Is there a correlation between e.g. location and depression?

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Outline of Talk

Copenhagen Center for Health Technology

- background & vision
- research & innovation

Digital Phenotyping in Mental Health

- background
- systematic review of correlations between ‘objective’ features and depression

Outlook

- technology for digital phenotyping
- standards for mobile health (mHealth)

Strategic Partnership

Technical University of Denmark

- Electrical Engineering
- Computer Science
- Nano-technology
- Management Engineering
- …

Faculty of Health Sciences @ University of Copenhagen

- Biomedical Sciences
- Public Health
- …

The Capital Region of Denmark

- all hospitals in Greater Copenhagen
- 1.8 mio. people
- 12 hospitals
- ~ 1.000 GPs

CITY OF COPENHAGEN

- all nursing homes++ in Copenhagen City
- 600.000 inhabitants
- primary care

Strategic Goals

#1 – RESEARCH

- initiate and host new research projects and initiatives across partners

#2 – GROWTH & INNOVATION

- fuel and support health innovation, entrepreneurship and commercial growth in GCPH

#3 – VISIBILITY

- increase visibility and impact of research in health technology in GCPH

Healthcare Challenges

Chronic diseases management
Accounting for 2/3 of all healthcare spend worldwide – and increasing – chronic disease management is and will be the main focus of health.

Preventive and predictive health
Obesity, lack of physical activity and unhealthy lifestyle are the major factors for health problems and needs to be addressed early

Regulatory
Legal and regulatory demands for protecting patient privacy, data, and safety will be enforced heavily as digital and personalized health emerge

Evidence & outcome-based health
New business models both for suppliers and vendors will be tied to clinical evidence and real-world patient outcome (efficiency)

Technology Opportunities

Personalized technology
Engaging, patient-centric, and participatory technology can deliver interventions tailored to the individual and sustain engagement “beyond-the-pill” outside traditional care settings.

Digitalization
The ubiquity of digital health and communication technology drive new models for virtual and semi-automated doctor-patient contact.

Health IoT
Pervasive, mobile and wearable technology for sensing and engaging with patients create a unique platform for personalized health delivery

Big data analytics
Computing power and advanced analytics and learning algorithms drive insight and prediction of patient behavior, treatment, and care costs

PART II
Digital Phenotyping in Mental Health

Figure 27: Ten leading causes of burden of disease, world, 2004 and 2030

2004 Disease or injury	As % of total DALYs	Rank
Lower respiratory infections	6.2	1
Diarrhoeal diseases	4.8	2
Unipolar depressive disorders	4.3	3
Ischaemic heart disease	4.1	4
HIV/AIDS	3.8	5
Cerebrovascular disease	3.1	6
Prematurity and low birth weight	2.9	7
Birth asphyxia and birth trauma	2.7	8
Road traffic accidents	2.7	9
Neonatal infections and other[a]	2.7	10
COPD	2.0	13
Refractive errors	1.8	14
Hearing loss, adult onset	1.8	15
Diabetes mellitus	1.3	19

Rank	As % of total DALYs	2030 Disease or injury
1	6.2	Unipolar depressive disorders
2	5.5	Ischaemic heart disease
3	4.9	Road traffic accidents
4	4.3	Cerebrovascular disease
5	3.8	COPD
6	3.2	
7	2.9	
8	2.7	
9	2.5	
10	2.3	
11	1.9	Neonatal infections and other[a]
12	1.9	Prematurity and low birth weight
15	1.9	Birth asphyxia and birth trauma
18	1.6	Diarrhoeal diseases

”Mental health will be the largest burden for society in the 2020s” – WHO 2012

The Smartphone

- Ubiquitous
- Unobtrusive
- Intimate
- Powerful
- Sensor-rich
- Connected – always!

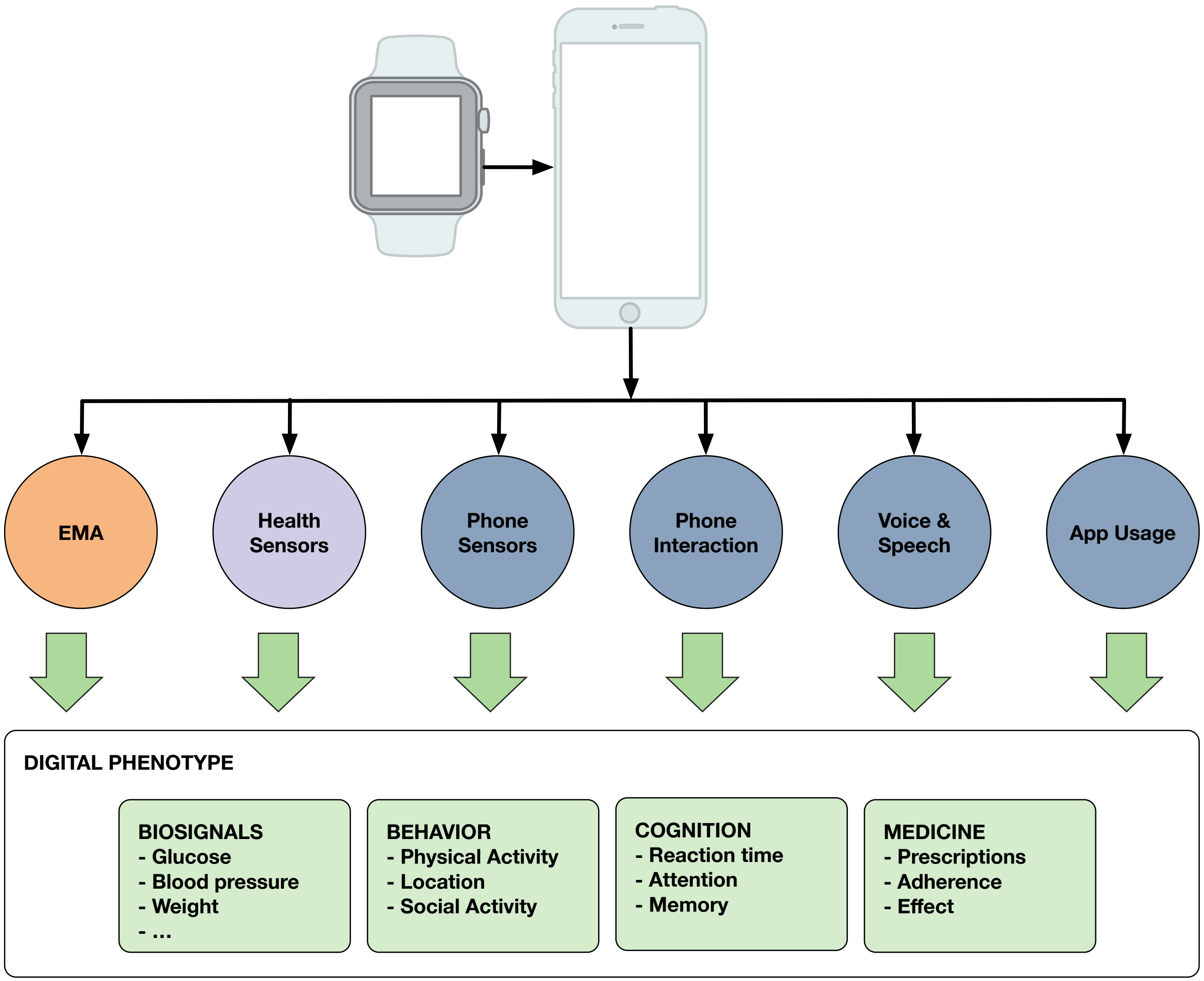
”... the mobile phone has become the most ubiquitous piece of technology in our recent history” – Oliver et. al. 2015

“Smartphones offer huge potential to gather **precise**, **objective**, **sustained**, and **ecologically valid** data on the **real-world behaviors** and experiences of **millions** of people where they **already are**” – Miller, 2015

Digital Phenotyping

Continuous and unobtrusive measurement and inference of health, behavior, and other parameters from wearable and mobile technology

"Even though smartphone technology promises to transform many aspects of health care, no area of medicine is likely to be changed more by this technology than psychiatry." [T. Insel, 2017]



- Jain, S. H., Powers, B. W., Hawkins, J. B., & Brownstein, J. S. (2015). The digital phenotype. *Nat Biotech*, 33(5), 462–463.
- Insel, T. R. (2017). Digital phenotyping: Technology for a new science of behavior. *JAMA*, *318*(13), 1215–1216.

EVIDENCE?

MONARCA

- Bipolar disorder (manio-depressive)
- EU STREP project | 2010-2014 | 13 partners
- Copenhagen team
  - The Copenhagen Clinic for Affective Disorder, Rigshospitalet, Psychiatric Center Copenhagen,
  - The Pervasive Interaction Technology Laboratory (PIT Lab), IT University of Copenhagen

- MONARCA system
  - Self-assessment
    - mood | sleep | stress | medicine | …
  - Auto-assessment
    - physical activity | mobility | social activity | phone usage
  - Feedback
    - visualizations | medication | actions-to-take | triggers | early-warning-signs | impact factors
  - Mood forecast
    - predict mood for next 5 days

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Clinical Evidence

Clinical evaluations have shown strong correlations between

- self-rated and clinically-rated mood
- objectively colle... rated mood

"Smartphones provide an easy and <u>objective</u> way to monitor illness activity and could serve as an <u>electronic biomarker</u> for depressive and manic symptoms in patients with bipolar disorder."

Table 2. Correlations between self-monitored data[a] collected using smartphones and depr
17 and YMRS, respectively[b]

	Unadjusted		
	Coefficient	95% CI	p-value
Mood (scale: −3 to +3)			
HDRS-17	−0.055	−0.067 to −0.042	<0.001
HDRS-17 sub-item 1 (mood)	−0.38	−0.45 to −0.30	<0.001
YMRS	0.39	0.016–0.062	<0.001
YMRS sub-item 1 (mood)	0.38	0.24–0.53	<0.001

Table 3. Correlations between automatically generated objective data[a] collected u
using the HDRS-17 and YMRS, respectively[b]

	Unadjusted		
	Coefficient	95% CI	p-value
/day)			
	0.022	−0.010 to 0.054	0.18
	0.060	0.016–0.100	0.007
ng calls (sec/day)			
	19.96	4.12–35.80	0.014
	28.54	5.17–51.90	0.017
sages (no./day)			
	−0.037	−0.18 to 0.14	0.61
	0.087	−0.10 to 0.28	0.37
/day)			
HDRS-17	0.031	−0.047 to 0.110	0.44
YMRS	0.15	0.045–0.250	0.005
Duration of outgoing calls (sec/day)			
HDRS-17	28.27	10.15–46.40	0.002
YMRS	23.87	−3.08 to 50.83	0.083
Outgoing text messages (no./day)			
HDRS-17	0.014	−0.16 to 0.19	0.88
YMRS	0.22	−0.006 to 0.450	0.057

M Faurholt-Jepsen et al. Smartphone data as an electronic biomarker of illness activity in bipolar disorder. Bipolar Disorders, 2015.

Voice & Mood

Collection of voice features in <u>naturalistic</u> setting

- N=28 | 12 week
- HDRS-17 (depre
- 179 clinical ratir
- openSMILE (em

Classification resu
(s.d.)

- depressive state : 70% (0.15)
- manic state : 61% (0.04)

Classification accuracy were not significantly increased when combining voice features with automatically generated objective data

"Voice features collected in <u>naturalistic settings</u> using smartphones may be used as <u>objective state markers</u> in patients with bipolar disorder. "

OPEN

Citation: Transl Psychiatry (2016) **6**, e856; doi:10.1038/tp.2016.123

www.nature.com/tp

ORIGINAL ARTICLE

Voice analysis as an objective state marker in bipolar disorder

M Faurholt-Jepsen[1], J Busk[2], M Frost[3], M Vinberg[1], EM Christensen[1], O Winther[2], JE Bardram[2] and LV Kessing[1]

Changes in speech have been suggested as sensitive and valid measures of depression and mania in bipolar disorder. The present study aimed at investigating (1) voice features collected during phone calls as objective markers of affective states in bipolar disorder and (2) if combining voice features with automatically generated objective smartphone data on behavioral activities (for example, number of text messages and phone calls per day) and electronic self-monitored data (mood) on illness activity would increase the accuracy as a marker of affective states. Using smartphones, voice features, automatically generated objective smartphone data on behavioral activities and electronic self-monitored data were collected from 28 outpatients with bipolar
daily basis during a period of 12 weeks. Depressive and manic symptoms were assessed
g Scale 17-item and the Young Mania Rating Scale, respectively, by a researcher blinded
zed using random forest algorithms. Affective states were classified using voice features
calls. Voice features were found to be more accurate, sensitive and specific in the classification
under the curve (AUC) = 0.89 compared with an AUC = 0.78 for the classification of depressive
automatically generated objective smartphone data on behavioral activities and electronic
curacy, sensitivity and specificity of classification of affective states slightly. Voice features
g smartphones may be used as objective state markers in patients with bipolar disorder.

6; doi:10.1038/tp.2016.123; published online 19 July 2016

such as the Hamilton
)[1] and the Young Mania
standards to assess the
mptoms when treating
using these clinical rating
er. Further, the severity of
termined by a subjective
interview with the risk of
bjective and continuous
t the clinical assessment
ods using continuous and
servable data on illness
be able to discriminate
linicians to improve the
ons for early intervention
r close and continuous
monitoring and collection of real-time data on depressive and manic symptoms outside clinical settings between outpatient visits.

Studies analyzing the spoken language in affective disorders date back as early as 1938.[5] A number of clinical observations suggest that reduced speech activity and changes in voice features such as pitch may be sensitive and valid measures of prodromal symptoms of depression and effect of treatment.[6–12] Conversely, it has been suggested that increased speech activity may predict a switch to hypomania.[13] Item number eight on the HAMD (psychomotor retardation) and item number six on the YMRS (speech amount and rate) are both related to changes in speech, illustrating that factors related to speech activity are important aspects to evaluate in the assessment of symptoms' severity in bipolar disorder. Based on these clinical observations there is an increasing interest in electronic systems for speech emotion recognition that can be used to extract useful semantics from speech and thereby provide information on the emotional state of the speaker (for example, information on pitch of the voice).[14]

Software for ecologically extracting data on multiple voice features during phone calls made in naturalistic settings over prolonged time-periods has been developed[15] and a few preliminary studies have been published.[16–20] One study extracted voice features in six patients with bipolar disorder type I using software on smartphones and demonstrated that changes in speech data were able to detect the presence of depressive and hypomanic symptoms assessed with weekly phone-based clinicians administrated ratings using the HAMD and the YMRS, respectively.[17] However, none of the patients in the study presented with manic symptoms during the study period, and the clinical assessments were phone-based. Another study on six patients with bipolar disorder showed that combining statistics on objectively collected duration of phone calls per day and extracted voice features on variance of pitch increased the accuracy of classification of affective states compared with solely using variance of pitch for classification.[18,19] The study did not state if and how the affective states were assessed during the monitoring period.

In addition to voice features, changes in behavioral activities such as physical activity/psychomotor activity[21–24] and the level of engagement in social activities[25] represent central aspects of

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E-mail: maria@faurholt-jepsen.dk
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M Faurholt-Jepsen, J Busk, M Frost, M Vinberg, EM Christensen, O Winther, JE Bardram, LV Kessing (2016,). Voice analysis as an objective state marker in bipolar disorder. *Transl Psychiatry.* Macmillan Publishers Limited.

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SYSTEMATIC EVIDENCE?

Systematic Review

- Systematic review
  - behavioral features
    - collected from mobile and wearable devices
  - depressive mood symptoms
  - patient w. affective disorders
    - major depression
    - bipolar disorder

Review

Correlations Between Objective Behavioral Features Collected From Mobile and Wearable Devices and Depressive Mood Symptoms in Patients With Affective Disorders: Systematic Review

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Abstract

Background: Several studies have recently reported on the correlation between objective behavioral features collected via mobile and wearable devices and depressive mood symptoms in patients with affective disorders (unipolar and bipolar disorders). However, individual studies have reported on different and sometimes contradicting results, and no quantitative systematic review of the correlation between objective behavioral features and depressive mood symptoms has been published.

Objective: The objectives of this systematic review were to (1) provide an overview of the correlations between objective behavioral features and depressive mood symptoms reported in the literature and (2) investigate the strength and statistical significance of these correlations across studies. The answers to these questions could potentially help identify which objective features have shown most promising results across studies.

Methods: We conducted a systematic review of the scientific literature, reported according to the preferred reporting items for systematic reviews and meta-analyses guidelines. IEEE Xplore, ACM Digital Library, Web of Sciences, PsychINFO, PubMed, DBLP computer science bibliography, HTA, DARE, Scopus, and Science Direct were searched and supplemented by hand examination of reference lists. The search ended on April 27, 2017, and was limited to studies published between 2007 and 2017.

Results: A total of 46 studies were eligible for the review. These studies identified and investigated 85 unique objective behavioral features, covering 17 various sensor data inputs. These features were divided into 7 categories. Several features were found to have statistically significant and consistent correlation directionality with mood assessment (eg, the amount of home stay, sleep duration, and vigorous activity), while others showed directionality discrepancies across the studies (eg, amount of text messages [short message service] sent, time spent between locations, and frequency of mobile phone screen activity).

Conclusions: Several studies showed consistent and statistically significant correlations between objective behavioral features collected via mobile and wearable devices and depressive mood symptoms. Hence, continuous and everyday monitoring of behavioral aspects in affective disorders could be a promising supplementary objective measure for estimating depressive mood symptoms. However, the evidence is limited by methodological issues in individual studies and by a lack of standardization of (1) the collected objective features, (2) the mood assessment methodology, and (3) the statistical methods applied. Therefore, consistency in data collection and analysis in future studies is needed, making replication studies as well as meta-analyses possible.

(JMIR Mhealth Uhealth 2018;6(8):e165) doi:10.2196/mhealth.9691

Rohani AD, Faurholt-Jepsen M, Kessing VL, Bardram EJ. Correlations Between Objective Behavioral Features Collected From Mobile and Wearable Devices and Depressive Mood Symptoms in Patients With Affective Disorders: Systematic Review. *JMIR Mhealth Uhealth*. 2018;6(8):e165. doi:10.2196/mhealth.9691.

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Methods

- 2,644 unique papers identified
- 929 full papers screened
- 46 papers included

- Studies divided into
  - clinical (i.e. diagnosed)
  - non-clinical ("healthy individuals")

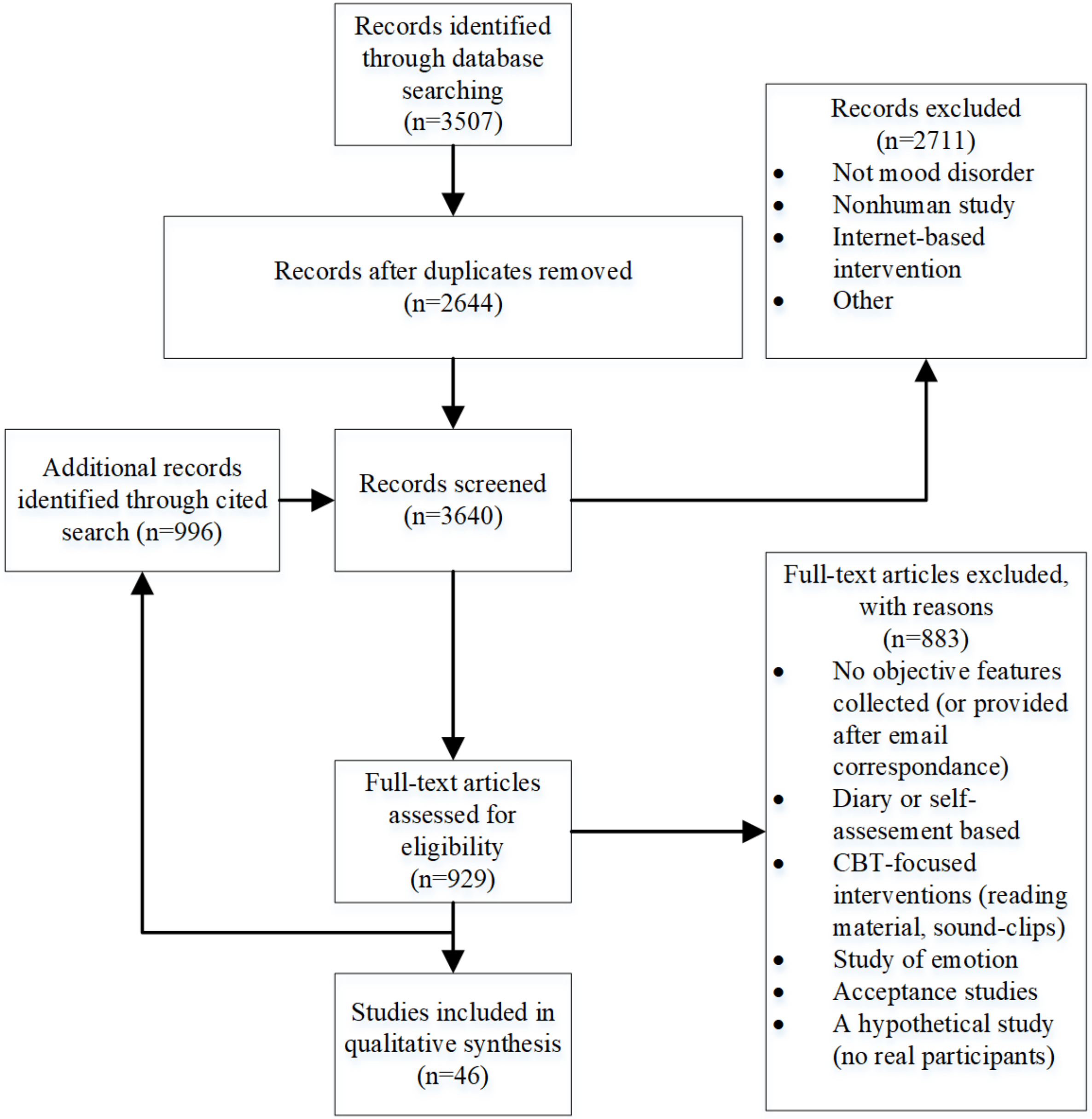

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Table 1. Summary of the included studies with nonclinical samples of participants.

Reference	Technology used	Participants (N=1189), n		Participant age (years), mean (SD)	Study duration (days)	Mood scale
		Male	Female			
Asselbergs et al, 2016 [15]	Android; Funf	5	22	21.1 (2.2)	36	10p mood
Baras et al, 2016 [40]	Android; EmotionStore	9	1	N/A[a]	14	BRUMS[b]
Becker et al, 2016 [41]	Android; Funf	5	22	N/A	42	Mood
Ben-Zeev et al, 2015 [42]	Android	37	10	22.5	70	PHQ-9[c]
Berke et al, 2011 [43]	Multisensor (waist)	4	4	85.3 (4.1)	10	CES-D[d]
Canzian and Musolesi, 2015 [9]	Android; MoodTraces	15	13	31	71	PHQ-8[e]
Cho et al, 2016 [44]	Phone records	234	298	57	N/A	BDI-21[f]
Chow et al, 2017 [45]	Android	35	37	19.8 (2.4)	17	DASS-21[g]
DeMasi et al, 2016 [46]	Android	17	27	N/A	56	BDI-21
Edwards and Loprinzi, 2016 [47]	Digi-Walker Pedometer	16	23	21.82	7	PHQ-9
Farhan et al, 2016 [17]	Android or iOS; LifeRhythm	21	58	18-25[h]	N/A	PHQ-9
Mark et al, 2016 [48]	Fitbit flex	20	20	N/A	12	Affect balance
Matic et al, 2011 [16]	Windows M. 6.5; MyExperience	6	3	28.4 (2.8)	7	rPOMS[i]
Mehrotra et al, 2016 [49]	Android	25[j]	N/A	N/A	30	PHQ-8
Mestry et al, 2015 [14]	Android	1	1	22	34	DASS21
Pillai et al, 2014 [50]	Actigraph	10	29	19.55 (3.2)	7	BDI-21
Saeb et al, 2015 [7]	Android; Purple robot	8	20	28.9 (10.1)	14	PHQ-9
Saeb et al, 2016 [39]	Android; Studentlife	38	10	N/A	70	PHQ-9

N=20

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Table 2. Summary of the included studies with clinical samples of participants diagnosed with unipolar (UD) or bipolar (BD) disorder.

Reference	Technology used	Participants (N=3094), n		Clinical diagnosis	Participant age (years), mean (SD)	Study duration (days)	Mood scale
		Male	Female				
Abdullah et al, 2016 [53]	Android; MoodRhythm	2	5	BD	25-64[a]	28	SRM II-5[b]
Alvarez-Lozano et al, 2014 [11]	Android; Monarca	18[c]	N/A[d]	BD	N/A	150	7p mood
Beiwinkel et al, 2016 [22]	Android; SIMBA	8	5	BD	47.2 (3.8)	365	HDRS[e]
Berle et al, 2010 [54]	Actigraph	10	13	UD	42.8 (11)	14	Group difference
Dickerson et al, 2011 [55]	iOS; Empath	0	1	UD	83	14	10p mood
Doryab et al, 2016 [18]	Android	3	3	UD	>18[f]	20	CES-D[g]
Faurholt-Jepsen et al, 2012 [56]	Actiheart	8	12	UD	45.2 (12)	3	Group difference
Faurholt-Jepsen et al, 2015 [57]	Actiheart	7	11	UD	45.6 (11.1)	3	HDRS-17
Faurholt-Jepsen et al, 2016 [58]	Android; Monarca	9	19	BD	30.3 (9.3)	84	HDRS-17
Faurholt-Jepsen et al 2014 [10]	Android; Monarca	5	12	BD	33.4 (9.5)	90	HDRS-17
Faurholt-Jepsen et al, 2015 [26]	Android; Monarca	20	41	BD	29.3 (8.4)	182	HDRS-17
Faurholt-Jepsen et al, 2016 [6]	Android; Monarca	11	18	BD	30.2 (8.8)	84	HDRS-17
Gershon et al, 2016 [59]	Actigraph	14	23	BD	34.4 (10.4)	46	Group difference
Gonzales et al, 2014 [60]	Actigraph	15	27	BD	41.0 (11.2)	7	IDS-C-30[h]
Grünerbl; 2015 [61]	Android	2	8	BD	33-48	84	7p mood
Guidi et al, 2015 [20]	Android	0	1	BD	36	98	mood state
Hauge et al, 2011 [62]	Actigraph	14	11	UD	42.9 (10.7)	14	Group difference
Krane-Gartiser et al, 2014 [63]	Actigraph	5	7	BD	39.9 (15.6)	1	Group difference
Loprinzi and Mahoney, 2014 [64]	Actigraph (hip)	1261	1313	UD	46.3	7	Group difference

N=26

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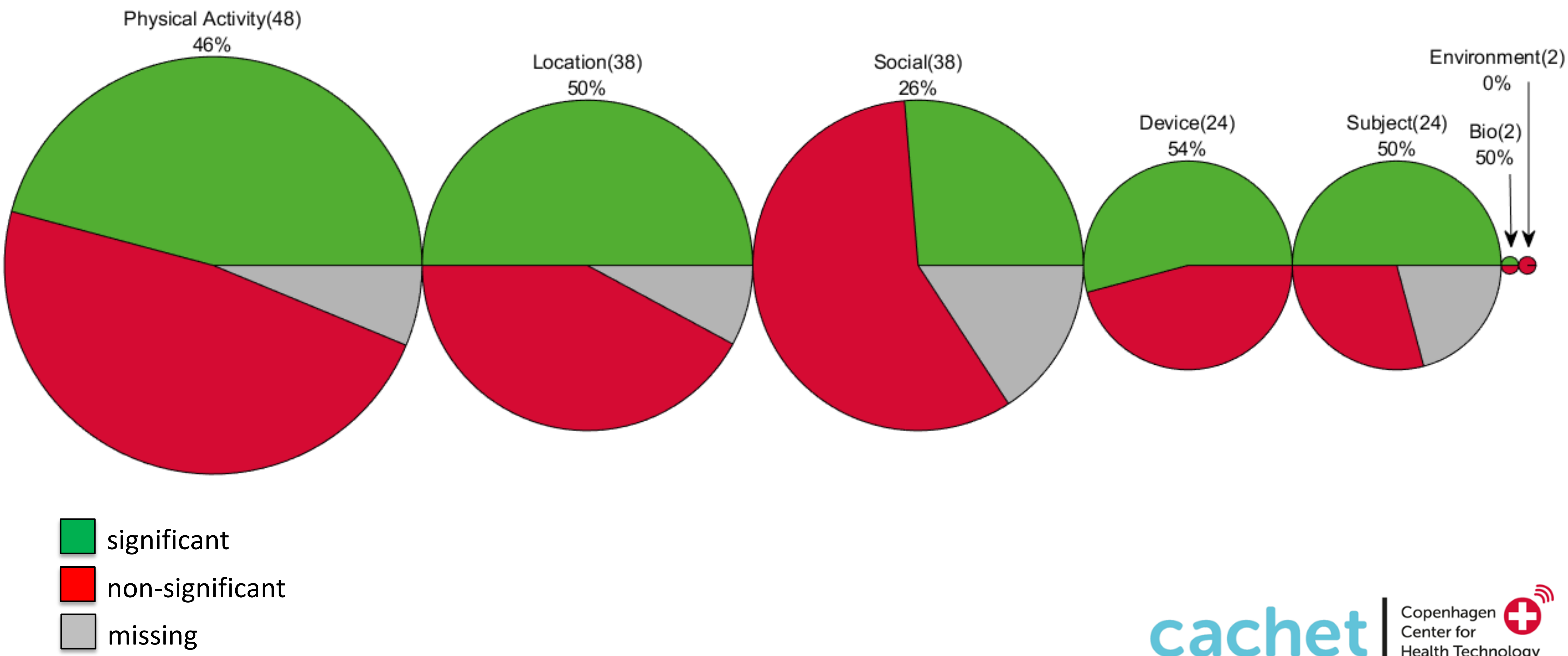
Feature Categories



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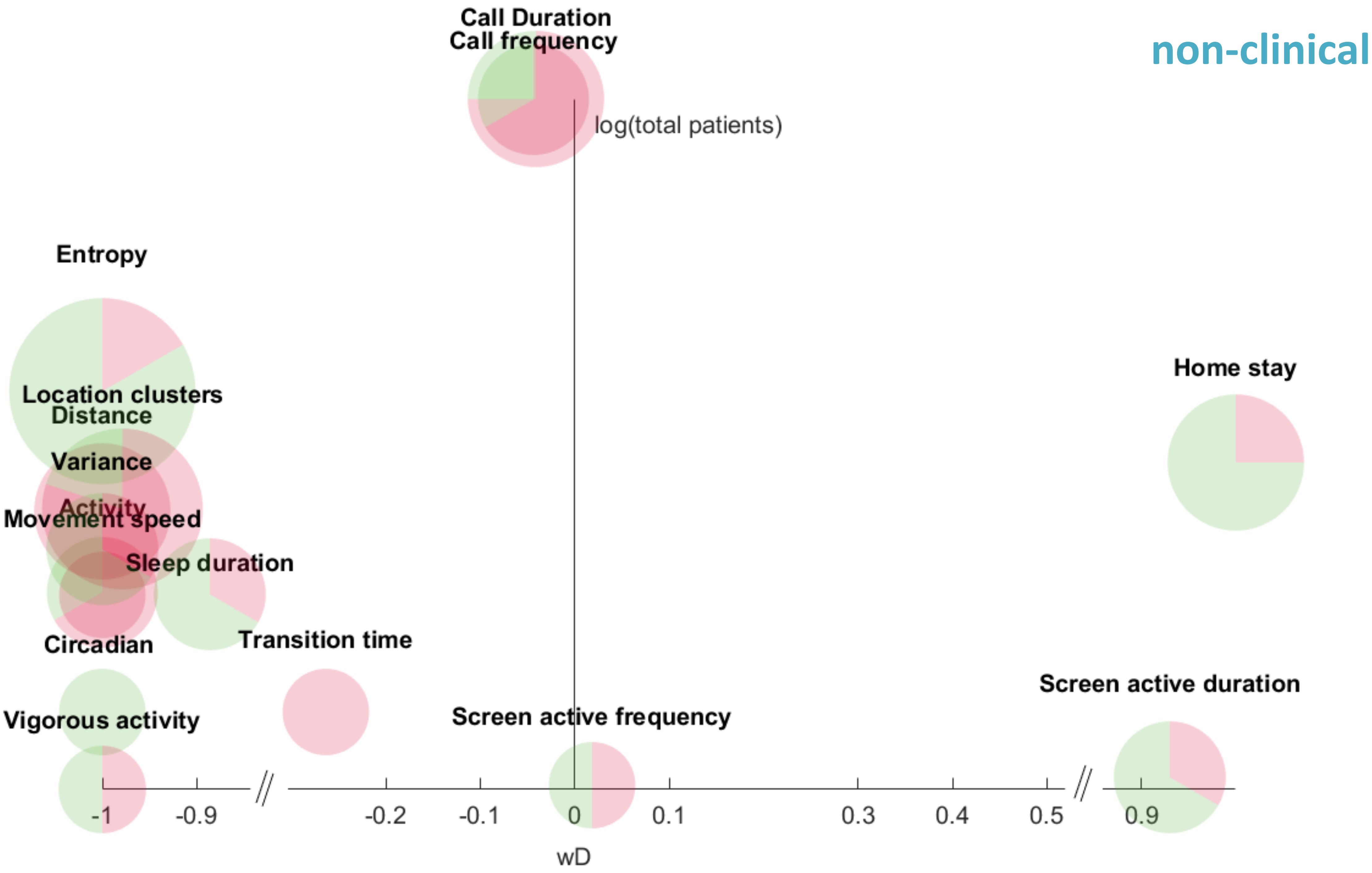
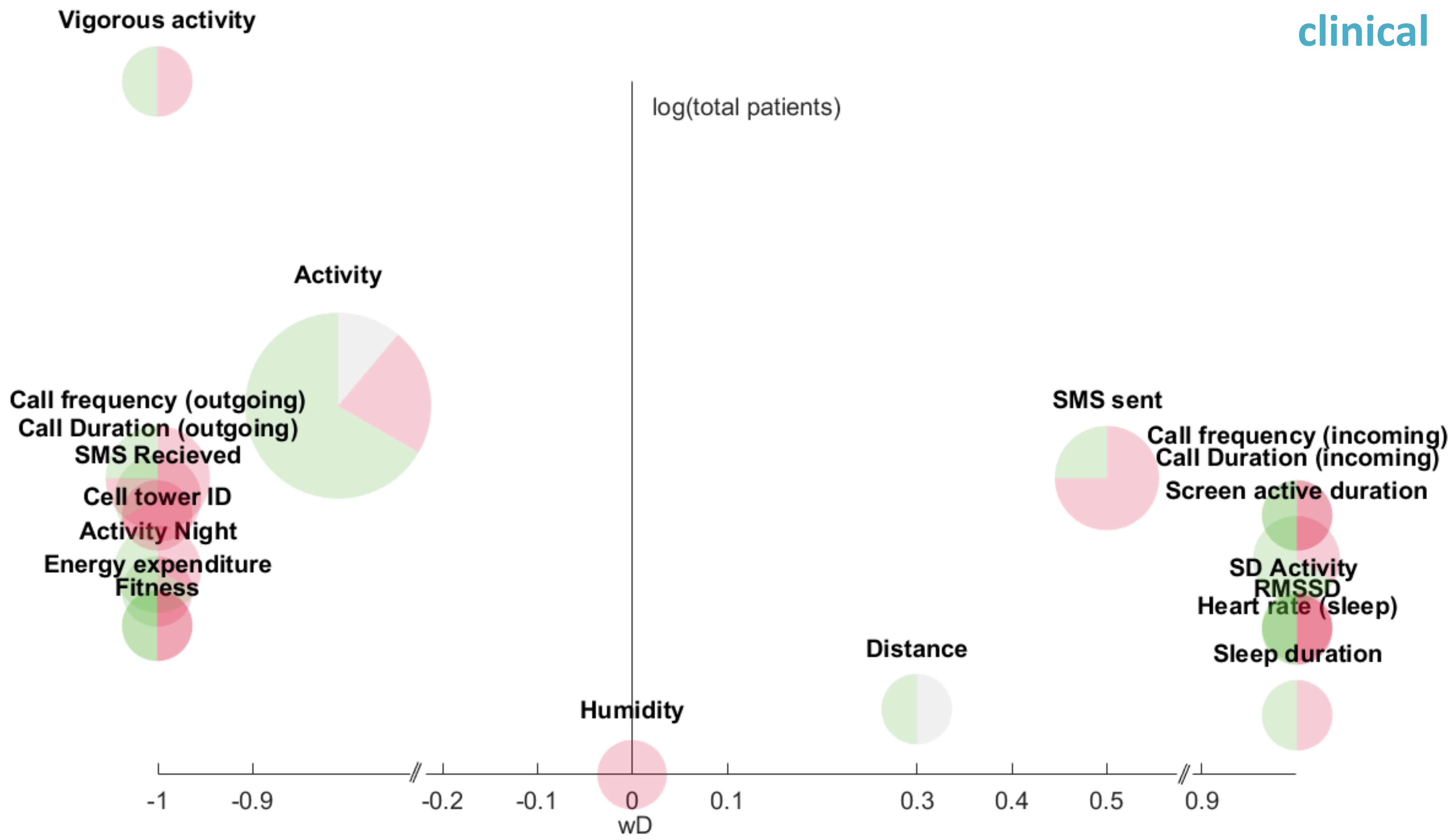

non-clinical
Call Duration
Call frequency
log(total patients)
Entropy
Location clusters
Distance
Variance
Activity
Movement speed
Sleep duration
Circadian
Transition time
Vigorous activity
Home stay
Screen active duration
Screen active frequency
-1
-0.9
-0.2
-0.1
0
0.1
0.3
0.4
0.5
0.9
wD



clinical
Vigorous activity
log(total patients)
Activity
Call frequency (outgoing)
Call Duration (outgoing)
SMS Recieved
Cell tower ID
Activity Night
Energy expenditure
Fitness
SMS sent
Call frequency (incoming)
Call Duration (incoming)
Screen active duration
SD Activity
RMSSD
Heart rate (sleep)
Sleep duration
Distance
Humidity
-1
-0.9
-0.2
-0.1
0
0.1
0.3
0.4
0.5
0.9
wD

However, ...

1. Standardized **data collection** and **features extraction** methods
   – the way that physical activity, social activity, and mobility features based on accelerometer and GPS data are extracted should be standardized across studies.
2. Standardized **mood assessment** tools.
   – a wide range of clinical (n=11) and nonclinical (n=9) mood rating scales were used
   – hard to compare correlations across studies when such different scales are used.
3. Standardized **statistical correlation** methodology.
   – studies applied more than 11 different methods for correlation values, with different time windows.

?!


PART III
OUTLOOK

CARP – CACHET Research Platform

Standardization

- part of open international standards
- FHIR, IEEE 1752, ORK, ORS, …

Sharing

- multi-study platform
- analysis of data across multiple studies

Privacy & Security

- enabling privacy & security as part of platform (GDPR)
- secure local hosting @DTU Computerome

Multi-project platform used in

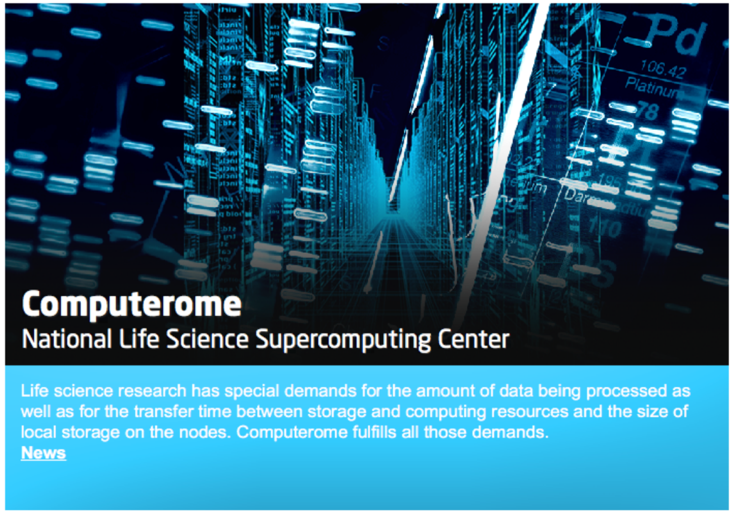
- REAFEL
- BHRP
- PhyPsy Trial
- …

Open mHealth

FHIR

IEEE Advancing Technology for Humanity

ResearchKit



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Technical University of Denmark DTU

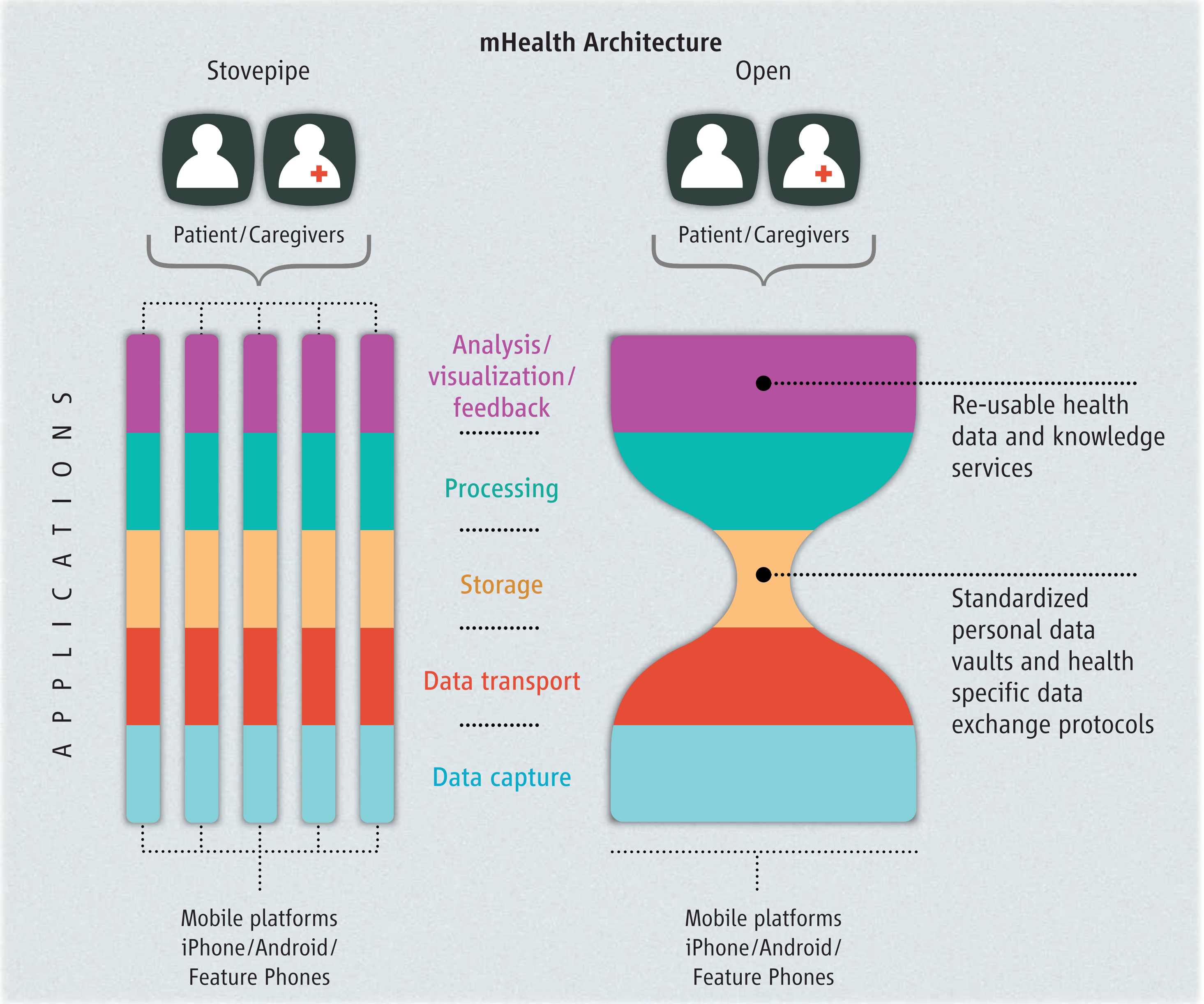
REGION H The Capital Region of Denmark

CITY OF COPENHAGEN

UNIVERSITY OF COPENHAGEN

Goal

- mHealth is emerging as a patchwork of **incompatible** applications serving narrow, albeit valuable, needs, and thus could benefit from more coordinated development
- Open architecture
  - standardized interfaces
  - standardized components
  - standardized data formats



mHealth architecture: Stovepipe versus Open. The narrow waist of the open hourglass will include at least health-specific syntactic and semantic data standards; patient identity standards; core data processing functions such as feature extraction and analytics; and data stores that allow for selective, patient-controlled sharing. Standards should be common with broader health IT standards whenever possible.

OMH Schemas

- A set of JSON standard for various mHealth data points
- Semantic standardization

- Design principles
- Templates
- Library

Sample Data

With descriptive statistic


```
{
    "systolic_blood_pressure": {
        "value": 160,
        "unit": "mmHg"
    },
    "diastolic_blood_pressure": {
        "value": 60,
        "unit": "mmHg"
```


Sample Data

Valid geoposition


```
{
    "latitude": {
        "value": 40.0596923828125,
        "unit": "deg"
    },
    "longitude": {
        "value": -105.21440124511719,
        "unit": "deg"
    },
    "effective_time_frame": {
        "date_time": "2013-02-05T07:25:00Z"
    },
    "positioning_system": "GPS"
}
```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Standardization

- IEEE P1752 – Open mHealth is now part of an IEEE standardization effort

- Standardization of
  - schemas
  - end-point APIs

- Relation to other (IEEE) standards
  - HL7 / FHIR
  - ISO/IEEE 11073 Personal Health Data (PHD)

IEEE P1752 Working Group IEEE

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Outline of Talk

Copenhagen Center for Health Technology

- background & vision
- research & innovation

Digital Phenotyping in Mental Health

- background
- systematic review of correlations between ‘objective’ features and depression

Outlook

- technology for digital phenotyping
- standards for mobile health (mHealth)

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