Health-related quality of life impact on patients with metabolic dysfunction-associated steatohepatitis: a targeted literature review

Tina Li[1], Yestle Kim[2], Melinda J Daumont[2], Daniela R Junqueira[1], John O'Donnell[2], Karissa Johnston[1]

[1]Broadstreet HEOR, Vancouver, Canada; [2]Madrigal Pharmaceuticals, West Conshohocken, PA, USA

HE-DART 2025
POSTER
#51

INTRODUCTION

Background

- Metabolic dysfunction-associated steatohepatitis (MASH), a severe form of metabolic dysfunction-associated steatotic liver disease (MASLD), is a progressive liver disease that can lead to cirrhosis and liver failure due to increasing fibrosis
- Patients with MASH face challenges related to their mental health, daily functioning, and overall well-being[1]
- While the impact of advanced fibrosis (F4) on health-related quality of life (HRQoL) is well-studied, the effects of earlier fibrosis stages (F0-F3) are less understood

Rationale

- Understanding how MASH impacts HRQoL in patients at different fibrosis stages is essential for guiding treatment and informing healthcare policy decisions to support patients
- Understanding the impact of MASH through patients' qualitative perceptions is crucial to uncover burdens that existing HRQoL instruments may not fully capture

OBJECTIVE

- To identify, via targeted review, and synthesize peer-reviewed literature on HRQoL and patient perceptions of the disease in patients with MASH at any fibrosis stage

METHODS

Search strategy

- Search period: January 2015 to July 2025
- Data sources: MEDLINE and Embase (via Ovid)

Study selection

- Title-abstract screening, followed by full-text publication screening, both conducted by a single reviewer
- Based on PECOS criteria (Table 1)

Descriptive synthesis

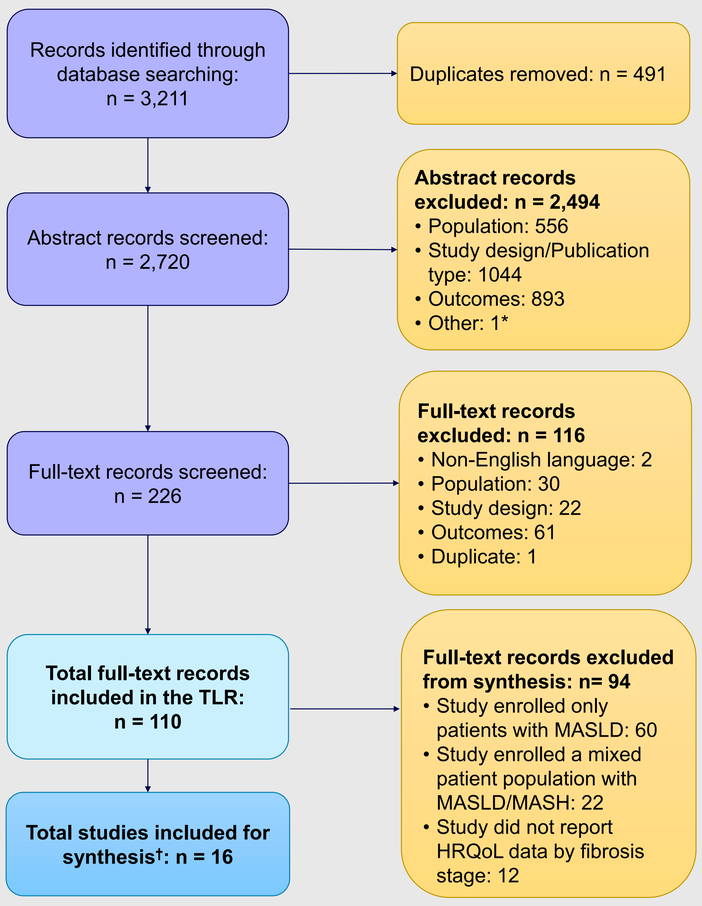
- Studies reporting on a patient population with at least 80% diagnosed with MASH
- Quantitative data on HRQoL described by fibrosis stages in patients receiving standard of care (SoC)/no treatment
  - For clinical trials, only baseline scores were summarized
  - To assess the clinical relevance of differences in scores between groups, differences were compared against minimal important differences (MIDs) from the literature
  - MIDs reflect the smallest difference between two values that can be interpreted as meaningful, so e.g. for a MID of 3, values of 80 vs. 83 would be considered meaningfully different while 80 vs. 82 would not. A variety of methods and terminologies are used (e.g. MCID, MSD); in this analysis all are collectively referred to as MID

TABLE 1. PECOS criteria

Domain	Inclusion
Population	• Adult patients diagnosed with MASH with none to advanced fibrosis (stages F0-F4) • MASH caregivers
Exposure/ Comparator	• Observational studies: SoC • Clinical trials: no treatment / placebo arm
Outcomes	• Outcomes reported according to fibrosis stage: – Generic HRQoL scales – Disease-specific HRQOL scales – Other validated or non-validated scales – Patient perceptions of disease burden and treatment
Study design	• Clinical trials (randomized and non-randomized) • Observational studies (including patient surveys and interviews)
Other	• Results published in a peer-reviewed journal • English language

INCLUDED STUDIES (PRISMA)

FIGURE 1. PRISMA diagram



*Study retracted evidence of systematic manipulation of the publication and peer-review process
† Studies included for synthesis reported on a patient population comprising ≥80% patients with a confirmed diagnosis of MASH and reporting on HRQoL according to fibrosis stages

RESULTS

Study characteristics

- Of 16 studies reporting HRQoL data for one or more fibrosis stages (Figure 1):
  - Seven were observational studies, including three patient interviews; seven were clinical trials, and two pooled analyses of RCTs
  - Sample size ranged from 20 to 3,754
  - Most studies (43.8%) included F1-F3 patients, with two studies (12.5%) not restricting the inclusion criteria to a specific fibrosis stage

Patient characteristics

- Observational studies vs. RCTs/pooled analysis:
  - Mean age: 42.4-56.9 vs. 50.3-58.4 years
  - % female: 50.0-82.0% vs. 44.0-69.4%
- Comorbidities prevalence (n=14 studies): T2DM (27-74%), diabetes (59-72%), hypertension (27-67%), hyperlipidemia / dyslipidemia (18-50%)

10 studies assessed HRQoL across fibrosis stages by applying generic instruments

- Patients assessed with generic HRQoL measures showed impairments compared to population norms across different fibrosis stages (Table 2):

TABLE 2. Mean scores, population norms, and clinically meaningful differences for generic HRQoL measures in patients with MASH

Instrument / Number of studies	Possible range of scores / Population norm*	Mean score range / Comparison with the population norm	Mean score range by fibrosis stage	Clinically meaningful differences
SF-36 PCS 6 studies	• Score range: 7.3-70.1; higher scores indicate better health • Population norm: 50	43.4-49.1[2-7] All scores below the population norm	F1-F3: 45.0-49.1[2-5] F3-F4: 43.4-47.1[2,6-7]	• Of the studies (n=2) that reported PCS scores stratified by fibrosis stages, no clinically meaningful difference among stages was observed • Reference MID: 3 points[8]
SF-36 MCS 6 studies	• Score range: 5.8-69.9; higher scores indicate better health • Population norm: 50	47.5-51.0[2-7] Scores below the population norm in four studies	F1-F3: 48.1-51.0[2-5] F3-F4: 49.3-50.6[2,6-7]	• Of the studies (n=2) that reported MCS scores stratified by fibrosis stages, no clinically meaningful difference among stages was observed • Reference MID: 3 points[8]
SF-6D Utility 5 studies	• Score range: 0-1; 1 represents perfect health, 0 represents a health state equivalent to death • Population norm: 0.78	0.57-0.69[2,6-7,9] All scores below the population norm	F1-F3: 0.67[2-3] F3-F4: 0.65-0.72[2,6-7,9]	• Of the studies (n=3) that reported SF-6D scores stratified by fibrosis stages, no minimally important difference in scores was observed • Reference MID: 0.038-0.081 points[10]
EQ-5D-5L Utility 5 studies	• Score range: 0-1; 1 represents perfect health, 0 represents a health state equivalent to death • Population norm: 0.85	0.08-0.84[3,7,9,11-2] All scores below the population norm	F0-F2: 0.67-0.82[3,11-12] F3-F4: 0.08-0.84[3,7,9,11-12]	• Of the studies (n=6) that reported scores stratified by fibrosis stages, clinically meaningful differences in scores between groups were seen in two studies • Reference MID: 0.058-0.158 points[10]
SIP 1 study	• Score range: 0%-100%; 100% indicates maximum dysfunction and 0% represents no dysfunction • Impairment observed in a healthy reference cohort: 3.4%†	Mean: 11.8%[13] Greater impairment vs. a healthy reference cohort† who had a mean score of 3.4%[13]	F0-F1: 18.9[13] F2: 14.3[13] F3-F4: 6.9[13] Differences between stages were not statistically significant.[13]	• Comparison by fibrosis stages shows clinically meaningful differences in dysfunction between F0-F1 vs. F3-F4 and F0-F1 vs. F2 • Reference MID: 5 points[14]

* Scores lower than the population norm indicate below-average HRQoL
† Scores >3.4% indicate higher impairment than the reference cohort[13]

9 studies assessed HRQoL across fibrosis stages by applying disease-specific instruments

- Patients assessed with disease-specific instruments validated for MASH and/or chronic liver disease also showed impairments across fibrosis stages:
  - **CLDQ (1=worst QoL, 7=best QoL; 2 studies)**: Mean scores for F2 and F3 were 4.8 and 5.0 (1 study[17]), and 4.9 for F4 (1 study[2]). Using a MID of 1,[8] no clinically meaningful difference in scores across fibrosis stages was observed
  - **CLDQ-NASH (1=worst QoL, 7=best QoL; 5 studies)**: Mean scores for F1 and F2 were 5.1-5.2, and 4.4-4.5 for F3-F4 [3,7,9,12,15].Using a MID of 0.3,[15-16] two studies found clinically meaningful differences in scores across fibrosis stages
  - **NASH-CHECK (**0=no impairment (best), and 10=complete impairment (worst); 2 studies): Patients with more severe fibrosis consistently showed greater impairment (mean scores ranged from 0.9-5.8 for F1-F3 patients).[11,18] No MIDs were identified for NASH-CHECK
  - **LDQOL** (1=poor QoL (worst), 100=good QoL (best), 1 study): Patients with fibrosis stages F1/F2 and F3 reported comparable levels of impairment (mean scores 78.2 and 78.1, respectively).[15] Using an MID of 5,[15] the difference between F1/F2 and F3 patients was not clinically meaningful

Three studies assessed the perception of the disease among patients with MASH

- Qualitative data on patient perceptions on symptom burden and disease impact were reported according to fibrosis stage in three studies:

Perceptions of symptom burden

- Across all three studies, the most frequently reported symptoms were fatigue/low energy and abdominal pain

Fatigue

F1: *You feel so bad like you don't want to do anything. You just want to sleep, but you can't sleep. It's hard to get motivated to do the things that you know you need to do*[2]

F2: *Yes. I constantly feel fatigued and I just haven't gotten enough sleep, no matter what I do. I'll wake up and it feels like all my muscles just wore out. Like I've gone and run a mile, but I haven't done anything*[2]

F3: *It's almost like you just feel whacked, like just not having any more energy to do anything*[11]

Abdominal pain

F1: *Some days it would feel like somebody was stabbing me*[11]

F2: *It's a real digging under the ribs, a real sharp pain*[11]

F3: *But I would get some stomach pains at times, I'd say…that's been a while. That would be on the side my liver would be on, the right-hand side*[20]

Perceptions of disease impact

- Across all three studies, patients reported impacts on activities and relationships, psychological and emotional well-being, and dietary restrictions

	Activities and relationships	Dietary restrictions	Psychological and emotional wellbeing
F1	*"So it's really disruptive because you can't do the things that you once enjoyed. It's hard to get motivated to do it"*[19]	*"It's …challenging because the diet and the health change psychological and emotional wellbeing and the habits that you have to change to try to stop it from continuing to harden, like weight management. Changing your whole lifestyle and diet basically around your illness is kind of challenging because some people are on a set budget for groceries … tricky because you have to balance everything all over"*[19]	*"And I was worried about it where I was like, oh my god, is my liver destroyed? Am I? So it was a very stressful, very uncertain time"*[20]
F2	*"I mean going out with friends for one is not something that I do, because most days I feel sluggish and tired and in pain"*[4]	*"…it's having to peel the skin off my chicken or cut the fat off a good, juicy steak. You know. Oh, yeah. I miss them tastes"*[19]	*"It worries me…you don't know like what's going to happen. Am I going to advance into full blown cirrhosis? Am I going to have like metabolic or hepatic encephalopathy? Do I need to take lactulose forever and a day so that I can get them on the level. You know these kinds of things, it bothers my mind"*[19]
F3	*"Never in my life did I think at almost 50 would my life be so restricted and unproductive. I feel like I'm a person in my 80s with not being very active, enjoying life. Making excuses not to go anywhere"*[20]	"Like I'm trying to eat less. Talking about quantity, less. And avoiding fried food, eating more vegetables"[19]	*"Yeah, it's very frustrating and it's very depressing. It makes you feel kind of less than a person. Not pulling your weight on everything"*[19]
F4	*No data available*	*"Well, it's impacting me as well as my spouse. Every day we're looking at what we're eating and trying to make the right choices. So when we go out, it's a little more difficult"*[20]	*No data available*

DISCUSSION & CONCLUSION

- This study highlights the significant HRQoL burden in patients with MASH, even in earlier fibrosis stages (F0-F2)
- The findings are supported by a semi-systematic review with formal search strategies, ensuring rigor and minimizing bias
- The demographic characteristics of patients were similar across studies, regardless of the study design
- Limited data availability prevents an evaluation of the impact of confounding factors due to comorbidities
- Consistent findings across quantitative and qualitative studies underscore the importance of early intervention to prevent or reverse the progression of fibrosis in patients with MASH
- Additional analyses of studies of mixed MASLD/MASH patients are needed to address unmet medical needs within the full spectrum of the disease

ABBREVIATIONS

CLDQ: Chronic Liver Disease Questionnaire; CLDQ-NAFLD: Chronic Liver Disease Questionnaire for Nonalcoholic Fatty Liver Disease; EQ-5D-5L: EQ 5 Dimensions, 5 Levels; F: Fibrosis stage; HRQoL: Health-related quality of life; LDQOL: Liver Disease Quality of Life; MASH: Metabolic dysfunction-associated steatohepatitis; MASLD: Metabolic dysfunction-associated steatotic liver disease; MCID: Minimum clinically important difference; MID: Minimum important difference; MSD: Meaningful score difference; NASH-CHECK: Patient-reported outcome measure for NASH; PECOS: Population, Exposure, Comparator, Outcome, Study design; QoL: Quality of life; RCT: Randomized controlled trial; SF-36 MCS: Short Form-36 Mental Component Summary; SF-36 PCS: Short Form-36 Physical Component Summary; SF-6D: Short Form-6 Dimensions (utility measure); SIP: Sickness Impact Profile; SoC: Standard of care; T1D / T2D: Type 1 Diabetes / Type 2 Diabetes

DISCLOSURES AND ACKNOWLEDGEMENTS

YK, MDJ, and JO are employees of Madrigal Pharmaceuticals. TL, DRJ, and KJ are employees of Broadstreet HEOR which was contracted by Madrigal Pharmaceuticals for the conduct of this study.

REFERENCES

1. Kennedy-Martin T. *Health-related quality of life burden of nonalcoholic steatohepatitis: a robust pragmatic literature review*. 2017;2:28. **2.** Younossi ZM. *Improvement of hepatic fibrosis and patient-reported outcomes in non-alcoholic steatohepatitis treated with selonsertib*. 2018;38:1849-1859. **3.** Younossi ZM. *Hepatic fat reduction due to resmetirom in patients with nonalcoholic steatohepatitis is associated with improvement of quality of life*. 2022;20(6):1354-1361. **4.** Romero-Gomez M. *Improved health-related quality of life with semaglutide in people with non-alcoholic steatohepatitis: a randomized trial*. 2023;58:395-403. **5.** McPherson S. *A randomized controlled trial of losartan as an anti-fibrotic agent in non-alcoholic steatohepatitis*. 2017;12(4):e0175717. **6.** Younossi ZM. *Patients with nonalcoholic steatohepatitis experience severe impairment of health-related quality of life*. 2019;114(10):1636-1641. **7.** Younossi ZM. *Reduced patient-reported outcome scores associate with level of fibrosis in patients with nonalcoholic steatohepatitis*. 2019;17:2552-2560. **8.** Desai AP. *Meaningful differences in patient-reported outcome measurement scores in liver disease*. 2025;9(6):e0727. **9.** Younossi ZM. *The association of histologic and noninvasive tests with adverse clinical and patient-reported outcomes in patients with advanced fibrosis due to nonalcoholic steatohepatitis*. 2021;160:1608-1619. **10.** Mulhem B. *Investigating the minimally important difference of the Diabetes Health Profile (DHP-18) and the EQ-5D and SF-6D in a UK diabetes population*. 2013; 5: 1045-1054. **11.** Aggio D. *Estimating utility values for non-alcoholic steatohepatitis health states: a discrete choice experiment*. 2024;13(2):e230033. **12.** O'Hara J. *Cost of non-alcoholic steatohepatitis in Europe and the USA: the GAIN study*. 2020;2(5):100142. **13.** Wernberg CW. *Steatotic liver disease is the most important somatic determinant of quality of life in patients with obesity: a cross-sectional study*. 2024;44:191-201. **14.** Bowers S. *Outcomes in cardiopulmonary physical therapy: sickness impact profile*. 2009; 20:19-24. **15.** Younossi ZM. *Health-related quality of life (HRQL) assessments in a 52-week, double-blind, randomized, placebo-controlled phase III study of resmetirom (MGL-3196) in patients with metabolic dysfunction-associated steatohepatitis (MASH) and fibrosis*. 2025;81:1318-1327. **16.** Younossi ZM. *A disease-specific quality of life instrument for nonalcoholic fatty liver disease and non-alcoholic steatohepatitis: CLDQ-NAFLD*. 2017;37:1209-1218. **17.** Chalasani N. *Effects of belapectin, an inhibitor of galectin-3, in patients with nonalcoholic steatohepatitis with cirrhosis and portal hypertension*. 2020;158:1334-1345. **18.** Twiss J. *Validation of NASH-CHECK: a novel patient-reported outcome measure for nonalcoholic steatohepatitis*. 2023;7(69):1-14. **19.** Shinde S. *Understanding the impact of non-alcoholic steatohepatitis with metabolic comorbidities on adults: a real-world qualitative study*. 2024;40(4): 665-676. **20.** Swain MG. *A qualitative patient interview study to understand the experience of patients with nonalcoholic steatohepatitis*. 2022;7:e0036

SCAN QR CODE
FOR DIGITAL POSTER

Madrigal