



White Paper 23-10

Parkinson's Disease - The Patient's Perspective

White Paper Summarizing Findings from the 23andMe Parkinson's Disease Research Community

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Introduction

At 23andMe, we strongly believe that the patient perspective is key to understanding how to approach and manage a disease as well as the development of new treatments. This is especially true for clinically heterogeneous and poorly understood diseases, such as Parkinson's disease ("PD").

Background

We recognize that PD is an important progressive neurological disorder with significant impact on affected individuals and their families, and we have worked with the PD community to sign-up over 11,000 individuals to be genotyped and join a PD research initiative. Inclusion criteria for participation include (i) being 18 years of age or older, (ii) diagnosed with PD by a medical professional and (iii) access to the Internet in order to complete online surveys. A recently published article (Dorsey, E.R. et al., 2015. Virtual research visits and direct-to-consumer genetic testing in Parkinson's disease. *Digital Health*, 1(0), pp.1–18 [Full text](#)) as well as the demographics of the 23andMe PD cohort ([Appendix A](#)) and the concordance of genetic findings with those using more traditionally defined cohorts, all support the accuracy of the self-reported diagnosis. In addition to genotyping, 23andMe research participants complete a number of online surveys covering a wide range of topics related to their PD and general medical conditions.

Conclusions

Mining of existing data as well as the distribution of a specific questionnaire enabled us to quickly generate input from a large number of individuals with PD addressing the questions posed by the FDA. This illustrates the value of such online disease communities as a source of the all-important patient perspective as well as providing insight into the natural history of the disease and opportunities for novel discoveries.

Symptoms

It is clear that even in a relatively recently diagnosed cohort such as the 23andMe Parkinson's community, symptoms can have a marked impact on both function and quality of life. Troublesome symptoms are not limited to the traditional movement related features of the disease but include non-traditional motor symptoms such as difficulties with handwriting and a wide array of non-motor symptoms. Indeed many of the symptoms scored as most

severe/impactful by these early stage individuals are non-motor such as sleep related disturbances, fatigue, pain and G.I. dysfunction etc. Since many of these are known to precede the classical diagnostic motor features this would argue that the classically defined prodromal phase may not be benign and could be considered early stage Parkinson's disease. Obviously this cannot be addressed directly in cohorts such as ours based on classical diagnosis, but is worthy of research especially in light of the need to discover and develop disease modifying therapies.

The significant variability in patients' perceptions of the severity of their disease and the impact of the somewhat hard to predict medication off periods present both challenges and opportunities. A high level of baseline variability is a challenge for clinical studies, especially those with quality of life related endpoints. This highlights the need for more objective measures and for "continuous" monitoring, both areas of significant research. Understanding the drivers of good versus bad days may provide opportunities to significantly improve management of the disease.

Treatments

Participants are conflicted regarding current medications, recognizing the significant benefit derived from current treatments, but variably aware of incomplete efficacy, an array of impactful side effects and progression of the underlying disease. As mentioned above off time is a major concern and suggests that there may be significant benefit to be gained from further optimization of current therapies, including genetics-based individualization of care. Related to this some of the responses to the questionnaire raise the question of how consistent management (both pharmaceutical and non-pharmaceutical) is across the population especially as it relates to non-motor symptoms. In fact it might be interesting to know in those individuals with low satisfaction regarding current treatment how this relates to poor efficacy of medications, suboptimal disease management or unrealistically high expectations.

There is a clear call for treatments that can slow or stop progression of the disease. New targets for disease modifying therapies will come from better understanding of the causes and pathophysiology of the disease and genetics will continue to play a key role in this. Support for ongoing and new research and development activities in this area should be a priority for the PD community, academic and commercial researchers and the FDA.

Results

Regular 23andMe PD Community Surveys

Over 9000 research participants have completed a comprehensive PD background survey, with smaller numbers completing additional surveys. Here we present an analysis of the responses as they relate to the questions posed by the FDA to the Parkinson's community.

The following are the key findings (see [Appendix A](#) for supporting data):

Symptoms

- Participants were asked to rate severity/impact of a range of symptoms as normal, slight, mild, moderate or severe (based on the self-reported sections of the MDS-UPDRS). These responses were used to generate a score reflecting the population level impact of the various symptoms in the 23andMe cohort (at the time of study entry)

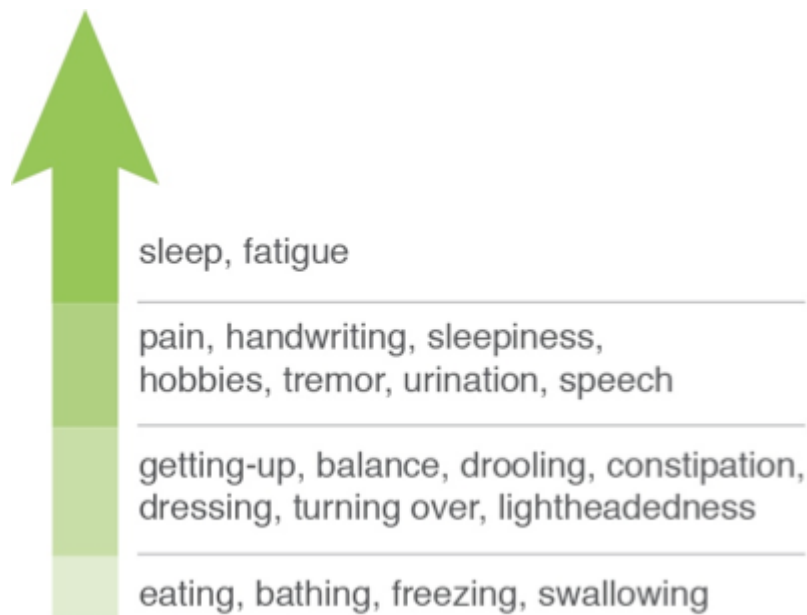


Figure 1 Patient Reported Impact of Symptoms

- Non-motor symptoms are very common and contribute significantly to disability from the perspective of individuals with PD
- The most impactful includes sleep disturbance, fatigue, pain,

Treatments

- See [Appendix A](#) for a summary of medication classes used by the cohort
- Participants were asked “On a typical day, how much of the time do you think your Parkinson's medications are working well?” Distribution of responses (2559 total) is as follows:

1/4 of the day or less	7.0%
More than 1/4 of the day, up to 1/2 of the day	15.4%
More than 1/2 of the day, up to 3/4 of the day	37.8%
More than 3/4 of the day, up to all day	37.6%

- It is significant that almost two thirds of respondents report having some “off” time since comparison of function (as determined by a modified Schwab and England scale) when medication are working and not working reveals that there is a distinct worsening of function in many individuals in the not working state

Function	Number of Respondents	
	Medication Working	Medication Not Working
Independent	1207	969
Moderately Dependent	121	293
Very Dependent	<20	100

- They were also asked “When your medications are working how well do they

	Control tremor?	Help with difficulty initiating movement?	Improve overall sense of wellbeing?
Not at all	1.0%	2.2%	1.1%
A little	5.2%	5.1%	4.6%
Somewhat	9.7%	11.4%	12.3%
A fair amount	24.7%	27.8%	30.7%
A great deal	59.4%	53.5%	52.4%
Number of Respondents	2022	2016	2414

- Only 50%-60% of respondents reported a strongly positive response to their current medication

Questionnaire Addressing Topics Related to FDA Questions

In addition to analyzing our existing data we informed the 23andMe PD community about the FDA meeting and encouraged them to participate. At the same time we also asked them to complete a brief online questionnaire addressing questions related to the topics of interest to the FDA. Greater than 1300 participants completed all or part of the questionnaire.

Full results can be found in [Appendix B](#), but key findings based on this cohort include:

Quality of Life Best or Worst Days

- Significant difference in perception of severity of impact of disease between best and worst days

Impact	Best Days	Worst Days
None	17%	3%
Slight	64%	41%
Significant	15%	42%
Severe	4%	14%

- This has some interesting implications:
 - A better understanding of the causes of good versus bad days, e.g. sleep, diet, exercise etc. may provide a significant opportunity to improve management of the disease
 - Any endpoints relying on a single time point report of self-assessed QoL are going to be prone to significant variability

Change in Ability to Cope and Symptom Variability

- 44% of individuals reported decreased ability to cope with their symptoms over time, whereas 37% reported no significant change. This likely reflects the relatively short average duration of disease in this cohort and the generally slow progression of the disease in most cases
- Medication Off Time: 70% reported that their symptoms “come and go”. This could have a number of causes, but one major one is likely wearing off of medication since this (along with the need for frequent dosing) was the most commonly cited downside of current treatments

Impaired Social Interaction

- Nearly two thirds of the respondents reported that the disease had impacted their social interactions. Not surprisingly this included a high percentage of those reporting significant or severe impact of the disease on their quality of life.

	Impact of Symptoms on QoL Best Days			
	None	Slight	Significant	Severe
% With Impact on Social Interaction (numbers/total)	32% (69/217)	70% (578/820)	93% (190/204)	96% (53/55)

- More surprising are the high number of individuals with only slight or no perceived impact on quality of life who report an adverse impact on social interaction. This suggests that this may be a significant impact early in the disease process, but that individuals with PD may underestimate the potential impact on their quality of life

Current Treatments

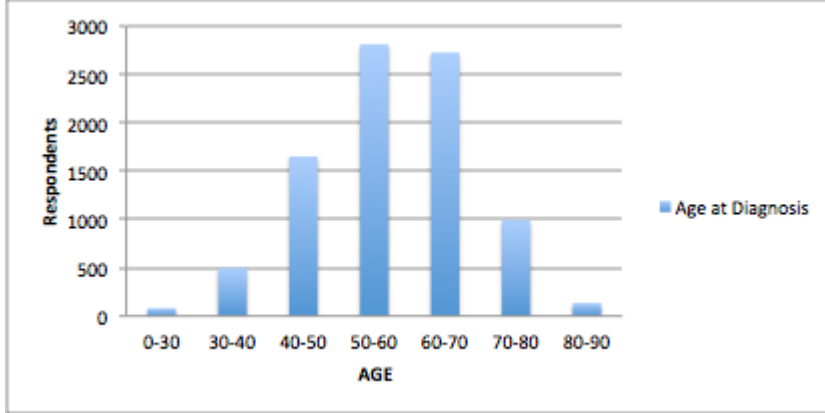
- Both in terms of symptoms and function, more than 80% of research participants reported that current treatment regimes work well or moderately well with only 12%-13% reporting poor or no efficacy
 - In contrast to the above, 38% reported poor efficacy as a significant downside of their current treatment
- The most common complaint (53%) regarding treatments is wearing off / need for frequent dosing. Side effects (34%) run the gamut with the most common being G.I. (nausea, constipation) and dyskinesia. However, a number of research participants also blamed their treatments for daytime sleepiness, cognitive and behavioral problems. Unfortunately, cost (28%) was also a frequent complaint

Future Treatments

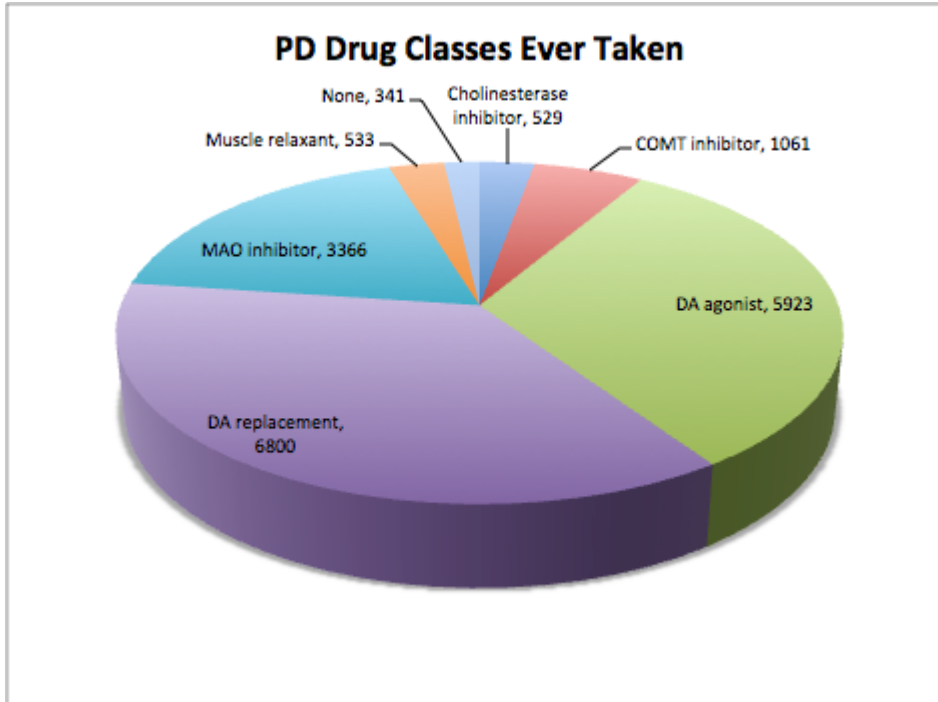
- Almost 80% of respondents want new treatments to slow or stop progression
 - At 10% the second most common request was better treatment of specific symptoms, with tremor and non-motor symptoms being the most commonly mentioned
 - It appears that some individuals affected with PD suffer from “treatment resistant” tremor. However, it is unclear whether this represents differences in underlying biology or disease management
 - It is interesting that a number of respondents request treatment for orthostatic hypotension, despite recent approval of medication for that specific indication

Appendix A: 23andMe Community Survey Responses

Age at Diagnosis



Classes of PD Medication Ever Taken



Severity/Impact of Symptoms

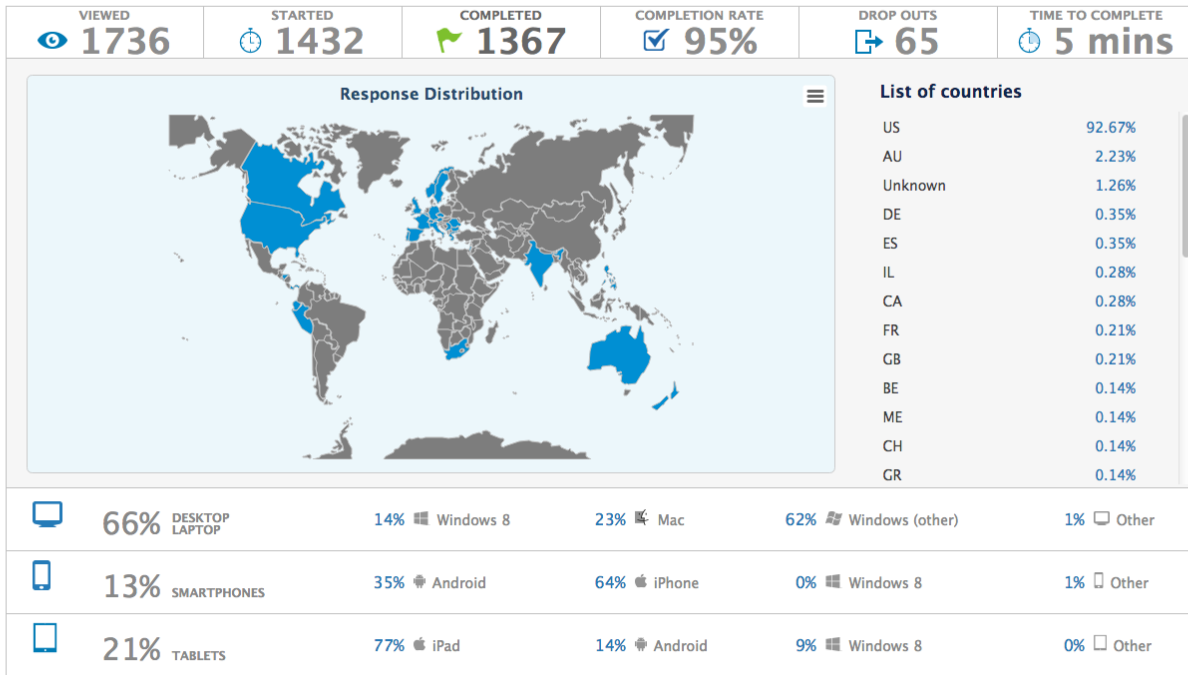
Symptom	Normal	Slight	Mild	Moderate	Severe
Tremor	1493	3966	2039	679	146
Fatigue	1610	3354	2052	1121	587
Daytime Sleepiness	1711	2693	3667	533	131
Sleep	1814	1791	2054	2410	666
Pain	2060	3195	1445	1483	552
Urination	2404	2640	1304	967	284
Hobbies	2534	2866	1888	865	565
Getting Up	2591	3687	1425	700	307
Handwriting	2680	2361	1837	1218	622
Balance	2743	3682	1004	949	332
Dressing	2908	3798	1511	285	216
Speech	3090	2231	2132	1112	158
Turning Over	3278	4110	763	297	262
Lightheaded	3348	2202	1168	441	87
Constipation	3470	3031	1196	942	96
Eating	3963	3061	1427	195	72
Saliva	4077	1514	1615	1194	323
Bathing	4292	3668	411	161	186
Swallowing	5814	2282	253	341	33
Freezing	5898	1431	629	470	282

Schwab And England Based Functional Rating Scale Comparing When Meds Are Working And When They Are Not

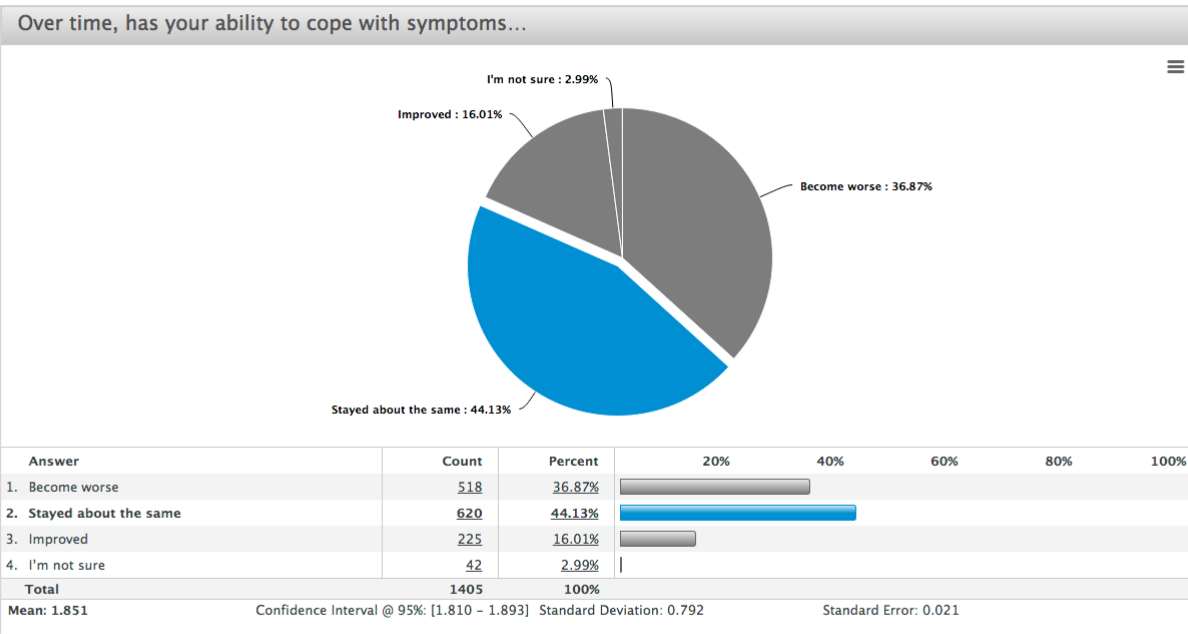
Description	Working	Not Working
Unaware of any difficulty. Completely independent	405	184
Beginning to be aware of difficulty. Completely independent	579	435
Conscious of difficulty and slowness. Completely independent	223	350
More difficulty with some chores. Not completely independent	53	131
Exceedingly slowly and with errors. Some dependency	48	96
Difficulty with everything. More dependent	20	66
Can assist with chores, but few alone. Very dependent	<20	37
A few chores alone. Much help needed	<20	37
Severe invalid. Nothing alone	<20	26
Complete invalid. Totally dependent, helpless.	<20	<20
Number of respondents	1328	1362

Appendix B: Questionnaire and Responses

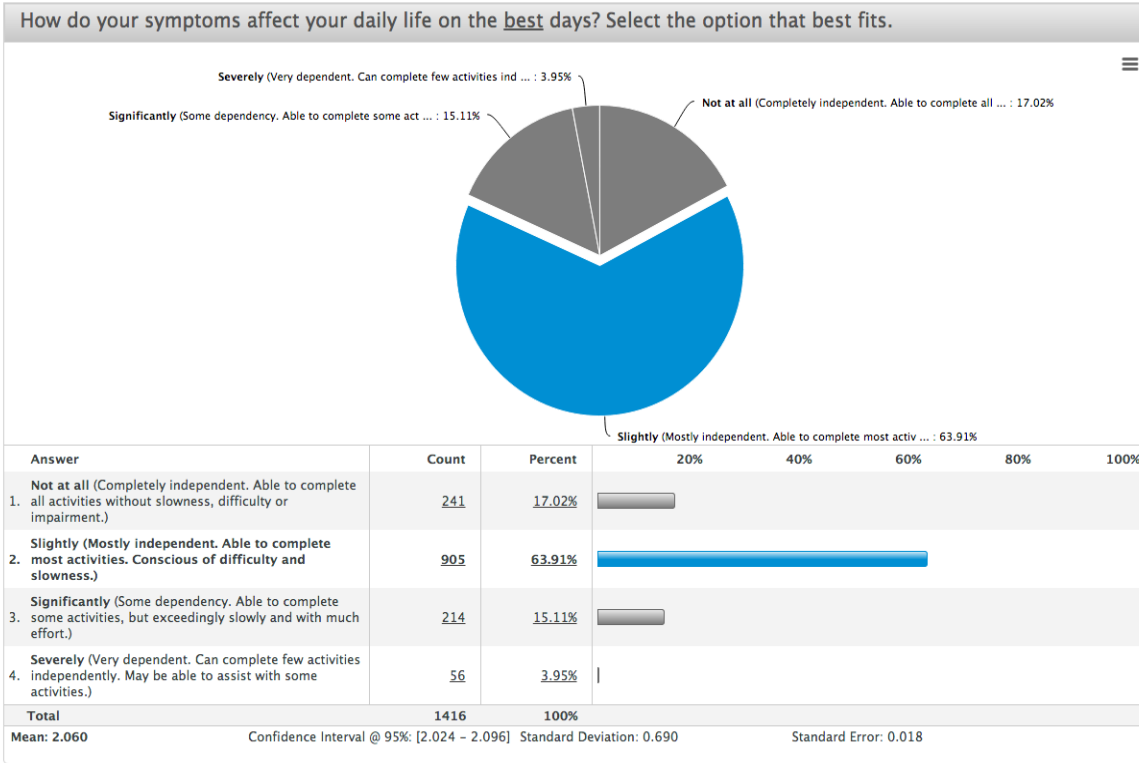
Completion Statistics



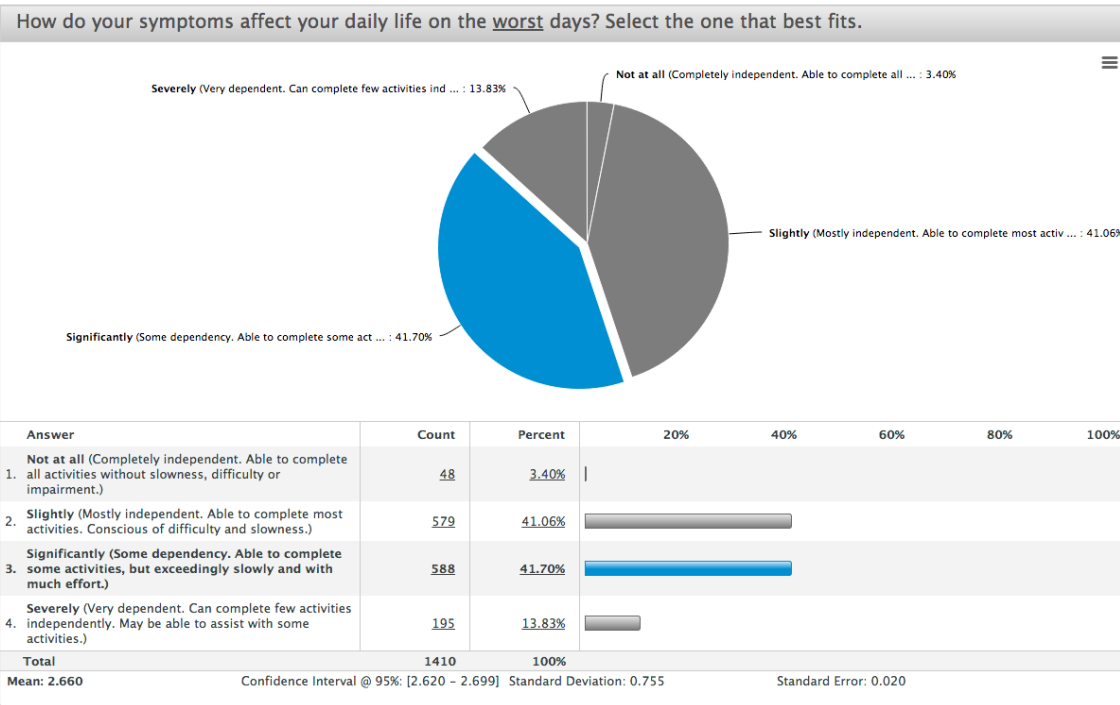
Ability to Cope Over Time



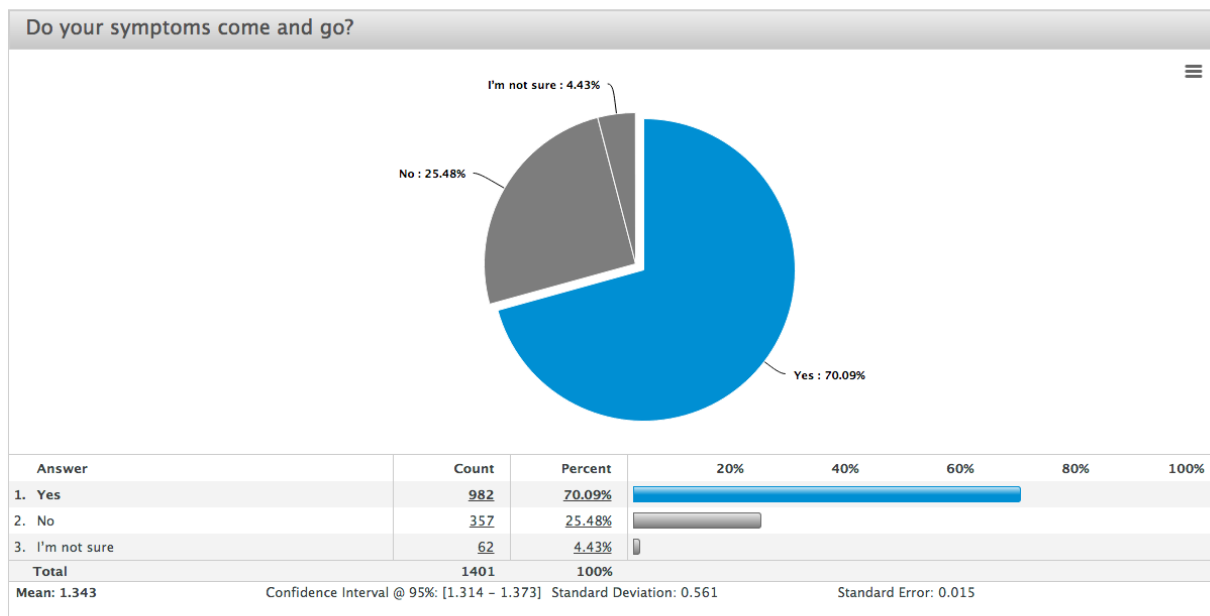
Impact on Best Days



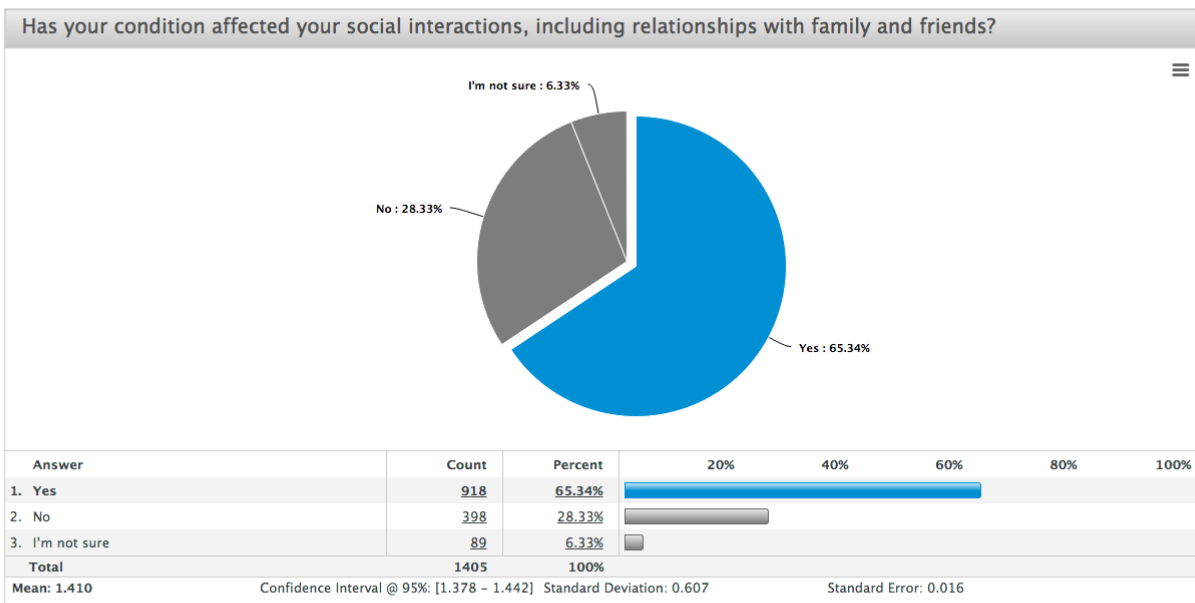
Impact on Worst Days



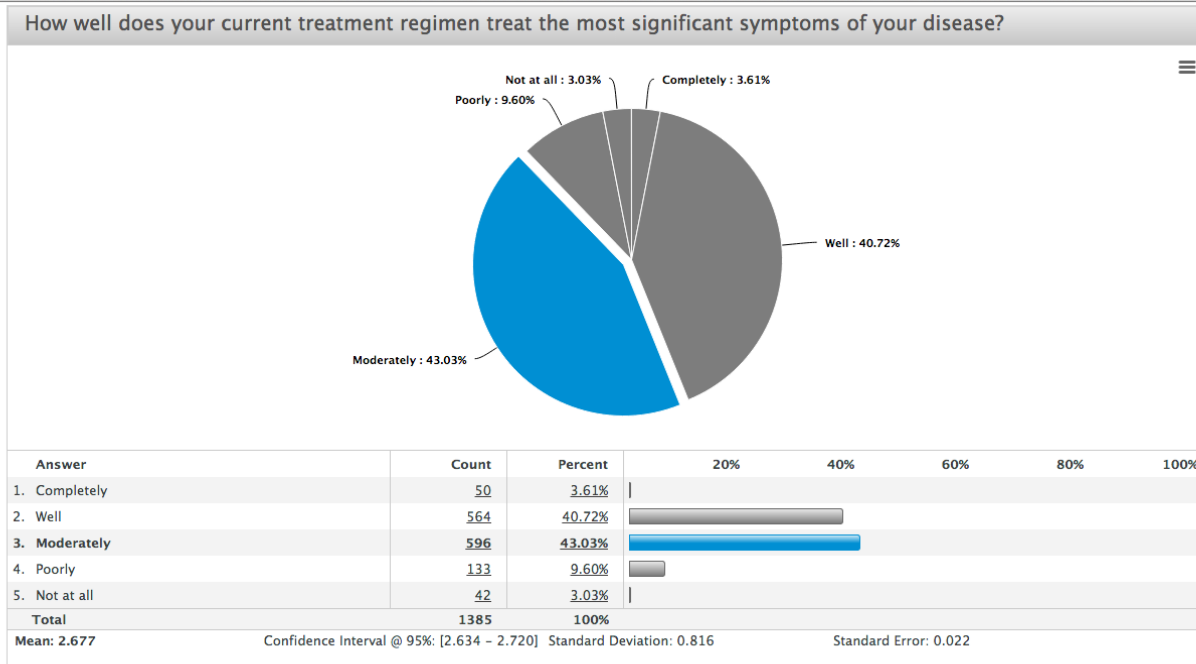
On and Off Times



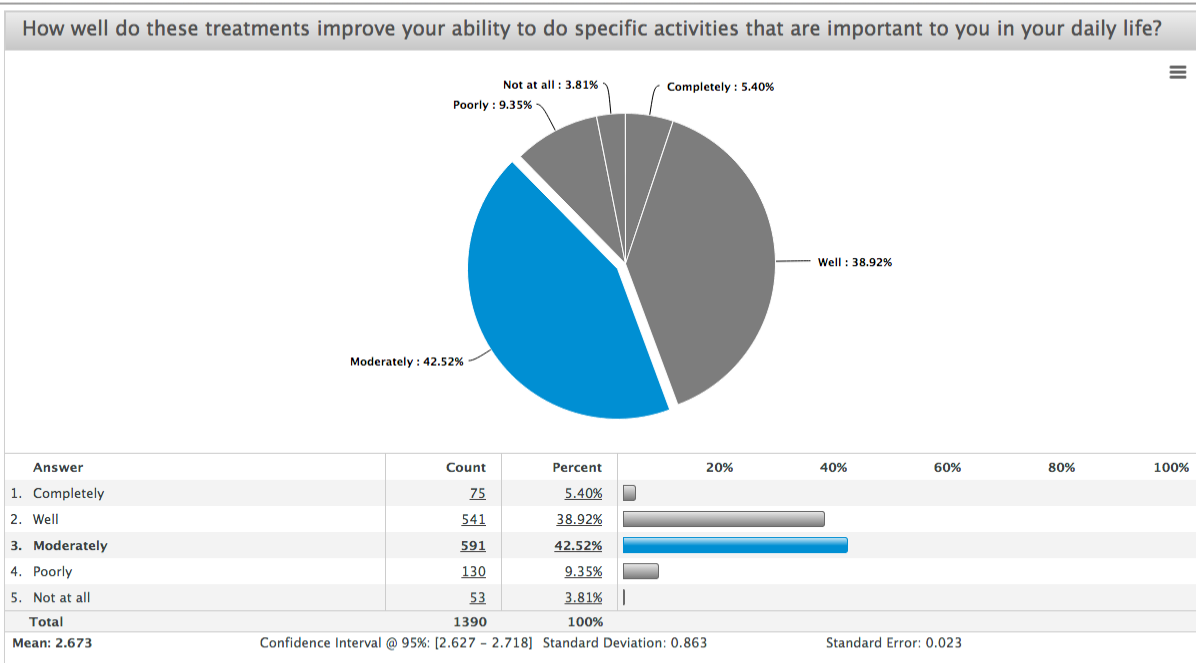
Impact on Social Interactions



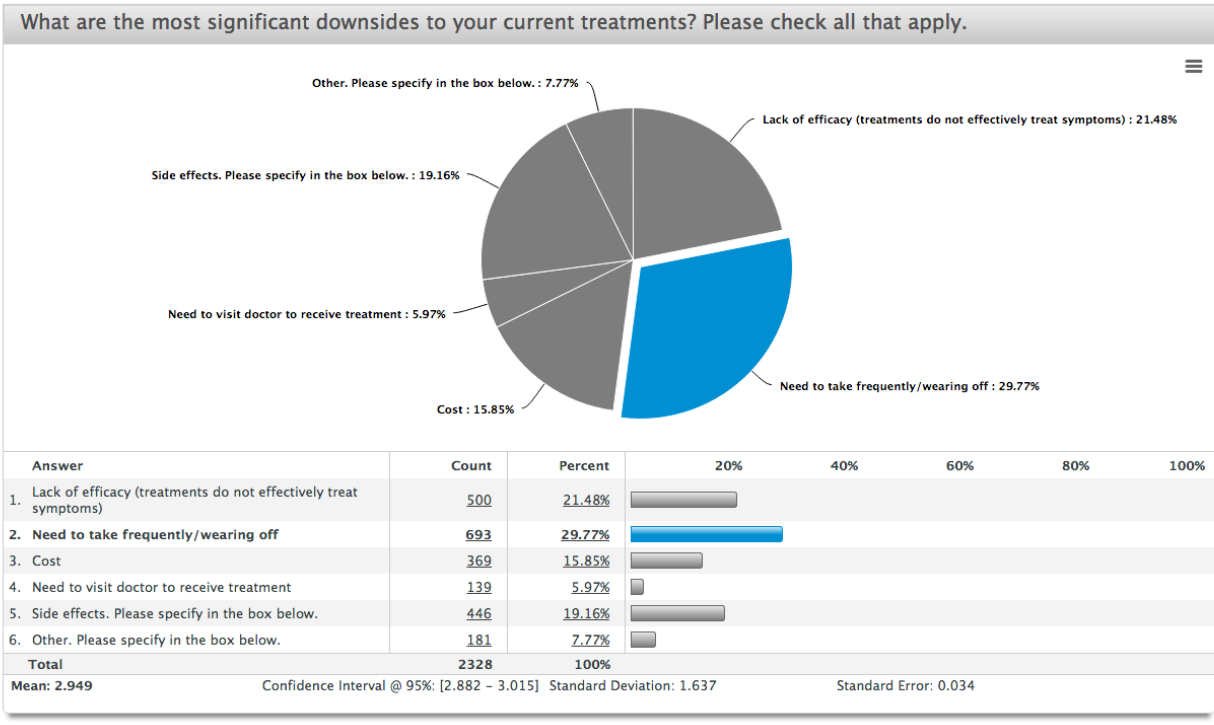
Treatment Effectiveness - Symptoms



Treatment Effectiveness - Function



Treatment Downsides



Ideal Treatment

