

SYMPTOM BURDEN IN PATIENTS WITH IDIOPATHIC MULTICENTRIC CASTLEMAN DISEASE AND ITS IMPACT ON DAILY LIFE: AN INTERNATIONAL PATIENT AND CAREGIVER SURVEY

Mukherjee S¹, Shupo F², Wayi-Wayi G², Zibelnik N², Kanhai K², Jones E³, Mason N³, Franklin M⁴, Brazier J⁴, Mileva Repasky⁵, Makarounas-Kirchmann K⁶

¹Cleveland Clinic, ²Recordati Rare Disease, ³Lumanity, ⁴Sheffield University, ⁵CDCN, ⁶KMC Health Care

Background

Idiopathic Multicentric Castleman disease (iMCD) is a subcategory of MCD, a rare lymphoproliferative disorder characterized by enlargement of the lymph nodes and lymphatic system. As no curative therapies exist for iMCD, the primary focus of clinical management remains symptom control. Currently, no assessment of symptom burden exists within this population. Incorporating patient and caregiver perspectives on the impact of iMCD symptoms can facilitate timely treatment, better symptom monitoring, and early flare-up detection, leading to greater patient satisfaction.

The aim of the study was to establish a comprehensive iMCD-centered symptom inventory from a patient perspective and to quantify the impact of symptom burden on various aspects of daily living. Secondly, to investigate caregivers' perspective on patients' iMCD-symptom burden and impact on the caregivers' daily life. Only the methodology and results for the patients are presented in this poster. More detailed results have been published elsewhere.¹

Methods

The iterative process followed is shown in Fig. 1. The initial literature review (April 2020) identified the MCD-SS, the CarerQoL-7D and the SF-36 as existing relevant scales. Also identified were symptom themes and these, together with their impact on daily life of patients and caregivers were explored further and validated by clinical experts.

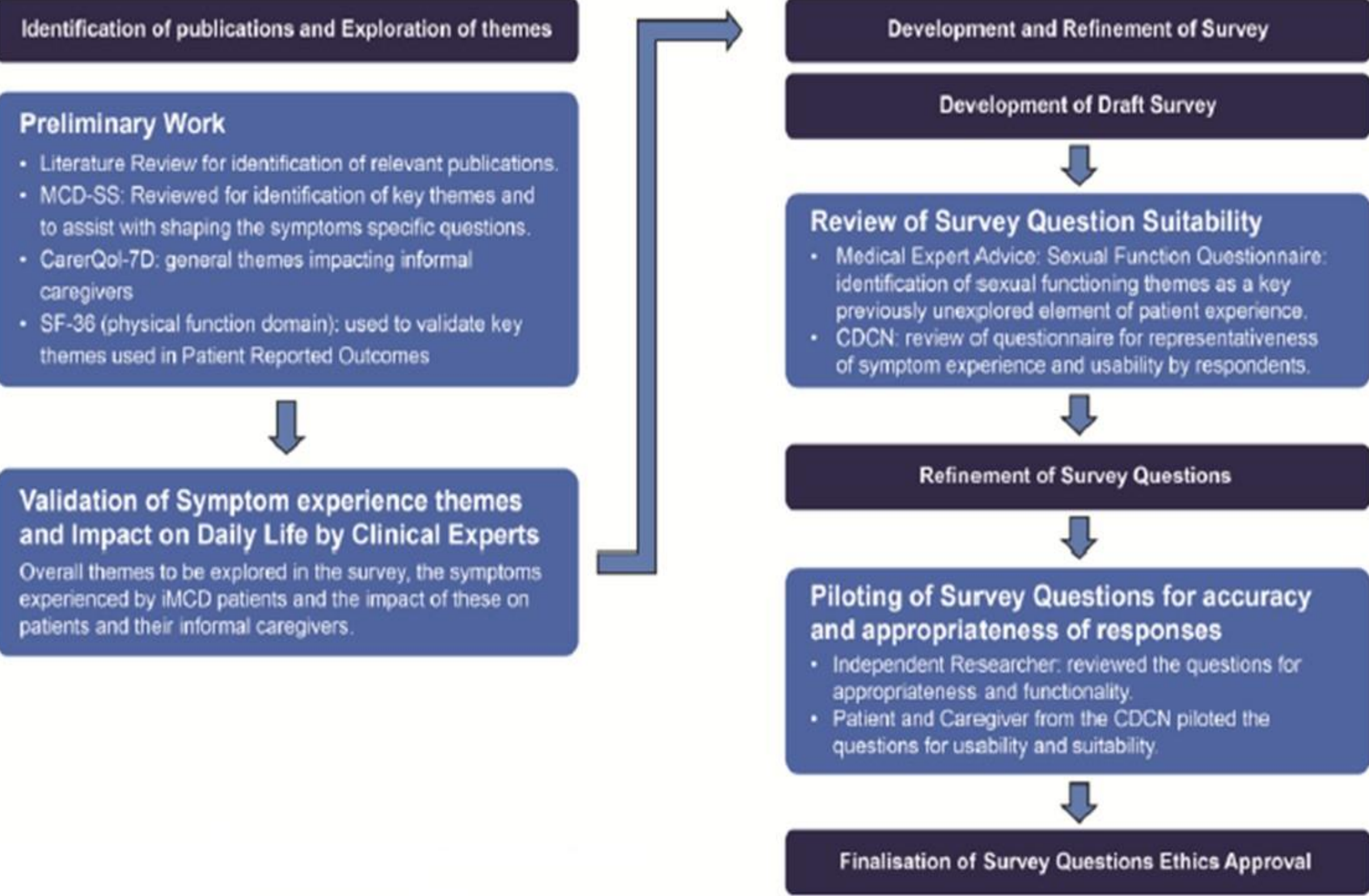


Fig. 1: Iterative derivation of iMCD survey

CDCN: Castleman Disease Collaborative Network; MCD-SS: Multicentric Castleman Disease Symptom Scale; iMCD: idiopathic Multicentric Castleman Disease; SF-36: Short Form 36

The questionnaire was developed in a stepwise manner to ensure appropriate stakeholder (patient, clinician, caregiver and researcher) engagement before being piloted. Survey Monkey® was used as the platform for the survey and was available to patients from April to November 2021. This non-interventional study consisted of 45-questions (11/45 open-ended, 34/45 closed-ended pre-defined) relating to symptomatology experienced, severity, and symptom impact on daily life in the past week (five severity level options, 0=no impact to 4=severe impact). Data storage remained with Lumanity, and question responses were de-identified and saved on password-encrypted servers. Ethics approval was obtained.

iMCD patients were recruited via the Castleman Disease Collaborative Network (CDCN). To participate, patients had to be ≥18 years, patients had to have a practitioner-confirmed diagnosis of iMCD. Patient consent was obtained for those participating in the study.

Descriptive analyses were performed on closed-ended questions. Ordinal logistic regression analysis was used to assess the relationship between number of symptoms and impact on different aspects of daily life. The effect is reported as an odds ratio (OR) with 95% confidence intervals (p<0.05). All statistical analyses were conducted in SPSS v23, and logistic regression utilized Minitab version 20.

Results

Detailed participant characteristics are shown in Table 1. Of the 51 patients self-reporting clinician diagnosed iMCD, 56.9% were female with a mean age of 47.4 years (range, 22–78 years). Of those who reported an informal caregiver (22/51), the patient's spouse was the primarily carer (22/51).

Of the 36 patients (70.6%) who reported receiving iMCD-directed treatment—23/51 (45.1%) received an intravenous treatment and 13/51 (25.5%) received a combination of intravenous and oral treatment. Approximately, 25% of patients who received intravenous and oral treatment reported receiving an oral steroid. Of the 36 patients (70.6%) receiving iMCD treatment, 31 (86.1%) reported receiving an anti-interleukin-6 monoclonal antibody with the frequency of administration varying between once-a-week to once every six weeks. Ordinal logistic regression analysis showed that the higher the number of symptoms, the more likely the symptoms negatively impacted the patient's daily life activities, shown across every daily life activity (OR <1; Fig. 2).

Table 1: Characteristics of Patients and Caregivers participating in the iMCD survey

Respondents Characteristics	Patient Respondents
Number of respondents, N	51
Gender, n (%)	
Female	29 (56.9%)
Male	22 (43.1%)
Prefer not to answer	
Age mean (SD, Range)	47.4 (1.9, 22 to 78)
Years under caregiver care, Mean (SD, range)	
Country, n (%)	
Australia	4 (7.8%)
Canada	4 (7.8%)
UK	3 (5.9%)
US	40 (78.4%)
Employment status, n (%)	
Disabled (unable to work/on disability allowances)	13 (25.5%)
Employed full time	21 (41.2%)
Employed part time	4 (7.8%)
Homemaker	3 (5.9%)
Prefer not to say	1 (2.0%)
Retired	3 (5.9%)
Unemployed/seeking opportunities	6 (11.8%)
Ethnic Group, n (%)	
Asian	7 (13.7%)
Black or African American	1 (2.0%)
Native Hawaiian or Other Pacific Islander	2 (3.9%)
Prefer not to answer	3 (5.9%)
White	38 (74.5%)
Hispanic	
Disease Characteristics of patients	Patient Survey
Sub Type, n (%)	
iMCD NOS	40 (78.4%)
TAFRO	11 (21.6%)
Treatment for iMCD Patients, n (%)	
Not receiving treatment	8 (15.7%)
Treatment for iMCD symptoms	3 (5.9%)
Receiving treatment for iMCD	36 (70.6%)
IV treatment only	23 (45.1%)
Both IV and oral treatment	13 (25.5%)
Missing	4 (7.8%)

iMCD: idiopathic multicentric Castleman's disease; iMCD NOS: idiopathic multicentric Castleman's disease not otherwise specified; SD: standard deviation; TAFRO: thrombocytopenia, anasarca, fever, reticuln marrow and organomegaly.

A total of 27 unique symptoms were experienced by the 51 patients in the week prior to completing the survey. Five patients experienced no symptoms. In patients reporting symptoms, tiredness was the most prevalent (78.4%), followed by weakness (41.2%), night sweats (39.2%) and numbness/tingling (37.3%).

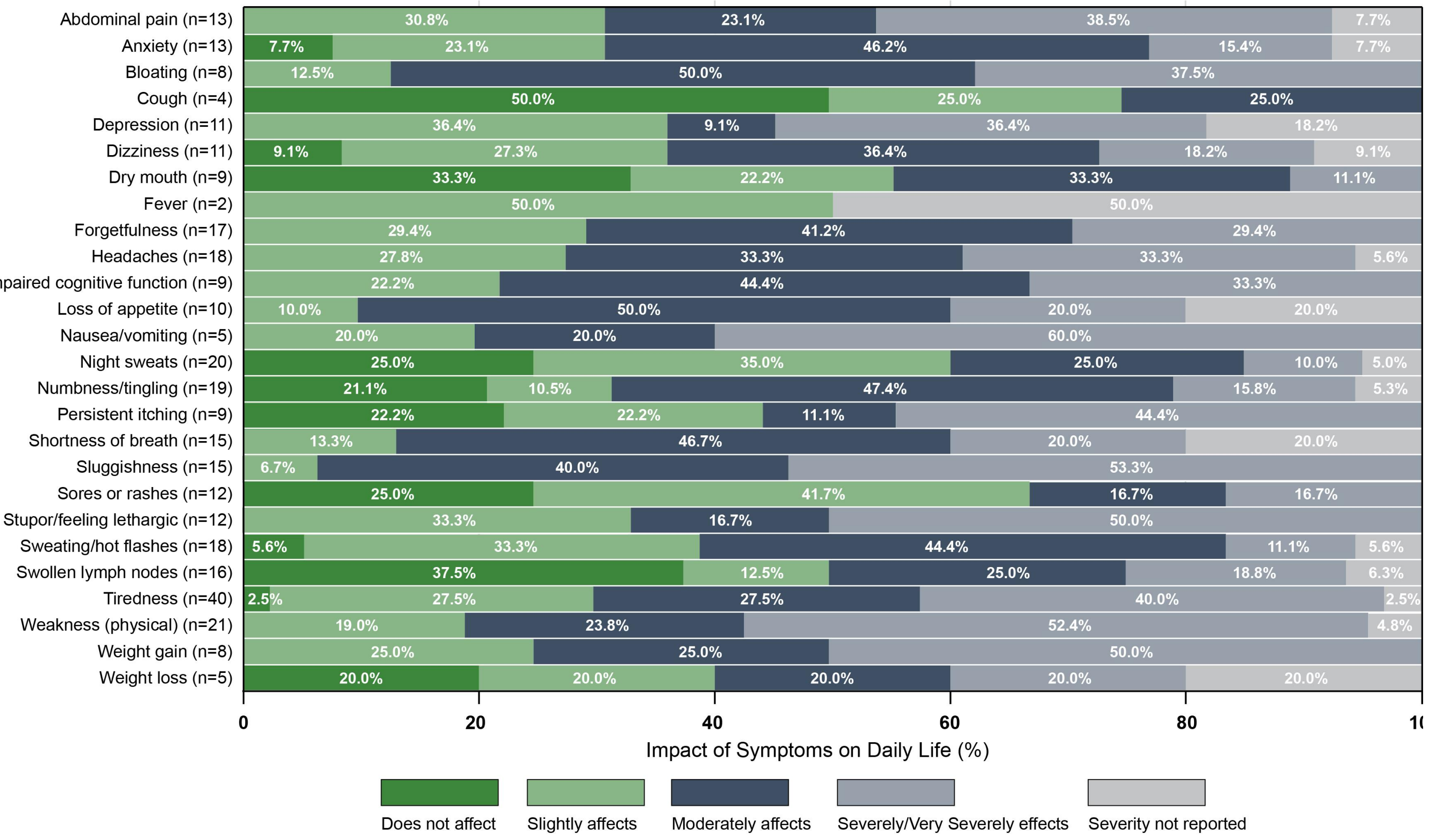


Fig. 2: The impact severity on daily life for iMCD patients experiencing a symptom

Note: Sample size of symptoms corresponds to the number of patients who reported experiencing the relevant symptoms one week prior to completing the survey

Patients reported that their symptoms had a slight to moderate effect on their daily life (Fig. 2). The symptoms having the most severe impact on daily life included nausea/vomiting (60.0%), sluggishness (53.3%), weakness (physical) (52.4%), weight gain (50.0%) and stupor/feeling lethargic (50.0%) (Fig. 2). When looking closely at the aspects of daily life most affected by these symptoms, a moderate to very severe impact was reported on aspects of daily life that related to patient pain/discomfort (65.2%), ability to travel (60.9%), sexual function (56.5%), emotional and psychological wellbeing (52.2%), general wellbeing (52.2%), financial wellbeing (52.2%) and social life (50.0%) (Fig. 3).

Ordinal logistic regression analysis showed that the higher the number of symptoms, the more likely the symptoms negatively impacted the patient's daily life activities, shown across every daily life activity (OR<1; Fig. 2).

Results

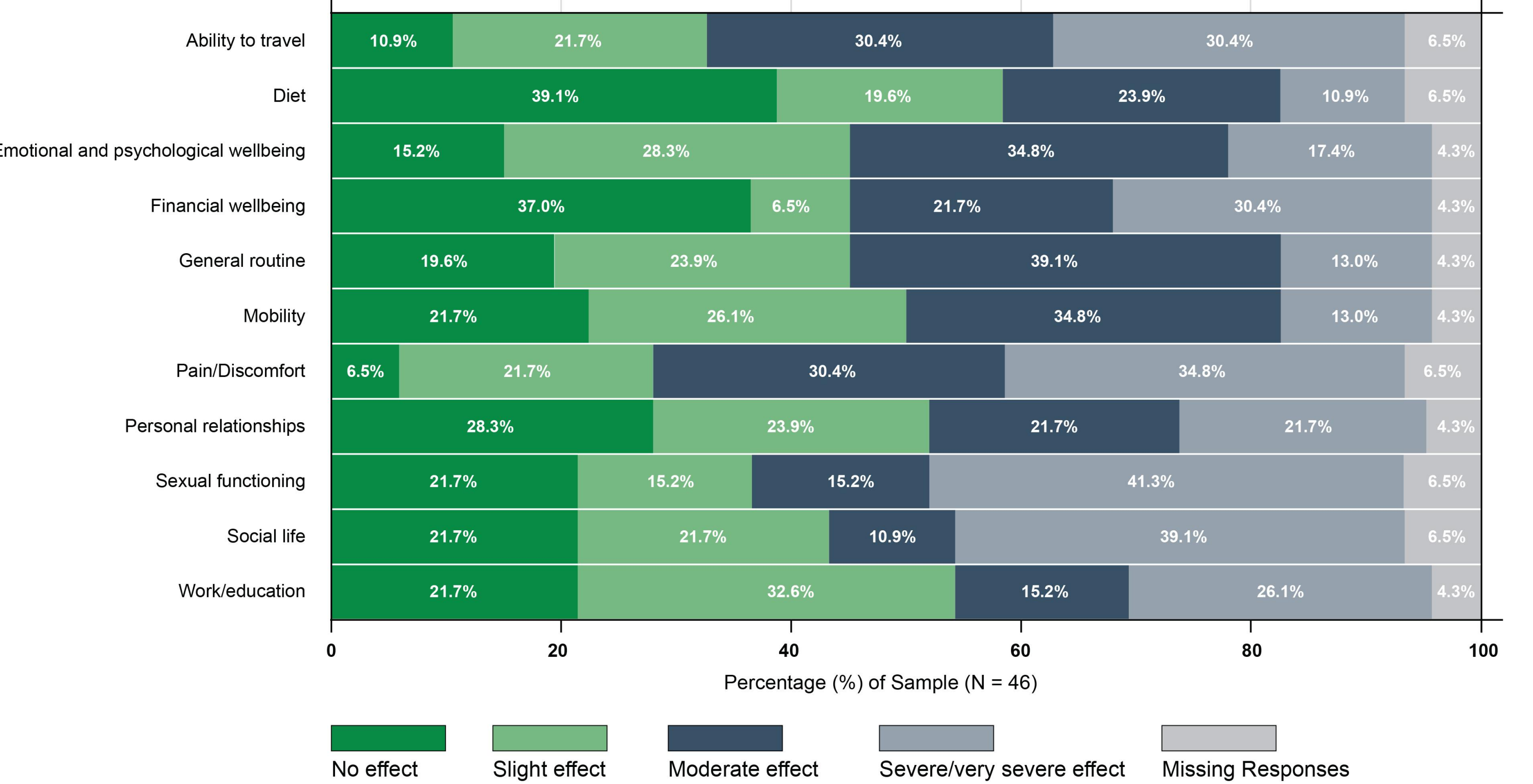


Fig. 3: Severity Impact of symptoms on aspects of daily life

Note: Sample size of N - 46 accounts for only those patients which reported experiencing symptoms, with five patients having reported not experiencing any iMCD symptoms.

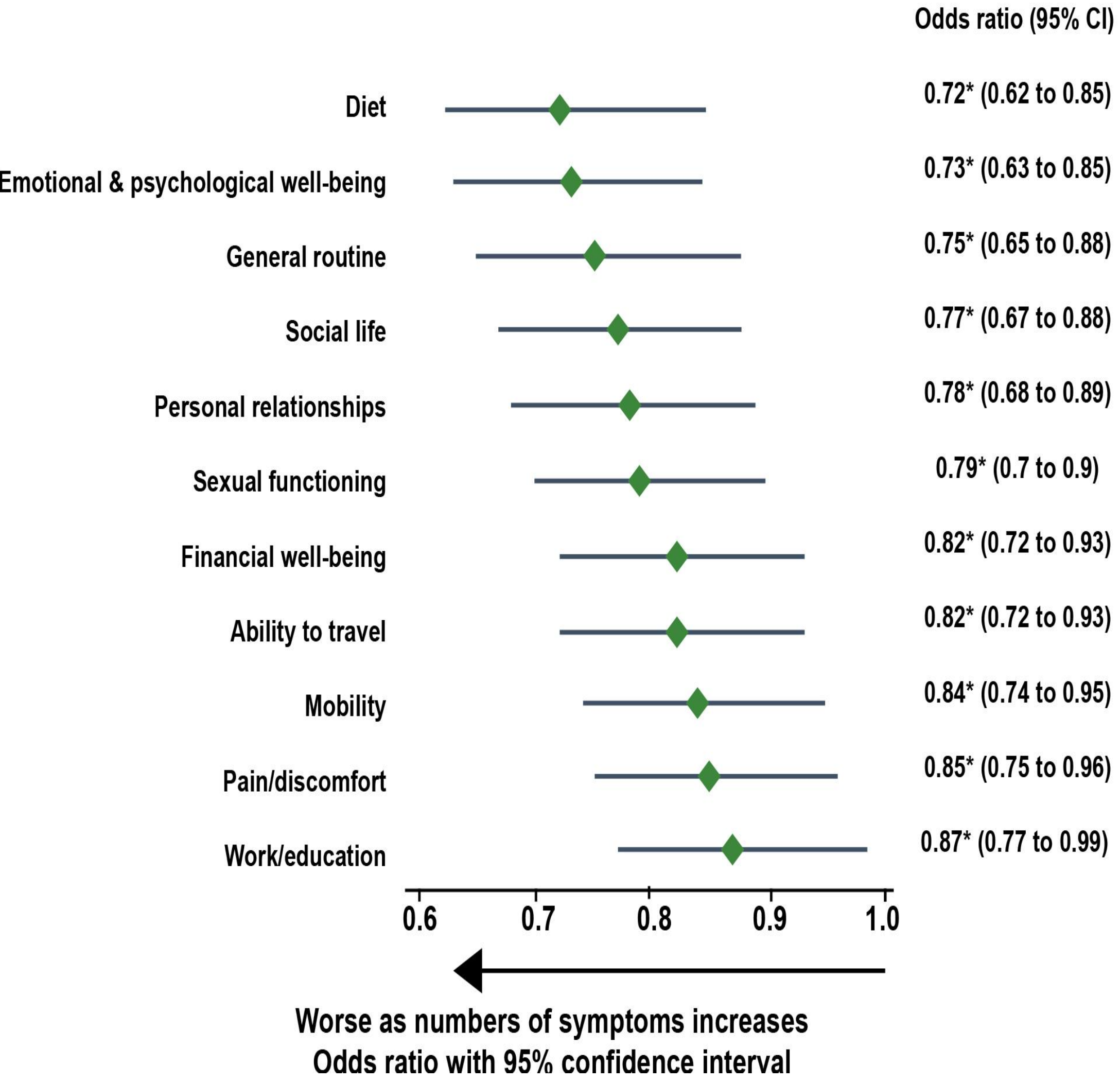


Fig. 4. Forest plot of the odds ratios of impact on daily life by Multiplicity of symptoms

The multivariate regression model was adjusted by age, gender, and number of symptoms. *Level of significance was set at p<0.05

Limitations

This international iMCD survey is, to our knowledge, the first large survey to systematically evaluate the spectrum of symptoms experienced by patients and the impact of symptom burden on everyday life from the patient perspective. It nonetheless had limitations that need to be considered. Firstly, identification of patients for this survey relied on respondents self-reporting their practitioner-confirmed diagnosis of iMCD as opposed to direct physician reporting or clinical documentation. Secondly, there were insufficient patient numbers to differentiate the impact by type of iMCD. Thirdly, though some treatment data were captured this was insufficient to determine the impact of this on symptoms and aspects of daily life. Lastly, COVID-19 restrictions may have impacted recruitment of patients.

Conclusions

In conclusion, this study outlines a methodical approach for creating patient-centered surveys. Its primary achievement is the creation of an extensive symptom inventory for iMCD. The survey's results reveal the far-reaching consequences of a high symptom burden on various aspects of daily life, affecting patients. These findings have the potential to influence the refinement of diagnostic criteria, enhance clinical assessments, and guide the development of patient-focused treatment plans. Ultimately, these findings lay the groundwork for our aspiration to establish the first-ever iMCD-specific symptom scale.