Psychometric Evaluation Of NASH-CHECK, a Patient-Reported Outcome Measure for Non-alcoholic Steatohepatitis

PGI51

Twiss J,[1] Whalley D,[1] Doward LC,[1] Balp MM,[2] Brass C,[2] Lopez P,[2] Loeffler J,[2] Cai J,[3] Cryer D,[4] Sanyal AJ*,[5] Anstee QM*[6]

[1]RTI Health Solutions, Manchester, United Kingdom; [2]Novartis Pharma AG, Basel, Switzerland; [3]Novartis Pharmaceuticals Corp, East Hanover, New Jersey, United States; [4]Global Liver Institute, Washington, DC, United States; [5]Virginia Commonwealth University, Richmond, Virginia, United States; [6]Newcastle University, Newcastle, United Kingdom; *Joint Senior Authors

Background

- Non-alcoholic steatohepatitis (NASH) is the form of non-alcoholic fatty liver disease characterised by liver fat accumulation, inflammation, cell injury, and fibrosis.[1-2]
- NASH-CHECK is a disease-specific patient-reported outcome measure that assesses symptoms and health-related quality of life (HRQOL) among patients with NASH. The instrument was developed based on qualitative research with patients with NASH[3-6] and according to the United States Food and Drug Administration (FDA) guidance.[7]

Objective

- To report a preliminary psychometric evaluation of NASH-CHECK:
  - Evaluation of the individual items of NASH-CHECK for potential removal
  - Assessment of the preliminary dimensional structure of NASH-CHECK

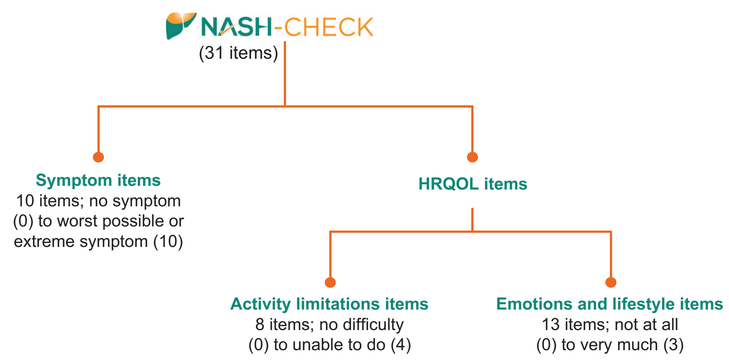
Methods

Study Design

- Data came from a 12-week, randomised, double-blind, placebo-controlled, phase 2 trial of tropifexor in adult patients with phenotypic NASH.[8]
- The analysis sample included randomised patients who completed NASH-CHECK at baseline, week 6, or week 12.

NASH-CHECK

Figure 1. NASH-CHECK structure Overview



Psychometric Analysis Methods

- NASH-CHECK symptom items and HRQOL items were analysed separately.
- **Item response frequency distributions:** Identifies items with high floor or ceiling effects.
- **Inter-item and corrected item-total correlations:** Correlations < 0.2 = unrelated items; correlations > 0.8 = redundant items.
- **Exploratory factor analysis (EFA):** Maximum likelihood (for symptoms items) or weighted least-squares (for HRQOL items) estimation with quartimin rotation.
  - Eigenvalues > 1 to identify separate factors.
  - Model fit: non-significant X^2 test statistic.
  - Goodness-of-fit statistics: comparative fit index (CFI) ≥ 0.95, Tucker-Lewis index (TLI) ≥ 0.95, root mean square error of approximation (RMSEA) ≤ 0.06, and standardised root mean square residual (SRMR) ≤ 0.08.
  - Item factor loadings < 0.30 to identify unrelated items.
  - Items loading onto multiple factors to identify items assessing multiple constructs.
- **Rasch analysis:**
  - Model fit: non-significant ($p > 0.05$) item-trait interaction X^2 statistic, item and person fit residuals with a mean of 0 and standard deviation (SD) of 1, and person separation index (PSI) > 0.70.
  - Individual item fit: non-significant ($p > 0.05$) X^2 statistic and item fit residuals between ± 2.5.

Results

Patient Sample

- The analysis sample included 104 patients diagnosed with NASH and fibrosis levels F1-F3 from 13 countries, with the largest samples from the United States (38.5%) and South Korea (22.1%) (**Table 1**).

Table 1. Patient Characteristics at Baseline

Sample Characteristic		Psychometric Analysis Sample (N = 104)
Gender, n (%)	Female	57 (54.8)
Age years, mean (SD) [range]		51.2 (12.7) [19.0-79.0]
Race, n (%)	Caucasian	60 (58.3)
	Asian	40 (38.8)
	Black	1 (1.0)
	Other	2 (1.9)
Type 2 diabetes, n (%)		68 (65.4)
Clinical assessments, mean (SD) [range]	BMI	32.5 (6.1) [20.9-49.3]
	ELF score	9.4 (1.1) [3.3-11.7]
	ALT level*	79.9 (41.1) [25.0-248.0]
	AST level*	57.5 (32.6) [16.5-224.0]
	GGT level*	73.3 (58.0) [12.0-385.0]
	Hepatic fat %	20.0 (6.9) [10.2-36.7]

ALT = alanine aminotransferase; AST = aspartate aminotransferase; BMI = body mass index; ELF = enhanced liver fibrosis; GGT = gamma-glutamyl transferase; SD = standard deviation; *units per liter

Item Response Frequency Distributions

- There were no item-level ceiling effects.
- Floor effects ranges:
  - Symptom items: 17.4%-69.8%
  - Activity limitations items: 51.2%-74.4%
  - Emotions and lifestyle items: 17.4%-83.7%

Item Correlations

- Inter-item and item-total correlations suggested some potential item redundancy:
  - Symptoms: fatigue items 3 and 4; cognitive items 6-9
  - HRQOL: daily activities items 11-13, ambulation items 15-18, relationship issues items 23-27, and leisure/work items 29 and 30
- Item 31 (food restriction) had low correlations (< 0.2) with other items.

Exploratory Factor Analysis

Symptoms Items

- For the symptoms items, a 3-factor solution was best supported in terms of model fit (**Table 2**). However, only one of the factors comprising cognitive symptoms (items 6-9) was conceptually supported and considered to form a meaningful scale.

Table 2. EFA Factor Loadings for NASH-CHECK Symptoms Items

NASH-CHECK Item	3-Factor Model[a]		
	Factor 1	Factor 2	Factor 3
1. Pain	**0.955***	—	—
2. Bloating	**0.422***	0.393*	—
3. Fatigue	—	**0.954***	—
4. Rest	—	**0.819***	—
5. Sleep	—	—	—
6. Focusing	—	—	**0.679***
7. Thinking	—	—	**1.060***
8. Conversation	—	—	**0.862***
9. Forgetful	—	0.309*	**0.506***
10. Itchy skin	**0.392**	—	—

* $p < 0.05$. **Bold** = highest loading for each item. Loadings < 0.3 are not presented.[a] $X^2[18, n = 103] = 23.89$, $p = 0.159$; RMSEA = 0.06; CFI = 0.99; TLI = 0.97; SRMR = 0.03.

HRQOL Items

- Initial analysis supported the separation of the activity limitations (items 11-18) and emotions and lifestyle (items 19-31) items.
- Activity limitations: both a 1-factor (an overall activity limitations summary scale) and a 2-factor (comprising a daily activities subscale and an ambulation subscale) solution were supported (**Table 3**).
- Emotions and lifestyle: both a 1-factor (an overall psychosocial summary scale) and a 2-factor (comprising an emotions subscale and a social subscale) solution were similarly supported (**Table 4**).

Table 3. EFA Item Factor Loadings for Activity Limitations Items

NASH-CHECK Item	1-Factor Model[a]	2-Factor Model[b]	
		Factor 1	Factor 2
11. Bending	0.914*	**0.933***	—
12. Light chores	0.959*	**0.997***	—
13. Heavy chores	0.945*	**0.743***	—
14. Heavy objects	0.852*	**0.904***	—
15. Short walk	0.901*	—	**0.947***
16. Long walk	0.920*	—	**1.031***
17. Brisk walk	0.926*	0.346*	**0.620***
18. Walk up	0.878*	—	**0.738***

* $p < 0.05$. **Bold** = highest factor loadings for each item. Loadings < 0.3 are not presented.
[a] $X^2[20, n = 103] = 50.835$; $p = 0.0002$; RMSEA = 0.12; CFI = 0.99; TLI = 0.99; SRMR = 0.05;
[b] $X^2[13, n = 103] = 16.37$, $p = 0.230$; RMSEA = 0.05; CFI = 1.0; TLI = 1.0; SRMR = 0.02.

Table 4. EFA Item Factor Loadings for Emotions and Lifestyle Items

NASH-CHECK Item	1-Factor Model[a]	2-Factor Model[b]	
		Factor 1	Factor 2
19. Worry	0.565*	**0.721***	—
20. Feel down	0.738*	**0.904***	—
21. Angry	0.729*	**0.667***	—
22. Judge me	0.585*	**0.499***	—
23. Relationships	0.886*	—	**0.818***
24. Daily activities	0.888*	—	**0.870***
25. Family life	0.985*	—	**0.923***
26. Worry to family	0.713*	0.368*	**0.418***
27. Intimacy	0.851*	—	**0.927***
28. Socialise	0.631*	—	**0.705***
29. Spare time	0.826*	—	**0.839***
30. Work or study	0.857*	—	**0.925***
31. Food restriction	0.426*	—	**0.305**

* $p < 0.05$. **Bold** denotes the highest factor loadings for each item. Loadings < 0.3 are not presented.
[a] $X^2[65, n = 103] = 94.09$, $p = 0.011$; RMSEA = 0.07; CFI = 0.98; TLI = 0.98; SRMR = 0.08.
[b] $X^2[53, n = 103] = 57.82$, $p = 0.302$; RMSEA = 0.03; CFI = 1.0; TLI = 1.0; SRMR = 0.06.

Rasch Analysis

- Rasch analysis was conducted for each of the item sets supported in the EFA (**Table 5**).
- The individual items showing misfit (X^2 $p < 0.05$) were as follows:
  - Cognitive symptoms: item 6
  - Overall activity limitations: item 13
  - Emotions: item 20
  - Social: items 24 and 28

Table 5. Rasch Analysis: Overall Fit Results

NASH-CHECK Scale	n	Item-Trait Interaction X^2 (p value)	PSI	Mean (SD) Item Fit Residual	Mean (SD) Person Fit Residual
Symptom items					
Cognitive symptoms (items 6-9)	75	12.84 (0.012)	0.76	–0.45 (1.18)	–0.38 (0.81)
HRQOL items					
Overall activity limitations (items 11-18)	69	12.77 (0.120)	0.87	–0.10 (1.10)	–0.29 (0.91)
Daily activities (items 11-14)	54	7.81 (0.099)	0.78	0.37 (1.07)	–0.21 (0.76)
Ambulation (items 15-18)	60	4.65 (0.326)	0.81	0.09 (0.56)	–0.13 (0.60)
Overall emotions and lifestyle (items 19-31)	98	21.63 (0.061)	0.77	–0.45 (1.13)	–0.32 (0.76)
Emotions (items 19-22)	84	8.42 (0.077)	0.33	–0.34 (0.30)	–0.28 (0.61)
Social (items 23-30)	71	24.60 (0.002)	0.68	–0.25 (1.20)	–0.26 (0.76)

HRQOL = health-related quality of life; PSI = person separation index; SD = standard deviation.

Preliminary Dimensional Structure for NASH-CHECK

- The preliminary dimensional structure for NASH-CHECK symptoms items and HRQOL items are shown in **Figure 2** and **Figure 3**, respectively.

Figure 2. Preliminary Dimensional Structure for NASH-CHECK Symptom Items

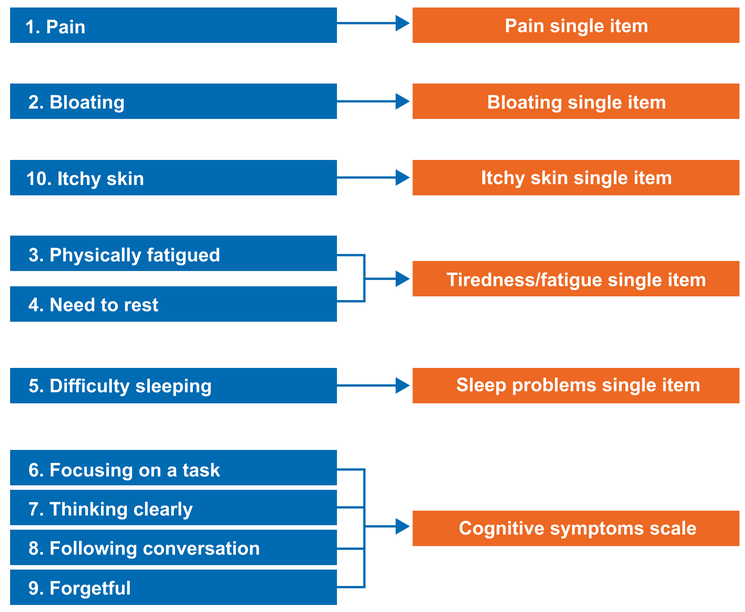
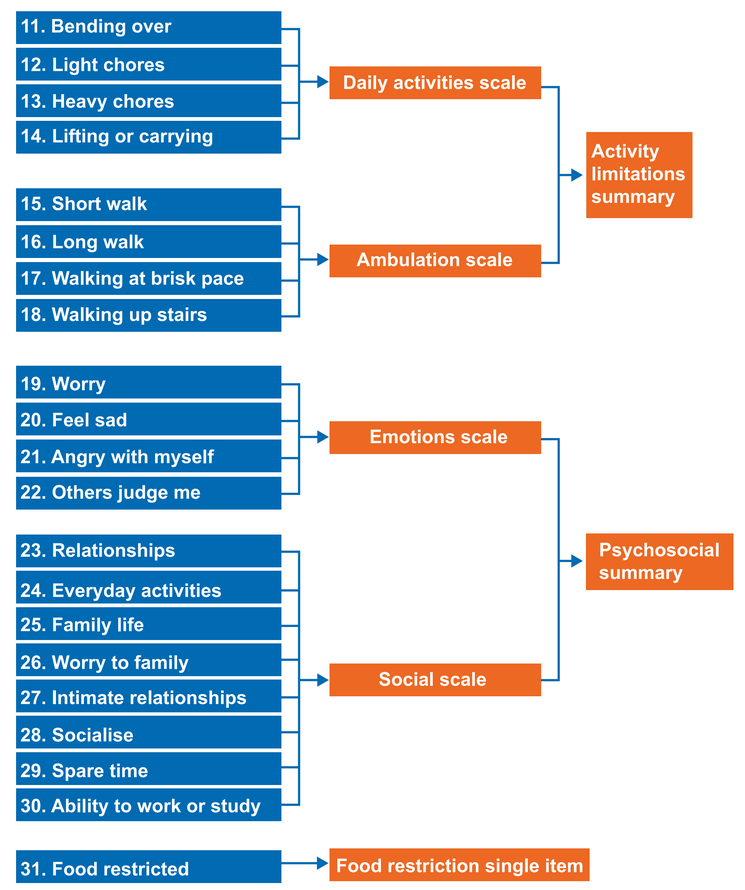


Figure 3. Preliminary Dimensional Structure for NASH-CHECK HRQOL Items



Conclusions

- The psychometric evaluation provided evidence for a preliminary dimensional structure for NASH-CHECK.
- Although based on a small sample the results of the analyses highlighted several items that may be redundant or that were not associated with other items; such items will be potential candidates for removal.
- NASH-CHECK will be evaluated further using additional clinical trial data sets to identify the final items for removal and confirm the final dimensional structure.

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Acknowledgements

This study was conducted under the LITMUS (Liver Investigation: Testing Marker Utility in Steatohepatitis) project and funded from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No. 777377. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

Presented at: ISPOR Europe 2019 (2–6 November 2019), Copenhagen, Denmark.

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