PD GENEration Sub-Studies: The Next Step to Engaging People with Parkinson's Disease in Research

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PD GENEration — POWERED BY THE PARKINSON'S FOUNDATION

asap Aligning Science Across Parkinson's

gp2 Global Parkinson's Genetics Program

Background

The PD GENEration study (NCT04994015), sponsored by the Parkinson's Foundation in partnership with the Global Parkinson's Genetics Program (GP2), offers whole genome sequencing (WGS) with genetic counseling and return of results to broad populations of people living with Parkinson's disease (PD), reaching over 30,000 participants. Historically, data collection occurred only in people with PD (PwP) and was limited to a baseline survey collected at time of consent. Responding to the urgency to better understand genetic forms of PD, new sub-studies were added to PD GENEration to enhance participant engagement and facilitate the collection of additional data.

Methods

PD GENEration Participants

PDGENE Surveys

Survey
Topics may include environmental exposures, diagnosis and medication changes, and more

PDGENE Family

Family Member Testing
Eligible PDGENE participants can invite their first-degree biological family members to enroll

PDGENE Insights

Clinical Data Collection
Participation includes self-report questionnaires and a clinical visit with a study physician

PDGENE Explore

Sample Collection
Plasma collection and UPSIT-R administration to PDGENE participants

PDGENE Family is enrolling

First-degree biological relatives of PDGENE participants who tested positive for at least one of the following gene variants:

Primary Panel	Secondary Panel
LRRK2	*ATP1A3*
SNCA	*RAB32*
VPS35	*CHCHD2*
PRKN	*GCH1*
PINK1	*GRN*
PARK7	*MAPT*

PDGENE Family Workflow

1) Proband Enrollment

PD GENEration proband is invited through direct email invite. Proband consents and provides family member contact information in study portal

2) Family Member Enrollment

1. **Family Member Consent** — Family member consents and completes baseline survey. Information is confirmed by a study coordinator via a confirmation call
2. **Pre-Test Counseling** — Family member meets with a genetic counselor for a pre-test genetic counseling session
3. **Sample Collection** — Whole blood sample collected via Tasso+ kit at the family member's home

2) Genetic Testing

1. DNA Extraction
2. Whole Genome Sequencing
3. Primary panel variant curation
4. Report generation and upload to OpenClinica

Additional Analysis

GP2 Neurobooster array

3) Genetic Counseling

Primary panel results returned to family member virtually through Indiana University's centralized genetic counseling core

Data Sharing

VCF BAM FASTQ

Raw genomic data to GP2 and AMP-PD

4) Secondary Health Findings

1. Family members decide if they would like to opt in to receiving results from either of the SHF panels. **If they decline, their participation in PDGENE Family is complete**
2. If family members opt into receiving any SHF results, additional genetic reports are generated according to the desired panels
- 3a **Positive results** are returned to family members through Indiana University's centralized genetic counseling core
- 3b **Negative results** are returned to family members via email

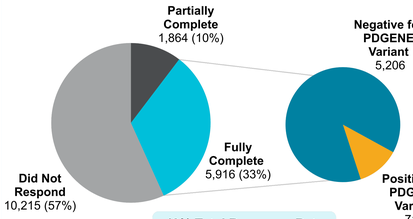
5) Study Complete

Results

Surveys

Survey 1: Environmental Impact and Lifestyle

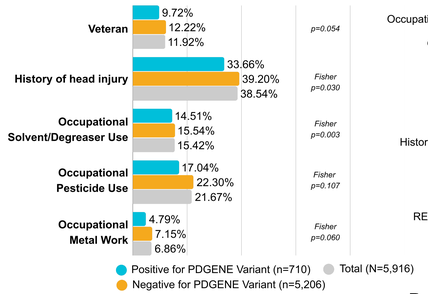
The first PDGENE survey was administered via REDCap to 17,995 PD GENEration participants between July-September 2025 to evaluate exposures related to occupation, lifestyle, and environment. The survey also screened participants for REM sleep behavior disorder (RBD) and offered an expanded survey for veterans to capture additional military-related exposures.



43% Total Response Rate

Exposures by PDGENE Variant Positivity

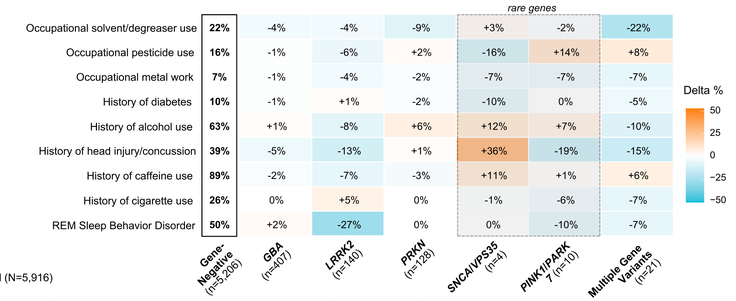
Participants without a PDGENE variant were more likely to report environmental or occupational exposures including history of head injury and working with solvents and degreasers, pesticides, or metal. These results seem to suggest that environmental factors may play a more influential role in a person developing Parkinson's disease when there isn't an underlying genetic variant driving risk.



Compared to the general survey population, veterans (n=684) reported higher frequencies of occupational exposures to pesticides (**28%** vs. **15%**), solvents/degreasers (**34%** vs. **22%**), and metal work (**15%** vs. **7%**)

Relative Environmental and Clinical Profiles by PDGENE Variant

Difference in prevalence (%) of clinical and environmental exposures between specific genetic cohorts and the gene-negative cohort. Blue tiles indicate where a genetic group has fewer reported exposures, suggesting that their disease onset may have been more influenced by genetic predisposition than by environmental factors. Orange tiles indicate a higher prevalence of exposures compared to the gene-negative group.



Family

Proband Enrollment by Gene Variant

When the PDGENE pilot opened to enrollment, only PD GENEration participants who tested positive for a LRRK2 variant were invited to participate. In February, the study eligibility criteria expanded to include those participants with pathological variants in the genes listed below.

	LRRK2	*PRKN*	*VPS35*	*SNCA*	*PINK1*	*PARK7*	*ATP1A3*	*RAB32*	*CHCHD2*	*GCH1*	*GRN*	*MAPT*	Multiple
Invited	90	150	1	5	8	5	1	0	0	6	1	3	29
Consented	20	16	0	2	0	1	0	0	0	0	0	3	4

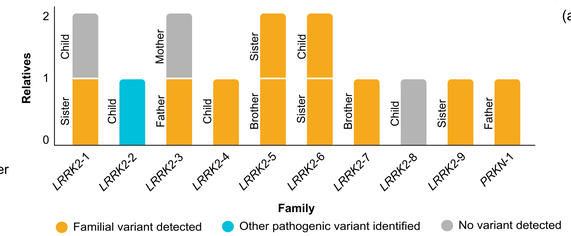
299 Probands Invited → **46** Probands Consented

103 Family Members Invited → **47** Family Members Consented

Overall PDGENE Family Enrollment

The PDGENE Family pilot enrolled the first proband on October 26, 2025, and the first family member on November 6, 2025.

To date, genetic results have been returned to **14 family members** participating in PDGENE Family. Of those who have completed testing, **10 family members tested positive** for a familial variant, representing **71%** of those tested.



PDGENE Family Member Genetic Status

Each column (above) represents a unique family group identified by the proband (*LRRK2*-X). The y-axis shows the number of invited relatives with completed testing, categorized by their relationship to the proband and variant status.

Panels (below) show the pedigrees for families *LRRK2-3* (left) and *LRRK2-1* (right).

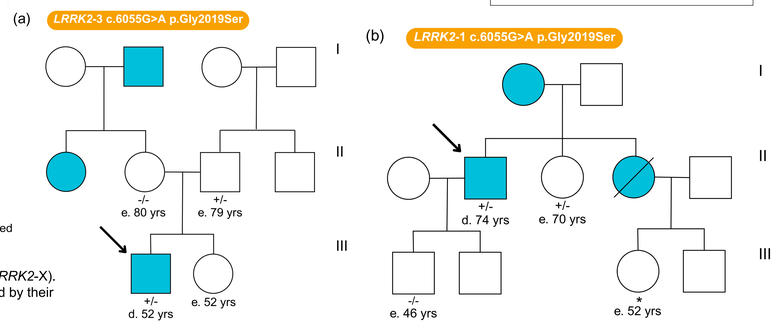
These diagrams illustrate the segregation of *LRRK2* variants alongside participant-reported family history of Parkinson's disease (PD) across multiple generations.

KEY

- Male
- Female
- Parkinson's disease (PD)
- Proband
- d. Age at PD diagnosis
- e. Age at enrollment

Variant Status

- +/- *LRRK2* heterozygous
- +/+ *LRRK2* homozygous
- -/- *LRRK2* variant negative
- * Genetic results pending



Insights

PDGENE Insights is enrolling

PDGENE or PDGENE Family participants Who tested positive for at least one of the following gene variants:

Primary Panel	Secondary Panel
LRRK2	*ATP1A3*
SNCA	*RAB32*
VPS35	*CHCHD2*
PRKN	*GCH1*
PINK1	*GRN*
PARK7	*MAPT*

- **OR** has been found to have a **potential PD candidate genetic variant** upon research analysis of PD GENEration data
- **OR** has early onset PD
- **OR** has idiopathic PD or no PD diagnosis and can act as a control

Mandatory Baseline Visits

1. **Consent Visit** — Participant consents and completes baseline clinical data collection and independent questionnaires
2. **Confirmation Visit** — Site staff connects with participant to review baseline data and questionnaires
3. **Clinical Visit** — Participant meets with clinician to complete the clinician-guided assessments and scales

Supplementary Visits

Genetic Counseling Sessions

- **Refresh Genetic Counseling** site-based or via telemedicine to review prior PD GENEration results
- **New Clinical Report** site-based or via telemedicine to review new genetic findings

Optional Assessments **Opt-In Consent Required**

- **Medical Record Collection** — Collection of prior medical records, including labs, clinician notes, and imaging reports
- **Return of Research Results** — Return of select research results to participants, including: MDS-UPDRS, MoCA, UPSIT

Longitudinal Data Collection **Optional Consent Required**

If participants consent, the following assessments are repeated at

Year 1 → Year 2 → Year 3

1. Consent Visit
2. Confirmation Visit
3. Clinical Visit

Study Complete

Explore

PDGENE Explore is enrolling

PD GENEration, PDGENE Family, or PDGENE Insights participants Aged 18 or older, with or without a diagnosis of PD

1) Consent

Participant reviews and signs informed consent form, consenting to one or both sample collections

2) Sample Collection

1. **Plasma Collection** — Blood sample collected and processed for plasma analysis and storage
2. **Smell Identification Test (UPSIT-R)** — Participants complete the revised UPSIT smell test and receive their results

3) Study Complete

Conclusion

PD GENEration acts as an accessible gateway for diverse communities of people with PD to be engaged with research. The incorporation of sub-studies into PD GENEration offers, for the first time, additional research opportunities to participants, further expanding participant engagement in research and ensuring the research community has even more data to further their work to find a cure for PD.

More about PD GENEration

PD Trial Navigator : personalized guidance on clinical trial enrollment for people living with Parkinson's disease

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Objectives

Precision medicine trials for Parkinson's disease (PD) face challenges in recruiting participants despite their great potential. The Parkinson's Foundation created the *PD Trial Navigator*, building on the success of the *PD GENEration* study to address the following primary objectives:

- ❑ **Accelerate enrollment in genetic and disease-modifying clinical trials for Parkinson's disease (PD)**
- ❑ **Build a clinical-trial–ready cohort through targeted education on clinical research and precision-medicine trials**
- ❑ **Empower individuals with PD to make informed decisions about participating in research**

Background

Clinical trials for Parkinson's disease (PD) face significant challenges with enrollment beyond simply recruiting those who meet the proper inclusion criteria. Limited awareness and understanding of trial opportunities and processes by participants, in addition to concerns about risks and benefits are considerable barriers (1,2). To address these, the Parkinson's Foundation created *PD Trial Navigator* to provide curated guidance for people living with PD about trial eligibility and to accelerate enrollment in genetic and disease- modifying focused trials.

Building from, *PD GENEration,* our international genetic study which has enrolled over 30,000 participants since 2019, those identified as having a PD-associated genetic variant (n=3,247 as of 2/1/2026) or meet trial eligibility criteria may will be invited to PD Trial Navigator. Interested participants can then complete a brief survey and receive personalized information about PD, clinical research, and available gene-targeted trials all through a direct connection with our clinical trial team.

Methods

A mixed-method approach was utilized to inform development of the *PD Trial Navigator* program and included: 1) focus groups to assess understanding and awareness of personalized medicine, disease modifying therapies, genetics and PD and clinical trials, and 2) retrospective review of survey data collected in 2024 among *PD GENEration* participants and in 2025 among the general PD community. Trial Navigators will use one-on-one virtual conversations, email, and/or phone as part of a multi-method approach. General education materials will include fact sheets, webinars, and podcasts.

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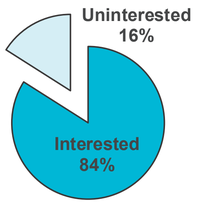
Results

2024 *PD GENEration* Survey

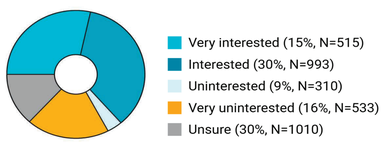


Recontact about future clinical trials (N=3,361)

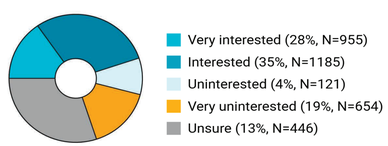
Nearly 85% of respondents reported that they were interested in being recontacted about future trials.

Almost 64% of respondents had some level interest in telehealth smartphone-based studies. The interest in trials was dramatically lower when a placebo control was included at 45%

Interest in Telehealth

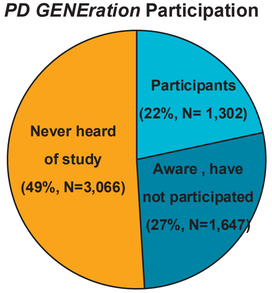


Interest in Placebo Controlled



2025 State of the Community Survey

***PD GENEration* Participation**



Participant Takeaways

Had not participated in a clinical trial or research study

Top concerns: Symptoms and Planning for the Future

Topics of interest: Treatment options, symptoms, research updates

Most used resources: Website, online programs and email updates

Among 6,060 PD constituents who took the 2025 State of the Community survey (English version), a total of 2,949 (1,302 + 1,647) are aware of PD GENEration with 44.2% (n=1,302) of those participating in PD GENEration..

Focus Group: Key Insights N=9

Precision Medicine

"I think that you need to make a difference between individualized medicines vs precision medicines when you are talking about having a big genetic component…because even if two people have the same gene, they are still going to respond different based on their beliefs, their social economic background, all of those things are just as crucial"

- **Varied understanding of precision medicine**
- **Frustrations over strict exclusion criteria, time and travel with clinical trials**
- **Communication about research with neurologist is fragmented**
- **PD Trial Navigator should offer flexible and personalized communication**

Barriers to Trial Participation

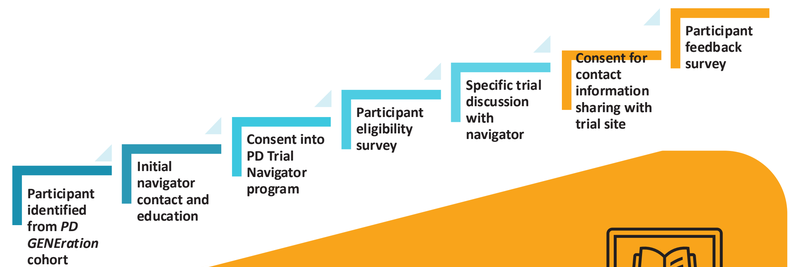
"Clinical Trials.gov is hard to navigate, You have to have baseline knowledge … including the stage you are in, terminology, your symptoms, and if you are newly diagnosed you may not have all of that information… most trials are 5-6 hours away which is hard to do, and if you are older, someone has to accompany them and a lot of the trials won't allow you to stay the night."

Educational Opportunities

Focus group and survey findings identified educational focus areas that will be addressed using diverse formats (handouts, fact sheets, webinars, podcasts):

- ❑ **Overview of disease-modifying therapies**
- ❑ **Introduction to precision medicine**
- ❑ **Understanding the research process**
- ❑ **Supporting shared decision-making during informed consent, including discussions with care teams and loved ones.**

The Steps of PD Trial Navigator



Want to find out more?

1. Visit our *PDGENEration* landing page at: https://www.parkinson.org/advancing-research/our-research/pdgeneration
2. Check out the post- study support for more about our *PD Trial Navigator program*.
3. See our press release here: https://www.parkinson.org/about-us/news/pd-trial-navigator-launch
4. Email our general inbox at: PDNavigator@parkinson.org or our Industry lead: mcaulfield@parkinson.org

Conclusions

Community feedback from focus groups and surveys played a critical role in shaping the *PD Trial Navigator* , ensuring that education, guidance, and outreach efforts directly reflect the needs and preferences of people with Parkinson's and their care partners. By grounding this work in lived experience, the initiative is better positioned to reduce barriers to participation and support informed decision-making. While *PD GENEration* continues to return genetic results to participants, the *PD Trial Navigator* will bridge the next step, providing personalized education and support to help individuals understand and act on their clinical trial options. Together, these complementary initiatives aim to strengthen the pipeline for precision-medicine trials, accelerate clinical research progress, and ultimately advance the shared goal of finding a cure for Parkinson's disease. [*References: 1) Fogel D. B. (2018). Contemp Clin Trials Commun. PMID: 30112460 2) Vaswani, P. A., Tropea, T. F., & Dahodwala, N. (2020). NeuroTherapeutics. PMID: 33150545]*

Assessing Provider Performance in Simulated Genetic Counseling Sessions Within the PD GENEration-LARGE-PD study

Martinna Raineri Tapies[1], Valentina Caceres[1], Katie Fiallos[1], Rebeca De León[2], Anny Coral[2], Miguel Inca[3], Ignacio F. Mata[3], Priscila D. Hodges[1]

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INTRODUCTION

The PD GENEration (PDGENE) study provides CLIA-certified genetic testing and counseling to individuals living with Parkinson's disease (PD). To enhance diversity in PD genetic research, the study expanded to Latin America through a collaboration with the Latin American Research Consortium on the GEnetics of Parkinson's Disease (LARGE-PD). As part of the expansion, a study-specific training was developed to support providers in the genetic counseling (GC) process.

METHODS

- Training via pre-recorded or live mock genetic counseling sessions.
- **Scenarios:** negative or positive results (*PRKN* + *GBA1* variants).
- Pre-provided checklist of core competencies and key topics.
- Standardized evaluation applied to all participants.
- Individualized written feedback after each session.
- **Remediation:** repeat video or live session if needed.
- Thematic analysis identified recurring strengths and weaknesses.

RESULTS

A total of 46 video feedback forms, from two training cycles, were analyzed (Fig.1). Areas of strength were found at least once in all feedback forms. Participants demonstrated strengths in the following relevant areas: pace of the session and allowing space for questions, speaking in simple terms, and contextualizing the conversation within PD (Fig. 2). In contrast, areas of weakness were also found at least once across all GC core competencies. With weaknesses seen in core GC concepts like familial risks/penetrance, session organization, and genotype/phenotype correlations (Fig. 3).

Fig. 1 Evaluations workflow and outcome

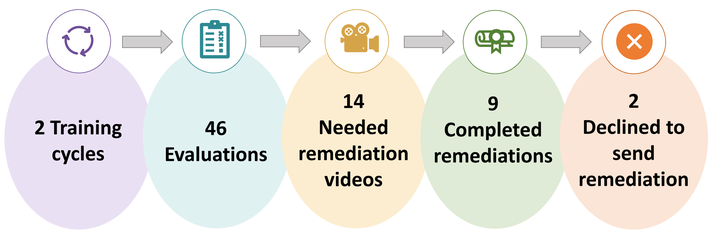


Fig. 2. Summary of common strengths

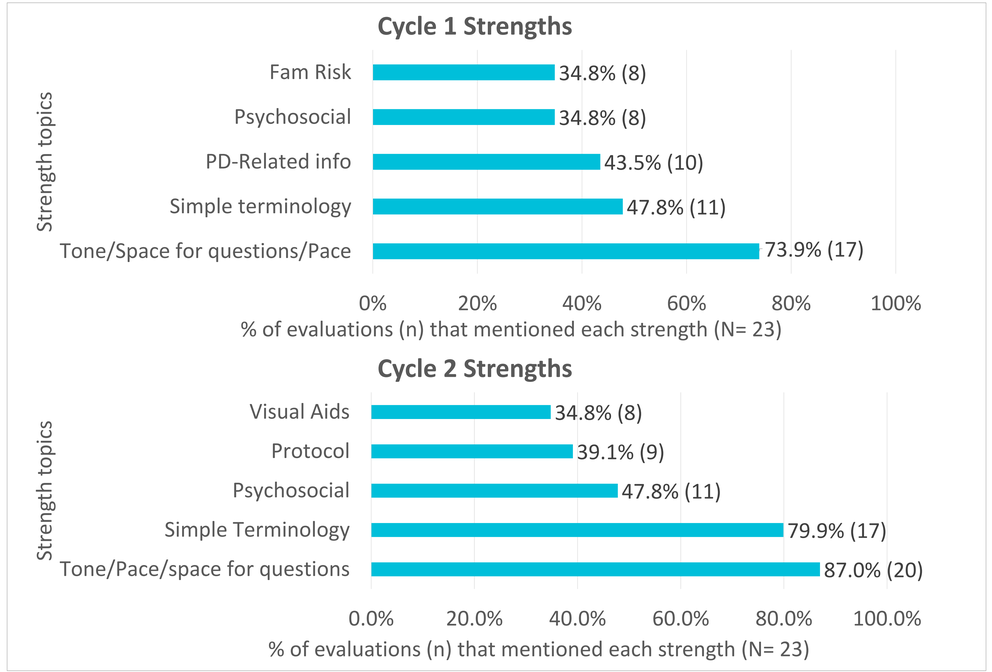
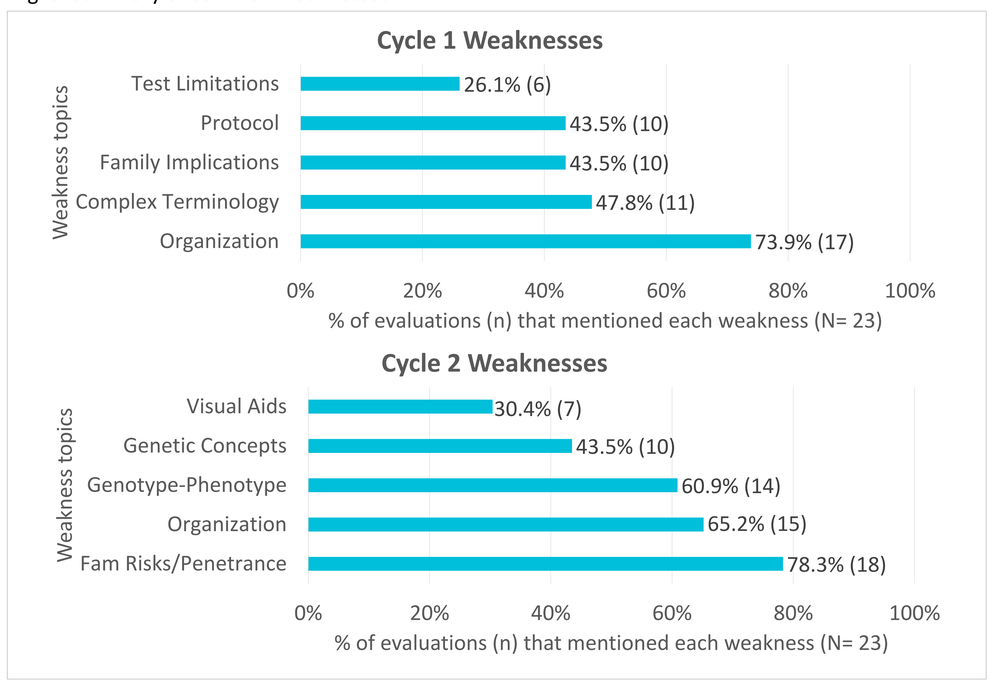


Fig. 3. Summary of common weaknesses



CONCLUSION

These findings highlight the important need of targeted genetic counseling training with feedback for clinicians that return genetic testing results. All clinicians that completed the video remediation, succeeded after detailed feedback of their first video. Suggesting that structured, iterative training programs can be an effective way of standardizing and strengthening genetic counseling skills. Continued capacity-building efforts are essential to ensure equitable and high-quality return of genetic results in large-scale international studies.

ACKNOWLEDGEMENTS

This project was supported by the Parkinson's Foundation and the Global Parkinson's Genetics Program (GP2). GP2 is funded by the Aligning Science Across Parkinson's (ASAP) initiative and implemented by The Michael J. Fox Foundation for Parkinson's Research (**https://gp2.org**). For a complete list of GP2 members see **https://gp2.org**.

The authors would also like to extend their heartfelt gratitude to all members of the Latin American Research Consortium on the GEnetics of Parkinson's Disease (LARGE-PD) for their invaluable time, dedication, and unwavering commitment to every aspect of the study.

RESOURCES

To learn more about PD GENEration

To learn more about LARGE-PD

LARGE-PD Latin American Research consortium on the GEnetics of Parkinson's Disease

INDIANA UNIVERSITY SCHOOL OF MEDICINE

Cleveland Clinic

Building genetic counseling capacity in Latin America to facilitate the sharing of genetic results with patients in the PD GENEration - LARGE-PD study

Priscila D. Hodges [1], Martinna Raineri Tapies [1], Katie Fiallos [1], Rebeca De León[2], Anny Coral[2], Miguel Inca[3], Ignacio F. Mata[3], Valentina Caceres[1], and The Parkinson's Foundation PD GENEration Study

[1] Indiana University School of Medicine, Indiana, USA, [2] Parkinson's Foundation, Miami, USA, [3]Genomic Medicine Institute, Cleveland Clinic, Ohio, USA

OBJECTIVE

To describe the creation, implementation, and outcomes of a structured genetic counseling training initiative designed for clinicians within the Latin American Research Consortium on the GEnetics of Parkinson's Disease (LARGE-PD), aimed at preparing them to deliver genetic test results as part of the PD GENEration (PDGENE) study.

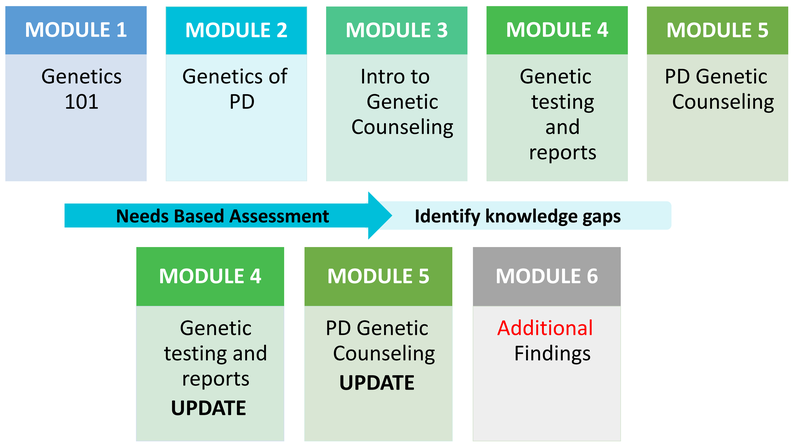
BACKGROUND

In 2019, PDGENE started providing CLIA-certified genetic testing and counseling at no cost to individuals diagnosed with Parkinson's disease (PD). In 2024, a strategic partnership with LARGE-PD was established to increase Hispanic/Latine participation in PD genetic research. Since the return of results in PDGENE is conducted through formal genetic counseling sessions, a study-specific training framework was designed to equip LARGE-PD clinicians with the competencies necessary to perform this role effectively.

METHODS

Five self-paced training modules were initially developed in Spanish, covering foundational genetics, Parkinson's disease genetics, genetic counseling principles, and results interpretation and disclosure (Fig. 1). To inform the training, a needs-based assessment (NBA) was distributed to LARGE-PD clinicians to identify knowledge gaps; it also informed targeted updates to existing modules and guided the development of a sixth module on secondary findings.

Fig. 1. Breakdown of training modules



RESULTS

The study-specific certification program was offered to all LARGE-PD members, and two training cycles have been completed to date. **Cycle 1:** 33 clinicians expressed interest, 26 completed the training, and 16 achieved certification. **Cycle 2:** 34 clinicians expressed interest, 26 completed the training, and 16 achieved certification (Table 1). Overall, 32 clinicians across 12 countries have been certified, ensuring that every LARGE-PD site has at least one trained clinician capable of delivering results through a formal genetic counseling session (Fig. 2). **To date, 1630 participant results are available, with 861 genetic counseling sessions successfully completed reflecting substantial progress in the return of results process.**

Fig. 2. Map of certified clinicians

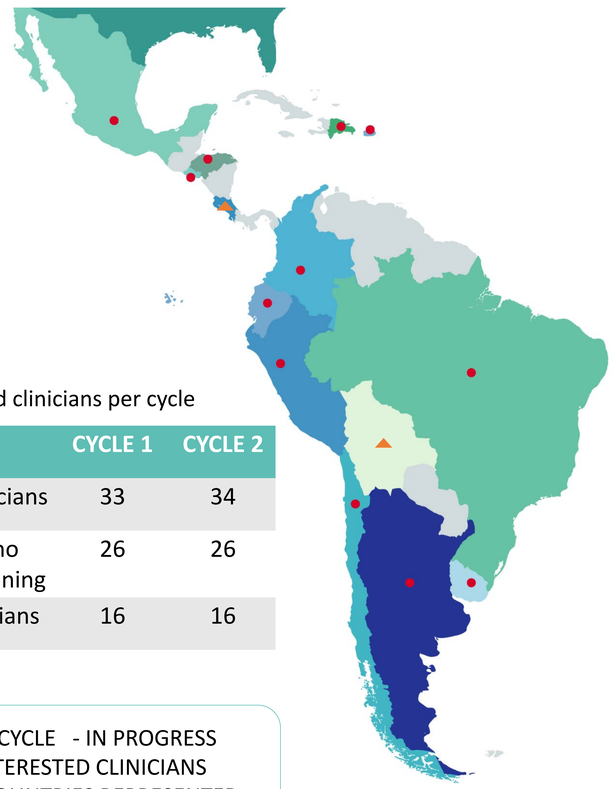


Table 1. Certified clinicians per cycle

	CYCLE 1	CYCLE 2
Interested clinicians	33	34
Clinicians who completed training	26	26
Certified clinicians	16	16

CONCLUSION

Since the study expansion into Latin America, the PDGENE-LARGE-PD collaboration has implemented and refined a study-specific training framework to build genetic counseling capacity in Latin America. This initiative shows that it is possible to train local clinicians to deliver genetic results in regions where specialized genetic counseling resources are limited. By building local expertise, this model improves access to genetic information, supports more inclusive research, and helps ensure that people with Parkinson's disease in Latin America can better understand their condition.

ACKNOWLEDGEMENTS

This project was supported by the Parkinson's Foundation and the Global Parkinson's Genetics Program (GP2). GP2 is funded by the Aligning Science Across Parkinson's (ASAP) initiative and implemented by The Michael J. Fox Foundation for Parkinson's Research (**https://gp2.org**). For a complete list of GP2 members see **https://gp2.org**.

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RESOURCES

To learn more about PD GENEration

To learn more about LARGE-PD