Journal of Parkinson's Disease 13 (2023) 637–640
DOI 10.3233/JPD-225015
IOS Press

Letter to the Editor

Enhancing Participant Engagement in Clinical Studies: Strategies Applied in the Personalized Parkinson Project

Marjan J. Meinders[a,*], William J. Marks Jr.[b], Sabine B.M. van Zundert[c], Ritu Kapur[b] and Bastiaan R. Bloem[c]

[a]*Radboud University Medical Center, Research Institute for Medical Innovation, Scientific Center for Quality of Healthcare, Nijmegen, the Netherlands*

[b]*Verily Life Sciences, South San Francisco, CA, USA*

[c]*Radboud University Medical Center, Donders Institute for Brain, Cognition and Behaviour, Department of neurology, Nijmegen, the Netherlands*

Accepted 29 March 2023
Pre-press 17 April 2023
Published 13 June 2023

A recent article by Kehagia et al. in this journal highlighted the extensive qualitative work that was conducted within the PD STAT trial, and that resulted in valuable insights and recommendations to enhance trial delivery in Parkinson's disease (PD) [1]. Future trials can benefit from a similar person-centered research protocol, addressing the needs of study participants, care partners and study staff. These include the need to alleviate the burden of OFF state assessments, the need for care partners to feel heard, the importance of the relationship between study staff and study participants and the possibility to personalize data collection protocols to maximize convenience, comfort, and privacy.

The Personalized Parkinson Project (PPP)—which was designed independently from PD STAT, and which started in 2017—also implemented many of these recommendations, plus several others, to create a comprehensive battery of recruitment and retainment measures [2]. Here, we share our experience with this battery that complements the PD STAT experience. Specifically, the PPP study aimed to gain more insight into the heterogeneous course of PD by means of including a representative sample of patients and by deploying an extensive protocol for deep phenotyping. The study enrolled persons with PD, all diagnosed<5 years. During three consecutive annual clinic visits, we collected clinimetrics, multiple biospecimens, and neuroimaging data. In addition, participants completed online questionnaires and wore a multi-sensor smartwatch (the Verily Study Watch) for up to 23 hours per day for at least two years, with the possibility to extend to up to three years [2]. From 2020 onwards, the smartwatch also supported data collection during eight structured motor tasks [3].

Right from the outset, participatory research principles guided the design of the PPP study. A panel of 20 people with PD served as an advisory board, and together with the study team they co-designed the study procedures, the recruitment strategies, and a comprehensive set of patient engagement measures, to optimize retention of participants (Box 1). After the first clinic visit, participants were invited to complete

*Correspondence to: Marjan J Meinders, PhD, Reinier Postlaan 4, 6525 GC Nijmegen, the Netherlands. Tel.: +31 24 361 5202; E-mail: marjan.meinders@radboudumc.nl.

an online survey about their initial study experiences. This resulted in 430 (response rate = 83%) completed surveys. We discuss the results from this survey to provide context to the recommendations made by Kehagia et al. [1].

Box 1. Strategies to enhance study retention in the Personalized Parkinson Project

- Personal assessor for every participant, who is the first point of contact throughout the entire study trajectory.
- Dedicated helpdesk, which can be reached by phone and email during business days. The helpdesk proactively assists participants, addresses problems and questions, and solves/communicates issues related to trial execution.
- Brief videos of all study procedures to inform potential participants and to prepare the participants for the clinic visits.
- Overnight stay and taxi service from a nearby hotel to the research center, at no costs, to reduce the burden of traveling in an OFF state.
- Lumbar puncture is an optional part of the protocol.
- Offering educational materials, i.e.,
  - Monthly newsletters, sent by email, to inform participants about the progress of the study.
  - Short video-messages on the study website, addressing participants questions about issues relating to their Parkinson's, shared not only with the participant who raised the question, but also with all other participants in the study.
  - Annual conference for participants, with updates about the study progress as well as advances in the Parkinson's disease field.
- The Principal Investigator tries to personally welcome every participant at their first visit.

During the course of three years, 520 participants were enrolled, with 59% men, a mean age of 61.7 ± 9.0 (mean $\pm$ SD) years and a mean time since diagnosis of 2.7 ± 1.5 years. After 2 years of follow-up, 24 participants withdrew their consent and four participants died, leading to a net dropout rate of 5.4%. Participants mentioned the intensive test protocol (9 times) and worsening of their health status (7 times) as the main reasons for study withdrawal (Table 1).

We will briefly discuss some of the PPP retention strategies (Box 1) in more detail below. Adequate information, written in layman's terms about the study for potential study participants can enhance the efficiency of the recruitment phase. Digital multimedia approaches are recommended, as they may confer particular benefits over paper-based information [1]. For PPP, we indeed provided brief video-clips detailing all study procedures, in addition to the written information letter and two telephone calls by the study staff with all participants during the enrollment phase. In the survey, 77% (269/350) of the participants indicated they had watched the videos and 82% rated them as useful or very useful.

From the PD STAT evaluation, a personal relationship between the study participant and study staff emerged as a strong asset for study retention [1]. For the PPP study we assigned a personal assessor for every participant, who acted as a first point of contact throughout the study. During the first clinic visit, the PPP participants highly valued this personal assessor, with 98% indicating to be satisfied or very satisfied. For research staff, a reciprocal relationship with their study participants is an important motivational factor [4]. Offering flexible and creative workarounds, with an assessment schedule which includes room for informal conservations, e.g., about vacation and general well-being, helped us to ensure a strong relationship between the participant and the assessor. Furthermore, being available by phone for support and providing frequent newsletters with updates about the study are strategies which we applied to further foster a personal relationship [4].

OFF state measurements during clinic visits are known to be burdensome for trial participants [1]. During the recruitment for the PPP study, only a few potential participants (6 out of 331 screen failures) refrained from study participation for this reason. Among the included participants, everybody came in the OFF state to the clinic, while this was 98.4% (429/436) at the first follow-up visit and 96.8% (456/471) during the second follow-up visit. To lessen the burden, we offered a stay in a nearby hotel for two persons and a taxi service from the hotel to the study site on the day of the OFF assessment, at no costs to the participants. This also allowed us to include people living further away from the clinic. Almost everybody (90%) used this hotel service, which was valued with a score of 9.1 ± 0.9 on a 1–10 point scale. Among those who used the taxi service (79%), 99% indicated that this had added value.

Another important component of the PPP retention toolbox is the availability of educational programs to engage participants, as part of the compensation for participating in the study. The content of the educational programs is driven by questions from the participants about issues relating to their Parkinson's, which are then answered in short video messages. The educational program is shared not only with the participant who raised the issue, but also with all other

Table 1
Reasons for drop-out (frequency (%)*)

	Between baseline visit and first follow-up visit	Between first and second follow-up visit	Total
Total	10 (1.9%)*	18 (3.2%)**	28 (5.4%)*
- Diagnosis not confirmed	1	2	3
- Protocol too burdensome	5	4	9
- Refusal to wear the smartwatch	1	2	3
- Unsatisfied with staff support	1	0	1
- Deceased	0	4	4
- Worsening of health status, unrelated to PD	1	5	6
- Worsening of health status, related to PD	1	0	1
- Refusal to come to study site	0	1	1

*Percentages based on the 520 participants who started the first year of follow-up; **Percentage based on the 510 participants who started the second year of follow-up.

participants in the study. This generates an extensive library of information that meets the needs of people living with PD. We also offer all participants the opportunity to visit an annual conference, where the study team provides updates about the progress of the study, where we discuss advances in the PD field and where participants can meet fellow participants. All participants also receive a monthly newsletter with information about the study, e.g., the number of participants, a personal story of a member of the study team or a participant who explains how he/she has experienced the clinic visit. We also provide information about new developments in the PD field.

In conclusion, our experiences in the PPP underline the recommendations made by Kehagia et al. [1] that dedicated participant-centered engagement strategies do matter and should be included as an integral part of any future clinical study. To optimize the package of strategies, balancing costs and benefits, we need a better understanding of the elements that drive compliance. Compliance might be driven by one factor, and making all others redundant, or conversely, that all of them somehow work together in a synergistic way, and everything in between. Participant-centric strategies make it possible to successfully execute complex and demanding study protocols which are required to answer the relevant research questions that we are facing in the journey to find cures for PD.

ACKNOWLEDGMENTS

The Personalized Parkinson Project is financially supported by Verily Life Sciences LLC, Radboud university medical center, Radboud University, the city of Nijmegen and the Province of Gelderland and by a PPP Allowance made available by Health∼Holland, Top Sector Life Sciences & Health, to stimulate public-private partnerships. The Radboudumc Center of Expertise for Parkinson & Movement Disorders is supported by a center of Excellence grant of the Parkinson's Foundation.

CONFLICT OF INTEREST

BR Bloem serves as the co-Editor in Chief for the Journal of Parkinson's disease but was not involved in the peer-review process nor had access to any information regarding its peer-review. He also serves on the editorial board of Practical Neurology and Digital Biomarkers, has received fees for serving on the scientific advisory board for UCB, Kyowa Kirin, Zambon and the Critical Path Institute (paid to the Institute), has received fees for speaking at conferences from AbbVie, Biogen, UCB, Zambon, Roche, GE Healthcare, Oruen and Bial (paid to the Institute), and has received research support from the Netherlands Organization for Health Research and Development, the Michael J Fox Foundation, UCB, the Stichting Parkinson Fonds, Hersenstichting Nederland, de Stichting Woelse Waard, Stichting Alkemade-Keuls, de Maag Lever Darm Stichting, Parkinson NL, Davis Phinney Foundation, the Parkinson's Foundation, Verily Life Sciences, Horizon 2020, the Topsector Life Sciences and Health, Nothing Impossible and the Parkinson Vereniging, outside the submitted work.

R Kapur and WJ Marks Jr receive salary and equity compensation as employees of Verily Life Sciences.

MJ Meinders and SBM van Zundert have no conflict of interest to report.

DATA AVAILABILITY

The data supporting the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

REFERENCES

[1] Kehagia AA, North TK, Grose J, Jeffery AN, Cocking L, Chapman R, Carroll C (2022) Enhancing trial delivery in Parkinson's disease: Qualitative insights from PD STAT. *J Parkinsons Dis* **12**, 1591-1604.

[2] Bloem BR, Marks WJ, Jr., Silva de Lima AL, Kuijf ML, van Laar T, Jacobs BPF, Verbeek MM, Helmich RC, van de Warrenburg BP, Evers LJW, intHout J, van de Zande T, Snyder TM, Kapur R, Meinders MJ (2019) The Personalized Parkinson Project: Examining disease progression through broad biomarkers in early Parkinson's disease. *BMC Neurol* **19**, 160.

[3] Burq M, Rainaldi E, Ho KC, Chen C, Bloem BR, Evers LJW, Helmich RC, Myers L, Marks WJ, Jr., Kapur R (2022) Virtual exam for Parkinson's disease enables frequent and reliable remote measurements of motor function. *NPJ Digit Med* **5**, 65.

[4] Siffels LE, Sharon T, Hoffman AS (2021) The participatory turn in health and medicine: The rise of the civic and the need to 'give back' in data-intensive medical research. *Humanit Soc Sci Commun* **8**, 306.