Telehealth and Mobile Measures in Parkinson’s Disease

Jamie Adams, MD

The University of Rochester Medical Center
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There is no password needed
Telehealth and Mobile Measures in Parkinson’s Disease

11:15 am – 12:15 pm | Gleason

Jamie Adams, MD

The University of Rochester Medical Center
Telehealth and Mobile Measures in Parkinson’s Disease

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Outline

• Technology in Research Overview/Rationale
• Virtual Visits in Clinical Trials
• Mobile Measures
• Telehealth in Clinical Care
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• Technology in Research Overview/Rationale
• Virtual Visits in Clinical Trials
• Mobile Measures
• Telehealth in Clinical Care
The global burden of Parkinson disease is rising

Current clinical assessments are subjective, categorical, insensitive, and episodic

Assessment of motor function in Parkinson disease

3.4 FINGER TAPPING

Instructions to examiner: Each hand is tested separately. Demonstrate the task, but do not continue to perform the task while the patient is being tested. Instruct the patient to tap the index finger on the thumb 10 times as quickly AND as big as possible. Rate each side separately, evaluating speed, amplitude, hesitations, halts and decrementing amplitude.

0: Normal: No problems.

1: Slight: Any of the following: a) the regular rhythm is broken with one or two interruptions or hesitations of the tapping movement; b) slight slowing; c) the amplitude decrements near the end of the 10 taps.

2: Mild: Any of the following: a) 3 to 5 interruptions during tapping; b) mild slowing; c) the amplitude decrements midway in the 10-tap sequence.

3: Moderate: Any of the following: a) more than 5 interruptions during tapping or at least one longer arrest (freeze) in ongoing movement; b) moderate slowing; c) the amplitude decrements starting after the 1st tap.

4: Severe: Cannot or can only barely perform the task because of slowing, interruptions or decrements.

Source: Movement Disorders Society. United Parkinson Disease Rating Scale, 2008
These rating scales lead to false and missed signals of efficacy.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Disease</th>
<th>Phase 2 Findings</th>
<th>Phase 3 Findings</th>
<th>N</th>
<th>Duration</th>
<th>Sponsor</th>
<th>Phase 3 Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatine</td>
<td>Parkinson disease</td>
<td>2.8 points improvement on total UPDRS over placebo</td>
<td>Failed, study terminated early due to futility</td>
<td>955</td>
<td>5 years</td>
<td>NIH</td>
<td>~$25 million</td>
</tr>
<tr>
<td>Coenzyme Q$_{10}$</td>
<td>Parkinson disease</td>
<td>1.2-5.3 points improvement on total UPDRS over placebo</td>
<td>Failed, study terminated early due to futility</td>
<td>600</td>
<td>16 months</td>
<td>NIH</td>
<td>~$14 million</td>
</tr>
<tr>
<td>Idalopirdine</td>
<td>Alzheimer disease</td>
<td>2.1 points improvement on ADAS-Cog over placebo</td>
<td>Failed, unchanged ADAS-Cog</td>
<td>2525</td>
<td>24 months</td>
<td>Lundbeck</td>
<td>~$600 million</td>
</tr>
<tr>
<td>Solanezumab</td>
<td>Alzheimer disease</td>
<td>1.9 points improvement on ADAS-Cog over placebo for lowest dose</td>
<td>Failed, unchanged ADAS-Cog</td>
<td>2100</td>
<td>18 months</td>
<td>Eli Lilly</td>
<td>~$600 million</td>
</tr>
<tr>
<td>Gammagard</td>
<td>Alzheimer disease</td>
<td>5.4 points improvement on ADAS-Cog over placebo</td>
<td>Failed, unchanged ADAS-Cog</td>
<td>390</td>
<td>18 months</td>
<td>Baxter</td>
<td>~$30 million</td>
</tr>
<tr>
<td>Coenzyme Q$_{10}$</td>
<td>Huntington disease</td>
<td>0.34 point improvement on Total Functional Capacity over placebo</td>
<td>Failed, study terminated early due to futility</td>
<td>609</td>
<td>5 years</td>
<td>NIH</td>
<td>~$22 million</td>
</tr>
<tr>
<td>Pridopidine</td>
<td>Huntington disease</td>
<td>1.0-1.2 point improvement on modified motor score over placebo in two trials</td>
<td>Failed, no significant improvement</td>
<td>400</td>
<td>6 months</td>
<td>Teva</td>
<td>~$100 million</td>
</tr>
</tbody>
</table>

UPDRS = Unified Parkinson's Disease Rating Scale; ADAS-Cog = Alzheimer's Disease Assessment Scale – Cognitive subscale
Sources: Dorsey ER, Papapetropoulos S, Xiong M, Kieburtz K. The First Frontier: Digital Biomarkers for Neurodegenerative Disorders. Digit Biomark 2017
Atri A et al. Effect of idalopirdine as adjunct to cholinesterase inhibitors on change in cognition in patients with Alzheimer disease: three randomized clinical trials. JAMA 2018
New tools can uncover new details about disease.
Future trials will incorporate new tools that transform clinical trials

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>20th Century</th>
<th>21st Century</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study design</td>
<td>Randomized, double-blind, parallel-group, placebo-controlled trial</td>
<td>Randomized, double-blind, parallel-group, placebo-controlled trial using adaptive designs</td>
</tr>
<tr>
<td>Study population</td>
<td>All comers with a given disease</td>
<td>Individuals selected based on phenotypic and genetic results</td>
</tr>
<tr>
<td>Study recruitment</td>
<td>Clinical practices</td>
<td>Global clinical trial registries and social networks organized by disease area</td>
</tr>
<tr>
<td>Trial visits</td>
<td>In person and audio calls</td>
<td>In person and audio and video calls</td>
</tr>
<tr>
<td>Data management</td>
<td>Paper and electronic forms</td>
<td>Electronic forms</td>
</tr>
<tr>
<td>Participant feedback</td>
<td>Limited, delayed</td>
<td>Almost universal, approximately real time</td>
</tr>
<tr>
<td>Outcome measures</td>
<td>Insensitive</td>
<td>Sensitive</td>
</tr>
<tr>
<td></td>
<td>Episodic</td>
<td>Frequent or continuous</td>
</tr>
<tr>
<td></td>
<td>Subjective</td>
<td>Objective</td>
</tr>
<tr>
<td></td>
<td>Provider centered</td>
<td>Patient centered</td>
</tr>
<tr>
<td></td>
<td>In clinic</td>
<td>Remote</td>
</tr>
<tr>
<td></td>
<td>Unidimensional</td>
<td>Multidimensional</td>
</tr>
</tbody>
</table>

New model for clinical trials

Recruit → Pre-screen → Enroll → Conduct interim assessments → Conduct final assessment → Follow participants longitudinally

Current:
- Site
- Site
- Site
- Site
- Site
- Site

Future:
- Centrally & remotely
- Site
- Remotely
- Site
- Centrally & remotely
Outline

• Technology in Research Overview/Rationale
• Virtual Visits in Clinical Trials
• Mobile Measures
• Telehealth in Clinical Care
Virtual studies offer many advantages over traditional site-based approaches

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Traditional Model</th>
<th>Virtual Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geographic Reach</td>
<td>Determined by site location</td>
<td>Determined by internet access</td>
</tr>
<tr>
<td>Sites</td>
<td>Many</td>
<td>One</td>
</tr>
<tr>
<td>Institutional Review Boards</td>
<td>Many</td>
<td>One</td>
</tr>
<tr>
<td>Time to initiate study</td>
<td>Long</td>
<td>Medium</td>
</tr>
<tr>
<td>Investigators</td>
<td>Many</td>
<td>Few</td>
</tr>
<tr>
<td>Time required for visits</td>
<td>Long</td>
<td>Short</td>
</tr>
<tr>
<td>Variance in assessments</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Burden on participants</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Cost</td>
<td>$$$$$$$</td>
<td>$$</td>
</tr>
</tbody>
</table>
National studies can be conducted from single sites

Map of participants in a virtual research study

Source: Journal of Parkinson's Disease, 2015; 5: 505-515
Research participants like virtual visits

Over 80% of participants said they would be more willing and able to participate in future research studies if could do so remotely.

Source: Journal of Parkinson's Disease, 2015; 5: 505-515
Virtual visits are being used for longitudinal follow-up of large clinical trials (AT-HOME PD)

**Objective:** To leverage modern technology to develop, pilot and implement a 100% virtual model for long-term follow up of clinical trial cohorts utilizing telemedicine and smartphone platforms for quantitative monitoring of clinician- and patient-reported outcomes.
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Mobile technologies can enable more objective, sensitive, and frequent measures of PD.
Smartphone and wearable sensor studies in neurology, 1992-2017

Source: PubMed searches of smartphone and wearable sensor studies for neurology and associated conditions on 12/31/2017
New tools enable research to be conducted at unprecedented scale and scope

Geographical representation of study participants (N~1000 participants)

Source: Smartphone PD
Smartphone research apps contain surveys, structured tests, and passive monitoring.
A mobile Parkinson disease score has been developed using a smartphone application.

The mobile Parkinson disease score reveals inter-day variation that the traditional assessments miss.

Individual with advanced Parkinson disease

Number of tests: 152

Source: Zhan et al. Calculating Parkinson disease severity from a smartphone: the mobile Parkinson disease score. *JAMA Neurol* [in press]
Smartphone apps can detect responses from medications

Comparison of change in mPDS and MDS UPDRS Part III between the OFF and ON medication states

Source: Sage Bionetworks
Despite the many benefits of health applications, they still face challenges

<table>
<thead>
<tr>
<th>Limitation</th>
<th>Description</th>
<th>Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selection bias</td>
<td>Most health applications and research studies are only available on iPhone</td>
<td>• Make health applications available on Android devices</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 77% of Americans currently own smartphones</td>
</tr>
<tr>
<td>Retention</td>
<td>After initial interest in health applications interest and use wanes</td>
<td>• Increase valuable feedback to participants</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Provide data relative to other participants</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Predict course of disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Increase engagement with healthcare team</td>
</tr>
<tr>
<td>Privacy</td>
<td>Study participants are concerned over the privacy of their health data</td>
<td>• Disclose who has access to data</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Give study participants ability to choose who gets their data and for what purpose</td>
</tr>
<tr>
<td>Validation</td>
<td>Health applications need to be validated and their efficacy determined</td>
<td>• Validate health applications in in-person observational studies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Use in clinical trials for validation</td>
</tr>
</tbody>
</table>

Source: http://www.pewresearch.org/fact-tank/2017/01/12/evolution-of-technology/
Wearable Sensors
We evaluated wearable sensors for Parkinson disease and Huntington disease

MC10 BioStampRC

Sensor-MD Overview:
- We enrolled 56 participants
  - 16 with Parkinson disease
  - 15 with Huntington disease
  - 5 with prodromal HD
  - 20 without a movement disorder
- Participants wore 5 sensors on their chest and limbs

Source: http://www.mc10inc.com/our-products/biostamprc
Sensors can distinguish between individuals with and without movement disorders

Comparison of gait between an individual with HD and a control

Source: Adams et al. Multiple wearable sensors in Parkinson and Huntington disease individuals: a pilot study in clinic and at home. Digital Biomarkers 2017
Not only can sensors track known motor symptoms over time...

Frequency and severity of tremor detected over one hour period

Source: Adams et al. Multiple wearable sensors in Parkinson and Huntington disease individuals: a pilot study in clinic and at home. Digital Biomarkers 2017
...but can also capture novel data objectively and continuously in clinic and at home

Proportion of day individuals spend lying down, sitting, standing, and walking

Control
n = 20

Sitting 34%

Standing 12%

Lying 34%

Stand/Sit 10%

Walking 10%

Proportion of time in each state
100%
80%
60%
40%
20%
0%

Parkinson disease
n = 16

Sitting 32%

Standing 9%

Lying 38%

Stand/Sit 13%

Walking 9%

Huntington disease
n = 14*

Sitting 26%

Lying 50%

Stand/Sit 7%

Standing 10%

Prodromal Huntington disease
n = 5

Sitting 27%

Lying 33%

Stand/Sit 15%

Walking 11%

Standing 15%

Source: Adams et al. Multiple wearable sensors in Parkinson and Huntington disease individuals: a pilot study in clinic and at home. Digital Biomarkers 2017
In collaboration with MIT, we are now using cellular waves to monitor gait and movement.

Source: http://www.emeraldforhome.com/
Video analytics are another emerging tool for measuring disease. Requires only webcam, microphone and an internet connection.
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Access to PD care is limited and has adverse health and economic consequences

40% of individuals with PD do not see a neurologist

Those who do not see a neurologist are...

- 15% more likely to have a hip fracture
- 20% more likely to be placed in a skilled nursing facility
- 20% more likely to die

New models bring care to patients rather than patients to care
Virtual visits flip the care paradigm

Patient time spent on in-person versus telemedicine visits

Connect.Parkinson: a national randomized controlled trial of telemedicine in PD

**Aims**

1. To demonstrate the feasibility of using telemedicine to deliver specialty care into the homes of individuals with PD
2. To evaluate its effect on quality of life
3. To assess the impact on quality of care
4. To evaluate the value of the approach to decrease caregiver burden, save time, and reduce travel

**Source:** National randomized controlled trial of virtual house calls for Parkinson disease. *Neurology* 2017
Connect.Parkinson was conducted nationally in collaboration with:

- Northwest Neurological, Inc.
- Oregon Health & Science University
- UC San Francisco
- The Parkinson's Institute and Clinical Center
- Mayo Clinic
- Park Nicollet
- University of Rochester Medical Center
- Feinberg School of Medicine
- Northwestern University
- Johns Hopkins Medicine
- Penn Medicine
- North Shore LIJ
- The University of Kansas Medical Center
- Duke Medicine
- GRU
- University of South Carolina
- UF
- UHealth
- University of Miami Miller School of Medicine
- National Parkinson Foundation
- PCORI
- SBR Health
- Deliver Care Anywhere
- patientslike.me
- Vidyo
Patients like virtual visits

Source: National randomized controlled trial of virtual house calls for Parkinson disease. *Neurology* 2017
Who: Any New Yorker with Parkinson disease
What: Multidisciplinary care including virtual visits with a Movement Disorders specialist
Where: New York state, especially the 9 counties surrounding Rochester
When: Now
Why: To provide comprehensive PD care to residents of New York state, especially the underserved

Supported by: Greater Rochester Health Foundation and the Edmond J. Safra Foundation

For more information: www.pdcny.org
We are reaching patients throughout New York state
Take-home points

• Technology is pushing the migration of care and research from the hospital/clinic to the home

• Telemedicine and mobile tools are poised for exponential growth and can improve research and clinical care for our patients
UR Named National Center of Excellence for Parkinson’s Research

Wednesday, October 03, 2018

The University of Rochester has been selected as a Morris K. Udall Center of Excellence in Parkinson’s Disease Research by the National Institute of Neurological Disorders and Stroke (NINDS). The new $9.2 million award brings together researchers from industry and multiple academic institutions to focus on the development of digital tools to enhance understanding of the disease, engage broad populations in research, and accelerate the development of new treatments for Parkinson’s disease.