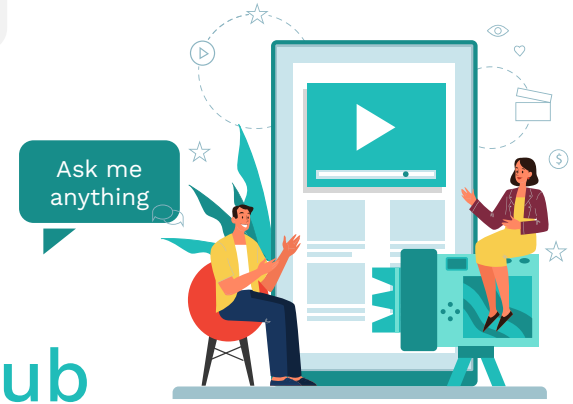
Virtual Journal club



Listen up! Using digital tools when designing patient-centric clinical trials

January 11th, 2022 11am ET

Cindy Zadikoff, MD
Medical Director, CPP Industry Co-Director
Abbvie

Martijn Müller, PhD
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Critical Path Institute

Mark Frasier, PhD
Chief Scientific Officer, Research Programs
Michael J. Fox Foundation

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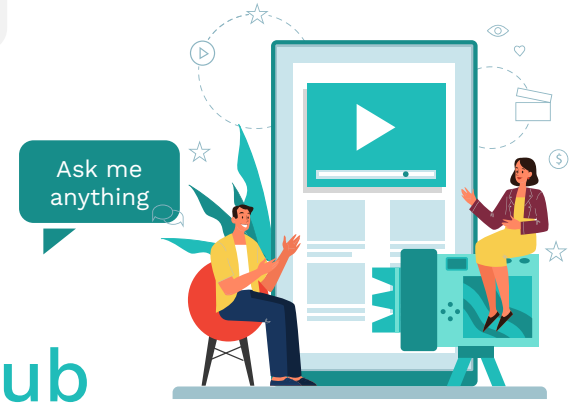
Senior Specialist in Patient Insights
Lundbeck

But first, housekeeping

- Please note today's session is being recorded
- To ask a question for discussion during Q&A, please:
    - Either 'raise your hand' in the participant window and moderator will unmute you to ask your question live, or
    - Type your question into the chat box
- Slides and recording will be available after today's session

Virtual Journal club



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Critical Path for Parkinson's Consortium | 3DT Initiative

Recommendations for involving people with Parkinson's in clinical studies using digital health tools

CPP PARKINSON'S CONSORTIUM

CRITICAL PATH INSTITUTE

About

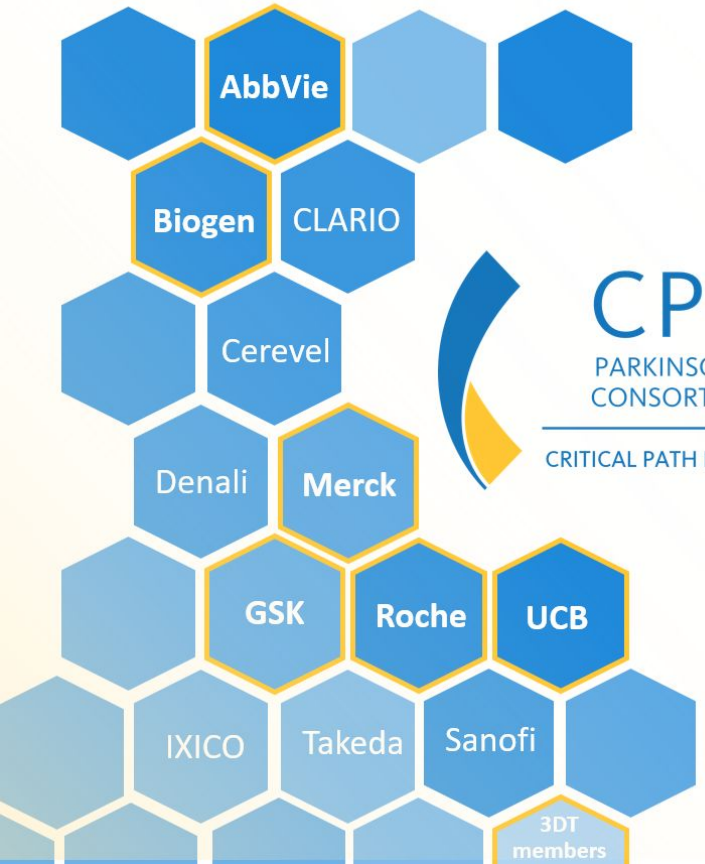
Critical Path for Parkinson's (CPP)

A global consortium that promises to pave the path to new treatments for Parkinson's. By facilitating collaboration among scientists from the biopharmaceutical industry, academic institutions, government agencies, and patient-advocacy associations, CPP fosters consensus and data-driven research to increase efficiency, safety, and speed in developing new therapies.

CPP's Digital Drug Development Tools (3DT)

An initiative launched in 2018 to leverage the unique role of CPP as a neutral convener, bringing stakeholders together in a pre-competitive space to collectively engage with regulatory agencies optimize the effective use of DHT in PD clinical trials.

Partnerships Overview



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PARKINSON'S CONSORTIUM
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Nonprofits
- **Parkinson's UK**
- **Michael J. Fox Foundation**
- National Institute of Neurological Disorders & Stroke
- Parkinson Canada

Nonprofits
- Davis Phinney Foundation
- Cure Parkinson's
- PMD Alliance
- International Parkinson & Movement Disorder Society

Academic Institutions
- University of Oxford
- University of Cambridge
- Newcastle University
- University of Glasgow
- Radboud University
- University of Rochester

Regulatory Agencies
- European Medicines Agency
- US Food and Drug Administration

Parkinson's Community
- People with Parkinson's
- Patient Advocates

Advisors
- Academic Contributors
- Individual Experts

Key takeaways

Participant engagement and integration of the voice of patients, at all stages of study design, is critical to ensure efficient recruitment and retention

Realities of DHT

Using digital health technologies (DHT) in clinical studies introduces unique design complexities

Effective engagement strategies

Human-centered design and participant engagement are paramount to success

Applications beyond Parkinson's

We believe these recommendations can be implemented in any trial/in a disease- and device-agnostic manner

Authors

This presentation was prepared as part of the Critical Path for Parkinson's consortium's Digital Drug Development Tools (3DT) initiative.

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Cindy Zadikoff, MD – Medical Director | AbbVie
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Diane Stephenson, PhD – Executive Director | Critical Path Institute
* *Work group co-chairs*

Project Manager:
Kimberly Ward Barowicz, CAPM, SHRM-CP – 3DT Project Manager | Critical Path Institute

Outline

The use of digital health technologies (DHT) in clinical studies introduces unique design complexities. The willingness and ability of people with Parkinson's (PwP) to engage in remote monitoring using DHT are paramount for the success of the trial. The **objective** of this slide deck is to produce guidelines, recommendations, and considerations for integration of DHT, regardless of the type of device, in PD clinical studies in order to improve the overall study design and execution, **with the engagement of PwP as a key component of this process**.

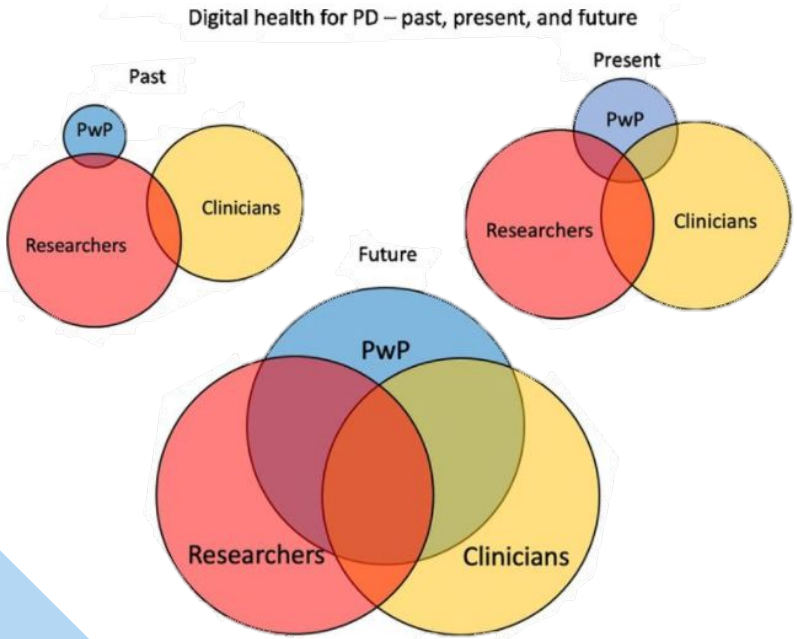
This slide deck provides examples of **the patient's perspective** in the use of DHT. A **review of the literature** was conducted that identified **barriers and facilitators for DHT use**. Based on these findings, r**ecommendations for protocol design, enrollment, and protocol compliance, and participant retention** were provided.

The use of DHT in clinical studies requires multiple stakeholders; clinicians, researchers, PwP, their partners, family, and careers alike. Successful engagement of PwP in clinical studies using DHT requires early and frequent involvement of all stakeholders in all aspects of the study. Patient experience data should also be generated to capture how PwP functions and feels, in accordance with regulatory advice.

Background

- There is a proliferation of clinical trials in Parkinson's (PD). (McFarthing *et al.,* 2020, JPD)
- Capturing intervention effects remains challenging. Assessments performed in a clinic may not adequately capture episodic symptoms and experiences of daily living that are important to persons with PD (PwP).
- The use of digital health technology (DHT), such as mobile phones, activity sensors, and smartwatches, forms an exciting opportunity to capture clinically relevant and meaningful features of PD in real life.
- While study sponsors and PwP understand the potential value of objective DHT measurements in interpreting clinical trial results, study participants will have a range of experiences and aptitude with technology and sensors. The willingness and ability of PwP to engage in remote monitoring using DHT are paramount for the success of the trial.
- Recent studies, for example, showed that adherence was acceptable for remote task-based assessments, but not perfect, with adherence rates between 61-68%. (Lipsmeier *et al.*, 2018, Mov Dis; Silva de Lima *et al*., 2017, Plos One)

The patient's perspective



In the past, PWP involvement in digital health development has been small and mainly in the context of technological research.

In the future, it is to be hoped that patient involvement will increase substantially and in equal partnership with researchers and clinicians.

Riggare et al., 2021, JPD

The patient's perspective

"I have been privileged to test drive an early prototype system (SENSE-PARK) of wearable-battery powered sensors which record a wide range of symptoms and ancillary information that is then converted by scientifically designed algorithms into comprehensive data from which a PwP can learn more about managing individual medical idiosyncrasies.

How will this help my Health-Related Quality of Life?
I expect the design of the chosen system to be capable of measuring critical symptomatic and autonomic elements of my Parkinson's condition and general health over extended periods and provide reliable data for me and my clinician to plan appropriate treatments that I can respond to and that can benefit me holistically. I believe that a reliably measured perspective of what to expect in the future will free me from constant preoccupation and allow me to concentrate on those activities that support my desired lifestyle."

Male, 88 years old, diagnosed with PD 15 years ago

Van Uem *et al.*, 2016, JPD

It takes a village | multiple stakeholders

The success of using DHT in clinical trials requires multiple stakeholders, including engagement of PwP in the use of remote DHT assessments. (Stephenson *et al.*, 2021, JPD)

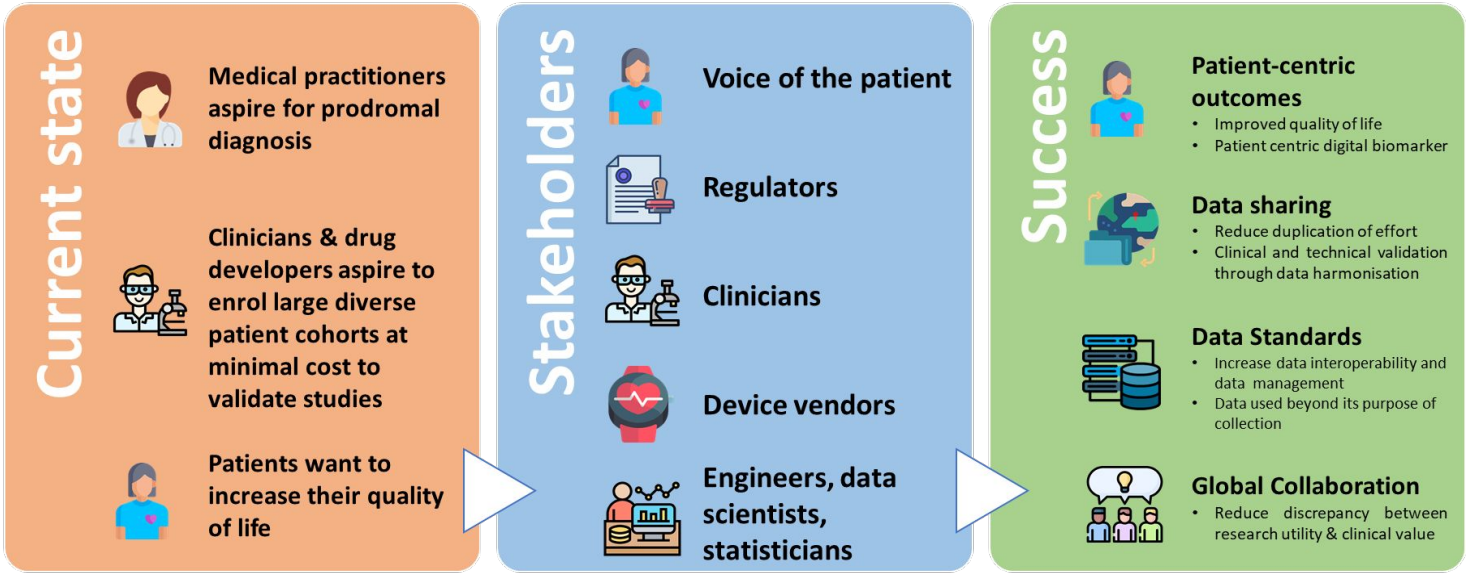
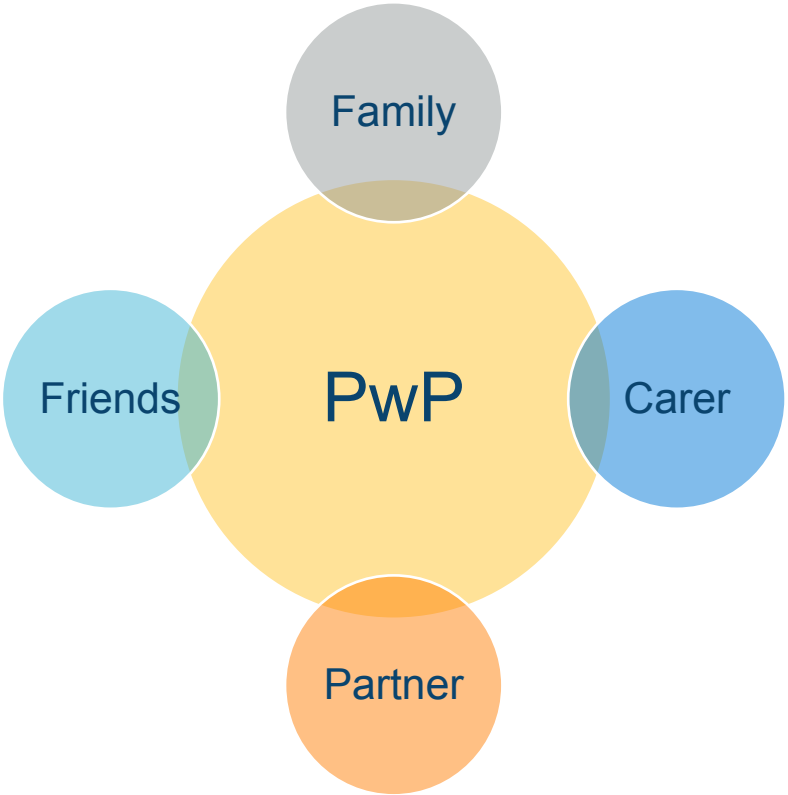


Fig. 1. Digital Biomarkers for Parkinson's: Opportunities for the future. An overview of the current state of digital biomarkers for PD, and what success can be achieved by bringing all key stakeholders to collaborate together. (Stephenson *et al.*, 2021, JPD)

It takes a village | PwP and their living & care environment

Successfully embedding DHT into clinical trials requires multiple stakeholders, including PwP.

Their perspective is informed by their immediate living & care environment.



Overview

Problem statement

The use of DHT introduces unique complexities in clinical study design and operations.

Objective

To produce guidelines, recommendations, and considerations for integration of DHT, regardless of the type of device, in PD clinical studies in order to improve the overall study design and execution, with the engagement of PwP as a key component of this process.

Audience

For CROs, investigators, sites, trial sponsors, etc. who are designing and executing PD clinical studies that include DHT.

Scope

In scope

- Designing a protocol that facilitates participant engagement
- Recommendations for materials that will enable efficient enrollment of study participants
- Providing information that maximizes protocol adherence for both passive and active monitoring
- Retain and keep participants motivated throughout the study
- Examples of suggestions/recommendations and good practice (e.g., vlogs, articles, materials currently in use) for each category above

Out of scope

- Device-specific recommendations
- Study protocols including PwP with cognitive impairment requiring additional considerations

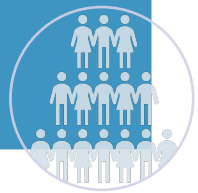
Why create guidelines and recommendations to consider?

Integration of digital technologies into clinical trials is becoming commonplace in PD.

Trends in the field

Reducing drop-out rates will lower sample sizes needed at enrollment and minimize costly delays.

Optimize studies



The inclusion of DHT may impose unique challenges on PwP, e.g., frequent testing in-home environments, that requires a comprehensive understanding of requirements and expectations from the PwP perspective.

Understand unique challenges

Patient engagement and integration of the voice of PwP, at all stages of study design, is critical to ensure efficient recruitment and retention

Literature review

barriers & facilitators for DHT use

A pragmatic exploration of the literature was conducted

- 12 feasibility studies, a combination of passive and active monitoring technologies.
- 1 qualitative study on general view on the use of wearable technologies.

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Literature review

barriers & facilitators for DHT use

Factors related to use of DHT itself

Barriers	Facilitators
• Text display too small[3] • Technical problems [6,7] • Connectivity issues cause missing data [2] • Unpleasant to carry a phone all day [10]	• Device should be comfortable, non-invasive, waterproof, durable, small, not visible, and easy to fasten[1,3,4] • Wrist is the preferred location for the device[1] • DHT does not require behavioral changes[2,13] • DHT does not obstruct everyday activities[3] • DHT does not require interaction[10,13] • Provide patient-facing summary[6] • Develop the DHT in co-design with patients[1,2,6] • Incorporate gaming activity[12]

Literature review

barriers & facilitators for DHT use

Factors related to the study participant

**inconclusive role*

Barriers

- Repetitive assessments tend to become boring[2]
- Concerns about the impression to others while wearing the device = public disclose of having a disease* [3,4]
- Concerns about proper attachment and use of the DHT[3,4]
- Attitude towards technology*[1]
- Difficulties in understanding reports, based on registered data[6]

Facilitators

- Availability of a caregiver to help to attach/use the DHT properly[4,9]

No influence

- No concerns about privacy[1]
- Gender[5,13]
- Age[5,13]
- Disease status at baseline[5,9,13]
- Attitude towards technology*[13]
- No concerns regarding device visibility, as it might indicate to the community that the patient needs help*[1,10]

Literature review

barriers & facilitators for DHT use

Factors related to the clinical study design

Barriers

- Delay in receiving a report, based on registered data[5]
- In-accurate capture of the symptoms[6]
- Frequent PROs over the day: evenings have lower completion rates[10]

Facilitators

- Collect data that is meaningful to the participant[2]
- Proper instruction before use[3,6,10,11]
- Intervention trial increases motivation[5]
- Schedules and unscheduled support calls[5,13]
- Helpdesk[5,13]
- Reminders[10]
- Short duration of the data-collection[10]
- Data collection at the same time every day[11]

No influence

- Day of the week[5]
- Holidays[5]

Recommendations
Protocol Design

- DHT is often used to assess motor fluctuations or fatigue. However, the use of DHT during these periods, especially, may place a high burden on PwP. How will DHT be used when PwP experiences fluctuations or fatigue? Can assessments be tailored to reduce the burden?
- What impact will the device and/or requested tasks have on participants' day-to-day lives, e.g., will they need to carry a device, does it need to be charged, how easy is it to take off or put on?
- How will seasonal weather and geographical differences affect DHT use?
- What is the duration of the study and the frequency of DHT assessments? An extended study or high frequency of assessments might mean reduced retention.
- Are there any cultural or socio-economic factors affecting the willingness to use DHT?
- Assess your participant population for circumstances/challenges that may play a role in DHT use in the trial. For example, a cognitively impaired population may require special recommendations
(out of scope for this slide deck).

Recommendations
Enrollment

- Provide informational materials, such as a pamphlet, in lay language clearly and concisely explaining:
- The rationale for the use of DHT in the study.
- What type/how much (personal DHT) data will be relayed during the study.
- The type of DHT assessments that will be conducted and what will be measured.
- Expectations from the study participant, e.g., time requirements, charging of devices, WiFi accessibility, physical environment, etc.
- Resources that are available to the study participant, e.g., technical support from a helpdesk, additional instruction in the use of the device if needed.
- What will happen with the data, e.g., who gets access, storage for how long, and privacy concerns in an FAQ section.

Recommendations
Protocol Compliance & Participant Retention

- The DHT should minimize/not cause significant behavioral changes or interfere with activities of daily living.
- Do participants need to delay any of their daily activities because they must complete DHT assessments?
- How is the daily living environment changed by the use of DHT, e.g., does furniture need to be moved?
- Will it interfere with doing exercise?
- Incorporate gaming activity (however, must consider ethical concerns of coercion or undue influence)
- Design, with input from the PwP participant, a user-friendly interface, and ease of use.
- Adherence is affected by the perceived nuisance of the device. How and how many devices are carried? In a pocket, on the wrist, on a belt or strap?
- Be proactive about sharing with sites lessons learned regarding DHT use during the conduct of the study in order to optimize participant experience.

Recommendations
Protocol Compliance & Participant Retention

- Engage participants early and frequently!
- Periodic retention events to build a community of participants engaged in research.
- Monthly newsletters or active study website/social media channel that frequently shares information with study participants, such as study updates and milestones.
- Messaging specifically about DHT use compliance at a group level, e.g.,
- *"Since the last visit, 74% of study participants have completed more than 7 consecutive days of tracking with the XYZ device. These are very valuable data. Please keep up the good work"*

Recommendations
Protocol Compliance & Participant Retention

- Points of contact:
  - Dedicated point of contact for each participant, easily contacted by phone/email (e.g., technical support/help desk)
  - Send personal reminders to participants
- Buddy system/ambassadors to pair experienced and new participants
- PwP may ask for their health-related results from the DHT. Providing this information may provide additional incentives for participation or protocol compliance and retention. While we firmly believe that participants are entitled to their own information, we recognize some of the concerns of investigators to provide this. Ethical concerns such as interpretation of clinically unvalidated observational DHT data will require an ongoing discussion between PwP, the investigators, and ethical review boards, and a disclosure plan is recommended. Similarly, research findings that may affect the management of a study participant's health, safety, or welfare require careful consideration by all stakeholders as well.

Recommendations
Summary

- Do not throw out the baby with the bathwater. Analog and digital measurement can be complementary. For certain assessments, diary studies may be preferred. (Vega *et al.*, 2018, CHI Proceedings)

- Follow regulators' advice to assess the PwPs' perspective of how they function and feel by performing qualitative studies, *e.g.,* entry and exit interviews that generate patient experience data. (Schultz-Knudsen, *et al.,* 2020, Ther Innov Regul Sci)

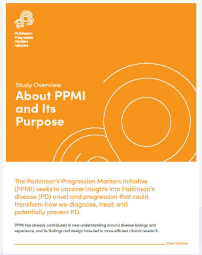
Conclusions

To ensure successful engagement of PwP in clinical studies that utilize DHT, **early and frequent involvement of PwP is required in all aspects of the study.**

The use of DHT in clinical trials is still in its infancy and many lessons can be learned. Continuous updating of these recommendations is needed. A standing working group including PwP that periodically reviews these recommendations may be required.

Resources

- https://www.ppmi-info.org/participants/ click here ->
- https://www.dimesociety.org/tag/patient-engagement/
- https://www.parkinsonopmaat.nl/parkinson-vraagbaak
- https://patientfocusedmedicine.org/the-patient-engagement-quality-guidance-download/
- Clinical-trial-charter-PDF.pdf (parkinsonsmovement.com)



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Key takeaways

Participant engagement and integration of the voice of patients, at all stages of study design, is critical to ensure efficient recruitment and retention

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Using digital health technologies (DHT) in clinical studies introduces unique design complexities

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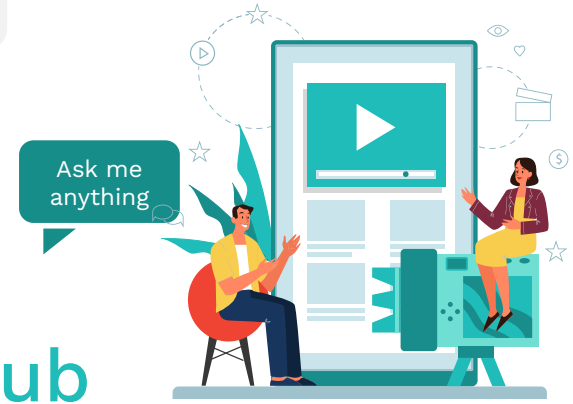

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State of digital medicine:
DiMe strategies to address key challenges in 2022

Wednesday, January 19 at 12pm ET

Jennifer Goldsack
Chief Executive Officer
Digital Medicine Society

Claire Meunier
Chief Operating Officer
Digital Medicine Society

Virtual Journal club

JMIR Publications
Advancing Digital Health & Open Science

Sensor Data Integration:

A New Cross-Industry Collaboration to Articulate Value, Define Needs, and Advance a Framework for Best Practices

February 2nd, 2022 12p ET

Ieuan Clay
Chief Scientific Officer
DiMe

Kimberly McManus
White House PIF
Veterans Affairs

David Drummond
Director
Evidation Health

Ingrid Oakley-Girvan
SVP Research & Academics
Medable

Shruti Iyer
Principal Innovation Architect
Oracle

Simona Carini
Programmer & Analyst
UCSF

THANK YOU

Cindy, Mark, Johan, and Martijn!

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