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## Time to embrace PROMIS-29 as the Standard Health-Related Quality of Life Instrument for Patients with Cirrhosis

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Cirrhosis is a common and serious illness characterized by a high burden of physical and psychological symptoms.(1, 2) Health-related quality of life (HRQOL) is often poor because of this symptom burden and represents a key unmet need for patients with cirrhosis. Efforts to characterize the depth and breadth of HRQOL deficits in patients with cirrhosis are limited by the lack of a standardized HRQOL screening tool. It's not that one doesn't exist—in fact, many have been studied in patients with cirrhosis(1, 3)—but what the hepatology field is lacking is *consensus* around a single instrument that balances breadth, depth, and pragmatism so that it can be widely used for patients with cirrhosis. Confusion around the “optimal” HRQOL tool has hampered incorporation of HRQOL measures in prospective cohorts and clinical trials, standardization of HRQOL reporting in publications, and uptake in clinical care.

### Why should we care about measuring HRQOL?

Beyond providing comprehensive evaluation of a patient's overall well-being, measuring HRQOL provides critical information for clinical decision-making that can inform screening recommendations and decisions to pursue or continue treatments. In observational studies, quantifying the range of HRQOL at baseline and the natural history of HRQOL over time can identify areas in need of drug development or other interventions to improve patients' well-being. In clinical trials, HRQOL assessment allows researchers to demonstrate holistic effects, expanding the impact of investigative therapeutics and allowing for patient-centered therapeutic label indications.

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## What makes an ideal HRQOL instrument?

The ideal HRQOL instrument is fast, free, flexible across disease severity and trajectories, and capable of capturing the full spectrum of the patient's lived experience without floor or ceiling effects. There is often a tension amongst experts about when to use disease-specific instruments developed for and within the affected population versus generic instruments developed for the general population. However, among patients with cirrhosis, studies have shown that generic instruments retain their performance.(4, 5)

## What HRQOL instruments have been studied in patients with cirrhosis?

Many instruments have been used to assess overall HRQOL in patients with cirrhosis. The simplest ask general questions. A commonly used visual analog scale (VAS) simply asks patients to rate how good or bad their health is on a scale of 0–100. Most instruments evaluate multiple domains of HRQOL such as physical, mental, and social well-being. These include the Short-Form 36 (and its shorter derivatives), Sickness Impact Profile (SIP), Chronic Liver Disease Questionnaire (CLDQ), EuroQol-5D, and Patient-Reported Outcomes Measurement Information System (PROMIS).(Table 1)

## PROMIS-29 is the optimal HRQOL instrument for research.

In this month's *Hepatology*, Dr. Archita Desai and her colleagues extend our understanding of PROMIS-29 in 4 ways with a cross-sectional study of 204 patients with chronic liver disease, 53% of whom had cirrhosis. First and simply put, patients like it. Second, it is quick to complete, beating out both SF-36 and CLDQ in completion time. Given prevalent fatigue and concentration deficits in concentration, efforts to minimize survey burden for patients with cirrhosis are critical for the feasibility of clinical trials. Third, the investigative team confirmed its validity and responsiveness to disease severity. Lastly and crucially, in contrast to SF-36 and CLDQ where floor and ceiling effects were common, there were none for PROMIS-29.

Further research will clarify the impact of PROMIS-29 for patients with cirrhosis. First, PROMIS-29 is reported in its component domains without single global HRQOL value. This can be challenging to interpret and report. However, by adding two questions about cognitive function - PROMIS-29+2 – which is important for patients with cirrhosis, it can be rendered into a health-state summary statistic called PROPr (range 0–1).(6) Second, given its cross-sectional design, this study did not assess the responsiveness of PROMIS-29 to clinical changes or interventions. Many HRQOL scales are predictive of poor outcomes but may not be responsive to therapeutic interventions.(7) Such change data are necessary to determine the minimum clinically important difference for PROMIS-29 among people with cirrhosis. These aims will be addressed with forthcoming data from the longitudinal cohort study of the NIH-funded Liver Cirrhosis Network ([NCT05740358](#)) and Transitional Liver Clinic ([NCT05733832](#)) and the PCORI-funded LIVE-SMART ([NCT05794555](#)), a randomized trial of lactulose and Tai-Chi, all of which utilize PROMIS-29+2.

## The future for HRQOL assessment in patients with cirrhosis

With these new data, we propose that the hepatology research community move forward with consensus around PROMIS-29 as the primary tool to measure HRQOL in patients with cirrhosis and chronic liver diseases in general. Of course, there is value in preserving a full range of tools to measure HRQOL, including common ones such as the SF-36 and CLDQ with which the PROMIS-29 had strong convergent validity. But investigators launching new studies should feel confident in their selection of PROMIS-29 as a valid tool that can capture the spectrum of HRQOL in this population. PROMIS-29 is also uniquely suited to pragmatic clinical trials which leverage the electronic health record for recruitment and follow-up. (8) PROMIS measures, including PROMIS-29 and PROPr, have been available in EPIC electronic health record software since 2012. Furthermore, we anticipate that consensus around a single optimal HRQOL metric will reduce ambiguity about the importance of assessing HRQOL and encourage more studies to include HRQOL as an endpoint in studies involving patients with cirrhosis and chronic liver disease.

### Conclusion

The aims of research seeking to enrich the lives of patients with cirrhosis are best supported by consensus around a HRQOL metric. As supported by these data from Desai and her team, patients prefer PROMIS-29—and so should researchers.

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**Table 1:** Common Health-Related Quality of Life Instruments Used in Studies of Patients with Cirrhosis

Instrument	Items	Domains	Scoring	Time (in minutes)	Cost
<b>PROMIS-29, PROMIS-29+2</b>	<b>29 31</b>	Physical function, Anxiety, Depression, Fatigue, Sleep, Social roles/activities, Pain interference, Pain Intensity; <i>Cognitive Function (+2)</i>	0–100 T-scores (compared to general US population) for each domain. The 29+2 can render a 0–100 summary score.	5.4±3.0	Free
<b>SF-36</b>	<b>36</b>	Physical function, Role limitations due to physical function, Emotional well-being, Role limitations due to emotional function, energy/fatigue, social functioning, pain, general health	0–100 scores for each domain or the physical or mental components, calibrated where 50 is the average.	6.7±3.3	Free version available
<b>Chronic Liver Disease Questionnaire</b>	<b>29</b>	Fatigue, Activity, Emotional function, abdominal symptoms, systemic symptoms, worry	6–42 overall with each of the six domains scored 1–7	6.5±5.2	License required
<b>Sickness Impact Profile</b>	<b>136</b>	Sleep and rest, Eating, work, home management, recreation, ambulation, mobility, body care and movement, social interaction, emotional behavior, and communication.	0–100 overall and for each domain	30	License required
<b>SF-Liver Disease Quality of Life</b>	<b>72</b>	Sexual dysfunction, stigma, hopelessness, sleep, concentration/memory, symptoms of liver disease, distress, loneliness, and SF-36	0–100 overall and for each component (LDQOL and SF-36 components)	18±9(9)	Free
<b>Eq5D-3L or 5L</b>	<b>15–25</b>	Mobility, Self-care, Usual activities, Pain / discomfort, Anxiety / Depression	0–100 overall	<3	License required, cost according to purpose
<b>Visual Analog Scale</b>	<b>1</b>	General health-related quality of life	0–100 overall	<1	Free