

# Decentralised Clinical Trials and the scope to include Digital Data

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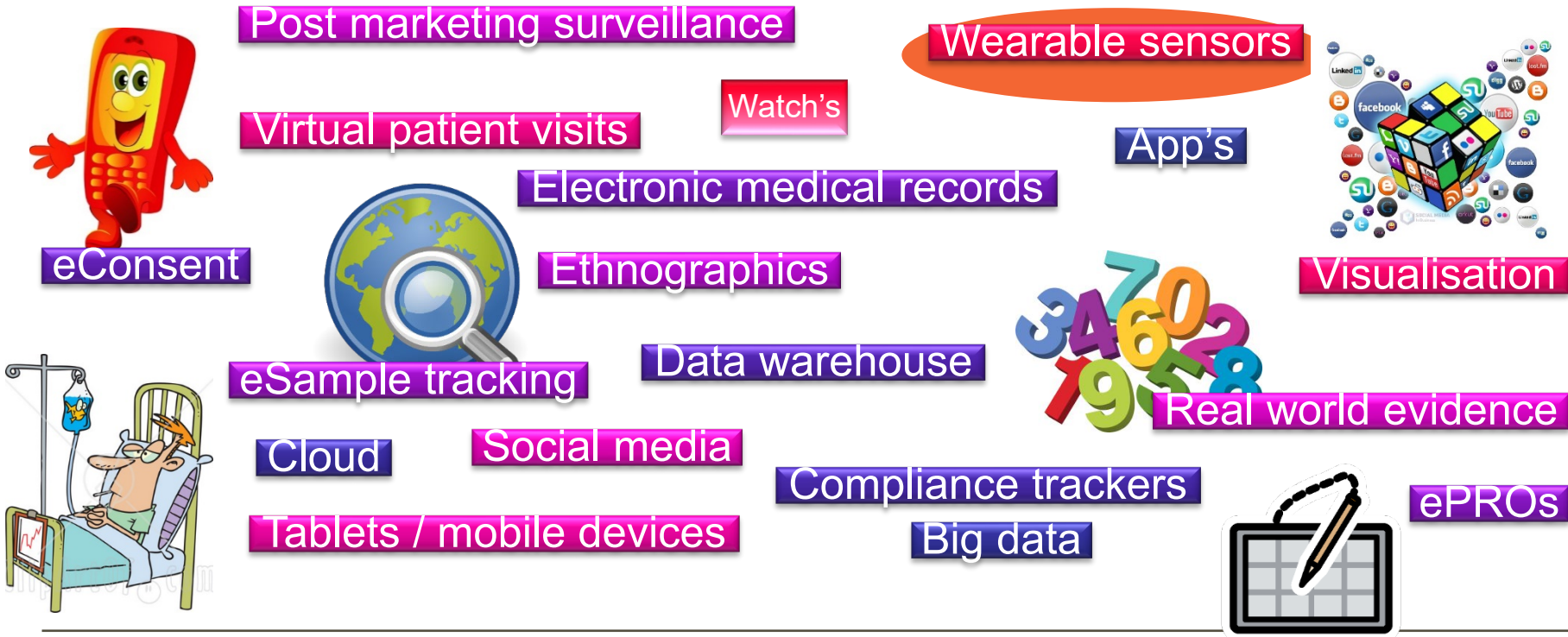
# Decentralised Clinical Trials



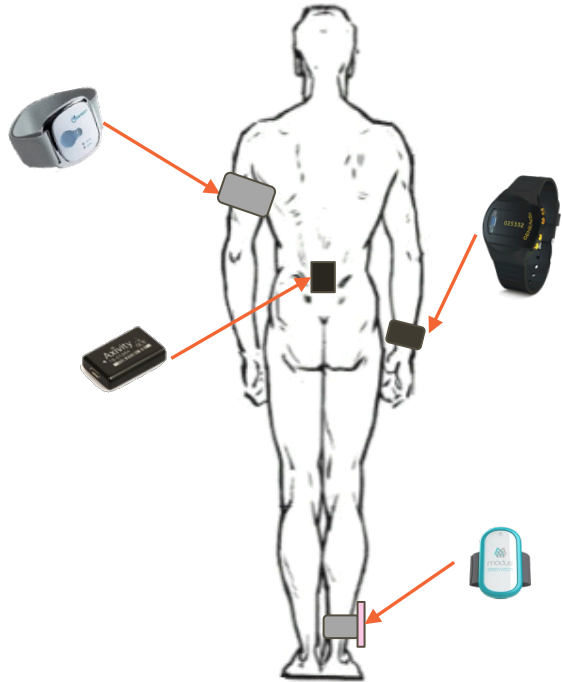
- Covid pandemic => virtual interactions with patients
- Need for technology to allow these interactions => advancements
- Decentralised clinical trials: Uses these virtual elements
- As move towards decentralised clinical trials, there is huge scope to incorporate digital data collection into clinical trials.



# What is Digital Data?



# Sensor data: Actigraphy



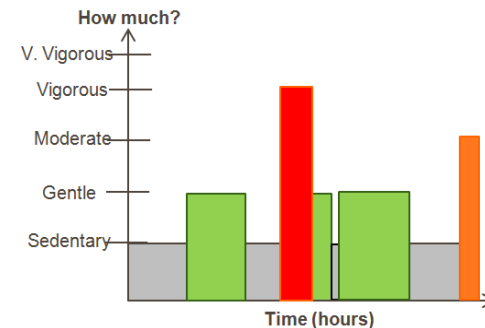
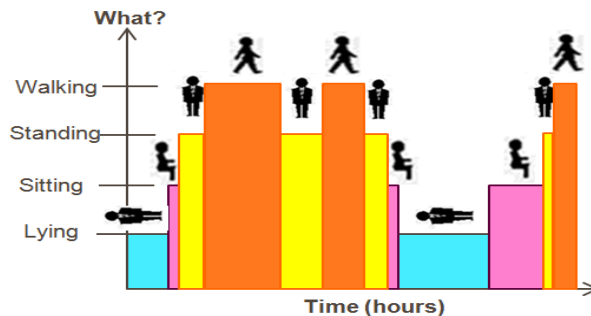
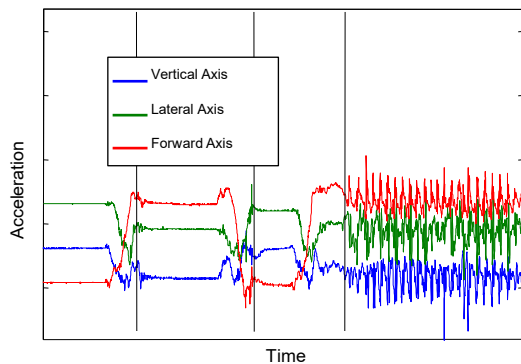
1 week

$300 \times 60 \times 60 \times 24 \times 7 = >180 \text{ million datapoints}$

# Actigraphy: Clinical trials

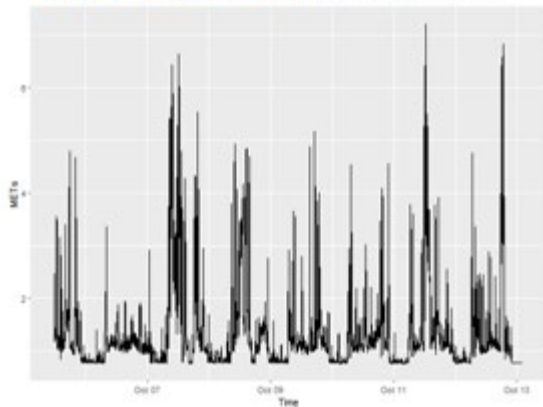


Raw data

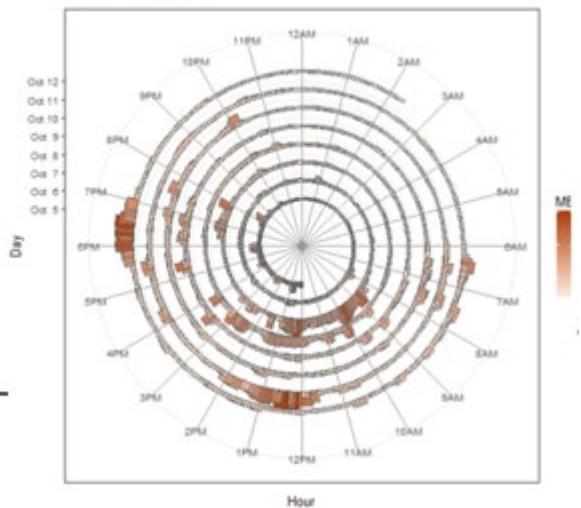


# Actigraphy: Clinical trials

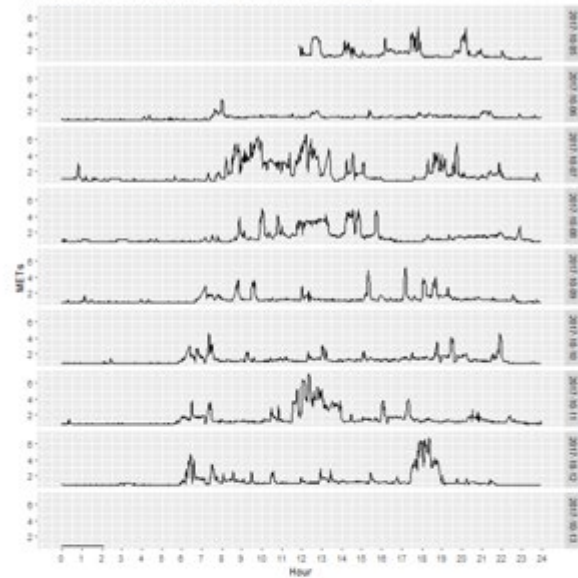
**A single time series:** rather uninformative



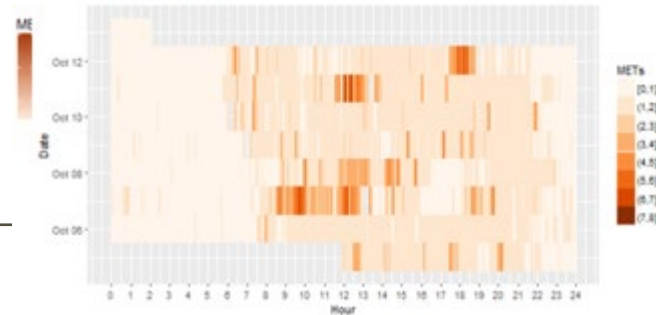
**Spiral plot:** Activity over 24h clock – cool!



**Stacked time series:** better appreciation of physical activity vs. time of the day



**Heatmap:** Requires categorising physical activity



- Amyotrophic Lateral Sclerosis (ALS)
  - Neurodegenerative neuromuscular disease with symptoms including muscle stiffness, gradual increases in weakness, difficulty in speaking/swallowing/breathing and eventually respiratory failure
  - ALS patients are expected to experience a gradual reduction in the level of daily physical activity
  - Study: Observational study of physical activity, night time rest, heart rate variability, speech
  
- Chronic Obstructive Pulmonary Disorder (COPD)
  - Group of lung conditions that cause breathing difficulties (emphysema, chronic bronchitis)
  - Study: Dose response study Phase II, Patients followed for 24 weeks
  - Sub study: 1 week of data at baseline, week 12, week 24

- Rheumatoid Arthritis
  - **PA**tient **R**heumatoid **A**rthritis **D**ata from the **rE**al world study (n~400)
  - Apple ResearchKit™ App
  - Real world patients could self recruit, consent, enroll, report entirely through iPhone
  - Participants were asked to provide demographics, comorbidities, medications, and RA symptoms including pain, fatigue, mood and morning stiffness.
  - Over 12 weeks completed validated questionnaires routinely used in RA clinical trials, namely HAQ, FACIT, and EQ-5D.
  - All data were self-reported and collected via their iPhone.
  
- [Using a ResearchKit Smartphone App to Collect Rheumatoid Arthritis Symptoms From Real-World Participants: Feasibility Study - PubMed \(nih.gov\)](#)



# Sensor data: Challenges

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## How do we choose a sensor type for the trial?

- Clinical hypothesis
- Patient population
- Wear location, duration, does it need to be waterproof?
- Design issues
  - Number of countries
  - Which country (import of devices, local country regulations)
- Ability to charge the device
- Data storage: volume of data that is required to be stored
- Downloadability of the data: can it be downloaded or backed up onto a phone
  - Format and content of actigraphy summary dataset may vary by vendor

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## What data processing is required?

- Is data access to cloud required in real time?
- Filter data corresponding to planned clinical visits
- Data quality rules pre-specified in the protocol
  - eg  $\geq 8$  hours for  $\geq 3$  days within the 7 day data collection period prior to the visit

## How can we analyse this type of data in a clinical trial to assess if the treatment works?

- Identify clinically meaningful endpoints
  - Summary measures
  - Consideration of continuous and categorical data on a minute by minute scale
- Apply appropriate statistical analysis techniques (eg Generalised Additive Models)
- Consideration: all sources of activity data could be correlated
- Need to consider computer capabilities

# Sensor data: Challenges



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**How can we analyse this data type in a clinical trial to learn about the patient population, disease progression, etc?**

- Identification of activity patterns? Differences between populations?
- How compare treatment groups

**What appropriate visualisation techniques should be applied to extensive data volume?**

- Identify appropriate visualisation techniques for representing the data

**Activity changes during the day, ie there are diurnal patterns; Or weekday v's weekend?**

- What happens in the second half of the day can vary by age
- How does the activity in the previous hour affect the activity in the next hour?
- Should this be considered in the statistical analysis?

**Relationship between novel digital endpoints and clinically standard ones?**

- eg how are FEV1 and actigraphy related in COPD patients?



# Sensor data: Challenges



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## How to deal with missing data?

- Compliance issues: consideration of how could be reduced (would DCTs help retention), and how dealt with in analysis
- Sometimes long gaps (up to a few hours) with missing data... in many subjects
- How deal with instances where have 0 steps, but >0 distance



## Longitudinal setting?

- Device worn at several periods during treatment phase
- How compare multiple time series within a patient?
- How do we produce a meaningful change from baseline?

## How do we ensure that the data is collected appropriately?

- Location of sensor – does it make a difference?
- How long should the sensor be worn, what volume of data is sufficient? eg how many days? What wear time within a day?
- Appropriate data format to fit into reporting systems



**Any Questions?**