Patient-Reported Symptoms and Impact in Nonalcoholic Steatohepatitis: An Evaluation of the NASH-CHECK, a Novel PROM in NASH

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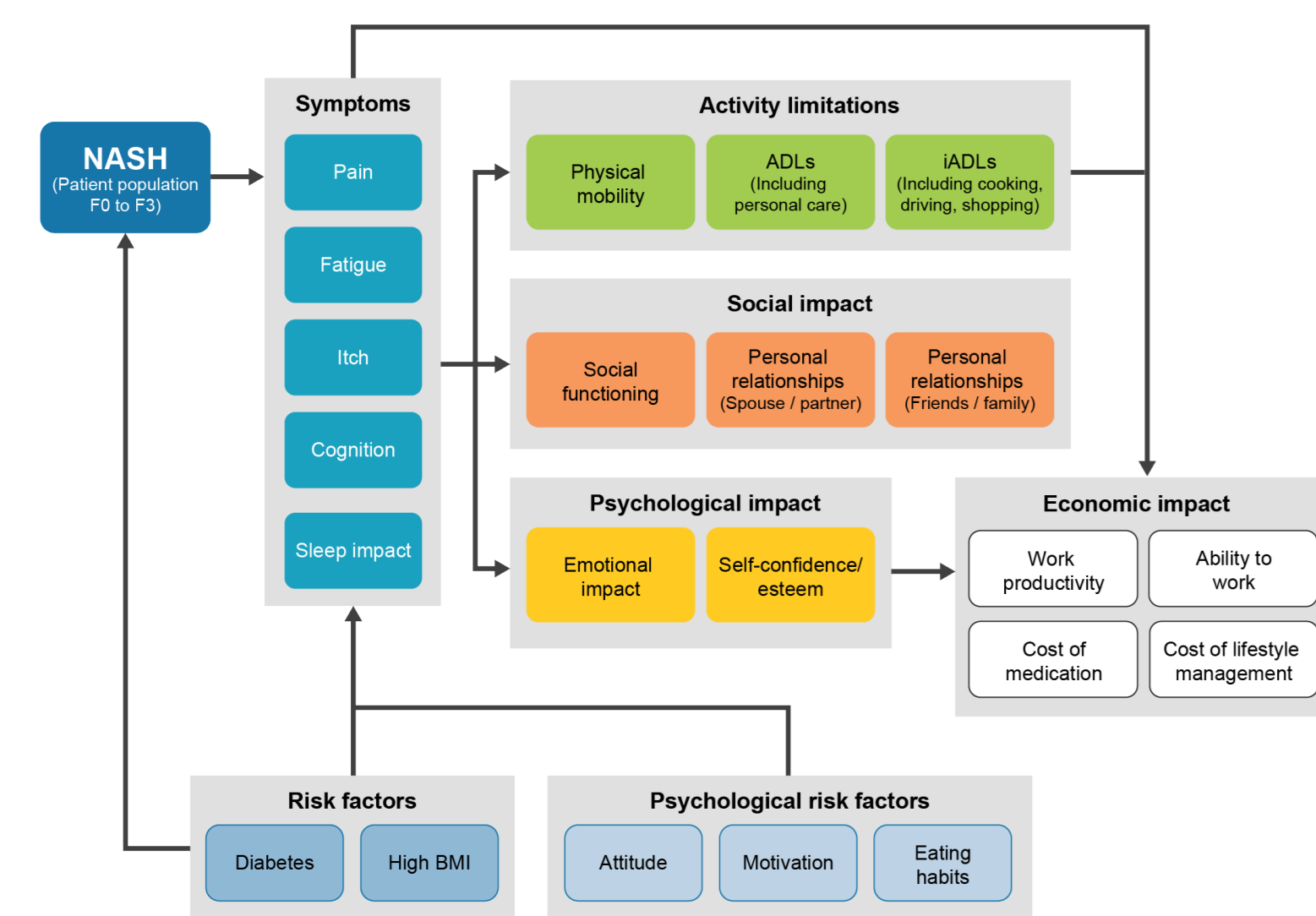
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1 INTRODUCTION

- NASH-CHECK is a novel, patient-reported outcome measure that was developed specifically to assess symptoms and health-related quality of life (HRQOL) in patients with nonalcoholic steatohepatitis (NASH).
- The development of NASH-CHECK was based on a conceptual model (**Figure 1**) derived from qualitative research with patients with NASH and input from clinical experts.[1-4]
- The draft measure comprised 10 symptoms items and 21 HRQOL items (activity limitations = 8 items; emotions and lifestyle issues = 13 items).

Figure 1. Conceptual Model of NASH

ADL = activity of daily living; iADL = instrumental activity of daily living; BMI = body mass index; NASH = nonalcoholic steatohepatitis.

2 AIM

- The aim of the study was to investigate the preliminary dimensional structure of NASH-CHECK in noncirrhotic patients.

3 METHODS

Study Design

- Data come from a 12-week, randomised, double-blind, placebo-controlled, phase 2 trial of tropifexor in adult noncirrhotic patients with NASH (fibrosis grades F1-F3).
- The analysis sample included randomised patients who completed NASH-CHECK at baseline, week 6, or week 12.

Analysis

- Analyses were conducted to explore associations among NASH-CHECK items to identify underlying dimensions. In line with the conceptual model, symptom items and HRQOL items were analysed separately.
- The following analyses were conducted:
  - Inter-item correlations to identify items that were potentially redundant (correlations > 0.8) or items that were not sufficiently related (correlations < 0.2).
  - Exploratory factor analysis (EFA) to explore patterns of associations between items to identify similar response patterns. The analysis used maximum likelihood estimation for symptoms items and weighted least-squares estimation for HRQOL items, with quartimin rotation. Overall model fit and item factor loadings were evaluated.
  - Rasch analysis to evaluate the extent to which NASH-CHECK items (or groups of items) can be considered to measure one underlying construct. The analysis used the partial-credit Rasch model and was conducted for each of the potential scales identified in the EFA. Overall model fit and item fit were evaluated.

4 RESULTS

Patient Sample

- The analysis sample included 104 patients diagnosed with NASH and fibrosis levels F1-F3.
- Among them, 54.8% were females, 58.3% Caucasians, 38.8% Asians, and 65.4% had type 2 diabetes.
- The mean (SD) BMI was 32.5 (6.1) and ALT was 79.9 (41.1) U/l.

NASH-CHECK Symptoms

Inter-Item Correlations

- High correlations suggesting potential content overlap between items 3 and 4 (fatigue and needing to rest, respectively), as well as between items 6 to 9 (cognitive symptoms)

Exploratory Factor Analysis

- For the symptoms items, EFA identified a model with three factors; item 5 (sleep) did not load onto any of the factors.
- Only one of the three identified factors, which comprised the 4 items assessing cognitive symptoms (6 to 9), was conceptually supported and considered to form a meaningful scale.
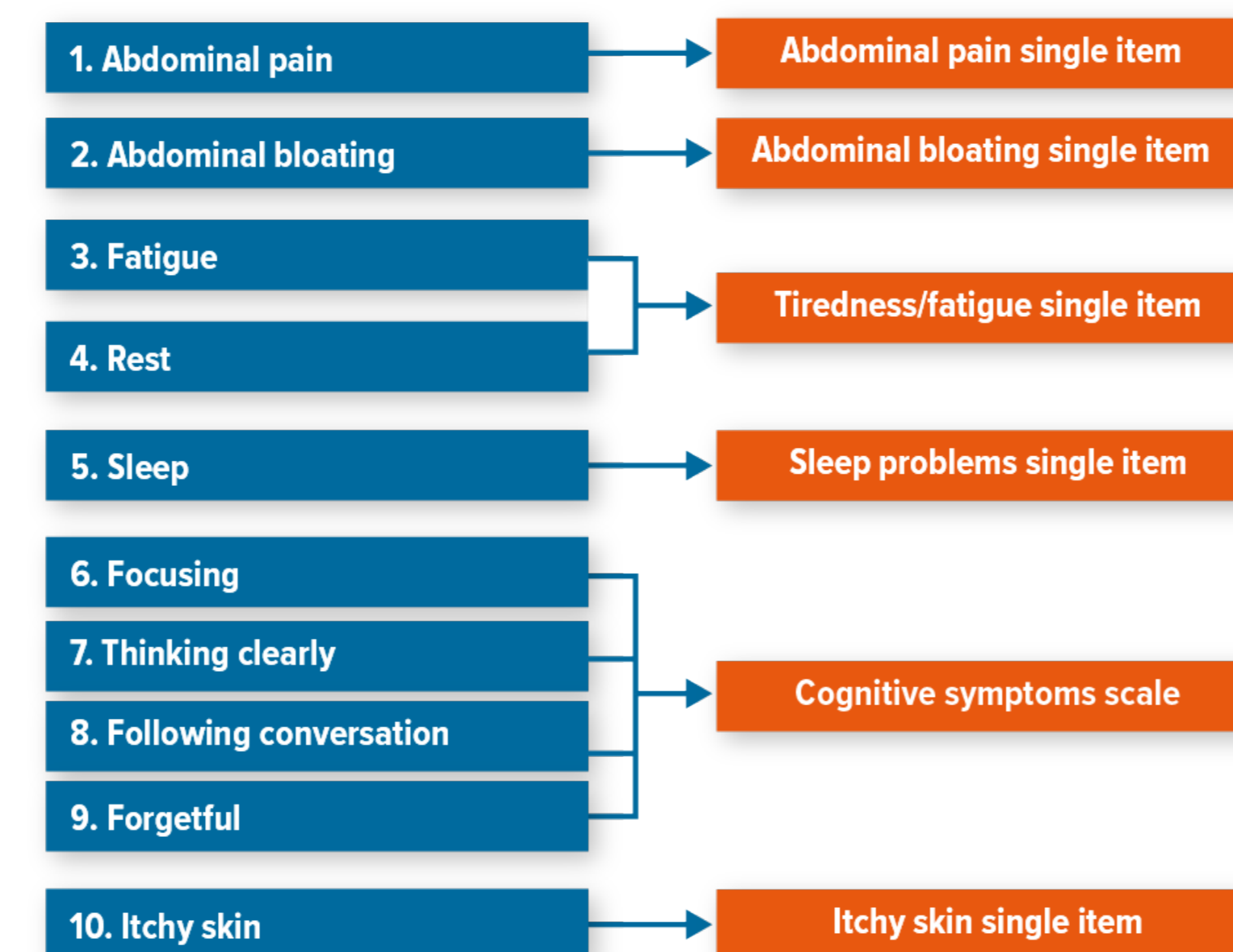
Rasch Analysis

- The 4-item cognitive symptoms scale identified in the EFA showed acceptable overall fit to the Rasch model.
- One item (item 6, forgetful) showed misfit to the Rasch model.

Preliminary Dimensional Structure for NASH-CHECK Symptoms Items

- Overall, the results supported a cognitive symptoms scale, with the remaining items proposed as single items (**Figure 2**).

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

NASH-CHECK HRQOL

Inter-Item Correlations

- High correlations suggesting potential content overlap were observed for the following items: daily activities items 11 to 13; ambulation items 15 to 18; relationship issues items 23 to 27; leisure/work items 29 and 30.
- Item 31 (food restriction) had low correlations with other items, suggesting content divergence.

Exploratory Factor Analysis

- Initial analysis supported the separation of the activity limitations items (11 to 18) and emotions and lifestyle items (19 to 31).

- **Activity limitations items:** EFA supported both a one-factor model and a two-factor model.
  - The one-factor model comprised all 8 items (11-18) (item loadings > 0.85)
  - The two-factor model comprised daily activities items (11-14) in the first factor (item loadings > 0.70) and ambulation items (15-18) in the second factor (item loadings > 0.60).
- **Emotions and lifestyle items:** EFA supported both a one-factor model and a two-factor model.
  - The one-factor model comprised all 13 items (19-31) (item loadings > 0.40).
  - The two-factor model comprised emotions items (19-22) in the first factor (item loadings > 0.45) and social items (23-31) in the second factor (item loadings > 0.30).
  - The loading for item 31 (food restriction) was low in both the one-factor and two-factor models (0.43 and 0.31, respectively) and was excluded from subsequent analysis.

Rasch Analysis

- All HRQOL scales identified in the EFA showed acceptable overall fit to the Rasch model, except for the model comprising social items 23 to 30.
- Individual items showing misfit were as follows:
  - Item 13 in the model comprising activity limitations items 11 to 18
  - Item 20 in the model comprising emotions items 19 to 22
  - Items 24 and 28 in the model comprising social items 23 to 30

Preliminary Dimensional Structure for NASH-CHECK HRQOL Items

- For activity limitations, the results supported an overall activity limitations scale in addition to two subscales assessing daily activities and ambulation, respectively (**Figure 3**).
- For emotions and lifestyle, the results supported an overall psychosocial scale in addition to two subscales assessing emotions and social issues, respectively (**Figure 3**).
- Item 31 (food restriction) did not adequately contribute to the scales identified; thus, if retained in the final measure, this item would be used a single item.

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

5 CONCLUSIONS

- The analyses supported a preliminary dimensional structure for NASH-CHECK that was consistent with the conceptual model developed previously from the qualitative research with patients with NASH.
- The results highlighted several items that may be redundant or that were not associated with other items; these items are potential candidates for removal.
- NASH-CHECK will be evaluated further using additional clinical trial data to identify the final items to be retained and confirm the final dimensional structure.

6 REFERENCES

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7 ACKNOWLEDGEMENTS

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