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## Symptom Distress in Patients with End-Stage Liver Disease toward the End of Life

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In the United States (U.S.) an estimated 5.5 million Americans have chronic liver disease (U.S. Department of Health and Human Services, 2004). It is one of the most expensive digestive diseases in terms of health care costs at a total cost of approximately \$1.6 billion annually, including \$222 million for indirect costs of work lost (U.S. Department of Health and Human Services, 2004). Chronic liver disease results in more than 350,000 hospitalizations and 750,000 physician office visits each year (Sandler, 2002). It is the fifth leading cause of death between the ages of 45 and 64 (Minino & Murphy, 2012), leading to more than 33,000 death each year (Hoyert & Xu, 2012). Chronic liver disease is a precursor to cirrhosis and ultimately end-stage liver disease (ESLD), reflecting irreversible damage to

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liver cells, structures, and functions of the liver. Cirrhosis can lead to profound liver failure - a terminal state. Toward the end of their lives many patients with ESLD experience symptoms such as fatigue, itching, peripheral edema, dyspnea, right upper quadrant pain, and changes in level of consciousness (Hansen, Sasaki, & Zucker, 2010; Ignatavicius, 2010; Sanchez & Talwalkar, 2006; Spengler, 2011). These symptoms are well known to health care professionals who care for patients with ESLD.

## Background

Research on *symptoms distress* experienced by adult patients with ESLD toward the end of their lives is lacking. Fewer than 20 articles have been published on this population (A. Hamilton, personal communication, July 8, 2013). Several are sub-studies based on data from the Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT) that used a sample of seriously ill hospitalized patients (Connors et al., 1995; Desbiens, Mueller-Rizner, Connors, Wenger, & Lynn, 1999; Desbiens & Wu, 2000; Desbiens et al., 1996; Freeborne, Lynn, & Desbiens, 2000; Roth, Lynn, Zhong, Borum, & Dawson, 2000). These studies focus on a limited number of symptoms such as pain, nausea, and anxiety, and do not address distress based on combined symptoms experienced by patients. Neither do the studies describe the variability in symptom distress experienced over time. In a study by Desbiens and Wu (2000), 60% of seriously ill hospitalized patients with liver failure experienced pain. This finding is important because the liver may be perceived as a relatively silent organ that does not cause pain. Pain is one of the most feared symptoms by patients, if not the most feared (Lemay et al., 2011).

A symptom checklist alone is not enough to provide the clinical insight needed by health care professionals to assess and manage outpatient symptom distress of patients with ESLD toward the end of life. Thus, the aims of this study were (1) to describe the presence, frequency, severity, and distress of symptoms in patients with ESLD who experience pain toward the end of life, and (2) to describe the variability in psychological and physical symptom distress between and within patients over time. Obtaining a detailed picture of the symptoms experienced by these patients will provide information to tailor effective symptom management strategies.

## Methods

A prospective descriptive design was used in this pilot study. Data were collected from patients once a month for a six month period. The study was approved by institutional review boards at Oregon Health & Science University (OHSU) and Portland Veterans Affairs Medical Center (PVAMC).

## Sample

The sample consisted of 20 outpatients with ESLD. Inclusion criteria consisted of: (a) 21 years of age, (b) ability to read and speak English, and (c) pain levels 3 on a 0 to 10 numeric rating scale. Liver disease was identified by medical record documentation of cirrhosis. Disease severity was assessed by a Model of End Stage Liver Disease (MELD) score. A MELD score of 18 was used as a cut-off because it is associated with increased

short term (3-month) mortality (Kamath & Kim, 2003; Kamath et al., 2001). Patients were excluded if they had a history of liver transplantation or hepatocellular carcinoma.

A purposive sampling strategy was used to enroll participants in this study. During scheduled appointments at the Hepatology Clinic at OHSU or PVAMC, potentially eligible patients for participation were approached by a nurse, nurse practitioner or physician to briefly explain the study and offer participation. Health care professionals supplied potential participants with written information regarding the study; those requiring more detail were referred to the principal investigator (PI). The PI then contacted the patient during the same clinic visit or later at home by telephone and explained the study in detail. Patients who agreed to participate provided written informed consent. Participants completed a symptom questionnaire at the time of recruitment. If it was inconvenient, the PI scheduled a convenient time for the participants to complete the questionnaire.

### Data Collection

Prior to enrollment in the study and before each data collection, patients' level of orientation and decisional capacity were assessed. Level of orientation was assessed by asking questions related to person, place, and time (Zator Estes, 2006). Decisional capacity was assessed by using the Guidance on Human Subject Research with Decisionally Impaired Adults (Oregon Health & Science University Office of Research Integrity, 2007). The Guidance includes five methods of assessing impairment, such as determining a person's ability to understand and express a reasoned choice. If patients were alert and oriented at the time of enrollment, but later became confused, the PI discontinued their participation in the study. The PI administered the questionnaire in-person once a month over the course of six months at a private location convenient for the participants. Participants were informed that they did not have to answer any questions. The PI telephoned the participants two weeks after each data collection point and the day prior to a scheduled data collection to facilitate continued study participation.

### Measure

The Memorial Symptom Assessment Scale (MSAS) was used to collect data on patients' symptoms. The MSAS is a Likert-type scale symptom checklist used to measure characteristics associated with 32 psychological and physical symptoms experienced in the preceding week (Portenoy et al., 1994). Patients were asked whether or not they experienced each of the 32 symptoms listed. If a patient was experiencing a particular symptom, he/she was asked to: (a) select how often the symptom occurred on a 1 – 4 scale (1 = *rarely* to 4 = *almost constantly*), (b) rate the symptom's severity on a 1 – 4 scale (1 = *slight* to 4 = *very severe*), and (c) indicate how much the symptom distressed him/her on a 1 – 5 scale (1 = *not at all* to 5 = *very much*). Based on the scoring instructions for the MSAS, distress scores were re-coded to a four point scale to insure consistency with the other two scales for the summary scores on the MSAS (Portenoy, et al., 1994). The MSAS consists of a total score, a global symptom distress index (GDI) score, a psychological symptom distress (PSYCH) score and a physical symptom distress (PHYS) score. The total MSAS score is computed by taking the average of all of the frequency, severity, and distress ratings. Symptom scores that were reported as not present were coded a 0. The PSYCH score is the average of the scores

on the severity, frequency, and distress scales for six symptoms (feeling sad, feeling irritable, feeling nervous, worrying, difficulty sleeping, and difficulty concentrating). The PHYS score is the average of the scores on the severity, frequency, and distress scales for 12 symptoms (lack of appetite, lack of energy, pain, feeling drowsy, feeling bloated, constipation, dry mouth, nausea, vomiting, change in taste, weight loss, and dizziness). The GDI is the average score for 10 symptoms that includes the frequency scores for feeling sad, worrying, feeling irritable and feeling nervous, and the distress scores for lack of appetite, lack of energy, pain, feeling drowsy, constipation, and dry mouth.

The completion time for the MSAS was 10 – 15 minutes for participants. Internal consistency of the MSAS scales has been established in patients with and without cancer near the end of life (Tranmer et al., 2003), and in patients with AIDS. In patients with AIDS, reported Cronbach's alpha for the GDI, PSYCH, and PHYS were .83, .82, and .83, respectively (Vogl et al., 1999). In the current data, the Cronbach's alphas at baseline for the GDI, PSYCH, PHYS, and MSAS total score were .83, .94, .87, and .93, respectively.

### Data Analysis

Data were analyzed using Stata 11 (College Station, TX; StataCorp 2009). Descriptive statistics, including frequency distributions, means, and standard deviations were used to summarize the data. Given the small sample size and exploratory nature of the study, descriptive statistics (i.e., frequency distribution, means, and standard deviations) rather than inferential statistics were used to summarize the data. Inter-individual variability was quantified as the between person standard deviation mean score averaged across time. Intra-individual variability was quantified as the within-person standard deviation of scores across time (Nesselrode & Ram, 2004).

### Results

To obtain a target sample of 20 patients from whom at least three months of data were collected, we enrolled 26 patients. At the time of study enrollment two patients declined to participate due to new life events such as moving to another city. During the study, no patients withdrew. Four patients died before three months of data were collected, one received a liver transplant and was therefore ineligible to continue to participate, and one was lost to follow-up. During the last three months of data collection, the sample size decreased to 10 patients. Four more patients died, two developed confusion, two experienced major medical events, a second received a liver transplant, and one moved away from the area. MELD scores ranged from 18 – 19 over time, corroborating the severity of patients' liver disease. Due to the disease severity, the PI collected the data in patients' homes to minimize missing data. Across all time points and participants, a total of 95 symptom scores were collected.

### Presence, Frequency, Severity, and Distress of Symptoms over Time

Demographics for the sample are presented in Table 1. The majority of patients were male and white. Frequency distributions were examined for the percentage of patients who indicated having each of the 32 symptoms listed on the MSAS over time (see Table 2).

Scores were aggregated across time as an initial step for obtaining a global understanding of how participants were responding to these items. The four most common symptoms reported were pain, lack of energy, feeling drowsy, and difficulty sleeping.

Mean ratings over time of the 10 most frequent, severe, and distressing symptoms of the MSAS are presented in Table 3. Patients reported lack of energy, pain, difficulty sleeping, and feeling drowsy as the most frequent, severe, and distressing symptoms. The fifth, sixth, and seventh most frequent and severe symptoms were dry mouth, difficulty concentrating, and itching, respectively. Difficulty concentrating was considered more distressing than dry mouth.

In addition to the presence, frequency, severity, and distress ratings, we also examined the total MSAS score for each symptom. The four symptoms with the highest scores were lack of energy ( $M = 3.1$ ;  $SD = 1.0$ ), pain ( $M = 3.0$ ;  $SD = 1.0$ ), difficult sleeping ( $M = 2.4$ ;  $SD = 1.5$ ), and feeling drowsy ( $M = 2.2$ ;  $SD = 1.4$ ). These symptoms are the same as the most common symptoms reported present by patients (see Table 2) but in a different rank order.

The means, standard deviation, and sample sizes for total MSAS Symptom, GDI (global distress), PSYCH (psychological distress), and PHYS (physical distress) scores over the six months of the study are presented in Table 4. Total MSAS score ranged from 1.2 to 1.6, and appeared to show a slight declining trend during the last three months. The GDI scores ranged from 2.6 to 2.9 and appeared relatively stable throughout the time periods. Patients mean scores on the PSYCH scale hovered between 1.6 and 1.9 during the six month time period. Patients mean scores on the PHYS scale ranged from 1.3 to 1.8, and appeared to decline during the last three months.

### Variability in Psychological and Physical Symptom Distress Between and Within Patients Over Time

The GDI variability was notable between and within individual patients (Table 5). Patient GDI scores ranged across time from 0.8 to 4.0 ( $M = 2.8$ ;  $SD = 0.7$ ); the standard deviations within patients across time ranged from 0.1 to 1.0 ( $M$  of  $SD = 0.4$ ). The intra-individual variability on the PSYCH scale ranged across time from 0.0 to 1.2 ( $M$  of  $SD = 0.5$ ). On the PHYS scale it ranged across time from 0.1 to 0.8 ( $M$  of  $SD = 0.4$ ).

## Discussion

To our knowledge, this is the first study to prospectively and longitudinally describe the psychological, physical, and global symptom distress in outpatients with ESLD who experience pain toward the end of life. The results from this pilot study provide a platform for commentary and hypothesis generation for future studies.

In addition to symptom distress, the results from the study include the presence, frequency, and severity of symptoms over time in patients with ESLD. The most common symptoms reported by patients were pain, lack of energy, feeling drowsy, and difficulty sleeping. Lack of energy was the most frequent and severe symptom but pain was the most distressing symptom. These findings differ from findings reported by S.-H. Kim, Oh, Lee, Kim, and

Han (2006) who used a cross-sectional design to examine symptom experiences in Korean patients with liver cirrhosis. They found the most frequent symptoms to be fatigue, abdominal distension and/or peripheral edema, change in appearance, dry mouth, and muscle cramps. They also measured symptom intensity and distress and found that fatigue was also the most intense and distressing symptom followed by muscle cramps and abdominal distension and/or peripheral edema. We did not measure fatigue, but we measured lack of energy and feeling drowsy. Both of these symptoms were among the four most frequent, severe, and distressing for patients in our study. In comparison to fatigue, lack of energy and feeling drowsy have received little attention in the liver literature. Fatigue has been listed as the most commonly experienced symptom in patients with chronic liver disease (Swain, 2006) and found to be most severe in patients with hepatitis C virus infection (Obhrai, Hall, & Anand, 2001). In our sample, the experience of lack of energy was severe and almost constant. Due to the stage of the liver disease, this finding was not surprising. Patients' lack of energy will likely increase as the disease progresses and may be influenced by numerous factors such as sleep disturbances and pain. As with other symptoms, the experience of lack of energy may not be static. Health care professionals should assess and address other factors influencing lack of energy. Patients should be counseled and reassured that this symptom is a normal part of advanced liver disease and should be included in routine discussions. Professionals should explore with patients when they have energy and decide how this energy is best spent as the disease worsens.

In a study by S.-H. Kim et al. (2006) pain was one of the least frequent, intense, and distressing symptoms experienced by patients. Right upper quadrant pain ranked as number 14 and bodily pain as number 16 of 18 symptoms measured. This is in contrast to our findings and may be related to our inclusion of only patients who experienced pain and who had worse disease severity. S.-H. Kim et al. (2006) measured disease severity by the Child-Pugh classification system and not the MELD score. In their study 94 of 129 patients were in the Child A and B classes (S.-H. Kim et al., 2006; MedicalCriteria.com, 2006). Child A classification is the least severe and Child C the most severe with a 45% one year survival rate (Albers, Hartmann, Bircher, & Creutzfeldt, 1989; Child & Turcotte, 1964; Pugh, Murray-Lyon, Dawson, Pietroni, & Williams, 1973). The frequency and intensity of pain experienced by patients with ESLD in our study are similar to findings by Roth et al. (2000). The researchers found that pain was moderately severe most of the time in one third of seriously ill hospitalized adults with ESLD (Roth et al., 2000, p. S122). Health care professionals under-treat pain in this population due to concerns about poor medication metabolism and hepatic encephalopathy (Larson & Curtis, 2006; Roth et al, 2000). Under-treatment of pain may also be due to an increased prevalence of substance abuse among patients with ESLD (Roth et al., 2000). Patients with ESLD toward the end of life need to be assured that pain control and comfort are the priorities, that addiction is rare, and that pain control should be initiated prior to the development of advanced hepatic encephalopathy. Because the frequency of encephalopathy may increase as patients approach death, inclusion of family members or caregivers early on in the care of these patients is critical. Early referral to hospice and palliative care services can be important resources for patients with ESLD and their family members or caregivers in managing pain and other distressing symptoms, and providing comfort.



An interesting finding revealed that patients in this study rated “having problems with sexual interest and activity” among the 10 most frequent symptoms. Inhibited sexual desire and decreased sexual activity have received little attention in this population. Previous studies focused on patients with stable liver disease (Simsek, Aslan, Akarsu, Koseoglu, & Esen, 2005) or patients pre and post liver transplant (Burra et al., 2010; Park & Villanueva, 2011; Sorrell & Brown, 2006), not on patients toward the end of life. According to Sorrell and Brown (2006) the effects of ESLD on sexual function is complex (p. 1473). They examined sexual dysfunction in patients with ESLD presenting for liver transplant evaluation (Sorrell & Brown, 2006). Women were found to have higher levels of sexual dysfunction than men, and the more severe the liver disease the lower the sexual frequency and satisfaction. However, in their study patients’ changes in sexual interest were not associated with their MELD score (Sorrell & Brown, 2006). Based on body changes and symptoms associated with ESLD that patients’ sexual interest and activity are compromised is no surprise. Therefore, it is critical for health care professionals to explore changes in sexuality and intimacy in this population toward the end of their life. Professionals should not make assumptions about these changes (Hordern & Street, 2007). To provide comprehensive care, professionals should routinely and explicitly initiate conversations about an individual’s or couple’s intimate relations, and encourage them to communicate their fears and concerns. To enhance sexual well-being, professionals should understand various forms of sexual expression and offer support and practical strategies, such as physical touch of any kind and expressions of love (Lamb, 2006).

The most important finding in our study is the amount of inter-individual and intra-individual variability on the MSAS over time. Despite a somewhat average trajectory of the group, PSYCH, PHYS, and CDI scores were labile between and within patients. Between patients the greatest range of variability was on the PHYS scale; within patients the greatest range was on the PSYCH scale. An interesting finding on symptom distress was reported by Davis, De-Nour, Shouval, and Nelmed (1998) who found that patients with minimal or no clinical symptoms from their liver disease experienced considerable amount of psychological distress. They measured psychological distress using the Brief Symptom Inventory (BSI) which is a 53-item questionnaire on psychological symptoms occurring in the preceding month. The amount of psychological distress experienced by patients may also be influenced by the etiology of the disease. Sigh, Gayowski, Wagener, and Marino (1997) found that patients with ESLD due to hepatitis C were more susceptible to psychological distress and depression than patients with other liver diseases. Due to the small sample in this study, the relationship between psychological distress and disease etiology was not explored.

Findings from our study and other studies speak to the importance of providing individualized care to address the specific psychological and physical symptom distress experienced by patients with ESLD at different points in their disease course. Health care professional should complete a detailed assessment of symptoms experienced by these patients at each clinic appointment. This assessment should use a multidimensional approach including presence, frequency, severity, and distress in developing and implementing symptom management strategies.

## Limitations

Although this study highlights the moderate level of distress experienced by outpatients with ESLD and their inter-individual and intra-individual variability, it has some limitations. First, the sample size was small. In addition, the sample did not include a comparison group (e.g, patients with hepatocellular carcinoma). Future research should include a larger and more ethnically diverse sample and use inferential statistics to explore variability in symptoms over time. Nevertheless, these findings emphasize the need to investigate the symptom frequency, severity, and distress experienced by patients with ESLD toward the end of life using a systematic approach to plan and design specific interventions. These interventions should be tailored to address the individual patient with ESLD based on the variability as well as the frequency, severity, and distress with which they experience individual symptoms.

## Implications for Practice and Research

Health care professionals should listen to and support patients with ESLD who are facing death and experience symptom distress. The level of global symptom distress (GDI) patients experienced in this study speaks to the importance of assessing which symptoms are experienced by individual patients over time. This assessment should include symptom frequency, severity, and how distressing symptoms are for patients. Addressing and intervening at individual symptoms may decrease the level of global symptom distress experienced by patients. In this study patients reported lack of energy, pain, difficulty sleeping, and feeling drowsy as the most frequent, severe, and distressing symptoms. Each of these symptoms is modifiable with the use of pharmacological and non-pharmacological interventions. Energy conserving behaviors by patients (e.g., naps) may be used to change the experience of lack of energy and feeling drowsy or better adapt to those experiences as the ESLD progresses. Therefore, it is important that health care professionals are educated in the use of interventions tailored to patients with ESLD and assist patients in receiving psychosocial support and effective pharmacological therapies. As appropriate, patients should be referred to clergy, psychologists, hospice and palliative care services. One of the goals of palliative care is to minimize symptoms and relieve suffering. Through assessment and early intervention of symptom distress in patients with ESLD, suffering may be decreased. Attention to prevention of symptom distress will shift the focus away from reacting to the disease as it progresses. This may provide patients and their family members or caregivers time to attend to what is most important in their lives and relationships.

Future research is needed that tests hypotheses related to the impact of psychological and physiological symptom distress on patients' quality of life at the end of life. With the information from such studies symptom management programs and palliative care interventions could be developed that are tailored for the individual and that optimize patients' well being as they are facing death. Such hypotheses may include the testing of whether or not inter-individual and intra-individual variability are related to personal characteristics and/or the etiology of ESLD. Other research needed may examine the concept of pain and the extent it is related to e.g., personal characteristics, etiology of ESLD, and disease severity. Including family members or caregivers in future research will be



important. Their quality of life will be affected due to burdensome and stressful physical and psychological experiences and challenges as the patient's disease progresses.

## Conclusion

Findings from this longitudinal study add to our understanding of the presence, frequency, severity, and distress of symptoms over time in patients with ESLD. This study also demonstrates the variability in psychological and physical symptom distress patients experience over time. Knowledge of these symptoms and the distress they cause are essential for health care professionals to effectively care for patients with ESLD toward the end of life.

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**Table 1**

## Characteristics of Patients with End-Stage Liver Disease (ESLD)

	<b>Patients (N=20)</b>
	<b>n (%)</b>
Sex	
Men	15 (75)
Women	5 (25)
Ethnicity	
Hispanic/Latino	3 (15)
Race	
White	15 (75)
African American	2 (10)
Multiracial	1 (5)
Unknown/Missing	2 (10)
Employment Status	
Disabled	14 (70)
Unemployed	3 (15)
Employed	3 (15)
Education level completed	
8 <sup>th</sup> grade or less	2 (10)
12 <sup>th</sup> grade or GED	4 (20)
Some college	11 (55)
College	3 (15)
Age, mean (SD)	59.0 (5.3)
	Range: 51 – 76
Reason for ESLD	
Hepatitis C	9 (45)
Alcoholic cirrhosis	5 (25)
Hepatitis C and alcoholic cirrhosis	2 (10)
Cryptogenic cirrhosis	2 (10)
Hepatitis B	1 (5)
Non-alcoholic steatohepatitis	1 (5)

Note. GED =General Education Development

**Table 2**

Presence of Symptoms as Reported by Patients with End-Stage Liver Disease

Variable	Patients <i>n</i> (%)
Pain	89 (94.7)
Lack of energy	87 (92.6)
Feeling drowsy	74 (78.7)
Difficulty sleeping	71 (75.5)
Difficulty concentrating	66 (70.2)
Lack of appetite	63 (67.0)
Feeling irritable	63 (67.0)
Itching	62 (66.0)
Dry mouth	61 (64.9)
Worrying	56 (59.6)
Nausea	55 (58.5)
Problems with sexual interest or activity	55 (58.5)
Swelling of arms or legs	54 (57.5)
Feeling bloated	52 (55.3)
Feeling sad	50 (53.2)
Numbness/tingling in hands and feet	46 (48.9)
Shortness of breath	44 (46.8)
Change in the way food tastes	43 (45.7)
Feeling nervous	43 (45.7)
Dizziness	41 (43.6)
Cough	40 (42.6)
Diarrhea	39 (41.5)
Changes in skin	36 (38.3)
I don't look like myself	34 (36.2)
Constipation	33 (35.1)
Problems with urination	32 (34.0)
Sweats	32 (34.0)
Vomiting	30 (31.9)
Difficulty swallowing	26 (27.7)
Weight loss	25 (26.6)
Hair loss	13 (13.8)
Mouth sores	12 (12.8)

*Note.* Table is sorted in descending relative frequency as indicated by the patient. Percentages and *n*'s reflect the total number of times across the study period a patient indicated a symptom was present.

**Table 3**  
 Ten Most Frequent, Severe and Distressing Symptoms Reported by Patients Across Time

Variable	Patients					
	Frequency <sup>a</sup>		Severity <sup>b</sup>		Distress <sup>c</sup>	
	n	M (SD)	n	M (SD)	n	M (SD)
Lack of energy	91	3.4 (1.1)	87	2.9 (1.1)	88	3.7 (1.5)
Pain	91	3.2 (1.1)	88	2.7 (1.1)	88	3.8 (1.4)
Difficulty sleeping	92	2.5 (1.6)	88	2.2 (1.5)	89	3.0 (2.0)
Feeling drowsy	91	2.3 (1.4)	87	2.1 (1.4)	88	2.8 (1.8)
Dry mouth	92	2.1 (1.7)	89	1.8 (1.6)	91	2.4 (2.1)
Difficulty concentrating	93	2.1 (1.6)	90	1.8 (1.4)	90	2.8 (2.1)
Itching	91	2.1 (1.7)	89	1.9 (1.6)	89	2.4 (2.0)
Swelling of arms or legs	91	1.9 (1.8)	89	1.7 (1.7)	89	2.2 (2.1)
Problems with sexual interest or activity	82	1.9 (1.9)				
Lack of appetite	91	1.8 (1.6)	85	1.6 (1.4)	86	2.2 (1.9)
Worrying			91	1.7 (1.6)	91	2.3 (2.1)

Note. Participant who indicated they were not experiencing a symptom were scored as a 0. Table is sorted in descending average frequency score. Average scores computed across all units of observation. M=mean, SD=standard deviation.

<sup>a</sup> Frequency scores range from 1=*Rarely* to 4=*Almost constantly*.

<sup>b</sup> Severity scores range from 1=*Slight* to 4=*Very severe*.

<sup>c</sup> Distress scores range from 1=*Not at all* to 5=*Very much*.



**Table 4**

Summary Scores on the Memorial Symptom Assessment Scale (MSAS) for each Time Point in Patients with End-Stage Liver Disease

Variable	Time	Patients	
		<i>n</i>	<i>M (SD)</i>
MSAS Global Distress Index (GDI)	Time 1	20	2.9 (0.4)
	Time 2	20	2.6 (0.8)
	Time 3	19	2.8 (0.6)
	Time 4	11	2.7 (0.7)
	Time 5	10	2.9 (0.8)
	Time 6	11	2.7 (1.0)
MSAS Psychological Symptom Scale (PSYCH)	Time 1	20	1.9 (1.2)
	Time 2	20	1.7 (1.4)
	Time 3	20	1.9 (1.3)
	Time 4	12	1.8 (1.4)
	Time 5	10	1.9 (1.3)
	Time 6	11	1.6 (1.3)
MSAS Physical Symptom Scale (PHYS)	Time 1	20	1.8 (0.7)
	Time 2	20	1.7 (0.9)
	Time 3	20	1.8 (0.9)
	Time 4	12	1.6 (1.2)
	Time 5	10	1.4 (0.8)
	Time 6	11	1.3 (0.8)
Total MSAS Score	Time 1	20	1.5 (0.7)
	Time 2	20	1.5 (0.8)
	Time 3	20	1.6 (0.8)
	Time 4	12	1.3 (1.0)
	Time 5	10	1.4 (0.8)
	Time 6	11	1.2 (0.7)

*Note.* MSAS Global Distress Index sample size for patients at Time 3 and 4 differs from sample size of other MSAS summary scores because certain participants did not answer certain items that make up the Global Distress Index at these time points. *M*=mean, *SD*=standard deviation.

**Table 5**

Between (averaged across time) and Within Patient with End-Stage Liver Disease Variability

Variable	Between patients		Within patient	
	<i>M (SD)</i>	Range	<i>M of SD (SD of SD)</i>	Range
MSAS Psychological Symptom Scale (PSYCH)	1.8 (1.3)	0.0 – 3.9	0.5 (0.4)	0.0 – 1.2
MSAS Physical Symptom Scale (PHYS)	1.7 (0.9)	0.0 – 4.0	0.4 (0.2)	0.1 – 0.8
MSAS Global Distress (GDI) Index	2.8 (0.7)	0.8 – 4.0	0.4 (0.2)	0.1 – 1.0
Total MSAS	1.4 (0.8)	0.2 – 3.3	0.3 (0.2)	0.0 – 0.6

Note. *M*=mean, *SD*=standard deviation.