Challenges to GCP Compliant Deployment of Biosensors in Cognitively Impaired Populations

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IXICO Overview

▶ **IXICO brings innovative digital technologies and services to those involved in researching and treating diseases of the brain**

▶ **IXICO's primary focus is on the needs of the pharmaceutical industry to support**

- Development of drugs in clinical trials
- Use of drugs in the clinic to improve patient safety and outcomes

▶ **Our background is in imaging-derived biomarkers for enrichment, safety and efficacy**

- The evolving biosensor-derived biomarkers landscape parallels imaging 15-20 years ago

▶ **Acquisition of Optimal Medicine in 2015 provides new capabilities and resources to apply to biosensors**

▶ **Collaborations with Withings/Nokia and Prof Yves Dauvilliers, Montpellier University Hospital Sleep Lab, DPUK**

Dementias Platform UK
Medical Research Council

imi
Innovative Medicines Initiative

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Challenges to GCP Compliant Deployment of Biosensors in Cognitively Impaired Populations

AGENDA

- IXICO overview
- **Overview of challenges**
    - **Ethical, privacy and security**
    - **Operational**
    - **Data validation**
        - **Authentication**
        - **Audit trail**
        - **Computer system validation**
        - **Data quality control**
- Case studies of deployment
    - Cygnus study
    - Context study

Ethics, Privacy and Security

▶ **Biosensors worn at home introduce particular challenges**

▶ **These increase if:**

- The data are accessed or shared within a study
- Real-time data are collection
- Using consumer devices via the cloud
- Patients are cognitively impaired

▶ **IXICO is particularly focussing on these issues in Cygnus**

- Protocol, ethics approval and informed consent challenges addressed with UK authorities and patient groups

Overview of Challenges to GCP Compliant Deployment

▶ **The challenges depend on the context of use**

▶ **Illustrated with two case studies from IXICO**

- To evaluate feasibility of biosensor & mobile technologies for collecting high quality and actionable data from cognitively impaired patients and their care givers
- Real world setting
- Linking to standard clinical care dataset about care delivery, cost and outcomes
- 250 patients presenting to memory services and 250 care givers
- Sub-group with wearables

- To explore the performance of biosensors compared with standard sleep assessment methods (polysomnography, sleep scales and sleep diaries) in healthy elderly subjects and individuals with neurodegenerative disorders
- To discover clinically valid actigraphy-derived sleep metrics (and beyond) that take into account physiology and pathology
- Commencing with elderly control subjects and Parkinson's disease

▶ **Device evaluation**

- Detailed assessment of a number of devices on parameters key to adoption and study success

	Price	Comfort	Step Count	Clock	Raw data	Ease of use	Data access	Battery life	Aesthetics
Fitbit Charge	80	Good	Yes	Yes	No	OK	Web	5 days	OK
Garmin Vivofit	60	Good	Yes	Yes	No	OK	Web	1 year	OK
Axivity	150	Poor	Yes	No	Yes	Good	Raw	30 days	Poor
wGT3X-BT Monitor	300+	?	with process	No	Yes	?	Raw	25 days	Poor
Withings Activite Pop	100	Good	Yes	Yes	No?	OK	API	8 months	Good
ActiGraph GT9X	180	Poor	Yes	Yes	Yes	OK	Raw	7 days	Poor

▶ **Focus groups**

- Highest scoring devices were evaluated in focus groups of people diagnosed with mild cognitive impairment/dementia and their care-givers

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Practical Considerations: Trade-offs

▶ **Long battery life and highly processed data vs. short battery life and raw data**

▶ **No charging worn 24/7 for battery life vs. removed for charging with data gaps**

▶ **Familiar appearance (watch) of consumer device but processed data**

CARING FOR DEMENTIA TOGETHER
Cygnus

- Withings Activité Pop
- 8 months battery life
- Processed data
- Requires app and website
- Syncs daily
- Near real-time QC of data
- Data can be "actioned" during study (ePRO questions, troubleshooting, technology issues...)

CONTEXT
Adding perspective to biosensor data

- Axivity AX3
- 14 days battery/data collection (depends on settings)
- Raw data
- Standalone device
- Data download, viewing and QC only at end of study period
- Subject behaviour not influenced by viewing data

→ **Three devices being used at present; Withings Activité Pop, Axivity and Actigraph Link**

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▶ **Authentication**

- How do we know who the data are coming from?

▶ **Audit trail**

- Especially for consumer devices, how do we identify and document changes to data made by people or systems?

▶ **Data quality control**

- Real-time verification e.g. syncing

- Artefact detection

  - Not being worn

  - Noise and error

  - …

→ **Risk based approach to computer system validation**

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Audit Trail and Computer System Validation For Consumer Devices

▶ **How do I know changes in sensor measurement are due to change in subject rather than change in sensor, its software, or artefact?**

- Reliable data
- Regulatory compliance for decision making

Subject — Consumer biosensor → **Cloud of unknown software in sensor device, smartphone, cloud servers etc.** → Uncontrolled output as software can change in unknown ways over time

▶ **Traditional approach**

- Vendor assessment of wearable supplier
- Validation of computer system (audit trail, access etc)
- Validate consumer wearable (inc. all systems) for "context of use" against "gold standard"
- Formal change control process if changes in device or software

Data QC - Near Real-Time Verification

Welcome janet.munro

👣	🌙	First Name	Last Name	UPI	Date Of Birth	Type	Consent Date	
✓	❗	*********	*********	02_PA_014	1944-06-01	Patient	2016-09-27	Edit
		*****	*****	02_SP_014	1954-12-28	Study Partner	2016-09-27	Edit
		******	******	03_PA_008	1932-03-04	Patient	2016-08-28	Edit
✓	✓	*****	*****	02_PA_016	1954-07-08	Patient	2016-09-29	Edit

***** ***** 02_PA_016 ⌚

Edit

👣 Activity last 14 days	Last sync at 17-Oct-2016 08:58:31
📊 ***** made 38 steps today and 3059 yesterday	Detail

🌙 Sleep last 14 days	Last sync at 17-Oct-2016 04:45:08
〰	Detail

🌙 Sleep last 14 days

Show Sleep Measures

Date Description	Day	Date	Duration To Sleep	Light Sleep Duration	Deep Sleep Duration	Wakeup Duration	Wakeup Count
today	Mon	17-Oct-2016	00h 01m	02h 39m	01h 02m	00h 02m	1
yesterday	Sun	16-Oct-2016	00h 00m	01h 44m	02h 11m	00h 26m	3
2 days ago	Sat	15-Oct-2016	00h 00m	04h 16m	02h 10m	00h 18m	3
3 days ago	Fri	14-Oct-2016	00h 00m	02h 11m	03h 05m	00h 16m	2
4 days ago	Thu	13-Oct-2016	00h 04m	02h 59m	05h 37m	00h 40m	3

Challenges to GCP Compliant Deployment of Biosensors in Cognitively Impaired Populations
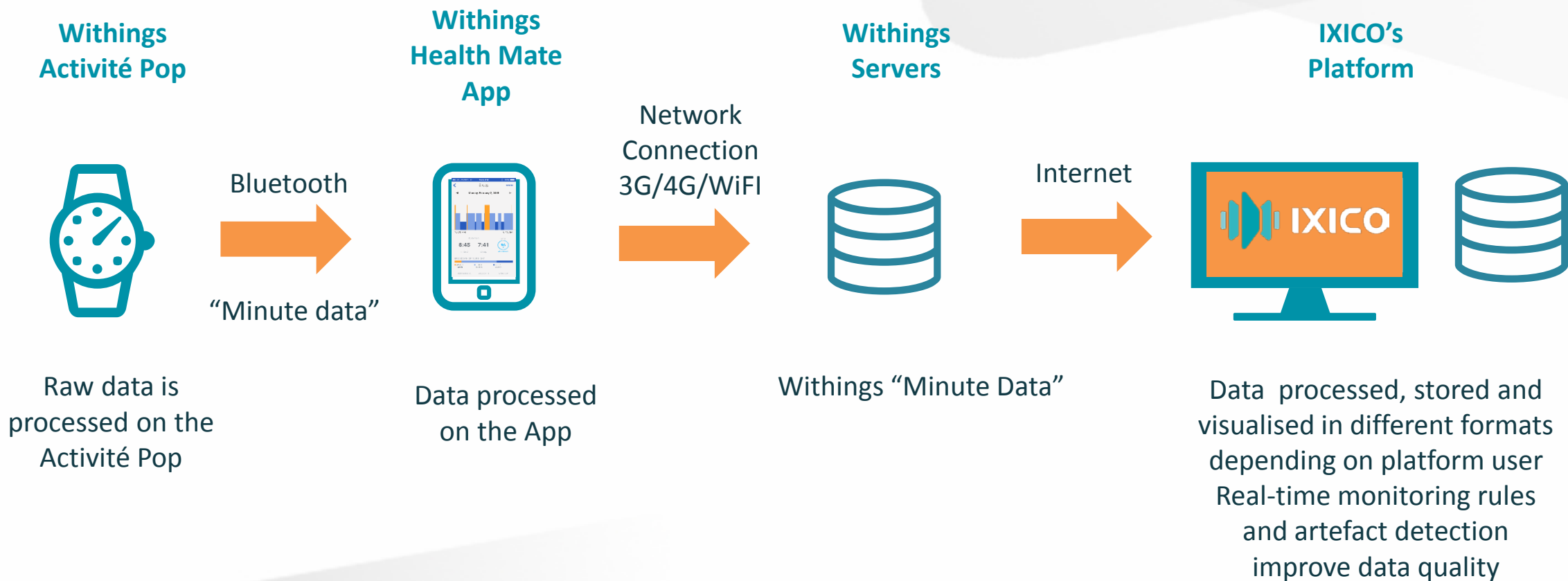
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Operationalising Wearables in the GCP Environment

▶ **Focus groups completed**

▶ **Ethics approval obtained**

▶ **Standard Operating Procedures established**

▶ **GCP compliant software platform with integrated wearables, ePRO and ObsPro (remote monitoring from patients and caregivers partners)**

▶ **>170 subjects recruited in main study**

▶ **Wearable sub-study data collection commenced**

▶ **Data artefact and syncing processes operational**

Dataflow from Withings Activité Pop to IXICO's Platform

Withings Activité Pop

Withings Health Mate App

Network Connection 3G/4G/WiFI

Withings Servers

Internet

IXICO's Platform

Bluetooth

"Minute data"

Raw data is processed on the Activité Pop

Data processed on the App

Withings "Minute Data"

Data processed, stored and visualised in different formats depending on platform user Real-time monitoring rules and artefact detection improve data quality

Withings "consumer" data

"Heat-maps" on Withings' website

Activity & sleep patterns

Week of 8 - 14 August 2016

70 000 steps / week | 38 % | 8 h of sleep / night | 92 %
27k steps | | 7h22

Inactive :   Activity :   soft   intense   Sleep :   light   deep

Sleep   Week   Day

8 - 14 August 2016

7 h 44 min of sleep   96   8 h 07 min in bed
08 min to sleep
8 HOURS   2 wake up

light 4 h 17 min   deep 3 h 27 min   awake 22 min
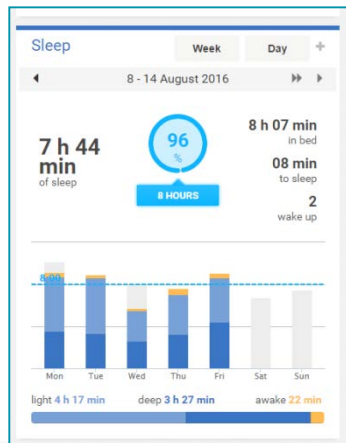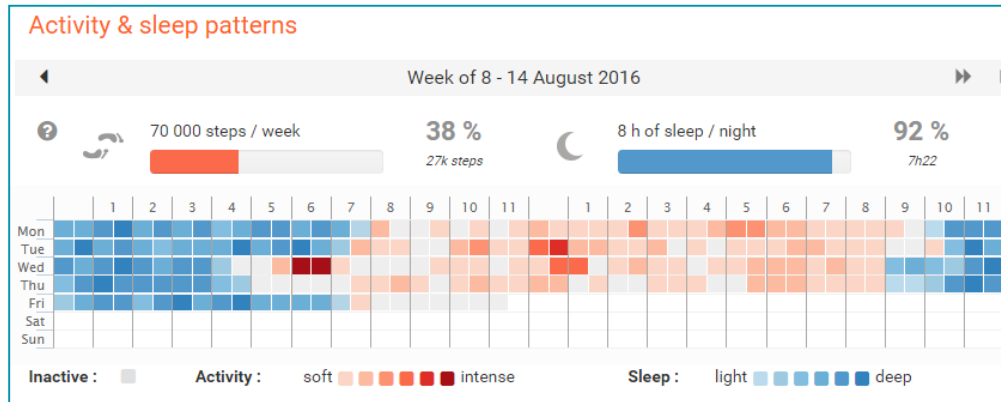
Graphs on Withings' App

Withings data from Oauth API

- Example of detailed sleep data

```
"id":16616514,
"timezone":"\"Europe/Paris\"",
"model":32,
"startdate":1410521659,
"enddate":1410542577,
"date":"2014-09-11",
"data":
{
    "wakeupduration":1800,
    "lightsleepduration":18540,
    "deepsleepduration":8460,
    "remsleepduration":10460,
    "durationtosleep":420,
    "durationtowakeup":360,
    "wakeupcount":3
```

API *"Get sleep data summary"*

Sample output converted to excel

state	Start time	End time	Start date	End date
awake	20:41:00	20:46:00	31/07/2016	31/07/2016
light sleep	20:46:00	20:49:00	31/07/2016	31/07/2016
deep sleep	20:49:00	21:09:00	31/07/2016	31/07/2016
light sleep	21:09:00	21:18:00	31/07/2016	31/07/2016
awake	21:18:00	21:30:00	31/07/2016	31/07/2016
light sleep	21:30:00	21:51:00	31/07/2016	31/07/2016
deep sleep	21:51:00	23:34:00	31/07/2016	31/07/2016
light sleep	23:34:00	23:45:00	31/07/2016	31/07/2016
awake	23:45:00	23:49:00	31/07/2016	31/07/2016
light sleep	23:49:00	23:58:00	31/07/2016	31/07/2016

Subject CY-01 "Minute data" Summaries

Activity Summary
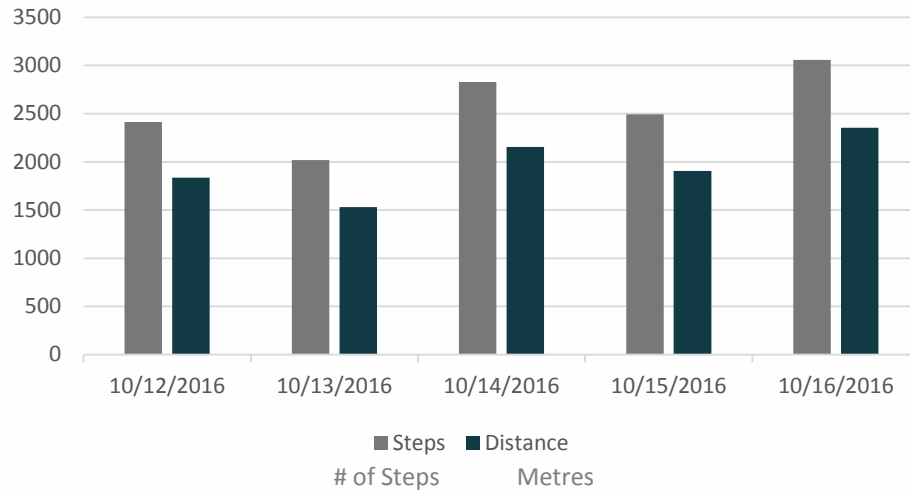
Intensity of exercise
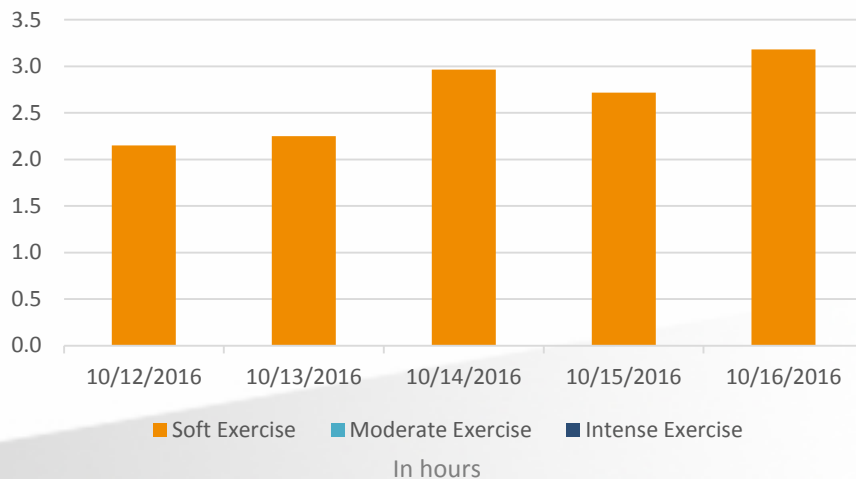
Sleep Summary
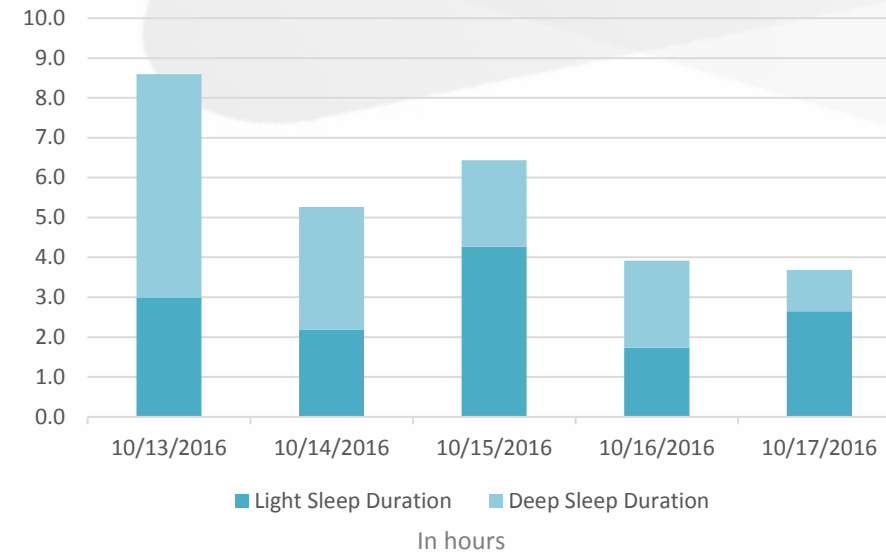
- ▶ **63 year old female**
- ▶ **Early onset Alzheimer's Disease**

CONTEXT Adding perspective to biosensor data

▶ **Advancing the understanding of the impact of clinical context on biosensor data**

- To explore the performance of biosensors compared with standard sleep assessment methods (polysomnography, sleep scales and sleep diaries) in healthy elderly subjects and individuals with neurodegenerative disorders

- To discover clinically valid actigraphy-derived sleep metrics that take into account physiology and pathology

- To identify bio-signatures of sleep disorders that influence sleep interpretation (REM- or sleep breathing-disorders, restless leg, etc)

▶ **Understanding complementary roles of different sleep assessment methods**

▶ **>15 subjects recruited; elderly control subjects (with detailed cognitive and clinical assessments) and Parkinson's disease patients**

Actigraphy vs Polysomnography PSG and Sleep Diaries

Sleep Laboratory

Home

- 20 + patients
- 20 + controls

Clinical and sleep assessments: e.g.
- REM Behaviour Sleep Disorder Screen
- Restless legs syndrome questionnaire
- Pittsburgh Sleep Quality Index
- Epworth Sleepiness Scale (daytime sleepiness)

- PSG & actigraphy
- 1 night

- Sleep diaries & actigraphy
- 14 nights

- Device data, PSG & sleep diary outcomes compared
- End points & algorithms defined for control & disease groups

CONTEXT

- **71-year old female**
- **Parkinson's disease**
- **1 night PSG plus Actigraphy**

Four sleep stages

Awake

Raw accelerometer
Blue: x-axis
Red: y-axis
Green: z-axis
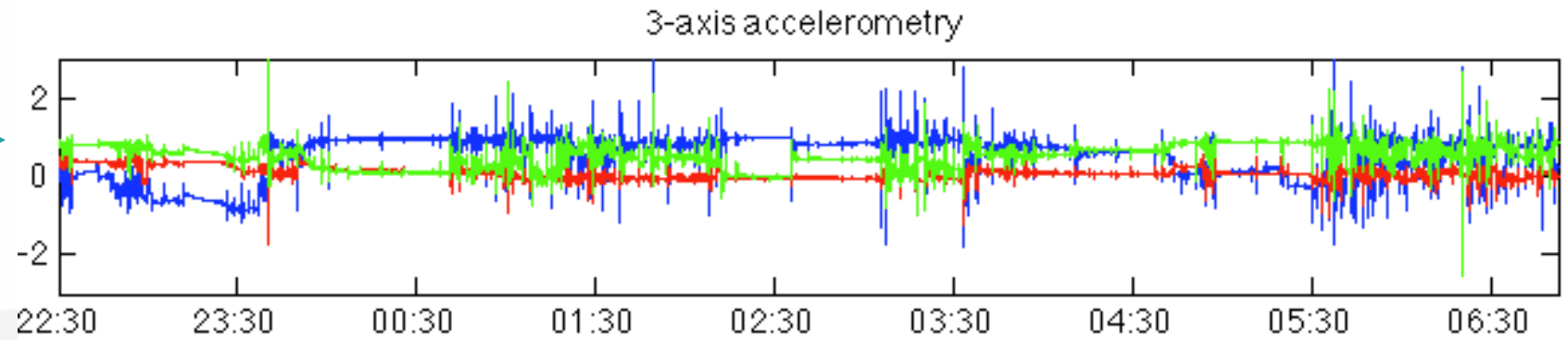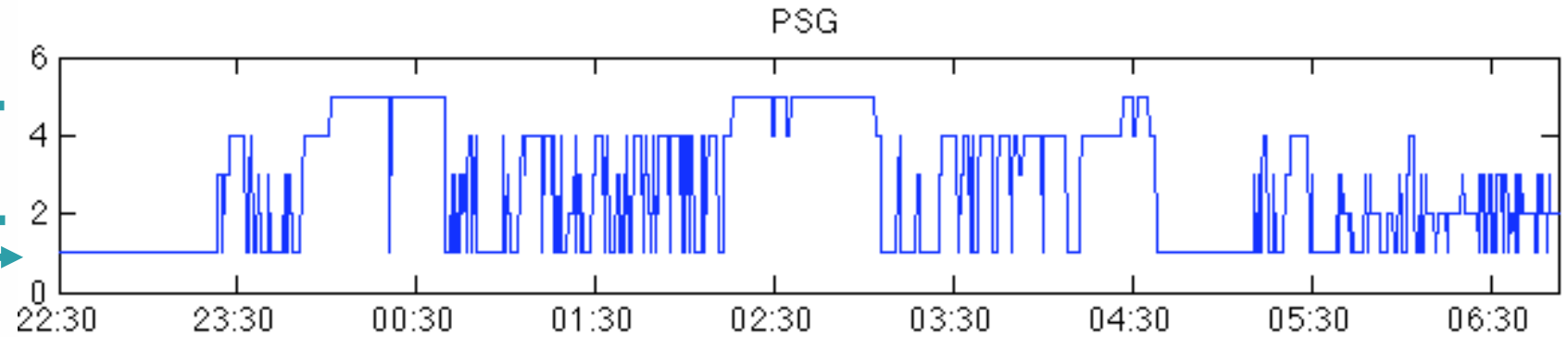
→ **Good correlation between PSG and raw actigraphy**

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Subject PD-1 "Processed Data"
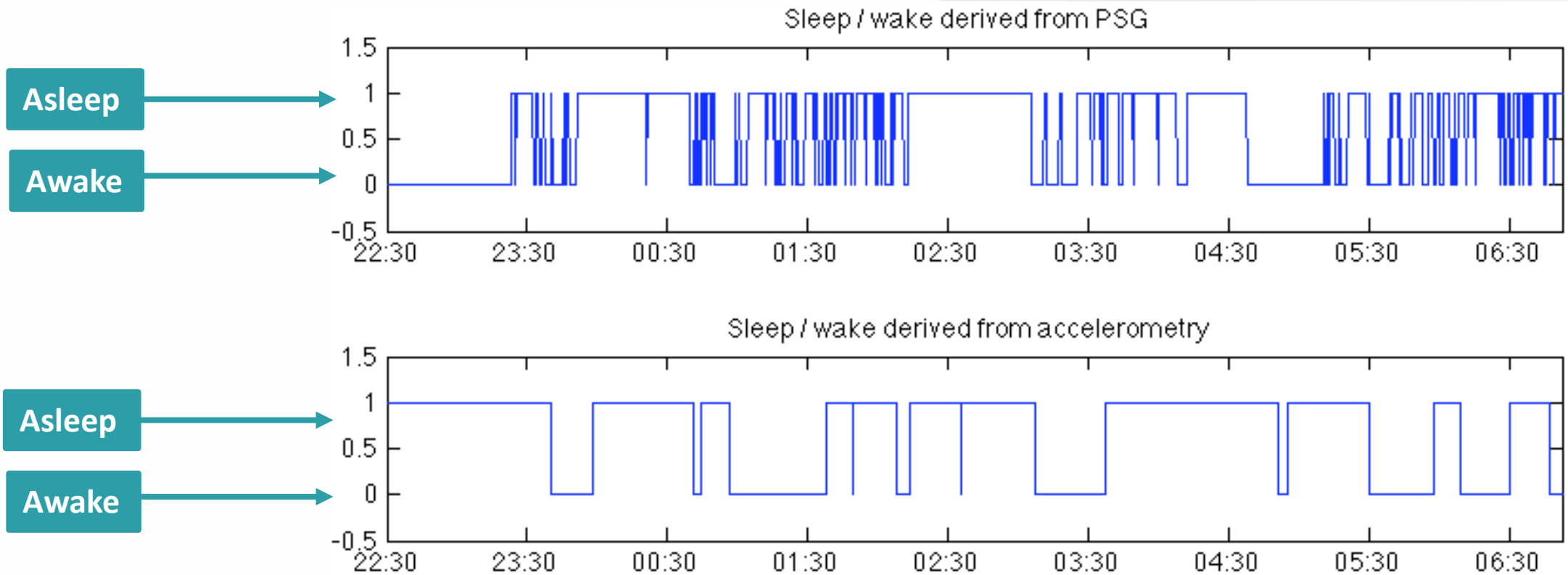
→ **Poor correlation between PSG and "processed" actigraphy using standard sleep algorithms**
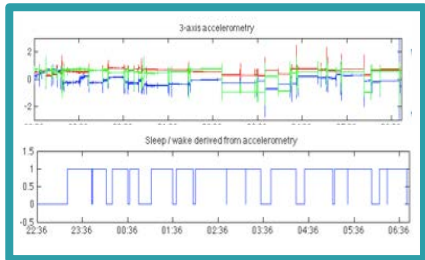
1 night sleep lab recording PSG & actigraphy

14 night home recording Sleep diary & actigraphy

14 day accelerometry

14 day sleep / wake measurement

1 = asleep

0 = awake

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Thank You

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