

Are we there yet? Evaluating new non-EDC data sources for clinical trial submission feasibility

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Agenda

- **Introduction**
- **Mobile Technologies, Types of Devices, Data Sources**
- **Data Flow, Standardization and Integration, Analysis**
- **Benefits and Challenges**
- **Resources**
- **Summary and Conclusion**



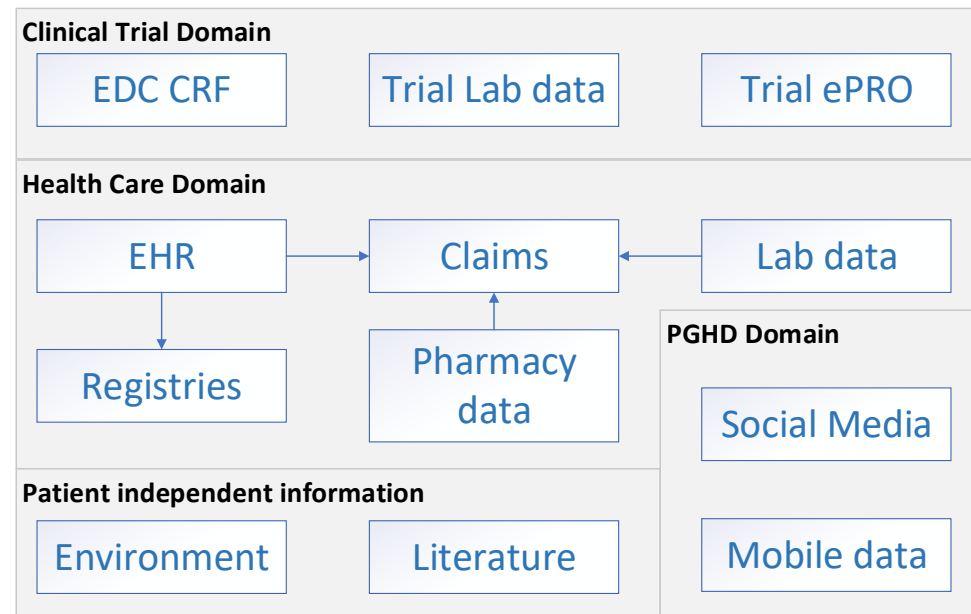
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Introduction

- **Work of PHUSE Data Engineering Project Sub Team Data Sources**
- **EU Connect 2019**
 - Classification of Data
 - FAIR, ALCOA+
 - Use Cases
- **Mobile Technologies**



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Mobile Technologies

- According to the **CTTI***, mobile technologies are defined as **“mobile applications and other wearables, ingestibles, implantables, and portable technologies containing sensors for the remote capture of outcomes data”**
- **Passive data**
- **Active Data**

* Clinical Trials Transformation Initiative



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Types of Devices

- **Devices available in the Market**
 - Commercial devices
 - Pros and Cons
- **Devices not available in the Market**
 - Specifically for Research
 - Pros and Cons



Data Sources

- **Devices, Apps**
- **Functionality**
- **Physical forms**
- **Therapeutic Areas**
- **Amount of Data**

Device and Data Stream	Sampling Frequency	Est. Size (MB) (per Participant/Day)
Watch - Accelerometer	100 Hz, while worn	> 200
Watch - Gyroscope	100 Hz, while worn	> 200
Watch - Pedometer	2-5 seconds	~ 0.1
Phone - Accelerometer	100 Hz, continuous	> 400
Phone - Gyroscope	100 Hz, continuous	> 400

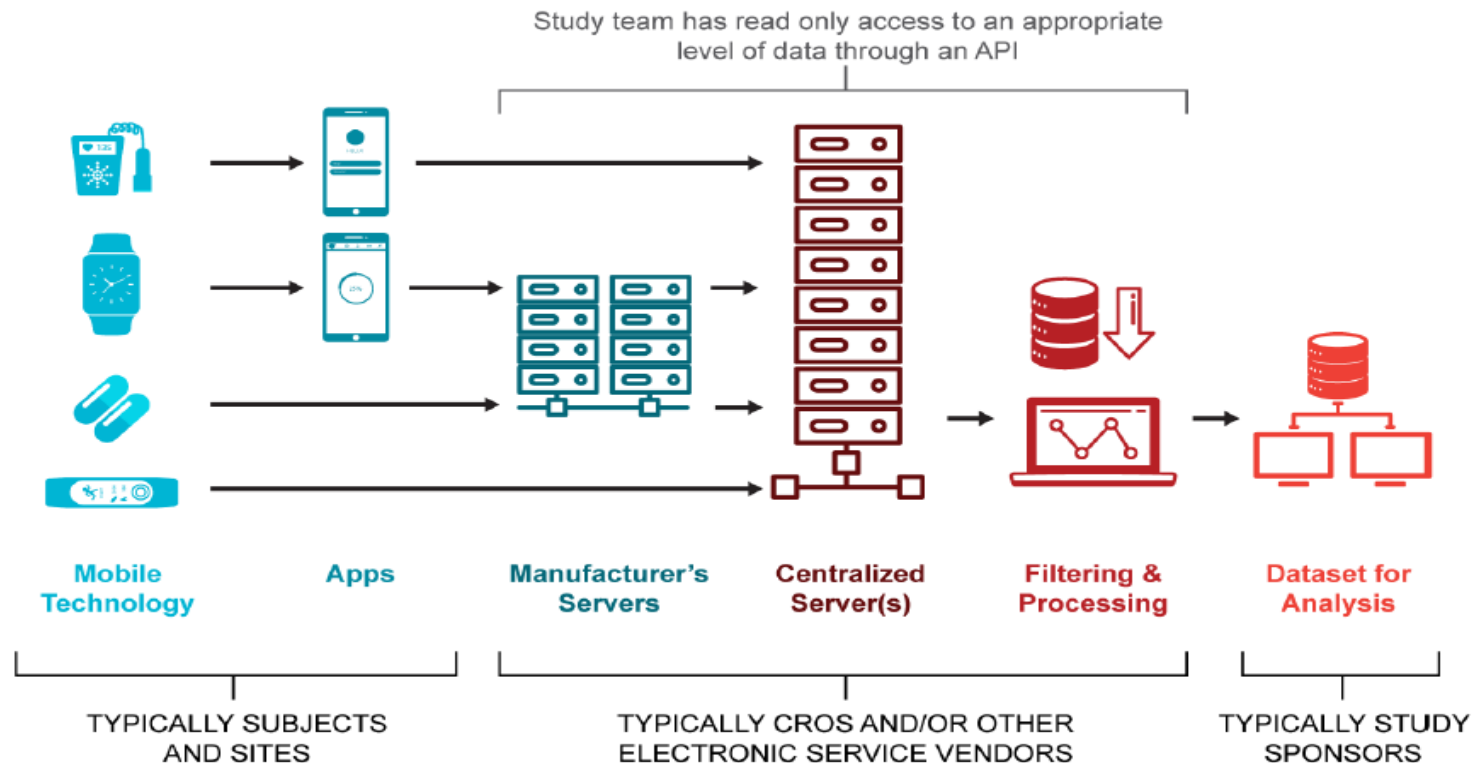
SOURCE: Developing Measures of Cognitive Impairment in the Real World from Consumer-Grade Multimodal Sensor Streams, KDD' 19

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Data Flow



SOURCE: CTTI



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Standardization and Integration

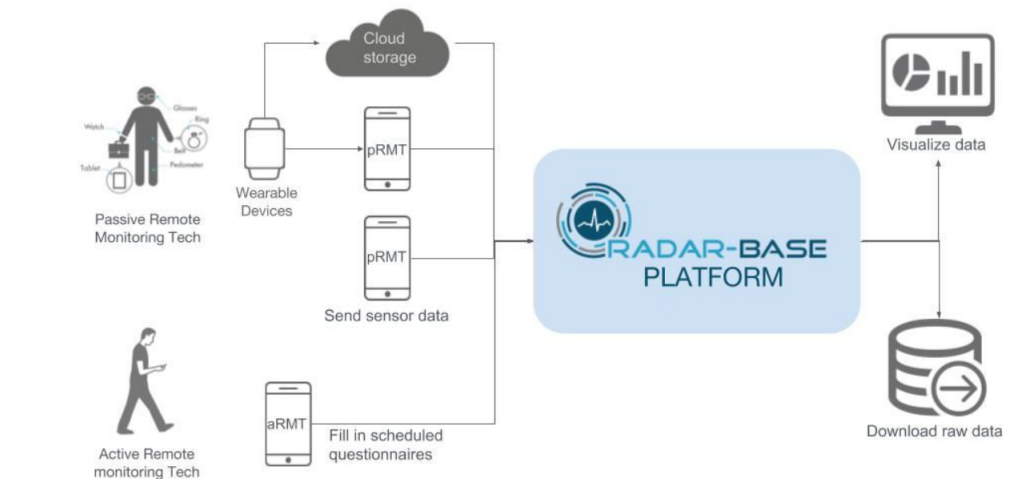
- **Retrieve, Standardize, Transfer, Linkage to Clinical Study Data**
- **Recognizable Format**
 - **Transform**
 - **Moving Averages, Removing Gaps and Spikes**
 - **Collaboration between Study Statisticians and Data Engineers**
 - **Anonymize Data**
 - **QR Code**
 - **Data Encryption**
- **Sensitive Data**
 - **Informed Consent**

Standardization and Integration

- **Data Schema**
 - **FAIR (Findable, Accessible, Interoperable and Reproducible)**
- **Technology Platforms**
 - **RADAR-Base [Open Source]**
 - **ANDROMEDA [EVIDATION]**
 - **Gather/validate/parse/normalize, datalake, slices, notebooks**

Standardization and Integration

- **RADAR-Base**
 - Remote Assessment of Disease And Relapses
 - Open source
 - Compliant to FAIR
 - Standardization
 - Privacy
 - Visualizations
 - Multiple Indications



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Standardization and Integration

- **RADAR-CNS**

- IMI (Innovative Medicines Initiative) project
- A collaborative research program
- Explore potential of wearable devices
- Prevent or help Central Nervous System disorders
 - Epilepsy
 - Multiple Sclerosis
 - Major depression



- **RADAR-AD**

- Alzheimer's Disease
- Vision:
 - Radically improve the assessment
 - Care for Alzheimer's patients
 - Using smart phones, wearables and home-based sensors
 - Measure disability progression associated with AD



Analysis

- **“Data Collection should focus on data necessary to implement the planned analysis, including the context” ICH E9 “Statistical principles for clinical trials”**
- **As defined in Protocol**
 - No data fishing
 - Data availability to study team
- **Avoid identification of personal traits**
- **Mis-interpretation of results**
- **Proper validated novel endpoints and analysis techniques**
 - Exploratory studies
 - Academic world to clinical trials

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Benefits

- **Enrollment, Retention**
- **Avoid trips to Clinical Site**
 - **Reduces Cost**
 - **Convenience**
- **Participant count**
- **Compliance, Quality of Data**
- **Avoid Site-induced inaccuracies**
- **Novel End points**
- **Real-time safety monitoring**
- **Medication adherence**



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Challenges

- **Device performance not as specified by manufacturers**
- **Privacy and Data Security**
- **Infrastructure necessary for handling large volume of data**
- **No acceptable endpoints available for many indications**
- **Technological devices not available as per study requirements**
- **Biopharmaceutical companies and device companies are separate and exploring mutual requirement is a challenge**

Challenges at each level: scientific, regulatory, ethical, legal, data management, infrastructure, analysis and security



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Resources

- CTTI Recommendations: Advancing the Use of Mobile Technologies for Data Capture & Improved Clinical Trials
- Feasibility studies data base: <https://feasibility-studies.ctti-clinicaltrials.org/>
- Atlas, an evidence-based catalog of connected technologies. <https://elektralabs.com/>
- RADAR-Base, Open source platform for remote assessment using wearable devices and mobile applications. <https://radar-base.org/index.php/home/about-us/>
- FDA Mystudies app: <https://www.fda.gov/drugs/science-and-research-drugs/fdas-mystudies-application-app>

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Summary and Conclusion

- **Context of “Are we There yet?”**
 - Device to submission supporting primary/key secondary endpoints
- **Feasibility Studies**
- **Data Management, Infrastructure, Analysis and security challenges**
 - Can be adopted from other industry use cases
- **Scientific and Regulatory Challenges**
 - Development of Novel Endpoints, Guidelines
- **Ethical and Legal Challenges**
 - Proper determination of data utilization as per protocol, adhering to consent obtained

Summary and Conclusion

Are we there yet?

Not yet, but we are on our way



Acknowledgements

- Guy Garrett, Bev Hayes and other members of Data Engineering Project
- Wendy Dobson from PHUSE
- Kevin Stanek, Raul Aguilar from Gilead Sciences Inc
- Dr Deniz Ones from University of Minnesota
- Rosa Bianca Gallo from The Hyve
- Gilead Sciences Inc

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Data Engineering Project

(Educating for the Future PHUSE Working Group)

<https://education.phuse.eu/eftf/data-engineering/>

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Any Questions?



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Back-up Slides



CTTI Feasibility Studies Database



CTTI Feasibility Studies Database

Select the columns you would like to display below (Max 8). *Note: All columns will be included in the downloaded data.*

- ☒ Title
- ☐ Authors
- ☐ Journal
- ☒ Year
- ☐ DOI
- ☐ Category
- ☒ Therapeutic Area
- ☐ Medical Condition
- ☒ Concept of Interest
- ☐ Outcome Assessment
- ☐ Comparator Measure
- ☒ Technology
- ☐ Sensor(s)
- ☒ Device Make and Model
- ☐ Wear Location(s)
- ☐ Algorithm / Analysis Software
- ☒ Sample Size
- ☐ Participant Age
- ☐ Participant Gender

The following 275 publications are feasibility studies on mobile clinical trials. Customize with Search and Filter, and then download your results.

Title	Year	Therapeutic Area	Concept of Interest	Technology	Device Make and Model	Sample Size
Quantifying the relative change in physical activity after Total Knee Arthroplasty using accelerometer based measurements More Info	2017	Musculoskeletal; Orthopedics/Orthopedic Surgery; Rheumatology	Physical activity patterns; Physical activity	Wearable	ActiGraph, GT1M	32

CTTI Feasibility Studies Database

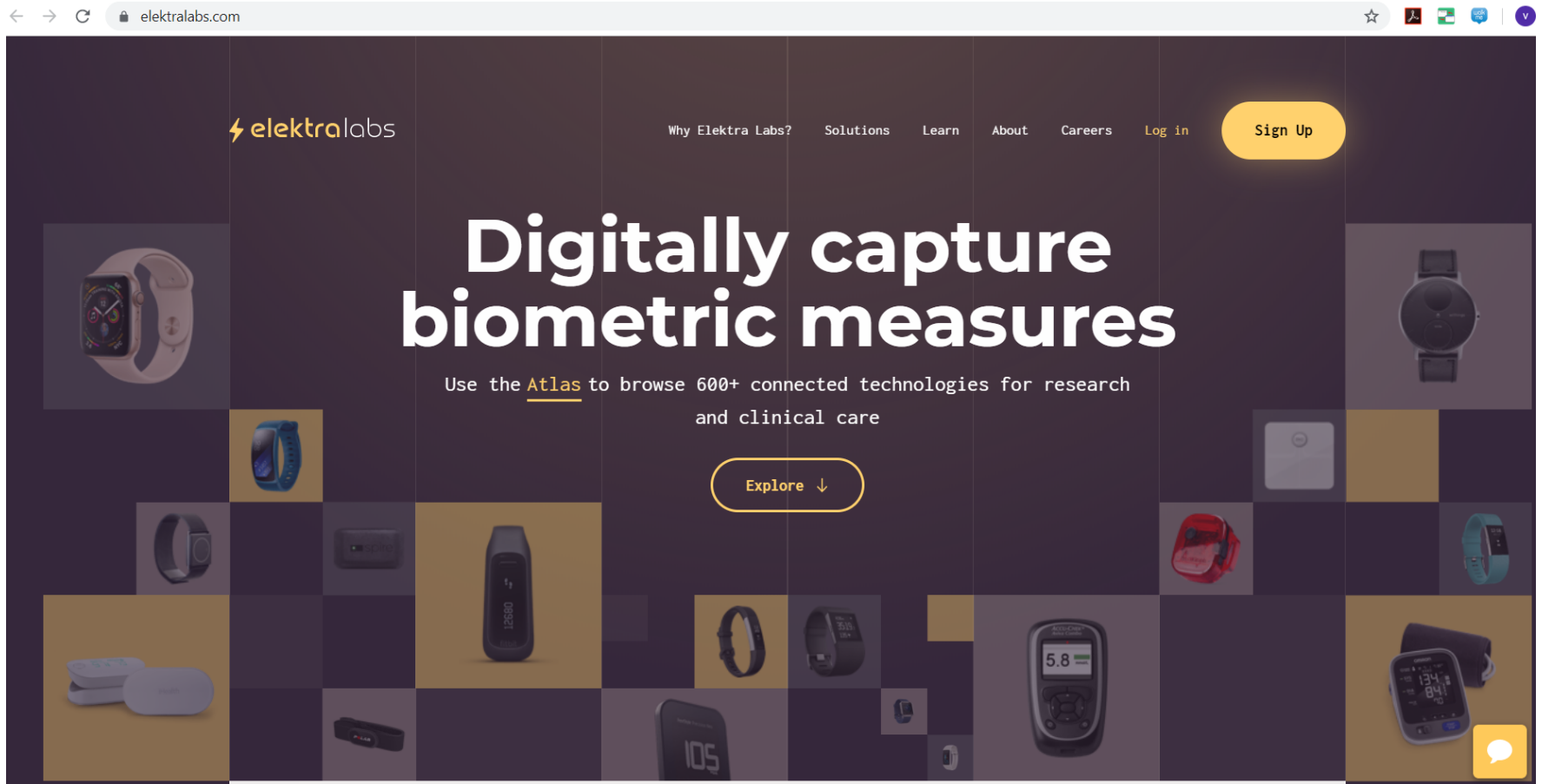
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Title	Year	Therapeutic Area	Concept of Interest	Technology	Device Make and Model	Sample Size
Impact of Arterial Stiffness on WatchPAT Variables in Patients With Obstructive Sleep Apnea More Info	2018	Cardiology; Pulmonary/Respiratory; Sleep	Arterial stiffness affect on respiratory variables	Portable technology	Itamar Medical Ltd., WatchPAT 200	61
The feasibility of using actigraphy to characterize sleep in Rett syndrome More Info	2018	Genetic Diseases; Neurology; Pediatrics; Rare Diseases/Disorders; Sleep	Sleep quality	Wearable	Philips Respironics, Actiwatch 2	13
Variables influencing wearable sensor outcome estimates in individuals with stroke and incomplete spinal cord injury: a pilot investigation validating two research grade sensors More Info	2018	Musculoskeletal; Neurology	Physical activity monitoring; Exercise capacity	Wearable; Patch	ActiGraph, wGT3X-BT; Metria IH1	28
Measurement of lower limb segmental excursion using inertial sensors during single limb stance More Info	2018	Orthopedics/Orthopedic Surgery	Motor function; Balance; Stability	Wearable sensor array	Custom CaneSense system	10
Nintendo Wii assessment of Hoehn and Yahr score with Parkinson's disease tremor More Info	2018	Musculoskeletal; Neurology	Motor function	Portable technology	Nintendo Wii remote	55
Quantification of whole-body bradykinesia in Parkinson's disease participants using multiple inertial sensors More Info	2018	Musculoskeletal; Neurology	Motor function	Wearable sensor array	Intertial Labs Inc.; Synertial Motion Capture system, IGS-180	41
The Pediatric SmartShoe: Wearable Sensor System for Ambulatory Monitoring of Physical Activity and Gait	2018	Musculoskeletal; Neurology;	Physical activity monitoring;	Smart	Interlink Inc.	21



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Atlas - Elektralabs

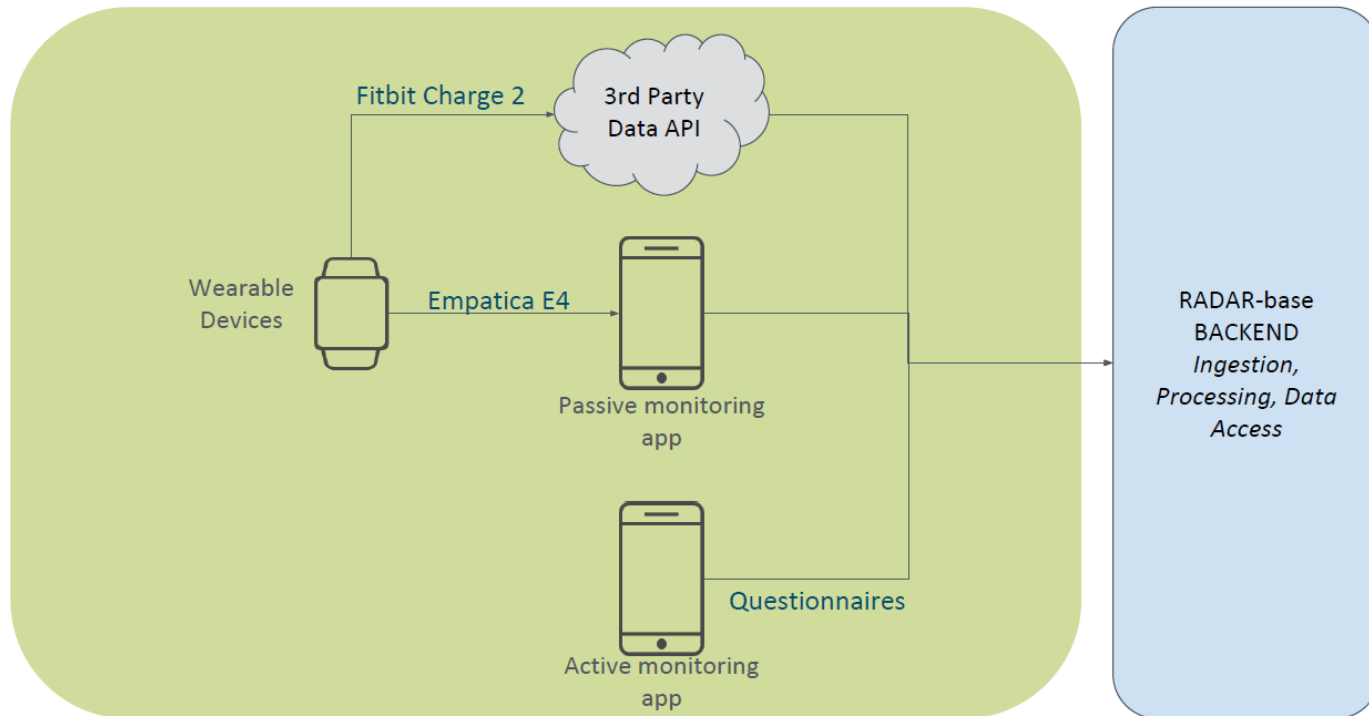


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RADAR-Base

Active and Passive Collection



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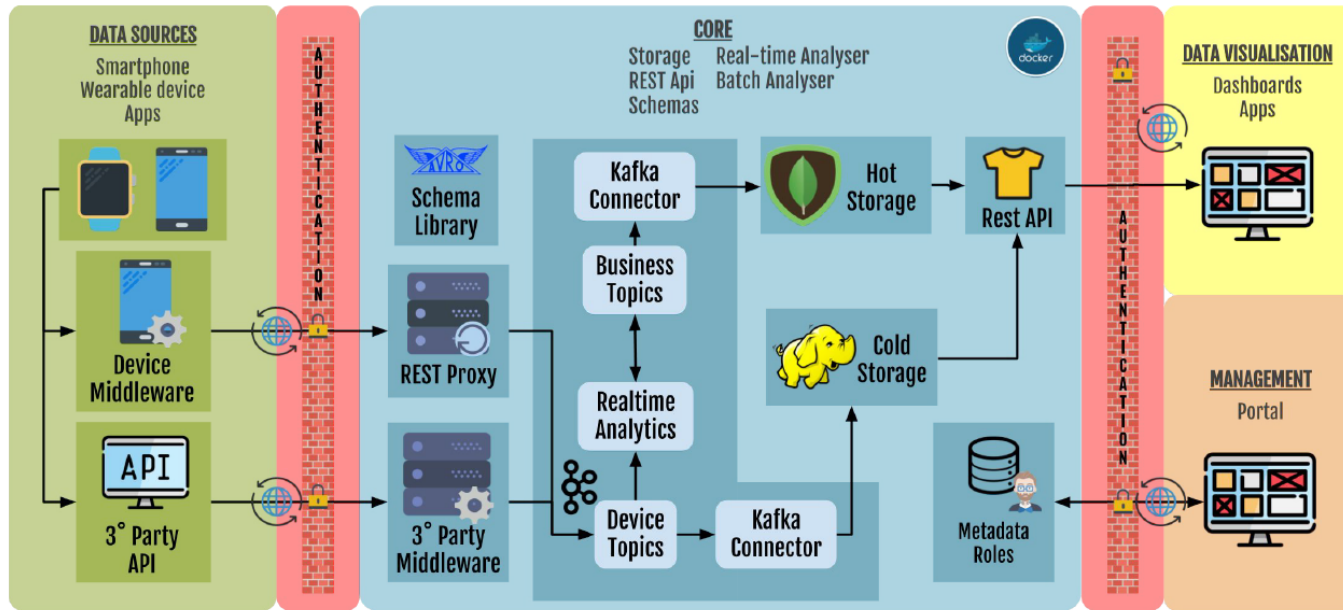


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RADAR-Base

The Open Source Stack



RADAR-Base

Data standardisation

Open data schema per type of sensor:



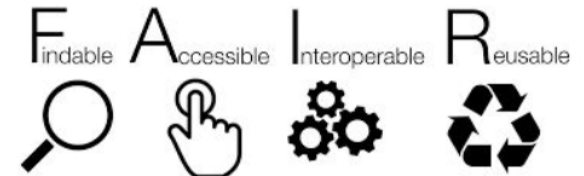
Pebble

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  ]
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```

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  "name": "EmpaticaE4Acceleration",
  "doc": "Data from 3-axis accelerometer sensor with gravitational constant g as unit."
  "fields": [
    { "name": "time", "type": "double", "doc": "Device timestamp in UTC (s)." },
    { "name": "timeReceived", "type": "double", "doc": "Device receiver timestamp in UTC (s)." },
    { "name": "x", "type": "float", "doc": "Acceleration in the x-axis (g)." },
    { "name": "y", "type": "float", "doc": "Acceleration in the y-axis (g)." },
    { "name": "z", "type": "float", "doc": "Acceleration in the z-axis (g)." }
  ]
}
```



Empatica



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- **RADAR-CNS**



https://www.linkedin.com/posts/radar-cns_watch-our-new-short-video-on-the-radar-cns-activity-6416979431360917504-kzU4



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