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Mapping meaningful symptoms and impacts of early Parkinson's disease to digital outcome measures

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et al.

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Quality in qualitative research statement

This study used COREQ criteria to guide reporting of qualitative findings.

Legends

Main manuscript Figure legends

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Figure 2. Online Interview Part 3 & 4: Mapping tasks and symptom concepts of interest to personal symptoms and impacts

Figure 3. Coding schema for analysis of symptom maps

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Abstract

Background: Digital health technologies have the potential to capture fine variations in symptoms across a range of diseases. However, it is not clear whether these measures are meaningful to patients, which is critical to guiding the selection of digital endpoints.

Objective: This manuscript describes novel methodology for mapping meaningful symptoms and impacts of disease and assessing personal relevance of digital measures from the patient perspective.

Methods: Participants with early Parkinson's from the WATCH-PD study [NCT03681015] completed online surveys (N=65), with a subset recruited for 1:1 online video-interviews (N=40) to explore symptoms, impacts and perceived relevance of selected digital measures. Interviews included: (1) symptom mapping to delineate and rank meaningful symptoms/impacts of Parkinson's, (2) cognitive interviewing on digital measures administered in the WATCH-PD study, and (3) mapping of these measures back to the personal symptom map to show relevance from the patient perspective. Content coding was used to assess frequencies and bothersomeness of symptoms/impacts, and perceived relevance of the technology. Thematic analysis was performed for narrative transcripts. Copies of maps were shared with participants.

Results: This approach was deeply engaging and satisfying to participants, who reported improved ability to describe and discuss their symptom experiences. Maps and interviews

provided detailed qualitative data on symptoms/impacts of early Parkinson's with concurrent ability to quantify symptom frequencies and bothersomeness along with perceived relevance of the digital measures.

Conclusion: Combining symptom mapping with cognitive interviewing can improve understanding of meaningful symptoms and impacts of disease and perceived relevance of digital measures from the patient perspective.

Background

Digital health technologies (DHTs) have the ability to capture fine variations in symptoms across a range of neurological conditions including Parkinson's disease (PD), and hold great potential for monitoring disease progression and responsiveness to treatment.[1-3] This has led to increasing use of digital measures in clinical practice and trials of new therapeutics as endpoints for therapeutic evaluation.[4-6] Although capable of detecting symptoms at more granular levels than can be achieved through standard clinical monitoring methods,[7-9] it is poorly understood whether these technologies are capturing symptoms or impacts of disease that are meaningful from the patient perspective.[10-12] Thus, some, such as Taylor et al. have advocated for patient centric approaches to developing digital outcome measures (i.e. prioritizing sensor features that are relevant to patients' functioning in everyday life),[10] and others such as the DiMe v3 framework and Clinical Trials Transformation Initiative strongly recommend defining meaningful aspects of health before selecting digital measures.[13,14]

Regardless of methods, standards, and technologies for collecting clinical outcome assessment data, relevant approaches for identifying symptoms and impacts that are meaningful to patients are urgently needed,[6,10,15] as there is currently limited ability to connect qualitative patient experiences to digital measures in a way that is easily interpretable, scalable, or translatable to other contexts.[16] Thus, the purpose of this manuscript is to describe a novel methodological approach to identifying (1) personally meaningful symptoms and impacts, and (2) relevance of digital outcome measures to monitor important aspects of disease from the patient perspective, as implemented within an early PD patient population.

Qualitative Study Methods

This study (University of Rochester IRB# 00006429) was designed under guidance of individuals from the Critical Path for Parkinson's Consortium, US Food & Drug Administration, multiple industry and academic partners, and people with Parkinson's, with the objective of understanding symptoms and impacts of early PD and perceived relevance of WATCH-PD (Wearable Assessments in The Clinic and at Home in PD) digital measures to monitor disease progression from the patient perspective.

Overview of parent study

The study was conducted in follow up to the parent WATCH-PD study (IRB#00003002; NCT03681015), a 12-month multi-center observational study that evaluated utility of a smartphone app, smartwatch, and research grade sensors for monitoring motor and cognitive function symptoms and progression in individuals with early, untreated PD (diagnosis ≤ 2 years, Hoehn & Yahr stage ≤ 2 at recruitment). Eighty-two individuals with PD and 50 controls were enrolled, with in-clinic visits at baseline and 1, 3, 6, 9, and 12 months, and home assessments of 10 brief smartphone/smartwatch-based tasks (**eTable 1**) related to motor and cognitive function completed bi-weekly for one year.

Setting, sample

Participants with Parkinson's who completed the parent study and consented to future contact were eligible for the qualitative study (N=78). Digital IRB-approved informed consent

was obtained prior to data collection, and incentives were offered for participation ($50/survey; $75/interview).

Data collection

A mixed-methods design was used, leveraging multiple convergent approaches to data collection to enable deeper understanding of the phenomena. This consisted of (A) a baseline web-based survey assessing PD symptoms and perceptions of WATCH-PD tasks, and (B) a 90-minute online interview with (1) symptom mapping to identify bothersome symptoms and impacts of disease; (2) cognitive interviewing to generate content validity evidence for assessments completed via DHTs in WATCH-PD ; and (3) mapping of digital measures back to personally important symptoms and (4) mapping selected research symptoms of interest.

Demographics. Demographic information from the parent study was obtained and reviewed for correctness during enrollment. This included age, gender, race/ethnicity, years since PD diagnosis, and any PD medication use.

Survey. All participants completed an online Redcap[17] survey including multiple choice, visual analog scale ratings, and open-response items evaluating symptoms of PD and relevance of the 10 smartphone/smartwatch tasks.

Online interviews. In-depth, 1:1 interviews were conducted with a purposeful subset (N=40). These were selected for demographic representativeness of the parent study, with inclusion of all minority participants (N=4). Those completing the parent study more than 6-months previously were not eligible for interviews due to increased risk of recall bias.[18] Interviews were conducted via Zoom video-conferencing, with screen sharing computer-to-

computer (years 2021—2022). A semi-structured interview protocol was used (**eSupplement A**). Interviews were conducted by JM and were recorded with permission.

Interview Part 1: Symptom mapping.

The first part of the interview focused on delineating personal symptoms and impacts of PD using a combination of traditional interviewing and novel symptom mapping techniques. Symptom mapping is a form of card-sorting that has been successfully used in other chronic diseases to define symptom trajectories and self-management behaviors.[19-21] This was adapted for the current study to a digital format, focusing on exploring symptoms and impacts. In this application, "card-sorting" was accomplished digitally using Xmind™ mind-mapping software: Yellow colored nodes were used to represent symptom "cards" and dependent line nodes were used to add details about symptoms and impacts (**Figure 1**).[22] Using screen sharing, the participant and interviewer simultaneously viewed and co-created the symptom map, ensuring that the participant's experience was accurately represented. Groupings of symptoms and impacts were arranged according to the participants perception of their PD experience.

Part 1, Step 1: Pre-interview map (preparation for interview). Each participant's survey responses were reviewed by the interviewer prior to the online interview and a map of the survey data was developed as a starting point for discussion. Reported symptoms (yellow nodes) were placed into one of the following categories based on survey scores: "Most bothersome;" "Somewhat bothersome;" "A little bothersome;" "Not bothersome," or "No current issues" as shown in **Figure 1**.

Part 1, Step 2. Mapping spontaneously reported symptoms. At the start of the interview, participants were oriented to the mapping process and shown the baseline map of their survey data. Building on this, participants were asked to identify and describe in detail all personally important symptoms of PD, correcting or redefining any symptoms entered from the survey. Concurrently, the interviewer entered these symptoms individually into the mutually viewable map.

Next, participants were asked to explain what made each individual symptom bothersome and how it affected them on a day-to-day basis, with the details about symptoms and impacts entered as related dependent lines. For example, a participant who experienced difficulty walking might define this as difficulty with foot lift, causing tripping on uneven surfaces, resulting in decreased ability to go hiking. When the participant finished describing a symptom and the related impacts, they were asked to review the symptom section for correctness and indicate if modifications were needed. Once validated, the section was collapsed to show only the primary symptom node to minimize total information on the screen at any time. As needed, symptom nodes could be reopened to add additional details arising during the course of the interview, enabling iterative correction and revision.

Part 1, Step 3: Mapping probed symptoms not spontaneously reported. After exploring all spontaneously reported symptoms and impacts, participants were systematically probed for common PD motor and non-motor symptoms not already reported (i.e. difficulties with tremor, walking, balance, fine motor, speech, thinking, mood, daytime sleepiness, tiredness/fatigue, depth-perception). If not experienced, symptoms were placed into the "No current issues" category, or "Not relevant to early PD" based on the participant's viewpoint.

When finished, the map was collapsed to show only primary symptoms in list view, with all supporting details and impacts hidden.

Part 1, Step 4: Reordering and ranking symptoms by bothersomeness. Next, participants were asked to review the condensed map to ensure all personally important symptoms were reflected, and then to reorder symptoms by how bothersome they were. This step focused on rearranging symptom nodes into the correct bothersomeness category (by dragging or cutting) and rank ordering by priority inside each category.

Part 1, Step 5: Identifying most important and most bothersome symptoms. Lastly, participants were asked to explain which symptoms were personally most important as well as most bothersome to them overall, and to delineate rationales and explain differences. These high-priority symptoms were identified using "call-out" brackets within the map that highlighted symptoms along with key rationales. The finished symptom map was saved and duplicated for progression to Part 3 of the online interview. (**Figure 2**).

Interview Part 2: Cognitive interviewing on WATCH-PD tasks

Immediately following symptom mapping, the interviewer performed cognitive interviewing on 10 digital tasks (**Table 1**) that were completed by participants biweekly during the parent study. No mapping was performed during this portion. The participant was shown a full-size image of each task via screen-sharing. They were then asked four standardized questions about each task. Questions were designed to assess if the participant (1) understood how to perform the task correctly, (2) if the task related to personally important symptoms, (3) if the task related to personal impacts and activities of daily living, and (4) if the participant

believed the task was relevant to monitoring the progression of their PD. General questions exploring perceptions of tasks were included, and follow-up probes were used to explore responses to questions (**eSupplement A**).

Interview Part 3: Mapping tasks back to personally important symptoms

Following cognitive interviewing, participants were asked to integrate a small pictograph (i.e. screenshot of task as it appeared on the iPhone) of each task into their personal symptom map. Task cards were placed next to the personal symptom(s) the participant felt it related to or monitored. This step was used to visually confirm the symptoms the participants felt each task related to, if the task captured (or failed to capture) meaningful aspects of disease, and whether tasks corresponded with more or less bothersome symptoms. This form of member checking served to validate and extend on information gathered in Part 2.

Interview Part 4: Mapping hypothesized motor and cognitive symptoms of interests to personal symptoms

Lastly, participants reviewed a set of blue colored nodes representing the symptoms of interest the WATCH-PD tasks were hypothesized to have measured. As with Part 3, Part 4 was used to visually confirm the extent to which symptoms of interest to the research team aligned with personally important symptoms for the patient. The interview concluded with closing questions and a final opportunity to review/modify the personal symptom map. Participants were emailed PDF copies of their personal symptom maps at the conclusion of the interview if desired.

Data analysis

Data analysis incorporated qualitative and quantitative content coding techniques[23] with thematic analysis[24] to derive a more holistic understanding of symptoms, impacts and relevance of digital measures. Coding was conducted by JM, RS, PY, GS (ethnically, occupationally, age and gender diverse).

Surveys. Descriptive statistics were computed for quantitative survey items and content coding was performed for qualitative items to identify important symptoms and rationales for bothersomeness.

Maps. Maps were analyzed for types, frequencies, and bothersomeness of symptoms and impacts, relevance of tasks to monitoring meaningful symptoms, and alignment of symptoms of interest to personally meaningful symptoms. For this step, each level in the map was assigned a Patient Reported Symptom Score (**PRSS**) for experienced symptoms (range 1-4) and personally important symptoms (range 0-4, where 0 indicates the symptom is important but not currently present), as shown in **Figure 3**. Presence and priority of symptoms, impacts, tasks and symptoms of interest were coded using this visual Likert scale schema as described below.

Content coding was performed via spreadsheet, with one sheet per domain (symptoms, impacts, tasks). Participant identifiers were listed across the top (i.e. P1, P2) and domain items were listed as rows to enable quantification. Symptoms and tasks were independently coded by two coders (JM, PY) and discrepancies resolved by comparison and discussion with the analytic team.

Coding was conducted as follows for all maps, with reference to transcripts as needed for clarification:

1) Open coding (i.e. without *a priori* schema) of maps to develop a comprehensive list of symptoms;
2) Re-coding of maps using the derived symptom checklist, with symptoms indicated as *not present* (".") or *present*, using Patient Reported Symptom Scores as show in **Figure 3** (PRSS; the highest level of bothersomeness a symptom occurred at within a given map; range 1-4);
3) Curation of individual symptoms into domains comparative to the Staunton et al. conceptual model of early PD;[25]
4) Open coding of all maps to develop a comprehensive list of impacts;
5) Re-coding of maps with derived list of impacts as for #2, with symptoms underlying the impact indicated as contributing (+) or not contributing ".";
6) Curation of individual impacts into domains comparative to Staunton et al.;[25]
7) Coding for relevance of WATCH-PD digital measures by association with personally important symptoms (PRSS range 0-4 and "." for not relevant);
8) Coding for alignment of symptoms of interest to meaningful symptoms (PRSS range 0-4 and "." for not relevant).

Interviews. Recorded interviews were transcribed and deidentified. Thematic analysis was conducted using Nvivo12 and Xmind™. Pattern coding was used to identify recurrent themes within and across interviews, with attention to similarities and differences between

participants.[26,27] Data tables were generated for themes with quotes to support validity and use of numeric identifiers to demonstrate representativeness.

Rigor and validity

Data collection instruments and procedures were developed under advisement from the FDA and in collaboration with people with Parkinson's disease (JC, JH), with pretesting prior to implementation. Observation of initial interviews was conducted for consistency of the interview process (RS). Triangulated data collection approaches and member checking were used to increase validity. Regular peer debriefing, multiple coders, intercoder reliability assessments, and a structured audit trail were used during the analytic stage.[28]

Data availability statement

Data are available to members of the Critical Path for Parkinson's Consortium 3DT Initiative Stage 2. For those who are not a part of 3DT Stage 2, a proposal may be made to the WATCH-PD Steering Committee (via the corresponding author) for de-identified datasets.

Methodological Results

Sample and interview characteristics

Of 78 participants in the PD cohort who completed the parent study, 65 were enrolled and completed surveys and 40 completed interviews (**Figure 4**). Eleven could not be recontacted and 2 declined. Demographics mirrored the parent study: mean age 65 (SD=8.8) 56.9% male, 95.4% Caucasian, and 2.3 years with PD (SD=0.92), with 47.7% starting any PD medications after enrollment in the parent study. Most participants engaged in the interview using a personal computer (N=37) with three via tablet or smartphone due to computer malfunction.

Feasibility. Interviews ranged from 60—139 minutes (average 102 minutes). Total time for the interviewer to conduct a visit was 3 hours, which included: mapping the survey prior to the visit (30 minutes), participant visit (2 hours), and data management procedures (30 minutes). Time to analyze surveys, maps, and interviews was approximately 10 hours per participant, including developing the structure of the analysis (iterative), coding for symptoms types and bothersomeness (30 minutes/map), impacts of disease and related symptoms (60 min/map), relationship of digital measures to important symptoms (10 min/map), content validity of digital measures (60 min/interview), and thematic analysis (6 hours/interview). Data saturation (i.e. point after which no new data was identified) for symptom types reported by >10% of the sample was 100% by the 17th interview, and 100% for impacts by the 10th interview in this relatively homogenous sample.

Data

As shown in e**Table 2**, this approach generated a wide range of both quantitative and qualitative data delineating symptoms and impacts of early Parkinson's disease by frequency and order of bothersomeness, and demonstrating participant perceived relevance of digital measures. There were four staged maps per participant (160 total maps): (1) baseline map from survey data; (2) map of personally important symptoms displayed by order of bothersomeness (collapsed form); (3) map of symptoms with details on symptoms characteristics and impacts of disease (expanded form); and (4) a final map showing the alignment of digital measures and symptoms of interest to personally important symptoms and impacts. Static images of maps #2-4 were shared with participants.

Perceptions of mapping

All participants reported being comfortable with the online interview and mapping process and indicated they were easily able to see and follow what was on the screen, including the three who engaged in interviews via tablet or smartphone. **Table 3** presents quotes illustrating participant experiences with symptom mapping. Nearly all (39/40) reported that use of mapping techniques enabled a more comprehensive discussion of their personal experience and helped them to define what was most bothersome about symptoms and why. For example:

> ***P1****: I'm feeling like I should pay you for this session. It's really hard to describe to your kids, "How's it going, Dad?" … I haven't thought about most bothersome to not bothersome to, "Well, what is it that bothers you?" This draws that out.*

While most participants indicated they enjoyed the interview, two found the in-depth discussion distressing at times and were offered the option to discontinue the interview. Distress was precipitated by deep reflection on impacts of PD and heightened awareness of personal decline in physical and mental capabilities. As one participant stated:

> ***P28****: This is really hard for me to talk about... It's distressing any time I think about this …*

Despite their distress, both participants chose to continue the interview and expressed positive perceptions of the online interview and mapping process. Of 40 participants, 95% (38/40) asked to receive copies of their personal maps, and several indicated that opportunity to receive the maps had been an incentive to participation.

> ***P37****: I would love to have [the maps]. I feel like I'm in all these studies, but I'm like, "I have no results!"…****Until now.***

Discussion

In this study we described novel methods for understanding and quantifying meaningful symptoms and impacts of early-stage PD and transparently demonstrating how these related to DHT assessments. In addition to generating a range of qualitative and quantitative data in support of the study aims, we found mapping was beneficial in several important ways, including (1) increased data granularity for identifying the prevalence and priority of symptoms and impacts in early PD; (2) improved ability to qualitatively and quantitatively demonstrate connections between meaningful symptoms and digital tasks; (3) greater participant engagement and reciprocity; and (4) enhanced rigor and validity in data collection and analysis processes.

The approach outlined in this report is unique as compared to strategies that others have employed to investigate clinical meaningfulness of measures derived from DHTs.[10,12-14] One clear benefit of the methodology used here is the unique opportunity to qualitatively describe experiences while simultaneously quantifying the prevalence and importance of different aspects of disease. In this study, mapping enabled systematic identification of a broad range of symptoms and impacts experienced by people with early PD, while further informing typological classification by quantitatively demonstrating prevalence and bothersomeness. This supported an in-depth understanding of early PD manifestations at the individual level, and what symptoms are most bothersome and important to those living with this disease. Granular data such as this can assist with identification of meaningful symptoms,[29] and inform the selection of endpoints critical to assess for disease progression.

We also found that mapping is a promising and useful technique for assessing the relevance of digital tasks to meaningful symptoms. Cognitive interviewing, included in this study, is a standardized approach to assess content validity.[30] Conducting mapping prior to this might have enhanced participants' ability to identify and verbalize connections between the DHT and personally meaningful symptoms. Mapping further extended on cognitive interviewing by showing explicitly how tasks relate to personal symptom hierarchies. This additional data can help to demonstrate whether tasks are adequately capturing the right set of symptoms for targeted groups, which will be important to the development of future COAs administered via DHTs.[31]

Based on feedback, mapping engaged participants intimately in the interview process, offering the opportunity to reflect deeply, add insights, or comment on the emerging "picture" of personal experiences. This is somewhat similar to traditional member checking, in which participants are asked to comment on or confirm the accuracy of understandings and validity of interpretations.[28] More than this, however, mapping enables individuals to be more active participants in data generation. Simply put, interviewing is primarily about "taking" words whereas mapping is primarily about "making" meaning. The difference lies in the act of intentional, visible co-creation, where a shared understanding is carefully crafted between two individuals in a transparent fashion amenable to identifying and correcting misunderstandings.

This process of co-creation contributes to overall study rigor and validity. Deep engagement, constant reflection, and iterative member checking are well-established means to enhance the validity of qualitative findings,[28] and are inherent in the mapping process. It can therefore be reasonably inferred that data resulting from co-created maps are likely to more

accurately represent participants' experiences than verbal interviews alone. This inference is supported by the participant comments in **Table 3**.

We found that mapping can also increase transparency and accuracy of data analysis, as key information is represented in concise visual formats easily amenable to external critical review. In this study, coding was easier and more efficient due to ability to visually identify key items within the Likert-scale structure of the map. In short, mapping offers ample flexibility to paint the highly personalized picture essential to good qualitative research with sufficient structure to enable systematic and reliable coding and quantification of key findings.

Lastly, online interviewing/mapping offers exciting new opportunities for the conduct of rigorous, high-quality qualitative research remotely, in ways that do not increase risk of exposure, maximize convenience, and minimize burden for participants and researchers. Online interviews have been normative for some period but with historically limited ability to engage with participants beyond talking and visualization. Interactive online processes such as mapping may offer additional means to collect data in ways that are both engaging and informative.

Although there are clear benefits to these methods, there are limitations to consider. This study was conducted in predominantly white, higher socio-economic status individuals within the context of a broader study exploring use of DHTs to monitor symptoms of PD. Participants were fluent in reading, comfortable with technology, and familiar with video-conferencing. People with reduced reading and technological literacy, or cognitive or visual impairments may find digital mapping techniques more challenging and may not benefit equally. Limited access to stable Wi-Fi or a computer with camera and microphone or

tablet/smartphone may also restrict use in rural, elderly, or lower income populations. These factors should be considered to ensure equitable access, and customization for these applications warrants further research in diverse populations.

In conclusion, we believe the techniques described here could translate across a range of chronic diseases and research objectives, enabling easier identification of meaningful symptoms and relevance of digital health technologies to monitoring personally important aspects of disease.

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Author contributions

Authorship contributions were as follows: planning and development of study (all), data collection (JM, JA PY, MK), data analysis (JA, JM, PY, GS, RS), drafting and revising of manuscript (all).

Conflict of interest statement

GTS is an employee of Rush University and has consulting and advisory board membership with honoraria for: Acadia Pharmaceuticals; Adamas Pharmaceuticals, Inc.; Biogen, Inc.; Ceregene, Inc.; CHDI Management, Inc.; the Cleveland Clinic Foundation; Ingenix Pharmaceutical Services (i3 Research); MedGenesis Therapeutix, Inc.; Neurocrine Biosciences, Inc.; Pfizer, Inc.; Tools-4-Patients; Ultragenyx, Inc.; and the Sunshine Care Foundation. He has received grants from and done research for: the National Institutes of Health, the Department of Defense, the Michael J. Fox Foundation for Parkinson's Research, the Dystonia Coalition, CHDI, the Cleveland Clinic Foundation, the International Parkinson and Movement Disorder Society, and CBD Solutions, and has received honoraria from: the International Parkinson and

Movement Disorder Society, the American Academy of Neurology, the Michael J. Fox Foundation for Parkinson's Research, the FDA, the National Institutes of Health, and the Alzheimer's Association. **JC** is Director of Digital Health Strategy at AbbVie and Industry Co-Director of CPP. **TD** Is Executive Medical Director at Biogen. **JH** Is Senior Scientist, Patient Insights at H. Lundbeck A/S, Valby, Denmark. **TS** has served as a consultant for Acadia, Blue Rock Therapeutics, Caraway Therapeutics, Critical Path for Parkinson's Consortium (CPP), Denali, General Electric (GE), Neuroderm, Sanofi, Sinopia, Sunovion, Roche, Takeda, MJFF, Vanqua Bio and Voyager. She served on the ad board for Acadia, Denali, General Electric (GE), Sunovion, Roche. She has served as a member of the scientific advisory board of Caraway Therapeutics, Neuroderm, Sanofi and UCB. She has received research funding from Biogen, Roche, Neuroderm, Sanofi, Sun Pharma, Amneal, Prevail, UCB, NINDS, MJFF, Parkinson's Foundation. **ERD** Has stock ownership in Grand Rounds, an online second opinion service, has received consultancy fees from 23andMe, Abbott, Abbvie, Amwell, Biogen, Clintrex, CuraSen, DeciBio, Denali Therapeutics, GlaxoSmithKline, Grand Rounds, Huntington Study Group, Informa Pharma Consulting, medical-legal services, Mednick Associates, Medopad, Olson Research Group, Origent Data Sciences, Inc., Pear Therapeutics, Prilenia, Roche, Sanofi, Shire, Spark Therapeutics, Sunovion Pharmaceuticals, Voyager Therapeutics, ZS Consulting, honoraria from Alzeimer's Drug Discovery Foundation, American Academy of Neurology, American Neurological Association, California Pacific Medical Center, Excellus BlueCross BlueShield, Food and Drug Administration, MCM Education, The Michael J Fox Foundation, Stanford University, UC Irvine, University of Michigan, and research funding from Abbvie, Acadia Pharmaceuticals, AMC Health, BioSensics, Burroughs Wellcome Fund, Greater Rochester Health Foundation,

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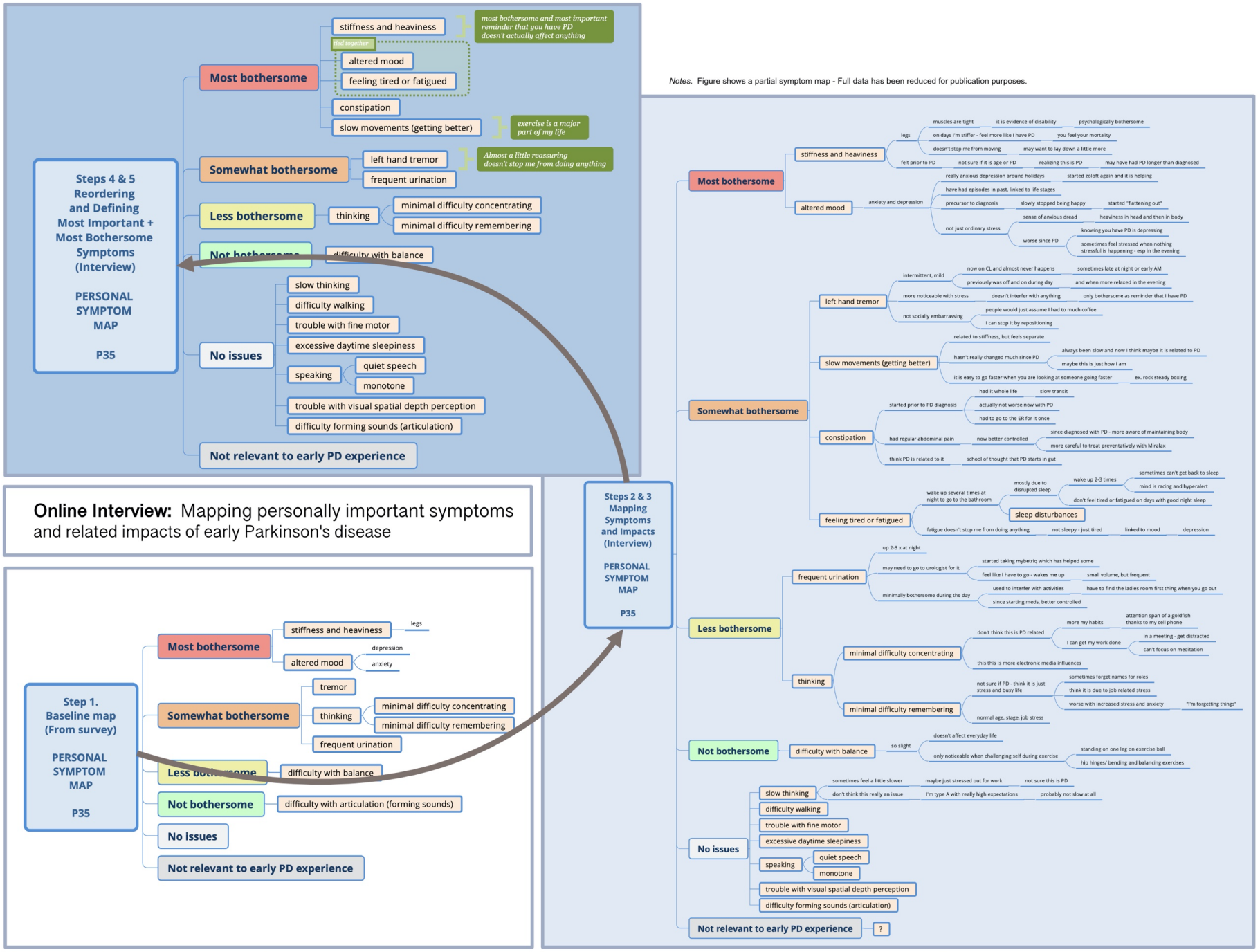
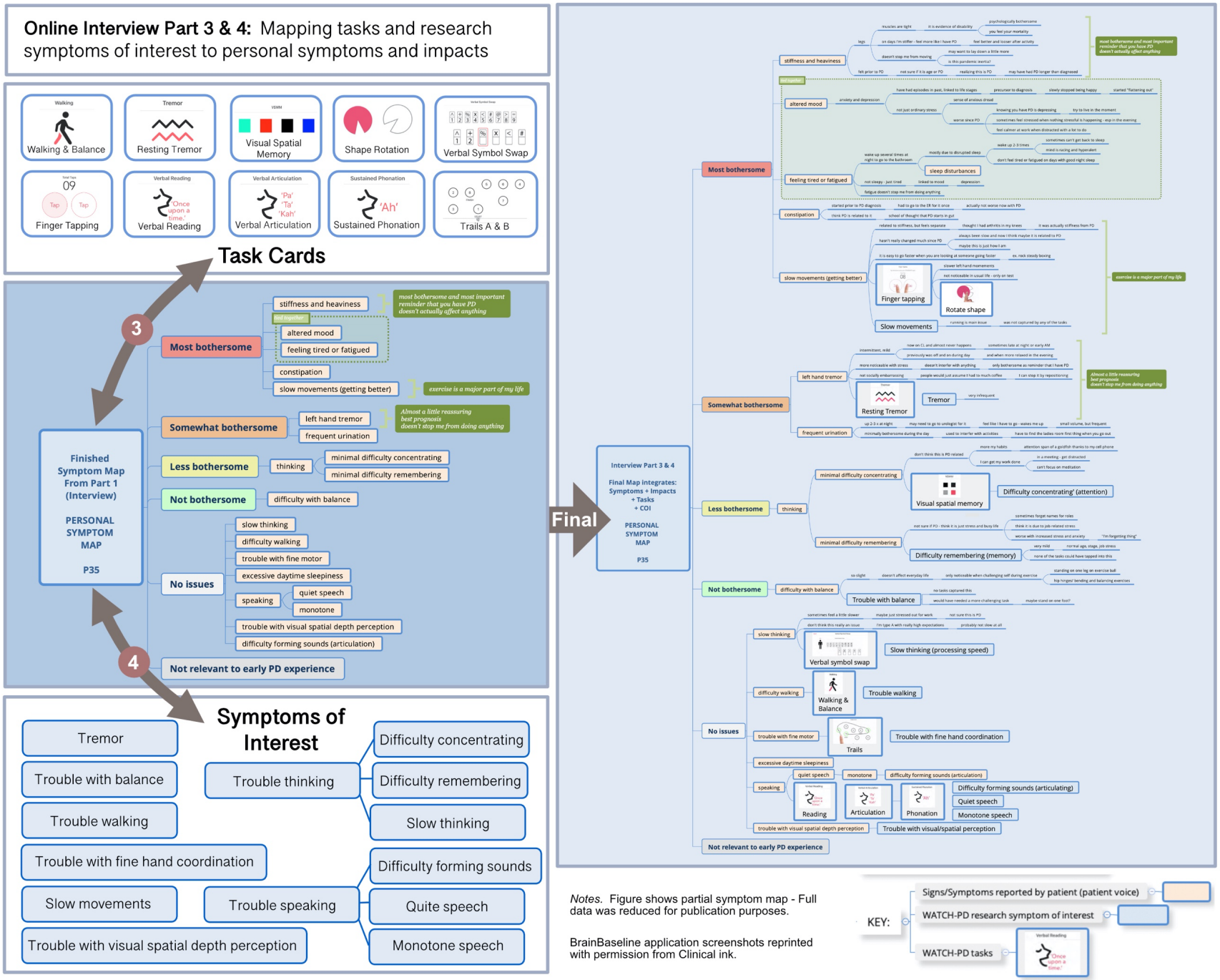


Figure 1. Online Interview Part 1: Mapping personally important symptoms and impacts of early PD



Notes. Figure shows partial symptom map - Full data was reduced for publication purposes.

BrainBaseline application screenshots reprinted with permission from Clinical ink.

Figure 2. Online Interview Part 3 & 4: Mapping tasks and symptom concepts of interest to personal symptoms and impacts

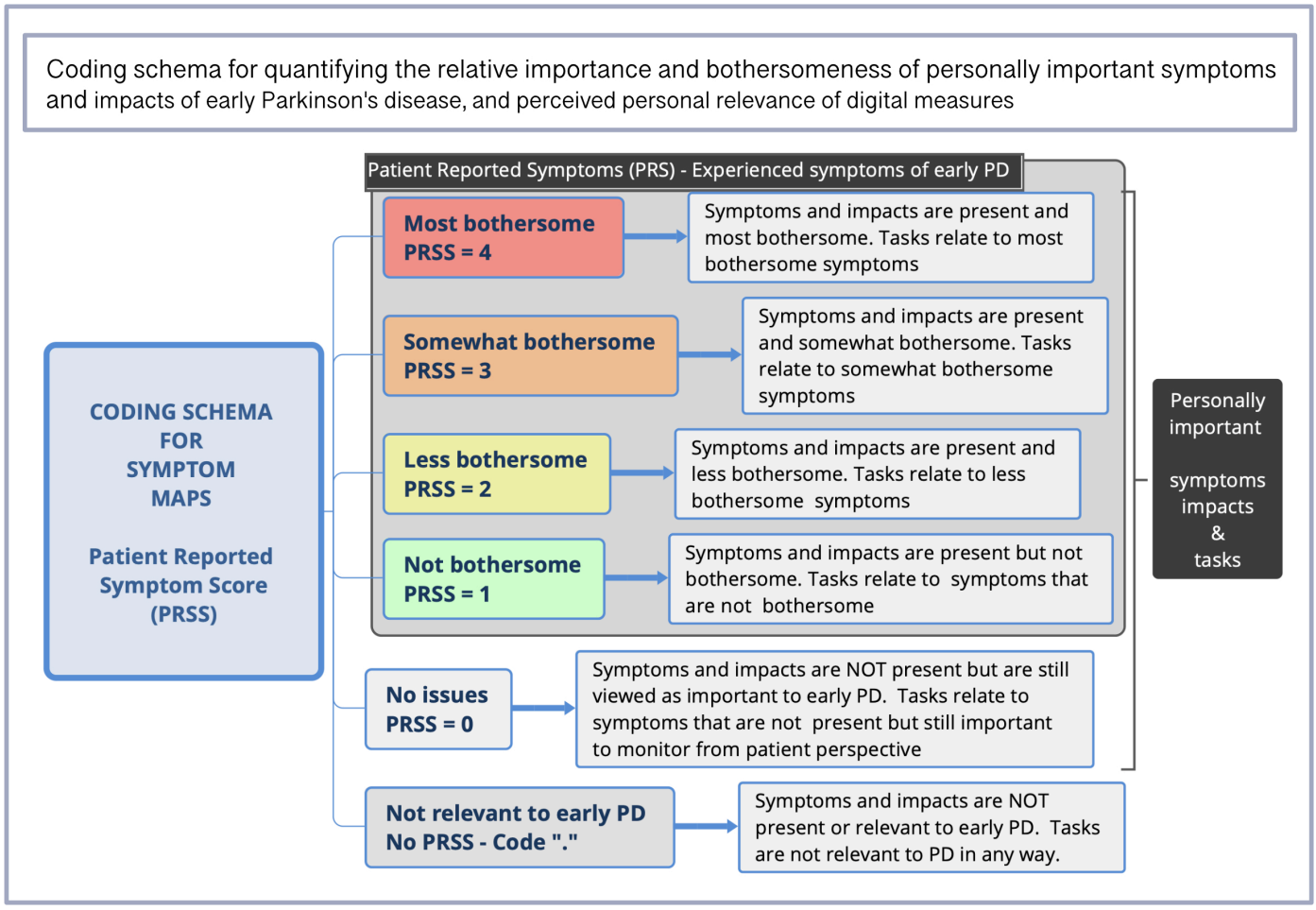


Figure 3. Coding schema for analysis of symptom maps

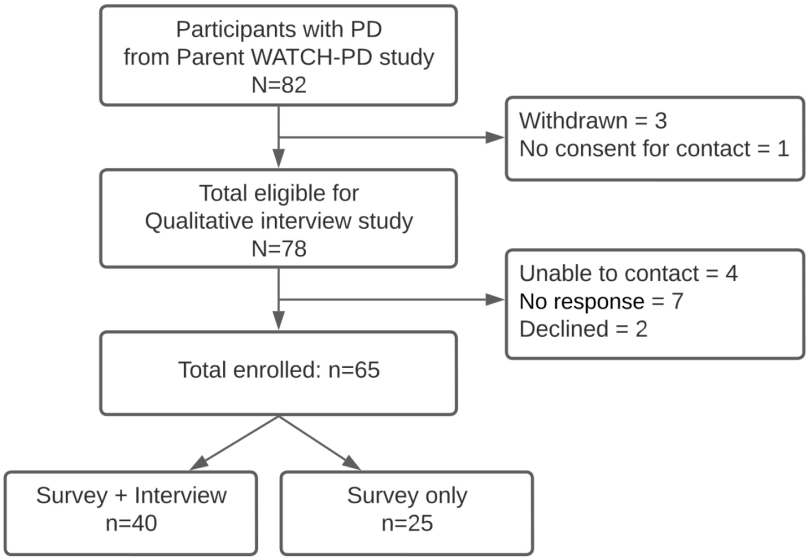


Figure 4. WATCH-PD qualitative study participant enrollment diagram

eTable 1. Digital tasks performed during the parent WATCH-PD study being evaluated for participant perceived relevance in the present study

Smartwatch	Timed Walking & Balance Task	The participant must walk in a straight line, turning at the end of their path, for 1 minute, then stand with arms at their side for 30 seconds.
	Tremor Task	The participant must rest their hands in their lap for 10 seconds, then extend their arms out in front of them for 10 seconds.
Smartphone Application	Finger Tapping Task (Fine Motor)	The participant performs rapid alternating finger movements by tapping two targets that appear side by side using their index and middle fingers.
	Shape rotation task (Fine Motor)	The participant must use 1-2 fingers to move and rotate a pink object into the object outline as quickly as possible.
	Verbal articulation task (Speech)	Participants must perform a sustained phonation task for 15 seconds
	Visual reading (Speech)	Participants must read a series of sentences printed on the screen.
	Sustained phonation task (Speech)	Participants must repeat the syllables “pa ta ka,” for 15 seconds.
	Digit Symbol Substitution Task (Thinking)	The participant is presented with a symbol and must speak aloud the corresponding number shown a key that connects symbols to numbers.
	Visuo-spatial Working Memory Task	The participant is briefly shown four colored boxes followed by a single, colored box and must indicate if that box was in the previous set of four.
	Trail Making Task (Thinking)	The participant must trace a set of dots as quickly and accurately as possible using the index finger on their dominant hand.

eTable 2. Quantitative and qualitative data resulting from analysis of symptom maps

Data	Data type
1. Comprehensive list of symptoms occurring in early PD	Categorical
2. Percent of patients experiencing each symptom type	Frequencies
3. Bothersomeness score for each symptom type	Likert scale 1-4
4. Rationales for what makes symptoms bothersome	Qualitative
5. Rankings of symptoms from most bothersome to not present	Ranked 0-4
6. Identification of most important most bothersome symptoms	Frequencies
7. Comprehensive list of impacts experienced in early PD	Categorical
8. Percent of patients experiencing each type of impact	Frequencies
9. Bothersomeness score for each type of impact	Likert scale 0-4
10. Identification of specific symptoms contributing to different impacts	Frequencies
11. Rationales for bothersomeness of impacts	Qualitative
12. Alignment of digital measures to personally important symptoms	Likert scale 0-4
13. Alignment of hypothesized symptom of interest to personal symptoms	Likert scale 0-4

Table 3. Quotes showing participant experiences with online symptom mapping as a method to understand personally meaningful symptoms and impacts of PD

ID	Quote
P1	It's really hard to describe to your kids, "How's it going, Dad?" …This maps that out. I haven't thought about most bothersome to not bothersome to, "Well, what is it that bothers you?" This draws that out
P8	I like this tool…this has been very interesting…Thank you for walking me through, I learned some things about myself.
P10	I'm accustomed to this sort of diagraming and I found it useful. Will I be able to get a copy of this?
P11	[This is] very good at quantifying, clarifying what I'm saying. I'm being very vague, but I'm appreciating that you're able [to map it out]…These are hard things to describe …. I'm impressed that you've been able to quantify my vagueness and put it into some semblance of order.
P12	It's an awesome program [and] interesting to look at it this way. Can I get a copy? I wanna review it with my wife and see if I've missed anything.
P14	It was easy. I'm impressed…it would've been much harder to do on the phone.
P16	This has been about as a detailed conversation that I've ever had with anybody about what goes on inside my head.
P26	I'm impressed … This has clarified my condition for me, laying it out like this. A lot of times, you want to avoid thinking about this and this sort of forces it, but in a fairly painless way… it was an easy way to do it.
P27	I learn and understand with visualization, so this actually brings it all to the forefront, makes it nice to see and understand. I like it. It puts it in perspective as to where I believe I am and the explanation. It's sort of like, oh, this makes sense to me…. absolutely recommend it.
P30	I am a visual learner. I like to see things mapped out… categorizing and making sense of it.
P31	It really makes sense for me. …. It's a great snapshot of now. I would love to see this in two years and in two years from there, depending on progression. I'm a list organization type person. This is a great way for me to see things, to see me on paper. it was great that you had the survey to start with, but this was much easier. I think with surveys, you tend to just [answer] whatever. You're not always—not truthful, it's just you're not quite sure…This picture is a really good way of taking that survey and organizing my thoughts and putting it correctly.
P34	Building the map together visually guided me without leading me. I'm impressed...It's logical and ordered.
P36	It's really hard to track your symptoms in a way that shows what's most important, what's not, and why…. I thought it was a really nice, clear, concise way of trying to describe what's most important to [me]….A lot of times, when you try to tell people about your symptoms, they don't really understand what you're saying. [This is] very good way of trying to describe it in a way that you can tell exactly what it is.
P37	I like it…. I get to think more about how I'm feeling, what I'm going through…I'm a visual person [so] it was much better seeing the screen. Then you can actually analyze what I'm talking about and… Then I can see it to move it down to the right categories.
P38	The map is useful—everything's interconnected, and everything has its own value. The map is useful to understand this situation, but discussion gets to the root of the issue how individuals are struggling… This is valuable as one of multiple approaches to understand the person.
P39	((participant with word finding issues))it think it was helpful. It…helped make it easier to [see] where things belonged or what matched what…it reaffirmed. It opens up everything. It's like—here's where I'm looking for a word … A confirmation [to be able to see it].

Supplement A - online only

WATCH-PD qualitative study interview guide

PARTICIPANT INTERVIEW GUIDE INSTRUCTIONS AND QUESTIONS

Note: *Below is a semi-structured interview guide. It is to be used as a guide only. The actual areas of conversation are fluid and may be discussed at moments different from the order appearing below. The interview will be approximately 60 minutes. The interviewer may adapt the guide in order to cover the topics in the amount of time allotted for the session or in order to best elicit concepts from the participants.*

Prior to the start of the discussion, please check off:

Participant has been deemed eligible	☐ Yes ☐ No
Participant has consented prior to the discussion	☐ Yes ☐ No

Notes to Interviewer:

- This interview guide is meant to help guide the discussion, but not to be used as a verbatim script; probes and questions may change slightly depending on individual feedback.
- Additional unscripted probes to be used to gain further information or clarification may include:
  - **Clarification:** I don't quite understand that.
  - **Expressing understanding:** How did you cope with that?
  - **Justification:** Can you tell me a little bit more about why you chose that for your answer?
  - **Importance:** How important is this for you?
  - **Relationship:** I'm not sure how these 2 things are linked.
  - **Extending narrative:** Tell me a bit more about that.
  - **Accuracy:** Let's see if I've got that right.

Key for Interviewer:

- Questions/text to be asked of the participant
- *Notes to the interviewer (Do not read to participant)*

Introduction

Thank you for taking the time to speak with me today. Before we can start with the interview let's go over the information for the study.

We are talking to people such as yourself who have been participants in the WATCH-PD study. The purpose of our conversation today is to better understand how the data captured in the WATCH-PD study relates to your experience with Parkinson's disease symptoms and impacts. The interview data we collect will be used to support the use of wearable devices or digital health technologies that can record important features of Parkinson's disease progression in future clinical trials.

It is expected that approximately 40 participants will be enrolled in this interview study. There are no treatments being tested in this study.

You are being asked to take part in one interview, which will be audio/video recorded to ensure we capture everything you say accurately. The interview will take between 60-90 minutes to complete. The recording will be transcribed and no names will appear in the written transcript. All your responses will be anonymous; your name will not be linked with any of your responses. Recording the interview is a required part of the study. If you do not want to be recorded, you may not take part in the study.

Your participation is voluntary, which means that you do not have to take part in the interview. You can skip any question you do not want to answer, and you can choose to stop the interview at any time. You will be compensated $X in the form of a gift card for your time after the interview.

Before we proceed, do you have any questions?

Address all questions the participant has before proceeding.

Before we get started, I would like to reiterate that this session will be audio recorded. However, your name will not be linked with the recording, transcription, or your responses during the interview.

Is it okay for me to record the conversation today?

If yes, continue to "Background for All Interviews."

If no: Unfortunately, since you do not agree to the recording of this session, you won't be able to participate in this study. Thank you for your willingness to consider participation in this study.

Background for All Interviews

- My role here is to ask questions and to listen. I will also be summarizing information at times. I will ask questions related to your experience and I will move the discussion from one question to the next to try to keep us on track so that we can finish on-time.
- I am not your medical doctor, so I am not qualified to give medical advice. I encourage you to follow-up with your regular doctor if you have any questions about your condition after this interview.
- Please feel free to let me know if you need a break. You can ask me questions at any time.

Any questions before we begin?

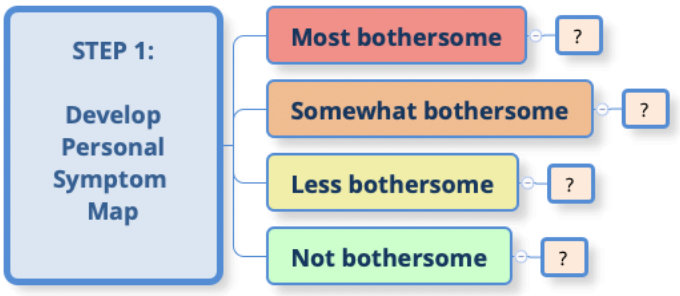
Begin Recorder: This is participant ID *[insert ID number here]* for the WATCH-PD Qualitative Sub Study on *[Date].* Do I have your permission to record this interview? *Verbal response required.* And can you please confirm that you read and signed the Informed Consent Form? *Verbal response required.*

Section 1. Personally Important Parkinson's Disease Symptoms

The purpose of our conversation today is to better understand how the data captured in the WATCH-PD study relates to your experience with Parkinson's disease symptoms and impacts. As part of this I'm going to ask you to describe your symptoms of Parkinson's and then I will create a map or a "picture" of symptoms that are important to you, based upon what you tell me. As I create the map, please point out anything you see that needs adjusting, as this will help me to best represent your experience.

1. First, would you tell me what Parkinson's disease-related symptoms you experience? From your responses on the survey, I see that you listed….

   [Step 1 of the symptom mapping activity begins here. As the participant directs, the interviewer will map the participants symptoms by order of personal importance.]



   - Probe: Are there other symptoms that you experience that you have not told me about and that I don't have in your map?
   - Probe [*yes/no*] on any they do not spontaneously state (tremor, slow movements, gait disturbances, fine motor coordination, speech articulation, cognitive impairment, daytime sleepiness, mood symptoms).

2. Of those symptoms you mentioned, explain to me which are the most bothersome to you. What specifically makes those symptoms bothersome, and in what situations?

   [The interviewer will add concise details to the symptom map delineating what makes specific symptoms important/bothersome. Example: if gait, is it foot lift or gait speed? Does it occur at home during regular daily activities or mostly when out exercising?]

3. Are the symptoms that are <u>most bothersome</u> also the <u>most important</u> to you, or is that different in some way?
   - Probe: Have we captured all the symptoms that you experience correctly? Is there anything we missed?

Section 2. Patient Perspectives on WATCH-PD Battery – Task Debriefing

In the WATCH-PD study you completed a range of tasks at home through use of the iPhone and Apple Watch and in the clinic. Now we will discuss those tasks.

The goal of the following questions is to determine if the tasks (and specifically what tasks) assessed via the WATCH-PD technologies are important/relevant/meaningful to patients. How do the tasks relate to how they feel and function?

1. You completed a **shapes task**. The screen looked like this:

   IMAGE HERE

   a. In your own words, what was this task asking you to do?

   b. What Parkinson's symptoms do you experience that are related to completion of this task?

   c. How is this task similar *[or relevant]* to tasks you do in your daily life?

   d. Do you believe completion of this task is important to measuring the progression of your Parkinson's? If not, why?

2. You completed a **trails task**. The screen looked like this:

   IMAGE HERE

   a. In your own words, what was this task asking you to do?

   b. What Parkinson's symptoms do you experience that are related to completion of this task?

   c. How is this task similar *[or relevant]* to tasks you do in your daily life?

   d. Do you believe completion of this task is important to measuring the progression of your Parkinson's? If not, why?

3. You completed a **finger tapping task**. The screen looked like this:

   IMAGE HERE

   a. In your own words, what was this task asking you to do?

   b. What Parkinson's symptoms do you experience that are related to completion of this task?

   c. How is this task similar *[or relevant]* to tasks you do in your daily life?

   d. Do you believe completion of this task is important to measuring the progression of your Parkinson's? If not, why?

4. You completed a **visual-spatial task**. The screen looked like this:

IMAGE HERE

a. In your own words, what was this task asking you to do?

b. What Parkinson's symptoms do you experience that are related to completion of this task?

c. How is this task similar *[or relevant]* to tasks you do in your daily life?

d. Do you believe completion of this task is important to measuring the progression of your Parkinson's? If not, why?

5. You completed **symbols swap task**. The screen looked like this:

IMAGE HERE

a. In your own words, what was this task asking you to do?

b. What Parkinson's symptoms do you experience that are related to completion of this task?

c. How is this task similar *[or relevant]* to tasks you do in your daily life?

d. Do you believe completion of this task is important to measuring the progression of your Parkinson's? If not, why?

6. You completed a **reading task**. The screen looked like this:

IMAGE HERE

a. In your own words, what was this task asking you to do?

b. What Parkinson's symptoms do you experience that are related to completion of this task?

c. How is this task similar *[or relevant]* to tasks you do in your daily life?

d. Do you believe completion of this task is important to measuring the progression of your Parkinson's? If not, why?

7. You completed a **phonation task**. The screen looked like this:

IMAGE HERE

a. In your own words, what was this task asking you to do?

b. What Parkinson's symptoms do you experience that are related to completion of this task?

c. How is this task similar *[or relevant]* to tasks you do in your daily life?

d. Do you believe completion of this task is important to measuring the progression of your Parkinson's? If not, why?

8. You completed an **articulation task**. The screen looked like this:

IMAGE HERE

a. In your own words, what was this task asking you to do?

b. What Parkinson's symptoms do you experience that are related to completion of this task?

c. How is this task similar *[or relevant]* to tasks you do in your daily life?

d. Do you believe completion of this task is important to measuring the progression of your Parkinson's? If not, why?

9. You completed a **walking and balance task**. The screen looked like this:

IMAGE HERE

a. In your own words, what was this task asking you to do?

b. What Parkinson's symptoms do you experience that are related to completion of this task?

c. How is this task similar *[or relevant]* to tasks you do in your daily life?

d. Do you believe completion of this task is important to measuring the progression of your Parkinson's? If not, why?

10. You completed a **tremor task**. The screen looked like this:

IMAGE HERE

a. In your own words, what was this task asking you to do?

b. What Parkinson's symptoms do you experience that are related to completion of this task?

c. How is this task similar *[or relevant]* to tasks you do in your daily life?

d. Do you believe completion of this task is important to measuring the progression of your Parkinson's? If not, why?

11. Overall, how well do you feel your Parkinson's symptoms were captured through the WATCH-PD iPhone and Apple Watch tasks you completed?

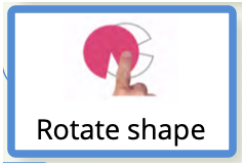
- Probe: What symptoms were NOT captured and why is that important to you?

Section 2A: Mapping Activity (Relating Tasks to Personal Symptoms)

Now let's incorporate each of the WATCH-PD **tasks** we just talked about into your personal symptom map where you feel they fit best. There is one task per card.

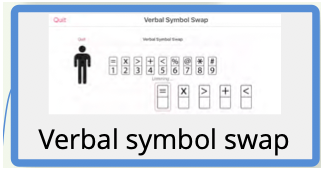
Movement

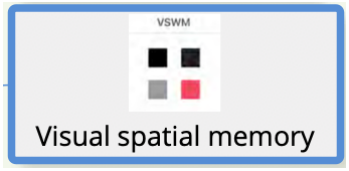
Fine coordination



Speaking

Thinking





BrainBaseline application screenshots reprinted with permission from Clinical ink.

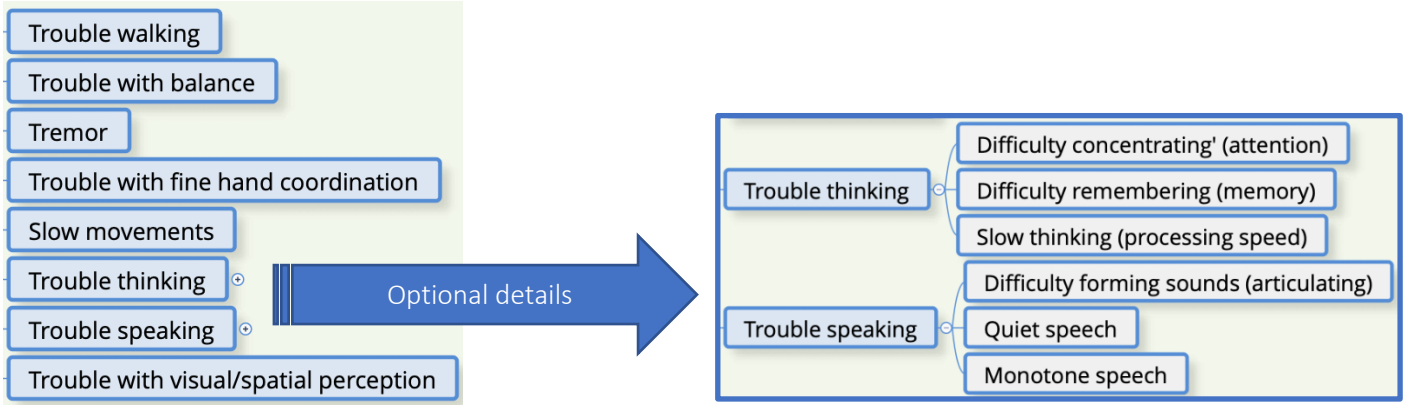
1. Where would you place each **task card** in relationship to the symptoms in your personal symptom map?

[As the participant directs, the interviewer will integrate the WATCH-PD tasks into the personal symptom map, relating each task to meaningful symptoms, or indicating if the task is not relevant to the participant, along with details as to what makes those tasks relevant or not relevant.]

Section 2B: Mapping Activity (Relating Concepts of Interest to Personal Symptoms)

Now that we have sorted each of the tasks, let's consider the various symptoms of Parkinson's Disease that the tasks were intended to measure. Again, there is one concept per card.

Main concepts of interest



2. Where would you place each of the [main concept] cards in relationship to the symptoms in your personal symptom map?

[As the participant directs, the interviewer will integrate the WATCH-PD concepts of interest into the personal symptom map, relating each concept to meaningful symptoms, or indicating if the concept is not relevant to the participant, along with details as to what makes the concepts relevant or not relevant. If able, participants will also be asked to consider the more granular concepts show in the call out box for trouble thinking and speaking.]

Closing

3. Are there any other things that come to mind when you think about your participation in WATCH-PD and the assessment of the Parkinson's disease symptoms and impacts that you have experienced?

Thank you for your time and for all the insightful information and experiences you have shared with me today. Now, let's discuss the next steps before we end the interview.

[Stop recording and go through any closing logistical items with the participant.]

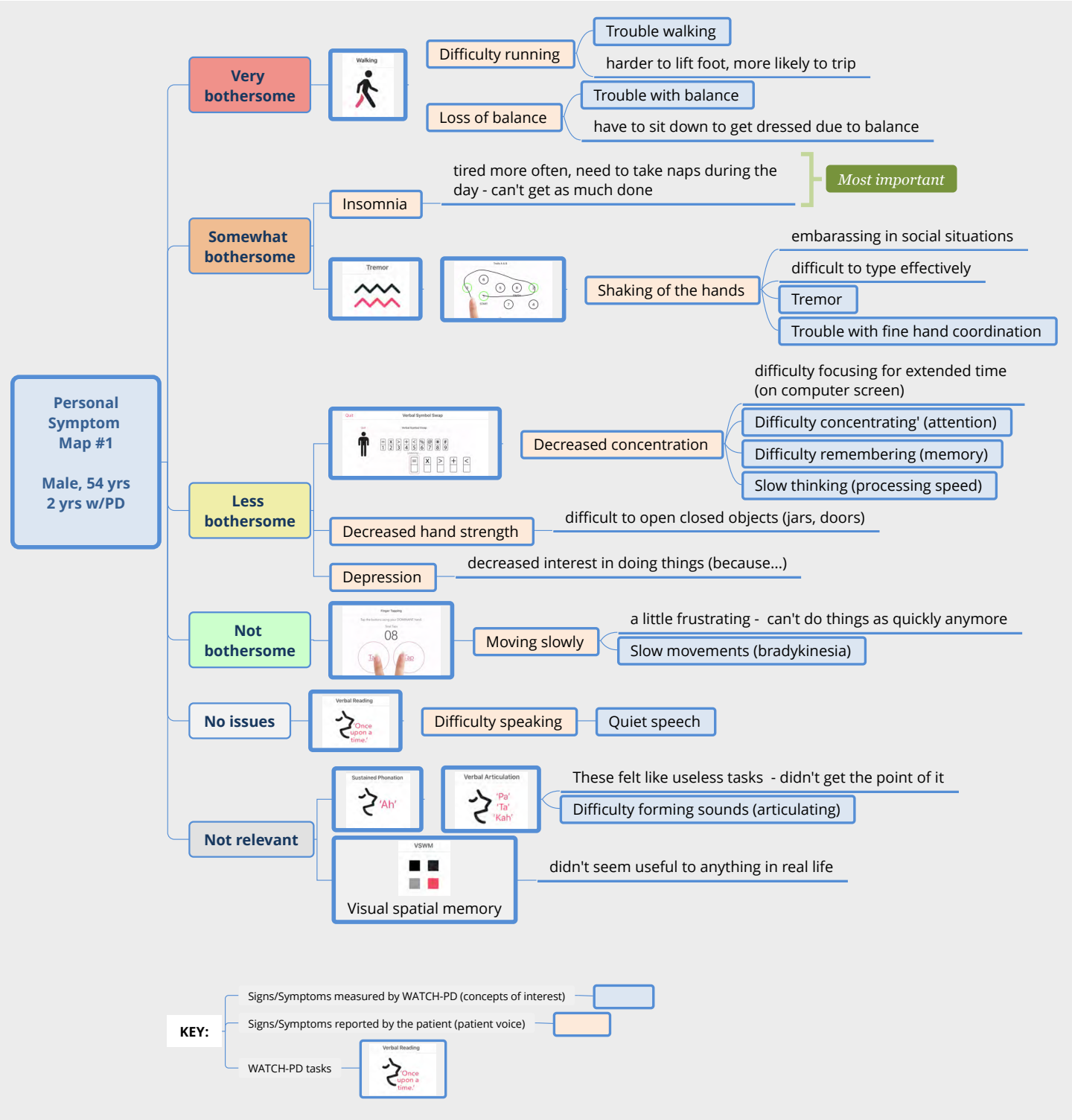


Figure 1. Sample personal symptom map showing perceived relevance of WATCH-PD tasks and concepts of interest