Parkinson's Disease Functional Impacts Digital Instrument (PD-FIDI): Studies Preceding Clinical Validation

Andrew Pearlmutter[1], Nicholas Wong[1], Molly Follette Story[1], Riliang Zheng[1] Robert Ellis[2], Peter Kelly[2], M Judith Peterschmitt[1]

[1]Sanofi, Cambridge, MA, USA; [2]Koneksa, New York, NY, USA

OBJECTIVE

- **Summarize the findings from three developmental studies of the Parkinson's Disease Functional Impacts Digital Instrument (PD-FIDI)**

CONCLUSIONS

- **PD-FIDI was developed via a comprehensive and iterative process, including**
  - **Confirmation that the underlying technology works as intended with healthy participants**
  - **Demonstration that ePRO components are accurate and understandable for PD patient end users**
  - **Testing and optimization of PD-FIDI's usability for PD patient end users**
- **Next steps include testing of PD-FIDI's validity, reliability, and sensitivity in a year-long multinational validation study (OBS16136)**

ABSTRACT

OBJECTIVE: Summarize the findings from 3 developmental studies of the Parkinson's Disease Functional Impacts Digital Instrument (PD-FIDI) – a novel endpoint for assessing PD symptoms.

BACKGROUND: PD-FIDI was developed to objectively assess PD symptoms in patients at home. PD-FIDI includes an iPhone application with electronic patient-reported outcomes (ePROs) and functional assessments, plus a wrist-worn device (ActiGraph GT9X) [figure1]. We report results of three studies that, in line with FDA guidance, assess PD-FIDI's analytical validity, safety, and usability prior to clinical validation.

METHODS: Study One had 2 objectives: To determine a) accelerometer accuracy for iPhone and GT9X compared with a Quanser Shake Table II [1] for accelerations observed in walking and tremor; and b) analytical validity and operational tolerance (deviation from instruction) of functional assessments and wrist-worn measures in 11 healthy volunteers compared with the observations of 3 trained raters. Agreement was measured via intraclass correlation coefficient (ICC) for assessments, and mean absolute percentage error (MAPE) was calculated for wrist-worn measures. Study Two covered expert review and interviews with 5 PD patients to assess comprehension and usability of PD-FIDI's 2 ePROs, adapted from MDS–Unified PD Rating Scale Part II and MDS–Unified Dyskinesia Rating Scale Part Ib. Study Three assessed PD-FIDI's safety and usability in a 2-phase formative human factors study with 9 PD patients.

RESULTS: For Study One, 99% of the ICC for iPhone and 92% of ICC for GT9X were acceptable (ICC ≥0.75) for acceleration >0.1 g. After optimization, ICC for 17 of 21 functional assessment measures were acceptable (ICC ≥0.75). For wrist-worn measures, MAPE was <6%. In Study Two, expert and patient reviews resulted in a number of minor changes to improve usability and comprehension of PD-FIDI's digital PROs. In Study Three – a two-phase formative human factors study – phase 1 revealed the need for minor user experience improvements, which were included and tested in phase 2 to confirm PD-FIDI's usability and safety.

CONCLUSIONS: The results of the 3 studies suggest that the PD-FIDI device and application show sufficient sensor precision, analytical validity (ICC ≥0.75), and usability to support use in a clinical validation study (OBS16136 – now enrolling patients).

INTRODUCTION

- Sanofi, in collaboration with Koneksa Health, has developed an at-home digital PD measurement tool, the PD-FIDI, including an iPhone application with ePROs and functional assessments, and a wrist-worn movement sensor (ActiGraph GT9X) (**Figure 1**)

References

1. https://www.quanser.com/products/shake-table-ii/

Acknowledgments and Disclosures

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METHODS

- **Study One** tested the technology behind Part III's iPhone app-based assessments and Part IV's wrist-worn ActiGraph GT9X Link digital actigraphy assessments – including device accelerometer accuracy, analytical validity, and operational tolerance for both devices used to collect PD-FIDI Parts III & IV data
- **Study Two** assessed the comprehensibility and usability of PD-FIDI's two ePRO components in Part I & II
- **Study Three** confirmed the usability of PD-FIDI Parts I-IV in a comprehensive, two-phase formative human factors study

Figure 1. Visual Overview of PD-FIDI and Developmental Studies

RESULTS

- For **Study One**, 99% of the ICC for iPhone and 92% of ICC for GT9X were acceptable (ICC ≥0.75) for acceleration >0.1 g (**Table 1**)
- In **Study Two**, expert and patient reviews resulted in a number of minor changes to improve usability and comprehensibility of PD-FIDI's ePROs (**Table 2**)
- In **Study Three**, phase 1 revealed minor usability issues and user interface optimization opportunities, and phase 2 showed that although the design changes meaningfully optimized usability, some users continued to have difficulty with the use tasks and functional assessments (**Figure 2**). Notably, many of the difficulties on the tasks were related to the patient's disease symptomology.

Table 1. Study One: Analytical Validity and Operational Tolerance

Analytical validity and operational tolerance of the Pronation/Supination functional assessment in 2 phases				
Study Phase	**Validation Test**		**Turns**	**Rotation Rate**
Phase 1	Analytical validity		0.642	0.935
	Operational tolerance (raising/lowering arm)		0.971	0.975
Phase 2	Operational tolerance (repeatedly turning/stopping)		0.995	0.990
	Operational tolerance (turn and then stop)		1.000	0.732

Analytical validity and operational tolerance of the Gait and Balance functional assessment					
Confirmatory Validity	**Duration (s)**	**Distance (m)**	**Steps**	**Speed (m/s)**	**Stride Period (s)**
Analytical validity (all walks: 5s, 10s, 15s, 20s)[a]	0.989	0.987	0.992	0.764	0.593
Operational tolerance (loose pocket)	0.066[b]	0.850	0.868	0.741	0.850
Operational tolerance (shoulder bag)	0[b]	0.932	0.858	0.837	0.798

Analytical validity measured by MAE, RMSE, and MAPE algorithms versus rater for wrist-worn measures[c]						
Confirmatory Validity		**Start Time (s)**	**End Time (s)**	**Duration (s)**	**Steps**	**Stride Period (s)**
Analytical validity (walk for 10s, stop for 10s)	MAE	0.874	0.521	0.494	0.628	0.039
	RMSE	0.999	0.626	0.629	0.816	0.051
	MAPE	-[d]	5.20%	5.00%	3.40%	3.60%
Analytical validity (walk for 20s, stop for 20s)	MAE	1.048	1.158	1.121	2.036	0.028
	RMSE	1.545	1.492	1.645	3.166	0.036
	MAPE	-[d]	5.80%	5.60%	5.40%	2.60%
Analytical validity (combined results)	MAE	0.943	0.776	0.745	1.191	0.033
	RMSE	1.246	1.061	1.149	2.1	0.042
	MAPE	-[d]	5.50%	5.20%	4.20%	3.10%

MAE=mean absolute error; RMSE=root mean square error. Numbers in green denote acceptable ICC (≥0.75). [a]Analytical validity was assessed over multiple walk durations: 5 seconds(s), 10s, 15s, and 20s; [b]Operational tolerance was only assessed over 20s walks in line with future planned studies which leads to small variation in rater duration (standard deviation <0.5 s) and therefore poor ICC for duration; [c]Wrist-worn measures assessed continuous walk detection (start and end time of walking period detected in raw data) and then duration, step count, and stride period for walk period; device raw data recorded on ActiGraph GT9X; [d]MAPE cannot be calculated for start time because the rater start time is always zero.

Figure 2. Study Three: Human Factors Formative Study

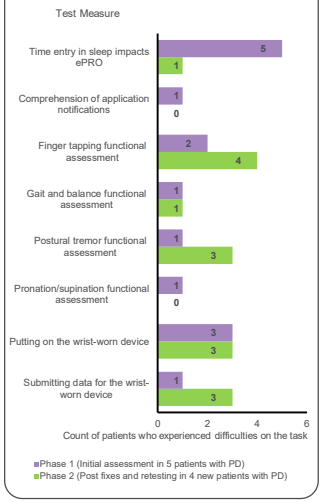

Table 2. Study Two: Expert and Patient Review of PD-FIDI's 2 ePROs

	Overall Usability of Application		**PD-FIDI Part I (MDS-UPDRS Part II)**		**PD-FIDI Part II (MDS-UDysRS Part Ib)**	
Study Phase	**Changes Implemented**	**Changes Not Implemented**	**Changes Implemented**	**Changes Not Implemented**	**Changes Implemented**	**Changes Not Implemented**
Initial expert review (using design files)	0	0	10	3	4	14
Final expert review (using smartphone application)	0	0	1	3	0	8
Patient review (smartphone application and posttesting interview)	2	3	0	1	0	1

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