Population precision medicine research in the digital economy

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Precision medicine

- The ambition:
  - *"a medical model that proposes the customization of healthcare, with medical decisions, practices, and/or products being tailored to the individual patient"*
  - *"an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person."*
- AKA:
  - Personalized medicine, personalized health, precision health, precision public health, precision oncology
- The present:
  - Focus on small, deep, validated cohort *omics studies
  - Rapt enthusiasm about expanding to broader genotype/ phenotype studies

Precision medicine

- Coming soon:
  - US Precision Medicine cohort -1,000,000 volunteers
    - EMR, genomic, social, biospecimens, outcomes, mobile
    - Distributed national centers, recruiting, management
    - Apps and marketing
- Anticipated challenges
  - Limited evidence of targeted genomics working at scale
  - Virtually no standardization of data sources, data ownership policy, or models of effective patient engagement
  - PMI underfunded (130MM$ = ~ $130/patient)
  - Multiple competing initiatives (PCORI, NCATS, 1MM Veterans, EU), no current interoperability
  - Academically driven

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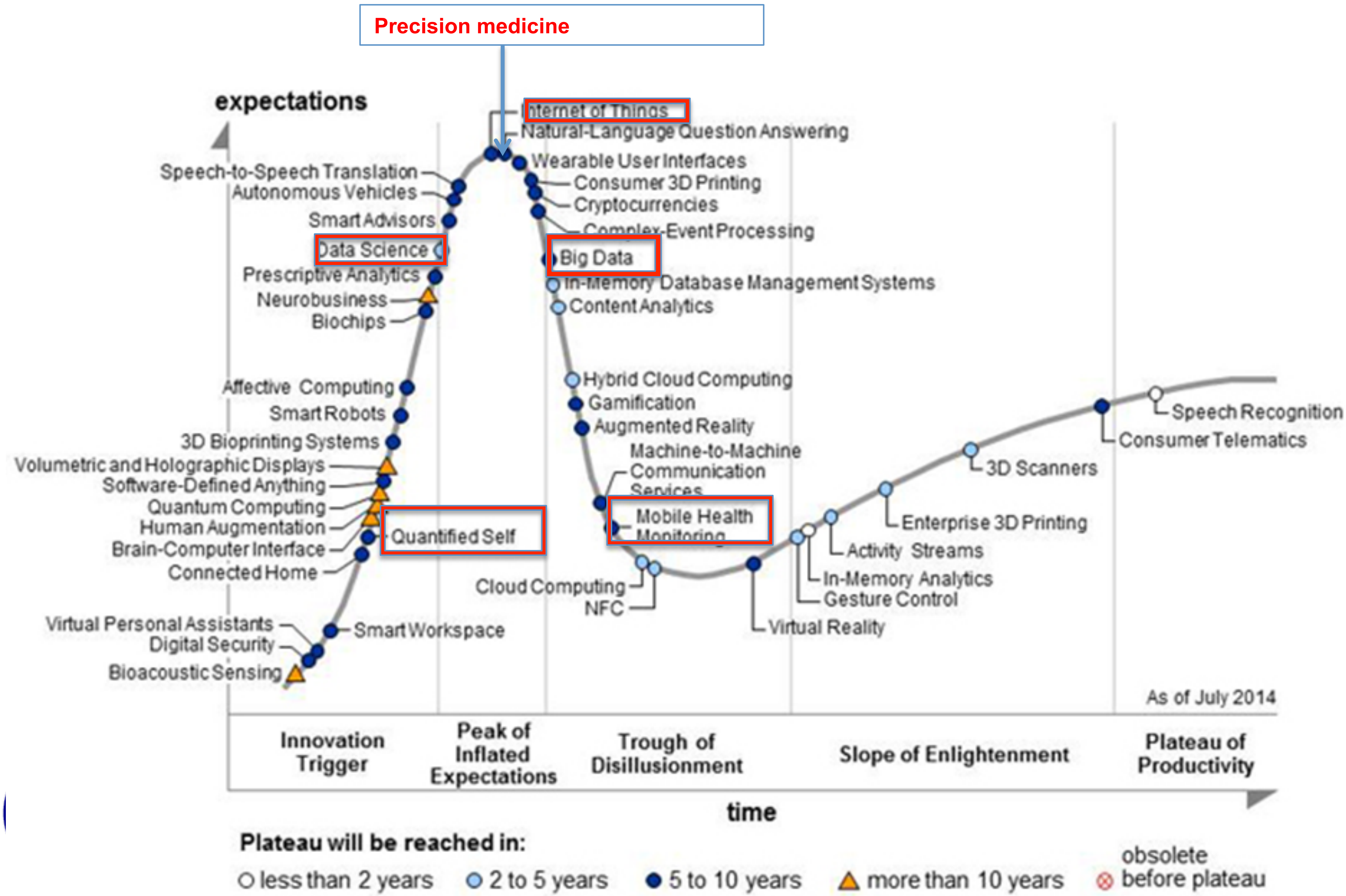
Gartners Hype Cycle 2015-2016



Consumer mHealth economy

- Vast ecosystem of products generating ~quantified biometrics
- $22+ billion economy by 2017
- 270+ million wireless subscribers in the US
- 30% of US smartphone users own at least 1 health app

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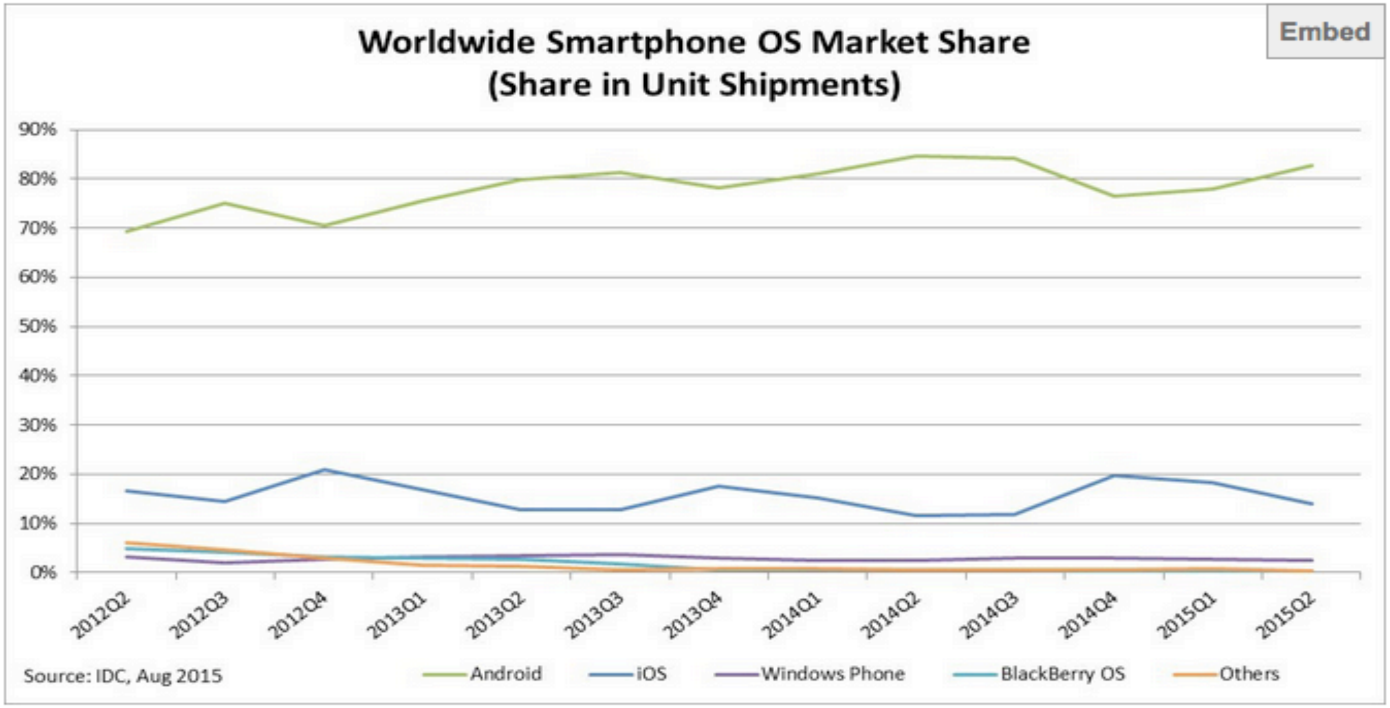

Period	Android	iOS	Windows Phone	BlackBerry OS	Others
2015Q2	82.8%	13.9%	2.6%	0.3%	0.4%
2014Q2	84.8%	11.6%	2.5%	0.5%	0.7%
2013Q2	79.8%	12.9%	3.4%	2.8%	1.2%
2012Q2	69.3%	16.6%	3.1%	4.9%	6.1%

Source: IDC, Aug 2015

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The trough of consumer mHealth

- 165,000+ apps in combined IOS and Android stores
- mHealth app or device average use 1-3 months
- Of active users, 65% use daily
- Over 85% use social media for health
- Emerging consumer suits against companies that don't perform as advertised
  - Fitbit
    - Sleep
    - Heart rate
  - Nike
    - Calories, steps, "nikefuel"
- …No one data stream tells the story

Precision mHealth challenges

- Majority of vendor data measures unvalidated, not reproducible or persistent
- Range of balkanized silos and aggregators:
  - Health maintenance
    - Apple HealthKit and now CareKit
    - Google Fit
  - Research
    - Apple ResearchKit
    - Research Stack (android)
  - Citizen science
    - Google Science Journal
    - Openhumans.org

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Small Data

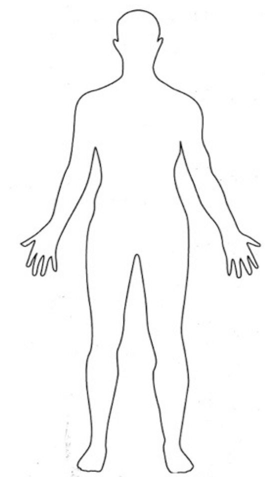
The data an individual generates implicitly, across a myriad of systems, and encounters

Household cable/tv box
- TV patterns (sleep/hearing)
- internet mediated patterns

Household utilities
- Diurnal rhythms
- Appliance use

Financial
- Purchases and Transactions
- Consumption
- Dietary patterns

Transportation
- Location/commute
- Physical mode (passive, active)
- Energy use
- Contextual stress



Social Media and Email
- Social/communciation
- Moods
- Family structure

Mobile Carriers
- Location/activity
- Call records
- Call patterns

Games/Music/Video
- Cognitive state
- Indicator/influence

Search
- State of mind
- Topic/concern
- Influence

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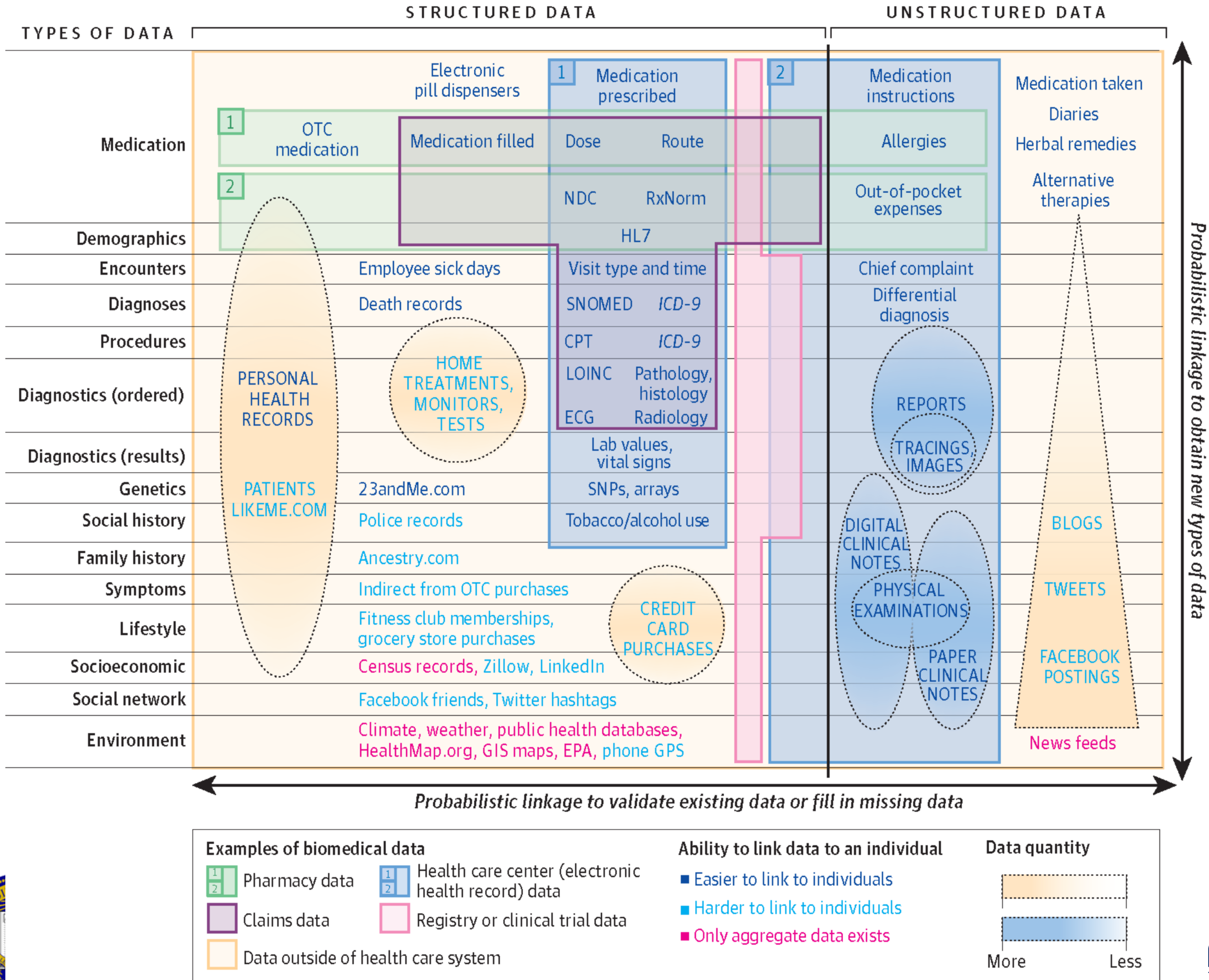

Weber et. al, JAMA 2014

Precision health in a legal and commercial world

- Few protections exist to prevent mHealth data from being shared without consent
  - CA bill to expand coverage of "HIPAA" like requirements to prohibit commercial health monitoring programs from sharing or selling data without explicit permission, and that mHealth data cannot be used by employers for employee discrimination.
- Broad restrictions and on sharing patient data
- Widely varying legal and social norm restrictions on sharing social media, movement, app usage data, - though it is for the most part already being shared.

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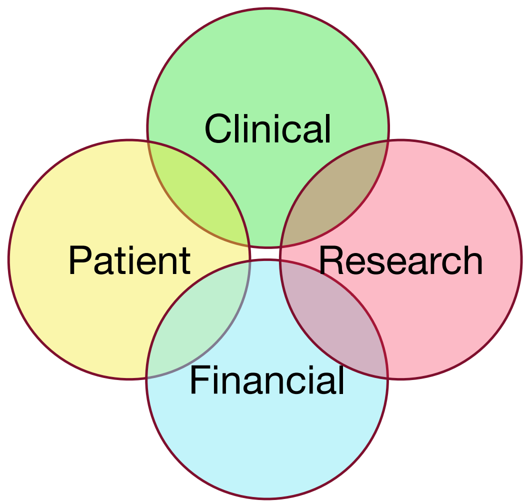
Data generation, ownership access and use

Owners: consumers, caretakers, companies, community
Sources: patients, companies, providers
Users: patients, providers, companies, R&D, payers
Examples: Vitals, fitness, chronic care, history, outcomes

Owners: providers, patients, labs
Sources: patients, providers, labs
Users: R&D, patients, providers
Ex: EMR, Dx, Tx, genetic tests



Owners: Academia, companies, gov
Sources: Providers, patients, companies
Users: Researchers, companies, pharma
Examples: Trials, screening, market research

Owners: Payers, patients, companies
Sources: providers, patients, companies
Users: payers, providers, regulators, companies, tbd
Examples: claims, cost, payment, utilization, allocation

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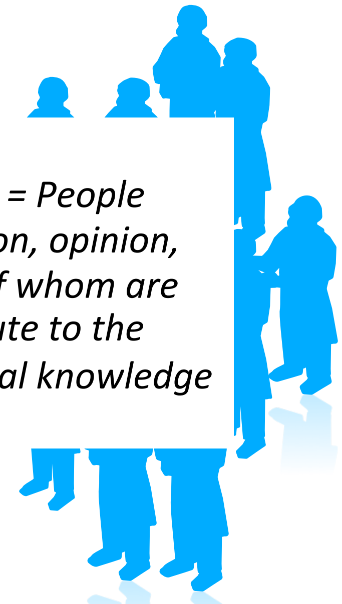
Data sharing and ownership challenges

"Data Seekers" *= Entities, people, tools, or applications that need to find and access sensitive personal health information*

- **personal, private, and highly sensitive**;
- protected by **national and jurisdictional laws**, strict **institutional policies**;
- Obscured by operational obstacles that maintain distance between researchers and potential **data subjects**



"Subjects of the Data" *= People with varying contribution, opinion, engagement – many of whom are quite willing to contribute to the discovery of new medical knowledge*

"Data Holders" *= Entities or people like hospitals, doctors offices, labs, pharmacies, insurers, medical specialists, devices, and apps with strict privacy obligations*

Dixie Baker, 2014

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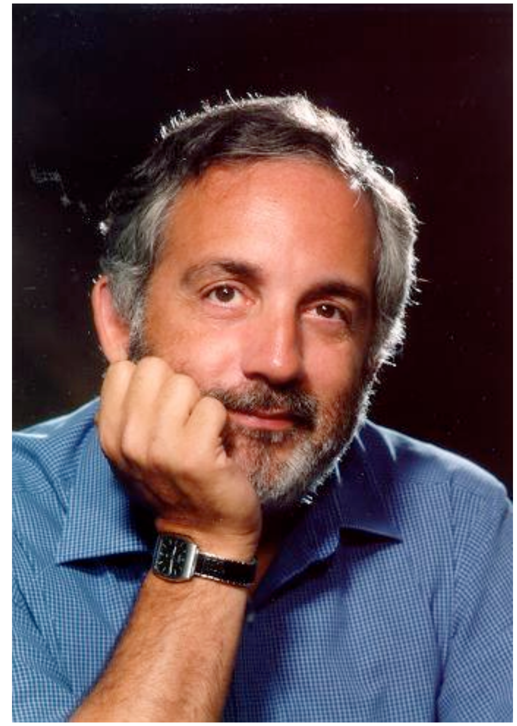
"The design of systems determines the kinds of politics that can take place in them, and designing a system is itself a political act". Mitch Kapor – Electronic Frontier Foundation



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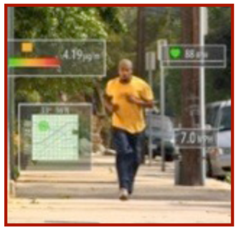
Behavioral Biomarkers

Specific behavioral traits to measure progress of disease and treatment

state classification
- sedentary/ambulatory
- at home/work
- app analytics (games, media...)
- communication



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Behavioral Biomarkers

Specific behavioral traits to measure progress of disease and treatment

summarization
- ambulatory/sedentary cumulative and durations,walking speed
- sleep times, meal times
- time spent key locations, diameter of day
- social interaction

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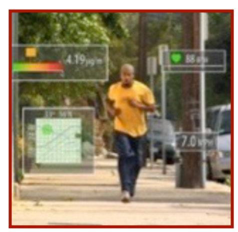

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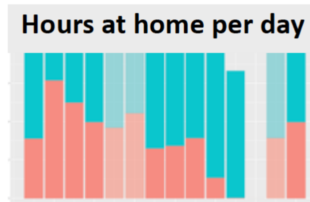
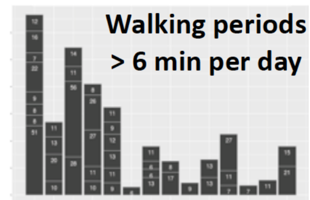
Behavioral Biomarkers

Specific behavioral traits to measure progress of disease and treatment

behavioral biomarker
- individual's patterns; relevance is symptom and condition dependent
- 'function, fatigue, pain, depression, insomnia, cognition, self-medication...





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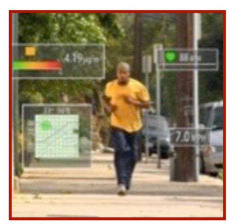

Predictive biomarkers via search

- ***Microsoft Finds Cancer Clues in Search Queries*** **- New York times June 7, 2016**
- "If we heard the whispers of people online, would it provide strong evidence or a clue that something's going on"
- Found that signals deduced from patterns of queries in search logs can predict the future appearance of queries that are highly suggestive of a diagnosis of pancreatic adenocarcinoma –
- \- which could inform *when* screening and assessment could improve subsequent symptom development health states
- Used Bing

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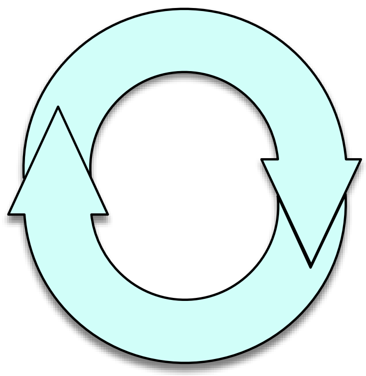
Link mHealth and small data to clinical care

Clinical history and context
Care plans

Participant self Care
How is this medication working for me?



Clinical care:
How is patient responding to new care plan?

Passive recorded data, location, activity

Mobile data outcomes, usage
Real-time sensor data

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Prescriptive data and digital biomarkers

Unknown
root cause

Patient
Not at Goal

- High cost patient
- Disease management candidate

Prescriptive data for 4 weeks

Differentiate patterns of adherence from non-adherence

Characterize behavioral reasons for non-adherence

Enable providers to make informed treatment decisions

4 week cycles capture robust data in typical Rx cycle

Alternative monitoring data to see if patient is on track

Root cause determined to be
treatable non-adherence

Sustain plan for 12 weeks

Designed for 12 week cycles to allow for habit formation

Treat non-adherence by supporting logistical, educational and motivational needs

Increase patient engagement through interaction with interfaces and enhanced communication with care team

Yearly
check-in

Patient
At Goal

Requires
on-going
support

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Building models

Personal	Public
Availability: Permission to share and access to data	**Aggregate data sets**
Standardization: harmonization and filtering	**Reference terminologies and data translations**
State classification: Ambulatory/mobile Home/work Application analytics Communication	**Classification models**
Summarization: Cumulative durations, speeds sleep times, meal times key locations, balance of activity social interactions/support	**Reference health phenotypes**
Patterns: Symptom and condition causality function: fatigue, pain, depression, insomnia, cognition	**Population health conditions**

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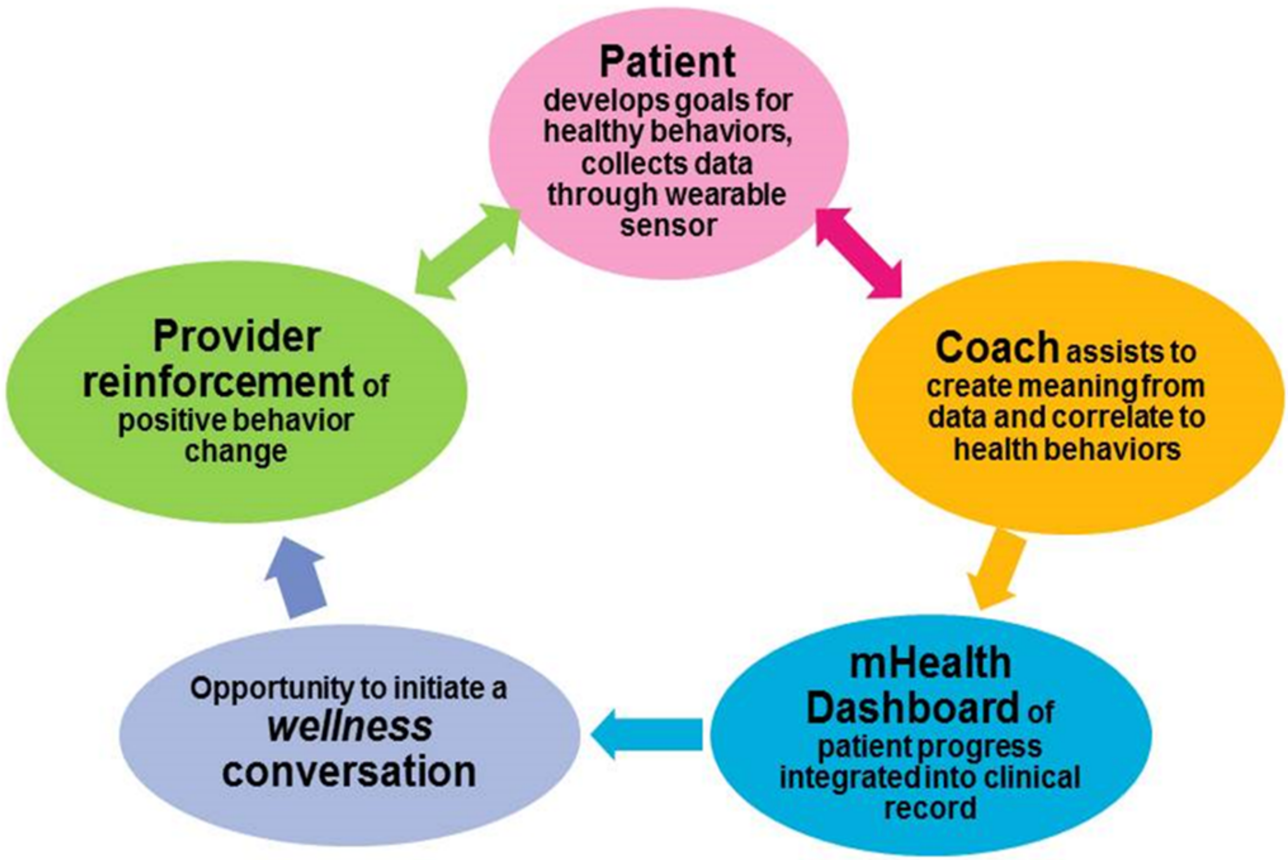
Challenges to digital biomarkers for precision medicine

- Quantity is not always better
- Potential biases require alternative validation approaches
- Critical:
  - Context and reproducibility critical
  - Patient trust and engagement

Prescriptive Digital health: Changing the patient/ data relationship



Questions?

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