Clinical trial efficiency using data and digital health tech

DIGITAL MEDICINE SOCIETY

Thursday, April 18, 2024

11 am - 12 pm ET

Michelle Holko, PhD, PMP
Vice President of Biorisk
Airfinity

Abigail Levine, PhD
Senior Director, Product & Portfolio Strategy
Evidation Health

Jacek K. Urbanek, PhD MEng
Director, Biostatistics
Regeneron Pharmaceuticals

Sarah Valentine
Partnerships Lead
DiMe
Moderator

But first, housekeeping

- Please note: **today's session is being recorded**
    - Slides and recording will be available on DiMe's webinar page after the session
- To ask a question for discussion during live Q&A, please either:
    - **'Raise your hand'** in the Reactions and the moderator will unmute you to ask your question live, or
    - **Type your question** into the chat box

*** Participants are not permitted to transcribe this webinar, violators will be removed from the session.

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Comprehensive view of real-world health, behaviors, and experiences

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Solutions for:

- **RECRUITMENT**
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Traditional RWD paired with direct from patient data builds a more complete health journey

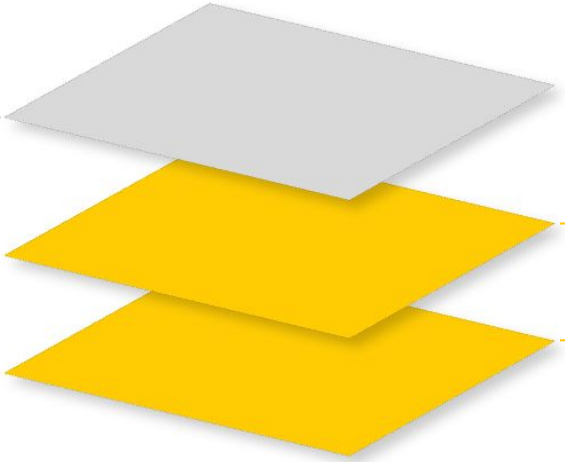
TRADITIONAL RWD SOURCES

Snapshots in time

Captures:

- Clinical measures, medication usage, and healthcare utilization
- Point-in-time or infrequent views into individuals' experiences with health and disease

Electronic health records
Health insurance claims



DIRECT FROM PATIENT DATA

Everyday life, over time

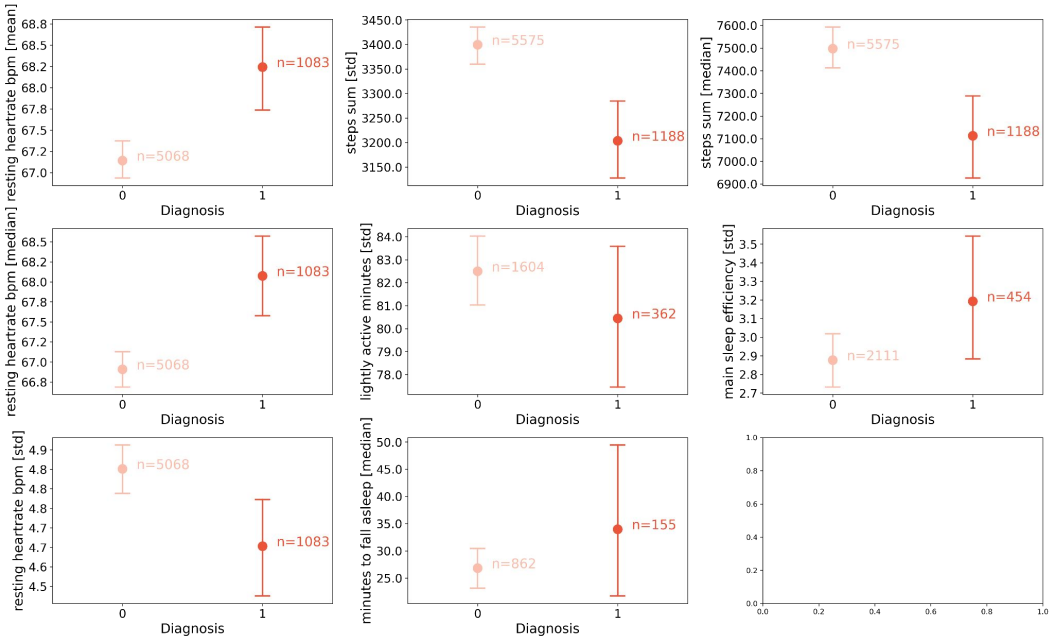
Captures:

- Insights into how life events and contextual factors influence health behaviors and access to care
- Daily changes in activity and other health measures close in time to when health events occur
- Day-to-day symptom burden, productivity, and other measures that are not easily observed

Low burden symptom diaries and periodic survey check-ins (e.g., ePROs)

Objective data from wearables other devices (e.g., activity levels, sleep patterns, heart rate)

Measuring the impact of endometriosis and uterine fibroids on daily activity



Trends in wearable data
Undiagnosed vs diagnosed

We analyzed trends in the most relevant* activity data features

Individuals with **diagnosed with endo and/or UF** tend to have **higher resting heart rate, fewer steps, and less variability in both of these.**

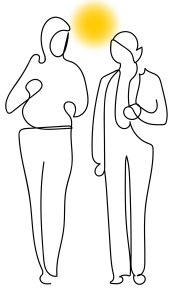
They also **tend to take longer to fall asleep**, and have more **variability** in their sleep efficiency**.**

*relevance was determined using the minimum redundancy, maximum relevance algorithm [https://pypi.org/project/mrmr-selection/0.2.4/]

FluSmart

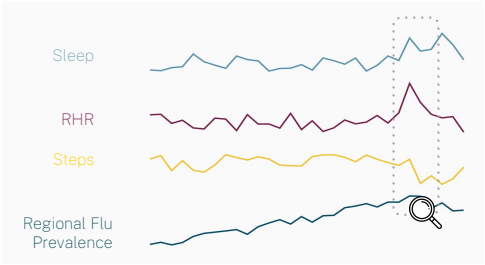
Evidation's cold and flu monitoring and education program

Engage & Monitor



- Surveys
- Symptom Trackers
- Wearables
- Content & Education

Measure & Detect



Machine learning model alerts participants based on behavioral pattern changes

Anomaly detected

Check in in real time with individual

Activate

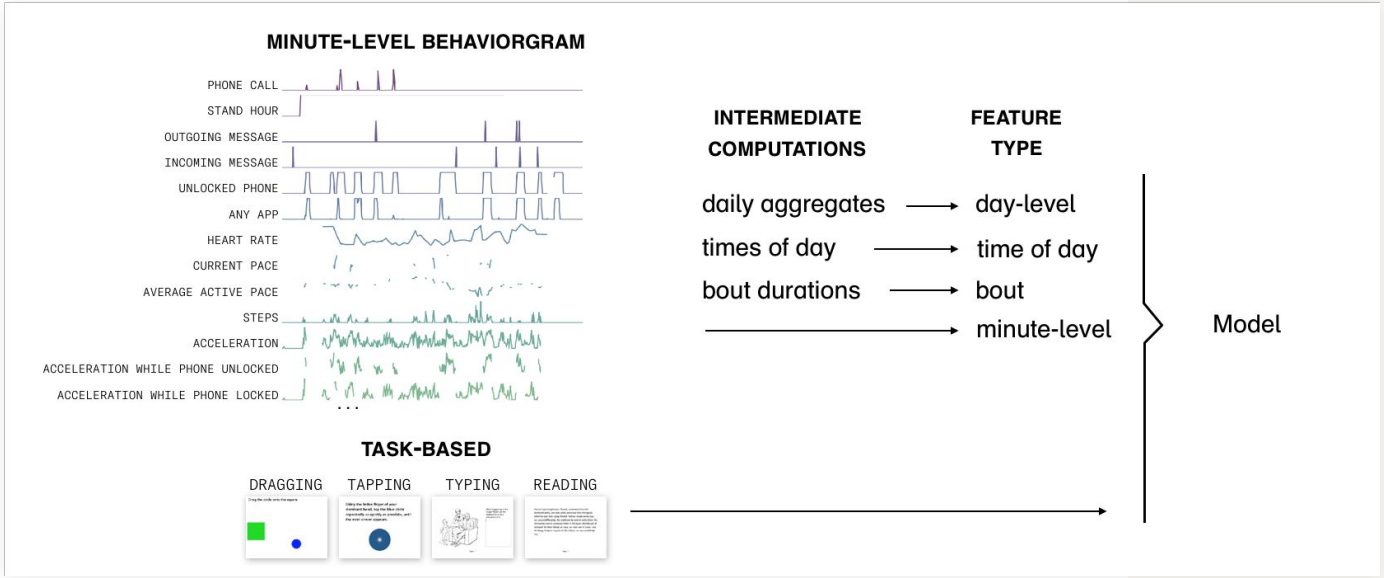
- → Proactively seek care
- → Answer symptom survey
- → Enroll in clinical research
- → Engage with relevant resources

2022 - 2023 Flu Season:

- **+189K** participants
- **90% completion rate** across content types over 8 months
- **>2.7 times more truly symptomatic people** vs. traditional recruitment advertising

Early detection of Alzheimer's

We extracted over 1,000 features from participants' behaviorgrams and iPad-based tasks that captured patterns in their activity, sleep, phone usage, and routines alongside the reading, typing, tapping, and dragging tasks.



04.18.2024

Large-Scale Observational Studies Enable Rapid Decision-Making in Digital Measurements Strategy for Clinical Trials

Case study in Parkinson's Disease

Jacek K. Urbanek, PhD MEng

Director, Biostatistics

Biostatistical Engineering

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There is a need for more sensitive markers of Parkinson's Disease progression

Goals

- Support the development of medicines for Parkinson's Disease
- To identify a set of potential outcome measures capturing progression of Parkinson's and technology to collect them

Challenges

- Existing instruments to measure Parkinson's Disease progression require large sample size
- There is no well-established digital measurement for Parkinson's Disease
- Many vendors propose solutions that need to be evaluated independently
- **Evaluation takes time and may require dedicated studies**

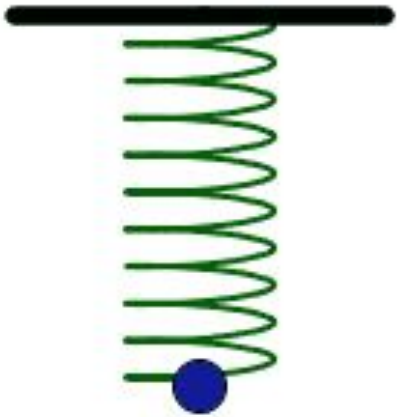
Proposed Solution

- Determine if **wrist-worn accelerometers** have potential to monitor severity of Parkinson's Disease
- Use existing, open-source National Health and Nutrition Examination Survey (NHANES) study accelerometry data

Wearable Accelerometers measure movement

Wearable accelerometers measure acceleration of the body part they are attached to

- In three orthogonal axes
- Continuously up to 100 observation per second for each axis
- Accelerometers are non-invasive, easy to implement devices that can collect characteristics of movement in free-living settings over multiple days at a time (continuously)
- Can be worn on different body parts (today we will focus on wrist)
- **It is just a ball on the spring**



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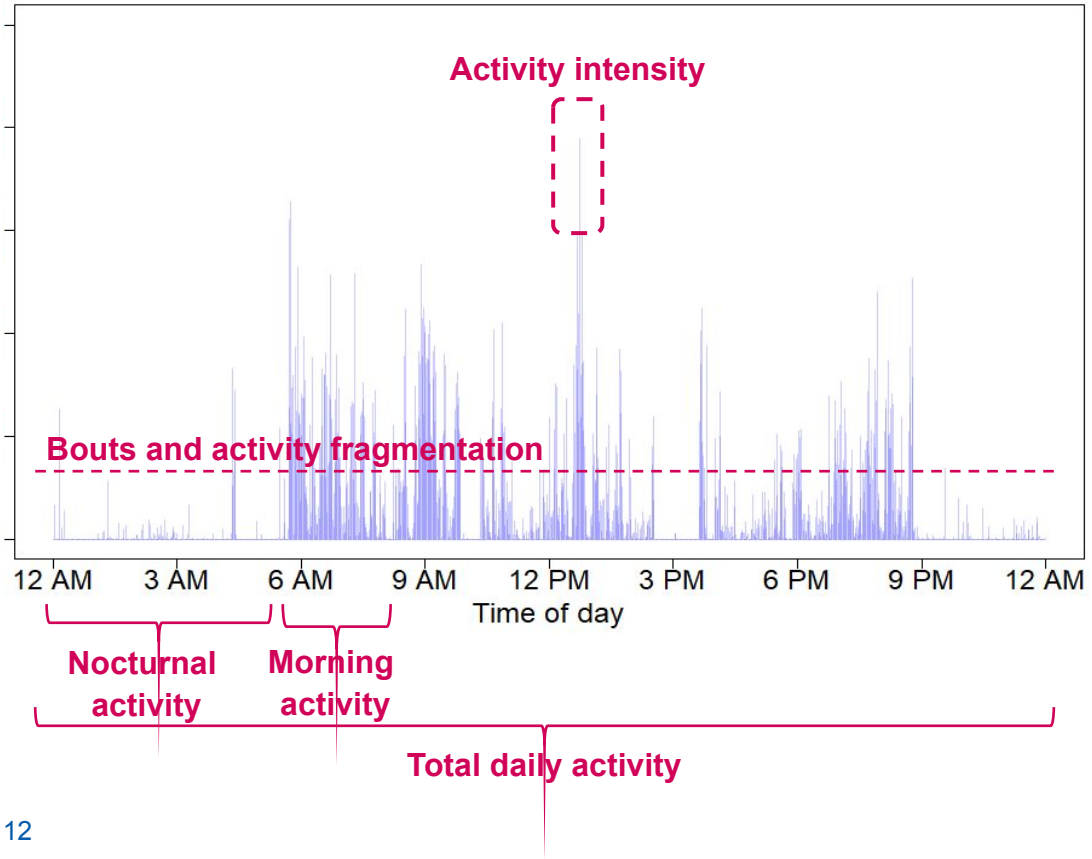
Accelerometry measurements can be a source of multiple outcome measures across different clinical modalities



Free-living accelerometry characteristics can capture multiple concepts

Total daily activity –> Functional independence

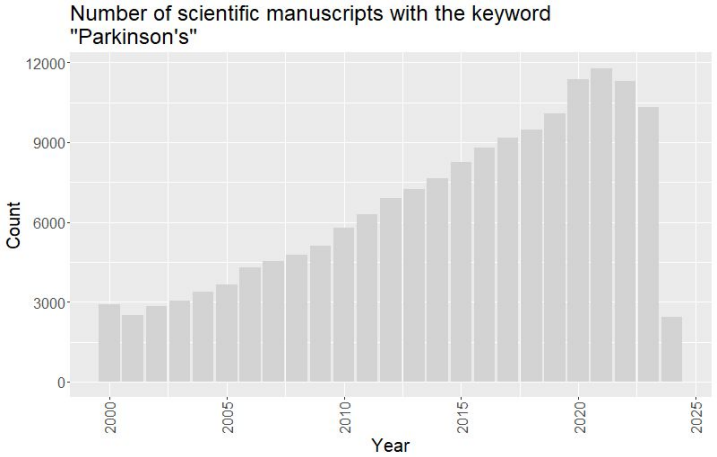
Nocturnal activity –> Sleep quality

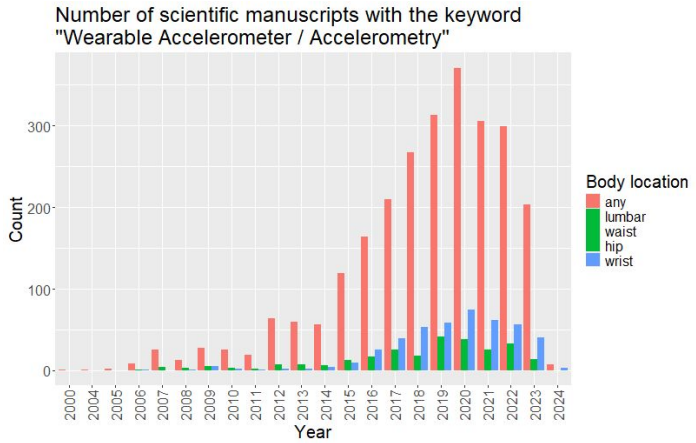
Morning activity –> Morning stiffness

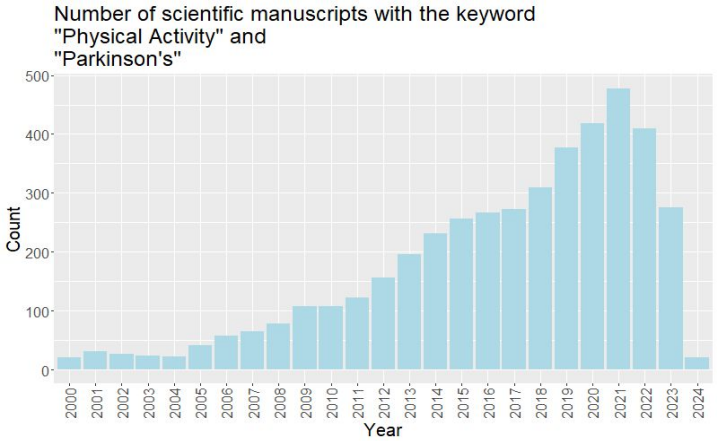
Activity intensity –> Mobility

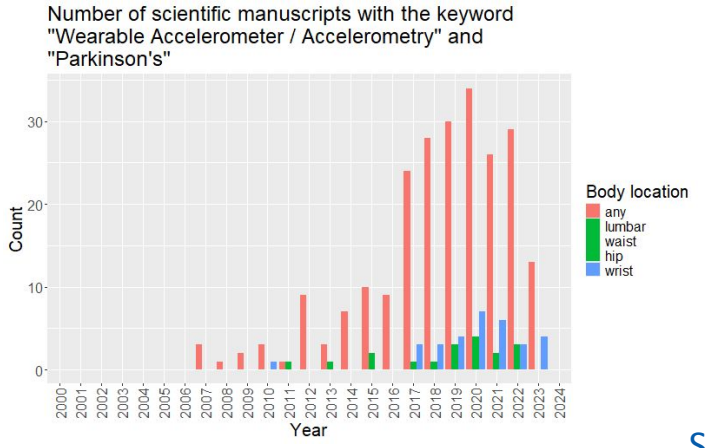
One measurement can result in multiple instruments.

Wearable accelerometers are getting more popular in academic Parkinson's research



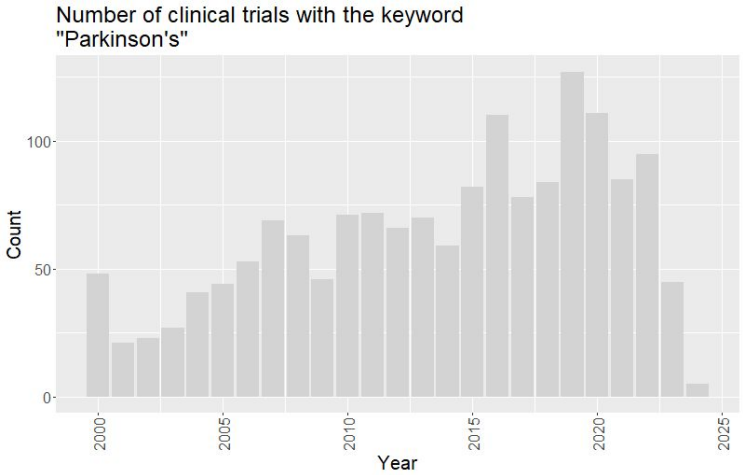


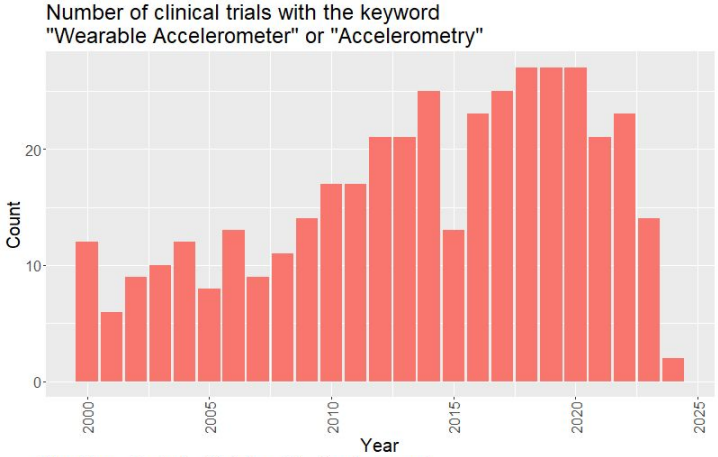


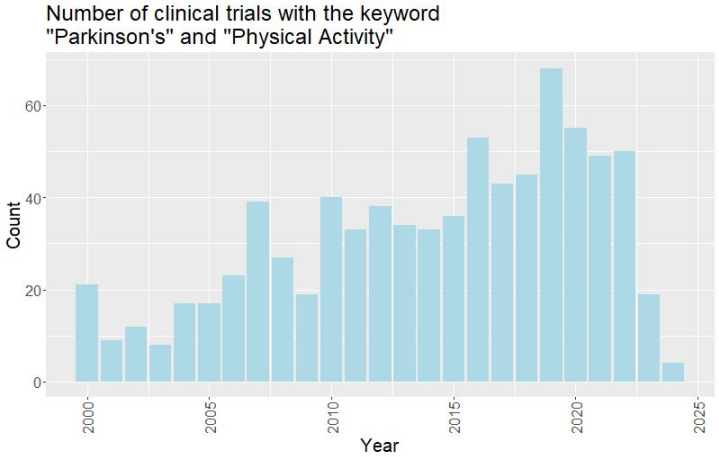


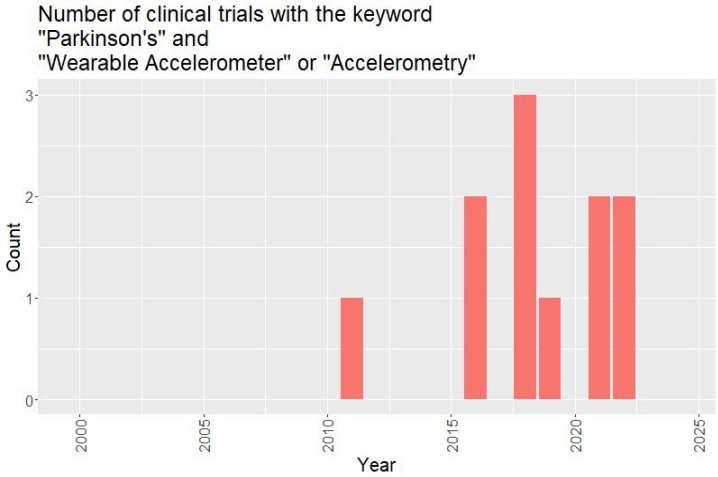
Source: **PubMed**

Application of wearable accelerometers in Parkinson's clinical trials is still sporadic



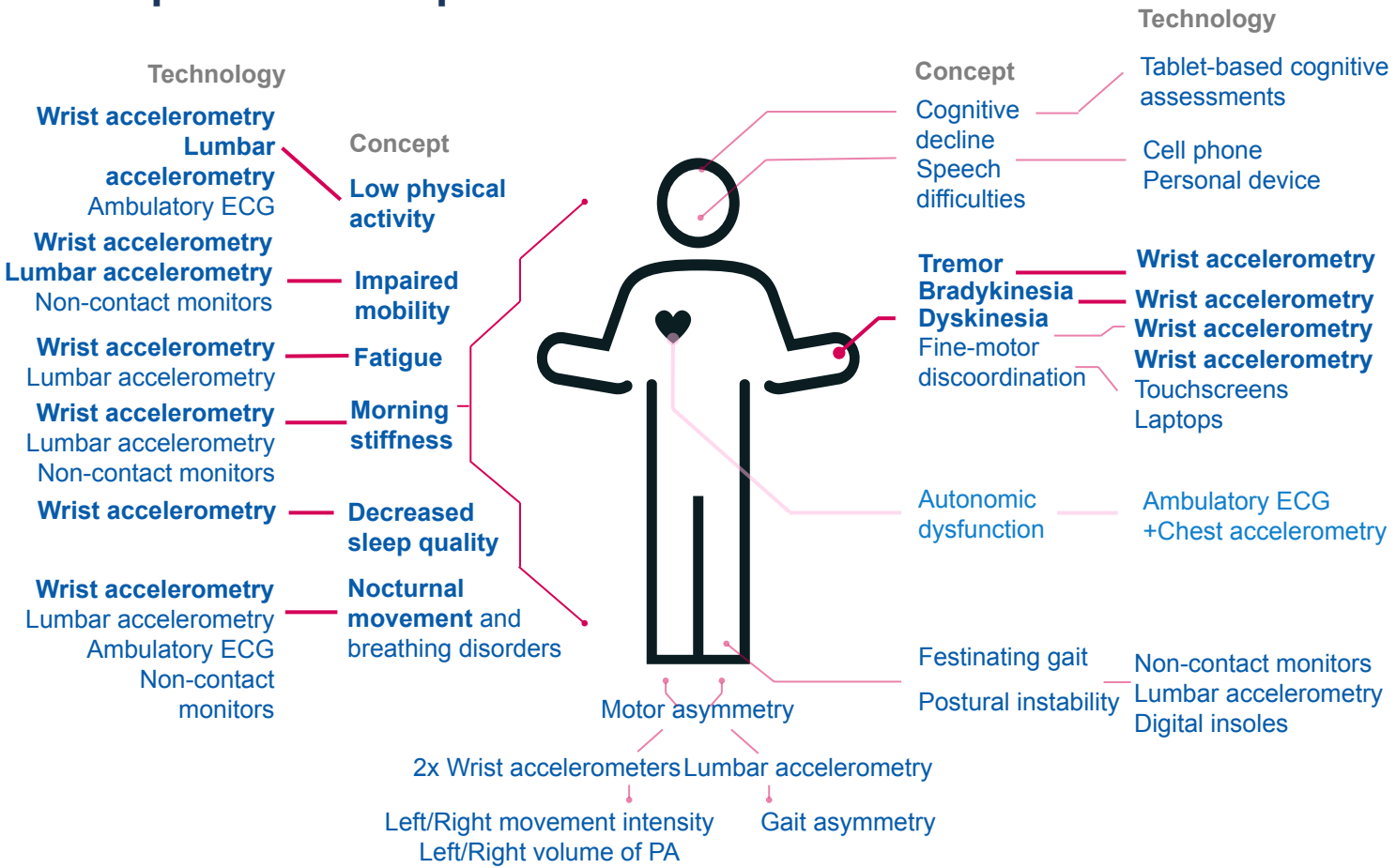






Source:
clinicaltrials.gov

Single wrist accelerometer can be applied in multiple Parkinson's-specific concepts



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In house analysis identified 20 Parkinson's patients with accelerometry data in National Health and Nutrition Examination Survey (NHANES)

National Health and Nutrition Examination Survey (NHANES)

Large cross-sectional cohort study, general population is representative of US

- Questionnaire data
- Limited clinical assessments
- Limited accelerometry measures

Identification of PD patients

- 50 years and older
- Included if Parkinson's medications:
  - Carbidopa
  - Levodopa
  - Pramipexole
  - Ropinirole
- Excluded if taking anti-psychotic or restless legs syndrome medications
- Diagnosis, if available
- 7 days of free-living accelerometry
  - Cohorts 2011-12 and 20013-14

Analysis

- Monitor-Independent Movement Summaries (MIMS) were pre-processed to:
  - Identify non-wear time
  - Impute missing data
- Minutes with MIMS below 10.59 were labeled as sedentary
- Days with more than 10% data missing were deemed invalid
- Participants with more than two invalid days were excluded

Following characteristics were calculated using ARCTOOLS R package

- *Total MIMS per day valid day -> Total daily activity*
- *Total MIMS per day valid night -> Nocturnal activity*
- *95th percentile of MIMS on valid days -> Activity intensity*
- *95th percentile of MIMS between 6AM and 9AM -> Morning Activity*
- *Probability of transitioning from active to sedentary state -> Activity Fragmentation*

Karas, M., Schrack, J., and Urbanek, J. (2021). ***arctools****: Processing and Physical Activity Summaries of Minute Level Activity Data. R package version 1.1.4.*

NHANES results replicate group level findings of differences in activity observed in UK Biobank

Our results - NHANES, N = 20

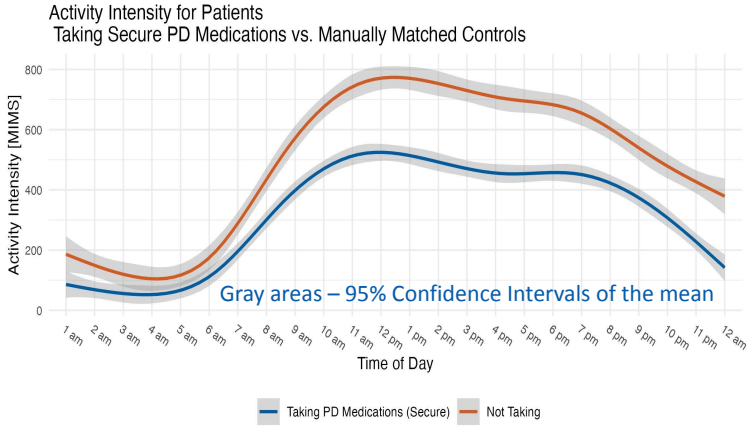

Fig 1. Average diurnal profiles of accelerometry between Parkinson's patients and healthy controls

Published results – UK Biobank, N = 273

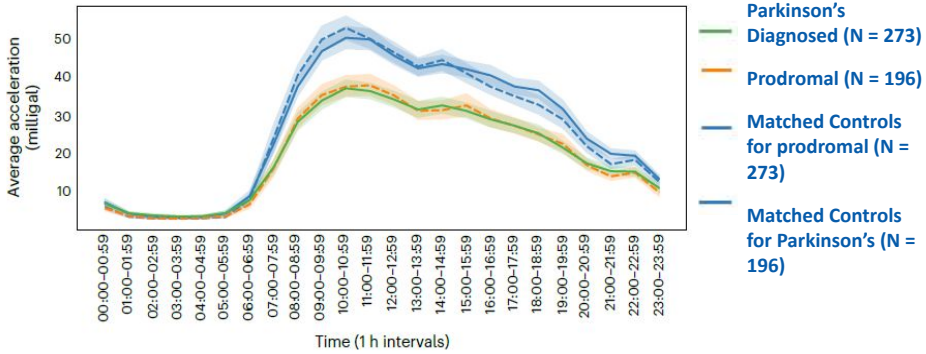

Fig. 2. Average acceleration profile between prodromal subjects, Parkinson's patients, and healthy controls [Schalkamp et al. 2023]

Hypotheses today

Compared to healthy controls, PD patients will be characterized by:

- Lower total activity
- Lower morning activity
- Higher nighttime activity
- Lower activity intensity
- More fragmented physical activity

NHANES - National Health and Nutrition Examination Survey
MIMS – Monitor independent Movement Summary

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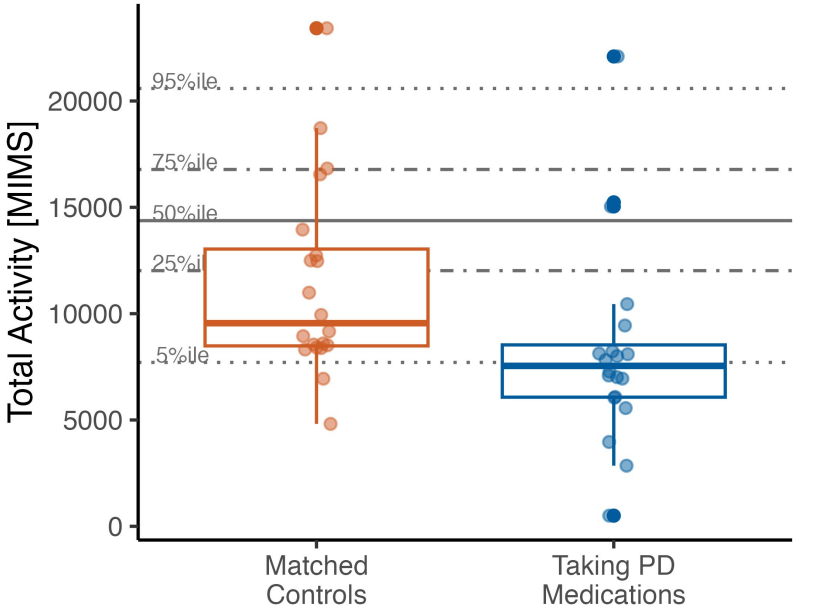
We have identified only 20 Parkinson's patients and 20 controls, but we are still leveraging big data to contextualize obtained results

Robust accelerometry characteristics are usually expressed on proprietary scales and might be difficult to interpret and translate

Patient's and Controls

- Parkinson's patients were matched to controls on age, sex, BMI, and ethnicity
- Controls were Parkinson's-free but they could have other health conditions



MC: 11436.43 (9556.28, 13356.70)
PD: 8292.72 (6239.38, 10297.24)
Diff: 3143.71 (663.65, 5749.90)

To improve interpretation, we provide percentile values for each characteristic in healthy adults

Reference Group

- *N* = 707 participants
- Age 25 to 50,
- BMI 18.5 to 25,
- No reported medications use
- No comorbidities

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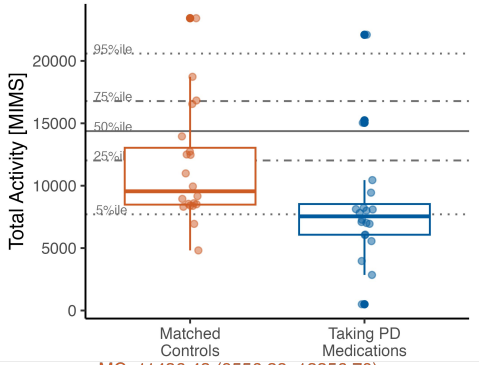
Tested accelerometry outcomes differ between Parkinson's patients and controls



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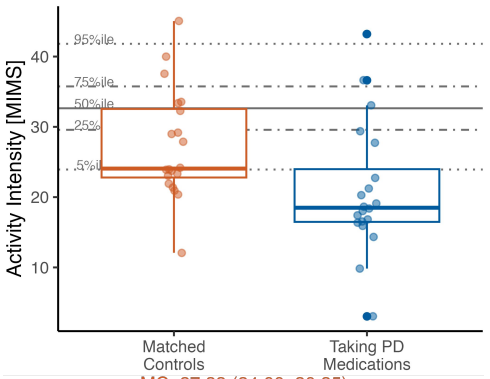
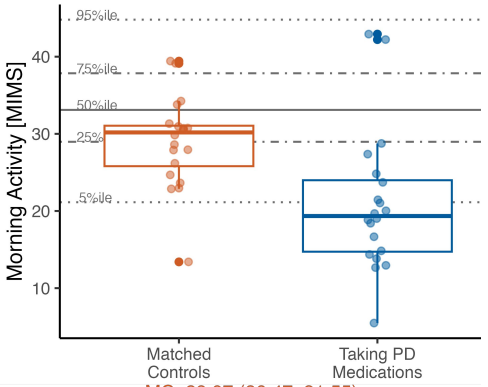
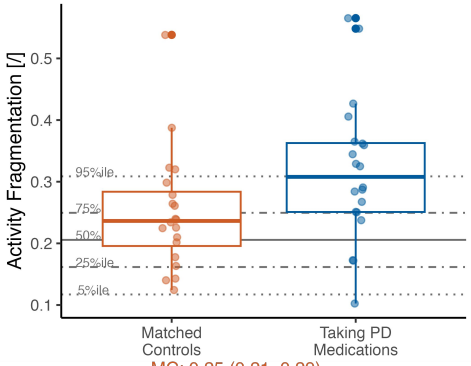


MC: 27.33 (24.00, 30.35)
PD: 20.93 (16.83, 24.73)
Diff: 6.41 (1.66, 11.04)



MC: 28.97 (26.47, 31.55)
PD: 20.95 (17.19, 24.83)
Diff: 8.02 (3.07, 13.16)



MC: 0.25 (0.21, 0.29)
PD: 0.32 (0.27, 0.36)
Diff: -0.07 (-0.12, -0.01)

Findings

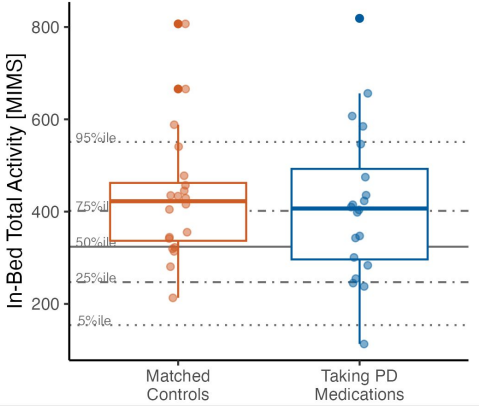
Total physical activity,

Activity intensity,

Activity fragmentation and

Morning activity are significantly different between controls and PD medication groups

In-bed activity is not



MC: 429.55 (369.24, 489.66)
PD: 414.94 (347.18, 481.87)
Diff: 14.62 (-59.28, 90.72)

n = 20 in both groups, Controls matched on age, sex, ethnicity, and BMI

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Summary

Recap

- We used **free** data, available to everyone, to explore the potential of wearable accelerometry in Parkinson's research
- We overcame limitations of NHANES by identifying likely Parkinson's patients using combination of medication
- Confirmed findings reported by others with in-house analysis

What have we accomplished

- Build confidence in wearable accelerometry across multidisciplinary study team
- Build analytical skillset to analyze and interpret these data
- Generate hypotheses to test in the longitudinal study
- … all with a minimal cost

Remaining gaps

- Ability of these metrics to capture progression of Parkinson's Disease still needs to be determined

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Advancing Sleep Research: New Core Digital Measures & Resources

Wednesday, April 24

11 a.m. - 12 p.m. ET

DATAcc

Digital Health Measurement Collaborative Community

by DiMe

Mark Aloia
Head of Sleep and Behavioral Sciences
Sleep Number

Jonathan Berent
CEO, Founder
NextSense, Inc

Bohdana Ratitch
Expert Statistician
Bayer

Farah Hasan
Expert Advisory Board Member and Patient Speaker
Project Sleep

Michael Kremliovsky
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Bayer

Nina Shaafi Kabiri
Research Scientist
Boston University

Eric Nofzinger
Senior sleep medicine consultant
Jazz Pharmaceuticals

Katerina Placek
Senior Implementation Manager
Takeda

Sudhir Sivakumaran
VP, Translational Medicine
Beacon Biosignals

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Building the **Business Case** *for* Digital Endpoints

DATAcc by DiME

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Don't miss out on our next DATAcc by DiMe project – **scan the QR code** to share your interest and learn more!

Source: https://pages.insightly.services/digital_endpoints

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