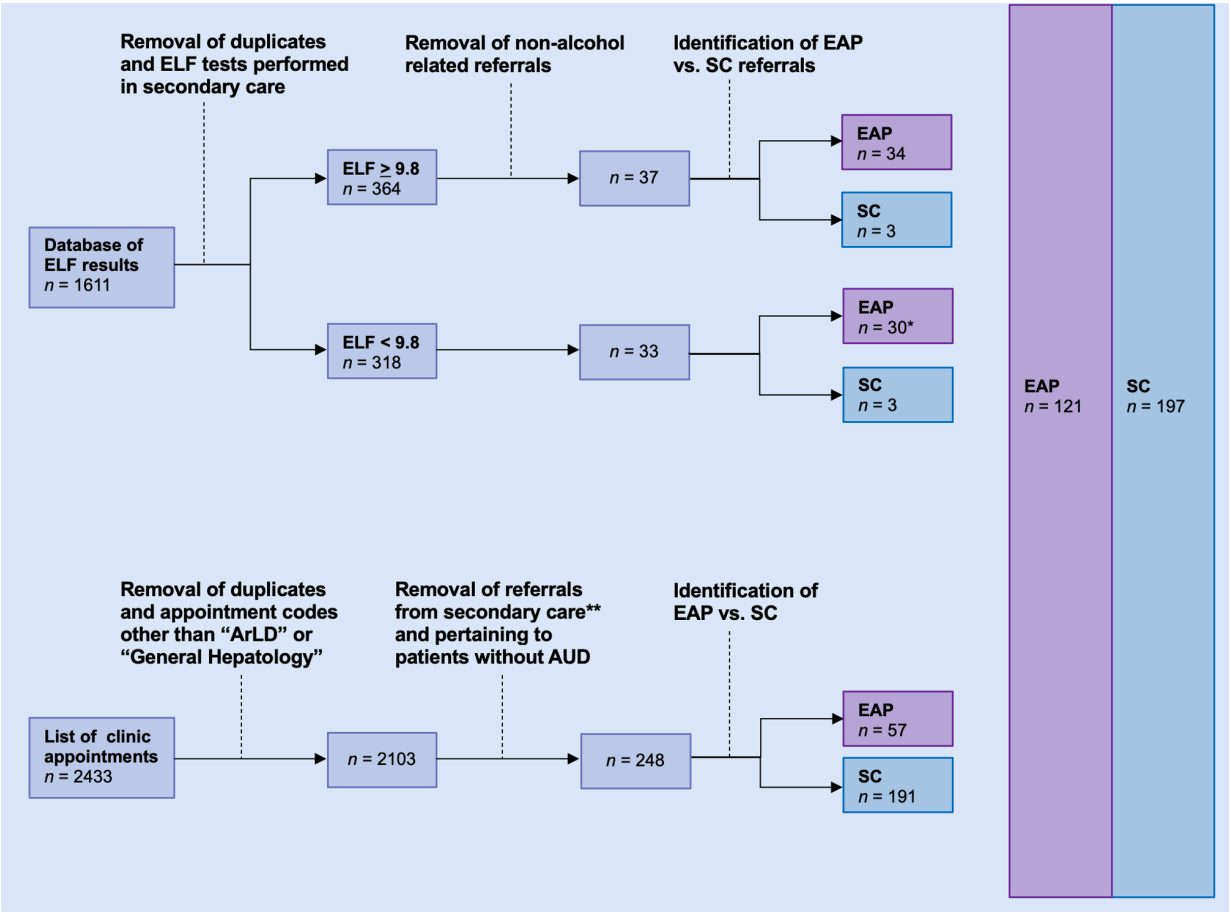

Figure 2 Flow diagram depicting the process for identification of secondary care referrals pertaining to patients with AUD. Flow diagram depicting the process for identification of specialist referrals from primary care made using the EAP or via SC. *This group of patients was assessed on the EAP and not referred (as ELF<9.8), with the exception of two patients for whom referrals were made but appropriately rejected in light of an ELF<9.8. **Post-discharge referrals from secondary care were analysed separately and presented in online supplemental data. AUD, alcohol use disorder; ArLD, alcohol-related liver disease; EAP, ELF alcohol pathway; ELF, enhanced liver fibrosis; SC, standard care.

liver specialists (AH, WMR) using objective predefined criteria (online supplemental table 1).

Outcomes

The primary outcomes of interest, in the context of this pathway evaluation, were: (1) the proportion of referrals deemed to be 'appropriate', on the basis of the presence of structural ArLD; (2) the prevalence of any alcohol-related liver pathology (including the prevalence of each degree of structural liver disease and/or hepatic decompensation on first clinic review). Secondary outcomes, some of which are particularly relevant with regards to the development of future guidelines, included the presence or absence of fibrosis. The proportion of patients assessed on the EAP who avoided unnecessary referral was based on the number of patients with AUD assessed in primary care on the EAP and found to have an ELF<9.8.

RESULTS

Baseline demographic and clinical characteristics are presented in table 1. For any variables with missing data points, the denominator has been adjusted to reflect the number of patients for whom data were available. Compared with patients referred via the EAP, patients referred via SC were significantly more likely to have higher recorded alcohol intake and higher levels of social deprivation, along with higher AST values, lower platelet counts and higher FIB-4 values. While the mean BMI of SC patients was lower than that of the EAP patients (the significance of which is unclear), the two groups were otherwise well-matched in terms of metabolic risk factors (such as dyslipidaemia, hypertension, type 2 diabetes and smoking history). While more patients in the EAP group underwent elastography, there were no significant differences between the proportion of patients in each group who had undergone imaging (largely ultrasonography) or liver biopsy.

During the evaluation period, 129 patients were initially enrolled in the EAP. However, of these, eight were aged >75 years and were thus excluded. Of the remaining 121 patients, referral was avoided for 24.8% (n=30) who were assessed via the EAP and found to have an ELF<9.8, none of whom have since presented with liver disease. The 91 patients referred using the EAP were compared

Table 1 Baseline demographic and clinical characteristics for the overall cohort, stratified by referral pathway

Patient characteristics	Total (n=288)	EAP (n=91)	SC (n=197)	Significance
Age (years), mean (SD)	56.2±12.7	60.5±12.1	54.0±12.4	p<0.001
Sex				p=0.205
Male, n (%)	198 (68.8)	68 (74.7)	131 (66.5)	
Female, n (%)	90 (31.3)	23 (25.3)	66 (33.5)	
Ethnicity				p=0.673
Caucasian, n (%)	165/235 (70.2)	52/71 (73.2)	113/164 (68.9)	
Asian, n (%)	13/235 (5.5)	6/71 (8.5)	7/164 (4.3)	
Black, n (%)	5/235 (2.1)	2/71 (2.8)	3/164 (1.8)	
Mixed, n (%)	2/235 (0.9)	1/71 (1.4)	1/164 (0.6)	
Other n (%)	50/235 (21.3)	10/71 (14.1)	40/164 (24.4)	
BMI, mean (SD)	29.5±7.0	31.2±6.7	28.8±7.1	p=0.001
n	217	67	150	
>25, n (%)	157 (72.4)	56 (83.6)	101 (67.3)	p=0.01
>30, n (%)	96 (44.2)	39 (58.2)	57 (38.0)	
Alcohol units/week, median (IQR)	84 (90)	63 (48)	100 (101)	p<0.001
n	252	85	167	
Diabetes, n (%)	45 (15.6)	15 (16.5)	30 (15.2)	p=0.922
Hypertension, n (%)	109 (37.8)	40 (44.0)	69 (35)	p=0.186
Dyslipidaemia, n (%)	71 (24.7)	24 (26.4)	47 (23.9)	p=0.754
Smoking status				p=0.446
Never smoked, n (%)	63/260 (24.2)	18 (19.8)	45/178 (25.3)	
Currently smoking, n (%)	101/260 (38.8)	28 (30.8)	73/178 (41.0)	
Previously smoked, n (%)	96/260 (36.9)	36 (39.6)	60/178 (33.7)	
Deprivation score rank, median (IQR)	13 777.0 (12115.0)	16 683.0 (10859.0)	12 597.5 (11389.3)	p<0.001
n	285	89	196	
Deprivation score, decile				p=0.01
1 (most deprived)	6 (2.1%)	2 (2.2%)	4 (2%)	
2	34 (13.9%)	10 (13.2%)	24 (14.2%)	
3	47 (30.2%)	7 (20.9%)	40 (34.5%)	
4	51 (47.9%)	15 (37.4%)	36 (52.8%)	
5	34 (59.7%)	11 (49.5%)	23 (64.5%)	
6	33 (71.2%)	10 (60.4%)	23 (76.1%)	
7	35 (83.8%)	16 (78%)	19 (85.8%)	
8	20 (90.3%)	9 (87.9%)	11 (91.4%)	
9	23 (98.3%)	11 (100%)	12 (97.5%)	
10 (least deprived)	5 (100%)	0 (100%)	5 (100%)	
ALT, median (IQR)	50 (45)	53 (49)	49 (43.5)	p<0.001
n	285	91	194	
AST, median (IQR)	58.5 (62.8)	49 (43)	66 (73)	p<0.001
n	278	89	189	
AST/ALT ratio, median (IQR)	1.1 (1.0)	0.9 (0.5)	1.3 (1.1)	p<0.001
n	278	89	189	
Platelets ($\times 10^9$), median (IQR)	211 (91.5)	222 (71.5)	206 (112)	p<0.001
n	282	91	191	
FIB-4 score, median (IQR)	2.1 (2.7)	1.7 (1.2)	2.5 (3.3)	p<0.001
n	276	89	187	

Continued

Table 1 Continued

Patient characteristics	Total (n=288)	EAP (n=91)	SC (n=197)	Significance
Liver biopsy, n (%)	6 (2.1)	1 (1.1)	5 (2.5)	p=0.702
Elastography (FibroScan), n (%)	228 (79.2)	83 (91.2)	145 (73.6)	p=0.002
Valid reading* (%)	223/228 (97.8)	83/83 (100)	140/145 (96.6)	
mLSM, kPa (IQR)	6.9 (9.13)	6.2 (4.75)	7.6 (12.73)	p<0.001
Ultrasound, n (%)	236 (81.9)	80 (87.9)	156 (79.2)	p=0.104
CT, n (%)	27 (9.4)	6 (6.6)	21 (10.7)	p=0.377

*FibroScan results were considered invalid if IQR>30% or success rate <60%.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; EAP, ELF alcohol pathway; ELF, enhanced liver fibrosis; FIB-4, Fibrosis-4 Index; mLSM, median liver stiffness measurement; SC, standard care.

with 197 patients referred using SC (including three patients with an ELF<9.8 who were referred by GPs on other grounds) during the same time period. Results stratified by minimum degree of fibrosis are presented in table 2 and depicted graphically in figure 3 (results for specific fibrosis categories are presented in online supplemental table 2 and shown in online supplemental figure 2). The vast majority of referrals made using SC or EAP had at least steatosis and, as such, were deemed appropriate (97.5% vs 92.3%, respectively). The cohort of patients referred using SC were found to have significantly worse liver damage than those referred via the EAP, with a higher proportion of patients having at least advanced fibrosis (46.2% vs 24.2%; OR 2.68 (1.50 to 4.93); p<0.001), cirrhosis (35.5% vs 7.7%; OR 6.58 (2.84 to 17.79); p<0.0001) and decompensated cirrhosis (10.7% vs 0%; p<0.001). This trend persisted when assessing the proportion of each cohort that could be classified as having compensated advanced CLD[24]: 35.5% for the SC cohort versus 24.2% for those referred using the EAP (OR 1.73 (0.96 to 3.19)). This suggests that use of the EAP resulted in earlier diagnosis of ArLD at a stage at which liver damage remains reversible.

As previously noted, patients referred following a liver-related inpatient stay were excluded from the main analysis as they did not follow either the SC or EAP. These patients were found to have more advanced liver disease at the time of evaluation than patients referred via SC or the EAP (data incorporating post-discharge referrals are presented in online supplemental tables 3 and 4.

Additional ELF thresholds were explored to determine the effect of their adoption in the EAP (online supplemental table 5). Use of the NICE-recommended ELF threshold of 10.51[25] would have reduced the pathway's sensitivity for detection of advanced fibrosis to 59.1% (with a specificity of 68.8%) and resulted in missing 9 cases of advanced fibrosis (40.9%) and 2 cases of cirrhosis (28.6%). Employing an ELF threshold >11.3 for the EAP yielded a specificity of 91.1% for diagnosing cirrhosis, but would have resulted in missing 16 cases of advanced fibrosis and four cases of cirrhosis (72.7% and 57.1%, respectively). While this pathway evaluation is not intended to serve as an additional validation cohort for either test (indeed, participant numbers are insufficient to do so), data showing the comparative performance of different ELF and FIB-4 thresholds are presented in online supplemental table 6 for completeness.

DISCUSSION

This was a retrospective evaluation of alcohol-related referrals to a specialist liver centre, following implementation of a regional primary care referral pathway using the ELF test to stratify fibrosis severity. Our findings

Table 2 Clinical liver status of AUD patients referred via the EAP versus via SC, stratified by minimum degree of disease

	SC (n=197)			EAP (n=91)						
CLD status (by minimum degree of disease)	n	%	Odds	n	%	Odds	OR	95% CIs		P value
Steatosis (or worse)	192	97.5	38.40	84	92.3	12.00	3.19	0.84	13.11	0.0564
Mild fibrosis (or worse)	116	58.9	1.43	46	50.5	1.02	1.40	0.82	2.38	0.2026
Advanced fibrosis (or worse)	91	46.2	0.86	22	24.2	0.32	2.68	1.50	4.93	0.0004
Cirrhosis	70	35.5	0.55	7	7.7	0.08	6.58	2.84	17.79	<0.0001
Decompensated cirrhosis	21	10.7	0.12	0	0	0	–	2.61	–	0.0004

(1) P values represent the degree of statistical significance as determined by Fisher's exact test; (2) CLD status represents the stage of liver disease at the time of referral; (3) for patients categorised as having cirrhosis, this encompasses patients with either compensated or decompensated cirrhosis.
AUD, alcohol use disorder; CLD, chronic liver disease; EAP, ELF alcohol pathway; ELF, enhanced liver fibrosis; SC, standard care referral pathway.

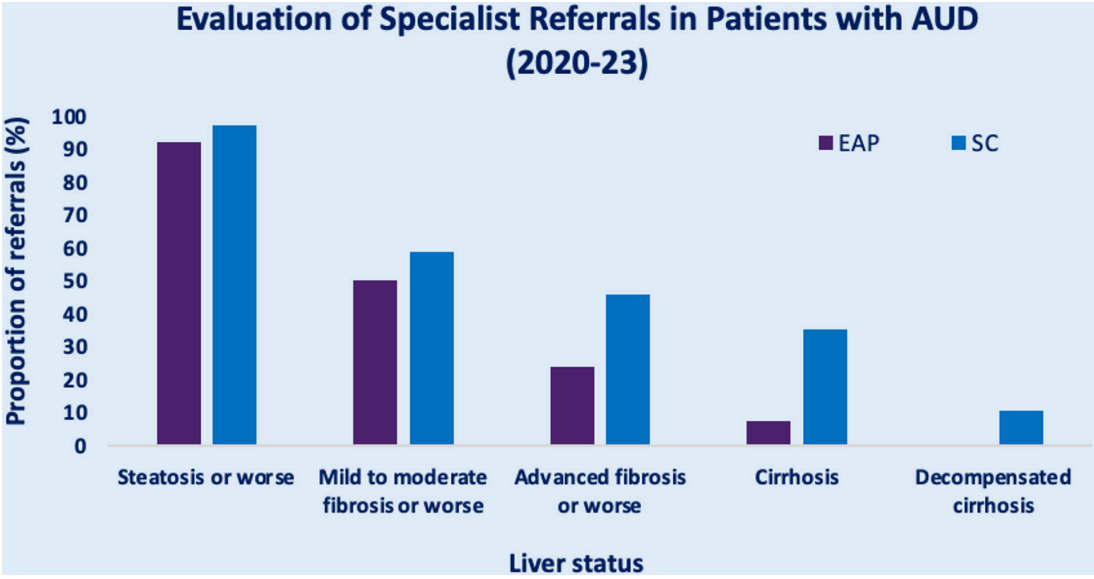

Figure 3 Clinical liver status of AUD patients referred via the EAP vs via SC, stratified by minimum degree of fibrosis. Bar chart demonstrating a comparison of clinical liver status (as determined using predefined criteria outlined in online supplemental table 1) for patients referred via the EAP versus via SC. Referrals are stratified by the minimum degree of fibrosis. AUD, alcohol use disorder; EAP, ELF alcohol pathway; ELF, enhanced liver fibrosis; SC, standard care.

highlight a number of advantages to the use of the EAP over SC.

Implementation of the EAP led to a reduction in unnecessary referrals (deemed in this study to be those without evidence of structural ArLD), with unwarranted specialist referral avoided in a quarter of cases assessed using the EAP. This approach could have an important impact on reducing the workload and costs associated with referral to secondary care. Additionally, with input from community alcohol support services, vital for all patients with AUD, those without evidence of liver disease can be directed to such services without delay.

Furthermore, the EAP facilitated identification of patients with ArLD at an earlier stage in their disease than those referred using SC, with 35.5% of patients referred via SC having established cirrhosis compared with 7.7% of EAP referrals. In keeping with this, the SC cohort had higher median FIB-4 scores and higher median LSM than the EAP cohort, while exhibiting similar rates of metabolic comorbidities. While the prevalence of ArLD was similar among both the SC and EAP group, liver damage was more advanced in the SC group. The greater severity of ArLD in the SC group was associated with higher median weekly alcohol intake which (along with FIB-4 scores) may have alerted their referring GPs to the likelihood of ArLD. Detection of ArLD at an earlier stage of liver damage in the EAP group was aided by the use of non-invasive blood tests for liver fibrosis, rather than relying on the level of alcohol consumption or abnormalities of conventional liver function tests. This study highlights the potential benefits associated with using more targeted approaches to detecting liver disease.

Our findings corroborate other reports of the use of non-invasive blood tests to stratify patients at risk of liver disease in primary care,[23] conferring advantages over risk scores based on simple liver tests and scores such as FIB-4 and APRI which are subject to confounding from active alcohol excess or liver inflammation. Our findings are similar to a recent Scottish study that reported a two-stage process involving the use of ELF to screen referrals made following calculation of FIB-4 values which reduced referral numbers by 34%. ELF was found to be not only highly sensitive at detecting cirrhosis at the 9.8 threshold, but also associated with higher area under the curve values for prediction of liver-related outcomes as compared with FIB-4.[26]

Limitations

This service evaluation was subject to a number of limitations. The uptake of the EAP was lower than anticipated and less than following the introduction of a similar pathway for metabolic dysfunction-associated liver disease (MASLD) in the same region. Dissemination and uptake of the EAP was undoubtedly impacted by the COVID-19 pandemic, which precluded the multiple in-person meetings with pathway stakeholders that had complemented the introduction of the MASLD pathway rolled out in the same region 6 years earlier.

The inherent challenges in both the quantification of alcohol intake and determination of its impact on an individual should not be overlooked. The initial assessment of this in primary care relied on patient-reported quantification of alcohol intake (which may be unreliable) and use of surveys such as the AUDIT-C (Alcohol Use Disorders Identification Test-Consumption). We did not use blood-based indicators of chronic alcohol excess, such as phosphatidylethanol or carbohydrate-deficient transferrin, which may be of use when combined with the above approaches, particularly in cases where self-reported alcohol intake may be unrepresentative.

Furthermore, the focus on quantification of intake, and on the identification of those with structural liver disease, may overlook some of the social and behavioural factors surrounding hazardous alcohol consumption. However, it should be noted that for all such patients, referral to alcohol support services forms an important part of holistic care where such factors may be explored in more detail.

It would have been optimal to evaluate all referrals on both pathways with liver biopsies as a reference standard for assessing liver fibrosis; however, it was deemed unethical to request liver biopsies on patients in primary care assessed as having AUD without ArLD. Among patients referred to secondary care, it was deemed appropriate and ethical to follow current national practice[16] and perform liver biopsies only where there was a specific indication. As such, few patients in either cohort underwent liver biopsies, with liver status determined primarily using a composite judgement involving blood tests, imaging and elastography. While a margin of error exists in the assessment of fibrosis using elastography and imaging, it is reasonable to assume that this would impact both pathways equally. Furthermore, as described above, efforts were made to standardise interpretation of the data when formulating the composite clinical judgements.

It should be acknowledged that we determined steatosis to be the minimum degree of ArLD indicative of an 'appropriate' referral for the purposes of this evaluation. As noted, this is in line with evidence which suggests that, for patients with AUD, any degree of structural liver disease confers poorer prognosis.[11 12] In this first phase of introduction of the EAP, it was deemed appropriate to design the pathway to have high sensitivity, reducing the likelihood of missing patients with CLD and enabling subsequent adjustment of the pathway's specificity in the context of the findings of the evaluation.

It was not possible to determine the true or false negative rates for the EAP as no further assessment of liver damage was performed on those patients allocated to remain in primary care (this information being located within the records of individual referring GP surgeries, which were not accessed). However, at the time of publication, only four of these patients have since been referred to the Trust's liver service, all of whom had continued to drink prior to referral. Two of these were found to have evidence of advanced fibrosis or cirrhosis.

Finally, this evaluation revealed marked heterogeneity in referral practice for the patients referred via SC with respect to both rationale for referral and the range of liver disease severity. This may indicate a need for clearer referral guidelines. An advantage of introducing the EAP is that it provides both guidance and a process which results in greater consistency in referral practice, with patients referred earlier in the course of their disease.

CONCLUSIONS

Our findings demonstrate that for patients with AUD, the introduction of a structured pathway incorporating assessment of liver fibrosis using ELF is associated with earlier detection of ArLD, enabling early referral for those warranting intervention. This also allows those without evidence of structural CLD to avoid unnecessary referral to liver specialists, inconveniencing patients, burdening specialist services and incurring unnecessary costs. This pathway evaluation supports the rollout of primary care-based approaches to the stratification of people at risk of liver disease and further validates the use of the ELF test in this context: to reduce unnecessary referrals to secondary care while simultaneously helping to identify occult liver disease at a stage where interventions carry a realistic prospect of improving prognosis.

Acknowledgements We would like to acknowledge patients, public health colleagues and commissioners involved in the Camden and Islington alcohol pathway.

Contributors AH contributed to data collection, formal analysis, writing (original draft) and writing (review and editing). CT contributed to data collection, formal analysis, writing (original draft) and writing (review and editing). FR contributed to writing (review and editing). JR contributed to writing (review and editing). WMR contributed to conceptualisation, formal analysis, funding acquisition, methodology and writing (review and editing). WMR is responsible for the overall content (as guarantor).

Funding AH is supported by a generous donation by the Whitmore family to the Royal Free Charity. WMR is supported by the UCLH NIHR Biomedical Research Centre and is a NIHR Senior Investigator Emeritus. This work was supported by Siemens Healthineers (grant no N/A).

Competing interests WMR is an inventor of the ELF test and has received support for research and speaker fees from Siemens Healthineers. FR is an associate editor at *BMJ Open Gastroenterology* but was not involved in the editorial process for this manuscript. Of the other authors, none have competing interests.

Patient consent for publication Not applicable.

Ethics approval The Research and Development Department of the Royal Free London NHS Foundation Trust categorised this study as an evaluation of a service improvement initiative, and all data were anonymised and routinely collected. Consequently, while the study was registered for audit purposes (IRAS number 272448), it did not require review or approval by an independent ethics committee. Individual patient consent was not solicited. All procedures adhered to the principles outlined in the Declaration of Helsinki (2013) guidelines.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

ORCID iDs
Alexander Hung http://orcid.org/0000-0002-8248-3290
Freya Rhodes http://orcid.org/0000-0002-6884-6235

REFERENCES

1 Huang DQ, Terrault NA, Tacke F, *et al*. Global epidemiology of cirrhosis - aetiology, trends and predictions. *Nat Rev Gastroenterol Hepatol* 2023;20:388–98.
2 Huang DQ, Mathurin P, Cortez-Pinto H, *et al*. Global epidemiology of alcohol-associated cirrhosis and HCC: trends, projections and risk factors. *Nat Rev Gastroenterol Hepatol* 2023;20:37–49.
3 BLT. Alcohol-related liver disease, Vol 2024. 2022.
4 Williams R, Aspinall R, Bellis M, *et al*. Addressing liver disease in the UK: a blueprint for attaining excellence in health care and reducing premature mortality from lifestyle issues of excess consumption of alcohol, obesity, and viral hepatitis. *Lancet* 2014;384:1953–97.
5 NHS. 2021. Statistics on alcohol, England 2021, Vol 2024. NHS Digital.
6 Rice P, Drummond C. The price of a drink: the potential of alcohol minimum unit pricing as a public health measure in the UK. *Br J Psychiatry* 2012;201:169–71.
7 Institute of Alcohol Studies. Economy - Institute of Alcohol Studies, Vol 2025. 2024.
8 NICE. NICE clinical knowledge summaries: alcohol – problem drinking, Vol 2024. 2023.
9 American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*, 5th ed., text revision (DSM-5-TR). Washington DC, 2022.
10 Arab JP, Addolorato G, Mathurin P, *et al*. Alcohol-Associated Liver Disease: Integrated Management With Alcohol Use Disorder. *Clin Gastroenterol Hepatol* 2023;21:2124–34.
11 Haflidadottir S, Jonasson JG, Norland H, *et al*. Long-term follow-up and liver-related death rate in patients with non-alcoholic and alcoholic related fatty liver disease. *BMC Gastroenterol* 2014;14:166.
12 Dam-Larsen S, Franzmann M, Andersen IB, *et al*. Long term prognosis of fatty liver: risk of chronic liver disease and death. *Gut* 2004;53:750–5.
13 Deleuran T, Grønbaek H, Vilstrup H, *et al*. Cirrhosis and mortality risks of biopsy-verified alcoholic pure steatosis and steatohepatitis: a nationwide registry-based study. *Aliment Pharmacol Ther* 2012;35:1336–42.
14 European Association for the Study of the Liver. EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis - 2021 update. *J Hepatol* 2021;75:659–89.
15 Darzi L. Independent investigation of the national health service in England, Vol. 2024. HM Department for Health and Social Care; 2024.
16 Abeysekera KWM, Srivastava A, Rowe I, *et al*. Exploring changing attitudes to non-invasive liver fibrosis tests in secondary care pathways: comparison of two national surveys. *Frontline Gastroenterol* 2023;14:483–90.
17 Thiele M, Madsen BS, Hansen JF, *et al*. Accuracy of the Enhanced Liver Fibrosis Test vs FibroTest, Elastography, and Indirect Markers in Detection of Advanced Fibrosis in Patients With Alcoholic Liver Disease. *Gastroenterology* 2018;154:1369–79.
18 Connoley D, Patel PJ, Hogan B, *et al*. The Enhanced Liver Fibrosis test maintains its diagnostic and prognostic performance in alcohol-related liver disease: a cohort study. *BMC Gastroenterol* 2021;21:268.
19 Sharma C, Cococcia S, Ellis N, *et al*. Systematic review: Accuracy of the enhanced liver fibrosis test for diagnosing advanced liver fibrosis and cirrhosis. *J Gastroenterol Hepatol* 2021;36:1788–802.
20 Punukollu B, Morgan S. NHS North Central London adult alcohol primary care clinical pathway. Vol. 2025. 2023.
21 NICE. Alcohol-use disorders: diagnosis and management of physical complications. London, 2017.
22 Day J, Patel P, Parkes J, *et al*. Derivation and Performance of Standardized Enhanced Liver Fibrosis (ELF) Test Thresholds for the Detection and Prognosis of Liver Fibrosis. *J Appl Lab Med* 2019;3:815–26.
23 Srivastava A, Gailer R, Tanwar S, *et al*. Prospective evaluation of a primary care referral pathway for patients with non-alcoholic fatty liver disease. *J Hepatol* 2019;71:371–8.
24 Pons M, Barreira A, Genescà J. Compensated advanced chronic liver disease (cACLD). In: *Baveno VII*. Cham: Springer, 2022.
25 NICE. Non-alcoholic fatty liver disease (NAFLD): assessment and management, Vol. 2024. 2016.
26 Pearson M, Nobes J, Macpherson I, *et al*. Enhanced liver fibrosis (ELF) score predicts hepatic decompensation and mortality. *JHEP Rep* 2024;6:101062.