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# Quality standards for the management of alcohol-related liver disease: consensus recommendations from the British Association for the Study of the Liver and British Society of Gastroenterology ARLD special interest group

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## ABSTRACT

**Objective** Alcohol-related liver disease (ALD) is the most common cause of liver-related ill health and liver-related deaths in the UK, and deaths from ALD have doubled in the last decade. The management of ALD requires treatment of both liver disease and alcohol use; this necessitates effective and constructive multidisciplinary working. To support this, we have developed quality standard recommendations for the management of ALD, based on evidence and consensus expert opinion, with the aim of improving patient care.

**Design** A multidisciplinary group of experts from the British Association for the Study of the Liver and British Society of Gastroenterology ALD Special Interest Group developed the quality standards, with input from the British Liver Trust and patient representatives.

**Results** The standards cover three broad themes: the recognition and diagnosis of people with ALD in primary care and the liver outpatient clinic; the management of acutely decompensated ALD including acute alcohol-related hepatitis and the posthospital care of people with advanced liver disease due to ALD. Draft quality standards were initially developed by smaller working groups and then an anonymous modified Delphi voting process was conducted by the entire group to assess the level of agreement with each statement. Statements were included when agreement was 85% or greater. Twenty-four quality standards were produced from this process which support best practice. From the final list of statements, a smaller number of auditable key performance indicators were selected to allow services to benchmark their practice and an audit tool provided.

**Conclusion** It is hoped that services will review their practice against these recommendations and key performance indicators and institute service development where needed to improve the care of patients with ALD.

### WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Alcohol related liver disease (ALD) is a common cause of ill health and premature death. Variations in the care of liver disease across the UK

### WHAT THIS STUDY ADDS

⇒ These consensus recommendations from the BASL/BSG ArLD special interest group are intended to improve quality and reduce variation in the management of ALD

### HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Recommendations for all aspects of management of ArLD are provided. To support implementation an audit tool is provided, based on the quality standards, and a template for patient information leaflet

## INTRODUCTION

Alcohol-related liver disease (ALD) is the major driver of liver-related morbidity and mortality in the UK. In 2019–2020, there were 74 220 admissions to hospital in England due to ALD[1] and 13 269 premature deaths (before the age of 75) between 2017 and 2019.[2] National Health Service (NHS) care for people with significant ALD is a major cost to the NHS—£1.8 billion for inpatient care related to alcohol.[3] ALD is intrinsically linked to alcohol misuse as the primary cause of liver disease, and in addition to the health costs of ALD, alcohol misuse is also causally associated to over 200 medical conditions and societal harms such as accidents, absenteeism and crime.[4] ALD is part of a wider spectrum of alcohol-related disease, which is linked to important comorbidities particularly mental health issues, cardiovascular disease and cancer,[5] and to other determinants of well-being particularly deprivation.[6] Recent data from the Office for Health Improvement and Disparities have highlighted the worsening situation: in 2020, 5608 alcoholic liver deaths were recorded in England, a rise of almost 21% compared with 2019. The spike in alcoholic liver deaths in 2020 occurred after a 43% increase in alcoholic liver deaths between 2001 and 2019.[7 8] The same publication highlighted that alcohol specific deaths have risen significantly since the onset of the COVID-19 pandemic. The treatment of ALD, therefore, requires the input of multiple practitioners and multiple different agencies.

ALD remains difficult to treat: a survey of outcomes from hospitals in England, Wales and Northern Ireland by the national confidential enquiry into patient outcomes and death found that death rates for patients remained high between two iterations of the survey in 2011 and 2019, and evidence of significant variations in care between centres.[9 10] This is consistent with NHS England data showing marked differences in the rates of death from liver disease across the country[11] and the observation that people with advanced liver disease admitted to hospital in emergency are 7–8 times more likely to die than those admitted for stroke or heart attack.[12]

Treatment guidelines for ALD have been produced by specialist hepatology societies to support the medical treatment of ALD, and the National Institute for Health and Care Excellence has also produced guidance in the UK[13 14] although this document has not been updated since 2017. The purpose of this initiative is to develop standards that would support the delivery of high-quality care for patients with ALD and reduce variation between areas.

## METHODS

A group of experts from the British Association for the Study of the Liver (BASL) and British Society of Gastroenterology (BSG) ALD Special Interest Group (SIG) developed the recommendations. RP chaired the group. All members of the ALD SIG were invited to participate via email and those expressing an interest were included in the working group. Ultimately, the group included a multidisciplinary team of 46 individuals from hepatology, psychiatry and psychology, dietetics, hepatology specialist nursing, pathology, primary care, pharmacy and addiction specialists.

The group was subdivided into three working groups that led the writing of draft recommendations for one of three parts of the document: (1) prehospital assessment and management of ALD (lead AS); (2) management of decompensated ALD in secondary care (lead JS) and (3) management after hospitalisation (lead RP). Each group produced a list of draft quality statements for the management of ALD diagnosis and management pathway to address within the standards document. The draft statements from three working parties were combined and an anonymous modified Delphi voting process was conducted individually by each member of the working group using an online survey tool to assess the level of agreement with each statement on a five-point scale (strongly disagree, disagree, neutral, agree or strongly agree). Members could abstain from questions that related to areas outside their usual clinical practice. After a round of voting, statements were redrafted if necessary through discussions via teleconference meetings. 'Agreement' was predefined when statements received a score of 'strongly agree' or 'agree', consensus predefined as when agreement was ≥85% after exclusion of abstentions. The result of this process produced a series of 24 recommendations (table 1). From this final list of statements, nine auditable key performance indicators (KPIs) were selected to allow services to benchmark their practice. The KPIs were chosen based on their potential to influence patient outcomes as well as being easily measurable. An audit tool based on these KPIs was produced to allow for assessment, benchmarking and monitoring of services.

### Patient and public partnership involvement

The quality standards group included a representative from the British Liver Trust (VH) and a patient representative (VL).

Terminology used in the document for ALD, and cirrhosis due to (ALD cirrhosis) is based on the most recent guideline document from the European society for the study of the liver, which recognised that use of the word 'alcoholic' is stigmatising and sought to move away from its use.[15] We have also used the term alcohol-related hepatitis (AH) to replace the previous term alcoholic hepatitis.

## QUALITY STANDARDS

### Prehospital assessment and management of ALD

#### People who are being asked about their alcohol use should have a validated alcohol questionnaire completed to identify any need for intervention

All patients in primary care should have an accurate recording of alcohol intake, which includes both quantity and frequency, updated at registration and

**Table 1** Summary of quality standards with level of agreement from the final round of the Delphi process

| | Agreement | Responses |
|---|---|---|
| People who are being asked about their alcohol use should have a validated alcohol questionnaire completed to identify any need for intervention. | 91% | 29% strongly agree<br>62% agree<br>6% disagree<br>2% strongly disagree |
| 1. Assessment of liver fibrosis should be<br>a. Offered to people who drink hazardously (35 units/week in women, 50 units/week in men).<br>b. Considered in people drinking alcohol in excess of maximum recommended levels (14 units/week) who have cofactors for liver disease (eg, obesity). | 94% | 55% strongly agree<br>39% agree<br>3% neutral<br>3% disagree |
| Assessment of hepatic fibrosis should be done using validated non-invasive liver fibrosis markers. | 100% | 78% strongly agree<br>22% agree |
| Patients identified at high risk of advanced fibrosis or cirrhosis should be offered referral for assessment by a gastroenterologist or hepatologist. | 97% | 74% strongly agree<br>24% agree<br>2% neutral |
| Patients presenting to hospital with liver disease should be screened for alcohol use disorder (AUD) and an estimation of typical no of units of alcohol per week recorded. | 76% | 38% strongly agree<br>44% agree<br>15% neutral<br>3% disagree |
| Patients admitted to hospital with ALD should be reviewed by a clinician trained in hepatology and the management of alcohol withdrawal within 24 hours of admission. | 88% | 49% strongly agree<br>39% agree<br>9% neutral<br>3% disagree |
| Patients admitted to hospital with ALD and AUD should be assessed by a specialist addiction practitioner during their admission and offered appropriate intervention and referral. | 97% | 68% strongly agree<br>29% agree<br>3% neutral |
| Alcohol withdrawal syndrome in patients with ALD with advanced liver disease, especially jaundice and/or encephalopathy, should be treated in a symptom-triggered fashion using a recognised symptom scoring system to avoid overuse of benzodiazepines. | 91% | 66% strongly agree<br>25% agree<br>9% neutral |
| It should be documented that patients have been advised that complete abstinence from alcohol is associated with better prognosis in ALD and that stopping alcohol entirely should be their goal. | 89% | 65% strongly agree<br>24% agree<br>12% neutral |
| Patients presenting with decompensated ALD or AH should be screened for infection. | 100% | 79% strongly agree<br>21% agree |
| All patients with decompensated ALD should have a nutritional assessment. | 100% | 85% strongly agree<br>15% agree |
| A plan for escalation of care in patients with ALD who develop acute-on-chronic liver failure (grades 2 or 3) should be clearly documented. | 100% | 78% strongly agree<br>22% agree |
| AH should be diagnosed in keeping with recognised clinical criteria, and patients suspected as having AH but who have confounding factors or do not fulfil all criteria should be considered for liver biopsy. | 93% | 59% strongly agree<br>35% agree<br>7% neutral |
| Patients with AH should have their prognosis assessed using a recognised prognostic scoring system (GAHS; MELD). | 100% | 77% strongly agree<br>23% agree |
| Corticosteroid treatment should be considered in patients with indicators of likely beneficial response (GAHS≥9; MELD 21–51; NLR 5–8) and without infection. | 85% | 58% strongly agree<br>27% agree<br>15% neutral |
| Response to treatment with corticosteroids should be assessed after 7 days and corticosteroid treatment discontinued if there is no response. | 86% | 45% strongly agree<br>41% agree<br>10% neutral<br>3% disagree |
| Patients should be provided with clear, written information about their liver disease in a manner that they can understand before they leave hospital. | 94% | 77% strongly agree<br>18% agree<br>6% neutral |
| The date and time of follow-up appointments should be arranged with patients before they leave hospital. | 88% | 56% strongly agree<br>32% agree<br>9% neutral<br>3% disagree |
| Patients hospitalised with decompensated ALD or AH should be followed up by clinicians with specialist interest in hepatology within 6 weeks of discharge. | 97% | 63% strongly agree<br>34% agree<br>3% neutral |

Continued

Table 1 Continued

| | Agreement | Responses |
|---|---|---|
| Patients with ALD with AUD should be offered community-based alcohol support after discharge from hospital. | 94% | 77% strongly agree<br>18% agree<br>6% neutral |
| Access to addiction specialists should be available, when indicated, for all patients with decompensated ALD after leaving hospital. | 91% | 61% strongly agree<br>30% agree<br>9% neutral |
| Medicines to support abstinence are beneficial and should be continued in primary care after being started in hospital or in alcohol treatment. | 85% | 50% strongly agree<br>35% agree<br>15% neutral |
| Patients with ALD with ongoing hepatic failure and a UKELD score greater than 49 should be considered for liver transplant referral if they are abstinent from alcohol. | 87% | 47% strongly agree<br>40% agree<br>7% neutral<br>7% disagree |
| Patients with ALD with an expected survival of less than 12 months should have their condition discussed with palliative care services. | 91% | 73% strongly agree<br>18% agree<br>6% neutral<br>3% disagree |

AH, alcohol-related hepatitis; ALD, alcohol-related liver disease; GAHS, Glasgow Alcoholic Hepatitis Score; MELD, model for end-stage liver disease; UKELD, UK Model for End-Stage Liver Disease.

opportunistically with a special focus on people who have an alcohol-related condition or who are at increased risk of harm from alcohol.[16] This is in line with the Public Health England initiative 'Making every contact count'.[17] Patients who drink above the recommended limits should be screened for alcohol use disorder (AUD) using a validated formal tool, for example alcohol use disorders identification test- C (AUDIT-C) or fast alcohol screening test (FAST). Those identified as drinking at higher risk or hazardous levels (35 units/week in women, 50 units/week in men) should receive feedback; a brief intervention and written information on their alcohol intake and how to address it.[18] Screening should occur at least annually for those deemed by clinical judgement to be at high risk of alcohol-related morbidity including (but not limited to) significant mental health problems and metabolic risk factors.

### Assessment of liver fibrosis should be offered to people who drink hazardously (35 units/week in women, 50 units/week in men) and considered in people drinking alcohol in excess of maximum recommended levels (14 units/week) who have cofactors for liver disease (eg, obesity)

The risk of liver disease increases with alcohol intake.[19] When males and females are stratified according to sex, the 35 units per week limit remains a reliable cut-off for increased advanced fibrosis risk in women, but for men, risk did not increase significantly until consuming 50 or more units per week.[20] When considering the value of fibrosis assessment in those who drink above recommended limits but below thresholds currently considered most harmful (35 units/week women; 50 units/week men), thought should be given to the presence of other significant drivers of liver disease, most notably obesity and diabetes mellitus.[21 22] The risk between alcohol intake and obesity is multiplicative[23]; in patients with a body mass index (BMI)>30 kg/m$^2$ drinking above UK recommended limits, the risk of chronic liver disease is five times greater than a patient with a normal BMI,[24] and those with severe obesity (BMI>35 kg/m$^2$) have double the risk of liver disease for any level of alcohol intake,[25] therefore, any intake over recommended limits in this group might prompt assessment of fibrosis. This approach is supported by clinical guidelines[26] but direct evidence for fibrosis testing at this threshold is lacking.

### Assessment of hepatic fibrosis should be done using validated non-invasive liver fibrosis markers

Identification of advanced fibrosis offers the opportunity for earlier referral to specialist support, earlier intervention for both the liver disease and significant cofactors/drivers, while avoiding unnecessary investigation in those without liver disease—only 20% of those with AUD for example, will develop significant liver disease.[27] Standard liver blood tests do not exclude the presence of significant liver fibrosis[28] and specific non-invasive tests (NITs) for liver fibrosis should therefore be used. NITs for detection of liver fibrosis are widely available in UK practice and are included in UK guidelines on investigation for fibrosis in AUD in primary care.[25] However, the evidence base to support the use of specific tests, or to provide cut-off values to exclude advanced fibrosis, is considerably smaller than in non-alcohol-related fatty liver disease.[29–31] NITs that have been used in ALD include panels based on standard blood tests (alanine transaminase (ALT), aspartate transaminase (AST), platelets) such as fibrosis-4 (FIB-4) and AST to platelet ratio index (APRI), stand-alone specialist blood tests such as Enhanced Liver Fibrosis (ELF) test, and imaging techniques such as transient elastography (TE).[32]

### Patients identified at high risk of advanced fibrosis or cirrhosis should be offered referral for assessment by a gastroenterologist or hepatologist

All patients identified at high risk of advanced fibrosis or cirrhosis after assessment with NIT should be referred to secondary care for further evaluation. Patients should be informed that an initial positive result highlights the need for further evaluation rather than confirming the presence of significant liver disease, given the modest positive predictive value with some NIT results. Those at low risk of advanced fibrosis or cirrhosis do not need referral to secondary care and can be managed safely in primary care or in community settings, with a focus on tailored lifestyle advice and access to support services, as no liver-specific treatments are indicated. In patients with metabolic or cardiovascular risk factors, managing these risk factors is important to reduce the risk of disease progression. Patients should be reassessed for liver fibrosis after 3–5 years if they continue to drink above recommended limits, using the tests described above.[14 33]

## Assessment and management of patients with acutely decompensated ALD cirrhosis or AH

### Patients presenting to hospital with liver disease should be screened for AUD and an estimation of typical number of units of alcohol per week recorded

Evaluation of alcohol intake is important for accurate diagnosis of liver disease and assessing the need for management of alcohol withdrawal. Screening for AUD should be done with validated tools such as AUDIT or its abbreviated forms such as AUDIT-C or FAST. Integrated care of liver disease and AUD requires the engagement of multiple practitioners to be effective and relies on prompt identification of patients who need care.[34] All those experiencing alcohol dependence should be monitored for the early signs of alcohol withdrawal (for example sweats, tremor, craving or agitation). Those typically drinking daily >15 units of alcohol are likely to experience moderate dependence. Those typically drinking daily >30 units of alcohol are likely to experience severe alcohol dependence and at greater risk of severe alcohol withdrawal symptoms.[35] In addition to the direct management of ALD, there is value in systematic screening for alcohol misuse in all patients admitted to hospital to better manage alcohol withdrawal and to identify those at risk of liver disease.[36]

### Patients admitted to hospital with ALD should be reviewed by a clinician trained in hepatology and the management of alcohol withdrawal within 24 hours of admission

Early consultant review improves outcomes in hospital admissions.[37] In patients with acutely decompensated ALD who may also require management of alcohol withdrawal, this complexity requires early specialist review. Timely review by senior specialist clinicians has been shown to reduce early mortality in patients admitted with decompensated liver disease.[38] All patients with decompensated ALD cirrhosis should have their initial management guided by the BSG/BASL Decompensated Cirrhosis Care Bundle.[39]

### Patients admitted to hospital with ALD and AUD should be assessed by a specialist addiction practitioner during their admission and offered appropriate intervention and referral

Alcohol treatment improves outcomes in patients with ALD and should be considered an integral part of holistic treatment.[40] Harmful alcohol use in the context of liver disease needs to be clearly addressed by practitioners with appropriate experience and training.[35] Specialist addiction practitioners may come from a variety of backgrounds including but not limited to nursing or medical training; their expertise in managing initial withdrawal and subsequent alcohol treatment is key. The international classification of alcohol use disorders (international classification of diseases (ICD) -10 or ICD-11) identify harmful drinking and alcohol dependence as conditions requiring access to specialist treatment interventions, which have shown to be effective in helping individuals to reduce or stop their alcohol use.[16] In centres with an alcohol care team (ACT), assessment and management of alcohol use is best done as part of the comprehensive care that ACTs provide.[41] Treatment and onward referral after an initial alcohol detoxification are supported by other guidelines.[35]

### Alcohol withdrawal syndrome in patients with ALD with advanced liver disease, especially jaundice and/or encephalopathy, should be treated in a symptom-triggered fashion using a recognised symptom scoring system to avoid overuse of benzodiazepines

Symptom triggered management should be the gold standard for management of withdrawal in patients with liver disease to avoid the risk of oversedation with benzodiazepines.[13] However, it is recognised that this requires a highly vigilant, trained workforce who are able to maintain the schedule of review and react accordingly. Where this gold standard cannot be delivered, a modification to the benzodiazepine type/dose may be required for high risk patients using fixed dose regimens.

Management of alcohol withdrawal syndrome in those with advanced liver disease should be undertaken in a symptom triggered fashion using recognised symptom scoring systems. These include the CIWA-Ar scale[42] and the Glasgow Modified Alcohol Withdrawal Score (GMAWS).[43] Metabolism of benzodiazepines is reduced in advanced liver disease with the risk of accumulation and subsequent oversedation and precipitation of hepatic encephalopathy if fixed dose regimens are used. However, staff should be competent in monitoring symptoms effectively and should have sufficient resources to allow them to do so frequently and safely. In those with decompensated liver disease,

especially severe jaundice and/or encephalopathy, modification to the benzodiazepine regimen may be required. This might include a reduction in the dose of benzodiazepine triggered by symptoms or perhaps the use of shorter acting benzodiazepines such as oxazepam or lorazepam.[16]

### It should be documented that patients have been advised that complete abstinence from alcohol is associated with better prognosis in ALD and that stopping alcohol entirely should be their goal

It is clear that abstinence from alcohol is associated with better outcomes compared with people who continue to drink.[44 45] Alcohol abstinence is also a prerequisite for consideration of liver transplantation should this become necessary. All patients with decompensated ALD cirrhosis including AH should therefore be advised that complete abstinence from alcohol should be the target of treatment. This may be an overwhelming goal and patients should be supported to work towards this target to avoid alienating them from treatment. This should be documented in patient notes, records and on electronic portals where possible with access for all clinicians involved in going care. A record of this advice should also be given to patients and general practitioners (usually via a discharge letter).

### Patients presenting with decompensated ALD or AH should be screened for infection

Alcohol consumption increases the risk of infection, and infection is a common cause of decompensated liver disease.[46] Infection may be present at presentation or occur during admission particularly in AH, and is associated with poorer outcomes.[47] This advice regarding screening for infection is consistent with the BSG/BASL decompensated cirrhosis bundle. Monitoring for signs of infection should continue throughout an admission with particular vigilance in patients with AH who are treated with corticosteroids where incident infection is associated with poor outcomes.[48] It is important to note that standard laboratory markers of infection for example, leukocytosis or elevated C reactive protein may be part of the syndrome of AH and not necessarily reflect active infection; these should be interpreted with caution and additional evidence for active infection should be sought. This said, given the adverse outcome with infection a low threshold for prescribing antibiotics is appropriate. The possibility of fungal infection should be considered: this may be more frequent in AH and associated with poor outcomes.[49] Prophylactic antibiotic treatment in AH has been shown not to improve mortality or morbidity in AH and should not replace careful monitoring for signs of infection.[50]

### All patients with decompensated ALD should have a nutritional assessment

Malnutrition (deficiencies in individual nutrients), sarcopenia (a reduction in muscle mass, strength and/or function[51]) and frailty (a clinical state of decreased physiological reserve and increased vulnerability to health stressors, predisposing individuals to adverse clinical outcomes[52]) are common in end-stage liver disease and in patients with AH.[53] Malnutrition risk can be assessed using subjective global assessment; however, there is risk of underestimation so caution is advised. Gold standard assessment of sarcopenia is through use of CT with analysis of Skeletal Muscle Index, however, if inaccessible then bedside measures through obtaining mid-arm muscle circumference are advised[54]: if malnutrition risk or sarcopenia/frailty are identified, patients should be seen by a dietician with specialist training and experience in hepatology.[55] Patients' food security should be considered when developing dietary plans for the post-discharge period and referral to social care made when appropriate.

Enteral nutrition via nasogastric tube has often been considered part of the treatment of patients with AH. More recent trial data failed to show an advantage of NG feeding over standard care but it was clear that adequate caloric intake was associated with better outcomes[56]; close attention should be paid to dietary intake.

### A plan for escalation of care in patients with ALD who develop acute-on-chronic liver failure (grades 2 or 3) should be clearly documented

Escalation decisions should be made on a patient-by-patient basis. Escalation decisions for patients with ALD must take account of factors such as pre-admission patient function, comorbidity, frailty, transplant eligibility and severity of liver disease; patient preferences must also be taken into account. Alcohol remains the the most common aetiology of acute on chronic liver failure (ACLF) in the UK[57]; ACLF grade and the need for renal replacement therapy are independently associated with 28-day mortality. Without transplantation, 28-day mortality falls between 18%–25% in grade 1 and 68%–89% grade 3.[58] With such high mortality early decision making and assessing appropriate candidacy is vital. A national cohort study of patients with ALD from the Scottish ITU registry confirmed a high mortality among this cohort, along with a significant long-term burden on subsequent healthcare resource utilisation.[59] Those admitted to ITU with ALD experience higher readmission rates, with more days in hospital and higher consequent costs, compared with ITU patients with other severe comorbidities. Therefore, careful liaison and shared decision-making about escalation, between the medical and ITU teams, alongside patients and their families is required. Escalation to intensive care units is often considered in the context of 'first presentation' of liver disease and the potential for patients to be a candidate for liver transplantation. Neither of these factors are known to be relevant to short term outcomes and may not be appropriate to inform care planning.

## Assessment and management of AH

### AH should be diagnosed in keeping with recognised clinical criteria; patients suspected as having AH but who have confounding factors or do not fulfil all criteria should be considered for liver biopsy

The diagnosis of AH has been controversial in the past. Previously it had been argued that a diagnosis of AH could only be made with confirmatory histology. For most AH patients this would require a transjugular liver biopsy the availability of which is variable and for which there is a technical failure rate of 3.2% and a diagnostically suboptimal sample obtained in up to 12%.[60] In addition, histological features of steatohepatitis may be present in patients with chronic liver disease without an acute illness.[61 62] AH is primarily a clinical diagnosis with recent onset jaundice being a cardinal feature. In order to standardise the clinical features of AH the National Institute on Alcohol Abuse and Alcoholism has published criteria which have received general acceptance.[63] Onset of jaundice (serum bilirubin>3 mg/dL or 50 µmol/L) within 8 weeks and excessive alcohol consumption within 60 days of presentation are key. The liver biochemistry should be compatible with AH with a raised AST, an AST-to-ALT ratio of >1.5 and neither value >400 IU/L. Fulfilment of these criteria without any confounding factors equates to a diagnosis of 'probable' AH which suffices for most clinical situations. A 'definite' diagnosis of AH is when these clinical features are fulfilled and there is additional confirmatory histology. However, if confounding factors are present then the level of diagnostic certainty falls to 'possible' AH in which case additional confirmatory histology would be recommended to make the diagnosis. Examples of such factors would be incompatible liver biochemistry, possible ischaemic liver injury (secondary to hypotension or cocaine use within 7 days), possible metabolic liver injury (Wilson's disease), possible drug induced liver injury (suspect drug within 30 days of jaundice) and uncertainty regarding timing of onset of jaundice. Liver biopsy rarely changes the diagnosis in individuals who meet the clinical criteria or history of alcohol excess.[64]

It should be noted that while these criteria have been accepted and form part of guidelines,[65] the threshold of serum bilirubin recommended is lower than that of most historical clinical studies of AH. These have tended to use a threshold of 80 µmol/L (4.7 mg/dL) or more. Therefore, the applicability of previous clinical studies to those with lower levels of serum bilirubin is unclear.

### Patients with AH should have their prognosis assessed using a recognised prognostic scoring system (Glasgow Alcoholic Hepatitis Score; model for end-stage liver disease)

Estimation of likely outcome from AH is important to identify those at greatest benefit from intervention as well as to allow informed discussion with the patient and their families regarding their expectations. 'Static' scores are those derived from variables available at a single point in time. The discriminant function (DF) has been used for many years with a threshold ≥32 identifying those with severe disease.[66 67] However, concerns have been raised regarding the reliability of the DF as it uses the absolute value of prothrombin time rather than a ratiometric value such as the international normalised ratio (INR).[68] Alternative scores have been proposed including the Glasgow Alcoholic Hepatitis Score (GAHS, and also its modified version, mGAHS using the neutrophil-to-lymphocyte ratio (NLR)),[69 70] the age, bilirubin, INR and creatinine score[71] and the model for end-stage liver disease (usually the pre-2016 UNOS variation of MELD, but also the modified MELD-Na version)[72] score. Recent studies have shown that these more recent scores are superior to the original DF.[72 73] In international guidelines, the GAHS and MELD have been most commonly cited as indicators of prognosis in clinical practice.[15 74] In the STOPAH trial, the 90-day mortality of AH with consistently low scores was: GAHS<9 110.2%; MELD<25 140.4%. A 90-day mortality in those with high scores (excluding those presenting with sepsis and/or gastrointestinal bleeding) was: GAHS≥9 380.4%; MELD≥25 390.6%.[73]

### Corticosteroid treatment should be considered in patients with indicators of likely beneficial response (GAHS≥9; MELD 21–51; NLR 5–8) and without infection

Corticosteroids are the only currently recommended pharmacological treatment. In the STOPAH trial, corticosteroids were associated with a modest improvement in mortality at 28 days, though the improvement did not reach conventional statistical significance (OR 0.72, 95% CI 0.52 to 1.01, p=0.06) and any benefit was not sustained at 90 days.[75] Subsequent meta-analysis supports the use of corticosteroids in selected patients to improve 28-day survival (HR 0.64, 95% CI 0.48 to 0.86, p=0.003), but also confirmed longer-term benefit was lost at 6 months.[76] Importantly, the rate of infection is significantly higher in patients with AH treated with steroids and in those who develop infection with AH, steroids increase 90-day mortality (OR 2.26, 95% CI 1.41 to 4.30, p=0.002).[48 77] Therefore, if steroids are to be used, they should be used cautiously after careful screening and aggressive treatment of infection at baseline. Furthermore, if a significant spontaneous decrease in bilirubin is observed after 7 days (<0.9×baseline bilirubin), 28-day survival may not be improved with steroids, and in this group the risks of steroid treatment could outweigh the benefits.[78] The standard dose of prednisolone is 40 mg daily, this is continued for 28 days in responders and then discontinued without weaning.

### Response to treatment with corticosteroids should be assessed after 7 days and corticosteroid treatment discontinued if there is no response

Dynamic prognostic scores, such as the Lille score,[79] predict mortality based on a reduction in bilirubin level in patients who have received corticosteroid therapy. The Lille score combines several variables, including age, renal function, albumin, prothrombin time and bilirubin

at baseline and 7 days. A non-response to corticosteroids is defined as a Lille score ≥0.45, and this is associated with a much poorer survival at 6 months compared with responders (25% vs 85%) and it is recommended that steroids are discontinued in this group. Calculating the Lille score at day four may give similar diagnostic accuracy in predicting 28-day and 90-day mortality compared with the day seven score, limiting unnecessary steroid exposure and reducing the risk of infection, but this requires further validation.[80]

## Posthospital management of ALD

### Patients should be provided with clear, written information about their liver disease in a manner that they can understand before they leave hospital

Patients should be supported to understand their health in the transition from hospital to the community.[81] Written information should include details about their liver disease, the reasons for hospital admission, treatment received and plans for follow-up including advice about abstinence and sources of alcohol support. Written information should take into account literacy level as the median UK reading age is 9 years old. A template information leaflet for decompensated alcohol-related cirrhosis is provided in the supporting information. The British Liver Trust also offers a range of resources designed to be accessible for patients (https://britishlivertrust.org.uk/). Where appropriate and with patients' consent, information should be shared with people significant or important to patients.

### The date and time of follow-up appointments should be arranged with patients before they leave hospital

Patients who attend outpatient hepatology outpatient clinics have been shown in retrospective reviews to have improved survival.[82 83] Early follow-up also facilitates discharge and may help prevent readmission, both of which can reduce pressure on inpatient services. Necessary investigations should where possible be completed during an index admission to reduce journeys and costs to patients. Measures to allow patients to lead follow-up arrangements by picking dates or times of appointments may also support engagement. Outpatient hepatology clinics have traditionally been delivered in hospitals, but could be placed in other centres which may improve attendance.

### Patients hospitalised with decompensated ALD or AH should be followed up by clinicians with specialist interest in hepatology within 6 weeks of discharge

In clinical studies, follow-up has been difficult.[84] Special efforts to engage patients with follow-up may be needed in excess of other patient groups. These efforts should ideally ensure that further engagement is made as easy as possible and, importantly, continually informed by patient experience. Additional efforts to engage patients through for example peer support, dedicated specialist nursing staff and using text messages have shown to improve attendance in people with hepatitis C[85 86]; similar initiatives may also be valuable in ALD.

### Patients with ALD with AUD should be offered community-based alcohol support after discharge from hospital

When accepted, contact with alcohol services should be established before leaving hospital. Team working including joint clinics between hepatology and alcohol practitioners may allow alcohol support to be offered to those declining community services. The management plan must address alcohol reduction and cessation.[15] Patients who have initially declined referral to alcohol services should be able to access this support if they change their minds. Motivational enhancement work by hepatology staff can help and reinforce the need for links between the services. Other substance use should also be addressed in addition to alcohol use. For example, there is a growing body of evidence that cigarette smoking is associated with increased progression of fibrosis and development of hepatocellular carcinoma. It is recommended that all patients with ALD be offered pharmacological and psychological smoking cessation support, particularly those being considered for liver transplantation.[87 88]

### Access to addiction specialists should be available, when indicated, for all patients with decompensated ALD after leaving hospital

Addiction specialist psychiatric specialists improve outcomes for people with advanced disease, for example, through reduced relapse rates after transplantation.[89] Most literature around the impact of this service is in the context of transplantation; the quality standard development group was clear that access to specialist addiction psychiatrists should not be reserved for such a highly selected group of patients. Good practice would include access to specialist psychiatrists for all patients.

### Medicines to support abstinence are beneficial and should be continued in primary care after being started in hospital or in alcohol treatment

A recent systematic review has demonstrated the benefits of either integrated or colocated addiction therapy for patients with ALD.[90] Compared with standard of care patients who received addiction treatment were less likely to suffer liver decompensation, require readmission (within 30 days) and had a lower risk of mortality. A similar pattern is seen in the use of relapse prevention medications: patients with cirrhosis were less likely to suffer hepatic decompensation.[40] This positive effect remained even when treatment was started after a diagnosis of cirrhosis indicating the ongoing value of treatment of AUD. Indications and medication doses should be reviewed in light of changes in liver function and patients' needs, and their engagement with addiction services. Disulfiram is associated with potentially serious hepatotoxicity and should be avoided in patients with advanced liver disease; its use in earlier disease may be

safe with careful monitoring. Acamprosate is renally excreted and baclofen has evidence of safety and efficacy in cirrhosis,[91 92] these agents may be preferred in cirrhosis. The use of relapse prevention medications is covered in other national UK guidance currently in development.

### Patients with ALD with ongoing hepatic failure and a UK Model for end-stage liver disease score greater than 49 should be considered for liver transplant referral if they are abstinent from alcohol

Liver transplant is an effective treatment option for selected patients with decompensated alcohol-related cirrhosis.[93] The development of decompensated disease (ascites, oedema, encephalopathy, bleeding) should prompt the consideration of transplant referral. The UK Liver Advisory Group[94] have recently provided updated guidelines for transplant assessment and referral which are specific to patients with alcohol-related disease. These supplement existing national criteria and guidelines for liver transplant.[95 96] Early discussion with a transplant centre should be considered in all cases, particularly where patients have demonstrated at least 3 months of alcohol abstinence or even earlier if they show good engagement with addiction services and an assessment may be prolonged because of medical complexity.[95] Referral should not be based on the 'rule of thumb' of 6 months abstinence before referral to a transplant unit.

The UK Model for End-Stage Liver Disease (UKELD) score is a compound measure of liver function intended to guide transplant candidacy in the UK. UKELD underpins minimal listing criteria for the elective waitlist. This is derived from the patient's serum sodium, creatinine, bilirubin and INR.[97] In chronic liver disease (CLD), a UKELD score ≥49 indicates survival advantage for LT over conservative management in patients with irreversible decompensation. A UKELD score of 49 is the equipoise at which the predicted 1-year mortality without liver transplantation (9%) matches that expected after liver transplantation, and is therefore the threshold of minimum listing criteria for elective liver transplantation in those with irreversible decompensation in the UK.[95] Calculators for the UKELD score are available on the NHS Blood and Transplant website.

### Patients with ALD with an expected survival of less than 12 months should have their condition discussed with palliative care services

Core palliative care is best delivered by the hepatology team in parallel with active disease management. This includes ensuring that discussions about disease trajectory and advanced care planning occur alongside active management of disease complications such as transplantation: one should not preclude the other.[98] Patients should be given the opportunity to be introduced to the palliative and supportive care team in hospital and a discussion in a suitable environment offered. If this is declined by the patient an opportunity to meet with the team postdischarge to discuss advanced care planning should be offered.

Planned admissions for paracentesis as a day case are well evidenced to improve patient and carer satisfaction. This can be done by a nurse-led service with the support of the medical team. The opportunity to use a multidisciplinary approach can be used including dietitian input, addictions specialist/ACT and introduction to supportive and palliative care. It allows continuity and advanced care planning. For patients enrolled in day case services, improvements in outcomes correlated with the proportion of large volume paracentesis procedures done in a day case (vs unplanned) setting. There are significant cost savings to planned admissions.[99]

Long-term indwelling ascitic drains (LTAD) drains could also be considered on a case-to-case basis in patients with refractory ascites who are not under consideration for/listed for liver transplantation or transjugular intrahepatic portosystemic shunt (TIPSS). The risks of indwelling drains need to be carefully weighed and decisions for LTAD insertion should be made by a multidisciplinary team.[100]

## RECOMMENDATIONS FOR FUTURE RESEARCH, AUDIT AND SERVICE DEVELOPMENT

### Earlier detection of liver disease

It has been clear for some time that people with ALD are more likely to present late, with more advanced disease, compared with those with other causes of liver disease.[101] Recent initiatives in the UK have sought to find cases of disease at an earlier stage, for example, by the use of TE in people at risk of disease.[102] Understanding the value of this approach and the best way to implement methods of early detection will be essential for future service development.

### NITs for risk assessment in ALD

There is a clear unmet need to understand which NITs have the greatest utility for the risk assessment of ALD, and the cut-off levels which are best suited to confirming or excluding advanced fibrosis and risk of liver-related ill health. The optimal timeframe for repeat testing in patients at low risk of disease at baseline also needs to be established.

### Treatments and services for decompensated disease and AH

There have been no new treatments for decompensated ALD cirrhosis or AH since the introduction of corticosteroids several decades ago. Given the increasing number of admissions and deaths from ALD this is an important gap in our ability to care for patients and improve outcomes. Research into new treatments is necessary. Research into new methods of delivering care is also required for example the value of 'hub and spoke' relationships between secondary and tertiary care for improved access to specialist services, and delivery of hepatology services outside of traditional hospital settings such as outpatient clinics based in community or alcohol treatment centres.

Innovative research methods may be necessary to effectively deliver research in this cohort since concomitant health and social issues may reduce the value of traditional trial methods.

## CONCLUSION

ALD continues to be a major cause of ill health and premature mortality. These quality standards should be used alongside clinical guidelines from other organisations and local protocols to direct the treatment of patients with ALD. Despite the prevalence of ALD, research has historically lagged behind other less common causes of liver disease. As such there remains some uncertainty about the best management of ALD. We have highlighted particular aspects of the care of patients with ALD that we feel are most in need of examination (online supplemental file 1). As information from clinical audit and research emerges, it is likely that these standards will need to be updated so that they remain relevant. It is hoped that these evidence-based quality standards will improve the care of ALD and reduce variation between units.

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# Audit tool

| | Numerator | Denominator | Target/setting |
|---|---|---|---|
| **Assessment of liver fibrosis** | | | Primary care and secondary care |
| 1. **Assessment of liver fibrosis should be:**<br>a. **offered to people who drink hazardously (35 units/week in women, 50 units/week in men)**<br>b. **considered in people drinking alcohol in excess of recommended levels (14 units/week) who have co-factors for liver disease** | Number of individual patients having a validated test for hepatic fibrosis | Patients who drink hazardously | 90% |
| **Hospital management** | | | Secondary care |
| 2. **Patients admitted to hospital with ALD should be seen by a liver specialist clinician within 24 hours** | Patients seen by a liver specialist clinician within 24 hours of being admitted to hospital | Patients admitted to hospital with a primary diagnosis of ALD | 95% |
| 3. **Patients admitted to hospital with ALD and AUD should be assessed by a specialist addiction practitioner during their admission and offered appropriate intervention and referral** | Patients reviewed by an alcohol practitioner during hospital admission | Patients admitted to hospital with a primary diagnosis of ALD and recent alcohol intake | 95% |
| 4. **Patients with decompensated ALD should have a specialist dietary and nutritional assessment by a dietician experienced in management of patients with liver disease** | Patients assessed for malnutrition | Patients admitted to hospital with a primary diagnosis of ALD | 95% |
| 5. Corticosteroid treatment should be considered in AH with indicators of likely beneficial response (GAHS≥9; MELD 21-51; NLR 5-8). | Documented decision regarding corticosteroid treatment | Patients with primary diagnosis of acute AH | 90% |
| 6. **Patients should be provided with clear, written information about their liver disease in a manner that they can understand before they leave hospital. Provision of this information should be** | Patients given written information about liver disease | Patients admitted to hospital with a primary diagnosis of ALD | 90% |

| | | | |
|---|---|---|---|
| **documented in medical notes or a discharge letter.** | | | |
| 7. **Patients hospitalised with decompensated ALD or AH should be followed up by clinicians with specialist interest in hepatology within 6 weeks of discharge.** | Patients seen in a liver clinic within 6 weeks of discharge | Patients admitted to hospital with a primary diagnosis of ALD | 90% |
| 8. **ALD patients with a UKELD ≥49 and ongoing hepatic failure who have been abstinent for at least 3 months should be considered for liver transplant referral.** | Patients referred to a transplant centre, or documented reason for not doing so | Patients with decompensated ALD in outpatient clinics or inpatients (?) | 90% |
| 9. **ALD patients with an expected survival of less than 12 months should be offered advanced care planning. Referral for liver transplantation should not preclude this.** | Documented referral to palliative care or reasons for not doing so documented | Patients with decompensated ALD in outpatient clinics or inpatients (?) | 90% |

# Supporting information

## Alcohol-related cirrhosis

You have been diagnosed with decompensated alcohol-related cirrhosis. This leaflet explains what it is, the risks to your health and what will happen after your discharge from hospital.

### What is cirrhosis?

Cirrhosis is a stage of liver disease where there is lots of scar tissue in your liver. It affects the whole liver. It is thought to be irreversible. In your case, cirrhosis has developed wholly or partly due to alcohol use.

### What is decompensated cirrhosis?

People can have cirrhosis for a long time without any symptoms where the liver carries on working well. This is known as compensated cirrhosis and people can live with this for many years. As the liver becomes more damaged and scarred, it stops working normally and signs of liver failure begin to appear. These are

- jaundice (yellowing of the eyes and skin)
- ascites ((bloating due to fluid in the tummy)
- encephalopathy (drowsiness or confusion
- varices (swollen veins in your gut, if they burst you can vomit blood or have blood in your poo)

When any of these happen, the liver condition is known as decompensated cirrhosis.People with cirrhosis also have an increased risk of developing liver cancer, although this happens in only a few patients.

### What do I need to do after I am discharged from hospital?

The most important thing you can do is stop drinking alcohol forever. This is known as being abstinent.

People with cirrhosis who continue to drink alcohol have a much higher chance of getting liver failure and dying than people who stop drinking.

You can be referred to local alcohol support services. They work with you to find the best way of stopping drinking for you and help you do it.

If you can't stop right away, cutting down is still better than carrying on as you are. The alcohol team can help you to cut down your drinking with the aim of stopping over time.

Stopping drinking usually helps your liver work a bit better. Your symptoms would be more likely to reduce or go away. So stopping drinking for the rest of your life is the best thing you can do for your health.

**When will I be seen in the outpatient clinic?**

Before you leave hospital, you will be given a date for an outpatient appointment in the gastroenterology/liver clinic within the next few weeks. This will probably be in person as the team may need to examine you. We may ask you to have blood tests on the day to monitor your liver function.

**What about liver transplantation?**

When people with liver disease due to alcohol stop drinking, the liver can dramatically improve, even with cirrhosis. For some people, even after stopping drinking alcohol, the liver cannot repair itself enough and the liver is still working poorly. This may mean that replacing the liver (i.e. a liver transplant) needs to be considered.

Liver transplantation is only an option for people who have stopped drinking alcohol for good. To be considered for a transplant you will need to show that you are committed to staying alcohol-free for the rest of your life.

Stopping drinking alcohol also gives your liver the best chance of recovering. It can improve enough that you won't need a transplant for some time or at all.

If you carry on drinking alcohol when your doctor has told you to stop, you will not be able to have a liver transplant. Even if your liver disease gets worse or your life is at risk. However, your doctors will look at all other possible treatments.

If you become unwell or have any questions or concern between clinic visits then you can call the Clinical Nurse Specialist on XXXXX. Your outpatient appointment can be brought forward or questions dealt with over the phone.

The British Liver Trust have support and information for everyone affected by liver disease. You can call their nurse-led helpline on 0800 652 7330

Visit their website to find out about their online community and support groups www.britishlivertrust.org.uk/support

Their website also has lots of information about liver disease for you to read, download or order.

www.britishlivertrust.org.uk/ARLD

www.britishlivertrust.org.uk/cirrhosis