Current Hepatology Reports (2018) 17:15–21
https://doi.org/10.1007/s11901-018-0385-y

MANAGEMENT OF CIRRHOTIC PATIENT (A CARDENAS AND P TANDON, SECTION EDITORS)

Quality of Life in Patients with Cirrhosis—Measurement and Clinical Impact

Zobair M. Younossi[1,2] · Linda Henry[3]

Published online: 7 February 2018

Abstract

Purpose of the Review As understanding of liver disease progression to cirrhosis has expanded, there has also been an acceleration in clinical trials and treatment options for the different underlying causes of cirrhosis to include chronic viral hepatitis, alcoholic and non-alcoholic fatty liver disease. It is imperative that healthcare practitioners fully appreciate the impact of liver disease and treatment from the patients' and society perspective.

Recent Findings An important aspect of patient-reported outcomes (PROs) is assessment of health-related quality of life (HRQL) completed using generic or disease-specific instruments. In the past decades, substantial evidence has been complied that demonstrates development of cirrhosis which has a significant negative impact on a patients' HRQL while effective treatment leads to significant gains in HRQL especially for patients with decompensated cirrhosis.

Summary Clinicians and clinical investigators must understand the importance of PROs for inclusion in clinical trials to fully assess the impact of cirrhosis on patients and the society.

Keywords SF-36 · CLDQ · CLDQ-HCV · CLDQ-NAFLD · Treatment · Decompensated cirrhosis

Introduction

Liver disease is a major cause of mortality and morbidity worldwide and the 12th leading cause of death in the USA [1]. In the USA and worldwide, the main causes of advanced liver disease or cirrhosis are alcohol-related liver disease, non-alcoholic steatohepatitis (NASH), and viral hepatitis [1].

Cirrhosis has had a tremendous clinical impact as a result of its complications including ascites, esophageal varices, liver failure, hepatic encephalopathy, hepatocellular carcinoma, and liver-related death. However, cirrhosis also has a negative impact on patient-reported outcomes (PROs) and on the resource utilization (the economic impact) [2••].

Measurement Tools for Quality of Life (Table 1)

In our previous work, we outlined the effect of cirrhosis and its associated complications on patients' health-related quality of life (HRQL) as well as discussing the different measurement tools used to measure HRQL [10]. Briefly, HRQL is defined as a "broad multidimensional concept that includes subjective evaluations of both positive and negative aspects of life" and are reports that come directly from the patient about the status of their health condition without amendment or interpretation by a clinician or anyone else [11].

There has been substantial investigation of HRQL assessment in patients with chronic liver disease. In this context, HRQL is influenced by the type and severity of liver disease [3•, 11–15]. In fact, patients with chronic hepatitis C have the most profound HRQL impairment while those with chronic hepatitis B have less impairment. Furthermore, patients with advanced cirrhosis experience severe impairment of HRQL impairments. The net overall effect is significant impairment of HRQL, whether due to mental impairment or limitations

This article is part of the Topical Collection on *Management of Cirrhotic Patient*

✉ Zobair M. Younossi
zobair.younossi@inova.org

[1] Center for Liver Diseases, Department of Medicine, Inova Fairfax Hospital, Falls Church, VA, USA

[2] Betty and Guy Beatty Center for Integrated Research, Inova Health System, Claude Moore Health Education and Research Building, 3300 Gallows Road, Falls Church, VA 22042, USA

[3] Center for Outcomes Research in Liver Disease, Washington, DC, USA

Table 1 Measurement tools used to measure patient-reported outcomes in patients with cirrhosis [3•, 4, 5••, 6••, 7••–9]

Name of tool	Health domains measured	Number of items	Strengths and limitations	Generic or disease-specific	How administered
SF-36	8 domains measuring functional health and well-being: general health, vitality, role emotional, role physical, social well-being, mental health, and physical functioning. Two summary scales of physical composite and mental composite scores	36 items	Strengths • Most widely used tool worldwide. • Established population norms for comparison. Limitations • It is a generic tool so may not be sensitive to disease-specific PRO impairments. • Asks for recall of how the patient is feeling over pat/week/month therefore depends on patients' accurate recall.	Generic-general health	Self-administered or can be done in person or over the telephone. Takes 5 to 10 min to complete.
Chronic Liver Disease Questionnaire (CLDQ)	Measures 4 domains: activity and energy, emotional, worry, systemic and assess HRQOL in chronic liver disease	29 items using Likert scale of 1–7 with higher scores meaning a better HRQL	Strengths • Widely used and validated tool to measure health-related quality of life in patients with chronic liver disease • Translated into many languages-see website (www.cldq.org)	Disease-specific	Paper and pencil—self-administered
Chronic Liver Disease Questionnaire-Hepatitis C Virus (CLDQ-HCV)	Measures 4 domains: activity and energy, emotional, worry, systemic and assess HRQOL in chronic liver disease and specifically in patients with HCV	29 items using a Likert scale of 1–7 with higher scores meaning a better HRQL but questions have been modified to be pertinent to patients with HCV	Strengths • Valid and reliable tool that was specifically designed to measure disease-specific health-related quality of life (HRQL) for patients living with chronic hepatitis C (CH-C)	Disease-specific	Paper and pencil—self administered
Chronic Liver Disease Questionnaire-Non-alcoholic Fatty Liver Disease/Non-alcoholic Steatohepatitis (CLDQ-NAFLD/NASH	Measure six domains: abdominal symptoms, activity, emotional, fatigue, systemic symptoms, and worry.	36 items—29 items from original CLDQ and 7 new items to reflect a greater influence of fatigue in the NAFLD population	Strengths • High correlations between presumably related domains of CLDQ-NAFLD and the widely used and extensively validated SF-36 • Female patients, patients of older age and patients with comorbidities were found to have lower scores in expected domains to include physical activity and depression. Limitations: • Further validation is needed in patients with NAFLD/NASH cirrhosis especially decompensated cirrhosis	Disease-specific	Paper and pencil—self administered
Primary Sclerosing Cholangitis Patient Reported Outcomes Tool	The severity of specific PSC symptoms (abdominal pain or discomfort, itching, fatigue, jaundice, difficulty	A 42-item instrument that contains 2 modules: symptoms and impact of symptoms	Strengths • Has good discriminatory power to differentiate patients according to the	Disease-specific	Self-administered via paper and pencil or available through an online domain

Table 1 (continued)

Name of tool	Health domains measured	Number of items	Strengths and limitations	Generic or disease-specific	How administered
(The PSC PRO)	with concentration, nausea, fever, chills, and sweats) are scored on a 0–10 scale with a 24-h recall period. The impact of PSC on their daily life—physical function, activities of daily living, work productivity, role function, emotional impact, social/leisure impact, and quality of life. Higher scores reflect worse health status.		presence and severity of cirrhosis and history of depression • The proposed minimally clinically important difference (MCID) for PSC PRO scores are suggested to be 4 for symptoms and 0.3 for the impact of symptoms. Limitations: • A newly developed tool so needs further validation in a larger population • Has not been well validated in patients with IBD.		
Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F)	Developed to measure four primary QOL domains: physical well-being, social/family well-being, emotional well-being, and functional well-being and the effect of fatigue on these domains	16 questions scores on a 0–4 likert scale with higher scores indicating fatigue interference with activity asked about.	Strengths • Written at the 4th grade-reading level, • Is specifically formatted for ease of self-administration • Takes a 4 to 6 min to complete • Validated for use with special populations such as with the elderly and those living in rural areas • Appropriate for use in patients with a variety of chronic health conditions, and in the general population Limitations • Fee based for other than English versions • Interviewer training is needed to minimize bias to patient responses.	Disease-specific	• Patient self-administration, either on paper or direct to computer. • Face-to-face or telephone interview; however, interview administration is appropriate with adequate training of interviewers to minimize bias to patient responses.
Work Productivity Activity Impairment-Specific Health Problem (WPAI-SHP)	Evaluates impairment in patients' daily activities and work productivity associated with a specific health problem	-There are 6 questions—5 for work activity and 1 for activity of daily living. Patients are asked to think about how their disease state impacts their life when answering the questions. Work productivity is divided into 2 parts—presenteeism how many hours during a work day are patients not productive as a result of their specific disease and absenteeism-how many days of work are missed as a result of ones' specific disease	Strengths • Tool able to capture lost productivity that can be used when determining economic impact of disease states. • The WPAI has been translated into more than 100 languages through a harmonization process consisting of several independent translations, back translations, expert review of the back translation, and local review by users • Free to use Limitations • The recall period is 7 days	Disease-specific	• Paper and pencil • Have developed a web based interactive platform

Table 1 (continued)

Name of tool	Health domains measured	Number of items	Strengths and limitations	Generic or disease-specific	How administered
		-Higher scores indicate poorer health status and impairment-range from 0 to 1	• Interviewer administration is associated with better accuracy of responses		

Adapted from Younossi Z. Patient Reported Outcomes for Patients with Chronic Liver Disease. CGH, 2018

affecting patients' ability to perform an activity of daily living such as HCV associated fatigue, cirrhosis associated muscle cramps and pruritus as well as the complications of cirrhosis, namely hepatic encephalopathy and ascites, which have their own unique impact on HRQL. In fact, ascites, hepatic encephalopathy, and hyponatremia have been found to be an independent predictor of severe impairment of HRQL possibly as a result of patients' acknowledgement of their liver disease progression [16–20, 21•, 22]. However, treatment of these complications leads to a positive impact on a patient's HRQL. In fact, the ultimate treatment of cirrhosis is liver transplantation which dramatically improves HRQL [19]. In this context, improvement in HRQL post liver transplantation is so profound that it can easily be captured with both a generic and a disease-specific HRQL instrument [19, 21•, 22].

As previously discussed, it is important to understand the different HRQL measurement tools and their properties that have been used for patients with liver disease [10]. The most commonly used tools to assess HRQL in patients with liver disease and cirrhosis include disease-specific tools: The Chronic Liver Disease Questionnaire (CLDQ) or the Liver Disease Quality of Life tool (LDQOL), and generic tools which include the widely used HRQL tool, the SF-36 and Sickness Impact Profile (SIP) [3•, 4, 23, 24].

As our understanding of the impact of different causes of liver disease on HRQL has deepened, more disease-specific instruments for types of CLD are being developed. In this context, recognizing that chronic hepatitis C (CH-C) is the most common cause of cirrhosis in the USA and the western world [1], a validated HCV-specific HRQL instrument (CLDQ-HCV) was developed and validated to measure the specific impact of HCV on patients' quality of life [5••]. In addition, due to the growing prevalence of NAFLD and NASH (global prevalence rate is 25%), NASH-NAFLD-specific CLDQ (CLDQ NASH-NAFLD) was also developed and validated [6••, 25]. Furthermore, clinical trials of new treatment regimens for Primary Sclerosing Cholangitis (PSC) have necessitated the development and validation of PSC PRO [7••].

Cirrhosis and Quality of Life for Associated Liver Diseases

A number of these instruments have been extensively used to assess HRQL in patients with HCV, HBV, and NASH as well as complication of cirrhosis (ascites, hepatic encephalopathy, and liver transplantation) [26•]. In this context, the recent approval of interferon-free and ribavirin free regimens has provided patients with a shorter time of treatment with very highly efficacious, safe, and cost-effective therapies but also significant increase in their health-related quality of life [27•, 28••, 29••]. In addition, the new treatments have been shown to improve patients HRQL and other Patient Reported

Outcomes (PROs) as early as 4 weeks into treatment [27•, 28••, 30]. In fact, these PRO improvements were also reported in patients with compensated and decompensated cirrhosis [27•]. Baseline HRQL (measured by the generic SF-36 and the disease-specific CLDQ-HCV) impairment has been found to be profound in patients with cirrhosis especially decompensated cirrhosis in the areas of activity, energy, vitality, and fatigue (measured with the FACIT-F). These noted decreases were present even after adjustment for baseline demographic disparities of the cirrhotic cohort. However, on average, cirrhotic patients PRO's increased about 10% across the majority of domains especially those that were most affected prior to treatment [27•]. In fact, patients with decompensated cirrhosis had the most significant gains after treatment though it is important to note that all patients who reached SVR had significant HRQL improvement as well but also that the gains obtained by patients with cirrhosis were similar or better than those gained by non-cirrhotics [30, 31].

In addition to HCV, there are HRQL studies of patients with NAFLD and NASH [32••, 33]. In fact, NAFLD patients show decrements in their HRQL when compared to the general population but is especially evident for patients with NAFLD associated cirrhosis. In one particular study which used the SF-36 to measure HRQL, investigators found that the domains most affected included role performance, vitality, role emotional, and the physical composite score, suggesting physical functioning in patients with NAFLD cirrhosis is profoundly affected [33]. Other studies have had similar findings [32••, 34]. There are no FDA approved treatments for NAFLD and NASH at this time; however, there are new medical treatments currently in development, and as they come to market, attention must be paid to how the treatments affect the patients' quality of life when judging the true effectiveness of the therapy [35].

Chronic hepatitis B virus (CH-B), primary biliary cholangitis (PBC), and primary sclerosing cholangitis (PSC) also lead to cirrhosis and cause significant decrements in HRQL. CH-B patients seem to have better HRQL than patients with CH-C and PBC. However, CH-B patients' overall utility scores are lower than population norms, whereas those with CH-C or PBC/PSC reported significantly lower HRQL scores than population norms while having cirrhosis was a predictive for decreased HRQL scores regardless of etiology of liver disease [36, 37•, 38•].

Importance to Clinicians

The most important lesson that clinicians should take away from HRQL studies of patients with chronic liver disease is that these patients not only face poor prognosis and survival but suffer from severe impairment of their HRQL. In this context, symptoms of cirrhosis (fatigue, muscle cramps, hepatic encephalopathy, ascites) can drive the impairment in HRQL and can cause tremendous negative impact on patients' functioning. Knowing this, treatment of cirrhosis should not just focus on clinical outcomes but also should include interventions that will improve patients' PROs. It is only with this comprehensive approach to patients with cirrhosis that we can capture the full impact of their disease and the impact of its treatment on PROs. Furthermore, focusing on HRQL as an outcome can build a bridge between disciplines as well as developing relationships between social, mental, and medical services, all health care entities which can help improve PRO's while at the same time meeting the Healthy People 2020 central public health campaign of improving people's quality of life (https://www.cdc.gov/hrqol/concept.htm).

Conclusion

Healthcare practitioners understanding of the impact of liver disease, cirrhosis, and treatment on patients' health-related quality of life has increased due to the development of liver disease-specific quality of life tools. Specifically, we now know that regardless of the cause of cirrhosis, cirrhosis is associated with a significant decline in quality of life especially for those that develop decompensated cirrhosis. However, treatment of the underlying cause of cirrhosis leads to substantial increase in the patients' health-related quality of life especially for those with decompensated cirrhosis. As such, assessment of quality of life should be a routine part of the clinical trials, as well as findings used in the clinical environment when treating patients with cirrhosis.

Compliance with Ethical Standards

Conflict of Interest Zobair Younossi and Linda Henry each declare no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. Younossi ZM, Stepanova M, Afendy M, Fang Y, Younossi Y, Mir H, et al. Changes in the prevalence of the most common causes of chronic liver diseases in the United States from 1988 to 2008. Clin Gastroenterol Hepatol. 2011;9(6):524–530.e1; quiz e60. https://doi.org/10.1016/j.cgh.2011.03.020.
2.•• Younossi ZM, Hepatitis C. Infection: a systemic disease. Clin Liver Dis. 2017;21(3):449–53. https://doi.org/10.1016/j.cld.2017.03.001.

A review of the impact of HCV to include clinically, quality of life, work productivity and economically as well as the impact of treatment on all aspects of HCV.

3.• Younossi ZM, Guyatt G, Kiwia M, et al. Development of a disease specific questionnaire to measure health related quality of life in patients with chronic liver disease. Gut. 1999;45(**2**):295–300. https://doi.org/10.1136/gut.45.2.295. **This study is the seminal work for the development of a disease specific tool to measure health related quality of life in patients with chronic liver disease.**

4. Ware JE, Kosinski M. Interpreting SF-36 summary health measures: a response. Qual Life Res. 2001;10(5):405–13; discussion 415-20. https://doi.org/10.1023/A:1012588218728.

5.•• Younossi ZM, Stepanova M, Henry L. Performance and validation of chronic liver disease questionnaire-hepatitis C version (CLDQ-HCV) in clinical trials of patients with chronic hepatitis C. Value Health. 2016;19(5):544–51. https://doi.org/10.1016/j.jval.2016.02.005. **A continuation of Younossi et al's work in developing disease specific tools that are spefically developed to measure the impact of HCV.**

6.•• Younossi ZM, Stepanova M, Henry L, Racila A, Lam B, Pham HT, et al. A disease-specific quality of life instrument for non-alcoholic fatty liver disease and non-alcoholic steatohepatitis: CLDQ-NAFLD. Liver Int. 2017;37(8):1209–18. https://doi.org/10.1111/liv.13391. **A continuation of Younossi et al's work in developing disease specific tools that are spefically developed to measure the impact of NAFLD.**

7.•• Younossi ZM, Afendy A, Stepanova M, Racila A, Nader F, Gomel R, et al. Development and validation of a primary sclerosing cholangitis (PSC) specific patient-reported outcome (PRO) instrument. Hepatology. 2017. https://doi.org/10.1002/hep.29664. **A continuation of Younossi et al's work in developing disease specific tools that are spefically developed to measure the impact of PSC.**

8. Webster K, Odom L, Peterman A, et al. The functional assessment of chronic illness therapy (FACIT) measurement system: validation of version 4 of the core questionnaire. Qual Life Res. 1999;8(7):604.

9. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. PharmacoEconomics. 1993;4(5):353–65. https://doi.org/10.2165/00019053-199304050-00006.

10. Younossi ZM, Henry L. Quality of life issues for patients with cirrhosis (Book Chapter). In Keaveny A, Cárdenas A, editors. Complications of cirrhosis: evaluation and management. Springer Publishing, Cham. 2015;323–336.

11. Centers for Disease Control- Health Related Quality of Life. Obtained from the world wide web at http://www.cdc.gov/HRQoL/concept.htm. Last accessed on 31 Aug 2017.

12. Younossi ZM, McCormick M, Price LL, Boparai N, Farquhar L, Henderson JM, et al. Impact of liver transplantation on health-related quality of life. Liver Transpl. 2000;6(6):779–83. https://doi.org/10.1053/jlts.2000.18499.

13. Martin LM, Sheridan MJ, Younossi ZM. The impact of liver disease on health-related quality of life: a review of the literature. Curr Gastroenterol Rep. 2002;4(1):79–83. https://doi.org/10.1007/s11894-002-0041-z.

14. Younossi ZM, Boparai N, McCormick M, Price LL, Guyatt G. Assessment of utilities and health-related quality of life in patients with chronic liver disease. Am J Gastroenterol. 2009;96(2):579–83.

15. Younossi ZM, Boparai N, Price LL, Kiwi ML, McCormick M, Guyatt G. Health-related quality of life in chronic liver disease: the impact of type and severity of disease. Am J Gastroenterol. 2001;96(7):2199–205. https://doi.org/10.1111/j.1572-0241.2001.03956.x.

16. Afendy A, Kallman JB, Stepanova M, Younoszai Z, Aquino RD, Bianchi G, et al. Predictors of health-related quality of life in patients with chronic liver disease. Aliment Pharmacol Ther. 2009;30(5):469–76. https://doi.org/10.1111/j.1365-2036.2009.04061.x.

17. Solà E, Watson H, Graupera I, Turón F, Barreto R, Rodríguez E, et al. Factors related to quality of life in patients with cirrhosis and ascites: relevance of serum sodium concentration and leg edema. J Hepatol. 2012;57(6):1199–206. https://doi.org/10.1016/j.jhep.2012.07.020.

18. Les I, Doval E, Flavià M, Jacas C, Cárdenas G, Esteban R, et al. Quality of life in cirrhosis is related to potentially treatable factors. Eur J Gastroenterol Hepatol. 2010;22(2):221–7. https://doi.org/10.1097/MEG.0b013e3283319975.

19. Two R, Verjee-Lorenz A, Clayson D, Dalal M, Grotzinger K, Younossi ZM. A methodology for successfully producing global translations of patient reported outcome measures for use in multiple countries. Value Health. 2010;13(1):128–31. https://doi.org/10.1111/j.1524-4733.2009.00585.x.

20. Loria A, Escheik C, Gerber NL, Younossi ZM. Quality of life in cirrhosis. Curr Gastroenterol Rep. 2013;15(1):301. https://doi.org/10.1007/s11894-012-0301-5.

21.• Loria A, Doyle K, Weinstein AA, Winter P, Escheik C, Price J, Wang L, Birerdinc A, Baranova A, Gerber L, Younossi ZM. Multiple factors predict physical performance in people with chronic liver disease. Am J Phys Rehabil. 2014;93(6):472–476. **A study that sought to determine the predictors of the physical functioning of patients with CLD as this is area that is most effected by any cause of CLD. Findings demonstrated that Poor physical performance is associated with physiologic, metabolic, and inflammatory abnormalities in subjects with nonalcoholic fatty liver disease and hepatitis C virus.**

22. Younossi ZM. Chronic liver disease and health-related quality of life. Gastroenterology. 2001;120(1):305–7. https://doi.org/10.1053/gast.2001.22073.

23. Gralnek IM, Hays RD, Kilbourne A, Rosen HR, Keeffe EB, Artinian L, et al. Development and evaluation of the liver disease quality of life instrument in persons with advanced, chronic liver disease—the LDQOL 1.0. Am J Gastroenterol. 2000;95(12):3552–65. https://doi.org/10.1111/j.1572-0241.2000.03375.x.

24. Bergner M, Bobbitt RA, Carter WB, Gilson BS. The sickness impact profile: development and final revision of a health status measure. Med Care. 1981;19(8):787–805. https://doi.org/10.1097/00005650-198108000-00001.

25. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease—meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology. 2016;64(1):73–84. https://doi.org/10.1002/hep.28431.

26.• Bureau C, Adebayo D, Chalret de Rieu M, Elkrief L, Valla D, Peck-Radosavljevic M, et al. Alfapump® system vs. large volume paracentesis for refractory ascites: a multicenter randomized controlled study. J Hepatol. 2017;67(5):940–9. https://doi.org/10.1016/j.jhep.2017.06.010. **This study highlights the positive impact of treatment on patients with decompensated cirrhosis.**

27.• Younossi ZM, Birerdinc A, Henry L. Hepatitis C infection: a multi-faceted systemic disease with clinical, patient reported and economic consequences. J Hepatol. 2016;65(1 Suppl):S109–19. https://doi.org/10.1016/j.jhep.2016.07.005. **A comprehensive review of the spectrum of the impact of HCV on patients and society.**

28.•• Younossi ZM, Stepanova M, Feld J, Zeuzem S, Sulkowski M, Foster GR, et al. Sofosbuvir and velpatasvir combination improves patient-reported outcomes for patients with HCV infection, without or with compensated or decompensated cirrhosis. Clin Gastroenterol Hepatol. 2017;15(3):421–430.e6. https://doi.org/10.1016/j.cgh.2016.10.037. **This study highlights the positive impact of treatment on patients with decompensated cirrhosis.**

29.•• Younossi ZM, Stepanova M, Nader F, Lam B, Hunt S. The patient's journey with chronic hepatitis C from interferon plus ribavirin to interferon- and ribavirin-free regimens: a study of health-related quality of life. Aliment Pharmacol Ther. 2015;42(3):286–95. https://doi.org/10.1111/apt.13269. **This study highlights the positive impact of the new treatment regimens with high "cure" rates on patients with HCV.**

30. Younossi ZM, Stepanova M, Nader F, Jacobson IM, Gane E, Nelson D, et al. Patient-reported outcomes in chronic hepatitis C patients with cirrhosis treated with sofosbuvir-containing regimens. Hepatology. 2014;59(6):2161–9. https://doi.org/10.1002/hep.27161.

31. Younossi ZM, Stepanova M, Charlton M, Curry MP, O'Leary JG, Brown RS, et al. Patient-reported outcomes with sofosbuvir and velpatasvir with or without ribavirin for hepatitis C virus-related decompensated cirrhosis: an exploratory analysis from the randomised, open-label ASTRAL-4 phase 3 trial. Lancet Gastroenterol Hepatol. 2016;1(2):122–32. https://doi.org/10.1016/S2468-1253(16)30009-7.

32.•• Golabi P, Otgonsuren M, Cable R, Felix S, Koenig A, Sayiner M, et al. Non-alcoholic fatty liver disease (NAFLD) is associated with impairment of health related quality of life (HRQOL). Health Qual Life Outcomes. 2016;14(1):18. https://doi.org/10.1186/s12955-016-0420-z. **One of the first studies that quantified the impact of NAFLD on patients reported quality of life.**

33. Sayiner M, Stepanova M, Pham H, Noor B, Walters M, Younossi ZM. Assessment of health utilities and quality of life in patients with non-alcoholic fatty liver disease. BMJ Open Gastroenterol. 2016;3(1):e000106. https://doi.org/10.1136/bmjgast-2016-000106.

34. Kowdley KV, Unalp A, Kanwal F, Brunt EM, Schwimmer JB, NASH CRN Research Group. Quality of life in adults with nonalcoholic fatty liver disease: baseline data from the nonalcoholic steatohepatitis clinical research network. Hepatology. 2009;49(6):1904–12. https://doi.org/10.1002/hep.22868.

35. Golabi P, Bush H, Younossi ZM. Treatment strategies for nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. Clin Liver Dis. 2017;21(4):739–53. https://doi.org/10.1016/j.cld.2017.06.010.

36. Bondini S, Kallman J, Dan A, Younoszai Z, Ramsey L, Nader F, et al. Health-related quality of life in patients with chronic hepatitis B. Liver Int. 2007;27(8):1119–25. https://doi.org/10.1111/j.1478-3231.2007.01558.x.

37.• Younossi ZM, Stepanova M, Tapper EB, Henry L, Sheikh AM, Nguyen M, et al. Long-term follow-up of patient-reported outcomes (PROs) in chronic hepatitis C (HCV) patients with compensated and decompensated cirrhosis with Sustained Virologic Response (SVR). Abstract: AASLD, Washington DC 2017. **This study highlights the positive impact of treatment on patients with decompensated cirrhosis sustained over the long term.**

38.• Younossi ZM, Stepanova M, Janssen HL, Agarwal K, Nguyen MH, Gane EJ, et al. The impact of treatment of chronic hepatitis B (CHB) on patient-reported outcomes (PROs). Abstract: AASLD, Washington DC 2017. **One of the first studies that highlights the positive impact of antiviral suppresion treatment on patients with HBV.**