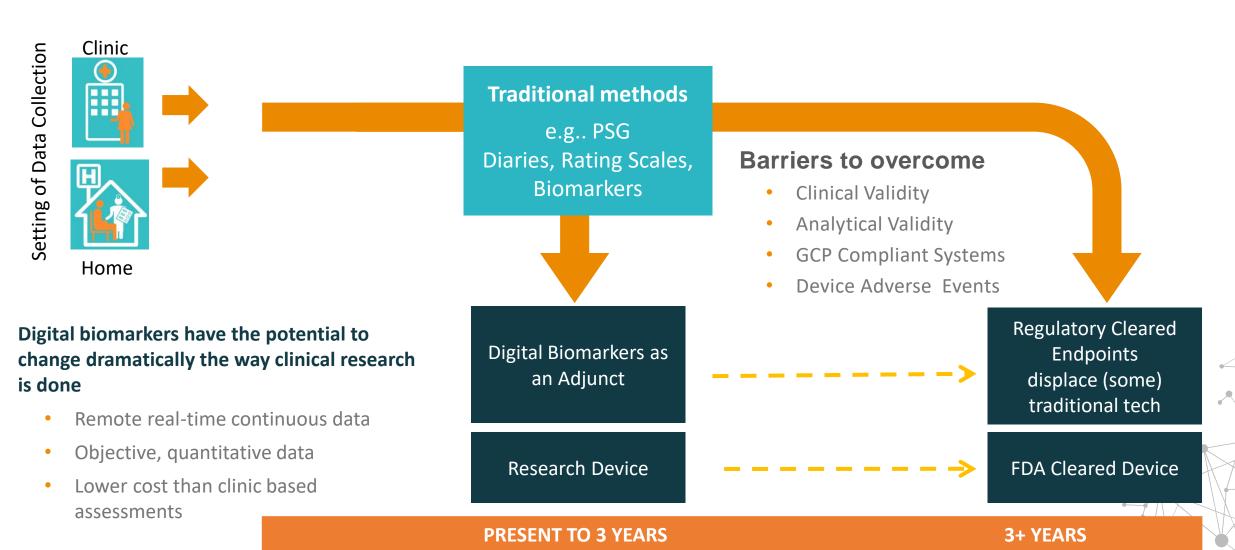


### Market evolution: biosensors and digital biomarkers





### Digital Biomarker Development



#### **Biomarker Discovery**

#### **Goals**

Evaluating biosensor measurements as markers of disease state and change

- Digital biomarker or disease signature identification with
  - Analytical Validation
  - Clinical Context
  - Clinical Validation
  - Regulatory pathway

#### Requirements

- Selection of most appropriate consumer or medical grade BMD for clinical population and research context
- Comparison of BMD & standard subjective assessment methods in different populations & disease states
- Development of state-specific algorithms
- Data management & QC
- Regulatory framework & compliant SOPs

#### **Clinical Trials**

#### Goals

### Using qualified biosensor outputs in exploratory, phase II/III clinical trials

- For population stratification/enrichment
- For monitoring of trial population
- As exploratory endpoints
- As secondary (or 1ry) endpoints
  - Safety
  - Efficacy

#### Requirements

- Building on expertise as lead imaging CRO in numerous CNS drug registration trials
- Working with regulatory bodies & pharma industry to define end-points
- Operational delivery capabilities
- Relationships
- Regulatory framework & SOPs
- Data management & QC

# **Clinical Practice Companion Digital Services**

#### **Goals**

### Using qualified biosensors to improve clinical outcomes

- Diagnosis
- Treatment targeting or switching
- Patient engagement & retention
- Monitoring & informing decision making
  - Disease progression
  - Relapse identification
  - Safety & efficacy
  - Adherence

#### Requirements

- Collection & analysis of actigraphy data from real-world settings
- Companion digital product experience
- Design of products with positive user experience
- Privacy & security
- Data management & QC

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# Framework for validation of biosensor derived endpoints - Example, Sleep in PD from a wrist worn accelerometer



**Biological Parameter** 

Wrist Movement

Sensor Data

Raw Accelerometer Units

Algorithm

Sleep / Wake

Endpoint

Clinically validated
Sleep Endpoints for
Parkinson's Disease

Sleep Measurement in PD through Wrist Movement

### Extracting Clinical Value From Actigraphy Metrics



#### Activity

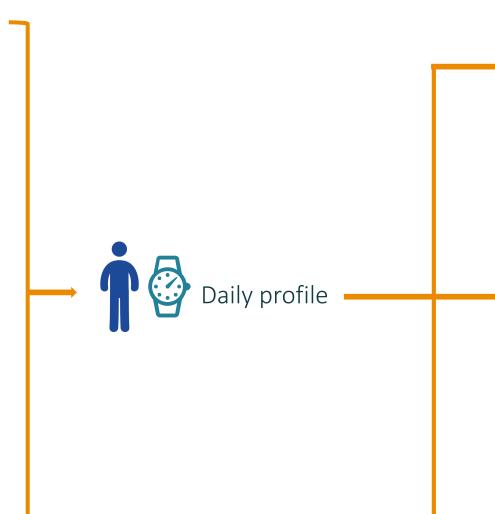
- day time activity
- evening activity
- nocturnal activity
- quantity and quality
- tremor
- bradykinesia
- PD on/off
- falls
- etc.

#### Sleep

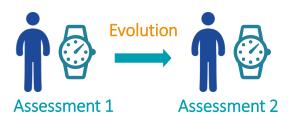
- sleep latency
- sleep efficiency
- number of awake times
- awake time duration
- circadian rhythm
- sleep stages
- etc.

#### Mood and Behaviour

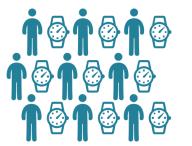
- Depression
- Social Withdrawal



Individual signature



Disease signature



Risk

Diagnosis

**Prognosis** 

Treatment response

e.g.. Alzheimer's, Parkinson's, ADHD, mood disorders, psychosis...

**Drug Effects** 



Risk
Side Effects

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## GCP compliant approach to wearables: IXICO's (current) approach I IXICO



Issue	(Current) IXICO Solution
GCP Compliant Data Collection	Closed data management Building on >10 years imaging
Data Privacy	Device handling by site. No cloud transmission
Data Format	Raw data - provides maximum flexibility in analysis
Device independent	"bridging strategy" to new technology
Clinically meaningful	"Gold Standard" Studies support algorithm development and validation
Data integrity	Simple device operation with data local download
Easy "User interface"	Data returned by hand or in post – no need for smart phone, Wi-Fi etc.
Low site and patient burden	Passive device - fit and forget
Blinded data collection	Passive device - fit and forget



### Digital Biomarker Discovery



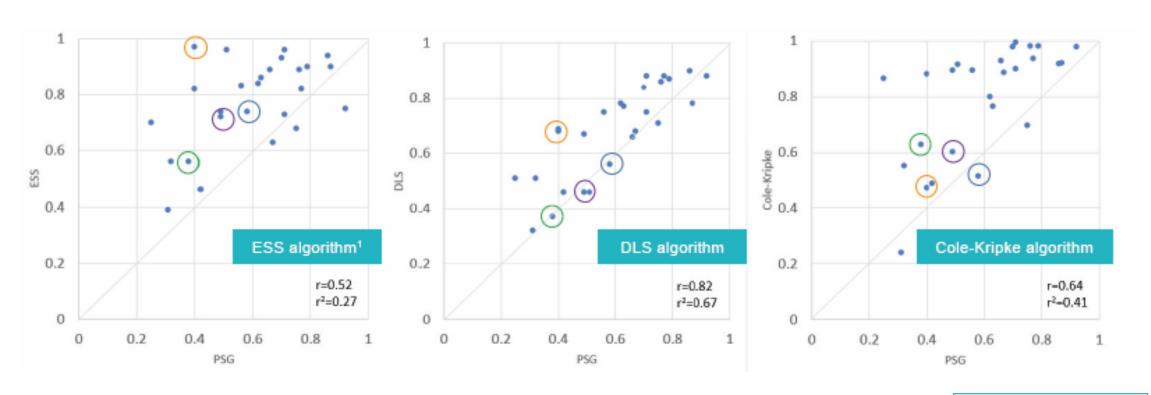
Example: Development of actigraphy-based measures for sleep using gold standard PSG data



### Digital Biomarker Discovery



Comparison of Actigraphy Algorithms Versus PSG



**ESNIEXI** 

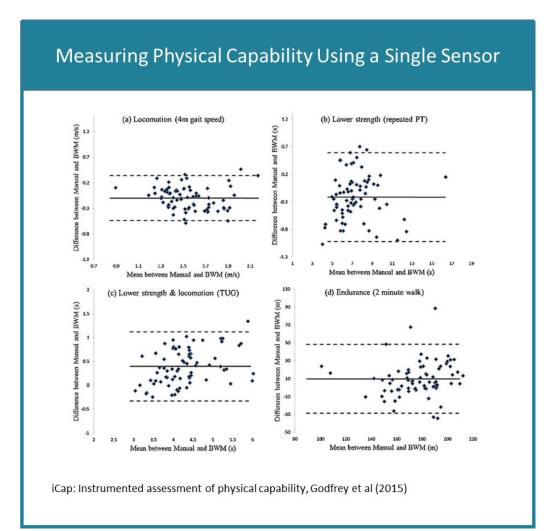
Presented at MDS 2017 (Vancouver) and Alzheimer's Association Research Round Table, June 2017

### Digital Biomarker Discovery



Developing Measures Avoiding Excessive Site and Patient Burden

## Correlating Step Count to EDSS using Consumer Device EDSS vs Daily Step Count Daily Step Count, Averaged Across Days, for All Patients 15000 10000 2-3.5 Average daily step count (measured using the Fitbit Flex) versus EDSS Block et al J Neurol. 2017 Feb;264(2):316-326. doi: 10.1007/s00415-016-8334-6. Epub 2016 Nov 28.

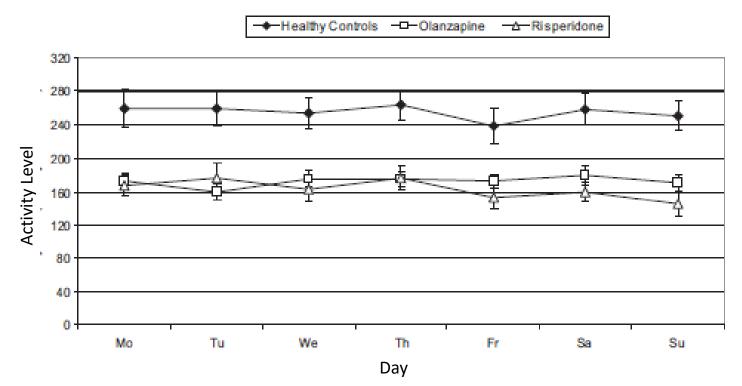




### Use of Actigraphy in Schizophrenia - Wichniak et al 2011



- Measured activity levels in subjects treated with olanzapine and risperidone versus healthy controls
- Found significant reduction in 24hr daily activity, lower daytime activity and longer time in bed
- Saw no difference in activity between olanzapine and risperidone treated groups
- Noted that choice of position of Actigraph is important and difficulty in comparing with other studies



Seventy-three patents with schizophrenia (n = 64) or schizophrenic form disorder (n = 9): Age (29.2± 10.2 years)

Wichniak A, et al 2011, Actigraphic monitoring of activity and rest in schizophrenic patients treated with olanzapine or risperidone. J Psychiatr Res. 2011 Oct;45(10):1381-6..

### Moving Forward through Building Partnerships



#### **Biomarker Discovery**

#### **Clinical Trials**

# **Clinical Practice Companion Digital Services**

#### **Collaborations**

- Academic collaborations to develop or test algorithms
- Device and technology companies collaborations to assess utility of new technology
- Patient advocacy groups and charities

#### **Collaborations**

- Deployment of exploratory measure in Commercial Pharma Drug Studies
- Deployment of validation measures in Commercial Pharm Drug Registration Studies
- · Clinical Data sharing
- CRO partnerships

#### **Collaborations**

- Data sharing e.g.. longitudinal studies
- Consortia to look at real world measures – e.g.. IMI ROADMAP
- Phase IV studies with pharma cos

Regulatory Pathway (e.g. CAMD)

Translation into Healthcare Practice (payers and Insurers)