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PROMIS computerised adaptive tests are dynamic instruments to measure health-related quality of life in patients with cirrhosis

J. S. Bajaj[*], **L. R. Thacker**[†], **J. B. Wade**[‡], **A. J. Sanyal**[*], **D. M. Heuman**[*], **R. K. Sterling**[*], **D. P. Gibson**[‡], **R. T. Stravitz**[*], **P. Puri**[*], **M. Fuchs**[*], **V. Luketic**[*], **N. Noble**[*], **M. White**[*], **D. Bell**[*], and **D. A. Revicki**[§]

[*]Division of Gastroenterology, Hepatology and Nutrition, Virginia Commonwealth University and McGuire VA Medical Center, Richmond, VA, USA

[†]Biostatistics, Virginia Commonwealth University and McGuire VA Medical Center, Richmond, VA, USA

[‡]Psychology, Virginia Commonwealth University and McGuire VA Medical Center, Richmond, VA, USA

[§]Department of Psychiatry, Georgetown University Medical Center and Center for Health Outcomes Research, United Biosource Corporation, Bethesda, MD, USA

Summary

Background—Cirrhotic patients have an impaired health-related quality of life (HRQOL), which is usually analysed using static paper-pencil questionnaires. The Patient Reported Outcomes Measurement Information System (PROMIS) computerised adaptive testing (CAT) are flexible, freely available, noncopyrighted, HRQOL instruments with US-based norms across 11 domains. CAT presents five to seven questions/domain depending on the patient's response, from large validated question banks. This provides brevity and precision equivalent to the entire question bank.

Aim—To evaluate PROMIS CAT tools against 'legacy instruments' for cirrhotics and their informal caregivers.

Methods—A total of 200 subjects: 100 cirrhotics (70 men, 53% decompensated) and 100 caregivers were administered the PROMIS and legacy instruments [Sickness Impact Profile (SIP), Beck depression/anxiety inventories, Pittsburgh Sleep-Quality Index (PSQI) and Epworth Sleepiness scale (ESS)] concurrently. Both legacy and PROMIS results for patients were compared with caregivers and US norms. These were also compared between compensated and decompensated patients. Preference for SIP or PROMIS was inquired of a selected group (n = 70, 50% patients). Test – retest reliability was assessed in another group of 20 patients.

Correspondence to: Dr J. S. Bajaj, Division of Gastroenterology, Hepatology and Nutrition, Virginia Commonwealth University and McGuire VA Medical Center, 1201 Broad Rock Boulevard, Richmond, VA 23249, USA. jsbajaj@vcu.edu.

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Results—Patients had significant impairment on all PROMIS domains apart from anger and anxiety compared with caregivers and US norms ($P < 0.02$ to <0.0001). Decompensated patients had significantly worse sleep, pain, social and physical function scores compared with compensated ones, similar to legacy instruments. There was a statistically significant correlation between PROMIS and their corresponding legacy instruments. The majority (71%) preferred PROMIS over SIP. PROMIS tools had significant test – retest reliability (ICC range 0.759–0.985) when administered 12 ± 6 days apart.

Conclusion—PROMIS computerised adaptive testing tools had significant concurrent and discriminant validity, test – retest reliability and subject preference for assessing HRQOL in cirrhotic patients.

Introduction

The impairment of quality of life in patients with cirrhosis is one of the most important issues that affect the well-being of the individual and their family.[1–5] The three major areas of health-related quality of life (HRQOL) – physical, psychological and social – are deeply affected in cirrhosis and have been shown to worsen with worsening cognition.[1, 6, 7] HRQOL can even predict mortality in patients with chronic liver disease.[8] However, the tools used to assess HRQOL are not standardised between studies.[9] Also, previously employed methods are static questionnaires that do not necessarily adapt to the patient's responses or are not specifically designed for liver disease.[2] In addition, some of the surveys recommended are copyrighted and do not have readily available normative data.[2, 7] The Sickness Impact Profile (SIP) is such an established HRQOL instrument which has been validated in cirrhosis and other chronic diseases.[10–12] Although it has good responsiveness and has been studied extensively in cirrhosis, the SIP is not routinely used due to its length and lack of norms.[12–15] As a result, the characterisation of HRQOL in cirrhosis is not performed routinely and an alternative approach is needed. A freely accessible, brief, but comprehensive method that could simplify the diagnosis of impaired HRQOL would increase the regular investigation of quality of life and encourage therapy to improve it.

The NIH-sponsored Patient Reported Outcomes Measurement Information System (PROMIS) tools are one such set of instruments.[16, 17] They have a dynamic and computerised adaptive measurement system (CAT), which offers a tailored yet comprehensive appraisal of several HRQOL domains. In the PROMIS system, each item has its own calibration in the overall HRQOL assessment.[18] The CAT also has the ability to reduce testing to within five to seven questions for a domain without loss of sensitivity or specificity of the response. This allows for brevity and precision instead of the lengthy, rigid and one-size-fits-all questionnaires that have been used previously. These tools are freely available at http://www.nihpromis.org and have extensive normative data that generate a report comparing the patient performance to the general US population and to someone of the patient's gender and age. This system, if validated in cirrhosis, would be a rapid and simple alternative to measure HRQOL in 11 domains, which would make investigation of HRQOL easier in practice and encourage treatments to improve it. The current study was undertaken to evaluate the PROMIS CAT to evaluate HRQOL in patients with cirrhosis

using their caregivers as controls and comparing the performance of PROMIS tools against key legacy instruments that ascertain HRQOL.

Methods

Consecutive patients with cirrhosis and their informal caregivers were enrolled prospectively from the hepatology clinics at Virginia Commonwealth University Medical Center and McGuire VA Medical Center. We excluded patients who were not able to give informed consent, did not have a caregiver available or those who were not familiar with the English language. Patients with hepatocellular cancer, those who were on disability before the diagnosis of cirrhosis and those with other significant end-stage organ diseases (congestive heart failure, chronic obstructive pulmonary disease requiring oxygen, on dialysis, non-HE psychiatric conditions requiring hospitalisation, those on antipsychotic and antiseizure medications and a current active cancer diagnosis) were also excluded. We chose to include caregivers in addition to the US normative sample to analyse the effect of confounding socio-economic factors in determining the outcomes of HRQOL testing as most caregivers share living space and lifestyles with the patients.[3] Patients with cirrhosis were divided into compensated and decompensated based on history of experiencing hepatic encephalopathy, variceal bleeding, spontaneous bacterial peritonitis or hepato-renal syndrome.

After written informed consent, the patients and their caregivers were interviewed separately and five validated questionnaires termed ‘legacy questionnaires’ SIP, Pittsburgh Sleep-Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Beck Depression and Anxiety Inventories] and PROMIS CAT were administered. A randomly selected group of patients and their caregivers were asked for their preference between SIP and the PROMIS CAT tools. They were asked to provide one reason for their stated preference. A random sample of 20 cirrhotic patients were administered the PROMIS twice within 15 days. We only included patients in whom there was no significant change in their cirrhosis condition or hospitalisation in between those two visits.

The legacy questionnaires that were used to study overall HRQOL, sleep and mood were:

(i) SIP for overall HRQOL assessment[10]: The SIP is a 136-part quality of life questionnaire that covers 12 different domains of daily functioning, which are sleep and rest, eating, work, home management, recreation and pastimes, ambulation, mobility, body care and movement, social interaction, alertness, emotional behaviour and communication.[10] Apart from a 12-dimension profile score and physical and psychosocial scores, a total score can be computed. Eating, recreation and pastimes, sleep and rest, and work are coded separately. Patients mark only items that relate to their health within 24 h and a high score indicates worse functioning. The SIP was chosen, as it is a disease nonspecific questionnaire (like PROMIS) that provides a comprehensive analysis of HRQOL and is validated in cirrhosis.[15] The short forms (SF-36 and SF-8) were not used, as their inquiry of HRQOL dimensions is limited compared with SIP. Also, as PROMIS tools are not specific to a disease, we did not use liver disease-specific questionnaires such as the Chronic Liver Disease Questionnaire (CLDQ) for comparison.[19] (ii) Mood inventories: The Beck Depression and Anxiety

Inventories were given to the patients and caregivers. The Beck Depression Inventory is a 21-part validated questionnaire on depression over the last 2 weeks.[20] A score <14 indicates normal mood, 14–19 is mild, 20–28 is moderate, whereas >29 indicates severe depression. The Beck Anxiety Inventory is also a 21-item questionnaire validated for anxiety over the last week; a score <9 is normal, whereas 10–18 reflects mild/moderate, 19–29 is moderate/severe and >30 is severe anxiety.[20, 21] (iii) Sleep questionnaires: The ESS and PSQI were administered. The ESS is a validated instrument to assess daytime sleepiness that ranges from a score of 0–24; 10 or higher indicates problem daytime sleepiness.[22] PSQI inquires about night-time sleep quality over the last month and a score >5 indicate poor sleep quality.[23]

The PROMIS CAT tools consist of the following 11 domains: (i) anger; (ii) anxiety; (iii) depression; (iv) fatigue; (v) pain-behaviour; (vi) pain-interference; (vii) physical function; (viii) satisfaction with discretionary social activities; (ix) satisfaction with social roles; (x) sleep disturbance; and (xi) sleep-related impairment. The patients are given CAT questions on a computer screen for each domain, and the scores are automatically calculated and stored.

Each item of the PROMIS tools has been developed individually using patients' representative of the 2000 US Census.[24] The resulting question pool varies between the domains. There are 29 questions each in the anger and anxiety domain, depression 28 questions, fatigue 95 questions, there are 39 questions in the pain-behaviour bank, 41 in the pain-interference domain, 124 in physical function, 27 questions in the sleep disturbance, 16 in the sleep impairment domain, 12 in the social impairment and 14 in social roles. The CAT presents a select group of questions out of these item pools for the subjects to answer (between 4 and 12 per domain). The CAT presents the first item in each domain and based on the response to that item, continues to present more items until it reaches a point where the responses satisfy the preset precision criteria of 80% reliability. Each question has five possible responses (never, rarely, sometimes, often or always) in 10 domains and six possible responses in the pain-behaviour domain (had no pain, never, rarely, sometimes, often or always). The CAT is tailored to the individual patient and can achieve comparable measurement using only a subset of the entire bank of items.[18]

The ultimate result is a *t*-score and standard deviation based on the standardised US population. The mean *t*-score is 50 and the standard deviation is 10. Importantly, there is no ‘total score’ for the PROMIS tools, but an individualised score for each domain. The scores provided for each domain are (i) total score, (ii) score compared with the general US population, (iii) score compared with patients in the same age group and (iv) score compared with persons of the same gender (Supplementary material). The scores are presented as either ‘worse than’ or ‘better than’ compared with the norms. Physical function, discretionary social activities and social roles are presented as ‘better than the population’, whereas the rest of the domains are presented as ‘worse than the population’. Therefore, a low score on physical function, discretionary social activities and social roles and a high score on the other domains implies worse HRQOL.

Statistical analysis

A comparison between the patients and caregivers was performed for all instruments using unpaired *t*-tests. The compensated cirrhotic patient group was compared with the decompensated patients for the legacy and the PROMIS measures using 95% confidence intervals and unpaired *t*-tests for assessing discriminant validity. PROMIS domain scores in the context of the US norms were also compared with respect to the patient and the caregiver groups using unpaired *t*-tests and ANOVA again to assess the ability to discriminate between patients and controls. As the CAT involves administration of different items depending on their initial response and also because a total score is not calculated, a Cronbach's alpha and factor analysis is not possible. Correlations between individual PROMIS domains and instruments pertaining to that domain were performed separately for patients and for caregivers using Pearson's correlations to evaluate concurrent validity. We also performed a stepwise regression analysis for each PROMIS domain using the following variables for each domain: age, gender, alcoholic aetiology, MELD score, medication use, compensated and decompensated status. In addition, legacy instruments pertinent to that domain were also included based on clinical and psychological judgment. For the mood domains (anger, anxiety and depression), the Beck inventories were used, whereas for fatigue the sleep instruments, Beck inventories, SIP recreation and pastimes were used. Physical function and the pain domains were regressed to SIP physical dimension, whereas PSQI, ESS and sleep and rest of the SIP were used to evaluate the sleep PROMIS domains. Social domains were tested using SIP recreation, and pastimes test – retest reliability was performed using the intraclass coefficients for each PROMIS domain. Time required to complete testing was compared.

Results

A total of 104 patients with cirrhosis and their caregivers were enrolled in the study; all completed the legacy instruments and 100 patients and caregivers completed the PROMIS CATs. The baseline demographics of the study population are shown in Table 1. The predominant aetiology of cirrhosis was chronic hepatitis C (44%), followed by non-alcoholic steato-hepatitis (23%), alcohol with hepatitis C (11%), alcohol alone (7%) and others (15%). Fifty-one (49%) were Veterans, whereas the rest had private insurance. Forty-five per cent of patients were recruited at the time of liver transplant evaluation. The majority (83%) were Caucasian, whereas 12% were African-American and 5% were Hispanic. The mean duration of cirrhosis diagnosis before the study was 8 ± 4 years. Fifty-three per cent of the cirrhotic patients were decompensated (44% had prior HE, 29% had ascites on therapy, 15% had prior variceal bleeding, 6% prior SBP, 6% prior hepato-renal syndrome and 1% hepatopulmonary syndrome). The median MELD score was 12 (range: 6–20). There was no significant difference in use of SSRI (8% vs. 12%, $P = 0.1$), other antidepressants (5% vs. 15%, $P = 0.07$), anti-anxiety medications (13% vs. 11%, $P = 0.8$), NSAIDS (3% vs. 15%, $P = 0.07$) or narcotics (25% vs. 11%, $P = 0.09$) between the decompensated and compensated groups. The mean relationship duration between caregivers and patients was 32 ± 14 years, and 77% were married partners [remaining:unmarried partners (12%), children (6%) or close friends (5%)]. Eighty-two percent shared living arrangements for a mean of 21 ± 16 years. There was a significantly

higher use of narcotics in patients compared with caregivers (Table 1), whereas the rest of the medication use was not statistically different.

Time and number of questions in PROMIS compared to legacy instruments

A median of six questions for anger, four for social role and social activity and five questions for the rest of the PROMIS domains were required to complete the CAT testing i.e. a median of 54 questions per patient. In contrast, the legacy instruments pose 205 questions for each patient. Correspondingly, the time required was significantly shorter for PROMIS in patients (10 ± 5 vs. 34 ± 11 min, $P < 0.0001$) and in caregivers (8 ± 4 vs. 25 ± 9 min, $P < 0.0001$).

Legacy instrument impairment within the patient group

The differences between the decompensated and compensated patients in total SIP%, physical, Sleep and Rest, Work and Eating domains were statistically significant, whereas the CI's for the psycho-social dimension and the Recreation and Pastimes domains of the SIP contained zero, i.e. were statistically similar (Table 2). The two patient groups' sleep indices (PSQI and ESS) were statistically similar as were the sleep-related domains of the PROMIS tools. The Beck Depression and Anxiety Inventory scores for the difference in the two patient groups were also similar.

PROMIS tests within the patient group

Paralleling this, two patient groups' emotional distress domains, anger, anxiety or depression using the PROMIS tools were statistically not significant. The PROMIS CAT tools demonstrated that the decompensated group was significantly more impaired on the discretionary social roles, social activities, physical function, pain-interference and pain-behaviour domains compared with the compensated patients (Table 2).

HRQOL impairment between patients and caregivers

Using the SIP, there was impairment across all domains in the patient group compared with their caregivers. Impairment was also observed in the sleep questionnaires and the two mood inventories (Table 1). Apart from anger and anxiety domains, patients with cirrhosis were significantly impaired compared with their caregivers on all other domains of the PROMIS tools (Table 3).

Comparison with US norms

There were no significant differences between caregivers compared with the general US population norms. In contrast, all of the patients' PROMIS scores were significantly impaired compared with the norms apart from the anger and anxiety domains (Supplementary Table S1).

Correlation between legacy instruments and PROMIS tools in patients

There was a significant correlation between the sleep impairment on PSQI with the PROMIS sleep impairment (r = 0.535) and PROMIS sleep disturbance ($r = 0.731$). A significant correlation was found between the physical domain of the SIP and PROMIS

pain-interference (r = 0.435), pain-behaviour (r = 0.364) and physical function (r = −0.679) scores. The Beck Depression Inventory was significantly correlated with the PROMIS depression (r = 0.585) and anxiety (r = 0.597) domains. This was also true for the Beck Anxiety Inventory, which was significantly correlated with the PROMIS anxiety (r = 0.647) and depression (r = 0.573) domains. A modestly significant correlation was also seen between the Sleep and Rest domain of the SIP and PROMIS sleep impairment (r = 0.324) and PROMIS sleep disturbance (r = 0.234) scores. There was no correlation between Epworth Sleepiness Scale and any of these instruments, including the SIP and PROMIS. This is probably because of ESS solely concentrates on daytime sleepiness, which may not have been an issue in our population.

Regression analysis of individual domains in PROMIS CAT in patients with cirrhosis

Each of the PROMIS domain scores were tested individually as outcomes with age, gender, alcoholic liver disease, MELD score, current medication use and legacy instruments relevant for those domains as the predictors (Supplementary Table S2).The results of the mood domains showed that the Beck Depression Inventory was the only significant predictor of the depression PROMIS domain, while it also predicted, along with Beck anxiety inventory, the anxiety domain. Interestingly, anger was only predicted by both Beck inventories, most likely because we did not specifically include an anger questionnaire in our legacy instruments.

Not surprisingly, the physical dimension of the SIP predicted the physical function, pain-interference and pain-behaviour and the recreation/pastimes domain of the SIP predicted social roles and disturbances. Decompensation was also associated with pain domains as well as sleep impairment (Supplementary Table S2).

Subject preferences

Thirty-five patients and 35 caregivers were randomly chosen to evaluate their preference for SIP or PROMIS measures. The majority in both groups (71% total; 69% of patients and 75% of caregivers) preferred PROMIS; the rest said they had no preference (25% of patients and 20% of caregivers) or preferred SIP (6% of patients and 5% of caregivers). Of the patients who preferred PROMIS, this preference was because it was briefer (36%), it had computerised interface (31%) and 1-week recall period (21%), whereas the remaining 12% did not have a specific reason for preferring it. The reasons that patients gave for preferring SIP were primarily their familiarity with the paper-pencil questionnaires (65%), whereas the remaining 35% who preferred SIP did not give a specific reason.

Test - retest reliability

A total of 20 patients with cirrhosis underwent the PROMIS tools 12 ± 6 days apart. There were no changes in the underlying condition of the patients during those visits. There was no significant difference in the test scores on any of the domains with high intra-class correlation coefficients ranging from 0.759 to 0.985 (Supplementary Table S3).

Discussion

Impairment of HRQOL in patients with cirrhosis is an important issue that needs to be considered during the clinical evaluation of these patients.[1] As this impairment is multi-faceted, and affected domains potentially differ between early and late-stage cirrhosis, an instrument that is capable of adapting to the patients' health status is needed.[1, 12] The study findings indicate that PROMIS domains parallel all legacy instruments pertinent to the study. The PROMIS CAT tools are dynamic assessment instruments that are tailored to the patient's health status, which is not seen in the currently available static paper-pencil instruments. We also found that HRQOL impairment on PROMIS domains were adversely affected in cirrhotic patients compared with caregivers, who acted as controls, on all domains except for anger and anxiety. The PROMIS measures as well as legacy instruments showed significant differences in physical function, pain as well as social roles domains of the HRQOL in decompensated patients compared with compensated ones. Most respondents preferred the PROMIS tools to SIP for HRQOL assessment, and these tools demonstrated good test – retest reliability.

With the prolongation of survival in patients with cirrhosis, the HRQOL impairments take centre-stage in the evaluation of these patients.[25] The multiple domains that are impacted in cirrhosis can not only alter patients' daily functioning but can also increase the financial and social burden they place on society and the medical system.[3–5, 7] HRQOL impairment is also associated with poor outcomes before and after transplant.[8, 26, 27] Therefore, a dynamic, freely available tool with readily interpretable results and normative values is needed to incorporate HRQOL assessment in the clinical evaluation of cirrhosis patients.

While a framework to identify the manifold aspects of distress in cirrhosis similar to that proposed for other gastrointestinal disorders is lacking, there is evidence that several of the components of HRQOL are impacted negatively in this condition.[28] Several instruments have been validated for use in cirrhosis, specifically the SIP and CLDQ.[10, 19, 29] The advantage of a simple tool like SF-36 is its brevity (36 questions) and extensive normative information; however, it is a static, generic instrument, and is not able to provide the depth of questioning due to its nonspecific nature and limited number of questions. Therefore, generic instruments such as SF-36 have given mixed results when used in cirrhotic patients.[2, 30–32] The SIP has been validated in cirrhosis.[7, 14] The SIP inquires about HRQOL over the last 24 h, which may minimise its ability to capture episodic, but troubling effects on HRQOL. Given the length of the SIP (136 questions), there is also a potentially significant patient burden associated with its administration. The CLDQ, is a simple, brief (29 questions) and freely available instrument that has good responsiveness in several stages of liver disease.[19, 29, 33] It has good validity in chronic liver disease, has been used in several countries and is also not copyrighted. However, its evaluation of the social and sleep disturbances is limited, and like other paper-pencil questionnaires, is a static instrument. We used SIP and not CLDQ in our study because of the SIP's higher coverage of social and behavioural domains and its disease non-specificity that replicates PROMIS tools.

This study shows that the PROMIS measures correlate well with the legacy instruments in the relevant domains. All PROMIS CAT tools that were available on the assessment centre

were used in this study as an exploratory analysis. Caregivers were also used as controls as we wanted to account for possible confounders such as living conditions and socio-economic status, because they were similar for patients and caregivers. The results indicate a significant impairment, not only between patients and the US norms but also between patients and caregivers. We found that there was no significant difference in anger and anxiety between the patients and caregivers, even when compared with respect to the US normative samples. This is interesting because anger issues have not been studied in patients with cirrhosis, whereas studies of anxiety have had mixed results between patients and caregivers.[34, 35] In our study, the Beck Anxiety Inventory scores did not differ between patients and their caregivers. Therefore, studies with PROMIS tools in cirrhosis would probably not benefit from including an anger domain, but anxiety may need to be further explored. Patients with cirrhosis were more likely to be depressed than their caregivers, which confirm prior observations.[36, 37] This difference was significant despite similar rate of use of antidepressants in both groups. Of interest, there was no significant difference in depression using either the Beck Depression Inventory or the PROMIS tools between compensated and decompensated cirrhotic patients. This was also not related to the antidepressant use which trended higher in the compensated group. These findings suggest that depression in these patients could potentially be related to their underlying disease aetiology, as the majority had hepatitis C and/or alcoholic cirrhosis or due to a cause unrelated to cirrhosis severity.[38]

An interesting observation was the severe impact on discretionary social activities and social roles in patients compared with caregivers and in decompensated patients compared with their compensated counterparts. This has been described before in the literature and seems to be related in our population to decompensation.[7] Prior studies have shown that even cirrhotics with cognitive impairment without obvious decompensation have difficulty with employment, driving and social roles.[39, 40] This was confirmed using PROMIS CAT tools. PROMIS tools were also able to confirm prior studies in which there was a restriction of physical function and more bodily pain in cirrhotics, especially in the decompensated patients.[41, 42] The pain questions in PROMIS tools do not specify physical or visceral pain, and therefore these findings could reflect the impaired neuro-muscular coordination and higher rates of abdominal pain in patients with decompensated cirrhosis.[19, 43]

The effect of sleep on HRQOL in patients with cirrhosis has been previously seen in this population with cirrhotic patients doing worse than caregivers in both the legacy and PROMIS CAT domains.[44, 45] We did not find any difference in PROMIS sleep domains or the PSQI and ESS between compensated and decompensated patients and there was an overall modest correlation between PROMIS and SIP sleep domains. This is probably due to the emphasis on daytime rest on the Sleep Rest domain compared with the night-sleep questions that are posed in PROMIS and PSQI. Also, the relatively low MELD range and the controlled symptoms of hepatic encephalopathy may be a factor in this lack of difference.

The validation of PROMIS tools in cirrhosis is important, because it can potentially create a secure online platform for clinicians to apply the CAT using nine domains (without anger and anxiety) in cirrhotic patients. The interface with its readily understandable report and

comparison with the US norms (supplementary Figure S1), can increase appreciation of the HRQOL abnormalities by both patients and clinicians. This could increase investigation of the underlying causes of impaired HRQOL in practice and encourage treatment to correct these issues.

The majority of patients preferred PROMIS tools over the SIP due to its brevity (median 54 questions compared with 136 in SIP), ability to capture events over the last week and due to its computerised interface. Patient preferences are important because a balance between the questionnaire length and comprehensiveness of the information that is collected is necessary to minimise respondent burden. It is also important to realise that the group who did not prefer PROMIS predominantly did so due to its computerised nature. Therefore, selection of the appropriate subject is important.

The PROMIS dataset is limited because it is not specifically tailored to a particular disease; therefore, we did not find anger and anxiety as measured by PROMIS to be helpful in cirrhosis. PROMIS CAT domains do not include inquiries about sexual dysfunction (this is under development at this time) and leg cramps specifically, which are important in patients with cirrhosis.[1] However, the current data shows that the PROMIS CAT tools have good concurrent validity, i.e. performance on the legacy instruments correlate strongly with the PROMIS tools, discriminant validity, i.e. performance differences in compensated and decompensated patients fall along expected domains and also correlate with legacy instrument differences and have good test – retest reliability in patients with cirrhosis. The study cohort has relatively advanced liver disease; therefore, generalisation to a cohort with earlier stages of liver disease may be limited.

We conclude that PROMIS CAT tools are dynamic and valid methods for assessment of HRQOL in cirrhosis which may be preferable to static paper-pencil questionnaires for their brevity, adaptability, lack of cost/copyrights, computerised interface and extensive normative comparison. It is likely that widespread use of the freely available and dynamic PROMIS could increase the inquiry into HRQOL in cirrhosis and potentially improve the quality of care that clinicians can provide their patients by targeting these issues.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1
Demographical and Legacy instrument comparison between patients and caregivers

	Patients (*n* = 100)	Caregivers (*n* = 100)	*P* value
Age	57.8 ± 6.7	51.6 ± 14.1	<**0.0001**
% Men	71	35	<**0.0001**
Years of education	13.2 ± 2.6	13.2 ± 2.5	0.968
Ethnicity (Caucasian/African-American, Hispanic)	81/11/8	84/10/6	0.824
Current medications			
SSRIs	13%	12.5%	0.161
Other antidepressants	10.5%	8.9%	0.726
Anti-anxiety	12.6%	5.6%	0.101
Opioids	18.9%	6.7%	**0.014**
NSAIDs	11.8%	22.1%	0.08
SIP scores (%)			
Total	19.9 ± 14.1	6.8 ± 10.0	<**0.0001**
Physical dimension	13.4 ± 13.5	3.66 ± 7.17	<**0.0001**
Psycho-social dimension	21.7 ± 25.1	9.3 ± 15.6	<**0.0001**
Work	53.0 ± 28.8	16.1 ± 28.0	<**0.0001**
Sleep and rest	32.9 ± 26.5	13.3 ± 17.0	<**0.0001**
Recreation and pastimes	27.5 ± 22.9	13.1 ± 18.9	<**0.0001**
Eating	6.23 ± 7.83	2.09 ± 6.47	<**0.0001**
Home management	24.9 ± 22.1	6.2 ± 12.2	<**0.0001**
Other legacy questionnaires			
Epworth Sleepiness Scale	9.85 ± 5.27	7.01 ± 4.42	<**0.0001**
Pittsburgh Sleep-Quality Index	8.91 ± 4.36	7.35 ± 4.37	**0.013**
Beck Depression Inventory	14.83 ± 9.56	10.40 ± 8.51	**0.001**
Beck Anxiety Inventory	12.4 ± 10.3	8.9 ± 10.1	**0.017**

SSRIs, selective serotonin reuptake inhibitors; SIP, Sickness Impact Profile; NSAID, non-steroidal anti-inflammatory drugs.

Bold text indicates significant differences.

Table 2
Comparison within the patient group on the basis of cirrhosis decompensation

	Decompensated patients (*n* = 53)	Compensated patients (*n* = 47)	95% CI for Difference (*t*-tests)
Legacy instruments			
Total SIP	23.2 ± 14.1	15.7 ± 13.2	**(2.2, 12.8)**
Physical dimension	16.7 ± 15.3	9.2 ± 9.5	**(2.6, 12.4)**
Sleep and rest	41.5 ± 28.1	22.0 ± 20.1	**(10.1, 28.9)**
Work	61.5 ± 22.1	41.6 ± 32.7	**(8.9, 30.9)**
Eating	7.9 ± 8.7	4.1 ± 6.2	**(0.9, 6.7)**
Psycho-social dimension	23.6 ± 23.7	19.6 ± 27.1	(−6.0, 14.0)
Recreation and pastime	31.2 ± 22.8	22.9 ± 22.6	(−0.5, 17.1)
Pittsburgh Sleep-Quality Index	9.1 ± 4.3	8.5 ± 4.5	(−1.1, 2.3)
Epworth Sleepiness Scale	10.4 ± 5.8	9.3 ± 4.5	(−0.9, 3.1)
Beck depression	15.4 ± 9.5	14.3 ± 9.7	(−2.6, 4.8)
Beck anxiety	13.0 ± 9.7	11.7 ± 11.2	(−.8, 5.4)
PROMIS tools			
Anger	52.6 ± 8.0	52.2 ± 9.1	(−2.9, 3.8)
Anxiety	53.9 ± 8.5	55.1 ± 7.3	(−4.2, 1.9)
Depression	53.1 ± 9.6	52.9 ± 8.7	(−3.3, 3.8)
Fatigue	59.2 ± 8.4	57.9 ± 7.4	(−1.8, 4.4)
Pain-behaviour	56.6 ± 6.3	52.1 ± 11.0	**(−7. 9, −1.1)**
Pain-interference	58.7 ± 6.6	55.3 ± 7.7	**(−6.2, −0.6)**
Physical function	38.0 ± 3.5	40.6 ± 5.5	**(−4.5, −0.8)**
Sleep disturbance	55.2 ± 11.0	55.7 ± 9.4	**(−4.5, 3.5)**
Sleep-related impairment	56.3 ± 8.1	55.7 ± 9.0	**(−2.8, 3.9)**
Discretionary social activities	42.6 ± 5.3	45.9 ± 6.7	**(−5.7, −0.9)**
Social roles	38.6 ± 5.9	43.0 ± 8.3	**(−7. 2, −1.5)**

SIP, Sickness Impact Profile; PROMIS, Patient Reported Outcomes Measurement Information System.

A high score on all legacy instruments indicate a worse quality of life. A low score on physical function, discretionary social activities and social roles and a high score on the rest of the domains implies worse quality of life. Bold text indicates significant differences.

Table 3
Comparison between PROMIS scores of patients and caregivers

Domain	Patient	Caregivers	*P* value
Anger	52.3 ± 8.5	52.5 ± 13.9	0.952
Anxiety	54.3 ± 8.0	54.4 ± 12.1	0.974
Depression	52.9 ± 9.1	48.6 ± 13.2	**0.018**
Fatigue	58.5 ± 7.9	48.5 ± 13.2	**<0.0001**
Pain-behaviour	54.0 ± 9.5	44.3 ± 19.8	**<0.0001**
Pain-interference	57.0 ± 9.8	44.4 ± 20.7	**<0.0001**
Physical function	39.2 ± 6.1	53.1 ± 14.6	**<0.0001**
Sleep disturbance	55.6 ± 10.2	50.2 ± 17.7	**0.020**
Sleep-related impairment	56.0 ± 8.4	47.2 ± 17.6	**<0.0001**
Discretionary social activities	44 ± 6.2	51.6 ± 14.8	**<0.0001**
Social roles	40.8 ± 7.4	53.6 ± 15.3	**<0.0001**

Patients had a significantly impaired HRQOL in all domains apart from anxiety and anger compared with their caregivers. A low score on physical function, discretionary social activities and social roles and a high score on the rest of the domains implies worse quality of life. Bold text indicates significant differences.