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Advanced chronic liver disease and the last year of life: a mixed methods study to understand how care in a specialist liver unit could be improved

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Abstract:

Objectives: To identify both the limitations in palliative care provision in the last year of life and the potential barriers to and enablers of shared approaches to care.

Design: Mixed methods study, using a retrospective case note review, qualitative focus groups and individual interviews.

Setting: A tertiary referral liver centre in the south of England (UK).

Participants: Purposively selected case notes of 30 people with cirrhosis, who attended the tertiary referral liver centre and died during an 18 month period. Twenty three liver health professionals participated in either focus groups or individual interviews.

Primary and secondary outcomes: Main data collected from case notes were hospital admissions, prognostic discussions and palliative care provision. Qualitative methods were used to explore topics on cirrhosis management, facilitators and barriers to palliative care.

Results: Participants had high rate of hospital admissions with high symptom burden. Clinicians rarely discussed prognosis and future care preferences as they lacked the skills and confidence to initiate these. Palliative care provision occurred late, as clinicians' were reluctant to refer due to the perceived recoverability of liver function, poor understanding of the palliative care role and the negative perception of palliative care from patients and family.

Conclusions: People dying with cirrhosis have unpredictable trajectories, but share a common pathway of frequent admissions and worsening symptoms as death approaches. The use of clinical tools to identify the point of irreversible deterioration and joint working between liver and palliative care may improve care for people with cirrhosis.

Strengths and limitations of this study

- The study is the first to look specifically at how care is provided to people with advanced liver disease in the last year of life, with the aim of identifying barriers that prevent better supportive care.
- A mixed methods approach enables identification of the structural difficulties to providing end of life care to people with advanced liver disease from different perspectives.
- Findings suggest pragmatic ways that supportive and end of life care can be improved for people with advanced liver disease.
- As this study was conducted in one tertiary liver unit in the south of England, the findings may not be generalised to other health settings.
- The retrospective nature of the case note data hampers the interpretation of the quantitative findings.

Background

Advanced chronic liver disease (cirrhosis) is a growing international public health problem and often affects people of working age.[1] It is the third most common cause of premature death in the United Kingdom (UK) [2], with more people affected by liver disease with the increase in alcohol consumption, viral hepatitis and obesity [3]. The majority dying from liver disease are not suitable for liver transplantation and of those suitable, 20% will die before a donor becomes available[4]. Living with cirrhosis may involve considerable symptom burden, and when liver failure ensues, the prognosis is poor. Death may occur either after a long period of decline with a fluctuant clinical picture, or may be sudden and unanticipated. In most cases, death from cirrhosis occurs in hospital [5].

People with cirrhosis have supportive and palliative care needs [6-9], in which liver professionals acknowledge they have a role in this aspect of care [10, 11], but perceive their skills are limited [10, 12]. Palliative care provision is limited [13], and knowledge of prescribing in liver failure is needed. Shared care, defined as using the skills and knowledge of many health professionals who share joint responsibility for an individual's care, may be useful [14]. Palliative care offered in parallel with optimised specialist and generalist care may benefit people with advanced cirrhosis [15]. One difficulty is knowing the appropriate time to make referrals and begin shared care [10]. Further data to understand how different specialities such as liver services and palliative care can work together may be helpful[14]. In this paper we report what we have learned from exploring practice in a tertiary treatment centre for liver disease in north London, UK. We used mixed methodology, guided by Rapid Participatory Appraisal in which data collected from different sources relating to a specific

healthcare provider are combined to describe both the service structure and care improvements in a specific health locality [16].

We conducted a case note review, focus groups and qualitative interviews to explore:

(i) How healthcare in liver services is provided in the last year of life to people with cirrhosis from any cause;

(ii) Potential barriers to palliative care provision in liver care and enablers of shared approaches to care between specialists in hepatology and palliative care.

Method

A mixed methods study, using a retrospective case note review, qualitative focus groups and individual interviews. Case note findings were used to quantify the types of healthcare inputs provided by the liver services to people in their last year of year and to identify potential limitations and barriers in the palliative care provided. The qualitative data identified reasons for these limitations and barriers to adopting shared care approaches, also highlighting potential enablers to improving this care for this group of people.

Setting

A tertiary referral liver transplant centre in north London UK, providing both a core diagnostic service for all conditions affecting the liver and long-term management of patients with all severities of liver disease.

Procedure

Retrospective case note review

As resources were limited, we purposively selected 30 people with cirrhosis from the 66 people who attended the tertiary referral liver centre and died between April 2010 and September 2011. We aimed to ensure that our sample represented the spectrum of people attending the centre and purposefully sampled according to age, gender and cause of liver failure.

We used a structured framework to extract data from patient records available from the centre for the 12 month period prior to death. We noted demographics, severity of liver disease at last admission, cause of cirrhosis, transplantation status, physical and psychological symptoms, and health service use in secondary care (inpatient admissions, hospital length of stay, intensive therapy unit (ITU), liver-related procedures). We recorded evidence of discussions about prognosis and future preference for care. We collected information on referrals to specialist palliative care (SPC), creation of care plans including evidence of advance care planning (ACP), resuscitation (DNACPR) status, preferred place of death and actual place of death. Data were extracted by the clinical researcher (SD) and inputted into Microsoft Excel.

Qualitative data

Both focus groups and semi-structured interviews were used to capture as many views of healthcare professionals as possible. All participants gave written consent prior to data collection. Focus groups and interviews were conducted in the period from July 2013 to May 2015.

Focus groups

Focus groups were used as a pragmatic method of gathering larger numbers of people together and using the group dynamic to generate discussion about care at the end of life in cirrhosis[17, 18]. A purposive sampling to ensure the views of all levels of the liver team across the disciplines (doctors, nurses and allied health professionals) were captured. Three focus groups were organised (lasting 45-60 minutes) and led by a clinical researcher (SD), with an observer (JL) taking field notes and co-facilitating. To guide these discussions, a topic guide (supplementary files) was developed by the members of research team (JL, SD, AM, DT, LG, KH, LJ) covering: challenges of providing care to patients in the last year of life; their perception of patient and family understanding of their liver disease; discussing prognosis and future care preferences; improving palliative care. All focus groups were audiotaped and transcribed verbatim.

Interviews

Professionals unable to attend the focus groups, were invited to take part in semi-structured individual interviews. These were conducted by SD using the focus group topic guide, and were audiotaped and transcribed verbatim.

Data analysis

Retrospective case notes: Descriptive statistics were used to describe hospital admissions and service use, documentation of prognostic discussions and preferences for future care,

and palliative care provision. Data were summarised to highlight limitations in palliative care service provision.

Qualitative data: A framework approach was used in analysing the transcripts[19], which were first read independently by two researchers (JL, SD). Thematic analysis was used to identify themes, from which a coding system was developed and applied to the whole data set systematically. Any disagreements in coding were resolved by consensus. The researchers considered independently and met to discuss how the themes identified were linked together by contextual factors. Independent analysis ensured validity and reliability of the themes identified. These themes were used to explain the limitations in palliative care provision found in the case notes, and to identify barriers and enablers to future palliative care for people with cirrhosis.

Results

Provision of healthcare in last year of life (case note findings)

Demographics and clinical characteristics (Table 1)

Our sample was predominately male (n=20, 67%) with a mean age of 58 years (range 25-75), in which alcohol-related liver disease (ARLD) was the predominant diagnosis (n=16; 53%). In 23 cases where data were available at last admission, our sample had a median (interquartile range) MELD score of 23 (16.5-23). Nineteen (63%) people were not considered for liver transplant due to poor health, five were on the liver transplant waiting list, and three had previously received a liver transplant. Eight (27%) people with cirrhosis had been referred to the tertiary centre from other 'out of area' hospitals either for a liver

transplant assessment, or for treatments such as a Transjugular Intrahepatic Portosystemic Shunt (TIPS) procedure or intensive management of bleeding.

The patients in our sample were highly symptomatic (table 2). Everyone was symptomatic three months before death, presenting with ascites (n=22, 73%), extensive peripheral oedema (n=20, 66%), severe fatigue and weakness (n=20; 66%) and pain (n= 13; 43%). In the last month of life, our participants presented with an average of 14 physical symptoms per person. The majority (n=19, 63%) were noted to have symptoms of Hepatic Encephalopathy such as confusion, disorientation, and agitation.

Health service use in tertiary care

Our sample of 30 had a mean of four inpatient admissions per person in the last year of life, and a mean length of stay of 37 days. Seventeen (57%) people were readmitted within 30 days of discharge. The frequency of admissions increased for most people (n=29; 97%) in the last 3 months of their life. Nineteen (63%) people had more than one admission in the month before death, during which the median number of admissions was two (IQR: 1-3). Most admissions were precipitated by cirrhotic complications, requiring invasive procedures such as blood transfusions, endoscopic treatment of varices, TIPS and paracentesis. During these admissions, each participant was seen by a mean of three different liver consultants (range 1-6) in the last year of life. Furthermore, nine (30%) people were regularly reviewed by the hospital nurse-led patient-at-risk team (PART), to decide whether to escalate or de-escalate their treatment. Six (20%) people with cirrhosis required treatment in the ITU during which three patients died.

Documentation of prognosis, future care discussions and palliative care provision

Liver consultants recorded having discussed prognosis mainly with family members (n=23, 77%), which occurred very late; in 16 (53%) cases this discussion occurred ≤ 34 days before the person died. Liver doctors recorded fewer discussions with patients about understanding of their disease or future care preferences (n=16, 53%), most of which occurred one month before death (n=9/16; 56%).

Although most people (n=26; 67%) had a DNACPR recorded in their medical notes, this was completed by medical personnel, with limited consultation from either the person with cirrhosis (n=5, 17%) or their family member (n=6, 20%). In seven cases, the liver team had to be alerted about completing a DNACPR by other clinical teams such as the PART team (n=4), ITU (n=2) and the emergency department (n=1). Most people (n=19, 63%) had no discussions with doctors about their preferred place of care.

Most people with cirrhosis (n=21; 70%) were referred to specialist palliative care a median of five days before death. Twelve (40%) people with cirrhosis documented as deteriorating were still receiving active treatment up until their death. For most people in our cohort, death occurred in hospital (n=25; 83%), three of which were in ITU. The remaining five people died either at home (n=3; 10%) or in a hospice (n=2; 7%). Only five people from the sample had clear discussions with health professionals about place of death, of which two died in the place of their choice (one at home and the other in hospital).

Barriers to and enablers of provision of palliative care (qualitative data)

Demographics of liver clinician sample: Thirteen liver health professionals took part in three focus groups (FG) [FG1: 3 doctors, 2 liver transplant nurses, a dietician and a pharmacist; FG2: 3 ward nurses and a healthcare assistant; FG3: 2 ward nurses). Nine health professionals took part in semi-structured interviews (5 doctors, 2 senior nurses in hepatology, a clinical nurse specialist in palliative care, an alcohol liaison nurse). No demographic information was collected for the liver clinician sample other than their discipline.

Key findings:

Initial analysis illustrated that liver clinicians recognised that although their patients were in poor health, they did not address quality of life issues with them and that palliative care options were only considered with patients who raised this topic first. Further analysis identified five emergent themes which illustrated why liver clinicians focused on reactive treatment for people at the expense of palliative care: unpredictable trajectory of liver disease, management of patient treatment expectations, clinician/patient perceptions of the palliative care role, poor continuity of care, perceived lack of skill and confidence.

Unpredictable trajectory of liver disease: The perceived ability of the liver to recover function made it difficult for doctors to estimate the point of irreversible liver decline, and so provided doctors with hope that trying different treatments will promote recovery, even with imminently dying patients on the wards. Part of this difficulty laid in the limited times that doctors saw patients in contrast with the ward nurses, who provide continuous care

and were confident in identifying those imminently dying, but who felt it was the doctors' responsibility, as the main clinical decision makers, to stop active treatment.

Management of patient expectations: Doctors' emphasis on active treatments is reinforced by their own perceptions of patients' treatment expectations. Part of this expectation may be reflected by the patients' young age, who doctors feel want 'life' at all costs. Furthermore, as many patients are referred by secondary care 'out of area' (as illustrated in our case notes), clinicians perceive these patients see referral to the tertiary liver centre as a last chance to 'cure' their liver disease. This in turn, reinforces clinicians' focus on active treatments, at the expense of discussing prognostic issues.

> *"We probably don't do enough of it (discuss future care preference), because most of the patients at a given time are not willing to engage with that question. The median age of patients is 53, so we are not talking about an 80 year old who has lived their life to the full. We are talking about people who still want life." (Consultant hepatologist 1, interview)*

Patients' unrealistic expectations, together with their limited knowledge of patients' own understanding of their disease, presented doctors with difficulties in managing these expectations and deciding what treatment options to pursue.

> *"They (patients) are often referred extremely late, full of expectation only to be told there's nothing we can do. The difficulty is, what do you then do with that patient? Do you let them go back to the referring trust or secondary care, how do you know that they are going to get palliative care or the treatment that they need" (Consultant hepatologist 2, interview)*

Misunderstanding of palliative care: Clinicians perceived that patients and their family members saw referral to palliative care negatively, as a move suggesting that clinicians had 'given up' on the patient. They felt that patients and families did not understand what palliative care could offer in terms of symptom control and psychosocial support, instead seeing palliative care as a service for people at the very end of life, as illustrated by this senior nurse.

> *"We've got a patient on the ward whose family are very opposed to palliative care, but wanted active treatment. The patient has had repeated admissions, even if the family can only have her for another extra few months. The nurse tried to tell them it is not just the last weeks and hours (input from palliative care), it can be longer than that and the palliative team have a lot to offer you even now." (ward senior nurse, interview)*

Although most liver clinicians saw a role for palliative care in caring for this group of patients, the debates on its utilisation centred more on understanding when a referral to palliative care was considered appropriate. Most had very limited experience in working with palliative care and knowing the best time to refer. This was further compounded by the difficulty of estimating the point of irreversible liver deterioration and the lack of clinical tools and guidelines to support them with this process.

> *"Would like to refer much earlier, but need to have an understanding at the point that Specialist palliative care would like involvement." (Consultant hepatologist, Multi-disciplinary focus group)*

Poor continuity of care: Liver clinicians felt the lack of adequate information systems and the rotation of medical staff (as identified in our case notes, which identified that each participant saw at least three liver consultants over the year), contributed to 'poor continuity of care' for patients. This lack of continuity is demonstrated when patients' treatment plans agreed with one consultant can be changed by another consultant due to a lack of shared information.

> *"This rotation of staff causes problems as some patients are treated and patched up, but come in under another consultant when readmitted and treatment happens again. However, the system does not allow for information to be exchanged about what exact changes have occurred in their condition." (Consultant hepatologist 3, interview)*

Perceived lack of skill and confidence: Doctors perceived they lacked skills and confidence in engaging in discussions about prognosis or palliative care with patients or family members. On liver wards, this perceived lack of skill and competence was further compounded by a lack of private space for clinicians to discuss sensitive topics with patients.

Enablers for improved palliative care: Liver clinicians suggested strategies to improve both continuity and enhancing the integration of palliative care and liver services: establishment of joint liver and palliative care clinics for people with decompensated liver disease and multidisciplinary team case conferences to coordinate care and treatment for those patients frequently admitted. This would enhance mutual understanding across specialities of liver-specific symptom management and the timing of referrals. To support liver clinicians in

identify patients suitable for early palliative care support, appropriate clinical tools with relevant guidelines need to be identified.

Discussion

Key summary

Our findings reflect the complicated clinical picture surrounding the provision of care of people with cirrhosis in their last year of life. We demonstrate that patients had a high symptom burden and increasing number of admissions in their last 3 months of life and a focus on active treatments as highlighted by inputs from both the nurse-led PART team and ITU. As with previous studies [12, 13], we highlighted the poor palliative care provision, in which discussions about prognosis and DNR orders were only raised in the final phase of life and referrals to palliative care made very close to death. We found that liver clinicians have difficulties in initiating discussions regarding prognosis, do not engage in parallel planning for potential deterioration as well as recovery and have a limited knowledge of palliative care.

Studies suggest that uncertainty plays an important role in making anticipatory care planning in advanced liver disease difficulty [12]. Our qualitative data further illustrated how five key factors interact in acting as a barrier to palliative care. Although liver clinicians may want to refer patients to palliative care earlier, active treatment is usually the de-facto choice unless patients specifically raise the topic of palliative care. The difficulty of identifying the point of irreversible liver deterioration, together with patients' expectations about finding a cure for their liver disease, together with liver clinicians' own perceived lack

of confidence and skills in addressing patients' palliative care needs, enabled them to focus on active treatment. A further barrier to accessing palliative care is the lack of contact and experience that liver clinicians have working with palliative care. This both prevents them from understanding what palliative care can offer, but also prevents palliative care clinicians from establishing earlier contact with patients and so become familiar faces with them. This culture of active treatment may stem from tertiary centres being seen as being at the forefront of technical innovation.

Clinical implications

Our findings suggested that the lack of knowledge about the role and benefits of palliative care may contribute to the late referral of liver patients to specialist palliative care. The formation of liver clinics specifically for people with decompensated liver failure, with joint input from liver and palliative care specialists, may promote understanding across specialties and an integrated and timely approach to care; enabling formulation of treatment plans, reduce the numbers of unplanned in-patient admissions to the liver service [12], improve symptom control, and enable liver and palliative care clinicians to engage in discussions about prognosis and future care preferences with patients at an earlier stage. Previous studies have already shown that early referral to specialist palliative care may reduce the rates of expensive hospitalisation, especially in the last month of life [20]. Such service developments could be explored, in line with guidance set by the end of life care good practice guide [21]. Consideration should be given to the care philosophy in a tertiary liver transplant centre, where many liver clinicians are reluctant to accept that active interventions have limited patient benefit. Furthermore, qualitative data indicated that liver

clinicians found it difficult to identify the point of irreversible liver deterioration, but our case note findings suggested that patients have increasing number of inpatient admissions and symptoms in their last three months of life. The introduction of clinical tools such as the Supportive & Palliative Indicators Care Tool [22] may support clinicians to identify when is timely to refer to palliative care, such as the 'point of irreversible deterioration of liver function'.

Strengths and Limitations

Our study explores care in advanced liver disease from different perspectives, but we accept our methodology limits the generalisabilty of our interpretation. Our case note data were retrospective and limited by the quality of recording in medical notes. Many in our case note sample were referred from other hospitals and did not include data recorded at these sites. For our qualitative arm, the health professionals were recruited from one hospital site and due to both time constraints and the limited pool of participants available, it is possible that theme saturation was not achieved. Our findings reflected practice in a tertiary liver transplant specialist unit in one country, and are therefore not representative of practice in wider secondary care or in health systems not similar to the UK. Nevertheless, our exploratory findings do provide new insights into how end of life care could be improved in people with cirrhosis, which deserve further exploration using more robust methodology.

A. Contributor ship statement: JL, SD, VV, LJ, LG and KH were responsible for the study concept and design; JL and SD were responsible to the acquisition of the data; JL, SD, VV, LJ, DT, AM, LG, KH, AL, AL were responsible for analysis or interpretation of the data; JL, SD, VV and LJ drafted the initial manuscript; DT, AM, LG, KH, AL, revised the manuscript critically for important intellectual content; all authors gave the final approval of the version to be published.

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Data sharing statement: Participants did not provide consent for the transcripts to be released outside of the remit of this study.

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Table 1: Patient demographics and clinical characteristics

Characteristic	n (%) (N=30)
Demographics	
Age mean (sd)	58 (11)
Gender	
Male	20 (67)
Female	10 (33)
Ethnicity	
White British	14 (58)
Black African	2 (8)
Asian	4 (17)
Other	4 (17)
Relationship Status	
Married	14 (54)
Divorced	5 (19)
Partner (previously divorced)	6 (23)
Widowed	1 (4)
Living arrangements	
With wife/partner	8 (35)
With wife and children	2 (9)
With children	3 (13)
With friends	2 (9)
Alone	5 (22)
Hostel	2 (9)
Hotel	1 (4)
Clinical characteristics	
Cause of cirrhosis	
Alcoholic (ALD)	11 (37)
Hepatitis C (Hep C), ALD	3 (10)
Hepatocellular carcinoma (HCC), Hep C, ALD	1 (3)
HCC, Hepatitis B (Hep B), Hep C, ALD	1 (3)
Hep C	4 (13)
Hep C, HCC	3 (10)
Non-alcoholic steatophepatitis (NASH)	2 (7)
NASH, HCC	1 (3)
Other (Primary biliary cirrhosis, Anti trypsin)	2 (7)
Previous transplant	2 (7)
On transplant list	5 (17)

460 **Table 2: Signs and symptoms during the last 3 months for the 30 patients**

Medical condition	*n* (%)	Medical condition	*n* (%)
Pain	**24 (80)**	**Fatigue** (Tiredness, lethargy)	**2 (40)**
Abdomen	15 (50)	Weakness	9 (30)
Back	6 (20)		
Legs	4 (13)	**Sepsis**	**5 (17)**
Chest	4 (13)	Tachycardia	4 (13)
Ribs	2 (7)	Temperature, chills/rigors	4 (13)
Ascites	**19 (63)**		
Distended abdomen	12 (40)	**Psychological**	**10 (33)**
Tense abdomen	6 (20)	Confusion	6 (20)
		Agitation	5 (20)
Encephalopathy	**19 (63)**	Drowsiness	5 (20)
Confusion	11 (37)	Distressed, crying, upset	4 (13)
Asterixs, hepatic flap	10 (33)	Depressed	4 (13)
Drowsiness	8 (27)	Low mood	3 (10)
Tremor	5 (17)	Hallucinations	3 (10)
Refusing treatment	4 (13)	Anxious	2 (7)
Agitation	4 (13)	Refusing treatments/observations	2 (7)
Distressed	2 (7)	Insomnia	2 (7)
Crying, upset	2 (7)	Suicidal	2 (7)
Aggressive	2 (7)		
Shouting/ screaming	2 (7)	**Digestive system**	
Disorientated	2 (7)	Anorexia	11 (37)
		Nausea	11 (37)
Bleeding	**12 (40)**	Vomiting	10 (33)
Blood in faeces	4 (13)	Incontinent of faeces	10 (33)
Blood in vomit	3 (10)	Constipation	6 (20)
Coffee ground vomit	3 (10)	Diarrhoea	4 (13)
Bleeding from rectum	4 (13)		
Bruising under skin	3 (10)	**Respiratory**	
Bleeding from mouth/nose	2 (7)	Shortness of breath	17 (57)
Bleeding from penis	2 (7)	Secretions	4 (13)
Blood in urine		Wheezy	2 (7)

2 (7)		**Urinary system**	
		Incontinent of urine	
Peripheral oedema (23)	**7**	8(27)	
Sacrum, testicles, scrotum	6 (2)	Oliguria	8(27)
Legs, thighs	3 (10)		
Ankles, feet	3 (10)	**Other**	
		Unsteady on feet/ gait	9 (30)
Skin other		Dizzy, faint,	(13)
Pruritis	7 (23)		
Rashes, erythema	5 (17)		
Cellulitis	3 (10)		

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Appendix i: Topic guide – Liver health professionals

Current experience of providing care to patients

What are the key issues or main challenges of caring for this patient group (in the last year of life) from your perspective?

Understanding of patient and family problems

What do you think are some of the problems or difficulties that patients with end stage liver disease face? What about their relatives?

Perception of patient and family understanding of liver disease diagnosis

What are your perceptions of patients' understanding of their own liver disease?

What is your perception of families understanding?

Discussion of prognosis and future preference of care

How do you address the issue of prognosis with patients? And when do you do it?

When do you address the issue of prognosis with the family?

How do you address patients' wishes for future care if. When do you think this is appropriate?

Would you document discussions about prognosis with the GP and patients future preferences for care?

Issues related to supportive and palliative care

How do you manage exacerbations of liver disease?

When do you refer to palliative care?

How do you identify when someone is actively dying?

What should good quality care for patients with ESLD look like?

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	8
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8- 9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	9
Bias	9	Describe any efforts to address potential sources of bias	N/A
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9-10
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	N/A
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	N/A
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-11
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	Report numbers of outcome events or summary measures over time	12
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	n/a
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	17
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	19
Generalisability	21	Discuss the generalisability (external validity) of the study results	19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	2

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Advanced chronic liver disease in the last year of life: a mixed methods study to understand how care in a specialist liver unit could be improved

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Title: Advanced chronic liver disease in the last year of life: a mixed methods study to understand how care in a specialist liver unit could be improved

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MeSH key terms: palliative care; cirrhosis; hepatology; mixed methods

Word count: 3909

Abstract:

Objectives: To identify the limitations in palliative care provision in the last year of life for people with liver cirrhosis and potential barriers to and enablers of palliative care.

Design: Mixed methods, including a retrospective case note review, qualitative focus groups and individual interviews.

Setting: A tertiary referral liver centre in the south of England (UK).

Participants: Purposively selected case notes of 30 people with cirrhosis who attended the tertiary referral liver centre and died during an 18 month period; a purposive sample of 22 liver health professionals who participated in either focus groups or individual interviews.

Primary and secondary outcomes: Data collected from case notes included hospital admissions, documented discussions of prognosis and palliative care provision. Qualitative methods explored management of people with cirrhosis, and barriers to and enablers of palliative care.

Results: Participants had high rates of hospital admissions and symptom burden. Clinicians rarely discussed prognosis or future care preferences; they lacked the skills and confidence to initiate discussions. Palliative care provision occurred late because clinicians were reluctant to refer due to their perception that reduced liver function is reversible, poor understanding of the potential of a palliative approach; palliative care was perceived negatively by patients and families.

Conclusions: People dying with cirrhosis have unpredictable trajectories, but share a common pathway of frequent admissions and worsening symptoms as death approaches.

The use of clinical tools to identify the point of irreversible deterioration and joint working between liver services and palliative care may improve care for people with cirrhosis.

Strengths and limitations of this study

- The study is the first to look specifically at how care is provided to people with advanced liver disease in the last year of life, with the aim of identifying barriers that limit a palliative approach to care.
- A mixed methods design enables exploration from different perspectives of the structural difficulties to providing end of life care to people with advanced liver disease.
- Findings suggest pragmatic ways that supportive and end of life care can be improved for people with advanced liver disease.
- As this study was conducted in one tertiary liver unit in the south of England, the findings may not be generalised to other healthcare settings.
- The retrospective nature of the case note data limits the interpretation of the quantitative findings.

Background

Advanced chronic liver disease (cirrhosis) is a growing international public health problem and often affects people of working age.[1] It is the third most common cause of premature death in the United Kingdom (UK) [2]; more people are affected by liver disease with the increases in alcohol consumption, viral hepatitis and obesity [3]. Most people dying from liver disease are not suitable for liver transplantation and, of those who are suitable, 20% will die before a donor becomes available[4]. Living with cirrhosis may involve considerable symptom burden, and when liver failure ensues the prognosis is poor. Death may occur either after a long period of decline with a fluctuant clinical picture, or may be sudden and unanticipated. In most cases, death from cirrhosis occurs in hospital [5].

People with cirrhosis have supportive and palliative care needs [6-9]. Liver professionals acknowledge they have a role to play in this aspect of care [10, 11], but feel that their skills are limited and may be inadequate to offer an effective palliative approach [10, 12]. Referrals to specialist palliative care may be necessary but palliative care provision is limited [13], and knowledge of prescribing in liver failure is needed. Shared care, defined as using the skills and knowledge of many health professionals who share joint responsibility for an individual's care, may be useful [14]. Palliative care offered in parallel with optimised specialist and generalist care may benefit people with advanced cirrhosis [15]. One difficulty is knowing the appropriate time to make referrals and begin shared care [10]. Further data to understand how different specialities such as liver and palliative care services can work together may be helpful[14]. In this paper we report what we have learned from exploring practice in a tertiary treatment centre for liver disease in north London, UK. We used mixed methodology, guided by Rapid Participatory Appraisal in which data collected from different

sources relating to a specific healthcare provider are combined to describe both the service structure and potential care improvements in a specific health locality [16]. Using mixed methods, we hoped to gain greater understanding of the limitations in the provision of palliative care for people with cirrhosis in the last year of life, and explore the reasons behind these limitations. This approach is commonly used in health service research to understand the complexity of health care[17].

We conducted a case note review, focus groups and qualitative interviews to explore:

(i) How healthcare in liver services is provided in the last year of life to people with advanced liver disease (cirrhosis) from any cause to identify limitations in palliative care provision;

(ii) Challenges in providing palliative care provision in liver care and how this provision might be improved in hepatology.

Method

A mixed methods study, using a retrospective case note review, qualitative focus groups and individual interviews. Case note findings were used to quantify the types of healthcare inputs provided by the liver services to people in their last year of year and to identify potential limitations in and barriers to the palliative care provided and a shared approach to care. The qualitative data identified reasons underlying these limitations and barriers, and highlighted potential enablers to improving care in this context.

Setting

A tertiary referral liver transplant centre in north London UK, providing both a core diagnostic service for all conditions affecting the liver and long-term management of patients with all severities of liver disease.

Procedure

Retrospective case note review

As resources were limited, we purposively selected 30 people with cirrhosis from the 66 people who attended the tertiary referral liver centre and died between April 2010 and September 2011. We aimed to ensure that our sample represented the spectrum of people attending the centre and purposefully sampled according to age, gender and cause of liver failure.

We used a structured framework to extract data from patient records available from the centre for the 12 month period prior to death. We noted demographics, severity of liver disease at last admission, cause of cirrhosis, transplantation status, physical and psychological symptoms, and health service use in secondary care (inpatient admissions, hospital length of stay, intensive therapy unit (ITU), liver-related procedures). We recorded documented evidence of discussions about prognosis and future preferences for care. We collected information on referrals to specialist palliative care (SPC), creation of care plans including evidence of advance care planning (ACP), resuscitation (DNACPR) status, preferred place of death and actual place of death. Data were extracted by the research nurse (SD) and inputted into Microsoft Excel.

Qualitative data

Both focus groups and semi-structured interviews were used to capture as many views of healthcare professionals as possible. All potential participants were first identified by a clinician (LG). The research nurse (SD) then contacted these participants face to face, by telephone, or by email. Participants were given information about the study, outlining the role of the research team, and gave written consent prior to data collection. All participants took part either in one focus group or a semi-structured interview (between July 2013-May 2014), which were conducted in the liver centre.

Focus groups

Focus groups were used as a pragmatic method of gathering larger numbers of people and using the group dynamic to generate discussion about care at the end of life in cirrhosis[18, 19]. Purposive sampling was used to ensure the views of those at all levels of the liver team across the disciplines (doctors, nurses and allied health professionals) were captured. Three focus groups were organised (each lasting 45-60 minutes) and led by a research nurse (SD – Master's degree qualification and 6 years of qualitative research experience), with an observer (JL – senior health researcher with a PhD and 20 years of experience in qualitative/mixed methods research) taking field notes and co-facilitating.

Topic guide

To guide discussions, a topic guide (supplementary files) was developed by the members of research team (JL, SD, AM, DT, LG, KH, LJ) covering: challenges of providing care to people in the last year of life; their perception of patient and family understanding of liver disease; discussing prognosis and future care preferences; improving palliative care. This guide was

developed pragmatically in the context of liver disease, guided by the principles of palliative care[20]. All focus groups were audiotaped and transcribed verbatim.

Interviews

Professionals unable to attend the focus groups, were invited to take part in semi-structured individual interviews. Nine interviews were conducted by SD (lasting 18 – 70 minutes) using the topic guide, and were audiotaped and transcribed verbatim.

Data analysis

Retrospective case notes: Descriptive statistics were used to describe hospital admissions and service use, documentation of prognostic discussions and preferences for future care, and palliative care provision. Data were summarised to highlight limitations in palliative care service provision.

Qualitative data: A framework approach was used to analyse the transcripts[21], which were first read independently by two researchers (JL, SD). Themes were identified, from which a coding system was developed and applied to the whole data set systematically. Any disagreements in coding were resolved by consensus. In organizing the data into appropriate themes, Microsoft Excel was used. The researchers considered themes independently and met to discuss the themes identified and how they were linked together by contextual factors. Independent analysis ensured validity and reliability of the themes and links identified. Findings were also shared with our clinical partners (AM, LG, DT, KH) in the research team to ensure that the findings were consistent with their experience of current clinical practice. These themes were used to explain the limitations in palliative care

provision found in the case notes, and to identify barriers and enablers to future palliative care for people with cirrhosis.

Ethical approval

Ethical approval was sought, but deemed unnecessary by the NRES Committee London - West London & GTAC (ref 14/LO/0799). NHS permission to conduct the clinical case-note review and the qualitative interviews with liver health professionals was obtained from the Royal Free London Clinical Governance Lead for Hepatology and Palliative Care under the remit of health service improvement.

Results

Provision of healthcare in last year of life (case note findings)

Demographics and clinical characteristics (Table 1)

Our sample was predominately male (n=20, 67%) with a median age of 59 years (IQR: 52-66; range 25-75), in which alcohol-related liver disease (ARLD) was the predominant diagnosis (n=16; 53%). A MELD score gives an indication of short term mortality, and is used to prioritise candidates on the orthotopic liver transplantation waiting list. In 23 cases where data were available at last admission, our sample had a median (interquartile range) MELD score of 23 (16.5-23), suggesting a 19.6 % chance of dying in the next 3 months [22]. Nineteen (63%) people were not considered for liver transplant due to poor health, four were on the transplant waiting list, and three had previously received a transplant. Eight (27%) people with cirrhosis had been referred to the tertiary centre from 'out of area' hospitals either for

a liver transplant assessment, or for specialist treatments such as a Transjugular Intrahepatic Portosystemic Shunt (TIPS) or intensive management of bleeding.

The people in our sample were highly symptomatic (table 2). All were symptomatic three months before death, presenting with ascites (n=22, 73%), extensive peripheral oedema (n=20, 66%), severe fatigue and weakness (n=20; 66%) and pain (n= 13; 43%). In the last month of life, our participants presented with an average of 14 physical symptoms per person. The majority (n=19, 63%) were noted to have symptoms of hepatic encephalopathy such as confusion, disorientation, and agitation.

Health service use in tertiary care

Our sample of 30 had a median of three inpatient admissions (IQR 2-5) per person in the last year of life, and a median length of stay of 31 days (IQR 19-55). Seventeen (57%) people were readmitted within 30 days of discharge. The frequency of admissions increased for most people (n=29; 97%) in the last 3 months of life. Nineteen (63%) people had more than one admission in the month before death, during which the median number of admissions was two (IQR: 1-3). Of the 78 admissions precipitated by cirrhotic complications, most required invasive procedures such as paracentesis (n=53/78, 68%), blood transfusions (n=13/78, 17%), endoscopic variceal banding (n=4/78, 5%) and TIPS (n=4/78, 5%). During these admissions, each participant was seen in the last year of life by a mean of three different liver consultants (range 1-6). Nine (30%) people were regularly reviewed by the hospital nurse-led patient-at-risk team (PART), to decide whether to escalate or de-escalate their treatment. Six (20%) people with cirrhosis required treatment in the intensive care unit (ITU) during which three patients died.

Documentation of prognosis, future care discussions and palliative care provision

Liver consultants recorded having discussed prognosis mainly with family members (n=23, 77%); discussions occurred very late, in 16 (53%) cases ≤ 34 days before the person died. Liver doctors recorded fewer discussions with patients about understanding of their disease or future care preferences (n=16, 53%), most of which occurred one month before death (n=9/16; 56%).

Although most people (n=26; 67%) had a DNACPR decision recorded in their medical notes, this was completed by medical personnel, with limited consultation with either the person with cirrhosis (n=5, 17%) or their family member (n=6, 20%). In seven cases, the liver team had to be alerted about completing a DNACPR by other clinicians such as the PART team (n=4), ITU (n=2) or the emergency department (n=1). Most people (n=19, 63%) had no discussions with doctors about their preferred place of care.

Most people with cirrhosis (n=21; 70%) were referred to specialist palliative care a median of five days before death. Twelve (40%) people with cirrhosis documented as deteriorating were still receiving active treatment up until their death. For most people, death occurred in hospital (n=25; 83%), three died in ITU. The remaining five people died either at home (n=3; 10%) or in a hospice (n=2; 7%). Only five people from the sample had clear discussions with health professionals about place of death; two of these died in the place of their choice (one at home and the other in hospital).

Challenges to and enablers of provision of palliative care (qualitative data)

Demographics of liver clinician sample: Thirteen liver health professionals took part in three focus groups (FG) [FG1: 3 doctors, 2 liver transplant nurses, a dietician and a pharmacist; FG2: 3 ward nurses and a healthcare assistant; FG3: 2 ward nurses). Nine health professionals took part in semi-structured interviews (5 doctors, 2 senior nurses in hepatology, a clinical nurse specialist in palliative care, an alcohol liaison nurse). No demographic information was collected for the liver clinician sample other than their discipline.

Key findings:

Initial analysis illustrated that liver clinicians recognised that although their patients were in poor health, they did not address quality of life issues with them and palliative care options were only considered with patients who raised this topic themselves. Further analysis identified five emergent themes which illustrated why liver clinicians focused on reactive treatment for people at the expense of palliative care: unpredictable trajectory of liver disease, management of patient treatment expectations, clinician/patient perceptions of the palliative care role, poor continuity of care, perceived lack of skill and confidence.

Unpredictable trajectory of liver disease: The perceived ability of the liver to recover function made it difficult for doctors to estimate the point of irreversible liver decline, and so provided doctors with hope that trying different treatments would promote recovery, even with patients on the wards who were imminently dying. Nurses felt that part of this difficulty was the short periods that doctors spend with patients in contrast with the ward

nurses, who provide continuous care and were confident in identifying those imminently dying. However, nurses considered that cessation of active treatment was the responsibility of doctors as main clinical decision makers.

> *"We (ward nurses) have constant contact with patients… enables us to identify those patients who are both aware of their deterioration and want to die at home to be fast tracked to specialist palliative care"* Ward nurse, *Nurse focus group 1.*

Management of patient expectations: Doctors' emphasis on active treatments is reinforced by their own perceptions of patients' treatment expectations. Part of this expectation may be reflected by the patients' younger ages, who doctors feel want life at all costs. Furthermore, as many patients are referred by secondary care 'out of area' (as illustrated in our case notes), clinicians perceive these patients see referral to the tertiary liver centre as a last chance to 'cure' their liver disease. This in turn, reinforces clinicians' focus on active treatments, at the expense of discussing prognostic issues.

> "*We probably don't do enough of it (discuss future care preference), because most of the patients at a given time are not willing to engage with that question. The median age of patients is 53, so we are not talking about an 80 year old who has lived their life to the full. We are talking about people who still want life." (Consultant hepatologist 1, interview)*

Patients' unrealistic expectations, and their limited knowledge and understanding of their own disease, presented doctors with difficulties in managing these expectations and deciding what treatment options to pursue.

"They (patients) are often referred extremely late, full of expectation only to be told there's nothing we can do. The difficulty is, what do you then do with that patient? Do you let them go back to the referring trust or secondary care, how do you know that they are going to get palliative care or the treatment that they need"

(Consultant hepatologist 2, interview)

Misunderstanding of palliative care: Clinicians perceived that patients and their family members saw referral to palliative care negatively, as a move suggesting that clinicians had 'given up' on the patient. They felt that patients and families did not understand what palliative care could offer in terms of symptom control and psychosocial support, instead seeing palliative care as a service for people at the very end of life, as illustrated by this senior nurse.

"We've got a patient on the ward whose family are very opposed to palliative care, but wanted active treatment. The patient has had repeated admissions, even if the family can only have her for another extra few months. The nurse tried to tell them it is not just the last weeks and hours (input from palliative care), it can be longer than that and the palliative team have a lot to offer you even now." (ward senior nurse, interview)

Although most liver clinicians saw a role for palliative care, the debate on its utilisation centred more on understanding when a referral to palliative care was considered appropriate. Most had very limited experience in working with palliative care and were unsure of the best time to refer. This was further compounded by the difficulty of

estimating the point of irreversible liver deterioration and the lack of clinical tools and guidelines to support them with this process.

"Would like to refer much earlier, but need to have an understanding at the point that specialist palliative care would like involvement." (Consultant hepatologist, Multi-disciplinary focus group)

Poor continuity of care: Liver clinicians felt the lack of adequate information systems and the rotation of medical staff (our case notes showed that each participant saw at least three liver consultants over the year), contributed to 'poor continuity of care'. This lack of continuity is demonstrated when treatment plans agreed with one consultant can be changed by another consultant due to a lack of shared information.

"This rotation of staff causes problems as some patients are treated and patched up, but come in under another consultant when readmitted and treatment happens again. However, the system does not allow for information to be exchanged about what exact changes have occurred in their condition." (Consultant hepatologist 3, interview)

Perceived lack of skill and confidence: Both doctors and nurses perceived they lacked skills and confidence in engaging in discussions about prognosis or palliative care with patients or family members. On liver wards, this was further compounded by a lack of private space to discuss sensitive topics.

Enablers for improved palliative care: Liver clinicians suggested strategies to enhance both continuity and integration of palliative care and liver services, such as joint liver and palliative care clinics for people with decompensated liver disease and multidisciplinary team case conferences to coordinate care and treatment for those patients frequently admitted. Such initiatives would enhance mutual understanding across specialities of liver-specific symptom management and the timing of referrals. To support liver clinicians in identifying patients suitable for early palliative care support, appropriate clinical tools with relevant guidelines need to be identified.

Discussion

Key summary

Our findings reflect the complicated clinical picture surrounding the provision of care of people with cirrhosis in their last year of life. We demonstrate that patients have a high symptom burden, increasing number of admissions in their last 3 months of life and a focus on active, disease-directed treatments. As with previous studies [12, 13], we highlight poor palliative care provision, in which discussions about prognosis and resuscitation orders were only raised in the last few days of life and referrals to palliative care were made very close to death. We found that liver clinicians have difficulties in initiating discussions regarding prognosis, do not engage in parallel planning for potential deterioration as well as recovery and have a limited knowledge of palliative care.

Studies suggest that uncertainty is an important barrier to anticipatory care planning in advanced liver disease [12]. Our qualitative data further illustrate how five key factors

interact as barriers to palliative care. Although liver clinicians may wish to refer patients to palliative care earlier, active treatment is usually the *de-facto* choice unless patients themselves specifically raise the topic. The difficulty of identifying the point of irreversible liver deterioration, patients' expectations of finding a cure, together with liver clinicians' perceived lack of confidence and skills in addressing palliative care issues enabled a focus on active treatment. A further barrier is the lack of contact and experience that liver clinicians have of working with palliative care specialists. This prevents them from understanding what palliative care can offer, and prevents palliative care clinicians from establishing earlier contact with patients which might enable them to become familiar faces for patients and families. This culture of active treatment may stem from tertiary centres being seen as at the forefront of technical innovation.

Clinical implications

Our findings suggest that lack of knowledge about the role and potential benefits of palliative care may contribute to the late referral of liver patients to specialist palliative care. The formation of liver clinics specifically for people with decompensated liver failure, with joint input from liver and palliative care specialists is recommended. This may promote understanding across specialties, an integrated and timely approach to care, formulation of treatment plans and a reduction in unplanned in-patient admissions to the liver service [12]. It may also improve symptom control and enable clinicians to engage in discussions about prognosis and future care preferences with patients and families at an earlier stage. Previous studies have shown that early referral to specialist palliative care may reduce the rates of expensive hospitalisation, especially in the last month of life [23]. Such service

developments could be explored, in line with guidance set by the 'End of life care good practice guide' [24]. Consideration should be given to the care philosophy in a tertiary liver transplant centre, where many liver clinicians are reluctant to accept that active interventions have limited patient benefit. Qualitative data indicate that liver clinicians found it difficult to identify the point of irreversible liver deterioration; our case note findings suggest that inpatient admissions and symptoms increase in frequency in the last three months of life. The introduction of clinical tools such as the Supportive & Palliative Indicators Care Tool [25] may support clinicians to identify when is timely to refer to palliative care, such as the 'point of irreversible deterioration of liver function'.

Strengths and Limitations

Our study explores care in advanced liver disease from different perspectives, but we accept our methodology limits the generalisabilty of our interpretation. Our case note data were retrospective and limited by the quality of recording in medical notes. Many in our case note sample were referred from other hospitals and did not include data recorded at these sites. Due to time constraints, we reviewed a purposive sample of case notes of those who died, so there is a potential for selection bias and error in the notes that were reviewed. Our case note sample only reflects patients who died during follow-up and not those who were still alive, or who had a transplant. This is important since these patients are also often recipients of palliative care. For our qualitative arm, the health professionals were recruited from one hospital site and due to both time constraints and the limited pool of participants available, it is possible that theme saturation was not fully achieved. We did not explore the views of close family members and informal carers in this study and may have missed

important insights on experiences of living and dying with liver disease and how care might be improved. Our findings reflected practice in a tertiary liver transplant specialist unit in one country; whilst clinical issues are likely to be similar in other settings, organisational issues and person-centred attitudes will vary across other healthcare systems. Nevertheless, our exploratory findings do provide new insights into how care towards the end of life could be improved in people with cirrhosis, which deserve further exploration using more robust methodology.

A. Contributorship statement: JL, SD, VV, LJ, LG and KH were responsible for the study concept and design; JL and SD were responsible to the acquisition of the data; JL, SD, VV, LJ, DT, AM, LG, KH, AL, AL were responsible for analysis or interpretation of the data; JL, SD, VV and LJ drafted the initial manuscript; DT, AM, LG, KH, AL, revised the manuscript critically for important intellectual content; all authors gave the final approval of the version to be published.

B. Competing interest: None declared

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Data sharing statement: Participants did not provide consent for the transcripts to be released outside of the remit of this study.

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Table 1: Patient demographics and clinical characteristics

Characteristic		n (%) (N=30)
Demographics		
Age	mean (sd)	58 (11)
	min - max	25-79
Gender		
	Male	20 (67)
	Female	10 (33)
Ethnicity (n=24)		
	White British	14 (58)
	Black African	2 (8)
	Asian	4 (17)
	Other	4 (17)
Relationship Status (n=26)		
	Married	14 (54)
	Divorced	5 (19)
	Partner (previously divorced)	6 (23)
	Widowed	1 (4)
Living arrangements (n=28)		
	With wife/partner	8 (35)
	With wife and children	2 (9)
	With children	3 (13)
	With friends	2 (9)
	Alone	5 (22)
	Hostel	2 (9)
	Hotel	1 (4)
Clinical characteristics		
Cause of cirrhosis		
	Alcoholic (ALD)	11 (37)
	Hepatitis C (Hep C), ALD	3 (10)
	Hepatocellular carcinoma (HCC), Hep C, ALD	1 (3)
	HCC, Hepatitis B (Hep B), Hep C, ALD	1 (3)
	Hep C	4 (13)
	Hep C, HCC	3 (10)
	Non-alcoholic steatophepatitis (NASH)	2 (7)
	NASH, HCC	1 (3)
	Other (Primary biliary cirrhosis, Anti trypsin)	2 (7)
Previous transplant		2 (7)
On transplant list		5 (17)

501 **Table 2: Signs and symptoms during the last 3 months for the 30 patients**

Medical condition	*n* (%)	Medical condition	*n* (%)
Pain	**24 (80)**	**Fatigue** (Tiredness, lethargy)	**2 (40)**
Abdomen	15 (50)	Weakness	9 (30)
Back	6 (20)		
Legs	4 (13)	**Sepsis**	**8 (27)**
Chest	4 (13)	Tachycardia	4 (13)
Ribs	2 (7)	Temperature, chills/rigors	4 (13)
Ascites	**19 (63)**		
Distended abdomen	12 (40)	**Psychological**	**10 (33)**
Tense abdomen	6 (20)	Distressed, crying, upset	4 (13)
Encephalopathy	**19 (63)**	Depressed	4 (13)
Confusion	11 (37)	Low mood	3 (10)
Asterixs, hepatic flap	10 (33)	Hallucinations	3 (10)
Drowsiness	8 (27)	Anxious	2 (7)
Tremor	5 (17)	Refusing treatments/observations	2 (7)
Refusing treatment	4 (13)	Insomnia	2 (7)
Agitation	4 (13)	Suicidal	2 (7)
Distressed	2 (7)	**Digestive system**	
Crying, upset	2 (7)	Anorexia	11 (37)
Aggressive	2 (7)	Nausea	11 (37)
Shouting/ screaming	2 (7)	Vomiting	10 (33)
Disorientated	2 (7)	Incontinent of faeces	10 (33)
		Constipation	6 (20)
Bleeding	**12 (40)**	Diarrhoea	4 (13)
Blood in faeces	4 (13)	**Respiratory**	
Blood in vomit	3 (10)	Shortness of breath	17 (57)
Coffee ground vomit	3 (10)	Secretions	4 (13)
Bleeding from rectum	4 (13)	Wheezy	2 (7)
Bruising under skin	3 (10)		
Bleeding from mouth/nose	2 (7)	**Urinary system**	
Bleeding from penis	2 (7)	Incontinent of urine	8(27)
Blood in urine			

2 (7)		Oliguria	8(27)
Peripheral oedema (23)	**7**	**Other**	
Sacrum, testicles, scrotum	6 (2)	Confusion (variety of causes)	6 (20)
Legs, thighs	3 (10)	Unsteady on feet/ gait	9 (30)
Ankles, feet	3 (10)	Dizzy, faint,	(13)
Skin other		Agitation	2 (7)
Pruritis	7 (23)		
Rashes, erythema	5 (17)		
Cellulitis	3 (10)		

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Appendix i: Topic guide – Liver health professionals

Current experience of providing care to patients

What are the key issues or main challenges of caring for this patient group (in the last year of life) from your perspective?

Understanding of patient and family problems

What do you think are some of the problems or difficulties that patients with end stage liver disease face? What about their relatives?

Perception of patient and family understanding of liver disease diagnosis

What are your perceptions of patients' understanding of their own liver disease?

What is your perception of families understanding?

Discussion of prognosis and future preference of care

How do you address the issue of prognosis with patients? And when do you do it?

When do you address the issue of prognosis with the family?

How do you address patients' wishes for future care if. When do you think this is appropriate?

Would you document discussions about prognosis with the GP and patients future preferences for care?

Issues related to supportive and palliative care

How do you manage exacerbations of liver disease?

When do you refer to palliative care?

How do you identify when someone is actively dying?

What should good quality care for patients with ESLD look like?

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	8
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8- 9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	9
Bias	9	Describe any efforts to address potential sources of bias	N/A
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9-10
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	N/A
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	N/A
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-11
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	Report numbers of outcome events or summary measures over time	12
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	n/a
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	17
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	19
Generalisability	21	Discuss the generalisability (external validity) of the study results	19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	2

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

Developed from:
Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

No. Item	Guide questions/description	Reported on Page #
Domain 1: Research team and reflexivity		
Personal Characteristics		
1. Interviewer/facilitator	Which author/s conducted the interview or focus group?	9
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	9
3. Occupation	What was their occupation at the time of the study?	9
4. Gender	Was the researcher male or female?	1
5. Experience and training	What experience or training did the researcher have?	9
Relationship with participants		
6. Relationship established	Was a relationship established prior to study commencement?	no
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	9
8. Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	N/A -
Domain 2: study design		
Theoretical framework		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	7
Participant selection		
10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	9
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	9
12. Sample size	How many participants were in the study?	13
13. Non-participation	How many people refused to participate or	N/A

	dropped out? Reasons?	
Setting		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	9
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	9-10
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	13
Data collection		
17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	9
18. Repeat interviews	Were repeat interviews carried out? If yes, how many?	No
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	9
20. Field notes	Were field notes made during and/or after the inter view or focus group?	9, 10
21. Duration	What was the duration of the interviews or focus group?	9, 10
22. Data saturation	Was data saturation discussed?	20
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	No
Domain 3: analysis and findings		
Data analysis		
24. Number of data coders	How many data coders coded the data?	10
25. Description of the coding tree	Did authors provide a description of the coding tree?	NA
26. Derivation of themes	Were themes identified in advance or derived from the data?	10
27. Software	What software, if applicable, was used to manage the data?	10
28. Participant checking	Did participants provide feedback on the findings?	10
Reporting		
29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	15-17
30. Data and findings consistent	Was there consistency between the data presented and the findings?	15-17
31. Clarity of major themes	Were major themes clearly presented in the findings?	15-17
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	NA