

Understanding the Patient-Perceived Impact of Nonalcoholic Steatohepatitis: Raising the Volume on a Silent Disease



Doward LC¹, Balp M-M², Twiss J¹, Slota C³, Cryer D⁴, Langford A⁵, Collen R⁶, Agashivala N⁷, Brass CA⁷, Anstee QM⁸, Sanyal AJ⁶ (The NASH-PRO TASK FORCE)

¹RTI-Health Solutions, Manchester, United Kingdom; ²Novartis Pharma AG, Basel, Switzerland; ³RTI-Health Solutions, Research Triangle Park, NC, USA; ⁴Global Liver Institute, Washington, DC, USA; ⁵British Liver Trust, Bournemouth, United Kingdom; ⁶Virginia Commonwealth University, VA, USA; ⁷Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; ⁸Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, United Kingdom

RESULTS

BACKGROUND

• Nonalcoholic steatohepatitis (NASH) is a progressive form of nonalcoholic fatty liver disease (NAFLD), characterized by excessive liver fat accumulation, inflammation, cell injury and fibrosis. Although NASH is often considered an asymptomatic 'silent' disease in its early stages, patients with NASH/NAFLD experience significantly higher rates of anxiety, depression and experience lower health-related quality of life (HRQoL) than the general population. However, no qualitative studies have been published exploring in-depth, the patient-perceived impact of NASH

OBJECTIVE

• This study aimed to identify the symptomatic and HRQoL impact of NASH from the patient perspective via concept elicitation (CE) interviews conducted with patients diagnosed with NASH

METHODS

• Institutional Review Board (IRB) approval was granted for the study by Western IRB (USA)

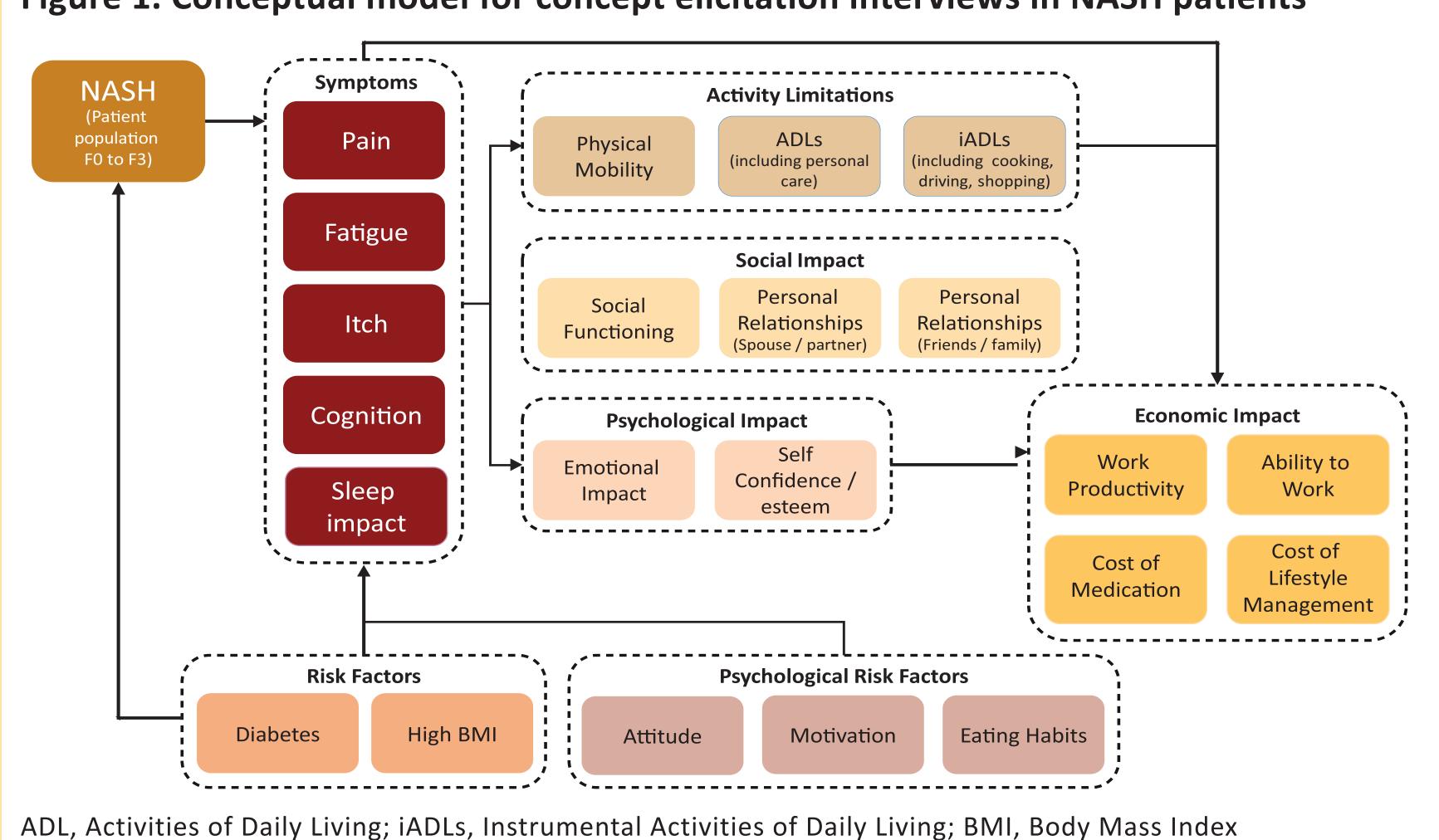
Patient Population:

- Patients with NASH recruited from a tertiary care center in Virginia, USA.
- Key inclusion criteria: Adults aged 18 75 years with NASH diagnosis confirmed by biopsy (in fibrosis stage F1, F2, or F3) or phenotypic diagnosis (ALT levels [≥ 60 IU/L for males or ≥ 40 IU/L for females] and body mass index (BMI) [≥ 23 kg/m² in Asians or ≥ 27 kg/m² in non-Asians] and type II diabetes)
- Key exclusion criteria: Presence of other liver disease, clinical evidence of steatohepatitis
 F4 (cirrhosis), excessive alcohol consumption, active substance use, severe mental illness, extreme obesity and poorly controlled diabetes

Concept Elicitation (CE) Interviews: Process and Qualitative Analysis

- A semi-structured interview guide was developed based on a conceptual model (**Figure 1**) developed previously.⁴ Interviews explored patient experiences of NASH symptoms and the impact of NASH on the way patients feel and function
- Interviews were audio-recorded and transcripts were produced
- Patient sociodemographic data were obtained from a patient-completed background questionnaire and medical data from patient records
- Thematic analysis was conducted by two independent researchers to evaluate key areas of symptomatic and HRQoL impact from the patient perspective
- Interview transcripts were analyzed in sets of five until coding saturation was reached

Figure 1. Conceptual model for concept elicitation interviews in NASH patients



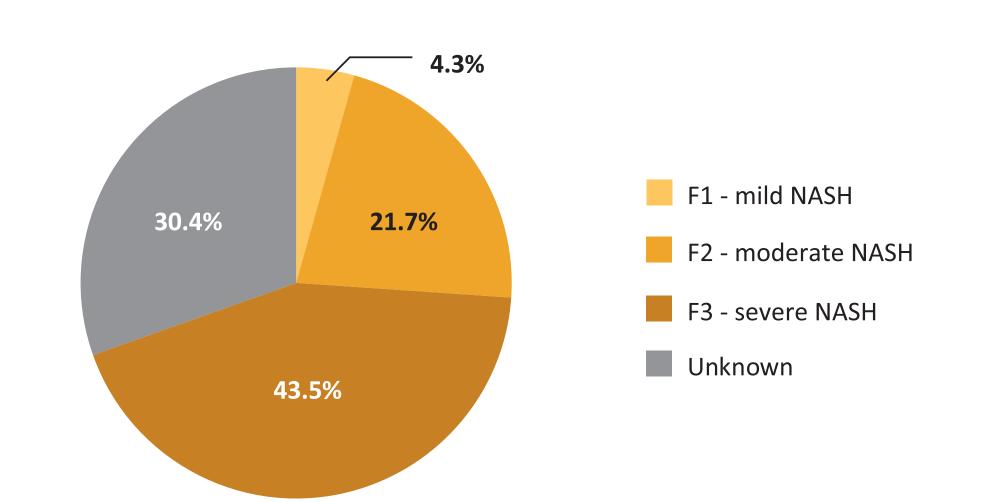
Study sample

- Initially, 27 patients were interviewed; 4 of them were excluded from the analysis due to existing severe comorbid conditions considered likely to have a current greater impact on patients' lives than NASH
- The final sample for analysis comprised 23 patients

Patient demographics and comorbid conditions:

- The mean (SD) age of the patients was 55.9 (10.0) years; 78% of the patients were female, 83% were white and 43.5% of the patients were employed
- Seven patients (30.4%) had phenotypic-diagnosed NASH and 16 (69.6%) had biopsy-confirmed NASH (**Figure 2**). The mean (SD) time since NASH diagnosis was 3.9 (2.9) years
- The most common comorbidities present in these patients were obesity (mean BMI=34.8 kg/m²), hypertension (65.2%), high cholesterol (47.8%) and type II diabetes (60.9%)

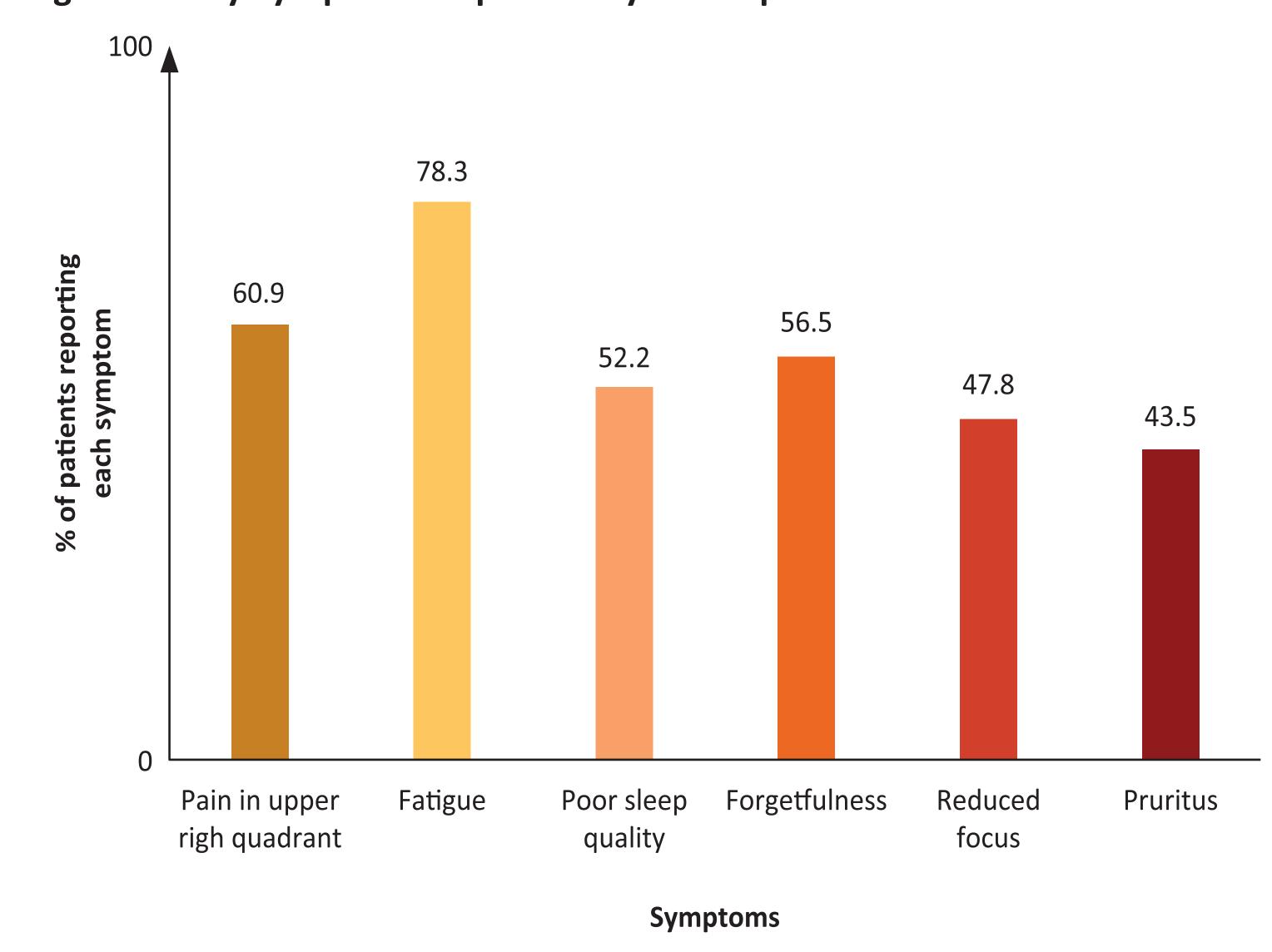
Figure 2. Fibrosis grade in NASH patients obtained from medical records



Symptoms reported by NASH patients:

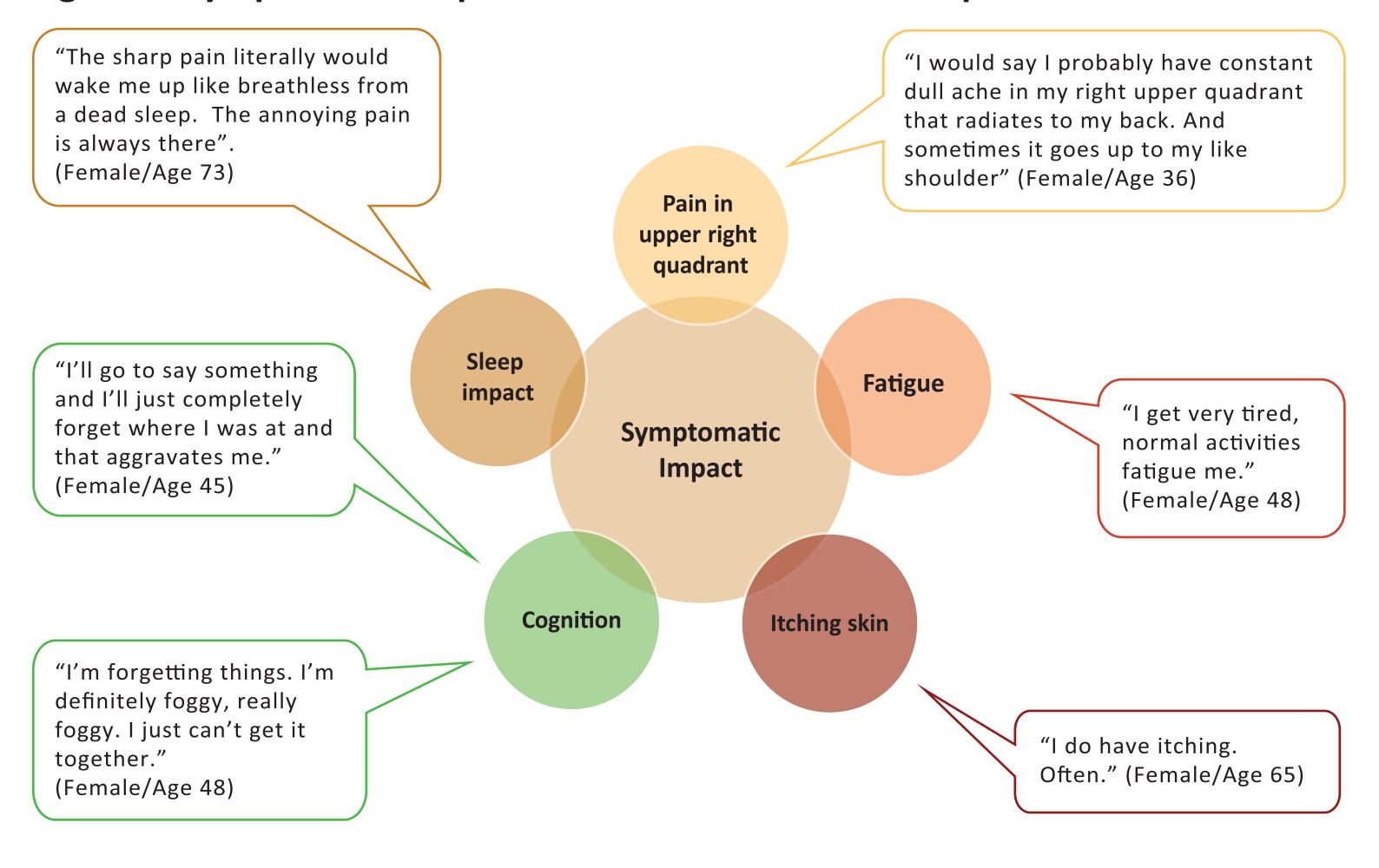
 Key symptoms reported comprised fatigue, abdominal pain, poor sleep quality pruritus (Figure 3)

Figure 3. Key symptoms reported by NASH patients



Symptomatic impact of NASH – Patient experience

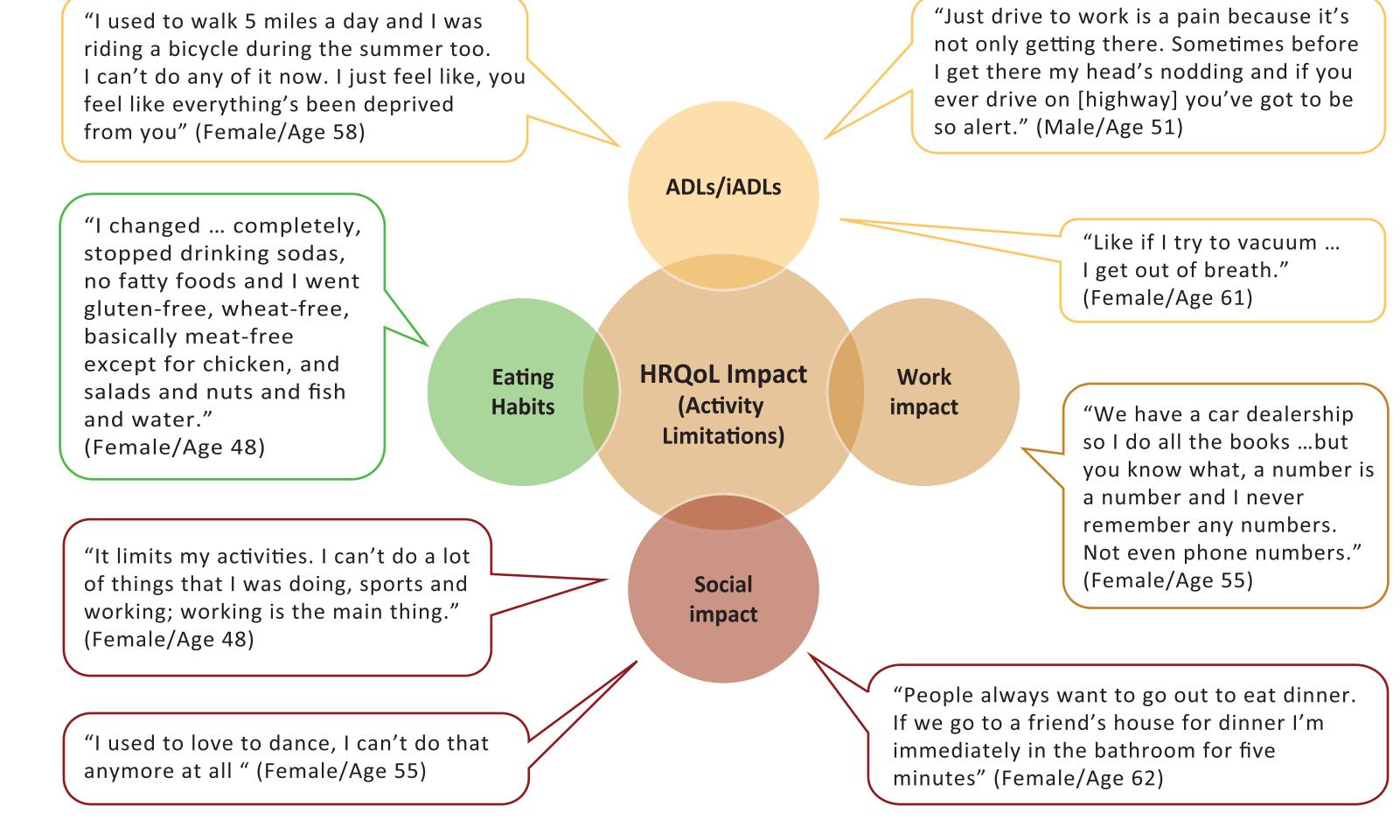
Figure 4. Symptomatic impact of NASH – Statements of patients with NASH



Impact of NASH on HRQoL – Patient experience:

- Patients reported that NASH impacted on many aspects of their daily life:
- Activity limitations, work and social life (Figure 5): NASH symptoms, particularly fatigue and cognitive problems, affected patients' ability to carry out ADLs and iADLs and impacted healthy eating choices, social and work life

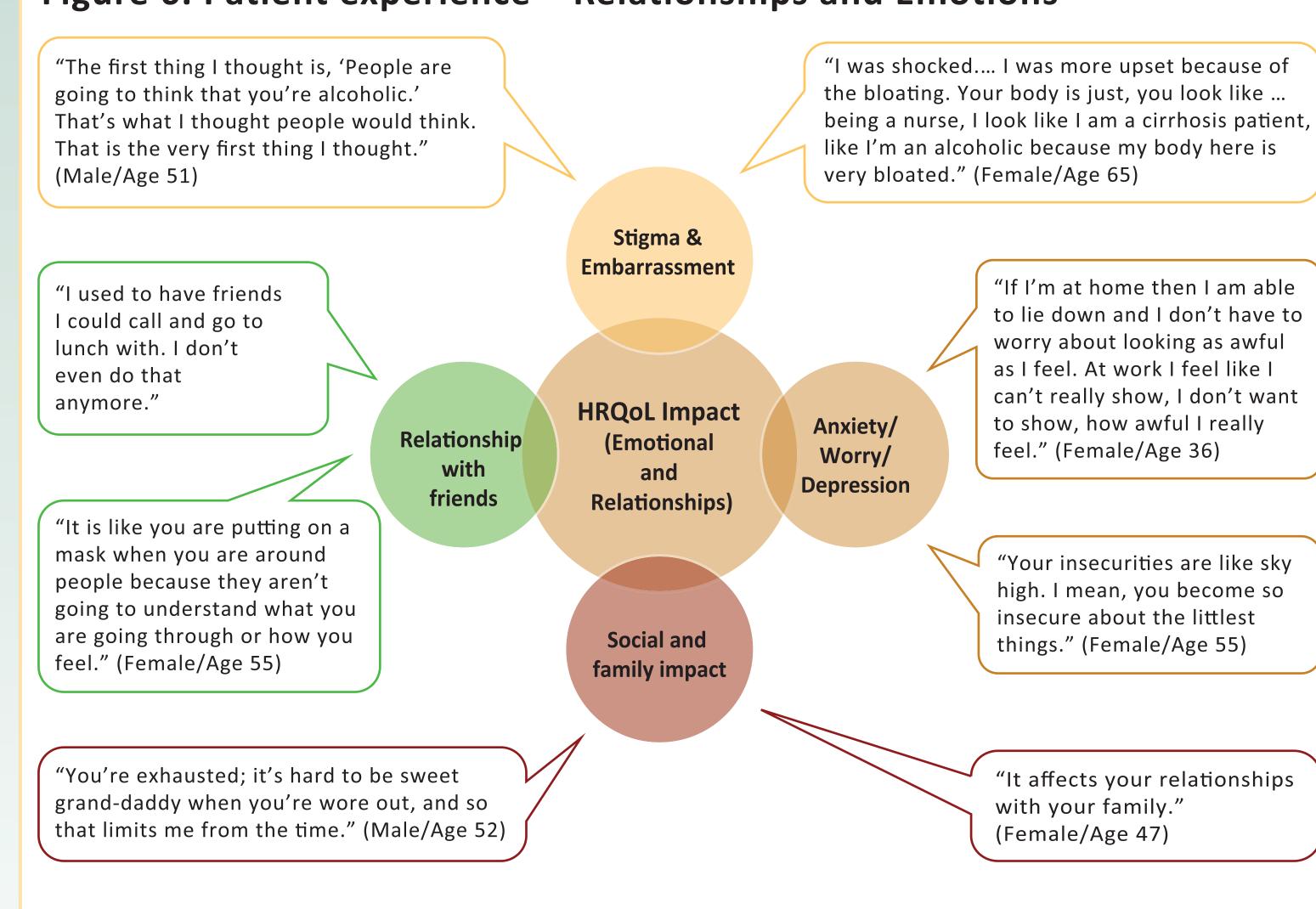
Figure 5. Patient experience – Activity limitations, Work and Social life



- Personal relationships and emotions (Figure 6): Both the experience of symptoms and the daily awareness of living with NASH also had a profound psychological impact on many patients, with negative impact on the quality of relationships with family and friends
- Some patients reported being worried about perceived NASH-stigma, hiding their symptoms to reduce worry for family members and self-consciousness/ embarrassment related to body shape/appearance
- Patients also reported anxiety and depression

RESULTS

Figure 6. Patient experience – Relationships and Emotions



CONCLUSION

- The interviews identified key symptoms experienced by NASH patients such as pain, poor sleep quality and cognitive problems
- The interviews also provided an insight into the negative impact of NASH on patients' HRQoL in terms of physical functioning, work and social life. NASH also impacted negatively on patients' emotional life and family/personal relationships
- Findings from this study challenges the notion that NASH is an asymptomatic condition and supports future patient-centered research initiatives in NASH
- These findings reinforce the need to develop a NASH-specific patient-reported outcome measure (PROM) in order to better quantify and capture the humanistic burden associated with NASH
- The development of PROM should follow FDA guidance⁵
- The next step will be to generate the content of a NASH-specific PROM based on the output of the CE interview

REFERENCES

- 1. Kopec KL and Burns D. *Nutr Clin Pract* 2011; 26: 565–76
- 2. Elwing JE et al. *Psychosom Med* 2006; 68: 563–569
- 3. David K et al. *Hepatol* 2009; 49: 1904–12
- 4. Doward LC *Hepatol* 2017; 66(1) S422–S423
- 5. US FDA Guidance for Industry 2009. Available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM193282.pdf

Acknowledgement

This research was conducted by the NASH-PRO Task Force. Harini Chinthapatla and Satabdi Chatterjee of Novartis provided medical writing support. The authors would like to thank the patients who contributed to the research.

Funding

This study was funded by Novartis Pharma AG, Basel, Switzerland.

