

Alcohol-related Liver Disease JLA Priority Setting Partnership

Total number of verified uncertainties identified by the PSP = 45

Date of priority setting workshop 16th September 2016

Question Rank	Uncertainty	Explanatory note / original uncertainties	Evidence	Source of Uncertainty	Health Research Classification System
1	What are the most effective ways to help people with alcohol-related liver disease stop drinking?	While it is widely accepted that stopping drinking alcohol is the most important first step in treating ARLD, "there is little certainty about which treatments are available to people affected by alcohol-related liver disease that usefully (i.e. that there is a good evidence base of efficacy for) reduces alcohol consumption - and therefore ongoing disease progress. In particular, patients hospitalised with complications of cirrhosis, who are most at risk and who benefit most from stopping drinking, are excluded from most trials. There is one trial of baclofen, but no other agents with a role in alcohol relapse prevention have any evidence base yet. Given that the STOPAH study confirmed that resuming alcohol intake was the major cause of mortality in alcoholic hepatitis there is an urgent need for such studies."	None identified.	12 Patients, 10 Carers, 53 Professionals.	Oral and Gastrointestinal
2	What are the most effective ways of delivering healthcare education and information about excessive alcohol consumption, the warning signs and the risks of alcohol-related liver disease to different demographics (including young people)?	A common concern is how best to inform people of the risks associated with alcohol consumption. "How can you educate people about the dangers of alcohol without appearing to preach?". "How are health professionals trying to make people aware of the addictive nature of regular consumption of alcohol?" The risk to young people is a particular concern "Does early education of risks associated with alcohol reduce alcohol problems developing in young people?". The use of information technology to educate people is a recurring theme "Exploring YouTube / interactive educational apps for delivering health education in different settings for the prevention of ARLD."	Systematic review: Scott-Sheldon LA; Terry DL; Carey KB; Garey L; Carey MP. Efficacy of expectancy challenge interventions to reduce college student drinking: a meta-analytic review. Psychology of Addictive Behaviors. 2012;26(3):393-405.	25 Patients, 15 Carers, 48 Professionals.	Oral and Gastrointestinal
3	What is the most effective model of community-based care for patients with alcohol-related liver disease?	The organisation and effectiveness of care and support in the home or community are important issues across all groups with an interest in this topic. "What care models work best to support people who cannot stop drinking and their carers? Currently most alcohol services will not provide input for people who continue to drink yet these are the people most at risk of serious health outcomes.". "Which services in the community are most able to prevent alcohol-related liver disease?" Care at home is another important issue "How can we offer better support including outreaching more into the house?"	None identified.	2 Patients, 2 Carers, 2 Professionals.	Oral and Gastrointestinal
4	What is the patient's experience of alcohol-related liver disease?	How does a diagnosis of alcohol-related liver disease affect other aspects of a persons physical or mental health, and their relationships or interaction with members of their family and wider social circle? This question relates to how ARLD affects other aspects of a persons health or life. "How does reported quality of life of ARLD patients compare to others with other physical disorders or conditions?" "How do persons experience the diagnosis of ARLD within a medical, family and social context?"	None identified.	1 Patient, 4 Professionals.	Oral and Gastrointestinal
5	Do attitudes to perceived 'self-induced illness' amongst healthcare professionals affect treatment, care provision and compassion for individuals with alcohol-related liver disease?	This question reflects concerns among both patients "Is ARLD put as a lower priority because it is deemed self inflicted?" and professionals "I have perceived at different times a lack of interest in actively managing the care of patients with alcohol related liver disease because they have it in their power to make the single biggest difference to their health." It is not just an issue of doctor-patient relations, but can have an impact on outcome. "Why do Dr.s just assume that (alcohol) is the only issue ?" "How does a diagnosis of an alcoholic affect care and treatment outcomes? "	None identified.	7 Patients, 8 Carers, 6 Professionals.	Oral and Gastrointestinal
6	What are the most effective strategies to reduce the risk of alcohol-related liver disease in heavy drinkers?	"What are the most effective interventions for reducing alcohol consumption, both at societal level and individual level?" What treatments are available to people affected by alcohol-related liver disease that usefully (i.e. that there is a good evidence base of efficacy) reduces alcohol consumption - and therefore ongoing disease progress?" "What strategies work in supporting heavy, dependent alcoholics remain abstinent?"	None identified.	5 Patients, 2 Carers, 9 Professionals.	Oral and Gastrointestinal
7	Does the stigma associated with alcohol misuse affect the willingness of people with alcohol-related liver disease to ask for help?	Stigmatisation of patients with alcohol problems is seen as an issue by professionals, and to an extent by those using health services. "What more can be done to ease stigma and prejudice towards people with alcohol issues to allow them to come forward for help more readily and before major damage has been caused?"	None identified.	2 Patients, 2 Carers, 6 Professionals.	Oral and Gastrointestinal

8	What interventions improve survival in individuals with complications of advanced alcohol-related cirrhosis?	This question largely relates to the use of steroids. "How can we identify which patients with severe alcoholic hepatitis benefit from steroids?" "What is the optimal duration of steroid therapy in severe alcoholic hepatitis (assuming initial response by Lille criteria)?" "How can you predict if someone will respond to a treatment or not?"	Protocol for a systematic review: Thorley H; Porter K; Fleming C; Jones T; Kesten J; Marques E; et al. Interventions for preventing or treating malnutrition in problem drinkers who are homeless or vulnerably housed: protocol for a systematic review. <i>Systems Review</i> . 2014;4:131.	21 Professionals.	Oral and Gastrointestinal
9	How should depression be managed in the context of alcohol-related liver disease?	This is a straightforward question related to the need to be aware that depression can be both a cause of and result of heavy drinking.	None identified.	1 Patient.	Oral and Gastrointestinal
10	What models of involvement of palliative care services in advanced alcohol-related liver disease are most beneficial?	"What are the barriers to this group of patients receiving palliative care?" "How can we define better which patients need end of life care? This is a challenge in ARLD as if abstinence is achieved recovery may occur." "How can these patient services be developed/funded to allow them to stay at home for end of life care instead of having to go to hospital?"	None identified.	6 Professionals.	Oral and Gastrointestinal
11	Are there any early signs of alcohol-related liver disease?	It is well recognised amongst liver specialists that the first time a person may know they have alcohol-related liver disease is when they come into hospital with a serious complication of advanced liver disease, an event that they may well not survive. Drinkers commonly assume no damage is occurring.	None identified.	4 Patients, 2 Carers, 7 Professionals.	Oral and Gastrointestinal
12	What are the factors that determine who gets significant/advanced alcohol-related liver disease (affect progression)?	It is well recognised that although the more alcohol a person drinks the more likely they are to get alcohol-related liver disease, there is a large variation in susceptibility to this condition. A knowledge of the factors that affect the risk to an individual is important for the individual to understand as well as for healthcare professionals in order that they may provide advice tailored to that person. Some factors are genetic, but other factors are likely to be dietary as well as other unknown elements. Genetic factors are the main interest here: "Can you be genetically pre-dispositioned - either to be dependent or to be more susceptible to liver damage from drinking?" "Though some other issues are raised: "Is there any evidence that some people are more susceptible to alcohol-related liver disease and, if so, is it useful to communicate this to patients?" "What are the gender differences in determinants and consequences of a diagnosis of ARLD?"	None identified.	4 Patients, 8 Carers, 29 Professionals.	Oral and Gastrointestinal
13	What effect would greater alcohol-related liver disease education/training of GPs and secondary care clinicians have on the mortality outcome of alcohol-related liver disease?	This question is important for two reasons: ARLD is all too infrequently identified at primary care level and on presenting at hospitals - usually with advanced liver disease - most ARLD patients are treated by non-hepatologists who lack the detailed experience and knowledge of how best to treat this complex disease. Research to identify the knowledge gaps and their effect on outcomes could lead to focused training/education of involved clinicians and potentially a significant decrease in disease progression and mortality. "What effect would there be on liver disease mortality if GP's had to undergo obligatory focused education on early diagnosis of liver disease? Currently they are largely too ignorant." "Would educating doctors - including consultants, other hospital doctors and GPs in the optimum diet/nutrition for ARLD patients prevent more harm and deaths?" "How can doctors be trained to avoid inappropriate prescribing of drugs to ARLD patients?"	None identified.	2 Patients, 4 Carers.	Oral and Gastrointestinal
14	What is the relationship between alcohol-related liver disease and mental illness?	While research has shown an association between psychological distress and liver disease generally, the extent of such a relationship in ARLD patients and mental illness as a contributing aetiology and/or effect of ARLD is unknown. "What is the correlation with mental health and alcohol-related liver disease?" "Is alcohol-related liver disease associated with an increased risk of mental illness and if so is this different compared with similar drinkers who do not have liver disease?"	None identified.	1 Patient, 1 Professional.	Oral and Gastrointestinal

15	What dietary recommendations or supplements (including herbal and vitamins) are beneficial in patients at risk of or with established alcohol-related liver disease?	This question covers a number of issues. It is important for a person to feel that they have some control over their condition and therefore, apart from stopping alcohol consumption, are there certain things they should or should not eat in order to help the liver cope and recover. A much greater understanding is developing over the last few years of how specific dietary constituents may affect the gut and thereby potentially affect the liver. It was felt that this area required further research as well as whether specific dietary supplements could help this condition. The importance of diet as an aid to recovery from ARLD is a recurring theme: "What is the correct amount of vitamins to give to patients when presenting in alcohol withdrawal?" "Are there any vitamins that it would be worth taking and any to avoid?" The use of dietary supplements, particularly milk thistle, is also of interest to many "Is milk thistle (<i>Silybum marianum</i>) beneficial to the liver?"	Systematic reviews: Salameh H., Bonkovsky H., Kuo Y.-F., Singal A. Impact of nutritional supplementation in patients with alcoholic cirrhosis and alcoholic hepatitis: A meta-analysis of randomized placebo controlled trials. <i>Am J Gastroenterol</i> 2013;108;S133. doi:10.1038/ajg.2013.265. Fialla A.D., Israelsen M., Hamberg O., Krag A., Gluud L.L. Nutritional therapy in cirrhosis or alcoholic hepatitis: A systematic review and meta-analysis. <i>Liver Int</i> 2015;35(9):2072-8. doi: 10.1111/liv.12798. Antar R. Wong P, Ghali P. A meta-analysis of nutritional supplementation for management of hospitalized alcoholic hepatitis. <i>Can J Gastroenterol</i> 2012;26(7):463-7.	10 Patients, 4 Carers, 14 Professionals.	Oral and Gastrointestinal
16	What effect does combining treatment of the liver disease with psychiatric support have on prognosis/mortality?	In alcohol-related liver disease, there are commonly two conditions - firstly the pattern of heavy alcohol consumption, and secondly, the resulting liver disease. Care of these two factors in a joined up, coherent, fashion would therefore seem logically to be beneficial. Understanding whether this is the case and how this can be delivered most effectively for the patient is therefore an important area of current uncertainty. "Where diagnosis is made, should patients be automatically referred to mental health services or a parallel service offering psychiatric support/counselling/treatment?"	None identified.	2 Carers.	Oral and Gastrointestinal
17	What are the most effective messages and how are they best delivered in helping a patient with alcohol-related liver disease understand the condition and the importance of abstinence?	Providing the motivation for a person to change a behaviour, such as to stop alcohol, consumption can be very difficult to achieve. The potential factors leading to the heavy alcohol use and the information or message that may trigger this being controlled and stopping are individual and poorly understood. More important than medication or therapies to aid alcohol cessation is a person deciding they are going to stop drinking and therefore knowing how best to lead a person to this point is central to allowing a person to recover, their liver disease to improve, with a consequent dramatically improved survival. "The effects of drinking need to be more specific. I was given numbers from my blood test that meant absolutely nothing to me. I needed to see people who were suffering/pictures of what it was doing to your body on the inside. Perhaps that would have made me understand what effect the alcohol was having on my body."	None identified.	1 Patient, 1 Carer, 1 Professional.	Oral and Gastrointestinal
18	Are there any effective treatments for alcohol-related liver disease apart from abstinence from alcohol?	The issues here are less about the effectiveness of drugs, but focus more on other types of treatment. Underlying many questions is the issue of whether there is any real alternative to abstinence from alcohol. "What intervention is most successful in the prevention of alcohol related liver disease?" "Are treatments cost effective or is the real aim alcohol abstinence?" "Treatment seems largely focussed on symptom management I am interested to hear about developments in gene therapy and other novel approaches to ARLD."	None identified.	9 Patients, 6 Carers, 25 Professionals.	Oral and Gastrointestinal
19	What are the obstacles for individuals to modification of their alcohol consumption?	"What are the common problems that people with ARLD have when modifying their alcohol use?"	None identified.	1 Professional.	Oral and Gastrointestinal
20	What lifestyle interventions improve outcomes in alcohol-related liver disease?	"Does diet or exercise help someone with ARLD?" These are the main lifestyle aspects that people are interested in, mostly as means of reducing or avoiding the need for pharmacological or surgical treatment.	None identified.	3 Patients, 1 Carer, 4 Professionals.	Oral and Gastrointestinal
21	What level and pattern of drinking behaviour affects the risk of getting alcohol-related liver disease (taking into account other risk factors for alcohol-related liver disease)?	The principal issue is whether binge drinking or constant use of alcohol affects the likelihood of developing ARLD. "Is chronic exposure or binge drinking more harmful?" "Is the severity of alcohol-related liver disease associated with quantity, frequency or type of alcohol consumed?" "Is the severity of alcohol-related liver disease associated with age at onset of drinking or the number of years of drinking?"	None identified.	6 Patients, 5 Carers, 14 Professionals.	Oral and Gastrointestinal
22	To what degree is established liver disease reversible?	The chances of their liver recovering from alcohol related damage is a major issue for many patients. "What are the chances of improving? Over what timescale?" "Is there a threshold beyond which alcohol-related liver disease is irreparable?" "How readily (if at all) early stage liver disease can be treated and the general recovery pattern if mild liver disease has been caused?"	None identified.	3 Patients, 10 Carers, 11 Professionals.	Oral and Gastrointestinal

23	What are the most effective interventions delivered in combined clinics in the setting of secondary care for alcohol-related liver disease?	There are general questions, mostly from professionals, about the effectiveness of different models of care. "Do hospital-based alcohol care teams produce better longterm results than community alcohol support services?" "How effective are specialist centres/wards/teams and what is the difference in the day to day care they provide compared to a general ward?" "Are ARLD patients given brief interventions? If so, what happens afterwards. From this we can develop health prevention information and approaches." There are also questions on the effectiveness of specific professional services such as psychologists and alcohol liaison nurses.	None identified.	1 Carer, 6 Professionals.	Oral and Gastrointestinal
24	What interventions improve survival in severe alcohol-related hepatitis?	The issues of concern here are "Which patients with alcohol-related liver disease should be given long-term antibiotic prophylaxis against spontaneous bacterial peritonitis?" and "What is the optimal fluid resuscitation in patients with alcohol-related liver disease who develop sepsis?"	None identified.	2 Professionals.	Oral and Gastrointestinal
25	Is there a difference between the outcome of alcohol-related liver disease patients treated by specialised liver disease units/hepatologists versus general gastro-enterologists?	"What is the outcome of ARLD patients treated by specialised liver disease units/hepatologists versus general gastro-enterologists and what can be done to educate the latter which would benefit mortality rates?"	None identified.	2 Carers, 1 Professional.	Oral and Gastrointestinal
Question not discussed and ranked at workshop	Do specific interventions involving family members/social support improve maintenance of alcohol abstinence in individuals with alcohol-related liver disease?	Questions relate to the effectiveness and cost effectiveness of interventions that involve families and social networks compared with those aimed at individuals alone. Relate to such therapies in general, as well as specific: "What is the effectiveness of motivational enhancement therapy and systemic family therapy techniques (problem/solution talk and resource talk) in the treatment of heavy drinking / ARLD in a hospital setting?"	None identified.	3 Professionals	Oral and Gastrointestinal
Question not discussed and ranked at workshop	Does the type of alcohol affect the risk, or progression, of alcohol-related liver disease?	"Do certain alcohol products confer a higher risk of ARLD than others - eg strong white ciders, spirits, etc - or is it simply a matter of total units consumed?"	None identified.	3 Patients, 1 Professional.	Oral and Gastrointestinal
Question not discussed and ranked at workshop	Does the media portray excessive drinking in an inappropriately positive way and does this affect behaviour?	"The vast majority of 'drunk scenes' on film and TV are used for comic effect - how can this message be put across that alcohol abuse can have serious consequences?" "We tend to 'celebrate' notable drinkers (Oliver Reed, Richard Burton) - What can be done to change this culture?"	None identified.	2 Carers, 2 Professionals.	Oral and Gastrointestinal
Question not discussed and ranked at workshop	What is the impact on drinking behaviour of the ready availability of alcohol in social environments, at home and elsewhere?	As patterns of drinking behaviour change, with more alcohol being drunk at home rather than in pubs or at social occasions, the factors that influence behaviour may change and need different approaches when tackling drinking behaviour.	None identified.	3 Professionals.	Oral and Gastrointestinal
Question not discussed and ranked at workshop	Why is alcohol-related liver disease more prevalent in low socio-economic groups?	There is a perception that alcohol abuse is more common in lower socio-economic groups. Exploring the reasons for this and developing strategies targeting these groups may need to be developed.	None identified.	1 Patient, 2 Professionals.	Oral and Gastrointestinal
Question not discussed and ranked at workshop	What role do dietary factors have in susceptibility and prevention to of alcohol-related liver disease?	"How does nutrition affect the development of ARLD?" "Does diet have a role in the management of ARLD?" "How can one recommend the most appropriate diet to optimise nutrition?"	None identified.	5 Patients, 8 Professionals.	Oral and Gastrointestinal
Question not discussed and ranked at workshop	What interventions best aid patients with alcohol-related liver disease maintain and manage employment?	"How can patients deal with work colleagues and HR?"	None identified.	2 Professionals.	Oral and Gastrointestinal
Question not discussed and ranked at workshop	What is the best screening test for alcohol-related liver disease and how should it be applied?	Questions relate to the importance of correct diagnosis in primary care: "What is the best way to raise awareness of alcohol related liver disease in general practice?" and also to the effectiveness of current screening tools and methods "Are current screening methods effective?" The ability to monitor your own condition is also desirable "Is there a personal early warning system like blood glucose test or app score software that people could use in the future?"	None identified.	10 Patients, 6 Carers, 14 Professionals.	Oral and Gastrointestinal
Question not discussed and ranked at workshop	Should there be routine screening for alcohol-related liver disease?	The desirability of screening is itself an issue "Should tests for early signs of liver damage be routine for all patients at GP surgeries in order to raise awareness of the patient, identify problems early and offer appropriate interventions/advice before further more serious liver disease occurs?"	None identified.	8 Patients, 2 Carers, 14 Professionals.	Oral and Gastrointestinal
Question not discussed and ranked at workshop	Should screening for primary liver cancer in patients with alcohol-related liver disease be routinely performed?	"What evidence do you have to support the current practice of annual liver US in people with fatty livers or cirrhosis? the incidence of HCC diagnosed in relatively asymptomatic patients must be vanishingly small. the amount of scan time consumed by this pointless activity is large. Where is the evidence base for this fashion?"	None identified.	1 Professional.	Oral and Gastrointestinal

Question not discussed and ranked at workshop	What is the best method for diagnosing alcohol-related liver disease and where is this best done? How does the experience of diagnosis affect outcome?	Current methods of diagnosis are questioned "How effective are current diagnostic tools to identify ARLD? Biochemical markers vs. self report questionnaires. Can they be improved?", as well as where diagnosis should be carried out "Can ARLD be diagnosed in the community?"	Systematic reviews: Stevenson M, Lloyd-Jones M, Morgan MY, Wong R. Non-invasive diagnostic assessment tools for the detection of liver fibrosis in patients with suspected alcohol-related liver disease: a systematic review and economic evaluation. Health Technol Assess. 2012; 16(4):1-174. Parkes J, Guha IN, Harris S, Rosenberg WM, Roderick PJ. Systematic review of the diagnostic performance of serum markers of liver fibrosis in alcoholic liver disease. Comparative Hepatol. 2012;11(1):5. Pavlov CS, Casazza G, Pavlova M, Nikolova D, Tsochatzis E, Liusina E, et al. Ultrasonography for diagnosis of cirrhosis in people with alcoholic liver disease. Cochrane Database of Systematic Reviews .2016, Issue 1.	16 Patients, 10 Carers, 34 Professionals.	Oral and Gastrointestinal
Question not discussed and ranked at workshop	What are the needs and best methods for delivering support to care-givers both for themselves and the patient with alcohol-related liver disease?	There are a broad range of issues here, from whether families should be involved in care "Does specific advice from health professionals to the families and carers of those with alcoholic liver disease about supporting the patient mentally and physically improve patient outcomes and reduce the negative impacts on families and carers." to carers who clearly feel they should be involved "Caregiver needs are completely overlooked in this group." How to address these needs remains unclear "What are the unmet needs of ARLD patient's carers?"	None identified.	1 Patient, 10 Carers, 19 Professionals.	Oral and Gastrointestinal
Question not discussed and ranked at workshop	What are the optimal ways of staging alcohol-related liver disease?	Optimal methods for assessing the stage of development of ARLD remain unclear. "Which measures of markers for ARLD are generally regarded as a "danger"?" "Clearly need to develop a blood test that reliably diagnoses significant liver injury." "Biggest problem is that LFTs may be normal, or nearly so, until alcoholic liver disease is quite advanced. Any better tests?"	Systematic review: Pavlov CS, Casazza G, Nikolova D, Tsochatzis E, Burroughs AK, Ivashkin VT, et al. Transient elastography for diagnosis of stages of hepatic fibrosis and cirrhosis in people with alcoholic liver disease. Cochrane Database of Systematic Reviews: 2015, Issue 1. DOI: 10.1002/14651858.CD010542.pub2	7 Patients, 3 Carers, 18 Professionals.	Oral and Gastrointestinal
Question not discussed and ranked at workshop	What medications for other conditions are the most effective and safe for use in patients with alcohol-related liver disease?	Interactions between drugs given for ARLD and for other conditions is a concern, both for co-existing conditions "What drugs which might be prescribed for co-existing conditions (e.g. statins) are best avoided to prevent further harm to the liver?" and for treatment of side effects of liver disease "What are the best analgesics for acute and chronic pain for people with liver disease?"	None identified.	5 Patients, 1 Carer, 3 Professionals.	Oral and Gastrointestinal
Question not discussed and ranked at workshop	What are the best means of diagnosing hepatic encephalopathy (HE) what is the role of new methods of diagnosing HE?	"How can we improve the recognition and diagnosis of early forms of (treatable) chronic hepatic encephalopathy in the community and hospital settings?"	None identified.	1 Carer, 2 Professionals.	Oral and Gastrointestinal
Question not discussed and ranked at workshop	What factors in a person with alcohol-related liver disease indicate a favourable outcome following liver transplantation?	"What factors indicate favourable outcome following liver transplant?" "What factors predict a return to drinking in people transplanted for alcohol-related liver disease?" "Is there an age cut-off for liver transplants, and should this be calendar or biological age?"	None identified.	3 Patients, 2 Carers, 4 Professionals.	Oral and Gastrointestinal
Question not discussed and ranked at workshop	What treatments are safe and effective in treating alcohol withdrawal in patients with alcohol-related liver disease?	"How do we manage alcohol withdrawal in the critically ill group?"	None identified.	4 Professionals.	Oral and Gastrointestinal
Question not discussed and ranked at workshop	What are the appropriate quality markers for care in alcohol-related liver disease?	"What are the appropriate quality markers for care in alcohol-related liver disease?"	None identified.	1 Professional.	Oral and Gastrointestinal
Question not discussed and ranked at workshop	Which liver-assist machines can help survival to liver transplantation?	"Extracorporeal therapies to bridge to transplant?"	None identified.	2 Professionals.	Oral and Gastrointestinal
Question not discussed and ranked at workshop	What is the best way of identifying which patients with severe alcohol-related liver disease needing Intensive Care support will survive?	"What criteria should be used to transfer to level 3 care?" "How best should we care for ALD patients when they become critically ill?"	None identified.	2 Carers, 4 Professionals.	Oral and Gastrointestinal