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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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3 1 **Title:** Advanced chronic liver disease and the last year of life: a mixed methods study to
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5 2 understand how care in a specialist liver unit could be improved
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For peer review only

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2
3 32 **Abstract:**
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6 33 **Objectives:** To identify both the limitations in palliative care provision in the last year of life
7
8 34 and the potential barriers to and enablers of shared approaches to care.
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11 35 **Design:** Mixed methods study, using a retrospective case note review, qualitative focus
12
13 36 groups and individual interviews.
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16
17 37 **Setting:** A tertiary referral liver centre in the south of England (UK).
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19
20 38 **Participants:** Purposively selected case notes of 30 people with cirrhosis, who attended the
21
22 39 tertiary referral liver centre and died during an 18 month period. Twenty three liver health
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24 40 professionals participated in either focus groups or individual interviews.
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26

27
28 41 **Primary and secondary outcomes:** Main data collected from case notes were hospital
29
30 42 admissions, prognostic discussions and palliative care provision. Qualitative methods were
31
32 43 used to explore topics on cirrhosis management, facilitators and barriers to palliative care.
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34

35 44 **Results:** Participants had high rate of hospital admissions with high symptom burden.
36
37 45 Clinicians rarely discussed prognosis and future care preferences as they lacked the skills
38
39 46 and confidence to initiate these. Palliative care provision occurred late, as clinicians' were
40
41 47 reluctant to refer due to the perceived recoverability of liver function, poor understanding
42
43 48 of the palliative care role and the negative perception of palliative care from patients and
44
45 49 family.
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50 50 **Conclusions:** People dying with cirrhosis have unpredictable trajectories, but share a
51
52 51 common pathway of frequent admissions and worsening symptoms as death approaches.
53
54 52 The use of clinical tools to identify the point of irreversible deterioration and joint working
55
56 53 between liver and palliative care may improve care for people with cirrhosis.
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3 54 **Strengths and limitations of this study**
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7 55 • The study is the first to look specifically at how care is provided to people with
8 56 advanced liver disease in the last year of life, with the aim of identifying barriers that
9 57 prevent better supportive care.
10 58
11 59 • A mixed methods approach enables identification of the structural difficulties to
12 60 providing end of life care to people with advanced liver disease from different
13 61 perspectives.
14 62
15 63 • Findings suggest pragmatic ways that supportive and end of life care can be
16 64 improved for people with advanced liver disease.
17 65
18 66 • As this study was conducted in one tertiary liver unit in the south of England, the
19 67 findings may not be generalised to other health settings.
20 68
21 69 • The retrospective nature of the case note data hampers the interpretation of the
22 70 quantitative findings.
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3 71 **Background**
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6 72 Advanced chronic liver disease (cirrhosis) is a growing international public health problem
7
8 73 and often affects people of working age.[1] It is the third most common cause of premature
9
10 74 death in the United Kingdom (UK) [2], with more people affected by liver disease with the
11
12 75 increase in alcohol consumption, viral hepatitis and obesity [3]. The majority dying from
13
14 76 liver disease are not suitable for liver transplantation and of those suitable, 20% will die
15
16 77 before a donor becomes available[4]. Living with cirrhosis may involve considerable
17
18 78 symptom burden, and when liver failure ensues, the prognosis is poor. Death may occur
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20 79 either after a long period of decline with a fluctuant clinical picture, or may be sudden and
21
22 80 unanticipated. In most cases, death from cirrhosis occurs in hospital [5].
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28 81 People with cirrhosis have supportive and palliative care needs [6-9], in which liver
29
30 82 professionals acknowledge they have a role in this aspect of care [10, 11], but perceive their
31
32 83 skills are limited [10, 12]. Palliative care provision is limited [13], and knowledge of
33
34 84 prescribing in liver failure is needed. Shared care, defined as using the skills and knowledge
35
36 85 of many health professionals who share joint responsibility for an individual's care, may be
37
38 86 useful [14]. Palliative care offered in parallel with optimised specialist and generalist care
39
40 87 may benefit people with advanced cirrhosis [15]. One difficulty is knowing the appropriate
41
42 88 time to make referrals and begin shared care [10]. Further data to understand how different
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44 89 specialities such as liver services and palliative care can work together may be helpful[14].
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49 90 In this paper we report what we have learned from exploring practice in a tertiary treatment
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51 91 centre for liver disease in north London, UK. We used mixed methodology, guided by Rapid
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53 92 Participatory Appraisal in which data collected from different sources relating to a specific
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3 93 healthcare provider are combined to describe both the service structure and care
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5 94 improvements in a specific health locality [16].
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11 96 We conducted a case note review, focus groups and qualitative interviews to explore:
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- 13
14 97 (i) How healthcare in liver services is provided in the last year of life to
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16 98 people with cirrhosis from any cause;
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18 99 (ii) Potential barriers to palliative care provision in liver care and enablers of
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20 shared approaches to care between specialists in hepatology and
21 100
22 palliative care.
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29 103 **Method**

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32 104 A mixed methods study, using a retrospective case note review, qualitative focus groups and
33
34 105 individual interviews. Case note findings were used to quantify the types of healthcare
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36 106 inputs provided by the liver services to people in their last year of year and to identify
37
38 107 potential limitations and barriers in the palliative care provided. The qualitative data
39
40 108 identified reasons for these limitations and barriers to adopting shared care approaches,
41
42 109 also highlighting potential enablers to improving this care for this group of people.
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48 111 **Setting**

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52 112 A tertiary referral liver transplant centre in north London UK, providing both a core
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54 113 diagnostic service for all conditions affecting the liver and long-term management of
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56 114 patients with all severities of liver disease.
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3 1154
5 116 Procedure6
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8 117 Retrospective case note review9
10 118 As resources were limited, we purposively selected 30 people with cirrhosis from the 66
11
12 119 people who attended the tertiary referral liver centre and died between April 2010 and
13
14 120 September 2011. We aimed to ensure that our sample represented the spectrum of people
15
16 121 attending the centre and purposefully sampled according to age, gender and cause of liver
17
18 122 failure.19
20 123 We used a structured framework to extract data from patient records available from the
21
22 124 centre for the 12 month period prior to death. We noted demographics, severity of liver
23
24 125 disease at last admission, cause of cirrhosis, transplantation status, physical and
25
26 126 psychological symptoms, and health service use in secondary care (inpatient admissions,
27
28 127 hospital length of stay, intensive therapy unit (ITU), liver-related procedures). We recorded
29
30 128 evidence of discussions about prognosis and future preference for care. We collected
31
32 129 information on referrals to specialist palliative care (SPC), creation of care plans including
33
34 130 evidence of advance care planning (ACP), resuscitation (DNACPR) status, preferred place of
35
36 131 death and actual place of death. Data were extracted by the clinical researcher (SD) and
37
38 132 inputted into Microsoft Excel.39
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47 133 Qualitative data48
49 134 Both focus groups and semi-structured interviews were used to capture as many views of
50
51 135 healthcare professionals as possible. All participants gave written consent prior to data
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53 136 collection. Focus groups and interviews were conducted in the period from July 2013 to May
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55 137 2015.
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3 138
45 139 *Focus groups*
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7 140 Focus groups were used as a pragmatic method of gathering larger numbers of people
8
9 141 together and using the group dynamic to generate discussion about care at the end of life in
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11 142 cirrhosis[17, 18]. A purposive sampling to ensure the views of all levels of the liver team
12
13 143 across the disciplines (doctors, nurses and allied health professionals) were captured. Three
14
15 144 focus groups were organised (lasting 45-60 minutes) and led by a clinical researcher (SD),
16
17 145 with an observer (JL) taking field notes and co-facilitating. To guide these discussions, a topic
18
19 146 guide (supplementary files) was developed by the members of research team (JL, SD, AM,
20
21 147 DT, LG, KH, LJ) covering: challenges of providing care to patients in the last year of life; their
22
23 148 perception of patient and family understanding of their liver disease; discussing prognosis
24
25 149 and future care preferences; improving palliative care. All focus groups were audiotaped
26
27 150 and transcribed verbatim.
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33 151
3435 152 *Interviews*
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37 153 Professionals unable to attend the focus groups, were invited to take part in semi-
38
39 154 structured individual interviews. These were conducted by SD using the focus group topic
40
41 155 guide, and were audiotaped and transcribed verbatim.
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46 156
4748 157 **Data analysis**
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51 158 Retrospective case notes: Descriptive statistics were used to describe hospital admissions
52
53 159 and service use, documentation of prognostic discussions and preferences for future care,
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3 160 and palliative care provision. Data were summarised to highlight limitations in palliative care
4
5 161 service provision.
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8 162 Qualitative data: A framework approach was used in analysing the transcripts[19], which
9
10 163 were first read independently by two researchers (JL, SD). Thematic analysis was used to
11
12 164 identify themes, from which a coding system was developed and applied to the whole data
13
14 165 set systematically. Any disagreements in coding were resolved by consensus. The
15
16 166 researchers considered independently and met to discuss how the themes identified were
17
18 167 linked together by contextual factors. Independent analysis ensured validity and reliability
19
20 168 of the themes identified. These themes were used to explain the limitations in palliative
21
22 169 care provision found in the case notes, and to identify barriers and enablers to future
23
24 170 palliative care for people with cirrhosis.
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31 172 **Results**

32 173 ***Provision of healthcare in last year of life (case note findings)***

33 174 ***Demographics and clinical characteristics (Table 1)***

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36 175 Our sample was predominately male (n=20, 67%) with a mean age of 58 years (range 25-75),
37
38 176 in which alcohol-related liver disease (ARLD) was the predominant diagnosis (n=16; 53%). In
39
40 177 23 cases where data were available at last admission, our sample had a median
41
42 178 (interquartile range) MELD score of 23 (16.5-23). Nineteen (63%) people were not
43
44 179 considered for liver transplant due to poor health, five were on the liver transplant waiting
45
46 180 list, and three had previously received a liver transplant. Eight (27%) people with cirrhosis
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48 181 had been referred to the tertiary centre from other 'out of area' hospitals either for a liver
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3 182 transplant assessment, or for treatments such as a Transjugular Intrahepatic Portosystemic
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5 183 Shunt (TIPS) procedure or intensive management of bleeding.
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8 184 The patients in our sample were highly symptomatic (table 2). Everyone was symptomatic
9
10 185 three months before death, presenting with ascites (n=22, 73%), extensive peripheral
11
12 186 oedema (n=20, 66%), severe fatigue and weakness (n=20; 66%) and pain (n= 13; 43%). In the
13
14 187 last month of life, our participants presented with an average of 14 physical symptoms per
15
16 188 person. The majority (n=19, 63%) were noted to have symptoms of Hepatic Encephalopathy
17
18 189 such as confusion, disorientation, and agitation.
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24 25 26 191 **Health service use in tertiary care**

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29 192 Our sample of 30 had a mean of four inpatient admissions per person in the last year of life,
30
31 193 and a mean length of stay of 37 days. Seventeen (57%) people were readmitted within 30
32
33 194 days of discharge. The frequency of admissions increased for most people (n=29; 97%) in
34
35 195 the last 3 months of their life. Nineteen (63%) people had more than one admission in the
36
37 196 month before death, during which the median number of admissions was two (IQR: 1-3).
38
39 197 Most admissions were precipitated by cirrhotic complications, requiring invasive procedures
40
41 198 such as blood transfusions, endoscopic treatment of varices, TIPS and paracentesis. During
42
43 199 these admissions, each participant was seen by a mean of three different liver consultants
44
45 200 (range 1-6) in the last year of life. Furthermore, nine (30%) people were regularly reviewed
46
47 201 by the hospital nurse-led patient-at-risk team (PART), to decide whether to escalate or de-
48
49 202 escalate their treatment. Six (20%) people with cirrhosis required treatment in the ITU
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51 203 during which three patients died.
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205 Documentation of prognosis, future care discussions and palliative care provision

206 Liver consultants recorded having discussed prognosis mainly with family members (n=23,
207 77%), which occurred very late; in 16 (53%) cases this discussion occurred \leq 34 days before
208 the person died. Liver doctors recorded fewer discussions with patients about
209 understanding of their disease or future care preferences (n=16, 53%), most of which
210 occurred one month before death (n=9/16; 56%).

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

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

224

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

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3 226 Demographics of liver clinician sample: Thirteen liver health professionals took part in three
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5 227 focus groups (FG) [FG1: 3 doctors, 2 liver transplant nurses, a dietician and a pharmacist;
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7 228 FG2: 3 ward nurses and a healthcare assistant; FG3: 2 ward nurses). Nine health
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10 229 professionals took part in semi-structured interviews (5 doctors, 2 senior nurses in
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12 230 hepatology, a clinical nurse specialist in palliative care, an alcohol liaison nurse). No
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14 231 demographic information was collected for the liver clinician sample other than their
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16 232 discipline.
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23 234 **Key findings:**

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26 235 Initial analysis illustrated that liver clinicians recognised that although their patients were in
27
28 236 poor health, they did not address quality of life issues with them and that palliative care
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30 237 options were only considered with patients who raised this topic first. Further analysis
31
32 238 identified five emergent themes which illustrated why liver clinicians focused on reactive
33
34 239 treatment for people at the expense of palliative care: unpredictable trajectory of liver
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36 240 disease, management of patient treatment expectations, clinician/patient perceptions of
37
38 241 the palliative care role, poor continuity of care, perceived lack of skill and confidence.
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46 243 Unpredictable trajectory of liver disease: The perceived ability of the liver to recover
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48 244 function made it difficult for doctors to estimate the point of irreversible liver decline, and
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50 245 so provided doctors with hope that trying different treatments will promote recovery, even
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52 246 with imminently dying patients on the wards. Part of this difficulty laid in the limited times
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54 247 that doctors saw patients in contrast with the ward nurses, who provide continuous care
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3 248 and were confident in identifying those imminently dying, but who felt it was the doctors'
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5 249 responsibility, as the main clinical decision makers, to stop active treatment.
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8 250 Management of patient expectations: Doctors' emphasis on active treatments is reinforced
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10 251 by their own perceptions of patients' treatment expectations. Part of this expectation may
11
12 252 be reflected by the patients' young age, who doctors feel want 'life' at all costs.
13
14 253 Furthermore, as many patients are referred by secondary care 'out of area' (as illustrated in
15
16 254 our case notes), clinicians perceive these patients see referral to the tertiary liver centre as a
17
18 255 last chance to 'cure' their liver disease. This in turn, reinforces clinicians' focus on active
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20 256 treatments, at the expense of discussing prognostic issues.
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25 257 *"We probably don't do enough of it (discuss future care preference), because most of*
26
27 258 *the patients at a given time are not willing to engage with that question. The median*
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29 259 *age of patients is 53, so we are not talking about an 80 year old who has lived their*
30
31 260 *life to the full. We are talking about people who still want life."* (Consultant
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33 261 *hepatologist 1, interview)*
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38 262 Patients' unrealistic expectations, together with their limited knowledge of patients' own
39
40 263 understanding of their disease, presented doctors with difficulties in managing these
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42 264 expectations and deciding what treatment options to pursue.
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45 265 *"They (patients) are often referred extremely late, full of expectation only to be told*
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47 266 *there's nothing we can do. The difficulty is, what do you then do with that patient?*
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49 267 *Do you let them go back to the referring trust or secondary care, how do you know*
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51 268 *that they are going to get palliative care or the treatment that they need"*
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53 269 *(Consultant hepatologist 2, interview)*
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3 271 *Misunderstanding of palliative care*: Clinicians perceived that patients and their family
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5 272 members saw referral to palliative care negatively, as a move suggesting that clinicians had
6
7 273 ‘given up’ on the patient. They felt that patients and families did not understand what
8
9 274 palliative care could offer in terms of symptom control and psychosocial support, instead
10
11 275 seeing palliative care as a service for people at the very end of life, as illustrated by this
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13 276 senior nurse.

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17 277 “We’ve got a patient on the ward whose family are very opposed to palliative care,
18
19 278 but wanted active treatment. The patient has had repeated admissions, even if the
20
21 279 family can only have her for another extra few months. The nurse tried to tell them it
22
23 280 is not just the last weeks and hours (input from palliative care), it can be longer than
24
25 281 that and the palliative team have a lot to offer you even now.” (ward senior nurse,
26
27 282 interview)

28 283 Although most liver clinicians saw a role for palliative care in caring for this group of
29
30 284 patients, the debates on its utilisation centred more on understanding when a referral to
31
32 285 palliative care was considered appropriate. Most had very limited experience in working
33
34 286 with palliative care and knowing the best time to refer. This was further compounded by the
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36 287 difficulty of estimating the point of irreversible liver deterioration and the lack of clinical
37
38 288 tools and guidelines to support them with this process.

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40 289 “Would like to refer much earlier, but need to have an understanding at the point
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42 290 that Specialist palliative care would like involvement.” (Consultant hepatologist,
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44 291 Multi-disciplinary focus group)

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3 293 Poor continuity of care: Liver clinicians felt the lack of adequate information systems and the
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5 294 rotation of medical staff (as identified in our case notes, which identified that each
6
7 295 participant saw at least three liver consultants over the year), contributed to 'poor
8
9
10 296 continuity of care' for patients. This lack of continuity is demonstrated when patients'
11
12 297 treatment plans agreed with one consultant can be changed by another consultant due to a
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14
15 298 lack of shared information.

16
17 299 *"This rotation of staff causes problems as some patients are treated and patched up,*
18
19 300 *but come in under another consultant when readmitted and treatment happens*
20
21 301 *again. However, the system does not allow for information to be exchanged about*
22
23 302 *what exact changes have occurred in their condition."* (Consultant hepatologist 3,
24
25 303 *interview)*

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31
32 305 Perceived lack of skill and confidence: Doctors perceived they lacked skills and confidence in
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34 306 engaging in discussions about prognosis or palliative care with patients or family members.
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36 307 On liver wards, this perceived lack of skill and competence was further compounded by a
37
38 308 lack of private space for clinicians to discuss sensitive topics with patients.

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45 310 Enablers for improved palliative care: Liver clinicians suggested strategies to improve both
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47 311 continuity and enhancing the integration of palliative care and liver services: establishment
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49 312 of joint liver and palliative care clinics for people with decompensated liver disease and
50
51 313 multidisciplinary team case conferences to coordinate care and treatment for those patients
52
53 314 frequently admitted. This would enhance mutual understanding across specialities of liver-
54
55 315 specific symptom management and the timing of referrals. To support liver clinicians in

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3 316 identify patients suitable for early palliative care support, appropriate clinical tools with
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5 317 relevant guidelines need to be identified.
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11 319 **Discussion**
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14 320 *Key summary*
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16
17 321 Our findings reflect the complicated clinical picture surrounding the provision of care of
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19 322 people with cirrhosis in their last year of life. We demonstrate that patients had a high
20
21 323 symptom burden and increasing number of admissions in their last 3 months of life and a
22
23 324 focus on active treatments as highlighted by inputs from both the nurse-led PART team and
24
25 325 ITU. As with previous studies [12, 13], we highlighted the poor palliative care provision, in
26
27 326 which discussions about prognosis and DNR orders were only raised in the final phase of life
28
29 327 and referrals to palliative care made very close to death. We found that liver clinicians have
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31 328 difficulties in initiating discussions regarding prognosis, do not engage in parallel planning
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33 329 for potential deterioration as well as recovery and have a limited knowledge of palliative
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35 330 care.
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41 331 Studies suggest that uncertainty plays an important role in making anticipatory care
42
43 332 planning in advanced liver disease difficult [12]. Our qualitative data further illustrated how
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45 333 five key factors interact in acting as a barrier to palliative care. Although liver clinicians may
46
47 334 want to refer patients to palliative care earlier, active treatment is usually the de-facto
48
49 335 choice unless patients specifically raise the topic of palliative care. The difficulty of
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51 336 identifying the point of irreversible liver deterioration, together with patients' expectations
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53 337 about finding a cure for their liver disease, together with liver clinicians' own perceived lack
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3 338 of confidence and skills in addressing patients' palliative care needs, enabled them to focus
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5 339 on active treatment. A further barrier to accessing palliative care is the lack of contact and
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7 340 experience that liver clinicians have working with palliative care. This both prevents them
8
9 341 from understanding what palliative care can offer, but also prevents palliative care clinicians
10
11 342 from establishing earlier contact with patients and so become familiar faces with them. This
12
13 343 culture of active treatment may stem from tertiary centres being seen as being at the
14
15 344 forefront of technical innovation.
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23 346 *Clinical implications*

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25
26 347 Our findings suggested that the lack of knowledge about the role and benefits of palliative
27
28 348 care may contribute to the late referral of liver patients to specialist palliative care. The
29
30 349 formation of liver clinics specifically for people with decompensated liver failure, with joint
31
32 350 input from liver and palliative care specialists, may promote understanding across
33
34 351 specialties and an integrated and timely approach to care; enabling formulation of
35
36 352 treatment plans, reduce the numbers of unplanned in-patient admissions to the liver service
37
38 353 [12], improve symptom control, and enable liver and palliative care clinicians to engage in
39
40 354 discussions about prognosis and future care preferences with patients at an earlier stage.
41
42 355 Previous studies have already shown that early referral to specialist palliative care may
43
44 356 reduce the rates of expensive hospitalisation, especially in the last month of life [20]. Such
45
46 357 service developments could be explored, in line with guidance set by the end of life care
47
48 358 good practice guide [21]. Consideration should be given to the care philosophy in a tertiary
49
50 359 liver transplant centre, where many liver clinicians are reluctant to accept that active
51
52 360 interventions have limited patient benefit. Furthermore, qualitative data indicated that liver
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3 361 clinicians found it difficult to identify the point of irreversible liver deterioration, but our
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5 362 case note findings suggested that patients have increasing number of inpatient admissions
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7
8 363 and symptoms in their last three months of life. The introduction of clinical tools such as the
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10 364 Supportive & Palliative Indicators Care Tool [22] may support clinicians to identify when is
11
12 365 timely to refer to palliative care, such as the 'point of irreversible deterioration of liver
13
14 366 function'.

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21 368 *Strengths and Limitations*

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24 369 Our study explores care in advanced liver disease from different perspectives, but we accept
25
26 370 our methodology limits the generalisability of our interpretation. Our case note data were
27
28 371 retrospective and limited by the quality of recording in medical notes. Many in our case
29
30 372 note sample were referred from other hospitals and did not include data recorded at these
31
32 373 sites. For our qualitative arm, the health professionals were recruited from one hospital site
33
34 374 and due to both time constraints and the limited pool of participants available, it is possible
35
36 375 that theme saturation was not achieved. Our findings reflected practice in a tertiary liver
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38 376 transplant specialist unit in one country, and are therefore not representative of practice in
39
40 377 wider secondary care or in health systems not similar to the UK. Nevertheless, our
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42 378 exploratory findings do provide new insights into how end of life care could be improved in
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44 379 people with cirrhosis, which deserve further exploration using more robust methodology.
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3 386 **A. Contributor ship statement:** JL, SD, VV, LJ, LG and KH were responsible for the study
4
5 387 concept and design; JL and SD were responsible to the acquisition of the data; JL, SD, VV, LJ,
6
7 388 DT, AM, LG, KH, AL, AL were responsible for analysis or interpretation of the data; JL, SD, VV
8
9 389 and LJ drafted the initial manuscript; DT, AM, LG, KH, AL, revised the manuscript critically for
10
11 390 important intellectual content; all authors gave the final approval of the version to be
12
13 391 published.
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23 394 commercial or not-for-profit sectors, but the Research Department responsible for this
24
25 395 study is provided core funding by Marie Curie in order to conduct the study.
26
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28 396 **Data sharing statement:** Participants did not provide consent for the transcripts to be
29
30 397 released outside of the remit of this study.
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457 **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)

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

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

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

BMJ Open

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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Primary Subject Heading:	Gastroenterology and hepatology
Secondary Subject Heading:	Palliative care
Keywords:	Hepatology < INTERNAL MEDICINE, cirrhosis, PALLIATIVE CARE, mixed methods

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3 1 **Title:** Advanced chronic liver disease in the last year of life: a mixed methods study to
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MeSH key terms: palliative care; cirrhosis; hepatology; mixed methods

Word count: 3909

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3 32 **Abstract:**
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6 33 **Objectives:** To identify the limitations in palliative care provision in the last year of life for
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8 34 people with liver cirrhosis and potential barriers to and enablers of palliative care.
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11 35 **Design:** Mixed methods, including a retrospective case note review, qualitative focus groups
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13 36 and individual interviews.
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17 37 **Setting:** A tertiary referral liver centre in the south of England (UK).
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19
20 38 **Participants:** Purposively selected case notes of 30 people with cirrhosis who attended the
21
22 39 tertiary referral liver centre and died during an 18 month period; a purposive sample of 22
23
24 40 liver health professionals who participated in either focus groups or individual interviews.
25

26
27 41 **Primary and secondary outcomes:** Data collected from case notes included hospital
28
29 42 admissions, documented discussions of prognosis and palliative care provision. Qualitative
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31 43 methods explored management of people with cirrhosis, and barriers to and enablers of
32
33 44 palliative care.
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37 45 **Results:** Participants had high rates of hospital admissions and symptom burden. Clinicians
38
39 46 rarely discussed prognosis or future care preferences; they lacked the skills and confidence
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41 47 to initiate discussions. Palliative care provision occurred late because clinicians were
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43 48 reluctant to refer due to their perception that reduced liver function is reversible, poor
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45 49 understanding of the potential of a palliative approach; palliative care was perceived
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47 50 negatively by patients and families.
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51 51 **Conclusions:** People dying with cirrhosis have unpredictable trajectories, but share a
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53 52 common pathway of frequent admissions and worsening symptoms as death approaches.
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3 53 The use of clinical tools to identify the point of irreversible deterioration and joint working
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5 54 between liver services and palliative care may improve care for people with cirrhosis.
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3 55 **Strengths and limitations of this study**
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- 6 56 • The study is the first to look specifically at how care is provided to people with
7 57 advanced liver disease in the last year of life, with the aim of identifying barriers that
8 58 limit a palliative approach to care.
9 59
10 60 • A mixed methods design enables exploration from different perspectives of the
11 61 structural difficulties to providing end of life care to people with advanced liver
12 62 disease.
13 63
14 64 • Findings suggest pragmatic ways that supportive and end of life care can be
15 65 improved for people with advanced liver disease.
16 66
17 67 • As this study was conducted in one tertiary liver unit in the south of England, the
18 68 findings may not be generalised to other healthcare settings.
19 69
20 70 • The retrospective nature of the case note data limits the interpretation of the
21 71 quantitative findings.
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3 72 **Background**
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6 73 Advanced chronic liver disease (cirrhosis) is a growing international public health problem
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8 74 and often affects people of working age.[1] It is the third most common cause of premature
9
10 75 death in the United Kingdom (UK) [2]; more people are affected by liver disease with the
11
12 76 increases in alcohol consumption, viral hepatitis and obesity [3]. Most people dying from
13
14 77 liver disease are not suitable for liver transplantation and, of those who are suitable, 20%
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16 78 will die before a donor becomes available[4]. Living with cirrhosis may involve considerable
17
18 79 symptom burden, and when liver failure ensues the prognosis is poor. Death may occur
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20 80 either after a long period of decline with a fluctuant clinical picture, or may be sudden and
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22 81 unanticipated. In most cases, death from cirrhosis occurs in hospital [5].
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28 82 People with cirrhosis have supportive and palliative care needs [6-9]. Liver professionals
29
30 83 acknowledge they have a role to play in this aspect of care [10, 11], but feel that their skills
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32 84 are limited and may be inadequate to offer an effective palliative approach [10, 12].
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35 85 Referrals to specialist palliative care may be necessary but palliative care provision is
36
37 86 limited [13], and knowledge of prescribing in liver failure is needed. Shared care, defined as
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39 87 using the skills and knowledge of many health professionals who share joint responsibility
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41 88 for an individual's care, may be useful [14]. Palliative care offered in parallel with optimised
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43 89 specialist and generalist care may benefit people with advanced cirrhosis [15]. One difficulty
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45 90 is knowing the appropriate time to make referrals and begin shared care [10]. Further data
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47 91 to understand how different specialities such as liver and palliative care services can work
48
49 92 together may be helpful[14]. In this paper we report what we have learned from exploring
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51 93 practice in a tertiary treatment centre for liver disease in north London, UK. We used mixed
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53 94 methodology, guided by Rapid Participatory Appraisal in which data collected from different
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3 95 sources relating to a specific healthcare provider are combined to describe both the service
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5 96 structure and potential care improvements in a specific health locality [16]. Using mixed
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7 97 methods, we hoped to gain greater understanding of the limitations in the provision of
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9 98 palliative care for people with cirrhosis in the last year of life, and explore the reasons
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11 99 behind these limitations. This approach is commonly used in health service research to
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13 100 understand the complexity of health care[17].
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20 102 We conducted a case note review, focus groups and qualitative interviews to explore:
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- 23 103 (i) How healthcare in liver services is provided in the last year of life to
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25 104 people with advanced liver disease (cirrhosis) from any cause to identify
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27 105 limitations in palliative care provision;
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30 106 (ii) Challenges in providing palliative care provision in liver care and how this
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32 107 provision might be improved in hepatology.
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39 109 **Method**

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41 110 A mixed methods study, using a retrospective case note review, qualitative focus groups and
42
43 111 individual interviews. Case note findings were used to quantify the types of healthcare
44
45 112 inputs provided by the liver services to people in their last year of year and to identify
46
47 113 potential limitations in and barriers to the palliative care provided and a shared approach to
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49 114 care. The qualitative data identified reasons underlying these limitations and barriers, and
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51 115 highlighted potential enablers to improving care in this context.
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3 117 Setting
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6 118 A tertiary referral liver transplant centre in north London UK, providing both a core
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8 119 diagnostic service for all conditions affecting the liver and long-term management of
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10 120 patients with all severities of liver disease.
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16 122 Procedure
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18 123 Retrospective case note review
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21 124 As resources were limited, we purposively selected 30 people with cirrhosis from the 66
22
23 125 people who attended the tertiary referral liver centre and died between April 2010 and
24
25 126 September 2011. We aimed to ensure that our sample represented the spectrum of people
26
27 127 attending the centre and purposefully sampled according to age, gender and cause of liver
28
29 128 failure.
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32
33 129 We used a structured framework to extract data from patient records available from the
34
35 130 centre for the 12 month period prior to death. We noted demographics, severity of liver
36
37 131 disease at last admission, cause of cirrhosis, transplantation status, physical and
38
39 132 psychological symptoms, and health service use in secondary care (inpatient admissions,
40
41 133 hospital length of stay, intensive therapy unit (ITU), liver-related procedures). We recorded
42
43 134 documented evidence of discussions about prognosis and future preferences for care. We
44
45 135 collected information on referrals to specialist palliative care (SPC), creation of care plans
46
47 136 including evidence of advance care planning (ACP), resuscitation (DNACPR) status, preferred
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49 137 place of death and actual place of death. Data were extracted by the research nurse (SD)
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51 138 and inputted into Microsoft Excel.
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3 139 Qualitative data
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5 140 Both focus groups and semi-structured interviews were used to capture as many views of
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7 141 healthcare professionals as possible. All potential participants were first identified by a
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9
10 142 clinician (LG). The research nurse (SD) then contacted these participants face to face, by
11
12 143 telephone, or by email. Participants were given information about the study, outlining the
13
14 144 role of the research team, and gave written consent prior to data collection. All participants
15
16 145 took part either in one focus group or a semi-structured interview (between July 2013-May
17
18 146 2014), which were conducted in the liver centre.
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23
24 148 *Focus groups*
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26 149 Focus groups were used as a pragmatic method of gathering larger numbers of people and
27
28 150 using the group dynamic to generate discussion about care at the end of life in cirrhosis[18,
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30 151 19]. Purposive sampling was used to ensure the views of those at all levels of the liver team
31
32 152 across the disciplines (doctors, nurses and allied health professionals) were captured. Three
33
34 153 focus groups were organised (each lasting 45-60 minutes) and led by a research nurse (SD –
35
36 154 Master's degree qualification and 6 years of qualitative research experience), with an
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38 155 observer (JL – senior health researcher with a PhD and 20 years of experience in
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40 156 qualitative/mixed methods research) taking field notes and co-facilitating.
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48 158 *Topic guide*
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50 159 To guide discussions, a topic guide (supplementary files) was developed by the members of
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52 160 research team (JL, SD, AM, DT, LG, KH, LJ) covering: challenges of providing care to people in
53
54 161 the last year of life; their perception of patient and family understanding of liver disease;
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56 162 discussing prognosis and future care preferences; improving palliative care. This guide was
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3 163 developed pragmatically in the context of liver disease, guided by the principles of palliative
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5 164 care[20]. All focus groups were audiotaped and transcribed verbatim.
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10 166 *Interviews*

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12 167 Professionals unable to attend the focus groups, were invited to take part in semi-
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14 168 structured individual interviews. Nine interviews were conducted by SD (lasting 18 – 70
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16 169 minutes) using the topic guide, and were audiotaped and transcribed verbatim.
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22 171 **Data analysis**

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24 172 Retrospective case notes: Descriptive statistics were used to describe hospital admissions
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26 173 and service use, documentation of prognostic discussions and preferences for future care,
27
28 174 and palliative care provision. Data were summarised to highlight limitations in palliative care
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30 175 service provision.
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35 176 Qualitative data: A framework approach was used to analyse the transcripts[21], which
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37 177 were first read independently by two researchers (JL, SD). Themes were identified, from
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39 178 which a coding system was developed and applied to the whole data set systematically. Any
40
41 179 disagreements in coding were resolved by consensus. In organizing the data into
42
43 180 appropriate themes, Microsoft Excel was used. The researchers considered themes
44
45 181 independently and met to discuss the themes identified and how they were linked together
46
47 182 by contextual factors. Independent analysis ensured validity and reliability of the themes
48
49 183 and links identified. Findings were also shared with our clinical partners (AM, LG, DT, KH) in
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51 184 the research team to ensure that the findings were consistent with their experience of
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53 185 current clinical practice. These themes were used to explain the limitations in palliative care
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186 provision found in the case notes, and to identify barriers and enablers to future palliative
187 care for people with cirrhosis.

188

189 Ethical approval

190 Ethical approval was sought, but deemed unnecessary by the NRES Committee London -

191 West London & GTAC (ref 14/LO/0799). NHS permission to conduct the clinical case-note

192 review and the qualitative interviews with liver health professionals was obtained from the

193 Royal Free London Clinical Governance Lead for Hepatology and Palliative Care under the

194 remit of health service improvement.

195

196 **Results**

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

198 ***Demographics and clinical characteristics (Table 1)***

199 Our sample was predominately male (n=20, 67%) with a median age of 59 years (IQR: 52-66;

200 range 25-75), in which alcohol-related liver disease (ARLD) was the predominant diagnosis

201 (n=16; 53%). A MELD score gives an indication of short term mortality, and is used to

202 prioritise candidates on the orthotopic liver transplantation waiting list. In 23 cases where data

203 were available at last admission, our sample had a median (interquartile range) MELD score

204 of 23 (16.5-23), suggesting a 19.6 % chance of dying in the next 3 months [22]. Nineteen

205 (63%) people were not considered for liver transplant due to poor health, four were on the

206 transplant waiting list, and three had previously received a transplant. Eight (27%) people

207 with cirrhosis had been referred to the tertiary centre from 'out of area' hospitals either for

1
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3 208 a liver transplant assessment, or for specialist treatments such as a Transjugular
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5 209 Intrahepatic Portosystemic Shunt (TIPS) or intensive management of bleeding.
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8 210 The people in our sample were highly symptomatic (table 2). All were symptomatic three
9
10 211 months before death, presenting with ascites (n=22, 73%), extensive peripheral oedema
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12 212 (n=20, 66%), severe fatigue and weakness (n=20; 66%) and pain (n= 13; 43%). In the last
13
14 213 month of life, our participants presented with an average of 14 physical symptoms per
15
16 214 person. The majority (n=19, 63%) were noted to have symptoms of hepatic encephalopathy
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18 215 such as confusion, disorientation, and agitation.
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26 217 **Health service use in tertiary care**

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29 218 Our sample of 30 had a median of three inpatient admissions (IQR 2-5) per person in the last
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31 219 year of life, and a median length of stay of 31 days (IQR 19-55). Seventeen (57%) people
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33 220 were readmitted within 30 days of discharge. The frequency of admissions increased for
34
35 221 most people (n=29; 97%) in the last 3 months of life. Nineteen (63%) people had more than
36
37 222 one admission in the month before death, during which the median number of admissions
38
39 223 was two (IQR: 1-3). Of the 78 admissions precipitated by cirrhotic complications, most
40
41 224 required invasive procedures such as paracentesis (n=53/78, 68%), blood transfusions
42
43 225 (n=13/78, 17%), endoscopic variceal banding (n=4/78, 5%) and TIPS (n=4/78, 5%). During
44
45 226 these admissions, each participant was seen in the last year of life by a mean of three
46
47 227 different liver consultants (range 1-6). Nine (30%) people were regularly reviewed by the
48
49 228 hospital nurse-led patient-at-risk team (PART), to decide whether to escalate or de-escalate
50
51 229 their treatment. Six (20%) people with cirrhosis required treatment in the intensive care unit
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53 230 (ITU) during which three patients died.
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232 Documentation of prognosis, future care discussions and palliative care provision

233 Liver consultants recorded having discussed prognosis mainly with family members (n=23,
234 77%); discussions occurred very late, in 16 (53%) cases \leq 34 days before the person died.

235 Liver doctors recorded fewer discussions with patients about understanding of their disease
236 or future care preferences (n=16, 53%), most of which occurred one month before death
237 (n=9/16; 56%).

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

244 Most people with cirrhosis (n=21; 70%) were referred to specialist palliative care a median
245 of five days before death. Twelve (40%) people with cirrhosis documented as deteriorating
246 were still receiving active treatment up until their death. For most people, death occurred in
247 hospital (n=25; 83%), three died in ITU. The remaining five people died either at home (n=3;
248 10%) or in a hospice (n=2; 7%). Only five people from the sample had clear discussions with
249 health professionals about place of death; two of these died in the place of their choice (one
250 at home and the other in hospital).

251

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

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3 253 Demographics of liver clinician sample: Thirteen liver health professionals took part in three
4
5 254 focus groups (FG) [FG1: 3 doctors, 2 liver transplant nurses, a dietician and a pharmacist;
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7 255 FG2: 3 ward nurses and a healthcare assistant; FG3: 2 ward nurses). Nine health
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9
10 256 professionals took part in semi-structured interviews (5 doctors, 2 senior nurses in
11
12 257 hepatology, a clinical nurse specialist in palliative care, an alcohol liaison nurse). No
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14 258 demographic information was collected for the liver clinician sample other than their
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16 259 discipline.
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23 **Key findings:**

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26 262 Initial analysis illustrated that liver clinicians recognised that although their patients were in
27
28 263 poor health, they did not address quality of life issues with them and palliative care options
29
30 264 were only considered with patients who raised this topic themselves. Further analysis
31
32 265 identified five emergent themes which illustrated why liver clinicians focused on reactive
33
34 266 treatment for people at the expense of palliative care: unpredictable trajectory of liver
35
36 267 disease, management of patient treatment expectations, clinician/patient perceptions of
37
38 268 the palliative care role, poor continuity of care, perceived lack of skill and confidence.
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46 270 Unpredictable trajectory of liver disease: The perceived ability of the liver to recover
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48 271 function made it difficult for doctors to estimate the point of irreversible liver decline, and
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50 272 so provided doctors with hope that trying different treatments would promote recovery,
51
52 273 even with patients on the wards who were imminently dying. Nurses felt that part of this
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54 274 difficulty was the short periods that doctors spend with patients in contrast with the ward
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3 275 nurses, who provide continuous care and were confident in identifying those imminently
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5 276 dying. However, nurses considered that cessation of active treatment was the responsibility
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8 277 of doctors as main clinical decision makers.
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11 278 *“We (ward nurses) have constant contact with patients... enables us to identify those*
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13 279 *patients who are both aware of their deterioration and want to die at home to be*
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15 280 *fast tracked to specialist palliative care” Ward nurse, Nurse focus group 1.*
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21 282 Management of patient expectations: Doctors’ emphasis on active treatments is reinforced
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23 283 by their own perceptions of patients’ treatment expectations. Part of this expectation may
24
25 284 be reflected by the patients’ younger ages, who doctors feel want life at all costs.
26
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28 285 Furthermore, as many patients are referred by secondary care ‘out of area’ (as illustrated in
29
30 286 our case notes), clinicians perceive these patients see referral to the tertiary liver centre as a
31
32 287 last chance to ‘cure’ their liver disease. This in turn, reinforces clinicians’ focus on active
33
34 288 treatments, at the expense of discussing prognostic issues.
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38 289 *“We probably don’t do enough of it (discuss future care preference), because most of*
39
40 290 *the patients at a given time are not willing to engage with that question. The median*
41
42 291 *age of patients is 53, so we are not talking about an 80 year old who has lived their*
43
44 292 *life to the full. We are talking about people who still want life.” (Consultant*
45
46 293 *hepatologist 1, interview)*
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51 294 Patients’ unrealistic expectations, and their limited knowledge and understanding of their
52
53 295 own disease, presented doctors with difficulties in managing these expectations and
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56 296 deciding what treatment options to pursue.
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3 297 *“They (patients) are often referred extremely late, full of expectation only to be told*
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5 298 *there’s nothing we can do. The difficulty is, what do you then do with that patient?*
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7 299 *Do you let them go back to the referring trust or secondary care, how do you know*
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10 300 *that they are going to get palliative care or the treatment that they need”*
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12 301 *(Consultant hepatologist 2, interview)*
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17 303 Misunderstanding of palliative care: Clinicians perceived that patients and their family
18
19 304 members saw referral to palliative care negatively, as a move suggesting that clinicians had
20
21 305 ‘given up’ on the patient. They felt that patients and families did not understand what
22
23 306 palliative care could offer in terms of symptom control and psychosocial support, instead
24
25 307 seeing palliative care as a service for people at the very end of life, as illustrated by this
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27 308 senior nurse.

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32 309 *“We’ve got a patient on the ward whose family are very opposed to palliative care,*
33
34 310 *but wanted active treatment. The patient has had repeated admissions, even if the*
35
36 311 *family can only have her for another extra few months. The nurse tried to tell them it*
37
38 312 *is not just the last weeks and hours (input from palliative care), it can be longer than*
39
40 313 *that and the palliative team have a lot to offer you even now.” (ward senior nurse,*
41
42 314 *interview)*
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47 315 Although most liver clinicians saw a role for palliative care, the debate on its utilisation
48
49 316 centred more on understanding when a referral to palliative care was considered
50
51 317 appropriate. Most had very limited experience in working with palliative care and were
52
53 318 unsure of the best time to refer. This was further compounded by the difficulty of
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3 319 estimating the point of irreversible liver deterioration and the lack of clinical tools and
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5 320 guidelines to support them with this process.
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8 321 *“Would like to refer much earlier, but need to have an understanding at the point*
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10 322 *that specialist palliative care would like involvement.” (Consultant hepatologist,*
11
12 323 *Multi-disciplinary focus group)*
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17 325 Poor continuity of care: Liver clinicians felt the lack of adequate information systems and the
18
19 326 rotation of medical staff (our case notes showed that each participant saw at least three
20
21 327 liver consultants over the year), contributed to ‘poor continuity of care’. This lack of
22
23 328 continuity is demonstrated when treatment plans agreed with one consultant can be
24
25 329 changed by another consultant due to a lack of shared information.
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28
29 330 *“This rotation of staff causes problems as some patients are treated and patched up,*
30
31 331 *but come in under another consultant when readmitted and treatment happens*
32
33 332 *again. However, the system does not allow for information to be exchanged about*
34
35 333 *what exact changes have occurred in their condition.” (Consultant hepatologist 3,*
36
37 334 *interview)*
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43 336 Perceived lack of skill and confidence: Both doctors and nurses perceived they lacked skills
44
45 337 and confidence in engaging in discussions about prognosis or palliative care with patients or
46
47 338 family members. On liver wards, this was further compounded by a lack of private space to
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49 339 discuss sensitive topics.
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3 341 Enablers for improved palliative care: Liver clinicians suggested strategies to enhance both
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5 342 continuity and integration of palliative care and liver services, such as joint liver and
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7 343 palliative care clinics for people with decompensated liver disease and multidisciplinary
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9 344 team case conferences to coordinate care and treatment for those patients frequently
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11 345 admitted. Such initiatives would enhance mutual understanding across specialities of liver-
12
13 346 specific symptom management and the timing of referrals. To support liver clinicians in
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15 347 identifying patients suitable for early palliative care support, appropriate clinical tools with
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17 348 relevant guidelines need to be identified.
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350 **Discussion**

351 *Key summary*

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

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

1
2
3 363 interact as barriers to palliative care. Although liver clinicians may wish to refer patients to
4
5 364 palliative care earlier, active treatment is usually the *de-facto* choice unless patients
6
7 365 themselves specifically raise the topic. The difficulty of identifying the point of irreversible
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10 366 liver deterioration, patients' expectations of finding a cure, together with liver clinicians'
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12 367 perceived lack of confidence and skills in addressing palliative care issues enabled a focus on
13
14 368 active treatment. A further barrier is the lack of contact and experience that liver clinicians
15
16 369 have of working with palliative care specialists. This prevents them from understanding
17
18 370 what palliative care can offer, and prevents palliative care clinicians from establishing earlier
19
20 371 contact with patients which might enable them to become familiar faces for patients and
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22 372 families. This culture of active treatment may stem from tertiary centres being seen as at
23
24 373 the forefront of technical innovation.
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33 375 *Clinical implications*

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35 376 Our findings suggest that lack of knowledge about the role and potential benefits of
36
37 377 palliative care may contribute to the late referral of liver patients to specialist palliative care.
38
39 378 The formation of liver clinics specifically for people with decompensated liver failure, with
40
41 379 joint input from liver and palliative care specialists is recommended. This may promote
42
43 380 understanding across specialties, an integrated and timely approach to care, formulation of
44
45 381 treatment plans and a reduction in unplanned in-patient admissions to the liver service [12].
46
47 382 It may also improve symptom control and enable clinicians to engage in discussions about
48
49 383 prognosis and future care preferences with patients and families at an earlier stage.
50
51 384 Previous studies have shown that early referral to specialist palliative care may reduce the
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53 385 rates of expensive hospitalisation, especially in the last month of life [23]. Such service
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3 386 developments could be explored, in line with guidance set by the 'End of life care good
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5 387 practice guide' [24]. Consideration should be given to the care philosophy in a tertiary liver
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7 388 transplant centre, where many liver clinicians are reluctant to accept that active
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10 389 interventions have limited patient benefit. Qualitative data indicate that liver clinicians
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12 390 found it difficult to identify the point of irreversible liver deterioration; our case note
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14 391 findings suggest that inpatient admissions and symptoms increase in frequency in the last
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16
17 392 three months of life. The introduction of clinical tools such as the Supportive & Palliative
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19 393 Indicators Care Tool [25] may support clinicians to identify when is timely to refer to
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21 394 palliative care, such as the 'point of irreversible deterioration of liver function'.
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28 396 *Strengths and Limitations*

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31 397 Our study explores care in advanced liver disease from different perspectives, but we accept
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33 398 our methodology limits the generalisability of our interpretation. Our case note data were
34
35 399 retrospective and limited by the quality of recording in medical notes. Many in our case
36
37 400 note sample were referred from other hospitals and did not include data recorded at these
38
39 401 sites. Due to time constraints, we reviewed a purposive sample of case notes of those who
40
41 402 died, so there is a potential for selection bias and error in the notes that were reviewed. Our
42
43 403 case note sample only reflects patients who died during follow-up and not those who were
44
45 404 still alive, or who had a transplant. This is important since these patients are also often
46
47 405 recipients of palliative care. For our qualitative arm, the health professionals were recruited
48
49 406 from one hospital site and due to both time constraints and the limited pool of participants
50
51 407 available, it is possible that theme saturation was not fully achieved. We did not explore the
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53 408 views of close family members and informal carers in this study and may have missed
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409 important insights on experiences of living and dying with liver disease and how care might
410 be improved. Our findings reflected practice in a tertiary liver transplant specialist unit in
411 one country; whilst clinical issues are likely to be similar in other settings, organisational
412 issues and person-centred attitudes will vary across other healthcare systems.
413 Nevertheless, our exploratory findings do provide new insights into how care towards the
414 end of life could be improved in people with cirrhosis, which deserve further exploration
415 using more robust methodology.

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3 423 **A. Contributorship statement:** JL, SD, VV, LJ, LG and KH were responsible for the study
4
5 424 concept and design; JL and SD were responsible to the acquisition of the data; JL, SD, VV, LJ,
6
7 425 DT, AM, LG, KH, AL, AL were responsible for analysis or interpretation of the data; JL, SD, VV
8
9 426 and LJ drafted the initial manuscript; DT, AM, LG, KH, AL, revised the manuscript critically for
10
11 427 important intellectual content; all authors gave the final approval of the version to be
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13 428 published.
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18 429 **B. Competing interest:** None declared
19
20

21 430 **C. Funding:** This study received no specific grant from any funding agency in the public,
22
23 431 commercial or not-for-profit sectors, but the Research Department responsible for this
24
25 432 study is provided core funding by Marie Curie in order to conduct the study.
26
27

28 433 **Data sharing statement:** Participants did not provide consent for the transcripts to be
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30 434 released outside of the remit of this study.
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498 **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)

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

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