MEASURING WHAT MATTERS TO PATIENTS: THE DEVELOPMENT OF THE NASH-CHECK, A NEW PATIENT-REPORTED OUTCOME INSTRUMENT FOR NON-ALCOHOLIC STEATOHEPATITIS

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NASH-PRO TASKFORCE

INTRODUCTION

- Non-alcoholic steatohepatitis (NASH) is a progressive form of non-alcoholic fatty liver disease (NAFLD), and is characterized by excessive liver fat accumulation, inflammation, and fibrosis[1]
- Previous research[2,3] investigated the impact of NASH from the patients' perspective and highlighted the need for a new NASH-specific patient-reported outcome (PRO) measure based on USA Food and Drug Administration (FDA) guidance[4]

AIM

- The aim of this study was to develop a PRO measure for patients diagnosed with NASH and fibrosis levels F1-F3 (mild-severe fibrosis), suitable for clinical trials and clinical practice

METHODS

- An international NASH-PRO Task Force comprising PRO researchers, clinical experts, patient advocacy, and pharmaceutical industry representatives supervised the development of the new PRO measure following FDA PRO guidance[4]
- Review of published/grey literature, social media patient narratives and medical/patient experts (USA/UK) assisted to provide the framework for the initial conceptual model[3]
- The qualitative work to develop the new instrument was conducted in two phases; item generation and content validation
- All interviewees were recruited from a tertiary care centre in the USA, had a diagnosis of NASH and fibrosis F1-F3
- Fibrosis levels were established using the NASH CRN Histological Scoring System

Item generation

- Guided by the initial conceptual model, semi-structured concept elicitation (CE) interviews were conducted by PRO experts
- Thematic analysis of the data from the CE interviews was used to derive the final conceptual model, which was then used to guide item selection for the NASH-PRO measure in collaboration with NASH-PRO Task Force clinical experts and patient representatives

Content validation

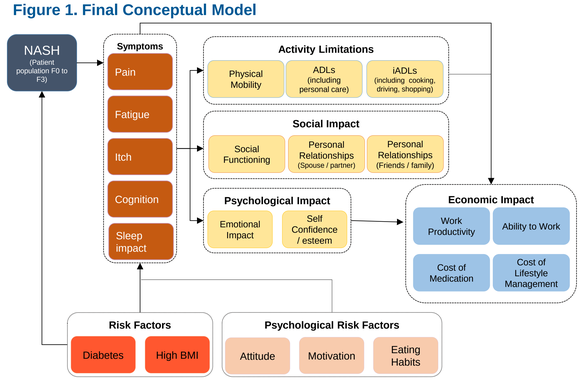
- Cognitive debriefing (CD) interviews were conducted to assess the content validity of the draft NASH-PRO measure
- Two rounds of interviews were conducted. This allowed for any necessary changes to be made to the instrument following the first round of interviews and further testing during the second round
- These interviews were designed to assess the comprehensibility, understandability, and relevance of the instructions, items, and response options for the NASH-PRO measure

RESULTS

Literature review & Conceptual model framework

- The draft conceptual model comprised the findings from the literature review confirming patient reported symptoms and impact on daily life and health related quality of life (HRQoL).[5-11] The final conceptual model[3] refined after the CE phase is presented in **Figure 1**

Figure 1. Final Conceptual Model



ADL: Activities of Daily Living; iADLs: Instrumental Activities of Daily Living; BMI: Body Mass Index

Patient Characteristics

- 23 patients were included in the CE and 15 patients for the CD
- Demographic and clinical characteristics were comparable among the two cohorts **(Table 1)**

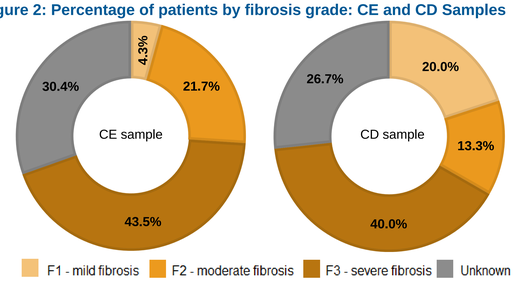
Table 1. Demographic and clinical characteristics (CE and CD Samples)

	CE Sample (N = 23)	CD Sample (N = 15)
Female, n (%)	18 (78.0%)	7 (46.7%)
Age, mean (SD) [range]	55.9 (10.0) [31.0-73.0]	53.6 (8.9) [31.0-68.0]
Years since diagnosis, mean (SD)	3.9 (2.9)	3.2 (2.8)
BMI, mean (SD)	34.8 (5.3)	36.4 (4.8)
Type 2 Diabetes, n (%)	14 (60.9)	11 (73.3)
Hypertension, n (%)	15 (66.2)	9 (60.0)

BMI: Body Mass Index; CE: Concept Elicitation; CD: Cognitive Debriefing

- The fibrosis stage across the two cohorts, based on the NASH CRN Histological Scoring System, is presented in **Figure 2**

Figure 2: Percentage of patients by fibrosis grade: CE and CD Samples

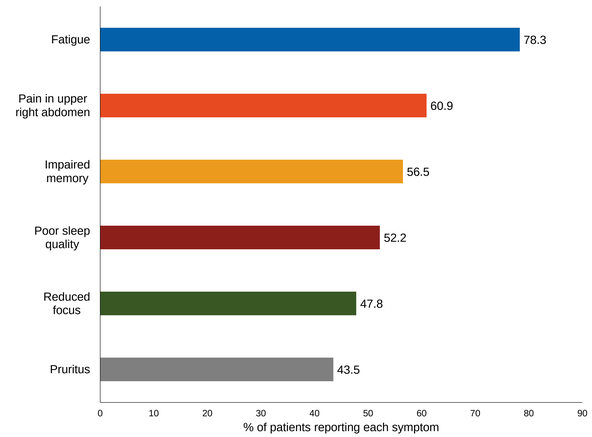


CE: Concept Elicitation; CD: Cognitive Debriefing

Item generation (concept elicitation)

- The CE interviews identified key symptoms of NASH and broader impact on patients' HRQoL:
  - Key symptoms reported include: fatigue, pain in upper right abdomen, poor sleep quality, and cognitive issues including impaired memory and reduced focus (**Figure 3**)
  - Key HRQoL impacts reported include: impaired physical functioning, ability to conduct daily living tasks, reduced quality of relationships, low mood, anxiety and self-consciousness
- The Task Force selected items for the first draft of the US-English NASH-PRO measure based on the key symptoms and HRQoL impacts
- The first draft of NASH-PRO measure included 52 items (16 symptom items and 36 HRQoL items) with a recall period of 7-days

Figure 3: Key symptoms reported by NASH patients (CE sample; N=23)

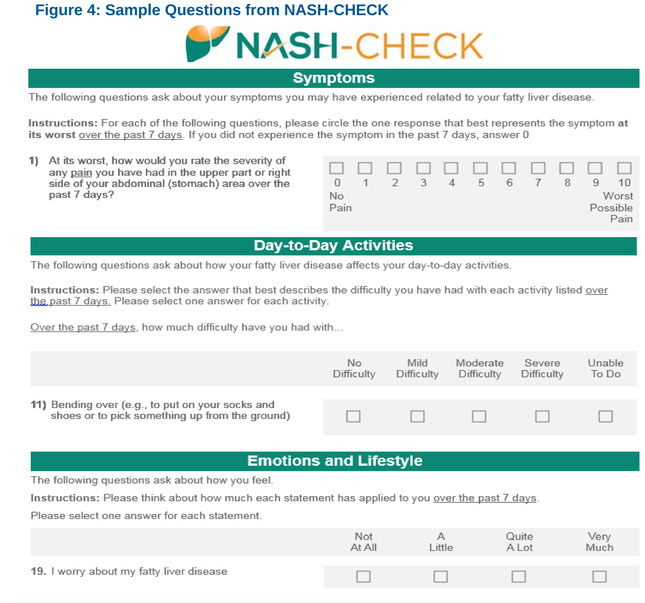


CE: Concept Elicitation

Content validation (cognitive debriefing)

- Based on patient preferences for item relevance, acceptability and comprehensibility, the NASH-PRO measure was refined to 31 items (10 symptom items and 21 HRQoL items)[12]
- The structure and concepts measured by the NASH-PRO were maintained during the instrument refinement. A sample symptoms item and HRQoL items are presented in **Figure 4**, respectively
- Patients found the final version of NASH-PRO measure to be relevant, acceptable, understandable, and clear and the measure was finally named **NASH-CHECK**

Figure 4: Sample Questions from NASH-CHECK


NASH-CHECK

Symptoms

The following questions ask about your symptoms you may have experienced related to your fatty liver disease.

Instructions: For each of the following questions, please circle the one response that best represents the symptom **at its worst** over the past 7 days. If you did not experience the symptom in the past 7 days, answer 0

1) At its worst, how would you rate the severity of any pain you have had in the upper part or right side of your abdominal (stomach) area over the past 7 days?

☐ 0 No Pain ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Worst Possible Pain

Day-to-Day Activities

The following questions ask about how your fatty liver disease affects your day-to-day activities.

Instructions: Please select the answer that best describes the difficulty you have had with each activity listed over the past 7 days. Please select one answer for each activity.

Over the past 7 days, how much difficulty have you had with…

	No Difficulty	Mild Difficulty	Moderate Difficulty	Severe Difficulty	Unable To Do
11) Bending over (e.g., to put on your socks and shoes or to pick something up from the ground)	☐	☐	☐	☐	☐

Emotions and Lifestyle

The following questions ask about how you feel.

Instructions: Please think about how much each statement has applied to you over the past 7 days.

Please select one answer for each statement.

	Not At All	A Little	Quite A Lot	Very Much
19. I worry about my fatty liver disease	☐	☐	☐	☐

CONCLUSIONS

- The impact of NASH might be underestimated in affected patients – fatigue, pain, poor sleep quality and cognitive issues are the key patient-reported symptoms and NASH has a profound impact on patients' day-to-day life
- The first development phase of a NASH-specific PRO measure (NASH-CHECK; US-English version) has been completed based on an initial literature review and CE and CD interviews with patients diagnosed with NASH F1-F3 fibrosis
- Further analysis will be performed to evaluate the dimensional structure and psychometric properties of NASH-CHECK

ACKNOWLEDGEMENTS

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