Remote Assessment of Disease and Relapse in Central Nervous System Disorders (RADAR-CNS)

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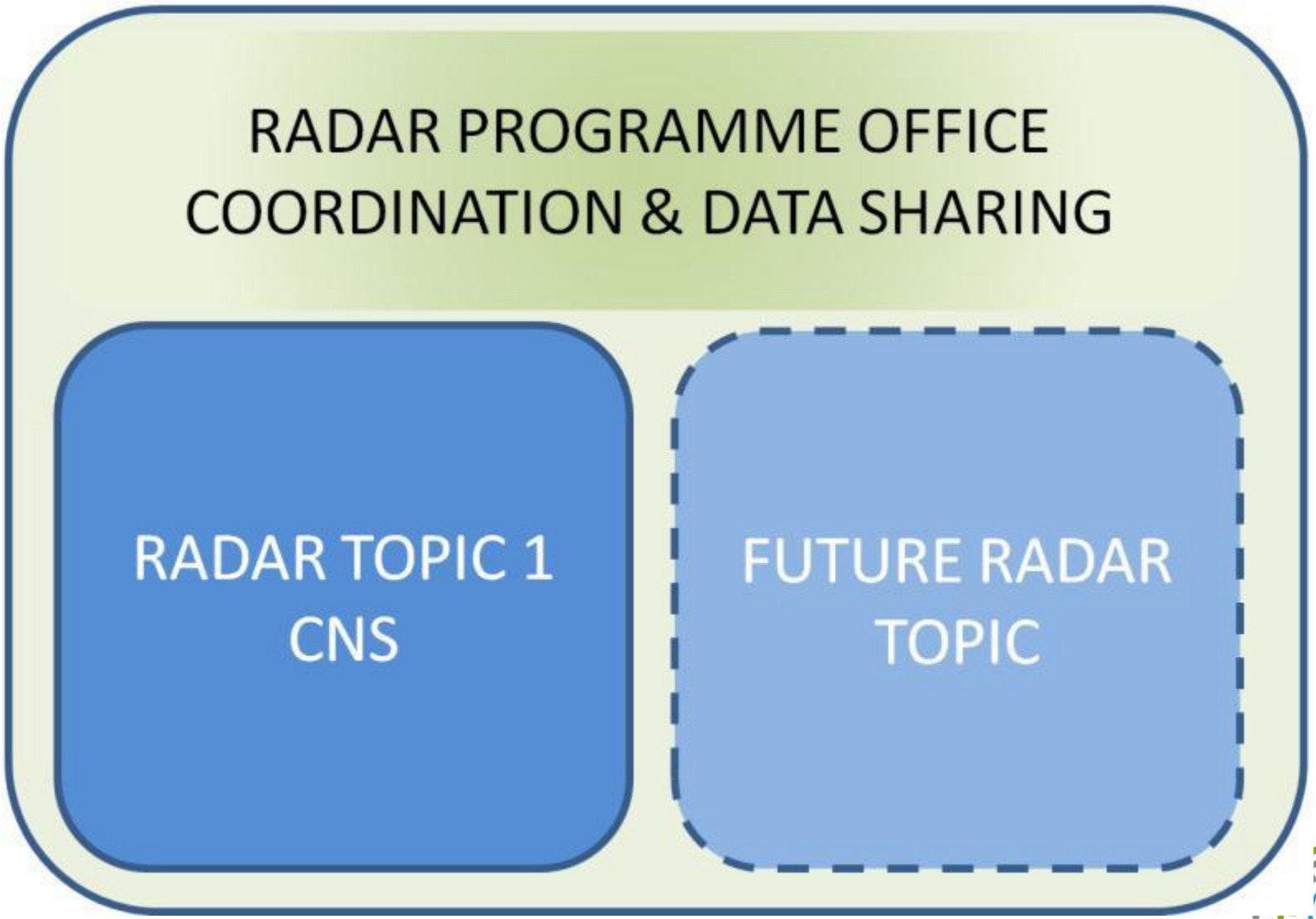
Introduction

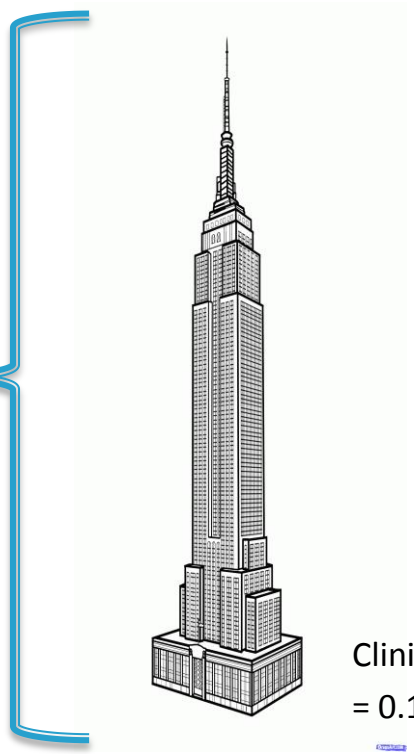
- Remote measurement technologies (RMT) could predict/avert negative outcomes by providing real-time information on **current clinical state** and predicting **future deterioration**.
- RADAR-CNS will develop and test **transformative platform** of RMT in three CNS diseases: epilepsy; multiple sclerosis (MS); and depression.
- The ultimate goal is to **improve patient outcomes** through remote assessment.

Original vision



A Data Challenge

Molecular Biological Data
= 380M

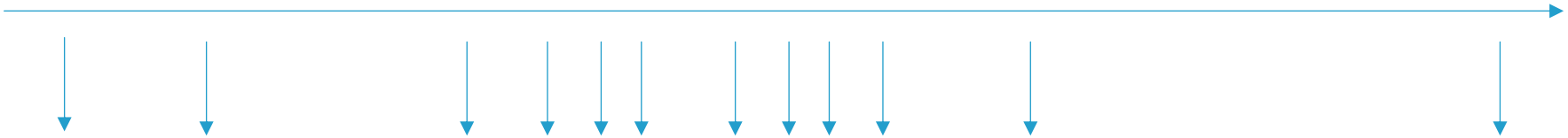


Clinical data
= 0.1 micron

Thanks to Ken Kubota and Michael J Fox Foundation

The traditional approach

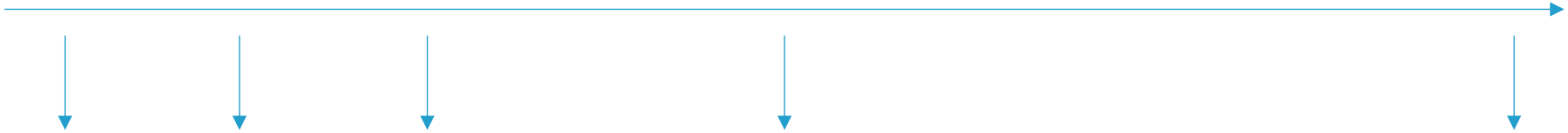
a. Clinical practice



Sporadic presentations to GP | Episode of specialist care | Sporadic presentations to GP

Lots of unstructured data, with incomplete measurement of outcomes & risk factors. Time points related to clinical state

b. Research



Detailed baseline assessment

Scheduled follow up visits at regular intervals

Snapshots of clinical outcomes, incomplete data, inefficiently used

Prediction of seizure likelihood with a long-term, implanted seizure advisory system in patients with drug-resistant epilepsy: a first-in-man study

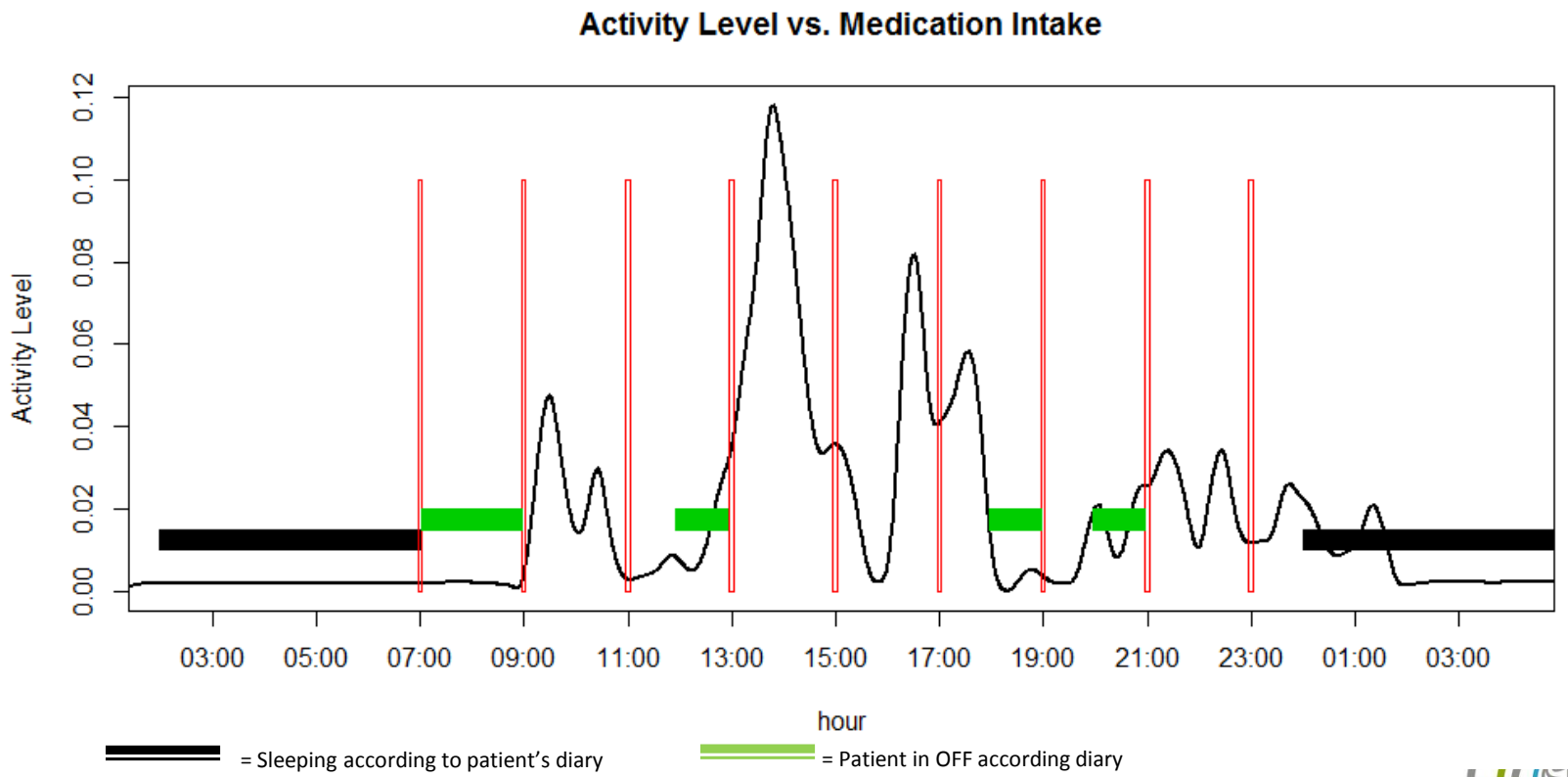
Mark J Cook, Terence J O'Brien, Samuel F Berkovic, Michael Murphy, Andrew Morokoff, Gavin Fabinyi, Wendyl D'Souza, Raju Yerra, John Archer, Lucas Litewka, Sean Hosking, Paul Lightfoot, Vanessa R

	Estimated monthly seizure rate at enrolment	Mean monthly seizure rate during study	Mean monthly seizure rate captured by intracranial electroencephalography	Spearman's rank correlation coefficient (ρ)	p
Patient 1	4	5·37	14·17	0·71	0·0063
Patient 2	3	0·00	1·52	..	..
Patient 3	7	0·00	126·65	..	..
Patient 4	5	1·16	3·61	−0·26	0·5742
Patient 5	4	0·00	1·32	..	..
Patient 6	2	0·55	6·32	−0·40	0·2223
Patient 8	4	5·55	42·32	0·59	0·0356
Patient 9	10	22·52	30·37	0·74	0·0134
Patient 10	4	24·06	52·28	0·45	0·1472
Patient 11	8	11·21	102·50	0·25	0·4357
Patient 12	5	0·25	0·37	0·71	0·0097
Patient 13	7	0·99	25·74	0·86	0·0007
Patient 14	3	0·00	0·00	..	..
Patient 15	5	4·80	6·28	0·55	0·1328

We eliminated outliers 1·5 times or more outside the IQR, which resulted in zero values for some patients with infrequent seizures.

Table 4: Seizure rates before and during the study, by patient

Example of 24 Hours of Ambulatory Data in Parkinson's Disease



Thanks to Ken Kubota and Michael J Fox Foundation

RADAR-CNS Objectives

1. Build a data collection, management, modelling and visualisation infrastructure. Including:
   - Generic RMT platform for active and passive RMT (aRMT/pRMT)
   - Data management pipeline, processing and analysis to identify bio-signatures
   - Data visualisation platform presenting user-friendly data for patients and clinicians.
   - Maximal interoperability with health systems e.g. electronic health records (EHRs) and patient health records.
   - Acceptable privacy protections to maximise patient confidence and acceptability.

2. Devise clinical studies using observational prospective designs to:
   - Test the acceptability of RMT
   - Determine added value of RMT to conventional markers of disease outcomes
   - Detect changes in disease state,
   - Changes in disease state due to drug effects
   - Prediction of change in disease state.

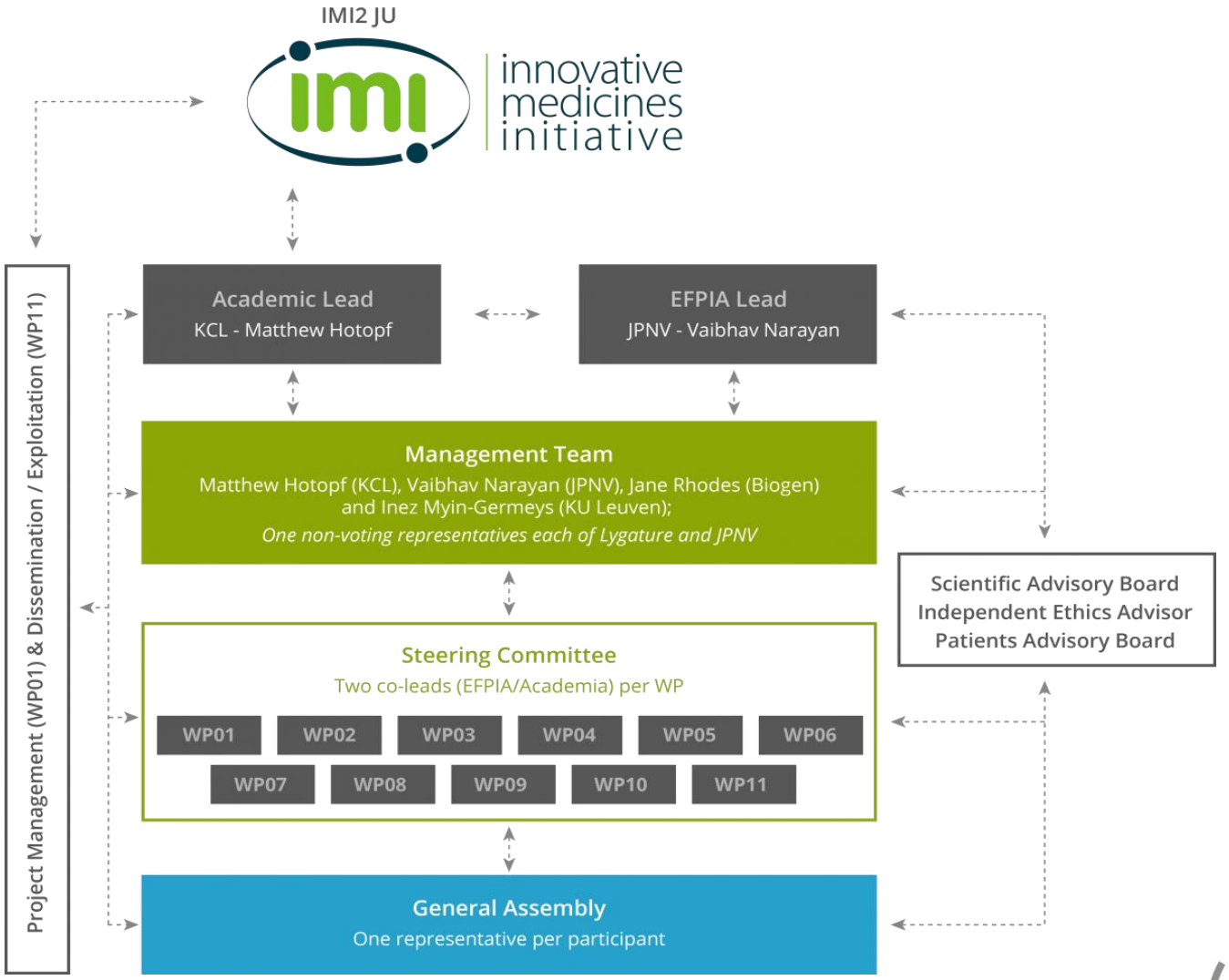
3. Engage stakeholders to maximise real world use of RMT and produce relevant and important questions to inform clinical study design.

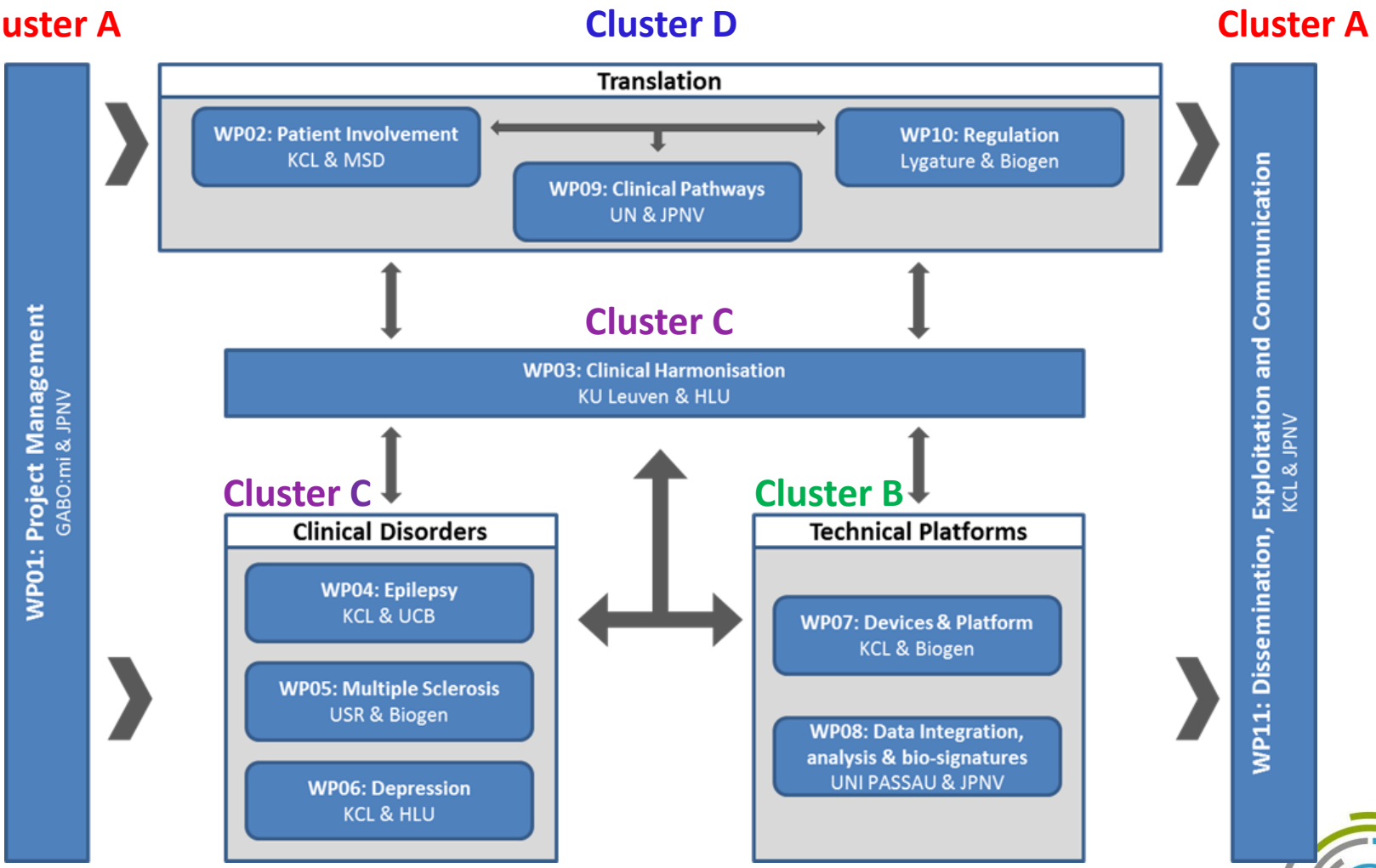
- Prioritise clinical endpoints of greatest relevance to patients, ensure RMT is use-friendly and acceptable.
- Test measures to ensure maximal adherence.
- Identify the priorities of clinicians and healthcare funders.
- Engage with regulators to identify key issues likely to be raised in relation to market authorisation of actionable bio-signatures.

Remote Assessment of Disease and Relapse in Central Nervous System Disorders (RADAR-CNS)

1	KCL	UK	13	KU Leuven	Belgium
2	IRCCS- FBF	Italy	14	NWU	USA
3	Lygature	Netherlands	15	UNI PASSAU	Germany
4	USR	Italy	16	UNIBG	Italy
5	VHIR	Spain	17	Charité	Germany
6	UN	UK	18	Intel	UK
7	CIBER	Spain	19	GABO:mi	Germany
8	Software AG	Germany	20	JPNV	Belgium
9	RegionH	Denmark	21	Biogen	UK
10	Vumc	Netherlands	22	HLU	Denmark
11	UKLFR	Germany	23	UCB	Belgium
12	IMEC-NL	Netherlands	24	MSD	Czech Republic

RADAR-CNS Governance




Cluster A
Cluster D
Cluster A
WP01: Project Management
GABO:mi & JPNV
Translation
WP02: Patient Involvement
KCL & MSD
WP09: Clinical Pathways
UN & JPNV
WP10: Regulation
Lygature & Biogen
Cluster C
WP03: Clinical Harmonisation
KU Leuven & HLU
Cluster C
Clinical Disorders
WP04: Epilepsy
KCL & UCB
WP05: Multiple Sclerosis
USR & Biogen
WP06: Depression
KCL & HLU
Cluster B
Technical Platforms
WP07: Devices & Platform
KCL & Biogen
WP08: Data Integration, analysis & bio-signatures
UNI PASSAU & JPNV
WP11: Dissemination, Exploitation and Communication
KCL & JPNV

Scientific Advisory Board: Ken Kobuta, Norman Sartorius, Tom Insel

The SAB advise on a **high standard of research and monitor the main progress of the Action**

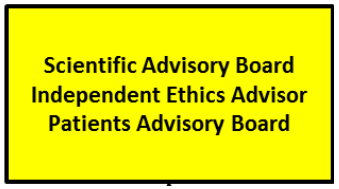
Ethics Advisor: Felicity Callard

The IEA advise on a in a non-binding way on: **ethical issues and good clinical practices guidelines** and will contribute to the researchers' awareness of ethical issues

Patients Advisory Board: representatives of

- Italian MS Society
- MS Society
- Epilepsy Action
- GAMIAN
- Netherlands Knowledge Center of Anxiety and Depression

The PAB provide a focus of **expertise in patient experience**, and offer a natural vehicle for **patient engagement** in the Action's activities

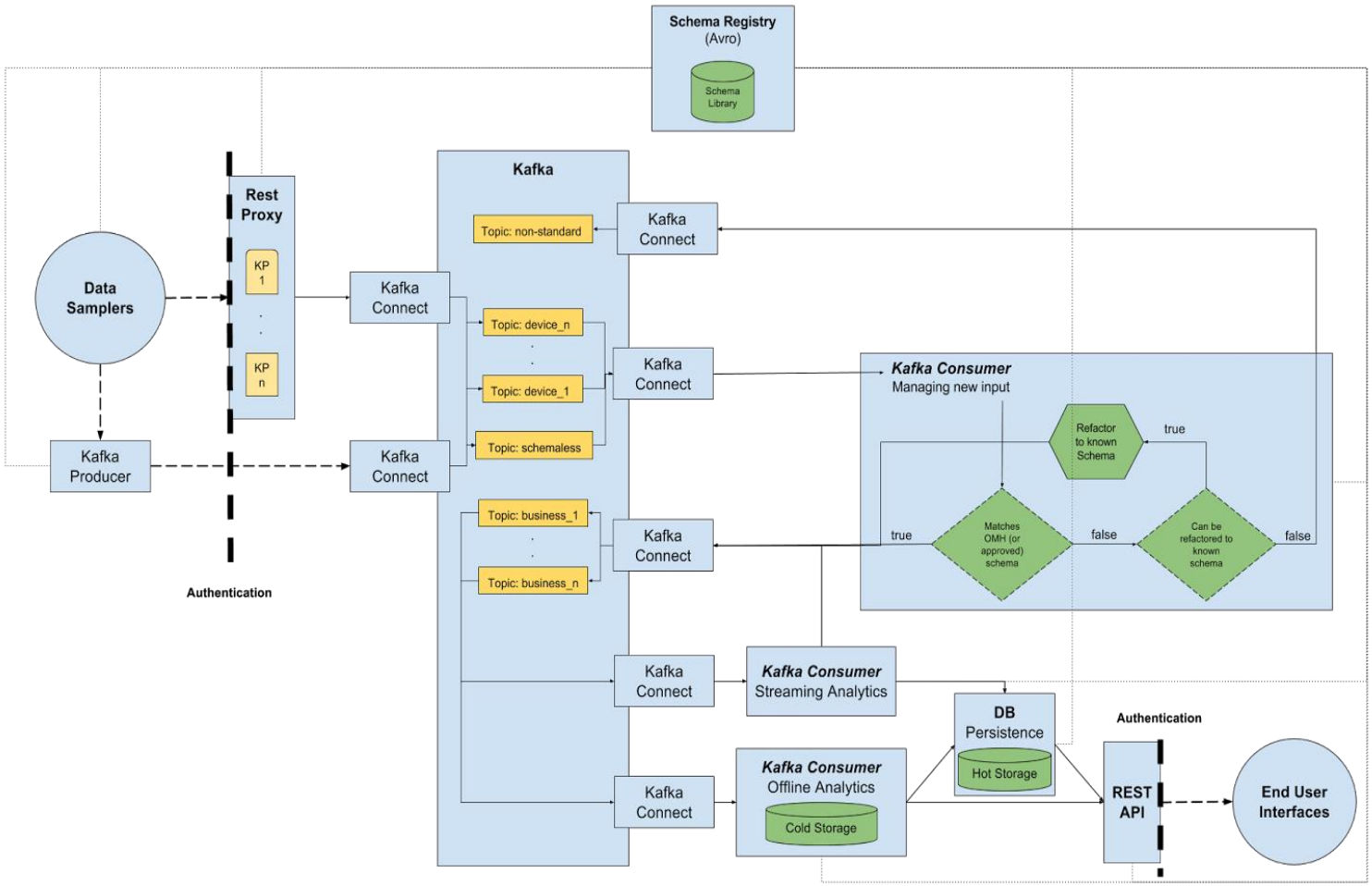


- WP02: Patient Involvement
  - Til Wykes (KCL) / Peter Gamble (Merck)
  - WP02 provides information on requirements of patient stakeholders
- WP09: Clinical Pathways
  - Michael Craven (UN) / Claudia Tamasy (JPNV)
  - WP09 focuses on the requirements of clinical stakeholders with respect to integration of RMT into care pathways in European healthcare systems.
- WP10: Regulation
  - Andre Broekmans (Lygature) / Steve Dew (Biogen)
  - WP10 focuses on the requirements of both medical device regulators and medicinal product regulators.

- WP07: Devices and Platform
  - Richard Dobson (KCL) / Shoibal Datta (Biogen)
  - WP07 will build an end-to-end system for RADAR-CNS clinical work-packages supporting pRMT and aRMT measurement and feedback using mobile and web technologies.

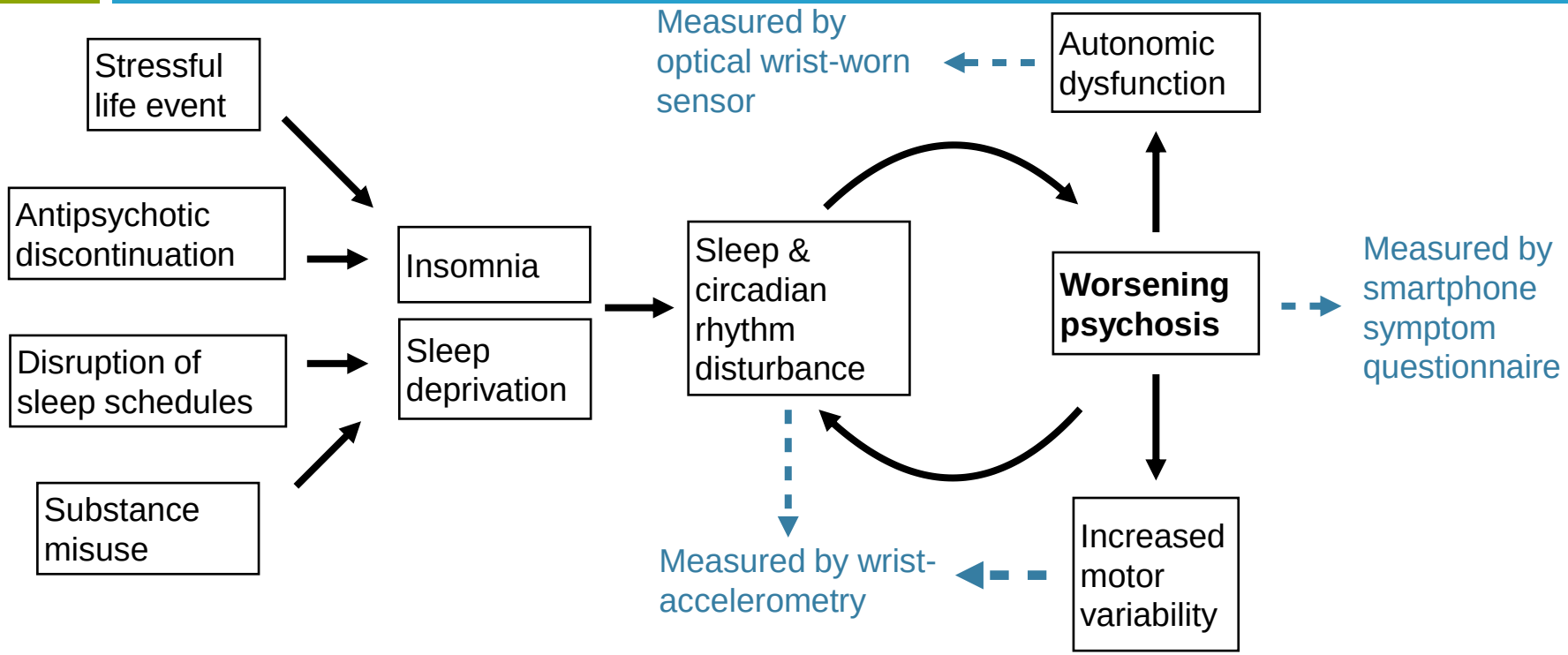
- WP08: Data integration, analysis and biosignatures
  - Björn Schuller (UNI PASSAU) / Anthony Rowe (JPNV)
  - WP8 will enable analysis of the collected data to understand the association between RMT and remission, relapse, and recurrence of the CNS disorders and to classify and predict the disease status.

Architecture



- WP03: Clinical Harmonisation
  - Inez Myin-Germeys (KU LEUVEN) / Michiel Ringkjøbing-Elema (Lundbeck)
  - WP03 provides an overarching assessment and analysis scheme across clinical disorders, combining aRMT and pRMT.
- WP04: Epilepsy
  - Mark Richardson (KCL) / Nancy van Osselaer (UCB)
  - WP04 aims to evaluate the utility of multi-parametric RMT in people with epilepsy
- WP05: Multiple Sclerosis
  - Giancarlo Comi (USR) / Bernd Kieseier (Biogen)
  - WP05 aims to evaluate the utility of multi-parametric RMT in people with MS to improve characterisation of its clinical presentation, depression and gait disturbance.
- WP06: Depression
  - Matthew Hotopf (KCL) / Hans Eriksson (Lundbeck)
  - WP06 aims to evaluate the utility of multi-parametric RMT in people with depression.

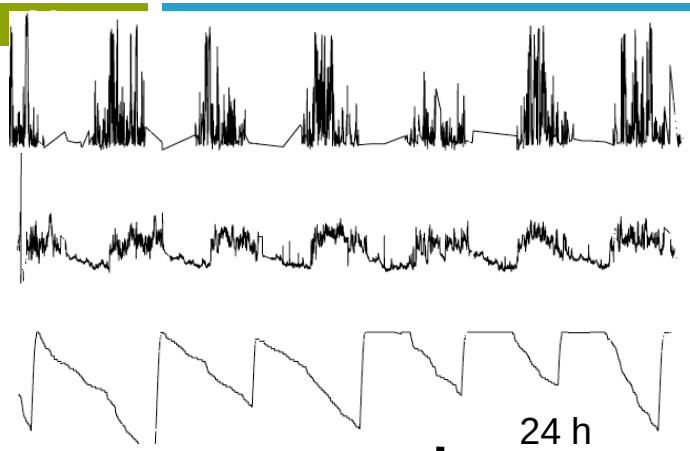
Passive Streams



Question: can physiological signals such as sleep patterns, motor activity and heart rate variability serve as useful <u>early-signs of relapse</u> in psychosis?

RADAR-CNS

SLEEPSIGHT



Motor activity

Mean heart rate

Battery charge

24 h

Automated real-time analysis

Intuitive visualisations

Care team

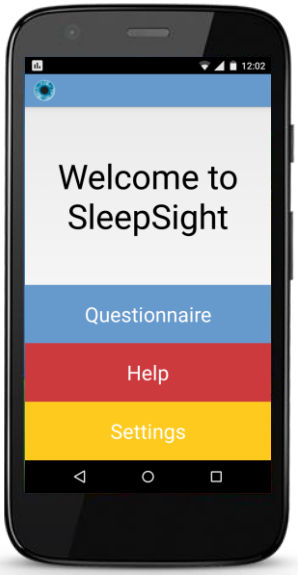
Relapse prevention

Patient

Improved self-management

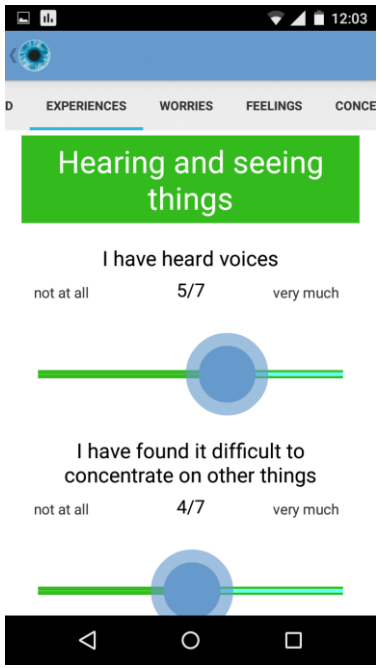
Wearable device

Passive



Smartphone sensors

Active



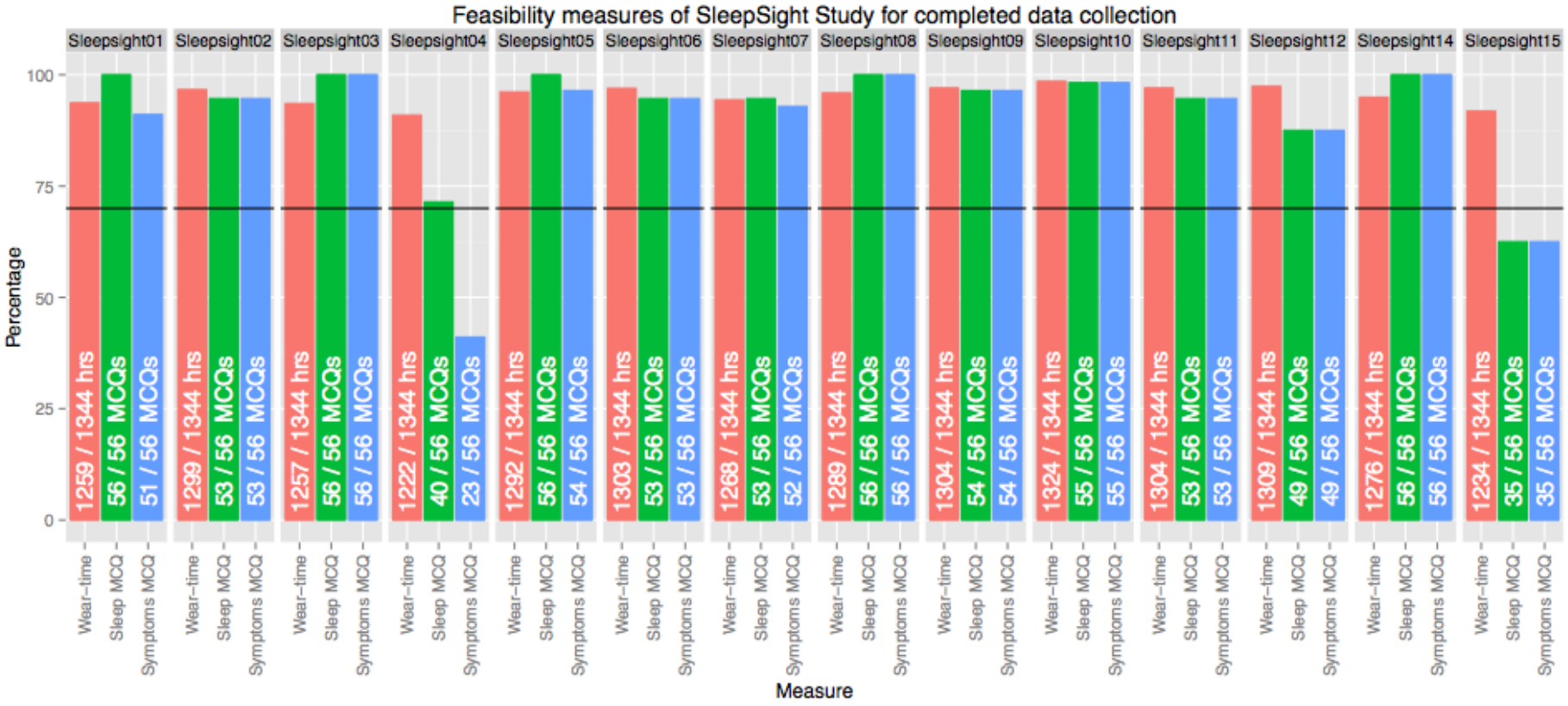
Symptom questionnaire

Mobile data upload

imi innovative medicines initiative

efpia

Acceptability - findings



Wear-time: 88%

Sleep diary: 89%

Symptom diary: 86%

http://www.radar-cns.org/ Follow us: @RADARCNS