Informing People with Parkinson’s Disease of Their Gene Variant Status: PD GENEration, a North American Observational and Registry Study

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Abstract

Objective: To describe genetic testing results of major genes for Parkinson’s disease (PD) in a North American cohort as part of PD GENEration. Background: Although seven genes (LRRK2, GBA1, PRKN, PINK1, SNCA, PARK7 and VPS35) are established as causative for PD, people with PD (PwP) often remain unaware of their genetic status since clinical testing is rarely offered. Three phases of PD GENEration: 1) Pilot study- launched in Sept. 2019 and aimed at feasibility 2) Clinical study- launched in Nov. 2020- continuation of the Pilot study at a larger scale, aimed at frequency and characterization of clinical phenotypes 3) Registry study- launched in Jan. 2021 and aims to make genetic counseling and testing accessible to 15,000 participants based on the needs of the patient and research community.

Methods: PD GENEration is a multi-center, observational study, offering genetic testing and counseling to those with PD in the United States, including Puerto Rico; Canada; and the Dominican Republic. DNA samples are analyzed by next-generation sequencing and deletion/duplication analysis (CLIA-certified; Fulgent Genetics). Variants classified as pathogenic/likely pathogenic and clinically actionable are disclosed. Demographic and clinical features are collected at baseline visits. Results: From September 2019 to January 2023 the study enrolled 7,550 participants across 35 sites and approximately 60 referral centers, with 6,328 tested. Study population characteristics were: 59% male; 90% White, 2% Asian, 2% Black/African American, 9% Hispanic/Latino; mean age of 66.4 ± 10.3 years. Sixteen percent had early-onset PD (age < 50 years), 15% were of high-risk ancestry (Ashkenazi Jewish, Spanish Basque, or North African Berber), and 22% had a first-degree relative with diagnosed PD. Of individuals tested, 842 (13.3%) had a reportable variant; 7.9% with variants in SNCA with two mutations or more (n=0) PRKN with two mutations or more (n=57) LRRK2 with two mutations or more (n=2) and 6% (n=1 in VPS35, PINK1, or PARK7). Twenty-seven (0.4%) participants had reportable variants in more than one gene. Conclusion: Genetic testing of well-established PD genes in this cohort resulted in a genetic diagnostic yield of 13.3%, overall, and, notably, 9.2%, in those unsuspected of harboring variants. Together with the increasing utility of self-knowledge of PD gene status, the findings support a shift to offering universal genetic testing to PwP. **The PD GENEration data shown below is an update as of June 1, 2023**

Methodology

PD GENEration was a multi-center, observational study, offering genetic testing and counseling to those with PD in the United States, including Puerto Rico; Canada; and the Dominican Republic. DNA samples are analyzed by next-generation sequencing and deletion/duplication analysis (CLIA-certified; Fulgent Genetics). Variants classified as pathogenic/likely pathogenic and clinically actionable are disclosed. Three phases of PD GENEration:

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Results

All results below are as of June 1, 2023. The PD GENEration study has enrolled 10,510 participants.

Study Enrollment Per Country

United States (US): 10,112
Puerto Rico (PR): 33
Dominican Republic (DR): 305
Canada: 60

58%:42% genetic sex of Male:Female
69 years average age at enrollment
62 years average age at diagnosis
58% diagnosed in the last 5 years

74% New to Clinical Research

Have you participated in research before? # of responses: 8,785

Yes 26% 2,312
No 74% 6,473

Racial Diversity in Cohort

American Indian/Alaskan Native 1,019
Asian 225
Black/African American 2,214
Hispanic 1,009
Native Hawaiian/Pacific Islander 7,079

Genetics

PD GENEration makes genetic testing and counseling accessible for PwP and their clinicians. The Parkinson’s Foundation’s plans to continue to recruit beyond 15,000 participants based on the needs of the patient and research community. By “opening the door” for genetic testing to all those interested and from all backgrounds, the study helps inform care, diversify the data, engage people in research, and qualify more for enrollment in precision medicine clinical trials for PD. Data generated from this study will be openly accessible to the research community.

For more information on the PD GENEration study, please scan the QR Code.
OBJECTIVE
To assess the feasibility and impact of systematic depression screening and management in movement disorders centers.

BACKGROUND
• Depression is common in Parkinson’s disease (PD) and has a significant adverse impact on quality of life.
• A survey of clinicians at Parkinson’s Foundation Centers of Excellence (PF COEs) revealed that most centers do not systematically screen for depression, and that the use of mental health professionals and antidepressants varies substantially, suggesting that clinical practice changes could improve care.

METHODS

Fig. 1 Study Overview

Fig. 2 Study Flow

Retrospective medical record review

Prospective follow-up

- Monitor proportion screened for depression at the site
- Assess screening impact: Follow screen-positives+

*Qualitative interviews to assess acceptability, feasibility, barriers and utility among: Patients and Care Partners, Health Care Providers

*Screen-positive = GDS-15 score ≥ 5

RESULTS

Retrospective review of depression screening
310 patients seen by 29 HCPs in the year prior to the implementation of systematic screening were reviewed.
Prior to implementation of formal GDS-15 screening:
• ~76% (range 56-100%) of patients were screened.
• Only 12% screened (range 0-57%) with a formal depression instrument.
• Instruments used other than the GDS-15: the Patient Health Questionnaire-2, MDS-Unified Parkinson’s Disease Rating Scale, Non-motor Symptoms Questionnaire, the Beck Depression Inventory, and the Beck Depression Inventory Fast Screen.

CONCLUSION
• Implementation of systematic screening using the GDS-15 is feasible among Parkinson’s Foundation Centers of Excellence.
• Time required is a barrier to formal screening.
• 77% recommended the screening program be implemented at other PF Centers of Excellence.
• Sites adopted GDS-15 administration based on practice
practicalities during the COVID-19 pandemic, substantially increasing the number of patients screened using a formal instrument.
• While overall quality of life measures did not change over 12 months, significant changes in GDS-15 scores were observed, suggesting improvements in depressive symptoms.
Introduction

People with Parkinson’s (PWP) and care partners (CP) have significant palliative care (PC) needs, however little is known about their preferences and knowledge of PC. There is sufficient support for implementing PC as a new standard of care for PWP and CP. As part of a national project on implementing outpatient PC in Parkinson’s Foundation Centers of Excellence (COE) we operationalized PC as the assessment and management of:

1. Non-motor symptoms
2. Patient grief/emotional/spiritual needs
3. CP needs
4. Completion of annual advance care planning (ACP)
5. Timely referrals to specialist PC and hospice

Methods

Using a qualitative descriptive design, we completed semi-structured interviews with PWP and CP (n=47- 23 PWP; 24 CP) recruited from 15 COE. All interviews were audio-recorded, de-identified, and transcribed. Data were coded and 5 themes were identified.

Results

To understand patient and family perceptions and knowledge of PC.

Table 1. Demographics of Patients and Care Partners

<table>
<thead>
<tr>
<th>People Living w/ PD (n=23)</th>
<th>Care Partners (n=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td></td>
</tr>
<tr>
<td>69.5 (8.14) years</td>
<td>68.88 (9.93) years</td>
</tr>
<tr>
<td>Years of PD symptoms, mean (SD)</td>
<td></td>
</tr>
<tr>
<td>13.73 (9.03) years</td>
<td></td>
</tr>
<tr>
<td>Years of additional household responsibilities</td>
<td>8.04 (5.65) years</td>
</tr>
<tr>
<td>Gender (female)</td>
<td></td>
</tr>
<tr>
<td>26.09% (17)</td>
<td>70.83% (17)</td>
</tr>
<tr>
<td>Hispanic/Latino (No)</td>
<td></td>
</tr>
<tr>
<td>95.65% (22)</td>
<td>95.83% (23)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td></td>
</tr>
<tr>
<td>78.26% (18)</td>
<td>91.67% (22)</td>
</tr>
<tr>
<td>Non-white</td>
<td></td>
</tr>
<tr>
<td>26.09% (6)</td>
<td>8.33% (2)</td>
</tr>
<tr>
<td>Married</td>
<td></td>
</tr>
<tr>
<td>62.61% (18)</td>
<td>87.50% (21)</td>
</tr>
<tr>
<td>Other relationship status</td>
<td></td>
</tr>
<tr>
<td>17.39% (4)</td>
<td>12.5% (3)</td>
</tr>
</tbody>
</table>

Acknowledgements

We thank our Patient & Care Partner advisory council for their input on the interview questions.

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Results Cont.

PWP and CP wanted more education and support to address their PC needs. Table 2 illustrates themes related to the 5 PC components that were identified.

Table 2. Themes and Illustrative Quotes

Theme 1: It’s the non-motor stuff that is driving everyone crazy.

Martha Patient: I’m impressed that [the new Neurologist] even asked me about bowel and bladder problems and things like that. She even brought something to my stomach and if I’ve had…a lot of sweating, and she’s talked to me about my drooling and my speech. I like that she’s very involved in helping with that.

Jennifer Care Partner: Can we stop calling this movement disorder because it’s the non-motor stuff that drives everybody crazy. Let’s give it another name.

Theme 2: It’s the caring, connection part that is missing

Mary Patient: He [Neurologist] said, “I think you’re depressed”…I don’t think I’m depressed. I think I’m sad… I’m trying everything I can to feel better.

Dorothy Care Partner: They’re an excellent [clinic]…they know about Parkinson’s, and they have excellent advice. It’s just…the caring part,…the connection part…it just sort of feel like…you’re a number and you’re kinda going through, and…then they’re on the next one.

Theme 3: Care partners want more education, guidance, and coping skills

William Patient: But they’re [carepartners] also human beings. They will have moments of doubt. They will…be overwhelmed. It’s kind of unfair to them.

Stephanie Care Partner: They [doctors] said that I have to take my—care of myself. I said, “I know, but how?”

Theme 4: Advance care planning conversations need to happen over time

Dorothy Patient: I don’t think we’ve planned much…I’d like to have somebody sit down and say, “What do you think…to answer some questions…but I don’t have anybody to talk to about that.

Andrew Care Partner: It’s hard to have those conversations too…we have not been offered any support that would kind of push us…into the ways of making those decisions and giving us…the education we might need to make some of those decisions.

Theme 5: Is palliative care about “end-of-life” or about “enhancing quality of life”?

Jason Patient: It means my life is coming close to an end.

Heather Care Partner: It’s enhancing quality of life.

Jennifer Care Partner: I think of it [PC] as sort of a whole person, whole family view of the situation and… um, you know, not doing the, “I’m the neurologist. I’m the pulmonary guy.”

Conclusion

Patients and families perceive gaps in the delivery of the services and are open to PC approaches to meet these needs. Providing additional education on the differences between hospice and palliative care is recommended.
Background

- Parkinson’s disease (PD) is a complex neurodegenerative disorder impacting everyday function and quality of life.
- Rehabilitation plays a crucial role in improving symptoms, function, and quality of life and reducing disability (1-3).
- However, rehabilitative care is under-recognized and under-utilized in PD and often only utilized in later disease stages, despite research and guidelines demonstrating its positive effects.
- Currently, there is a lack of consensus regarding fundamental topics related to rehabilitative care in PD.

Methods

- The Parkinson Foundation convened a Task Force of 21 international experts in PD rehabilitation and those with lived experience.
- Disciplines represented included:
  - Occupational Therapy (OT)
  - Physical Therapy (PT)
  - Speech Language Pathology (SLP)
  - Psychology/neuropsychology
  - Nursing
  - Neurology
  - Neuropsychology
  - Physiatry
  - Rehabilitation Science

- People living with PD and care partners

- Countries represented:
  - USA
  - Canada
  - France
  - Italy
  - UK
  - Australia
  - Netherlands
  - Switzerland
  - China

The Task Force and steering committee met virtually during 2021-2022 to discuss topics such as rehabilitative services, existing therapy guidelines and relevant literature in PD, and identify gaps and needs.

Conclusions

- The consensus-based framework is intended as a foundation for further multidisciplinary, integrated, and evidence-based research and guidelines demonstrating its positive effects.
- It is essential that providers understand the person with PD’s and care partners, and further evidence-based and scientific study are encouraged.

Acknowledgements

Practice and outcome variation across Parkinson’s Foundation Centers of Excellence

Abstract #92

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BACKGROUND

Variation in outcomes between patients with Parkinson’s disease (PD) is marked. Some of this variation is likely determined by factors intrinsic to the individual, but treatment practices may also influence outcome.

DESIGN/METHODS

• Parkinson Foundation (PF) Parkinson Outcomes Project data were used, with annual data collection on treatment received and outcomes in context of usual care at PF Centers of Excellence. People with PD seen at the center were enrolled without exclusions.
• Outcome assessments: health related quality of life (Parkinson Disease Questionnaire; PDQ-39), Hoehn and Yahr stage, and fall frequency.
• Adjusting for age, sex, education and number of comorbidities we compared a single center’s PD treatment and patient outcomes to the mean value for all centers stratified by disease duration ≤5 and >5 years.

RESULTS

• 12,664 PD participants from 31 PF Centers of Excellence were studied, with a mean age 68 (SD 10) and 63% men.
• 6,100 participants had PD duration ≤5 years from diagnosis and 6,405 had a PD duration >5 years at first study visit.

Figure 1: Dose/Frequency of primary treatment practices of interest by center, adjusted for comorbidities, age, sex, level of education

1a: Disease duration from diagnosis ≤5
Levodopa Use (%): 76% (n=4803) of participants were taking levodopa with 4 centers at a significantly higher (range 82-95%) and 7 centers at a lower proportion (59-74%).
Mean Levodopa daily dose: 250-600 mg
Dopamine agonist use: varied between 0 and 80% of patients.

1b: Disease duration from diagnosis >5 years
Mean Levodopa daily dose: ranged from 300mg/day to 900mg/day.
40% (n=2603) were sent to physical therapy with 8 centers higher (range 48-66%) and 10 centers lower (23-34%) than the mean.
20% (n=1251) had received DBS with 12 centers higher (range 22-41%) and 8 centers lower (2-10%) than the center average.

Figure 2: Distribution of outcomes of interest by center, adjusted for comorbidities, age, sex, level of education

2a: Disease duration from diagnosis ≤5 years
Mean PDQ-39 scores were 20 (sd 14) with 8 centers higher (range 21-27) and 6 centers lower (14-18).
22% (n=1331) participants had falls with 8 centers higher (range 28-38%) and 6 centers lower (6-16%) than the center average.

2b: Disease duration from diagnosis >5 years
Mean PDQ-39 scores were 29 (sd 16) with 7 centers higher (range 30-36) and 7 centers lower (23-27).
46% (n=2788) participants had falls with 7 centers higher (range 47-59%) and 8 centers lower (25-38%) than the center average.

CONCLUSIONS

There is substantial variation in both PD treatment practices and patient outcomes across centers of excellence. Our future analyses will examine the relationships between treatment patterns and outcomes to help guide high quality clinical care.

ACKNOWLEDGEMENTS

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Parkinson’s Team Training Is Beneficial For New and Established PD Centers

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Abstract #1934

OBJECTIVE
To determine if the Parkinson’s Foundation (PF) Team Training (TT) empowers Parkinson’s disease (PD) interprofessional healthcare teams to make changes in their care plans and treatment coordination that lead to better coordinated care for patients.

BACKGROUND
Since 2003, PF has offered the TT program to healthcare professionals in the community, both individual healthcare professionals and those who were working in, or establishing, PD programs using interprofessional care teams. It had not been formally studied as to whether PF TT could also be beneficial to an established PD care team.

METHODS
In October 2022, two large PD PF Centers of Excellence, including 39 team members participated in the TT in-person program, along with 53 attendees from various community PD care teams ranging from 3 to 8 team members. All team members were encouraged to attend, including physicians, nurse practitioners, physician assistants, nurses, psychologists, psychiatrists, neuropsychologists, dieticians, pharmacists, occupational, physical, speech, and music therapists, social workers, and other team members working with persons with PD. Participants completed surveys before, immediately after, and 6 months after the training to assess learning and benefit of the program.

RESULTS
A total of 73 participants completed the pre, immediate and 6-month surveys; 32 from established PD centers and 41 from community care teams. As noted in the graphs below, TT improved the confidence of team members of both community and established PD centers in caring for persons with PD and working with their care partners.

Prior to TT, 27% of the community team members strongly agreed that they had a clear understanding of the role of each team member which increased to 71% after TT. In the established teams, this increased from 44% before TT and 78% after. Finally, 100% of community teams agreed that TT had a positive impact to their care of persons with PD, compared to 97% of the established team members.

CONCLUSION
Team Training offered by the Parkinson’s Foundation was shown to have a positive impact on interprofessional team members of both established and community PD Centers. Attendees were more confident in the care they provide to both those with PD and care partners, more confident to improve quality of life of those with PD, increased their knowledge of the roles of other team members, and better understood their own roles within the PD care teams.