Digital Health in the Age of Big Data

Lena Granovsky, PhD
Director, Analytics & Big Data, Global R&D

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Technology and AI are here!

- As for November 2017, there were 318,000+ health apps and 340+ sensor devices available (with the number of apps doubling every two years)
- People are being equipped with new monitoring devices – portables, wearables, implantables or even digestibles!
- Patients are ready for the change
- Physicians have already adopted technology

But what about pharma?

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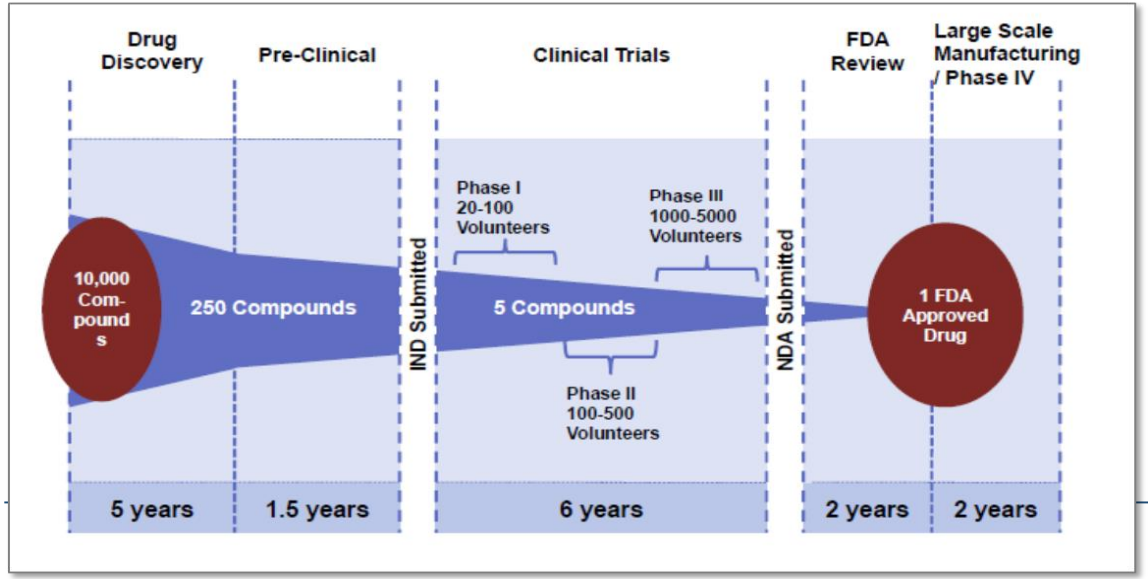
Clinical trials - the old way

- Remained relatively unchanged for the last 20 to 30 years
- Developing a new medicine takes about 10-15 years and several billion dollars
- Difficult to enroll and execute
- Centered around sites (and not patients)



Success rate is low

- Success rates in bringing a drug from discovery through to commercialization are low and getting worse, despite **increasing** costs
- Possible reasons for failure:
  - Subjective and biased reporting
  - Wrong patient populations
  - Wrong assumptions
  - Data quality issues
  - Operational failures

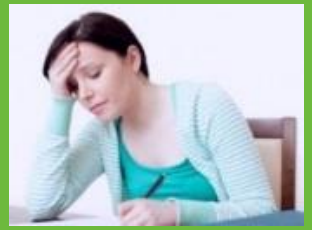
- Sometimes failure is caused by a limitation of the development process and not the pharmacology

Analytics and big data can be used to change it!

We can make the change - technology and AI are here!

Site selection:

Leverage advanced analytics to select better sites based on past performance and suitability for the trial



Patient selection, better retention:

- Enrolling through social media
- RWE to improve inclusion criteria (e.g. EMRs)
- Predictive models to estimate early termination rate

Overhauling study design

Leverage advanced analytics, RWE, historic trial data to develop study models and optimize study parameters

We can make the change - technology and AI are here!

Improving clinical data management

Real time and continuous monitoring of data

- Monitor the patient between site visits
- Develop novel digital markers that can be used as clinical objective endpoints
- Digital markers can be used as disease management tools and measures of quality of life
- Predictive algorithms can be build to estimate risk of worsening of medical condition

Case Study

Cluster Headache

Developing precise measures of disease severity & drug response

A Teva-Philips Collaboration

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Cluster Headache (CH)

Primary headache disorder characterized by repetitive attacks of excruciating unilateral head pain

- CH is one of the most painful conditions known to mankind
- A rare type of one-sided headache (affects 1 in 1,000)
- Prevalence of 0.1-0.4%, men 4-5 times more than women
- Attacks happen in distinct periods of time (episodic) or w/o remission (chronic)
- Age of onset 20-40 y/o
- Pathophysiology complex and not fully understood

Cluster Headache digital health sub-study

Teva using Philips Actiwatch and ERT eDiary

- Nocturnal attacks of CH are temporally related to the REM sleep phase, the first of which typically occurs roughly one hour after sleep onset
- Patients with cluster attacks do not try to rest in silent place like migraine patients, they move!

What Are We Exploring?

- Sleep/Wake patterns (sleep time, sleep onset latency, wake after sleep onset and sleep efficiency) on days with and without cluster headache attacks
- Steps, movement and physical activity on days with and without cluster attacks

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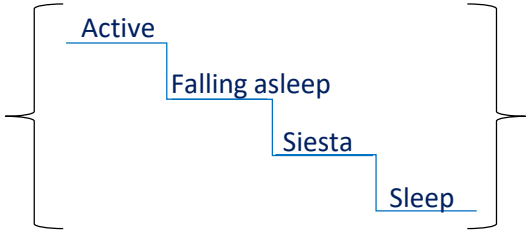
Using Sleep/Wake and activity data for CH detection and prediction

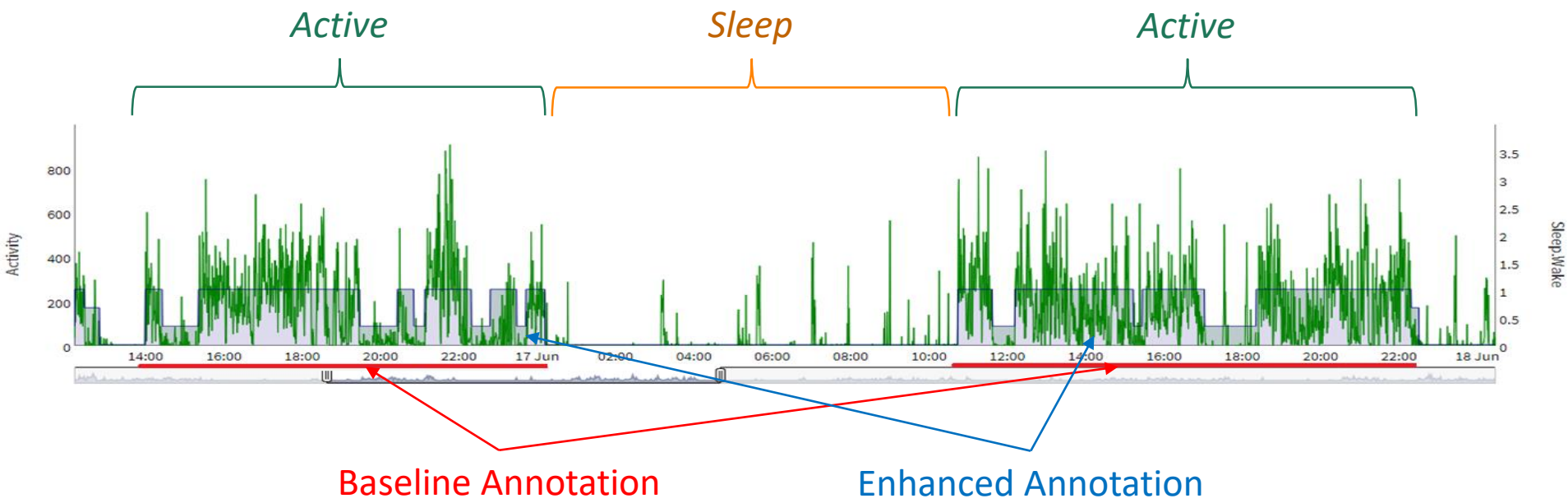
Goal: Determine whether activity and sleep/wake patterns in the data are associated with cluster headache attacks that ultimately can be used for diagnosis and/or prediction of the attack

Step 1: Refine traditional sleep/wake states

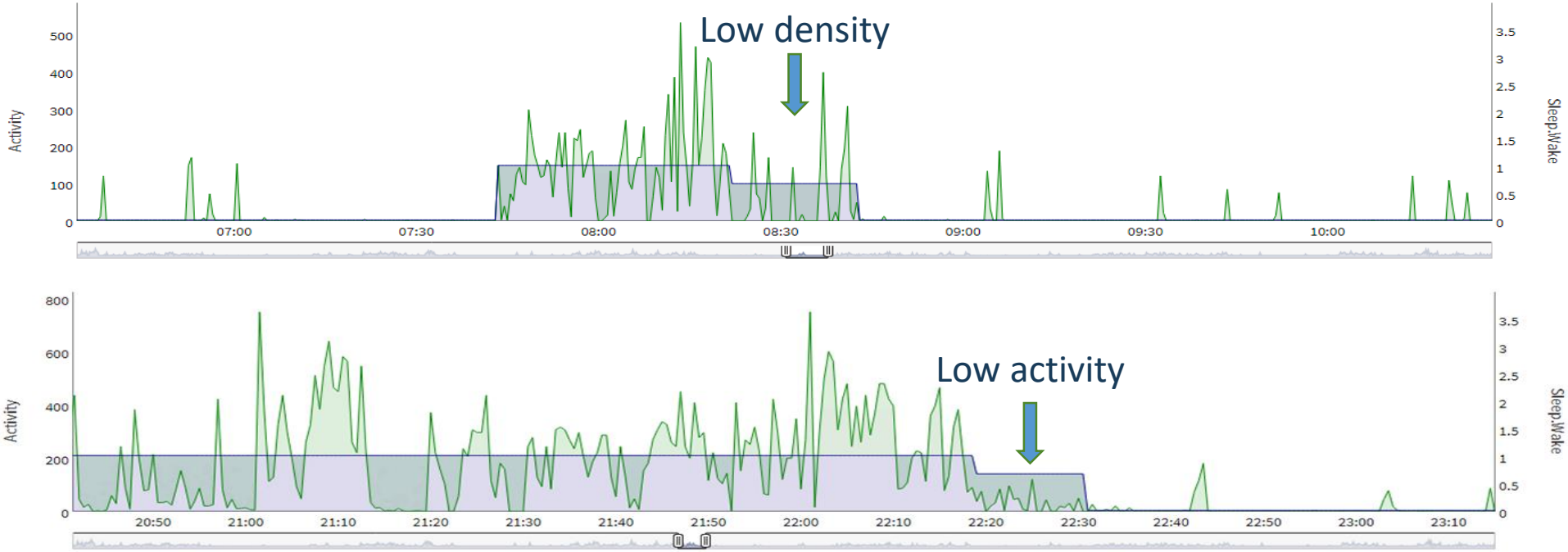


A	B	C	D
Date	Time	Activity	Sleep/Wake
02/15/2017	3:35:30 PM	154	1
02/15/2017	3:36:00 PM	105	1
02/15/2017	3:36:30 PM	215	1
02/15/2017	3:37:00 PM	159	1
02/15/2017	3:37:30 PM	56	1
02/15/2017	3:38:00 PM	134	1
02/15/2017	3:38:30 PM	76	1
02/15/2017	3:39:00 PM	245	1
02/15/2017	3:39:30 PM	253	1
02/15/2017	3:40:00 PM	208	1
02/15/2017	3:40:30 PM	176	1
02/15/2017	3:41:00 PM	70	1
02/15/2017	3:41:30 PM	125	1
02/15/2017	3:42:00 PM	424	1

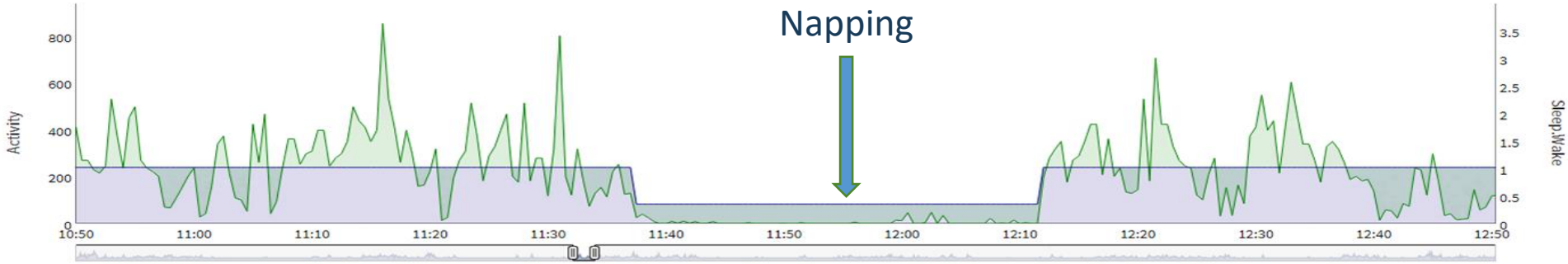
(Traditional) data annotation

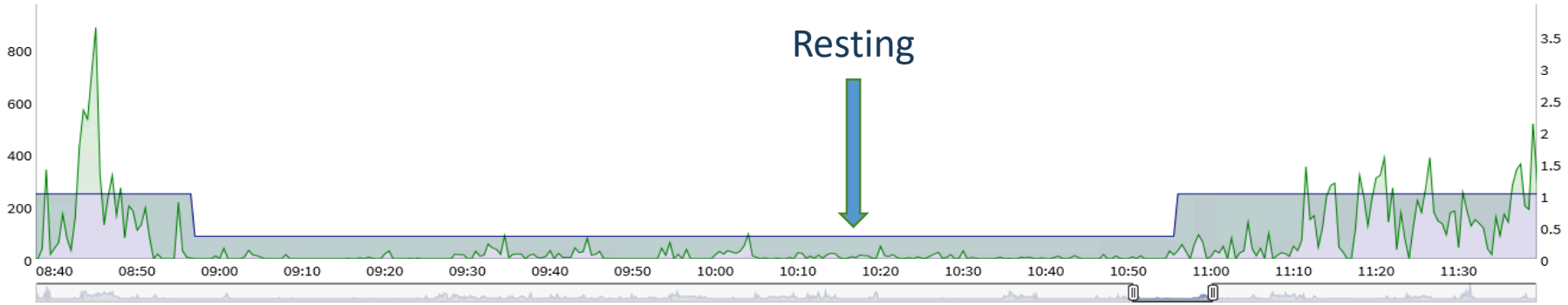


Refinement #1 – “Falling asleep”



Refinement #2 – “Siesta”

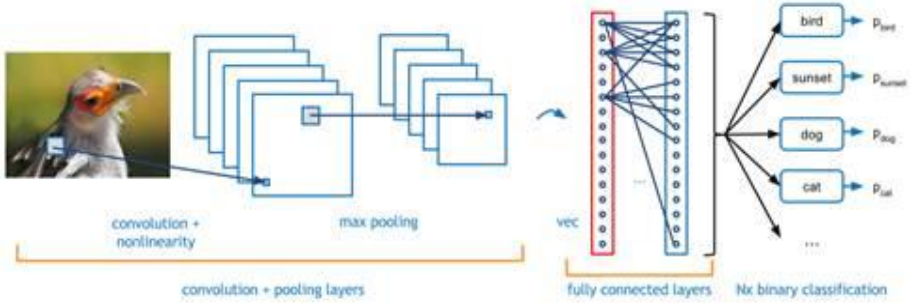




Development of digital markers in CH

<u>Step 1:</u>
We used advanced machine learning techniques to detect the refined sleep/wake states

<u>Step 2:</u>
These states (in addition to other data) are now used for developing personalized digital markers for objective measurements of headaches and cluster headaches



Case Study

Huntington Disease

Digital Health Study

A Teva-Intel Collaboration

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Huntington Disease digital sub-study

- Progressive brain disorder that causes uncontrolled movements, emotional problems, and loss of thinking ability (cognition)
- Motor symptoms in HD are typically evaluated by physicians using a rating scale
- Patients are forced to travel to undergo an exhausting 5-8hr visit

Teva to Develop Unique Wearable Tech and Machine Learning Platform for Continuous Measurement & Analysis of Huntington Disease Symptoms in Collaboration with Intel

September 15, 2016

Depiction of person with chorea

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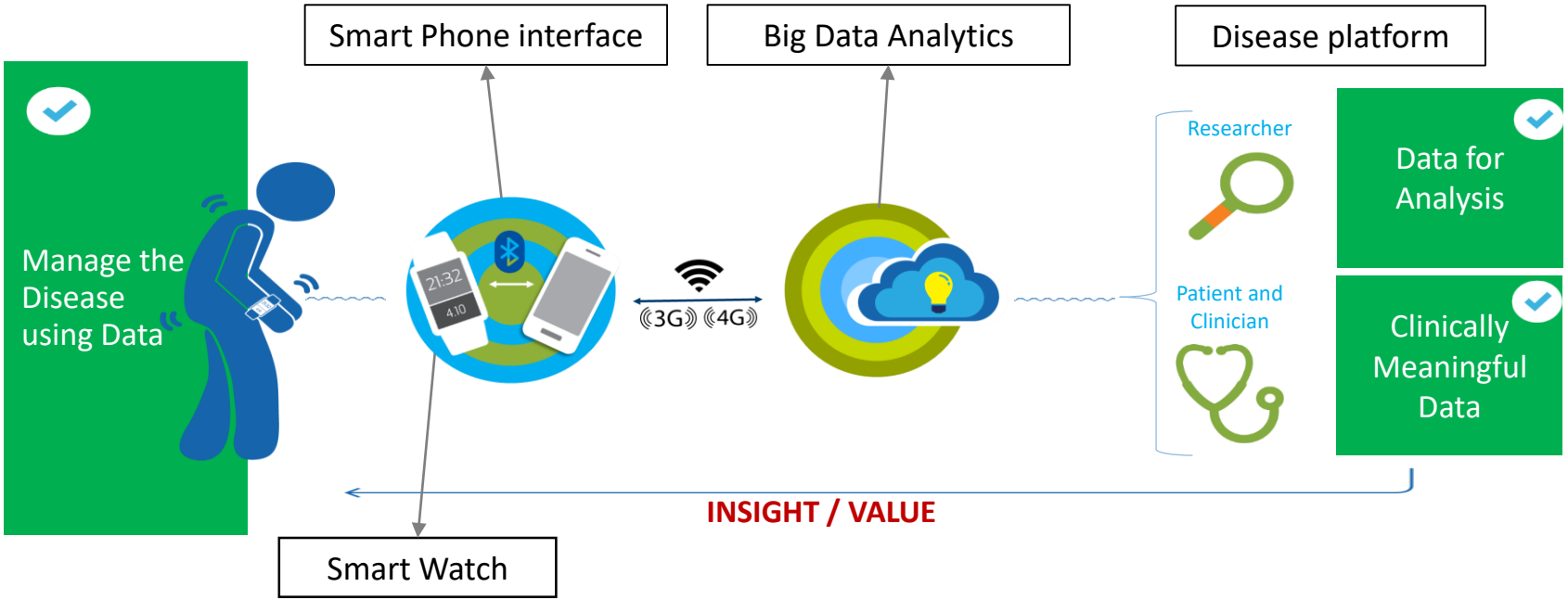
Digital Health Solution for Huntington Disease Patients*

A Teva-Intel Collaboration



Wearable Systems in Healthcare (a.k.a mHealth) are built on top of IoT technology

(*)Presented at the 9th European Huntington's Disease Network Plenary Meeting, Sept 16–18, 2016

The Mobile Application

The mobile application provides **assessment instructions** and **medication reminders**

Two types of assessment sessions

- **At-Home Assessment** – A short (2 tasks) session, conducted every other day
- **In-Clinic Assessment** – A longer (7 tasks) session, conducted at clinic visits

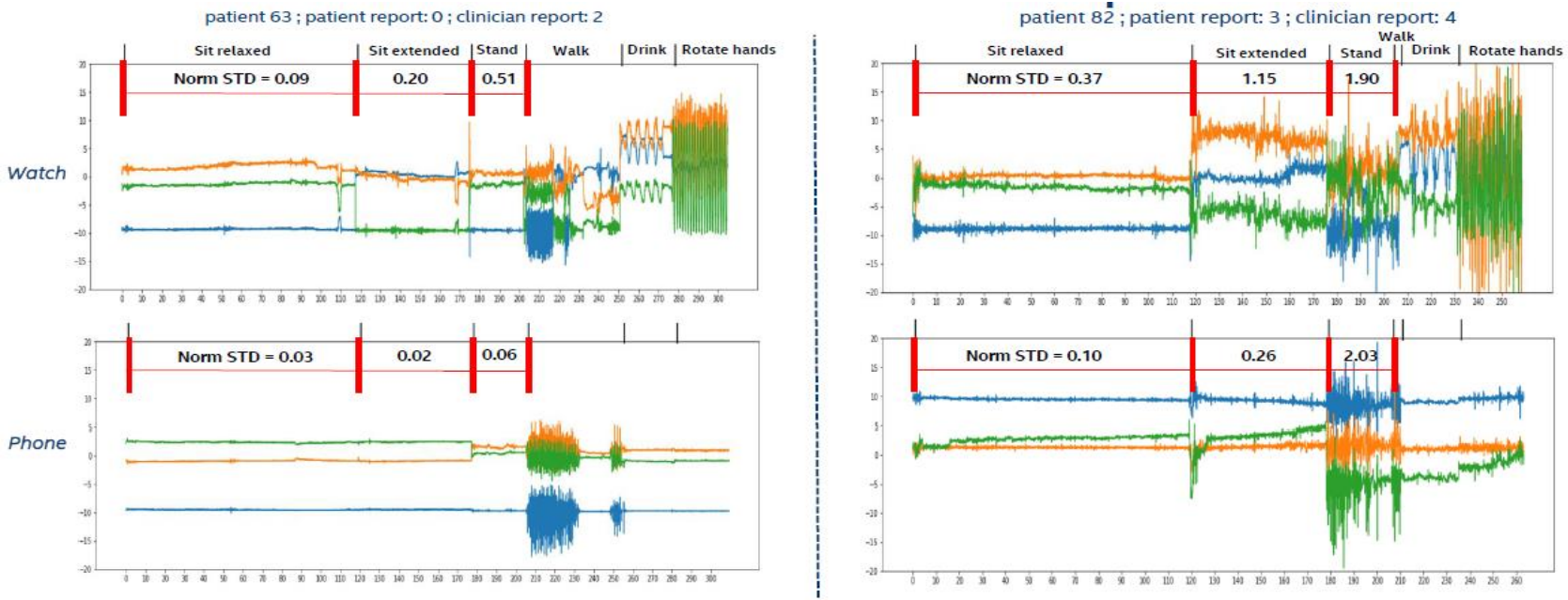
Self Assessment

1. Sitting at rest with arms relaxed
2. Standing at rest

In-Clinic Assessment

1. Timed Up and Go (TUG) test
2. Sitting at rest with arms relaxed
3. Sitting at rest with arms extended
4. Standing at rest
5. Ten-meter walking Test
6. Drinking from a cup test
7. Pronation-supination test

Preliminary Analysis



- Accelerometer signal variability indicates the existence and severity of Chorea
- Significant variability between body parts as captured by smartwatch and iPhone

Adoption of digital technology is slow!

- Infrastructure, data integration and analytics
- Quality of data and reliability of digital devices
- Privacy, security and safety of healthcare/trial interventions delivered using remote tech
- Impact of mobile tech on the quality of interactions between patients and site staff and possible bias caused by using the technology
- No clear statistical methodology for design of trials utilizing wearable data
- No clear pathway exists for regulatory validation and acceptance of trials using mobile technology

Global consortia

Pharma companies have formed new groups to create an open innovative initiative to reposition drugs.

<u>The key objectives of the programs:</u>

1. To identify appropriate digital devices & platforms for the transformation of the standard clinical endpoints into digital endpoints;
2. To experimentally test the validity of the proposed digital endpoints in clinical trials, with the final aim to select a few endpoints and progress them to obtain qualification from regulatory agencies;
3. Design of a clinical & regulatory plan with appropriate data analysis leading to a scientific validation for the proposed digital endpoint.

Vision of the Future

https://www.youtube.com/watch?v=rj_FGR8qwnE&feature=youtu.be

Concluding remarks

- Analytics & Big Data are key to the digital revolution in healthcare
- Companies can significantly shorten clinical trials, reduce costs and increase the consistency and integrity of their data
- Proof points and building blocks already exist
- According to recent report of BCG, implementing them together at scale will double the economic value of a pharmaceutical company's product
- Leading Information/Data sources
  - Today: Real World Evidence (EMR, Claims), Digital (Wearables, Sensors)
  - Next: Medical Images, Voice, Social Media

These are exciting times in Pharma and Healthcare where Analytics and Big Data are embraced
It is the ***Time to Innovate***

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Thank You!