



# Algorithms, clinical outcomes and digital biomarkers - Next generation endpoints

---

Adam Butler

Jane Tiller, MD, FRCPsych,  
MBA, MPhil



# Speakers

Anita Bajaj, MD, MPH

Adam Butler

Ariel Dowling, PhD

Ritu Kapur, PhD

Ian Marcus, MS

John Reynders, PhD

Jane Tiller, MD, FRCPsych,  
MBA, MPhil

# Algorithms, clinical outcomes, and digital biomarkers - Next generation endpoints

---

Introduction: Jane Tiller

# Disclosures

---

- CMO: of Neumora Therapeutics
  - Scientific Advisory Board: Woebot Therapeutics
  - Independent Board Member: Longboard Therapeutics
- 
- Thanks to Katherine Scangos for sharing her slides

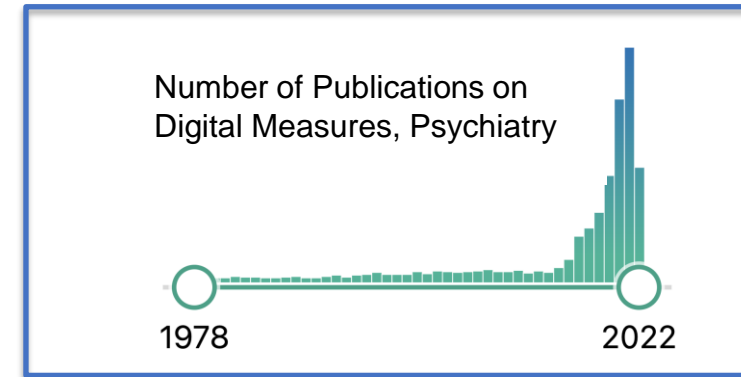
# Increasing Interest in Digital Biomarkers in CNS

## Opportunities

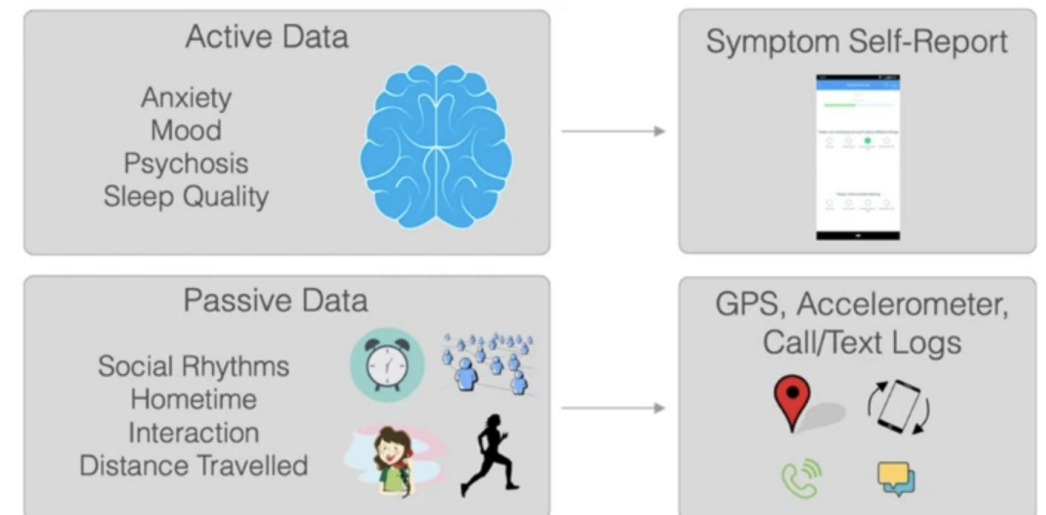
- Provides unique insights to quantify and characterize patient subtypes relevant for programs
- Facilitate study execution - via remote data collection. Can and increase the ability of underserved populations to participate in clinical trials
- Measurements can be more frequent or continuous; not restricted by scheduled clinic visits
- Assess disease metrics with objective measures and in patients' natural environment which may improve their accuracy (reduce noise) and separation of drug/placebo response.
- Opportunity to develop novel endpoints

## Challenges

- Immature digital infrastructure – practical deployment
- Significant methodological issues especially with continuous variables
- Verification, analytical and clinical validation
- Black box versus explainable AI



- Smartphone ownership: 44.9% worldwide
- Wearable device usage forecast to reach one billion by 2022



# Example: Remote Digital Assessments for Monitoring Change in Major Depression

Jacobson NC et al. npj Digital Medicine 2019

- Standard clinical care for MDD is time-consuming, resource-heavy, and often ineffective.
- Digital measures may allow passive detection of symptom severity changes to monitor
  - Clinical deterioration
  - Treatment response
  - Natural history

**Passive digital biomarkers:** scalable, unobtrusive, time-sensitive, cost-effective

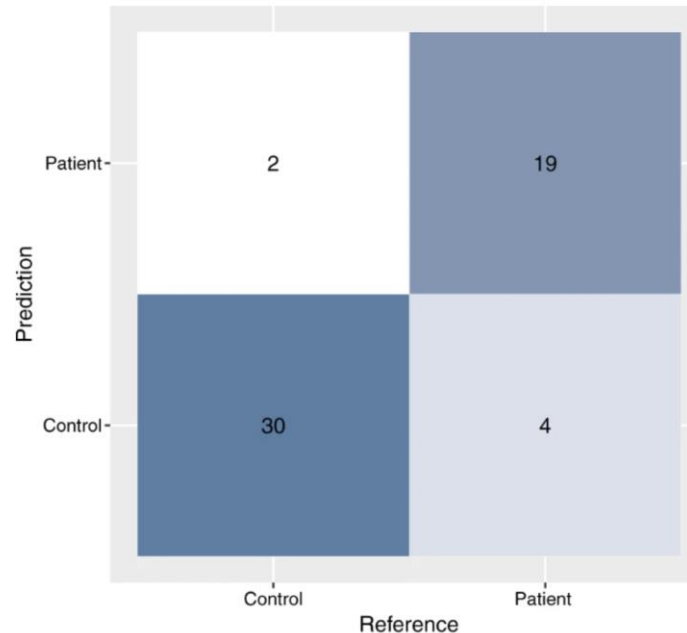
- **Actigraphs:**

- Movement data captures changes in goal-directed behavior, energy level, and movement
- Movement data + PPG (HR) sensors estimate changes in sleep onset, duration and architecture

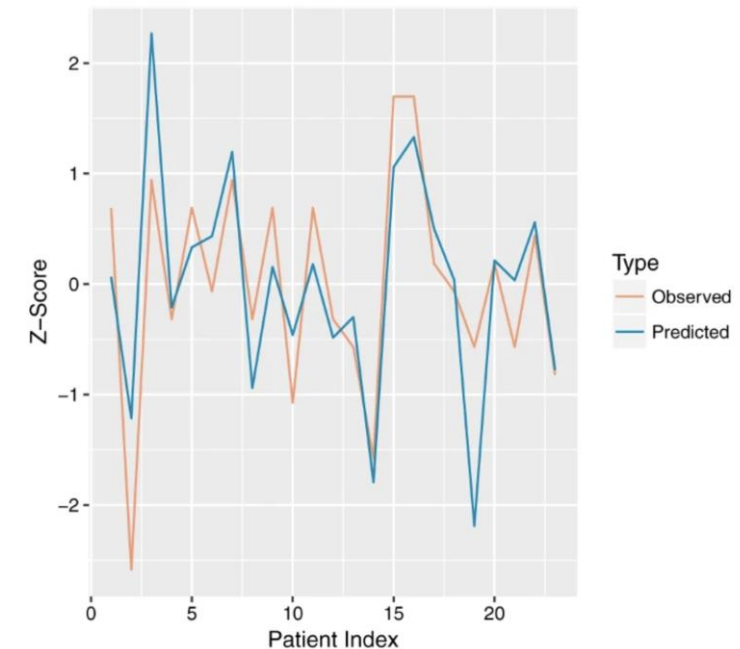
2 wks actigraphy data (actiwatch),  
N=23 MDD and BP patients  
Classification: xgboost, loocv

Predicted the majority of variation in patients' depression severity over ~2 weeks (MADRS pre-post difference scores).

Diagnostic Status  
Accuracy 89.1% Kappa 77.3%



Change in Depressive Symptoms  
 $r = 0.782$ ,  $p = 1.04e-05$



# RADAR-MDD Results: Longitudinal Collection of Remote Measures is Feasible

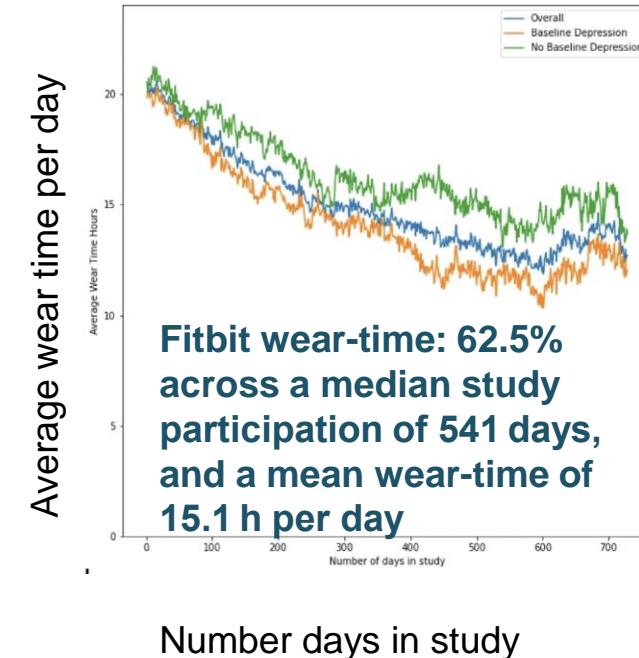
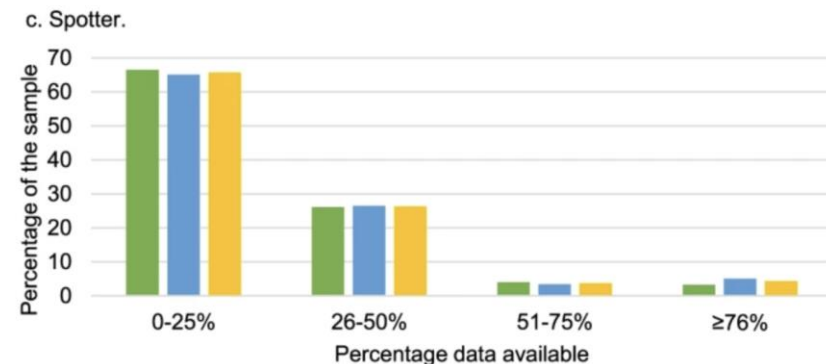
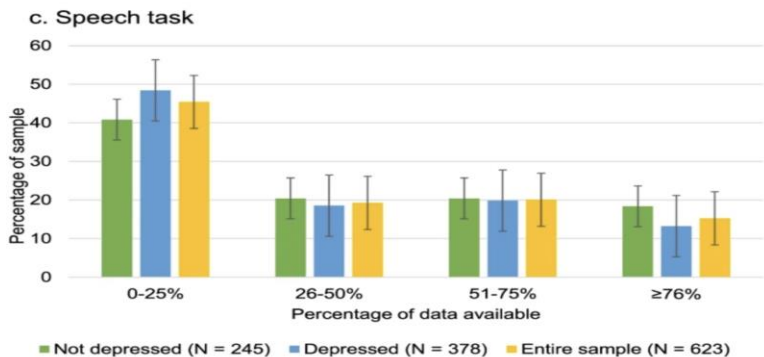
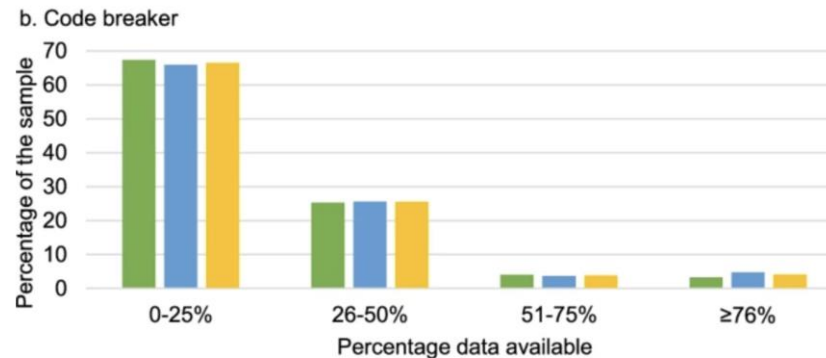
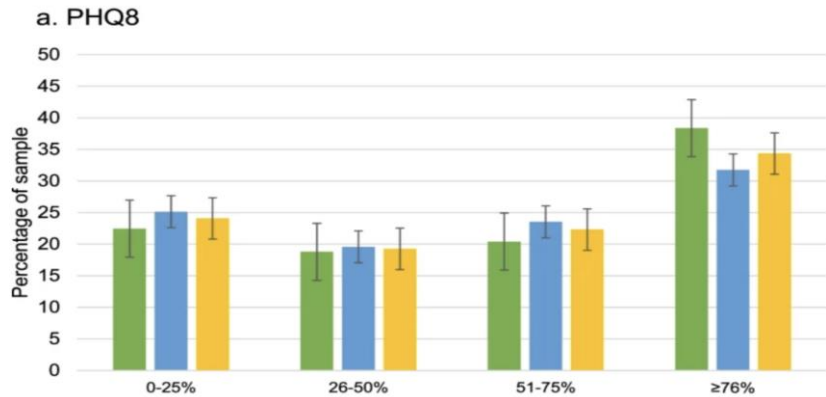
Faith Matcham et al BMC Psychiatry, 21 Feb (136) 2022 (Jansen and Kings College London)

**RADAR-MDD:** Multi-center, prospective 24 mo observational cohort study; N=623 MDD participants

## Smart-phone data:

- **Passive:** Global Positioning System (GPS), Bluetooth, gyroscope, phone screen interactions, ambient noise and light levels
- **Active:** questionnaires, cognitive tasks, speech sampling tasks

- Of the 623 participants enrolled, **445 (71.4%)** provided outcome data for 1-year, **181 (29.1%)** for full 2-years
- Comparable levels of data availability in active and passive forms of data collection
- Higher burden data sources (cognitive tasks, keeping wearable devices charged) reduces data availability



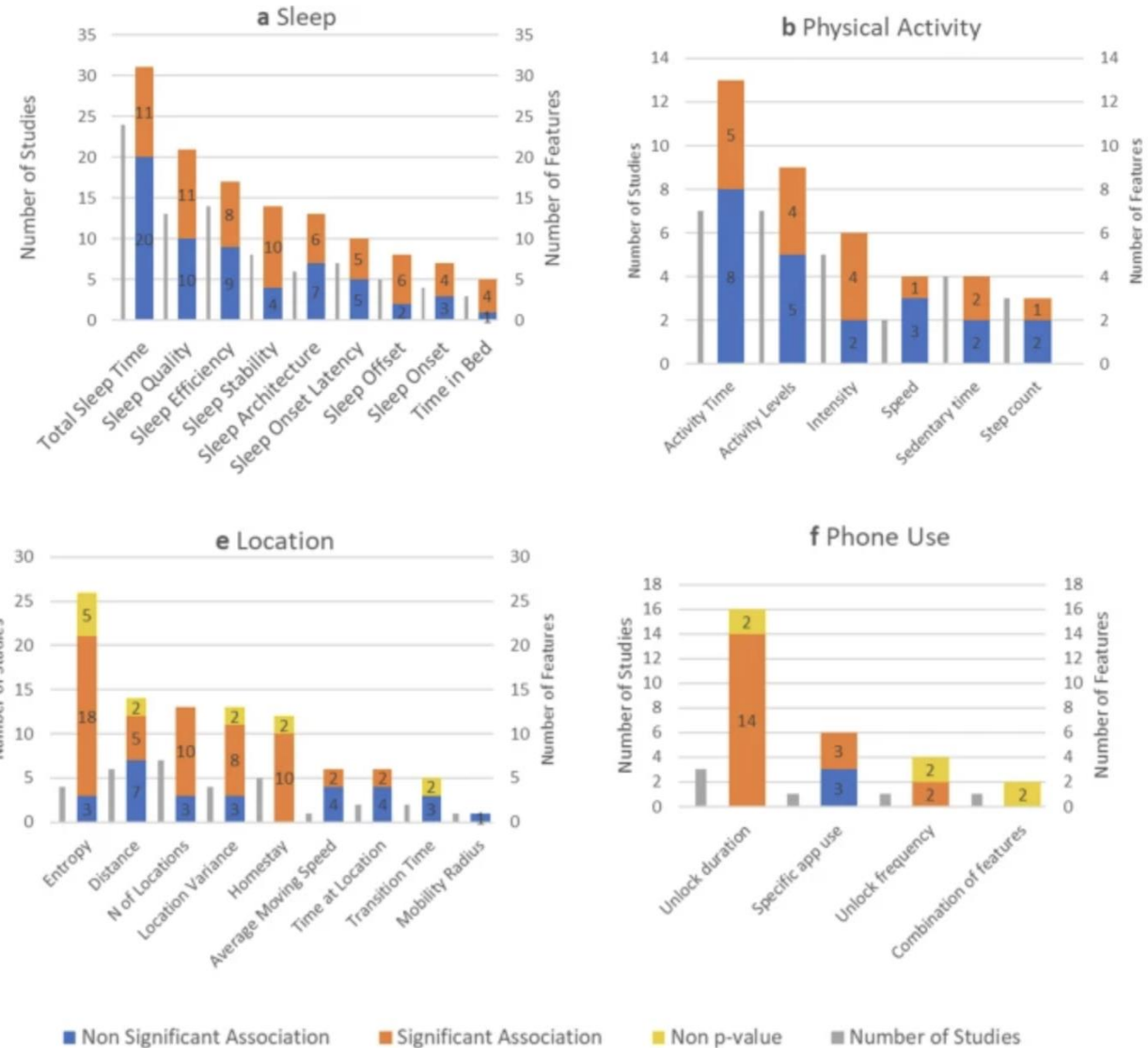
# DHTS for the passive monitoring of depression: fifty-one studies, N =16821

De Angel V et al npj Digital Medicine 2022: January 2007 - November 2019

## Important practical issues identified

- Many digital features correlated with depression – understanding feature importance and practicality vital
- Reasons for dropout: equipment malfunction, technical problems using devices (charging and network connectivity)
- Most studies employed opportunistic study designs, small sample sizes, short follow-up windows (2 wks)

## Feature associations with depression by behaviour type.





# Conclusions

- Digital Health Technology tools, advanced analytics and application of AI and machine learning have great promise in CNS diseases eg. to quantify behavior, monitor patients in their home environment and to develop novel endpoints
- However considerable challenges remain, such as: verification and validation, analytical methodology, practical deployment and regulatory considerations which will be the subject of this session