

# Qualitative interviews to understand patients' experiences of Glucocerebrosidase (GBA)-Parkinson's Disease

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## Background

- > Parkinson's disease (PD) is a progressive neurodegenerative condition characterized by three cardinal motor symptoms: resting tremor, bradykinesia and rigidity. Non-motor features include cognitive impairment, hallucinations, autonomic and sensory dysfunction and sleep disorders.<sup>1,2</sup>
- > Approximately 7-10% of Parkinson's disease (PD) patients possess a glucocerebrosidase mutation (GBA-PD).<sup>3</sup> There is some evidence that GBA mutations may influence the clinical course and phenotypic expression of PD.<sup>2</sup>

## Study specific objectives

- > A draft conceptual disease model of GBA-PD was developed based on published literature. However, there was a dearth of qualitative data in the literature relating to the patient experience of GBA-PD.
- > This study aimed to generate qualitative data on the patients' experiences of GBA-PD via the conduct of qualitative interviews with both GBA-PD expert clinicians and patients to refine the draft conceptual disease model of the GBA-PD patient experience.

## Methodology

### Study design

- > This was a non-interventional qualitative interview study with 20 PD patients in the US (15 with GBA-PD and 5 with idiopathic-PD [iPD]) and five international clinical experts (neurologists and clinical geneticists) actively involved in the treatment of patients with GBA-PD.
- > The patients took part in a two-hour face-to-face qualitative interview (with breaks). The expert clinicians (n=5) took part in qualitative interviews over the telephone lasting up to 75 minutes. Semi-structured interview guides were used to guide both the expert clinician and patient interviews to ensure that all topics of interest were discussed. Both the patient and clinician interviews included both open-ended concept elicitation questioning and cognitive debriefing questioning. However, the methods and results presented here will focus on the concept elicitation elements of the study.

### The clinicians:

- Were asked open-ended questions about the patient experience of GBA-PD and how this relates to the clinical characteristics of the disease.
- Reviewed and provided feedback on the draft conceptual model developed based on evidence from published literature.
- Were asked about differences between the patient experiences of iPD and GBA-PD.

### The patients:

- Were initially asked a series of broad open-ended questions about their experience of GBA-PD or iPD and how it affects their life. If the patients did not spontaneously mention a concept of interest, the interviewer used probes provided in the interview guide to explore these concepts directly with the patient.
- > The study was conducted in accordance with the Declaration of Helsinki and approved and overseen by a centralized Independent Review Board (IRB) in the US (reference: ADE1-17-542).

## Study sample

- > Both clinical expert and patient participants were recruited according to pre-defined inclusion and exclusion criteria.
  - Clinicians were required to be treating GBA-PD patients.
  - The patients had to have a clinician confirmed diagnosis of iPD or GBA-PD.
- > Quotas were used to ensure a diverse sample with representation of a range of demographic and clinical characteristics.

## Qualitative analysis

- > All interviews were audio-recorded and verbatim transcripts were analyzed using thematic analysis methods and Atlas.ti software.<sup>4</sup>
  - Patient quotes were grouped by code/theme and findings summarized and conclusions drawn.
- > Findings from the interviews were analyzed for evidence of data saturation (the point at which no new, concept-relevant information would emerge from further interviews/analysis).

## Results

### Demographic and clinical characteristics

- > Patients were aged between 46 and 80 years. Most were retired, although several patients reported working full or part time.
- > Patients were at stage 1, 2, or 3 on the H&Y scale. It was not possible to recruit patients above stage 3. Clinicians reported that 11 patients had complete functional independence, seven patients had modified functional independence, and two required minimal assistance.

Table 1. Demographic and clinical characteristics of GBA-PD and iPD patient samples

Demographic	Total GBA-PD (n=15)	Total iPD (n=5)	Total (n=20)	
Age, mean (range)	66.36 (52, 80)	62.60 (46, 78)	65.85 (46, 80)	
Age n (%)	46-55 years old 56-65 years old 66-75 years old 76-85 years old	1 (7%) 7 (46%) 4 (27%) 3 (20%)	2 (40%) 1 (20%) 0 (0%) 2 (40%)	3 (15%) 8 (40%) 4 (20%) 5 (25%)
Gender n (%)	Male Female	8 (53%) 7 (47%)	2 (40%) 3 (60%)	10 (50%) 10 (50%)
Hoehn & Yahr Scale n (%)	Stage 1 Stage 2 Stage 3	2 (13%) 9 (60%) 4 (27%)	2 (40%) 2 (40%) 1 (20%)	4 (20%) 11 (55%) 5 (25%)
Level of functional independence n (%)	Complete Modified Minimal assistance	9 (60%) 5 (33%) 1 (7%)	2 (40%) 2 (40%) 1 (20%)	11 (55%) 7 (35%) 2 (10%)
Race n (%)	White Black/African Hispanic	15 (100%) 0 (0%) 0 (0%)	3 (60%) 1 (20%) 1 (20%)	18 (90%) 1 (5%) 1 (5%)
Work status n (%)	Full/part time Not working due to PD Retired Full time volunteer	5 (33%) 0 (0%) 9 (60%) 1 (7%)	2 (40%) 1 (20%) 2 (40%) 0 (0%)	7 (35%) 1 (5%) 11 (55%) 1 (5%)

- > The clinicians were from the US, Israel and Italy and were neurologists or clinical geneticists.

Table 2. Summary clinician characteristics

Clinician and site characteristic	01-01	01-02	01-03	02-01	03-01	Total, n (%)
Location	US Israel Italy	X X X	X X X	X X X	X X X	3 (60%) 1 (20%) 1 (20%)
Speciality	Neurologist Clinical geneticist	X X	X X	X X	X X	4 (80%) 1 (20%)
Number of known GBA-PD patients at site	20-40 5 per week 100 >200	X X X X	X X X X	X X X X	X X X X	2 (40%) 1 (20%) 1 (20%) 1 (20%)
Type of patients at site	Mix of GBA & iPD Majority GBA-PD Did not state	X X X	X X X	X X X	X X X	3 (60%) 1 (20%) 1 (20%)

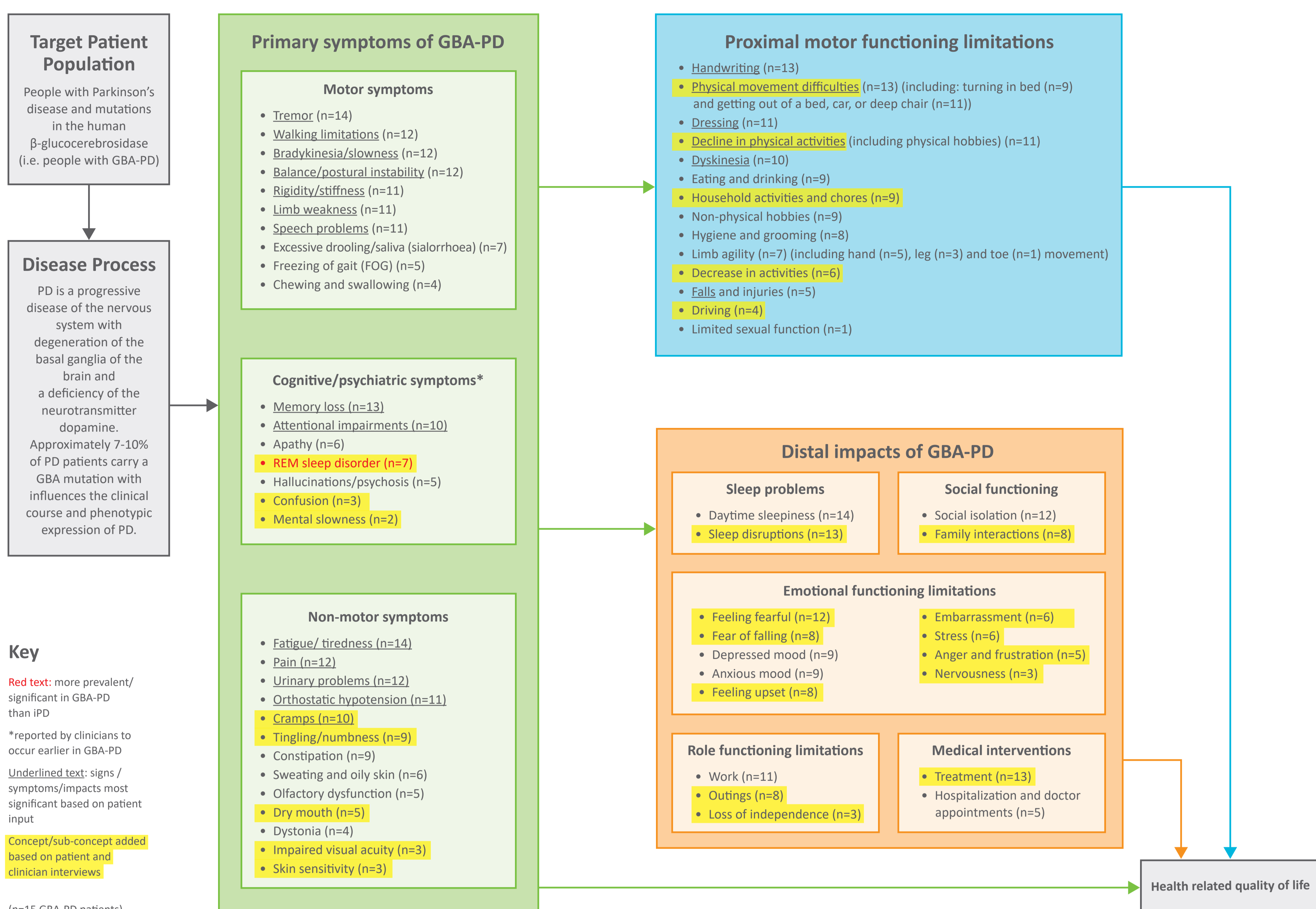


Figure 2. Updated conceptual model

## Symptoms

- > Patients discussed a total of 30 symptom concepts. A summary of the symptoms which were reported by 10 or more patients, and symptoms which patients thought were the most bothersome or important to treat is included in Table 3.

- > The majority of symptoms were reported by patients across the three stages on the H&Y scale represented in this study. The exceptions were excessive drooling/saliva, difficulty chewing or swallowing, apathy, excessive sweating, and dry mouth which were all reported only by H&Y stages 2 and 3 patients and by less than 10 patients.

- > Detailed findings for the symptoms reported to be most impactful and important for GBA-PD patients are included below:

- **Tremors** were reported to occur in the hands (n=13), arms (n=4), shoulder (n=3), or legs (n=4). They were considered one of the most bothersome symptoms by eight patients, and one of the most important symptoms to treat by six patients.

*"There was just a small rotation, uh, that was constant in the left hand, uh, shaking up and down I guess is the best way to describe it."* (H&Y stage 3 GBA patient)

- **Rigidity/stiffness** was reported to occur predominantly in the legs (n=7) and arms (n=6). The term 'stiffness' was most commonly used, and patients subsequently described the symptom as feeling like 'a tight rubber band'. Stiffness was often associated with pain.

*"I mean sometimes I can't read a book because I can't hold it. That's how stiff I am and painful."* (H&Y stage 2 GBA patient)

- **Speech problems** included: voices getting softer/quieter (n=7), too slow or fast (n=3), and difficulty pronouncing or enunciating words (n=5). These changes could sometimes be resolved with speech therapy, but they were still considered frustrating and made it difficult to communicate

*"I try to speak loud and slowly. If I can't do that, I start slurring like crazy...which makes it hard to speak."* (H&Y stage 3 GBA patient)

- **Memory loss** that patients reported included a decline in verbal fluency (n=14), which impacted their ability to have conversations, and difficult remembering things in every day life (n=6), such as where they left keys.

*"Now I'm losing my thoughts here, which is another thing that has affected me...I feel like I'm having memory loss."* (H&Y stage 2 GBA patient)

Table 3. Patient-reported 'most bothersome symptoms' and 'symptoms most important to treat'

Symptom (number of patients reported (N=20))	Number who considered the symptom one of the most bothersome			Number who considered the symptom one of the most important to treat		
	GBA-PD	iPD	Total	GBA-PD	iPD	Total
<b>Motor symptoms</b>						
Tremor (18/20)	5	3	8	4	2	6
Walking limitations (17/20)	2	0	2	2	1	3
Slowness/bradykinesia (17/20)	1	0	1	0	0	0
Balance/postural instability (16/20)	2	0	2	2	1	3
Rigidity/stiffness (16/20)	3	1	4	1	0	1
Limb weakness (16/20)	2	1	3	0	1	1
Speech problems (12/20)	4	0	4	2	0	2
<b>Cognitive/psychiatric symptoms</b>						
Memory loss (18/20)	3	1	4	2	0	2
Attentional impairments (14/20)	1	0	1	3	0	3
<b>Non-motor symptoms</b>						
Fatigue/tiredness (19/20)	3	1	4	0	0	0
Pain (17/20)	1	4	5	0	2	2
Urinary problems (17/20)	0	0	0	1	0	1
Orthostatic hypotension (16/20)	0	0	0	0	0	0
Cramps (14/20)	0	0	0	0	1	1
Constipation (13/20)	1	0	1	0	0	0
Tingling/numbness (10/20)	0	0	0	0	0	0

Considered one of the most bothersome symptoms by ≥3 patients

Considered one of the symptoms most important to treat by ≥3 patients

## Impacts

- > Six impact domains were reported; these were categorized into one proximal motor impact domain and five distal impact domains (Figure 1).

- **Proximal motor impacts** are those functioning impacts which were not directly symptoms of PD, and which produced other distal impacts and impacted quality of life. These impacts include physical movement difficulties (n=18) and handwriting changes (n=15) (among others):

*"Uh, every once in a while, if I have to write something, you know, I shake."* (H&Y stage 3 iPD patient)

- **Emotional impacts** were experienced by all 20 patients. The most commonly reported was fear (n=17), including specifically a fear of falling (n=13). Other commonly reported emotional impacts included depression (n=14) and anxiety (n=13).

*"With the legs it, uh—the weakness in my legs, I'm afraid I'm going to fall."* (H&Y stage 3 iPD patient)

*"It's depressing. Yes, it is. And mostly because...you don't know how much worse it's going to get and when."* (H&Y stage 2 GBA patient)

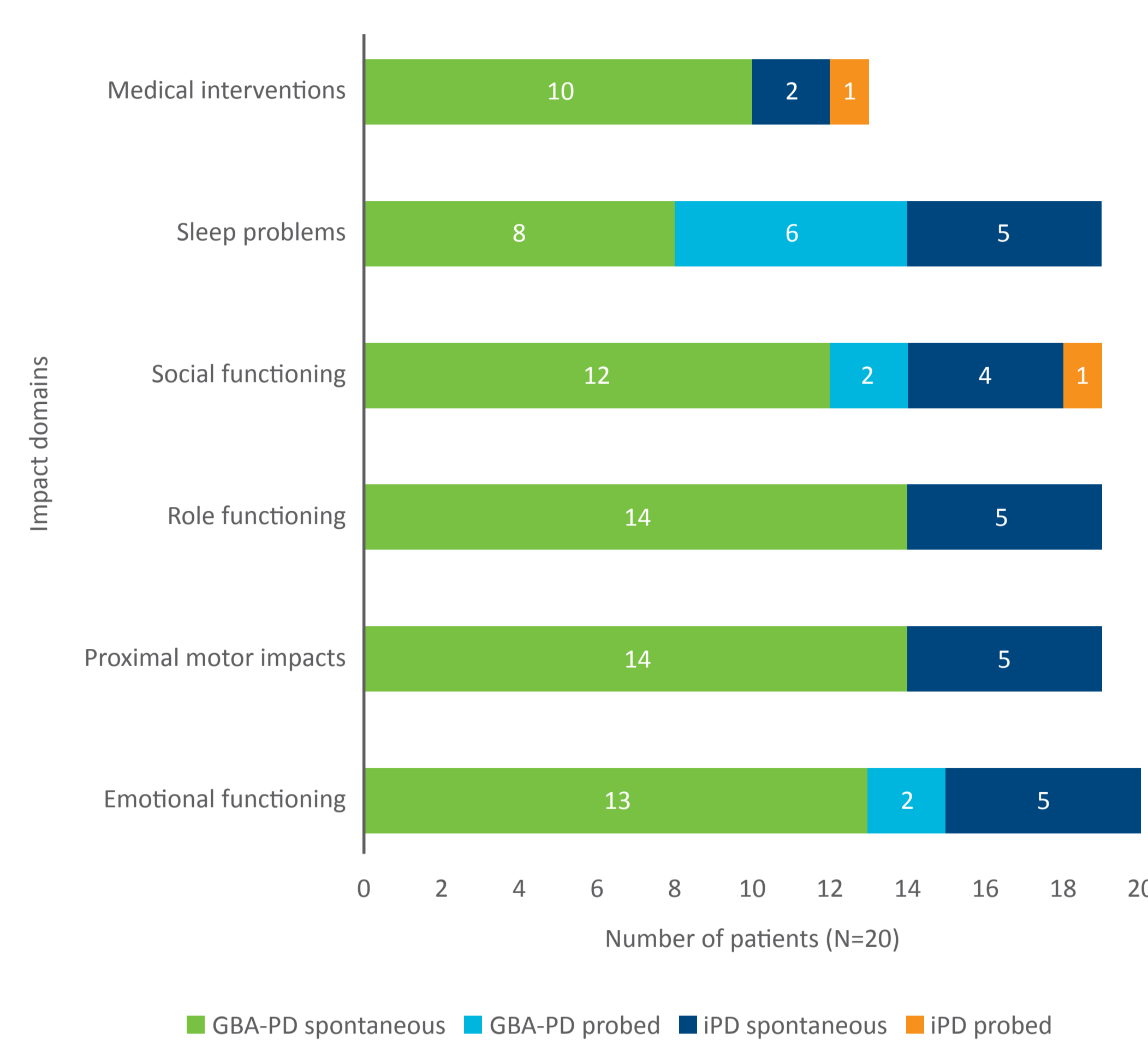


Figure 1. Overview of impact domains reported by patients

## Clinician discussion of symptoms

- > The clinicians confirmed that the concepts in the draft conceptual model were relevant to GBA-PD patients. They also suggested that a decline in visual acuity and rapid eye movement (REM) sleep disorder were also relevant symptoms.
- > The clinicians suggested that the GBA-PD and iPD patient disease experience was broadly similar. Most clinicians agreed that cognitive/psychiatric symptoms might present earlier and progress more rapidly in GBA-PD patients, as compared to iPD patients.

## Updated GBA-PD conceptual model

- > Based on findings from the patient and clinician interviews the draft conceptual model was updated. Figure 2 shows the updated conceptual model, including the number of GBA-PD patients (and not iPD patients) who reported each concept. The updates to the conceptual model included adding concepts which were spontaneously discussed during the patient interviews (some of which were confirmed in the clinician interviews), adding nuance to concepts which had previously been included, and updating to use the language used by patients.

- > The categorization of concepts as symptoms and impacts was also adjusted, and a proximal motor impacts domain was created to account for impacts closely related to symptoms which had further impacts on other aspects of life and overall patient quality of life.

- > Based on the clinician and patient interviews, the only category which might be considered more prevalent in the GBA-PD population was cognitive/psychiatric symptoms; and only patients with GBA-PD reported REM sleep disorder.

## Conclusions

- > The findings provide an in-depth understanding of the participant experience of GBA-PD and the impacts it has on health-related quality of life. The updated conceptual model developed based on these findings can be used to guide the selection of key measurement concepts for assessment in future clinical trials for GBA-PD.

- > The findings confirm that the concepts relevant to assess in GBA-PD patients are consistent with those relevant to assess in idiopathic-PD patients; however, slightly more consideration of cognitive/psychiatric symptoms may be warranted in GBA-PD populations.

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