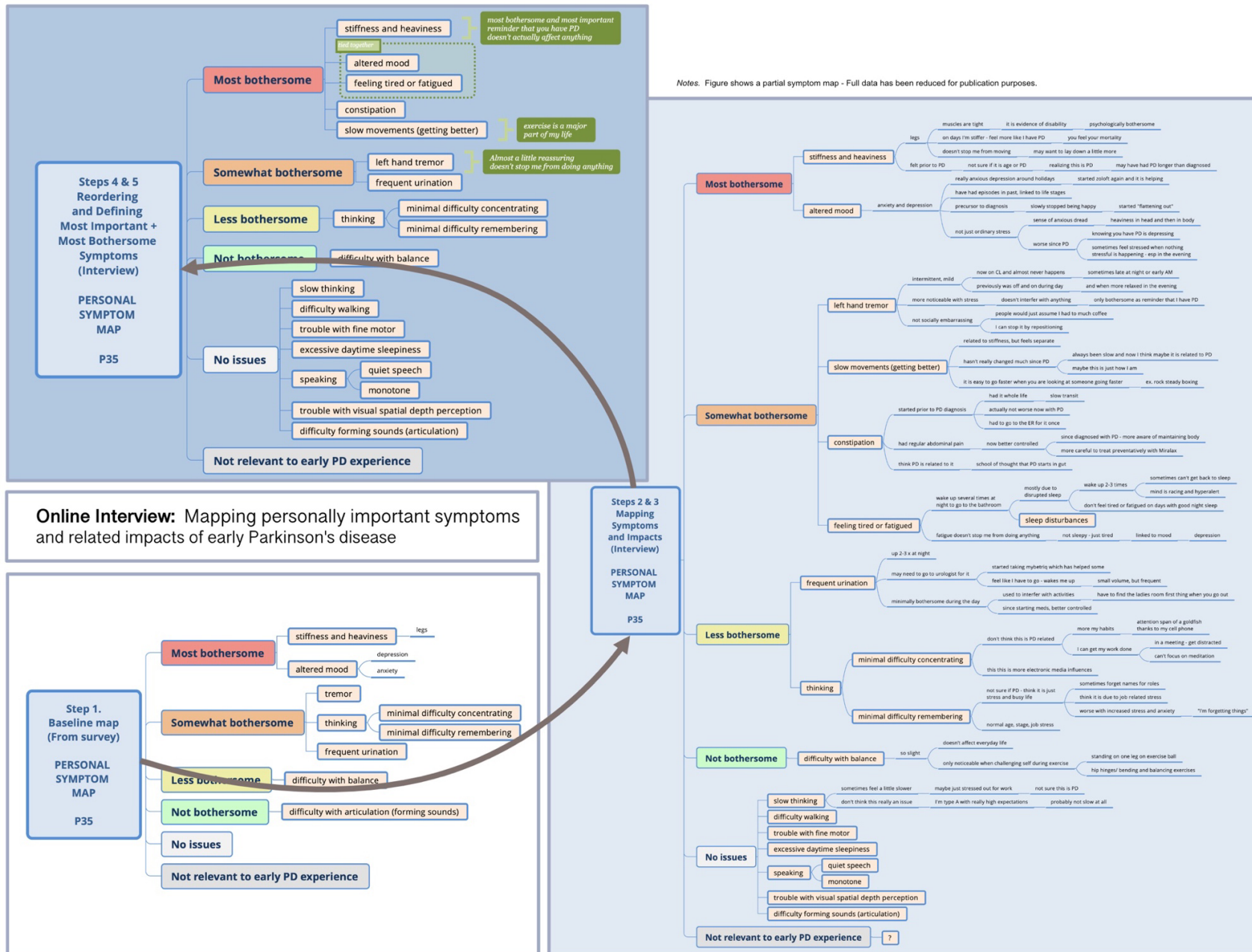


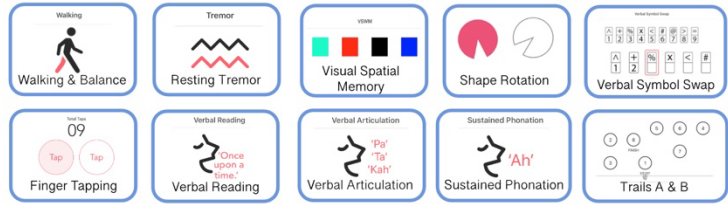
Supplementary Material

Mapping Relevance of Digital Measures to Meaningful Symptoms and Impacts in Early Parkinson's Disease

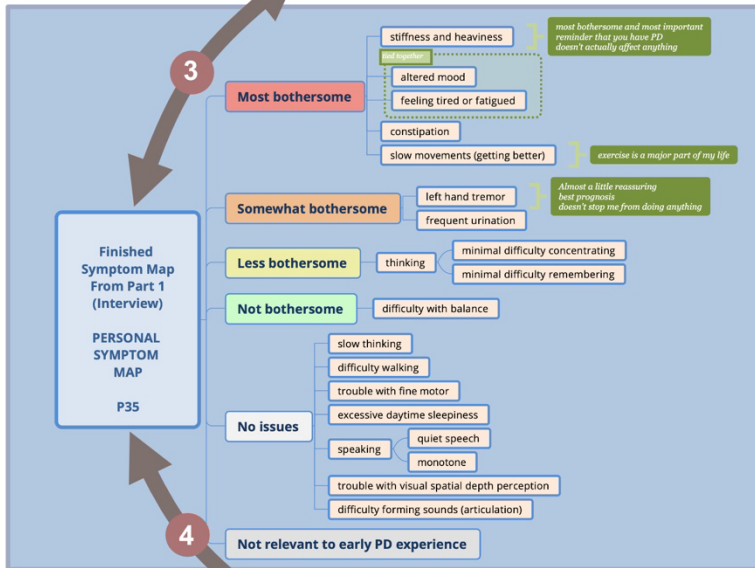


Supplement A. Online Interview Part 1 – Mapping personally important symptoms and impacts of early PD.

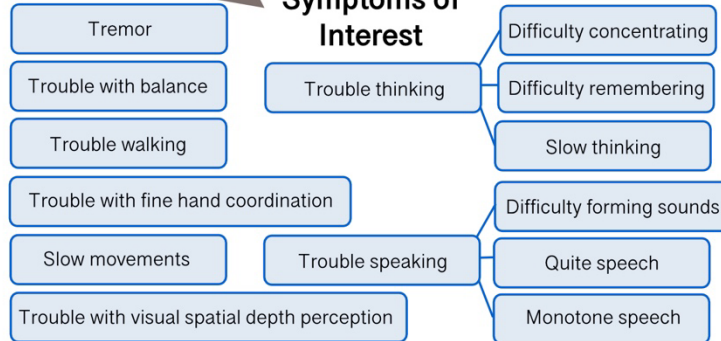
Online Interview Part 3 & 4: Mapping tasks and research symptoms of interest to personal symptoms and impacts



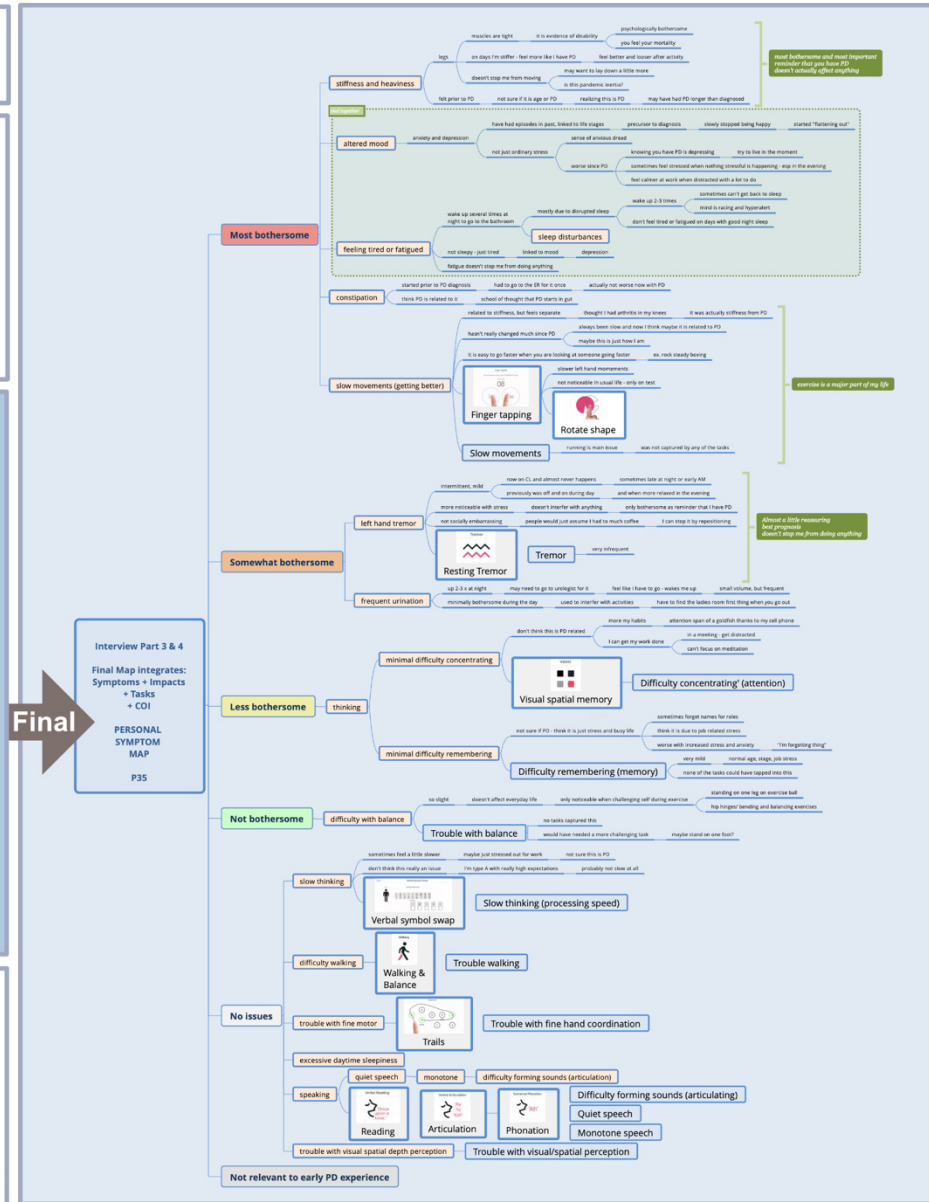
Task Cards



Symptoms of Interest



Final



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

BrainBaseline application screenshots reprinted with permission from Clinical ink.

Supplement B. Online Interview Part 3 & 4 – Mapping digital measures to personally important symptoms and impacts of early PD.

Supplement C. Feasibility metrics for online interviews with symptom mapping.

	Metric
Interview duration (Participant)	
Total time start to finish in minutes	120 minutes (range 90 – 155)
Recorded interview time in minutes	102 minutes (range 60—139)
Device used for online interview (Participant)	
Computer – N(%)	37 (47.5%)
Tablet – N(%)	2 (5%)
Smartphone – N(%)	1 (2.5%)
Data collection time (Researcher)	3 hours
Mapping survey prior to interview	30 minutes
Participant visit	2 hours
Data management procedures	30 minutes
Data analysis time – estimated time per interview (Researcher)	10 hours
Developing the code book	(iterative)
Coding for types and bothersomeness of symptoms	30 minutes
Coding for impacts and contributing symptoms	60 minutes
Coding for relevance of digital measures to symptoms	10 minutes
Coding of cognitive interview for content validity	60 minutes
Thematic analysis of narrative transcripts	6 hours
Data saturation (for items reported by > 10% of sample)	
Symptoms	17 th interview
Impacts	10 th interview
Tasks	(N/A)
Themes	20 th interview

Supplement D. Types of quantitative and qualitative data derived from mapping and data saturation points.

Data	Data type	Example	Data Saturation Interview #
SYMPTOMS OF PARKINSON'S DISEASE			
1. List of all symptoms occurring in early PD	Categorical	• Tremor, Slow movements, Insomnia, etc.	17
2. Percent of patients experiencing a given symptom	Frequencies	• The most commonly reported symptoms of early PD were ... [Symptom, N(%)...]	
3. Average bothersomeness of a given symptoms ^a	Likert scale	• On a scale from 0-4, average bothersomeness of difficulty thinking was [Mean = X] (SD)	11-38 ^b
4. Bothersomeness distribution of individual symptoms	Likert scale	[<i>Bar graph of symptoms by bothersomeness distribution</i>] • Most bothersome = N(%) • Somewhat bothersome = N(%) • Less bothersome = N(%) • Not bothersome = N(%) • No issues = N(%)	
5. Identification of "most important" symptoms	Frequencies, Ranked	• The single most important symptom to people with early PD was tremor, N(%)...	
6. Rationales for what makes symptoms bothersome or important	Qualitative	• P1: "It's bothersome because it affects almost everything"	
IMPACTS OF PARKINSON'S DISEASE			
7. List of impacts experienced in early PD	Categorical	• Altered ability to perform job, N(%) • Altered ability to communicate as usual N(%) • N(%)	10
8. Percent of patients experiencing each type of impact	Frequencies		
9. Specific symptoms contributing to individual impacts	Frequencies	[<i>Heat map impacts by contributing symptoms</i>] • Impact – N(%) attributed to Symptoms X, Y, Z	
10. Descriptions of how impacts affect the individual	Qualitative	P1: "It's a constant reminder that something is wrong with you..."	
RELEVANCE OF DIGITAL MEASURE TO MONITORING SYMPTOMS OF PARKINSON'S DISEASE			
11. Relevance of individual digital measures to monitoring personally important symptoms ^d	Likert scale	• The tasks which were rated as most relevant to personally important symptoms were [Task, N(%)...]	10-30 ^c
12. Rank ordered list of relevant measures from most to least relevant from the patient perspective	Ranked	• In all, nine out of ten tasks were viewed as relevant to monitoring important symptoms (past, present, anticipated)... However, only two [Task 1, Task 2] related to symptoms that were actively present and bothersome for more than 80% of the sample...	
THEMATIC FINDINGS			
13. Themes related to symptom experiences, impacts of disease, and perception of digital measures	Qualitative	Theme: People with PD find it difficult to differentiate between PD symptoms and changes that occur with normal aging.	2 ^e

Data saturation is the point after which no new data is identified and was calculated using symptoms reported by >10% of the sample. Data stability is the point at which the mean ratings of bothersomeness or relevance did not fluctuate more than +/-10%, suggesting adequacy of the sample size for the calculation.

^a Each symptom has an associated patient reported symptom scores (PRSS) based on placement in map from 4= Most bothersome to 0 =No issues

^b Stability of mean bothersomeness ratings of each symptoms (+/- 10% of final mean) occurred between 11 interviews [Tremor] to 38 interviews [Hypersalivation] for all symptoms expressed by >10% of the sample (SD=). On average, stability of symptom severity ratings occurred by the 29th interview. Symptoms with lower frequencies required a greater number of interviews to achieve stability for bothersomeness scores.

^c Stability of mean relevance rating (+/-10% of final average) occurred between 10 interviews [Tremor task] to 35 interviews [Visual Spatial Memory task]. On average, stability of relevance ratings for digital measures occurred by the Xth interview

^d Each digital measure is related to a symptom or level in the map and thus has an associated patient reported symptom scores (PRSS)

^e All key themes were identified within the first two interviews.

Supplement E. Theme 1 Supporting Data - Examples of task endorsement based on five criteria used by participants to explain rationales for personal relevance

Understood purpose	Important symptom	Good test of symptom	Related to daily life ^a	Experienced symptom ^b	Endorsed Task ^c	
C1	C2	C3	C4	C5	CASES IN WHICH PARTICIPANTS ENDORSED TASK	
✓	✓	✓	✓	✓	✓	<p>Interpretation: Personal relevance of digital tasks to patients for monitoring important aspects of disease is contingent upon:</p> <ul style="list-style-type: none"> • (C1) approximately understanding what symptom the task is assessing, • (C2) belief that the task is assessing an important symptom of the disease, and • (C3) belief that the task is a good test of that symptom. <p>The task does not have to be related to real life (C4) or an experienced symptom (C5) to be relevant. However, positive endorsement of these criteria can add value to perceived relevance of the measure.</p>
✓	✓	✓	✓	✓	✓	<p>P5: This was measuring fine motor ... I started to do the rapid tapping, I would lose control of my index finger and the middle finger and they would kind of spazz out. I could tap away a much greater rate with the right hand. [The task relates to my] dexterity, fine motor skills in my right hand. It's very similar to typing. Like I said, this one was the Parkinson's symptom that I'm noticing the most. Yes [it's important to measuring my PD progression]. (<i>Finger Tapping</i>)</p>
?	✓	✓	✓	✓	✓	<p>P25: I had to walk continuously for a minute and then at standstill for 30 seconds with my hands by my side. I think it was measuring my tremor while I was walking and standing still, since tremor is my only issue. I know it was probably in general looking at gait and balance as well [but I] don't really have those issues and that's why I wasn't focused on them. [The task is important and] similar to just standing still and walking. (<i>Walking & Balance Task</i>)</p>
✓	✓	✓	✓	✗	✓	<p>P24: There were four or five sentences that I had to read. My understanding is that sometimes people with Parkinson's have difficulty speaking, or their voice will kinda waver out. It'll get quieter. I don't think I have that problem. [but] Your ability to speak and make your needs known is important. [The task is similar to life because] I talk all the time, and if your voice is trialing off you have a problem communicating. [So the task] is very important. I think communication is key. Your ability to verbalize is extremely important. (<i>Verbal Reading Task</i>)</p>
✓	✓	✓	✓	✗	✓	<p>P26: It was asking me to walk for a full minute back and forth...it was sensoring for tremor and for gait. [I don't have this symptom [but] I do a lot of walking [and] I'm worried. This is one of the worrisome symptoms of PD, for me, not being able to get around, [so the task is important]. I mean I'm watching myself. When I stub my toe, I sit there and I go, was that [PD]? Yeah. I'm already monitoring it. (<i>Walking & Balance Task</i>)</p>
✓	✓	✓	✗	✓	✓	<p>P33: You sat down, and you put your hands in your lap and then You put your hands out. I thought this was measuring how much you were shaking. {I have] tremor in my hand. I don't sit around with my hands in my lap or my hands out. [But it's important] Because if the watch was picking up the intensity of the tremor, it would show that it was is getting worse. (<i>Tremor Task</i>)</p>
✓	✓	✓	✗	✓	✓	<p>P37: You keep tapping your index finger and your middle finger over and over, back and forth, both dominant and non-dominant...it's to see how your fine motor skills are working...I didn't realize this until I was doing this, how slow my right hand is compared to my left hand. I might hate this one, but this was one of the most important ones. (<i>Finger Tapping</i>)</p>
✓	✓	✓	✗	✓	✓	<p>P20: You had to move your fingers to the different numbers quickly...[it was measuring] motor skills, moving from one number to the next and doing it in a quick enough way, and some memory, 'cause you gotta go from one to two to three. [It relates to my difficulty with] motor skills as well as remembering. I think over a period of time, if you struggled with moving from one to two to three and so one, it would be measuring [progression] for sure. (<i>Trails A&B</i>)</p>
✓	✓	✓	✗	✗	✓	<p>P6: I don't have tremors... I understand why you're testing, and I think it's important to test, but, for my daily life, it wasn't particularly important to me at this point ...[it isn't like anything I do in real life, but] I can see where it would be very important. I absolutely believe it's valid, as valid as the walking, yes. (<i>Tremor Task</i>)</p>
✓	✓	✓	✗	✗	✓	<p>P21: It was asking me to repeat a three-syllable word, pa, ta, ka, pa, ta, ka, pa, ta, ka. [It was measuring] speech and ability to keep syllables separated. I don't think I have any [symptoms] that were related to that task. It's not at all similar [to things I do in daily life]. I have to articulate, but I don't say things over and over and over again. I don't try to squeeze in long sentences in one breath. [But] I think this task would be easy to see when deficits crept in ... it would be easy to see a decline with this task. I believe it's important. (<i>Verbal Articulation Task</i>)</p>
?	✓	?	✗	✗	✓	<p>P22: I was asked to repeat a nonsense word as many times as I could during a period of time. I had to take a deep breath, so that I could say it as many times as possible in that timeframe, so I thought it might have been measuring what my lung capacity was. I don't think I have any symptoms that relate to this task. Generally speaking, I'm not repeating words 15 or 16 times in a row so it's not an example of something that I would do in my everyday life. [But] I guess if</p>

C1	C2	C3	C4	C5	
					you were to look at the data over the course of several months, there might've been trend, so I feel like there might be meaning in the data, so that's what I mean by [I think it is an important task]. (<i>Verbal Articulation Task</i>)
CASES IN WHICH PARTICIPANTS DID NOT ENDORSE TASK					
✓	✓	✗	✓	✓	P14: [I had to] see if I can line up the solid circle with the outline circle and how long it would take me... I think[it measured] motor skills and dexterity. The reason I didn't like this one is I didn't think it measured Parkinson's; it just measures general coordination. This would be like trying to screw on a jar; I thought this one was too glitchy with the computer. there were times where my hand was moving, and the thing wasn't moving with me. I didn't think this measured accurately. (<i>Shape Rotation Task</i>)
✓	✓	✗	✓	✓	P26: It was asking me to take little pie slices and line them up. [It was measuring] my ability to control my hands. [But my] fingernails they get in the way on this exercise. It doesn't let you connect with the pad. To consciously keep that contact, I had to go slower than I normally would. [it's similar to] working on the computer. Yeah, using a mouse, using a track pad. I think that's relevant. [It relates to my trouble with] clicking on a link on your computer, and some of the fine motor skills. [But] I think there's too many things wrong with it for it to be important. Is it the Parkinson's or is it because I'm not positioned properly here? I don't trust this exercise. (<i>Shape Rotation Task</i>)
✓	✓	✗	✗	✓	P20: [The task measured] cognitive ability to remember colors. [It relates to] my issues remembering and being able to do things quickly. [But] You kinda give up on the task because it's so hard, and sometimes I just guessed... I think it would be challenging for anyone [regardless of PD], and I don't see where you would use it. My fiancée saw it and was like, "I don't think I could do that either." So I would question it's [validity] . (<i>Visual Spatial Memory Task</i>)
✓	✓	✗	✗	✗	P21: This [task] is where you'd see the four colored boxes and then have to say the one that they flashed up if it was one of four ...[It was measuring] Short term memory probably. It was frustrating... I'd get to the end of it and go, "Geez, did I get any of those right?" I don't think [I have] any [symptoms related to it], at least not yet. I don't have to make those kind of decisions that quickly in real life. I'm not sure it was relevant. I felt so crappy about how well I did at it. I don't know if that was related to my Parkinson's or not. I think I would've done crappy at it with Parkinson's or without Parkinson's. It just seems random ...I don't know if it showed a progression in my Parkinson's at all. (<i>Visual Spatial Memory Task</i>)
✓	✓	✗	✗	✗	P23: It's another fine motor task. You had to put two fingers on the colored circle and twist it and move it until it matched the circle on the inside. I don't have a lot of fine motor issues. I can't think of anything [in life it relates to]. it's not necessarily measuring fine motor skills. It's measuring your ability to learn how to game the system—it's affected by the length of your fingernails, and that doesn't have anything to do with fine motor skills. If it's measuring the length of my fingernails, that's a measurement error. (<i>Shape Rotation Task</i>)
?	✗	✗	✗	✗	P18: You had to remember these four colors, and then some other color, and match them up. I suppose it's [measuring] your memory. [but] I don't know how it relates to Parkinson's. [I've never had] very strong visualization. I'm not thinking of anything [in real life that it is similar to]. I guess I have no idea [if this is important to monitoring PD], which inclines me to think, no [it's not relevant]. I don't know ...I am not expert. (<i>Visual Spatial Memory Task</i>)
✗	✗	✗	✗	✗	P12: This task, I don't think I'm experiencing any symptoms, and I'm not sure what it was trying to measure. I don't see the connection to [daily life]and I'm not drawing the connection to the Parkinson's piece. (<i>Verbal Articulation</i>)
✗	✗	✗	✗	✗	P24: You have to look at one, two, three, four [colors], and then the fifth square at the bottom and figure out if that fifth square at the bottom is in any of those four. You know I'm not sure—I'm guessing that it's cognition, [but] ... I don't know what this would measure. I don't know [if I have related symptoms] because I don't understand the task. It's not similar to anything in life. I didn't like this. I was unsure of it and I found it extremely frustrating. It's not so much [the difficulty of] the test, it's trying to figure out how does it fit with Parkinson's? How is this going to benefit me, or other people? This was the only test that I recall, that made absolutely no sense whatsoever. I think, ultimately, that's the frustration. (<i>Visual Spatial Memory Task</i>)

Participant criteria for evaluating personal relevance of WATCH-PD tasks to monitoring personally important symptoms of Parkinson's disease.

C1. CRITERIA #1: Believed they knew what task was measuring

C2. CRITERIA #2: Believed the task related to an important symptoms of PD (experienced or not)

C3. CRITERIA #3: Believed the task was accurate, consistent, and reliable.

C4. CRITERIA #4: Believed task related to activities in performed in real life (^a Cognitive interview item Q3 – Task relates to activities in real life_

C5. CRITERIA #5: Personally experienced the symptom believed to be measured - past or present (^b Cognitive interview item Q2 – Task relates to personal symptom of PD)

Endorsed Task = Endorsed task as valuable for monitoring PD symptom progression over time. (^c Cognitive interview item Q4 – Task is relevant to monitoring personal PD progression)

Supplement F. Theme 2 Supporting Data

Theme 2. People with early PD believe it can be important to complete tasks measuring aspects of disease and symptoms that they do not currently experience.

P4: I just know that's something that does impact Parkinson's patients, so I thought that would've been something you could've measured.

P5 All of these things [are important], knowing whether or not there was any noticeable deterioration or whether they stayed the same or improved

P6: I don't recall that I even had any tremors at all. ... but I'm curious if it could tell beyond what I can sense. That would be of great interest to me.

P7: Well, it could be important a little longer term...you've got to compare it to something. That's what I'm wondering. It was valuable [to know] if it started and the cognitive issues maybe became more pertinent or speech was slurred or something... I think with a lot of these tasks that would be something that I would be interested in. Have they changed one way or the other over time or not changed at all over time?

P8: [It's important because] If I had difficulty walking, this [task] would have uncovered that. It would have diagnosed it and sent that information to somebody...or... if I was doing 200 taps, and then the next week only did 100 taps, that would show that something's going wrong, right? In my case, it did not, because not a lot is going on. I think this, again, falls into the general category that if over time, I noticed I was unable to do this, or I was getting worse at it, I would want to know that and use that as part of my discussions with my doctor. I think everything I did fell in that category.

P10: I suspect that this is something that over a longer duration of time would show evidence of deterioration. I think that the articulation issue is an important one and the one I experienced, but not maybe as noticeably at this point in my life. I do think it's important.

P15: I would say yes [it's important], because, over time, it may start to show up. It'll be like, "Okay, six months ago, it didn't tremor...a year later, now it tremors." It doesn't register anything now, but I think over time, if my hands started to tremor, then that would be valuable to know that it's progressing.

P19: I don't have an issue [with speech]. [But] I think the tasks are good to have in the test, because a lot of people with Parkinson's do have these issues. How would I know if I did or didn't have them without doing the task? [and] I'm gonna take back my last response about is this important for measuring Parkinson's, because maybe it is. Just because I didn't have problem with the cognitive doesn't mean that you wouldn't be able to identify issues with other people.

P24: I think it's not so much what you have currently, it's the progression. It's about whether new symptoms develop and if those symptoms become more severe over time. ... because you're always thinking at the back of your mind, "How much time do I have? Am I gonna be in a wheelchair? Am I gonna have dementia? Am I gonna be able to take care of myself?"...Symptoms they change, they get worse, or they suddenly show up, and you didn't have it before.

P26: My thinking is that the earlier you catch it, the better. Even if it wasn't a problem [now], I'd want to keep testing it because chances are, it's gonna show up, and we might as well know as early as possible. ... just because I don't [have] it now doesn't mean it's not gonna be relevant three months from now. You're going to find me saying yes to almost everything here unless I think it was ill-designed.

Supplement G. Theme 3 Supporting Data

Theme 3. Disease monitoring tasks can have negative emotional impact that affects sense of well-being and may impact perception of or engagement with the digital measure.

P1: Whenever I take a survey—they go through pages and pages of, "Have you choked yet? Have you fallen yet?" all these horrible things, "Are you constipated?" it's like, I don't have any of those things, but should I, will I? Will I have all of them? That's depressing

P5: I like to feel like I'm doing well, when I'm testing on these things in this way, I'm pretty clearly, I felt like it was not.

P6: I think in general, I'm mostly on top of things, but this I wasn't on top of. I just couldn't do it that fast...I wasn't going to let it stress me out. I just go, "Oh, I hate this. I know I'm not gonna do well." As hard as I tried to do well, I just never felt like I was on top of it.

P10: it made me aware of issues I didn't really know I had. I was blaming the game, not my cognitive difficulties, but it's a stupid game. It illustrated my problems with remembering. It's just right now that I'm remembering how stressful it was.

P11: I think I notice when I do this test that I have variations in tone and amplitude that I'm not in control of. I don't know if that's just everybody or if it's PD related, or if it's just me. It makes me conscious that I have less control in an area that I'm not really aware of.

P14: I hated doing. I guess it pointed out to me how slow my hand is getting. I was like, "Why can't I do this?" This one always made me feel really stupid. I never felt like I was doing it good. I think it was a tricky test, but I think it would measure whether your cognitive thinking, your ability to retain information and spit it back out is getting slower over time. I just didn't like it 'cause it made me feel dumb.

P15: That belongs under measure of insanity. I know I did very poorly on all the way through from the beginning.

P16: This one caused me the most anxiety. I bet that if you looked at the accuracy at the beginning of the test, and compare it with the accuracy at the end of the test, that the percentage correct answers would be far better in the beginning of the test than at the end. By the end, people are just so frustrated that they'll tap any finger. They won't care anymore.

P17: I felt like it was beating me. It's like playing poker with the house, the house wins every time. I felt like I did not have the cognitive ability to beat the house.... I felt like I was really bad at it.

P19: I didn't like being asked those questions every day ... Instead of just going about my day [happily] It made me feel moody. I was trying to do my best, but I was like, my best ain't good enough for this one.

P21: It was frustrating in the sense that I didn't feel like I was very good at it. I don't want to see the results I would get in that.

P23: A big issue with this, is you bring in previous frustration and it affects you even more. In other words, as frustration increases, the failure rate on the test is going to increase. Over time, you may be measuring more the frustration level than the Parkinson's level.

P26: when the doctor's testing you, you're really there to perform and so you get anxious. I felt like it was rigged against me. I felt like oh no, I can't handle this. This is gonna make me feel so inadequate and I'm gonna get depressed. ..After I was all done, I would go be depressed for an hour because it pointed out exactly what was going on—it pointed it out to me that I was having trouble with some of these things.

P27: I completed the test, but I dreaded it, and I'm like, "Can't I just skip this?" and I'm thinking, "No, you've gotta finish it all." But it made me anxious.... "Oh, my gosh. This is gonna be awful, and they're gonna think I've progressed." I just wanted to say, "Oh, the heck with this," {Someone} mentioned that this was hated by all of the participants, I felt better. I thought, "Okay, it's just not me. Everybody's screwin' up the test."

P33: Things that I could do when I started it, I couldn't do with my left hand... it was a reminder I was getting worse. When we did the study, they would ask you all these questions about symptoms, it'd be be depressing where you could be going with this. It would take me a day or two to forget about it.

P36: [it made me] little bit anxious approaching the test. Wondering what my numbers are gonna be, if it's getting worse.

P37: It was absolutely horrible. I didn't realize until I was doing this how bad my right hand is compared to my left hand....Is it getting worse? What do we need? Do we need to go on medication?" It's 100 things running through my brain.
