Qualitative analysis of patient characters, interviews on the burden of neuronopathic Gaucher disease in Japan

Shinichi Noto,[1] Midori Ono,[2] Yuta Koto,[3] Aya Narita,[4] Anna Lissa Hamada,[2] Norio Sakai[5]

[1]Niigata University of Health and Welfare, Niigata, Japan; [2]Japan Medical Office, Takeda Pharmaceutical Company Limited, Tokyo, Japan;
[3]School of Nursing, Faculty of Health Science, Osaka Aoyama University, Osaka, Japan;
[4]Division of Child Neurology, Institute of Neurological Sciences, Tottori University Faculty of Medicine, Yonago, Tottori, Japan;
[5]Child Healthcare and Genetic Laboratory, Division of Health Sciences, Osaka University Graduate School of Medicine, Osaka, Japan

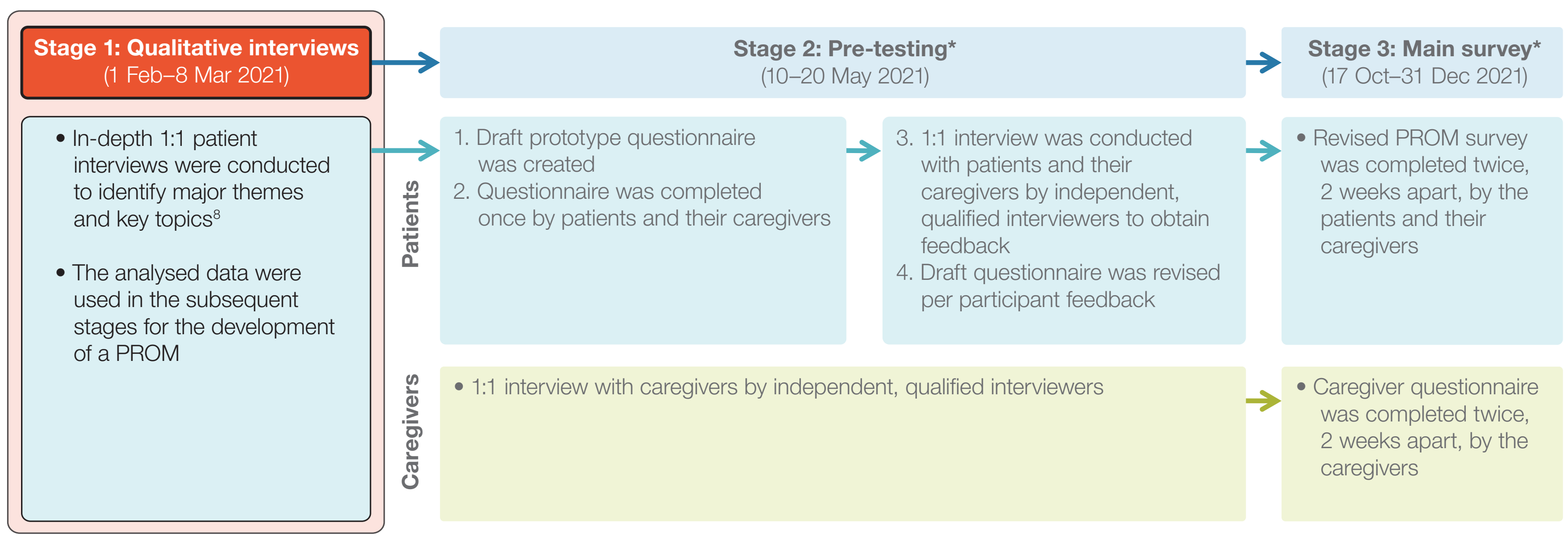
BACKGROUND

- Gaucher disease (GD) is a rare autosomal recessive lysosomal storage disorder.[1]
- GD is categorised into 3 clinical subtypes: type 1 (non-neuronopathic GD) and types 2 and 3 (neuronopathic GD [nGD]).[1]
  - Type 1 GD accounts for ~94% of cases in non-Japanese populations.[2]
  - In Japan, the prevalence of nGD is higher than in other countries,[3,4] accounting for ~60% of GD cases.[5]
- Patient-reported outcome measures (PROMs) enable a more comprehensive understanding of the burden of GD.
- However, the currently available PROM focuses only on type 1 GD[6,7] and is not suitable for patients with nGD.
- To develop a new PROM questionnaire that can be used for all GD types, we first conducted a qualitative analysis of interviews with patients with nGD.[8]
  - The aim of the qualitative analysis was to develop PROM questions specific to Japanese patients with nGD that can be added to the currently available PROM.

METHODS

- This was a cross-sectional observational study conducted in Japan comprising 3 stages (UMIN000042872).
  - Here we report the results from the qualitative interviews in Stage 1.

Figure 1. Study flow



Stage 1: Qualitative interviews
(1 Feb–8 Mar 2021)

- In-depth 1:1 patient interviews were conducted to identify major themes and key topics[8]
- The analysed data were used in the subsequent stages for the development of a PROM

Stage 2: Pre-testing*
(10–20 May 2021)

Stage 3: Main survey*
(17 Oct–31 Dec 2021)

Patients

1. Draft prototype questionnaire was created
2. Questionnaire was completed once by patients and their caregivers
3. 1:1 interview was conducted with patients and their caregivers by independent, qualified interviewers to obtain feedback
4. Draft questionnaire was revised per participant feedback

- Revised PROM survey was completed twice, 2 weeks apart, by the patients and their caregivers

Caregivers

- 1:1 interview with caregivers by independent, qualified interviewers
- Caregiver questionnaire was completed twice, 2 weeks apart, by the caregivers

Abbreviation: PROM, patient-reported outcome measure.
*The results of this stage are reported at Poster #PCR9.

Study population

- Included male or female patients with a confirmed type 2 or 3 GD diagnosis who had been treated for GD.
  - For patients aged <16 years, a caregiver (aged ≥20 years) participated on their behalf.
- Excluded participants who had cognitive disabilities, were not fluent in Japanese or were judged to be unsuitable for any other reason.

Qualitative interview

- Patients were recruited in Japan by referral from a patient association.
- The interviews were conducted using the interview guide developed by the authors based on the existing PROM for type 1 GD.[6,7]
  - The interview focused on 3 main themes; the appropriateness of these themes was confirmed during the interview.
- Interviews were conducted online in Japanese by one of the authors, who is a qualified nurse and has experience treating patients with GD.
- Interviews were audio-recorded with patients' approval and were transcribed.

Statistical analysis

- All interview transcripts were manually confirmed and were classified into 3 pre-proposed themes, confirming that no additional themes were necessary.
- Frequently occurring and co-occurring words were extracted by hierarchical cluster analysis and co-occurrence network analysis.
  - The Ward method was used to cluster words appearing ≥5 times; Jaccard distances between clusters were calculated.
  - The co-occurrence relation was calculated by the Jaccard index for words appearing ≥5 times and their word combinations.
- A co-occurrence network map was used to visually represent the resulting associations between words within sentences.

RESULTS

Patient demographics

Characteristics	Type 2 (N=4)	Type 3 (N=4)
Age range, years	2–11	4–57
Children (<18 years)	4	2
Adults (≥18 years)	0	2
Sex		
Male	2	3
Female	2	1
Daily activities		
Bedridden	3	0
Walk without assistance	0	3
Nursing assistance	1	0
No information	0	1
Interviewee		
Patient	0	2
Caregiver	4	2

Data are number of patients (N) unless otherwise indicated.

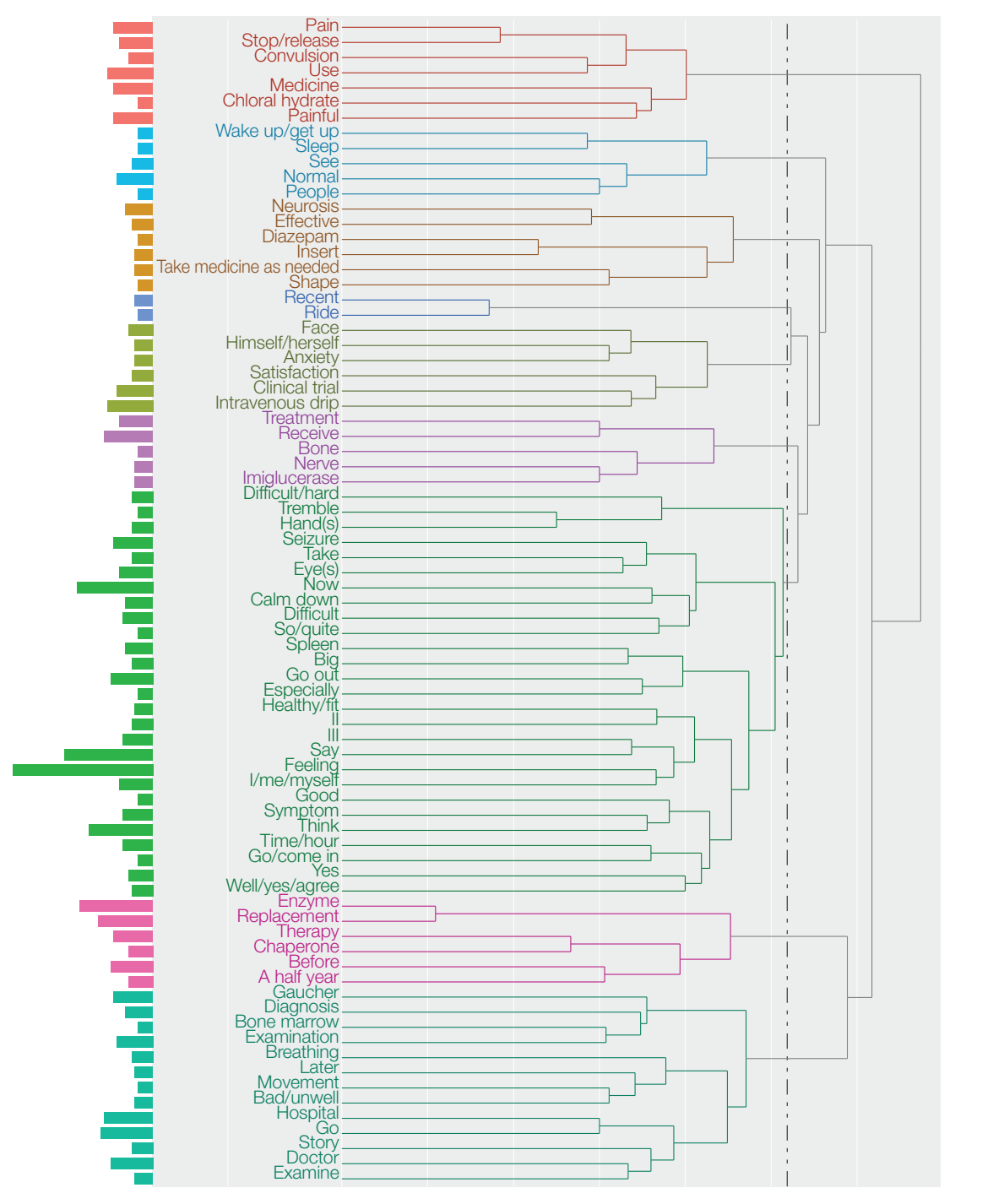
Conceptual framework identification

- Transcription analysis confirmed that the proposed themes, "treatment status", "patient burden" and "social support systems", are the main themes of disease burden.

Theme	Topic	Main content of remarks
Treatment status	Hearing impairment	Hearing loss
	Visual impairment	Squinted eyes, difficulty closing eyes
	Difficulty swallowing	Sputum-sticking sensation while sleeping
	Difficulty speaking	Difficulty talking
	Involuntary movement of extremities	Convulsive seizure, feeling that body and face are twitching
	Epileptic seizures	Epileptic seizures; anxiety about onset or possibility of epileptic seizures at school/in work
	Body aches	Fatigue after treatment; body tilting; body stiffness; bone fractures occurring when only changing position
Patient burden	Anxiety about symptoms	Epileptic seizures
	Difficulty with exercise and work	Anxiety about onset or possibility of epileptic seizures at school/in work
	Anxiety about continuing treatment	Feel uneasy about how long treatment will be continued
	Anxiety about going out	I feel anxious about the risk of infectious diseases when going out, including going to the hospital
	Tiredness from hospital visit or treatment	Burden of travelling because the hospital that can provide enzyme replacement therapy is not in the neighbourhood
Social support systems	Dissatisfaction about government service	As "Gaucher disease" is unrecognised as a disease name by government offices and public institutions, it is burdensome to explain
	Lack of social support	Do not have information about support system
	Information exchange in patient association	Can exchange information or have a consultation with patients with the same disease type

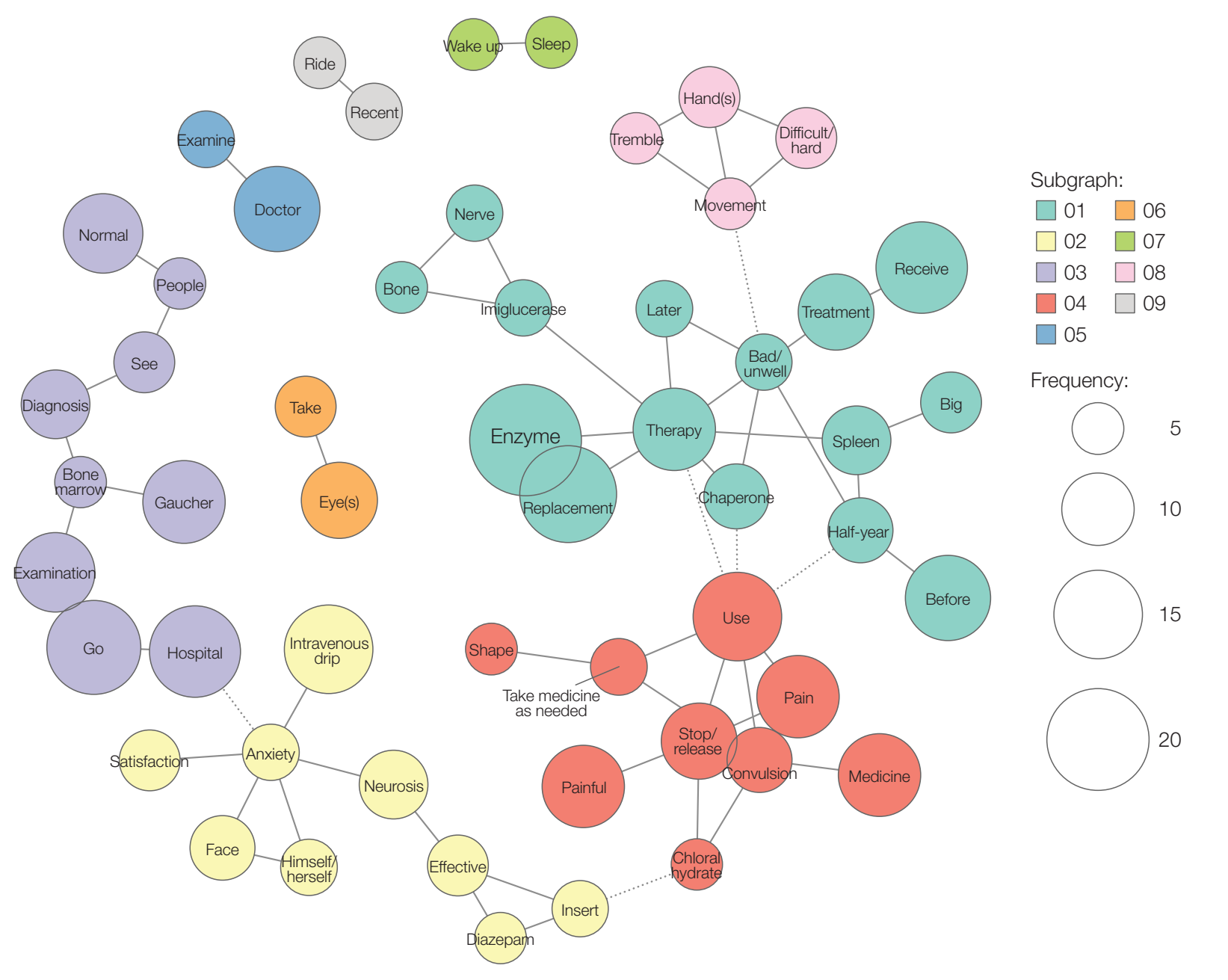
Adapted from Koto Y, et al. *Orphanet J Rare Dis* 2022;17:280.

Figure 2. Hierarchical cluster of extracted words for the theme "treatment status"



The dotted line shows the cut-off for the level of cluster analysis. The bar length on the left side indicates word frequency. Adapted from Koto Y, et al. *Orphanet J Rare Dis* 2022;17:280.

Figure 3. Co-occurrence network analysis of extracted words in the theme "treatment status"



The solid line shows words that appeared simultaneously in the same statement. The size of the circle indicates the frequency of the word's occurrence. Adapted from Koto Y, et al. *Orphanet J Rare Dis* 2022;17:280.

- 9 clusters of 2–27 words each were identified.
- Frequently appearing words were related to neurological symptoms and medication for seizure treatment.
  - Examples: "convulsions", "hands", "trembling", "diazepam", "chloral hydrate".
- Closely connected words related to medications were identified.
- Words and word connections suggest that patients with nGD are concerned about neurological symptoms.

Figure 4. Hierarchical cluster of extracted words for the theme "patient burden"

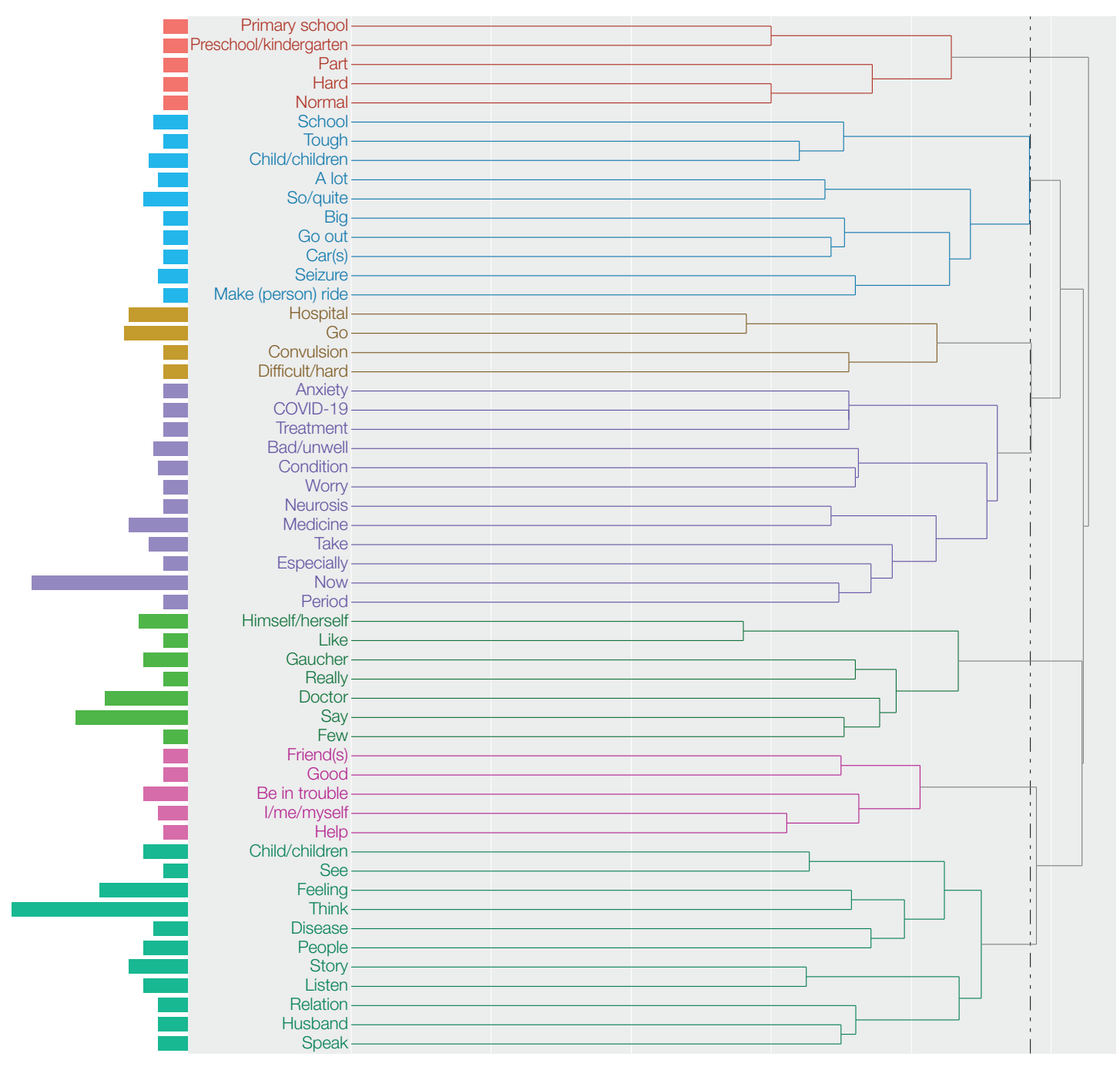


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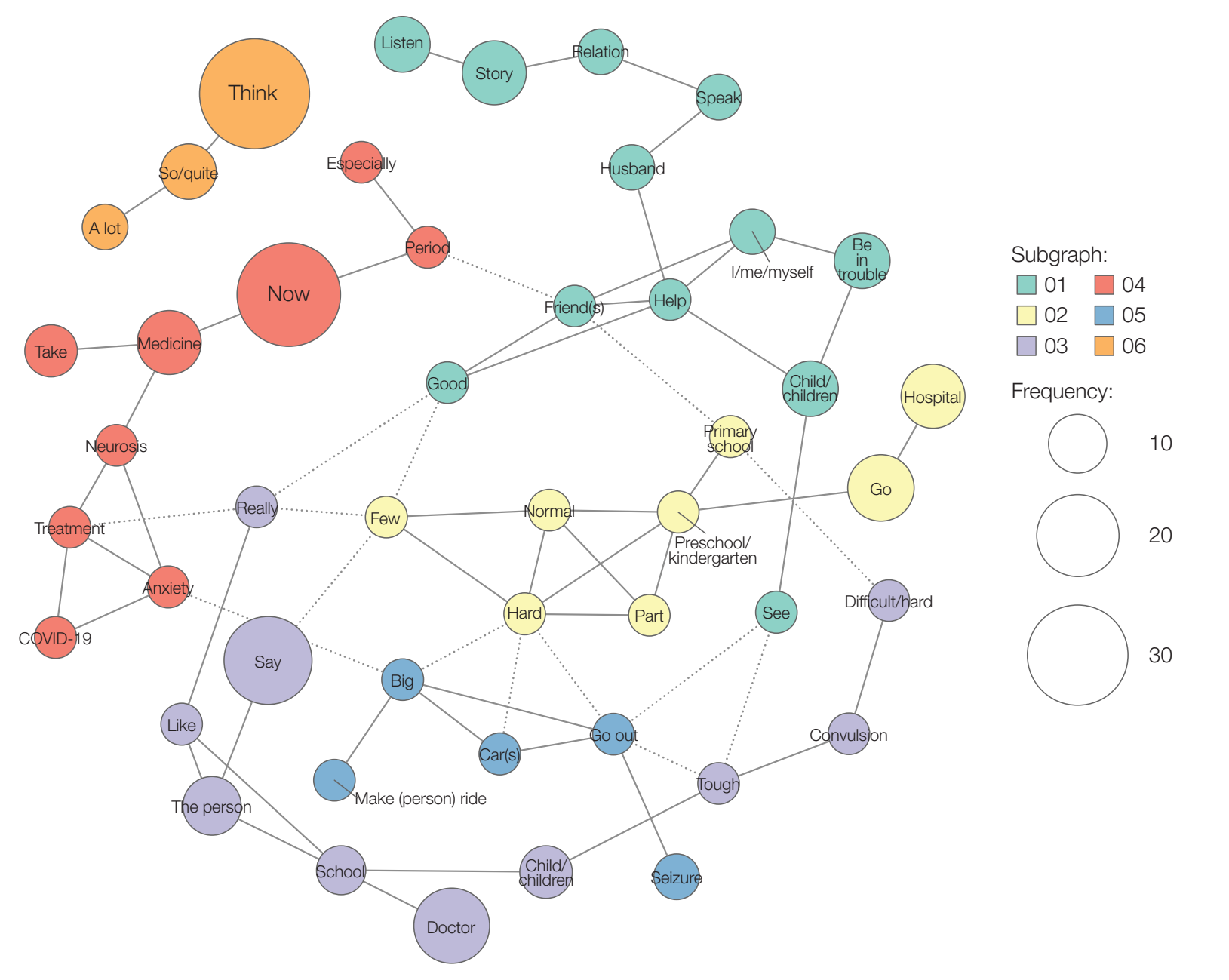
Figure 5. Co-occurrence network analysis of extracted words in the theme "patient burden"



The solid line shows words that appeared simultaneously in the same statement. The size of the circle indicates the frequency of the word's occurrence. Adapted from Koto Y, et al. *Orphanet J Rare Dis* 2022;17:280.

- 7 clusters of 4–12 words each were identified.
- Key clusters were for treatment burden (hospital visits and medications) and for the burden associated with schooling.
  - Examples: "hospital", "difficult/hard", "take", "medicine", "school", "tough", "primary school".
- There were weak but broad connections between words; no words were located at the centre of the network.

Figure 6. Hierarchical cluster of extracted words for the theme "social support systems"

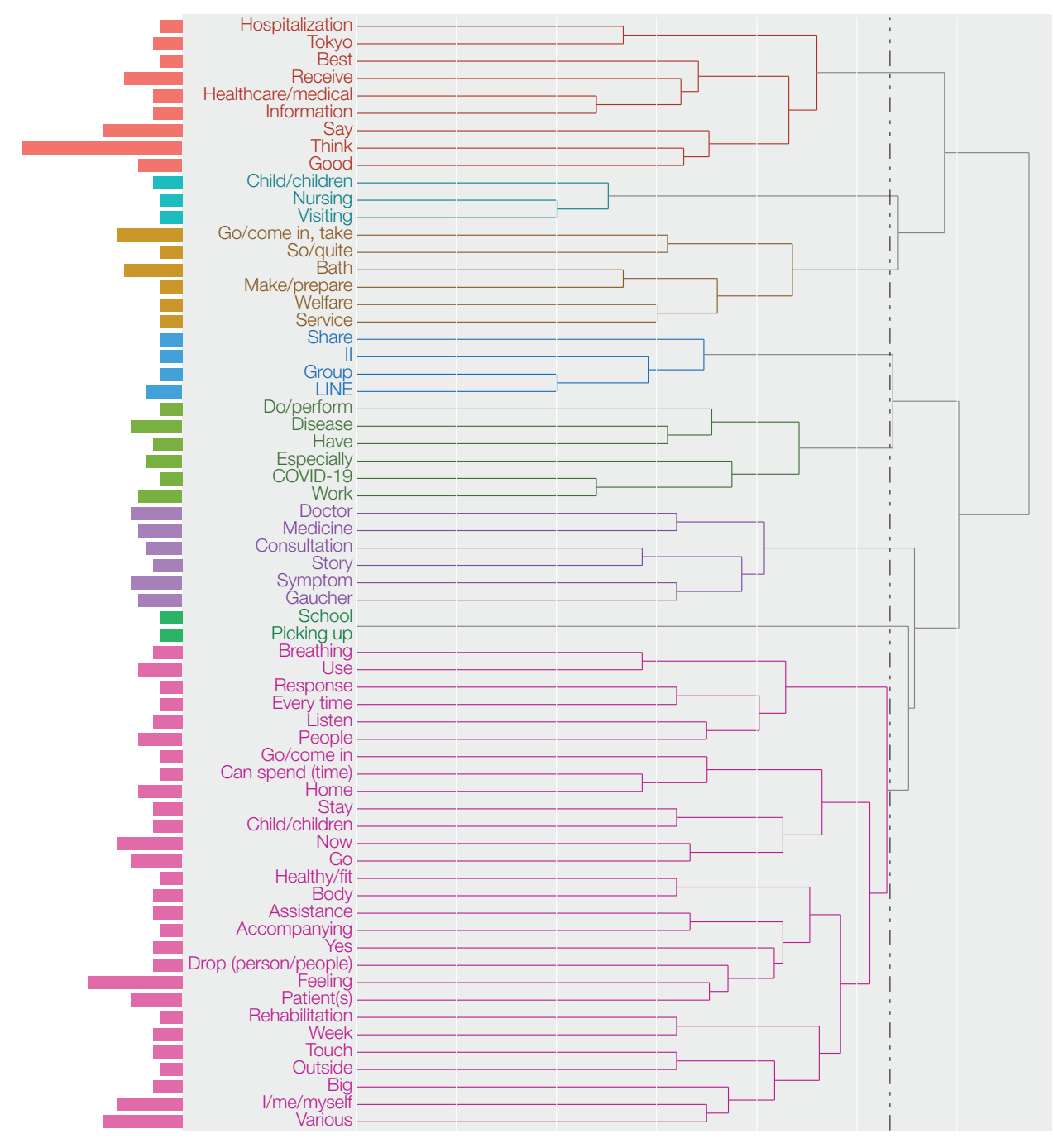


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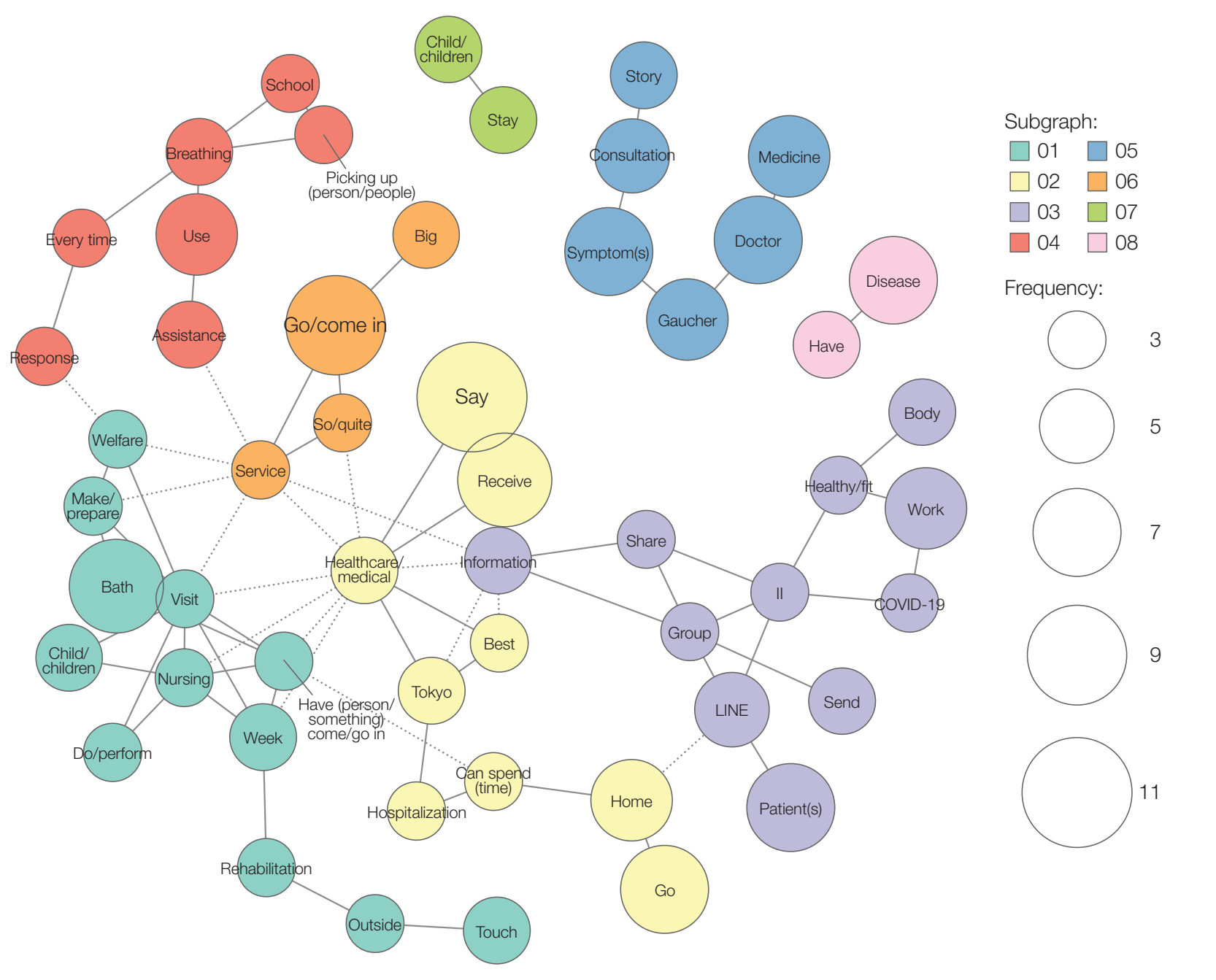
Figure 7. Co-occurrence network analysis of extracted words in the theme "social support systems"



The solid line shows words that appeared simultaneously in the same statement. The size of the circle indicates the frequency of the word's occurrence. Adapted from Koto Y, et al. *Orphanet J Rare Dis* 2022;17:280.

- 8 clusters of 2–28 words each were identified.
- Frequently appearing words were related to the types of services patients received.
  - Examples: "visiting", "nursing", "bath", "rehabilitation".
- The co-occurrence network analysis suggests that patients and their caregivers considered using social support systems when consulting with their doctors, and that sharing of information within the patient association was meaningful.

DISCUSSION

- This qualitative analysis confirmed 3 main themes that are important for patients with nGD: "treatment status", "patient burden" and "social support systems".
- These main themes enabled the identification of key topics within each theme, which can be used for the development of a PROM for patients with nGD.
  - "Treatment status" topics were related to ongoing symptoms (e.g. vision, hearing); these suggest a substantial unmet medical need with currently available treatments.
  - "Patient burden" topics included burden and anxiety with medicines, treatment and hospital visits, emphasising that the impact of nGD on health-related quality of life extends beyond the physical symptoms.
  - "Social support systems" topics suggest gaps between the current support system and patients' expectations, although social support systems are used during doctor consultations or through peer exchange via patient association(s) and social networking systems (e.g. LINE).

CONCLUSIONS

- This study was a qualitative analysis of the burden of nGD and was the first stage in the development of a validated PROM for patients with nGD in Japan.
  - Results from this analysis confirmed the need to include additional questions in the current PROM questionnaire to address current symptoms, including neurological symptoms, and patient burden and needs related to social support systems.
- Questionnaire items that are based on these themes and topics, when combined with the pre-existing PROM,[6] will produce a single PROM that can assess disease burden in patients with any type of GD.

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DISCLOSURES

S. Noto has served as a consultant for Takeda Pharmaceutical Company Limited (hereafter, Takeda). M. Ono and A. L. Hamada are employees of Takeda, and M. Ono is a stockholder of Takeda. Y. Koto, A. Narita and N. Sakai have received research funding from and have served as consultants and on speakers' bureaus for Takeda.

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