No conflicts to declare.

ISPOR 2020

Workshop 10

Advancing Real-World Evidence to Incorporate Patient-Generated Health Data

ISPOR 2020

Advancing Real-World Evidence to Incorporate Patient-Generated Health Data

Moderator

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#PGHDinRWE

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Digital health technology in clinical trials and beyond: A regulatory perspective

ISPOR Annual Meeting
May 19, 2020

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Acting Director, Division of Clinical Outcome Assessment
Office of Drug Evaluation Sciences
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Speaker Disclaimer

- The views expressed in this presentation are those of the speaker, and do not necessarily represent an official FDA position.

FDA's Comprehensive Effort to Advance New Innovations: Initiatives to Modernize for Innovation

August 29, 2018

By: Scott Gottlieb, M.D.

- *"Electronic capture of PRO data (ePRO) is also becoming standard, providing a rich pipeline of structured clinical data.*
- *...mobile wearable technologies can complement traditional PRO surveys by generating objective, continuous activity and physiologic data.*
- *Obtaining reliable wearable device data on activity level, coupled with direct patient report on their ability to carry out important day to day activities, can provide information on physical function that is directly relevant and important…."*

https://www.fda.gov/NewsEvents/Newsroom/FDAVoices/ucm619119.htm

Digital Health Technology (DHT)

- Digital health technology can be thought of as the convergence of computing power, connectivity, sensors, and software used in healthcare.

- Uses of DHT include (but are not limited to):
  - As a medical product or incorporated into a medical product
  - As a tool to develop or study a medical product (e.g., in study endpoints)
  - As a companion or adjunct to a medical product, including diagnostics and therapeutics
  - As a method of gathering insights into the patient experience

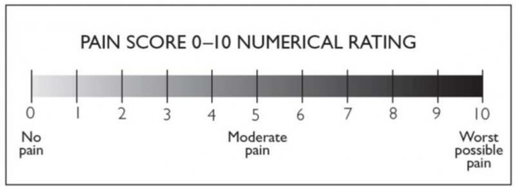
Person-Generated Health Data

- Growth of person-generated health data (PGHD) is enabled by DHT
- PGHD is wellness and/or health-related data created, recorded, or gathered by individuals for themselves (or by family members or others who care for an individual)*
  - Term “Patient-generated health data” is also used
- The individual or patient controls data collection and sharing

*Duke Margolis definition: https://healthpolicy.duke.edu/sites/default/files/u31/rwd_reliability.pdf

Assessment of Clinical Benefit:
How do we measure how patients feel and function?

Traditional Approaches



Novel Approaches

DHT and remote data capture: Opportunities

- Fewer barriers to clinical trial participation (e.g., travel)
- Larger, more inclusive, and more generalizable trials and evidence generation
- Enhancement of endpoints that matter to patients in daily life
- Ability to collect data from patients who cannot report (e.g., scratching in infants with atopic dermatitis)
- Ability to detect intermittent or rare events (e.g., falls, seizures, arrhythmias)
- Novel measures (e.g., behavior patterns in patients with depression)

Defining the endpoint

- Defining the endpoint rests on what is meaningful to patients and caregivers and what is expected to improve with a given treatment
- Input from multiple stakeholders is important: patients/caregivers, regulators, disease experts, clinicians, engineers, and others
- Considerations for a wearable activity monitor, for example, include:
  - Parameter definition (e.g., step counts, total distance walked, walking speed)
  - Determination of appropriate assessment periods (e.g., in a day, in a week)
  - Minimal time requirements for device wearing (e.g., during the day)
  - Data analysis: How do we summarize a large amount data over an extended period of time?
  - Data interpretation: How do we describe the benefit and what amount of change matters to a patient?

Examples of measures using DHT in development*

- Physical activity accelerometry assessment for analgesic clinical trials
- ActiMyo® in Duchenne muscular dystrophy
- Actibelt® in sarcopenia after surgical treatment of hip fracture
- Activity monitor based endpoint in chronic heart failure
- Virtual Reality Functional Capacity Assessment Tool (VRFCAT) cognition in patients with schizophrenia (a performance outcome assessment)
- Others

*For further information, please see CDER's Drug Development Tool (DDT) Clinical Outcome Assessment (COA) Qualification Program website

Real-world data to assess variation in opioid prescribing and use for acute pain

- FDA collaboration with Yale-Mayo CERSI*
- 1,550 patients from diverse populations prescribed short-acting opioid analgesics for new onset pain
- Hugo, a novel health data-sharing platform, will be used to collect:
  - Pain control and opioid use
  - Electronic medical records and pharmacy data
  - Activity and sleep patterns using wearable devices
  - Information about what patients did with unused opioids
- Goal: Evidence-based recommendations for opioid analgesic-prescribing

*Center of Excellence in Regulatory Science and Innovation

Closing thoughts

- DHT offers unique opportunities in assessing patient experience, both within trials and in the real world context
- Considerations include (but are not limited to):
  - Selection of important concept(s) to be assessed in the target population consistent with the medical product development goals
  - Development of a meaningful endpoint
  - Practical aspects of implementation, including analysis and interpretation
- Engage multiple stakeholders, including patients and caregivers, beginning as early as possible

Thank you!

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Resources

- Guidance for Industry: Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims
  - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-reported-outcome-measures-use-medical-product-development-support-labeling-claims
- CDER's Patient-Focused Drug Development Webpage:
  - https://www.fda.gov/drugs/development-approval-process-drugs/cder-patient-focused-drug-development
- Guidance for Industry: Electronic Source Data in Clinical Investigations
  - http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm328691.pdf
- Clinical Trials Transformation Initiative (CTTI) Novel Endpoints Project
  - https://www.ctti-clinicaltrials.org/projects/novel-endpoints
- Clinical Outcome Assessment Qualification Program
  - https://www.fda.gov/drugs/drug-development-tool-ddt-qualification-programs/clinical-outcome-assessments-coa-qualification-submissions
- Opioid Prescribing project
  - https://www.fda.gov/science-research/advancing-regulatory-science/real-world-data-assess-variation-opioid-prescribing-and-use-acute-pain-diverse-populations


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ADMINISTRATION

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What is PGHD and how can it be valuable in medical product development and RWD/RWE data generation?

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ADVANCING REAL-WORLD EVIDENCE TO INCORPORATE PATIENT-GENERATED HEALTH DATA | ISPOR 2020

May 19, 2020

Outline

Background: Person-Generated Health Data (PGHD)

Case Studies

1. Cognitive Impairment
2. Weight Loss Surgery
3. Asthma

Patients and their outcomes have historically been characterized using limited, visible-to-the-system data sets.

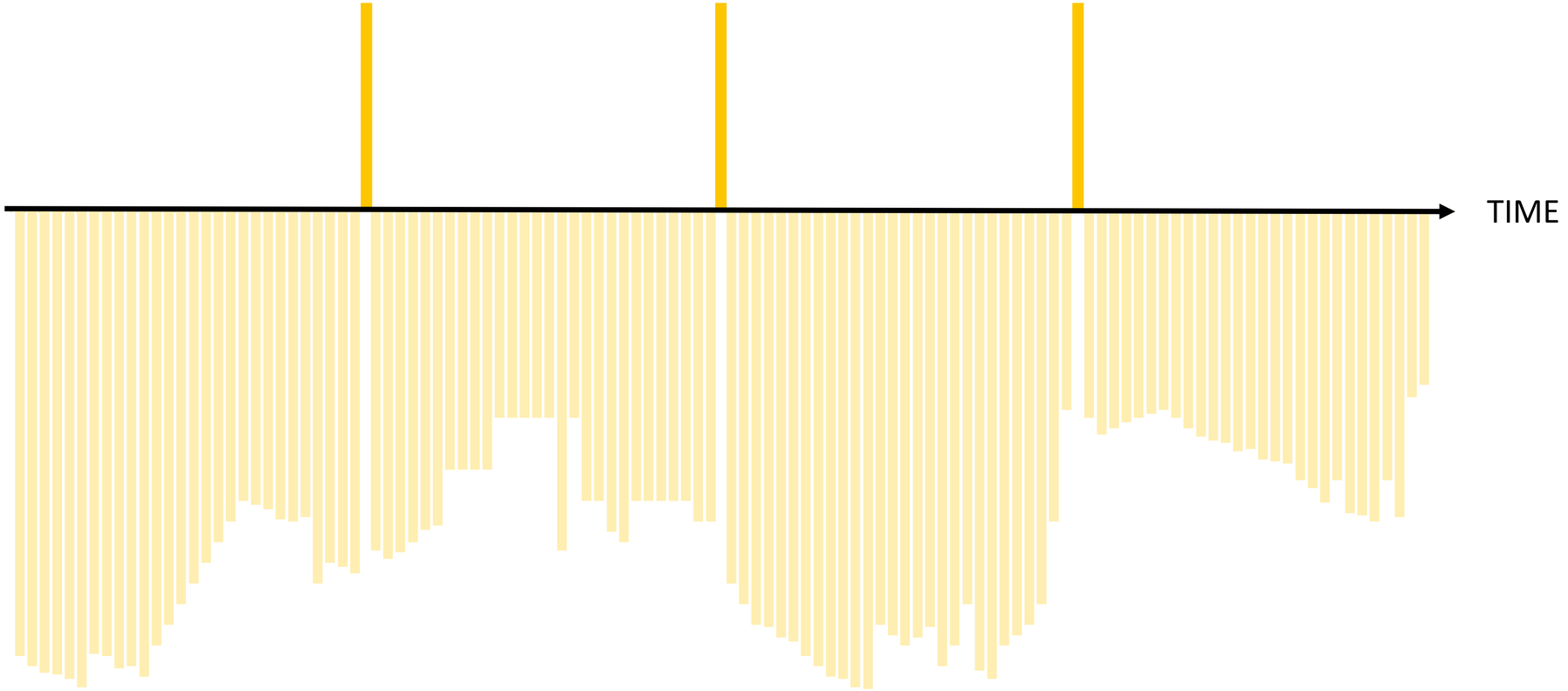
DATA POINTS

Visible

episodic

Invisible

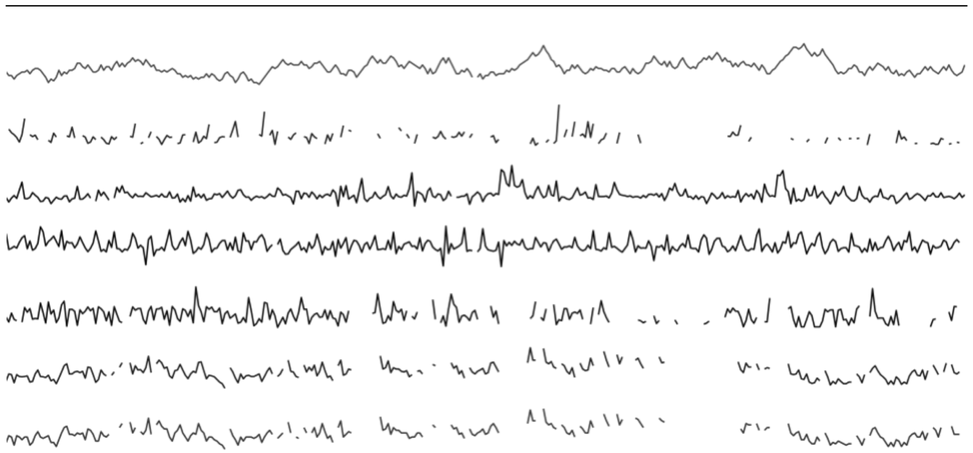
continuous, passive



Person-Generated Health Data (PGHD) is wellness and/or health-related data created, recorded, or gathered by individuals for themselves (or by family members or others who care for an individual)

OBJECTIVE EVERYDAY DATA

Collected via sensors and apps



PHENOTYPIC LABELS

Collected via questionnaires / ePROs

- Age
- Gender
- Ethnicity / race
- Medical diagnoses
- Prescription drugs
- Smoking
- Education
- Household
- Zip code
- Patient-reported outcomes
- Fast food consumption
- Employment status
- Employer
- Supplements
- Quality of life
- Alcohol use
- Insurance carrier
- Height / weight
- Major medical events
- Sleep quality

EXAMPLE DIGITAL MEASURES

Direct assessment
- Functional mobility
- Sleep reliability
- Weight range

Behavioral inference
- Routine/consistency
- Digital utilization
- Responsiveness

Clinical inference
- Exacerbation events
- Treatment utilization
- Disease progression

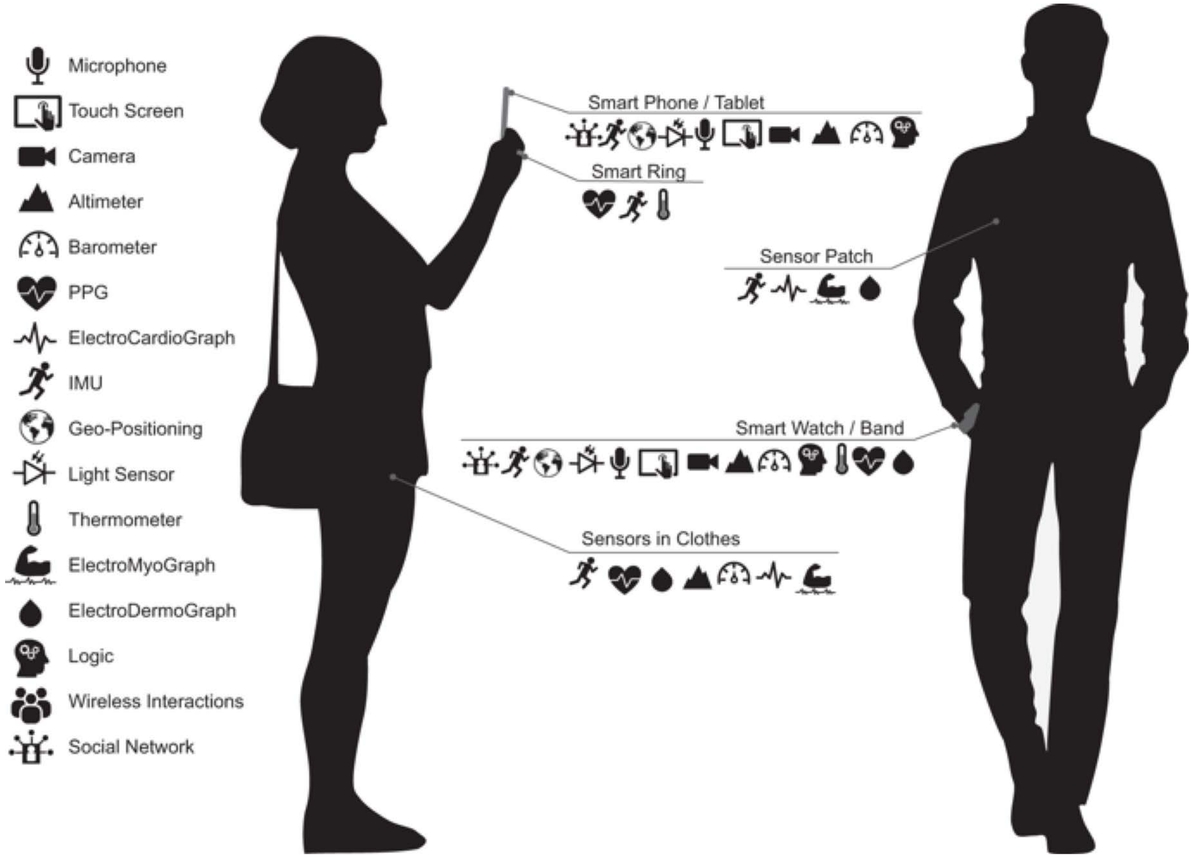
Definition: https://healthpolicy.duke.edu/sites/default/files/atoms/files/_determining_real-world_datas_fitness_for_use_and_the_role_of_reliability.pdf

Person-Generated Health Data (PGHD) can be obtained from a variety of sensors, services, and self-report methods

Sensors

Services

Surveys / ePROs



Kourtis, L. C., Regele, O. B., Wright, J. M., & Jones, G. B. (2019). Digital biomarkers for Alzheimer's disease: the mobile/wearable devices opportunity. *Npj Digital Medicine*, *2*(1), 9. https://doi.org/10.1038/s41746-019-0084-2

Outline

Background: Person-Generated Health Data (PGHD)

Case Studies

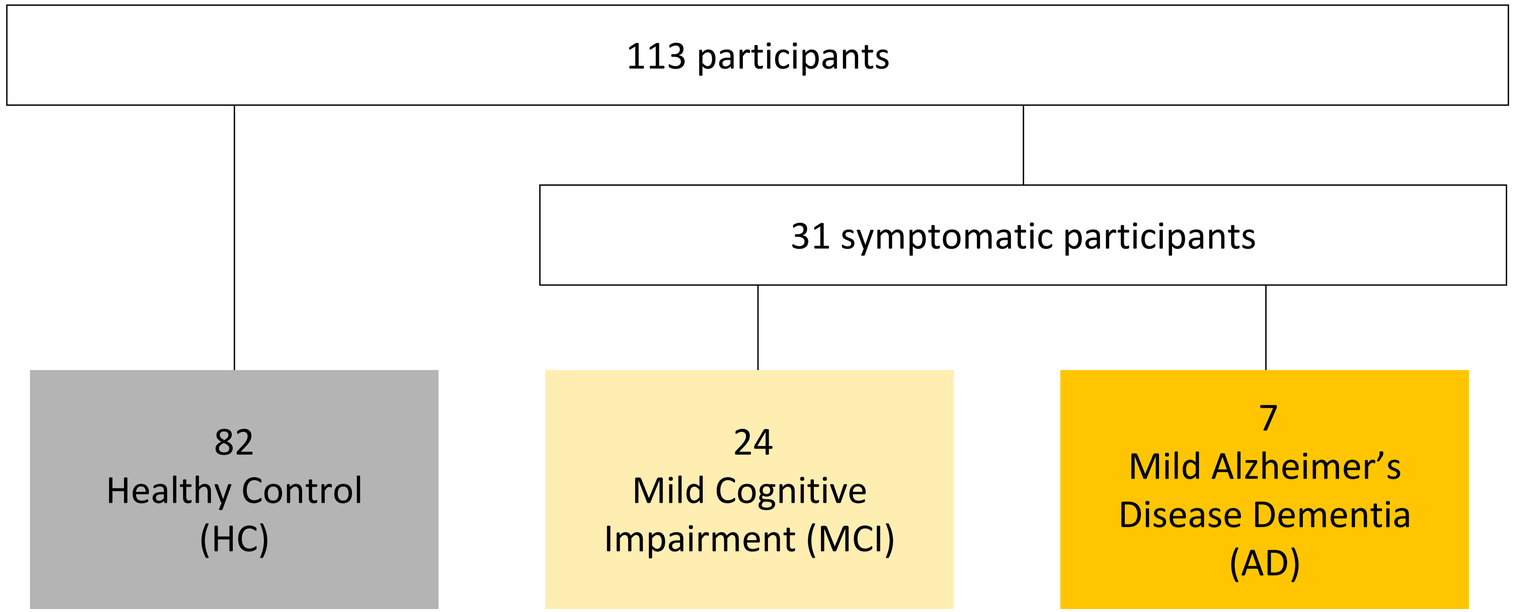
1. Cognitive Impairment
2. Weight Loss Surgery
3. Asthma

Case Study #1: Evidation, along with collaborators at Eli Lilly and Apple, recently completed a study using PGHD in participants with cognitive decline.

Objectives

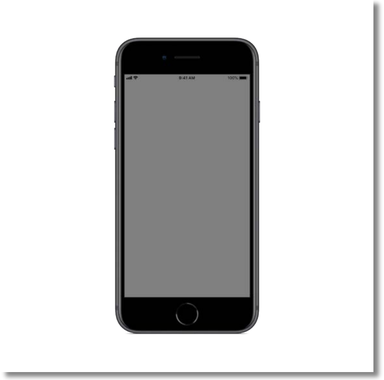
1. Assess the feasibility of collecting and processing data from multiple smart devices of older adults with and without cognitive impairment in their daily lives.

2. Test whether data from these devices can differentiate between healthy controls and participants with cognitive impairment.



Chen, Richard, et al. "Developing measures of cognitive impairment in the real world from consumer-grade multimodal sensor streams." Proceedings of the 25th ACM SIGKDD International Conference on Knowledge Discovery & Data Mining. 2019. DOI.ORG/10.1145/3292500.3330690

Participants were given an iPhone, Apple Watch, and Beddit sleep monitor to use as their primary devices over the course of the 12 week study, as well as an iPad to complete at-home cognitive tests.



acceleration
steps
calls
messages
app usage
distance
daily surveys

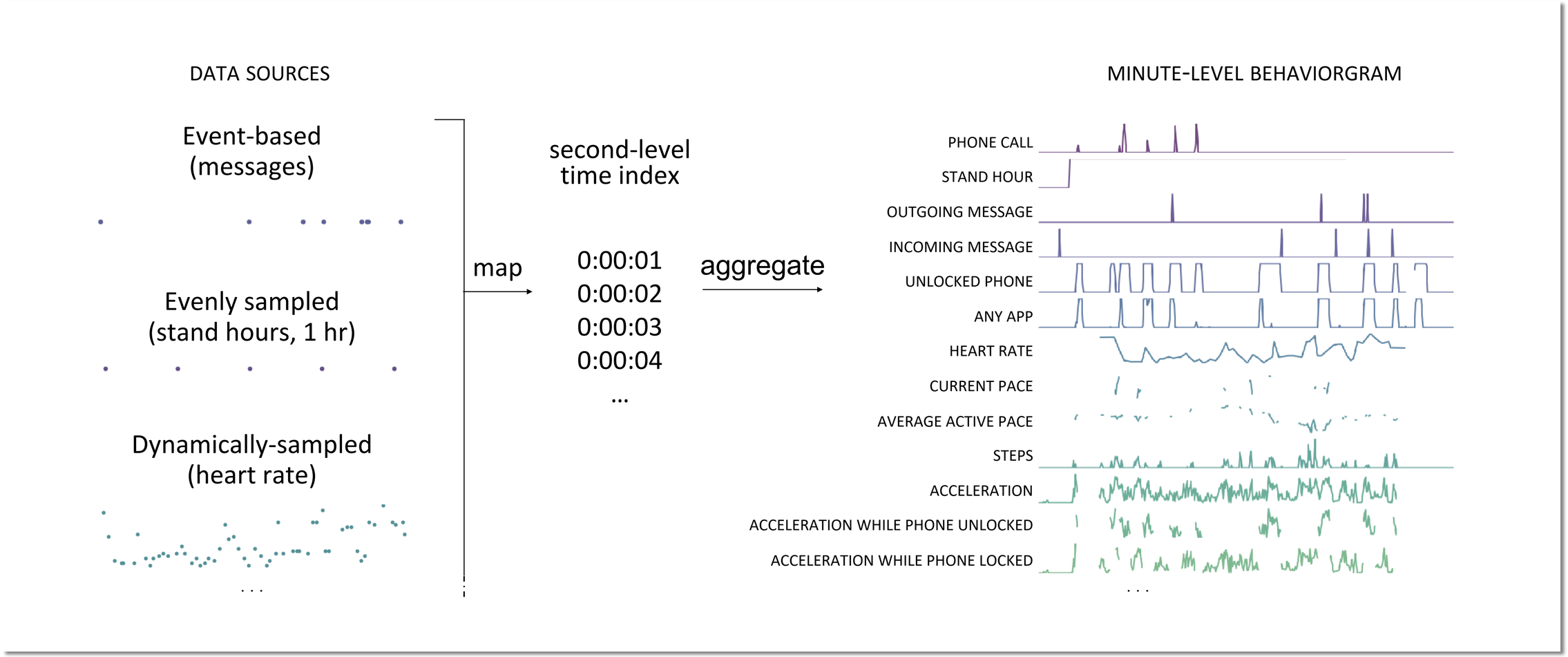
acceleration
steps
standing
heart rate
exercise

sleep

psychomotor skills
cognitive performance

Chen, Richard, et al. "Developing measures of cognitive impairment in the real world from consumer-grade multimodal sensor streams." Proceedings of the 25th ACM SIGKDD International Conference on Knowledge Discovery & Data Mining. 2019. DOI.ORG/10.1145/3292500.3330690

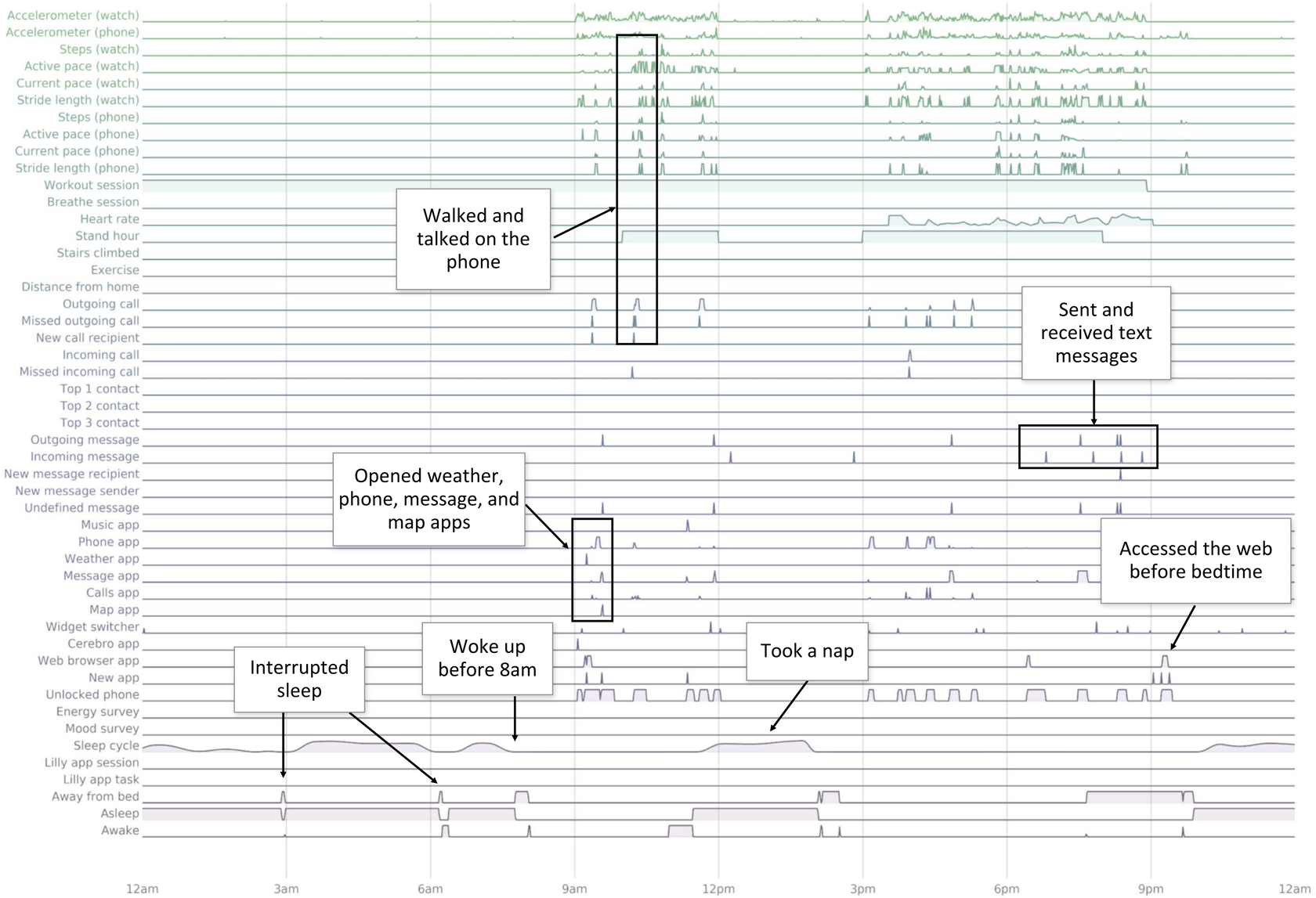
We processed, aligned, and combined data from all the different data sources to create a single behaviorgram for each participant.



Chen, Richard, et al. "Developing measures of cognitive impairment in the real world from consumer-grade multimodal sensor streams." Proceedings of the 25th ACM SIGKDD International Conference on Knowledge Discovery & Data Mining. 2019. DOI.ORG/10.1145/3292500.3330690

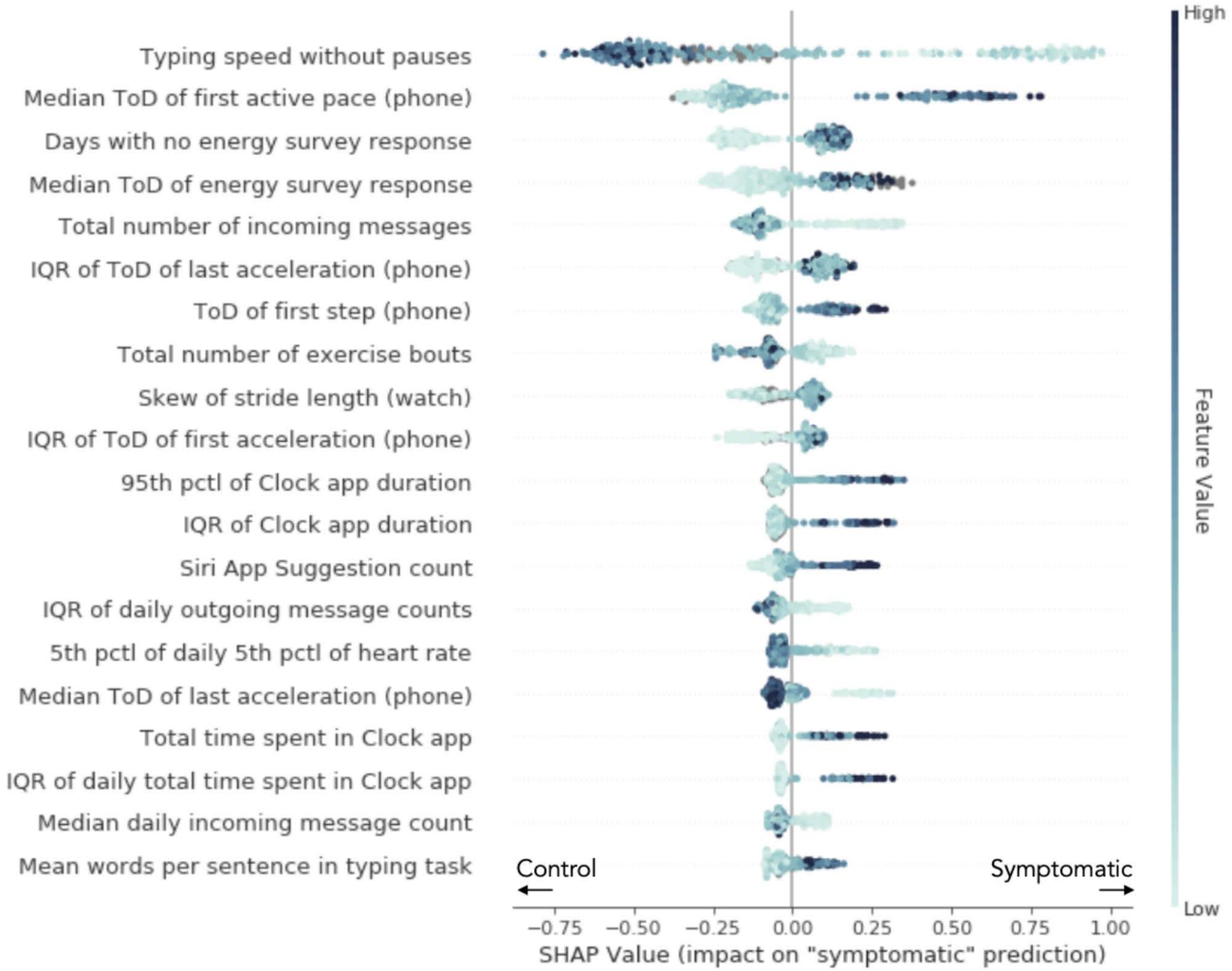
The behaviorgram offers a rich representation of an individual's behavior.

It also serves as a tool for data exploration, hypothesis generation, and as a way to inspect the quality of the data.



Chen, Richard, et al. "Developing measures of cognitive impairment in the real world from consumer-grade multimodal sensor streams." Proceedings of the 25th ACM SIGKDD International Conference on Knowledge Discovery & Data Mining. 2019. DOI.ORG/10.1145/3292500.3330690

Although exploratory, preliminary outcomes indicate that PGHD generated from consumer devices can identify symptomatic patients.



Study Outcomes

Important features for identifying symptomatic individuals during modeling:

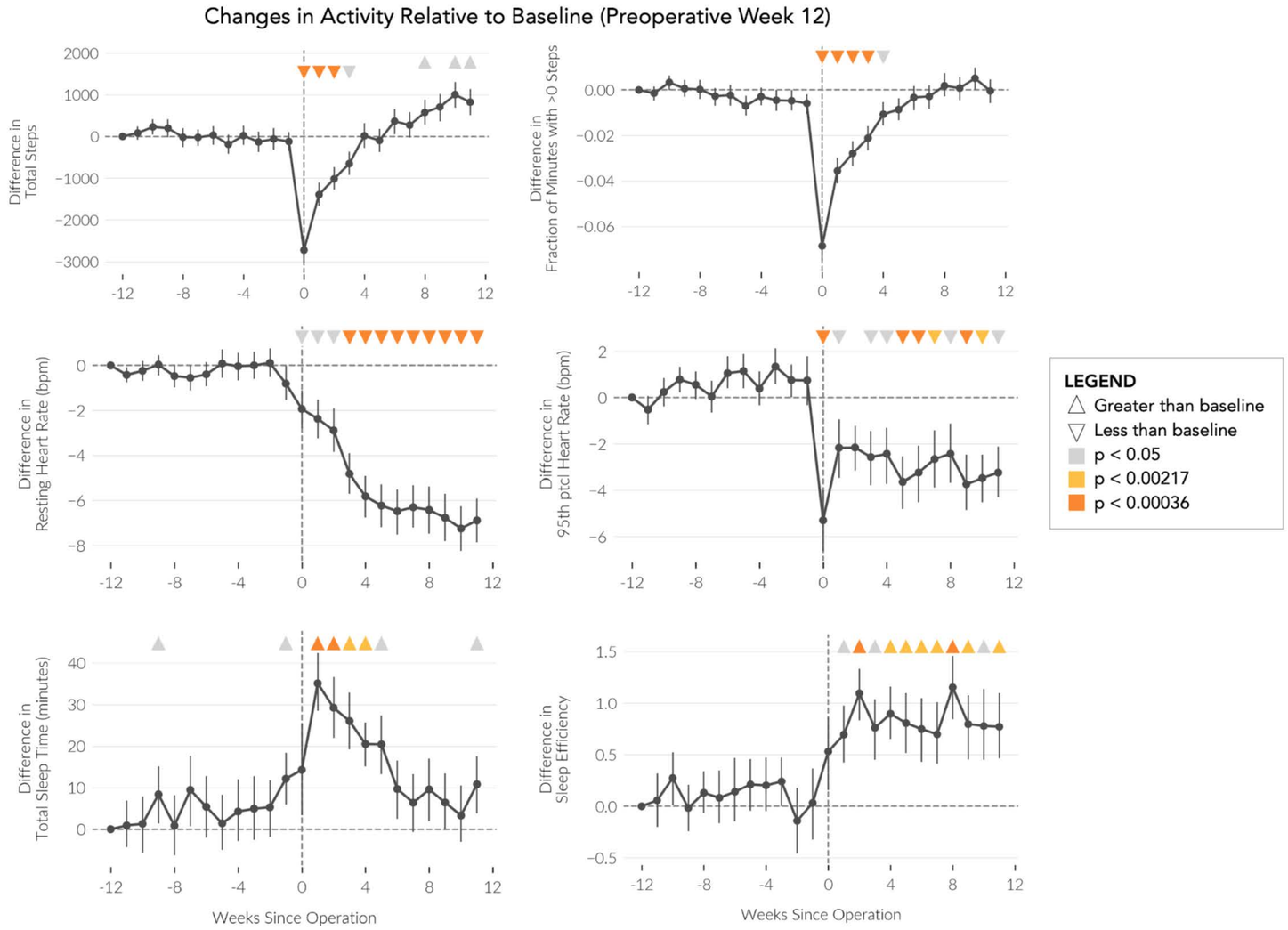
- Slower typing
- Less regularity and later first steps
- Fewer text messages
- Greater reliance on helper apps
- Poorer survey compliance

Chen, Richard, et al. "Developing measures of cognitive impairment in the real world from consumer-grade multimodal sensor streams." Proceedings of the 25th ACM SIGKDD International Conference on Knowledge Discovery & Data Mining. 2019. DOI.ORG/10.1145/3292500.3330690

Case study #2: PGHD can reveal important insight into postoperative behavior and physiology that is convenient, sensitive, scalable, individualized, and continuous

Study overview

- Self-reported surgical procedure and date
- Linked activity data spanning 12-weeks pre/postoperative
- Computed the weekly mean of each feature for each participant for each week of the observation window
- Compared each observed week to week -12 (baseline)
- Evidence that postoperative trajectories derived from PGHD can indicate important changes in behavior and physiology.



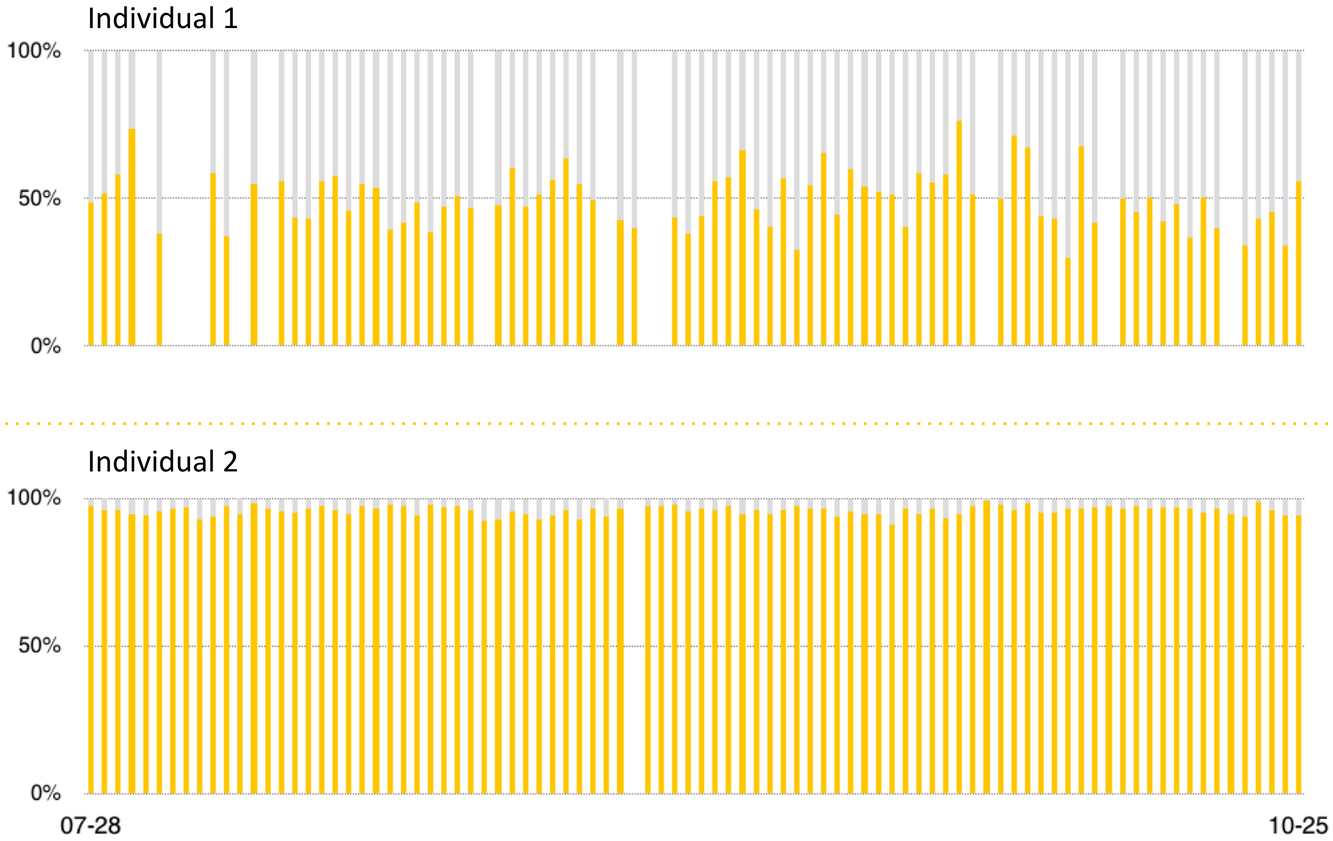
Ramirez, Ernesto, et al. "Continuous Digital Assessment for Weight Loss Surgery Patients." Digital Biomarkers 4.1 (2020): 13-20. DOI: 10.1159/000506417

Case study #3: Connecting directly to patients provides unprecedented resolution into asthma control and the true disease burden in everyday life.

Both Individuals

- Persistent moderate/ severe asthma
- Currently taking LABA/ICS
- Adhering to physician-prescribed treatment
- Non-smokers
- Use the same brand of wearable device

Percentage of time asleep while in bed (nightly)



- Reports waking up **often (every night or almost every night)** when asked how often they wake up at night due to asthma symptoms
- **49% time asleep** while in bed over last 90 days

- Reports waking up **2 or fewer days per month** when asked how often they wake up at night due to asthma symptoms
- **96% time asleep** while in bed over last 90 days

Note: time asleep data is objectively-derived from wearable devices; comparison is illustrative only and not controlled for any variable

evidation

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Sponsor Approach to Incorporating Patient-Generated Health Data into Real-World Evidence Plans

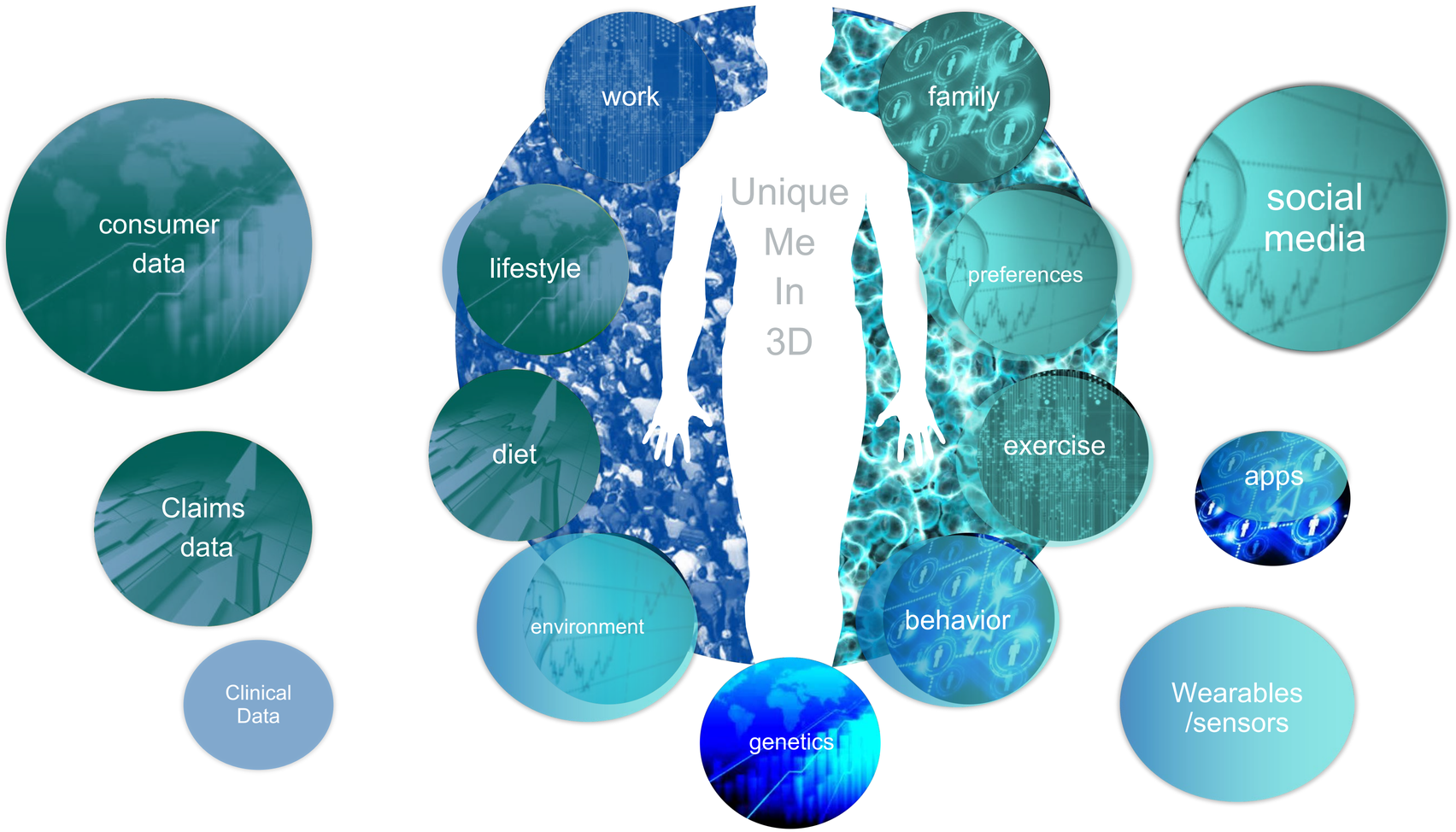
Kalahn Taylor-Clark, PhD, MPH
Global Head of Patient Solutions, Sanofi

Speaker Disclaimer

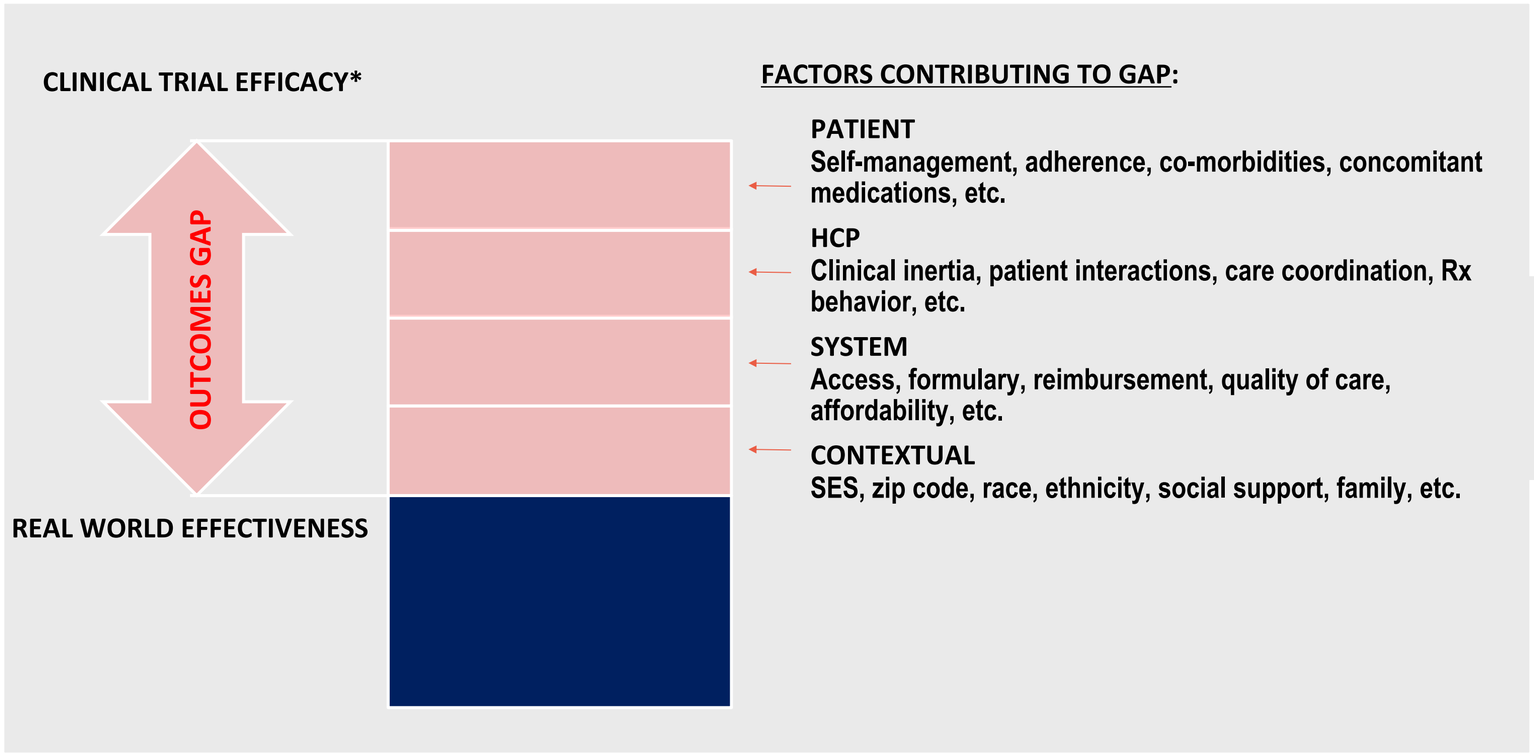
The views expressed in this presentation are those of the presenter and do not necessarily represent an official company position.

SANOFI

Why Patient-Generated Health Data and Insights in Pharma?



LEVERAGING BEHAVIORAL SCIENCE TO CLOSE THE GAP BETWEEN REAL-WORLD EFFECTIVENESS AND EFFICACY



- **Goal is to reduce gap** between clinical trial efficacy and real world effectiveness
- **PISO Team bridges this gap** through evidence-based interventions, including:
  - Understanding patient factors behind gap and associate them with outcomes
  - Designing interventions to influence key factors that will lead to improved outcomes

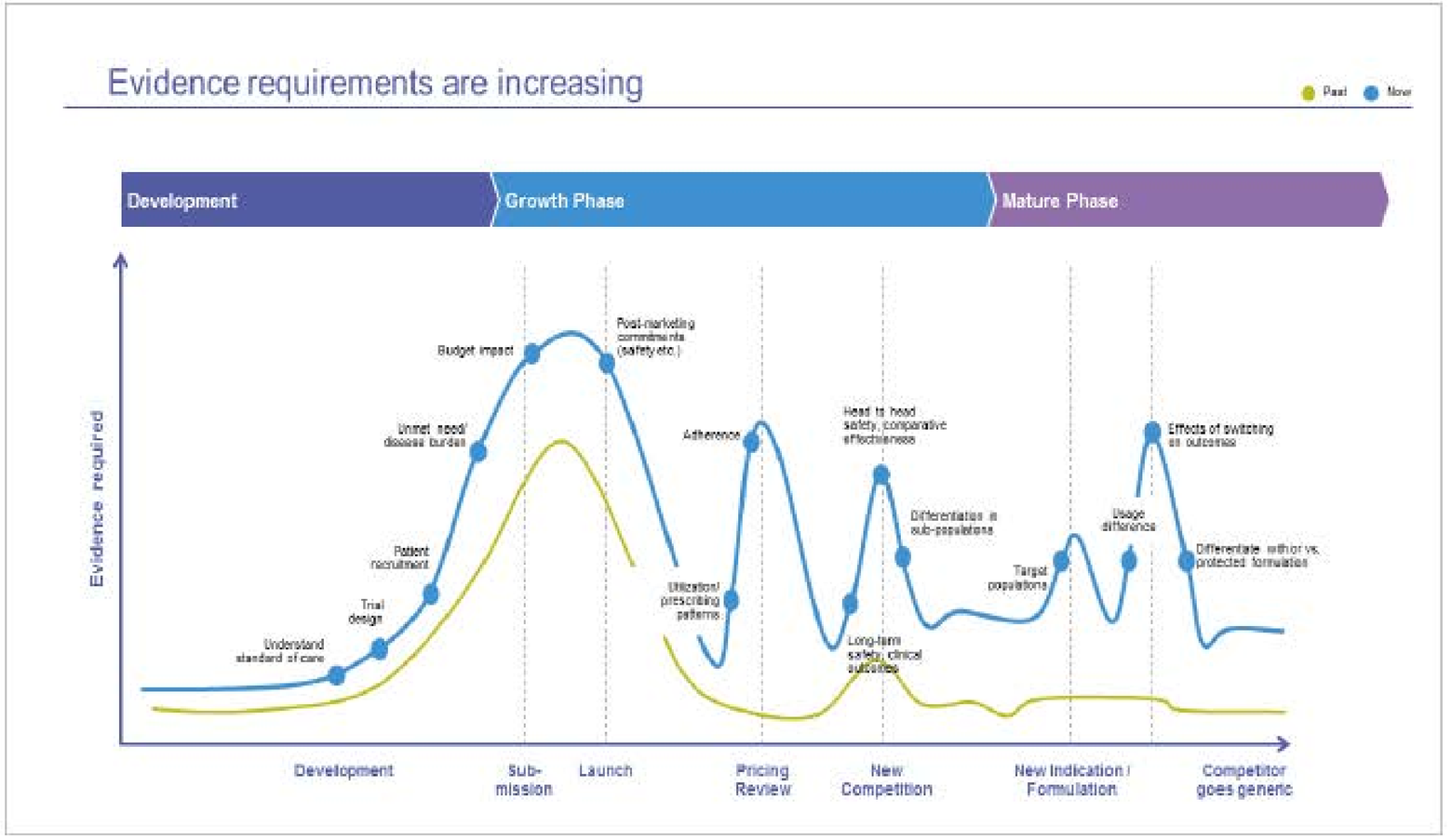
Behavioral Science can address clinical inertia, patient activation and non-adherence which are critical to reducing the gap and improving outcomes

**Relative scale of impact for patient factors, HCP, health system, and contextual factors varies case by case.*
Broader results/ outcomes differences in clinical trial efficacy and real world effectiveness may vary on a case by case basis.

THE PROBLEM TO SOLVE: UNCOVER NOVEL DATA SOURCES AND METHODOLOGIES FOR PATIENT EVIDENCE GENERATION

Patient Solutions

What are the promising practices? How can we industrialize them?



The need is increasing for:

NEW DATA SOURCES

NEW ANALYTIC METHODS

Sanofi Pasteur – Evidation DiaFlu Retrospective study

Original Article

Quantifying the Impact of Influenza Among Persons With Type 2 Diabetes Mellitus: A New Approach to Determine Medical and Physical Activity Impact

Sandrine I. Samson, PhD[1], Kevin Konty, PhD[2], Wei-Nchih Lee, MD, MPH, PhD[2], Tom Quisel, BS[2], Luca Foschini, PhD[2], David Kerr, MD[3], Jan Liska, MSc[4], Henry Mills, MS[5], Rosalind Hollingsworth, PhD[1], Michael Greenberg, MD, MPH[5], and Anne C. Beal, MD, MPH[4]

Journal of Diabetes Science and Technology
1–9

DOI: 10.1177/1932296819883340
journals.sagepub.com/home/dst
SAGE

1st Scientific, Peer-reviewed Publication

A retrospective study using multiple data sources, and wearable device demonstrated that:

- **Influenza increases rates of pneumonia, heart disease, and abnormal glucose levels among people with T2DM,**
- **Influenza also negatively impacts daily activities compared to controls**

SANOFI

Thank you!

Kalahn Taylor-Clark, PhD, MPH
Global Head of Patient Solutions, Sanofi
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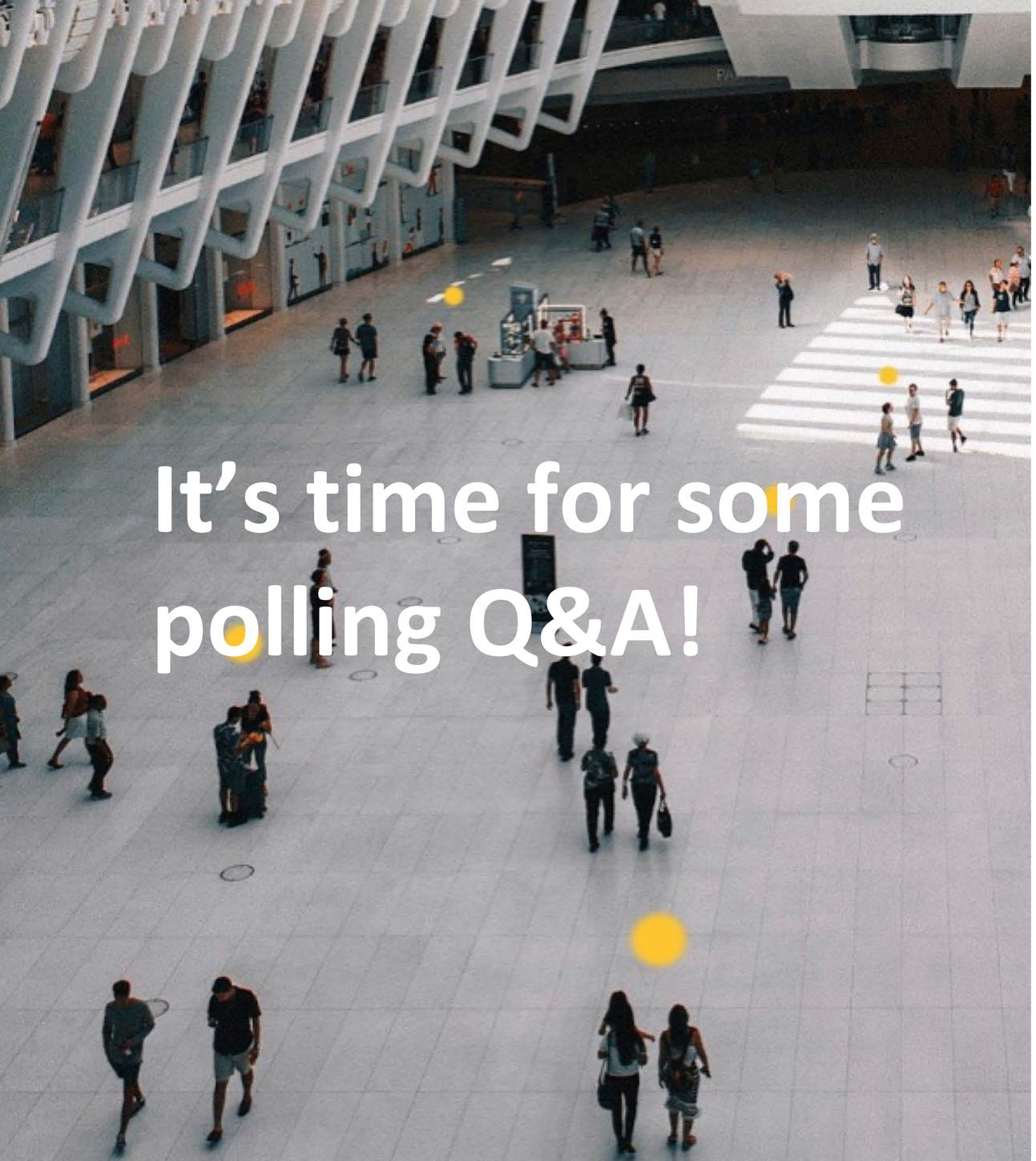
SANOFI

Key Session Takeaways

1. PGHD provides the opportunity to enhance endpoints that matter to patients in daily life by:

- More frequently and sensitively measuring a patient's real-world experience with a disease or condition outside the clinic
- Revealing new insights about treatment toxicity, quality of life, functional mobility, sleep, pain, mood, and more

2. PGHD can be incorporated into real-world evidence plans to better understand safety and clinical benefit, and differentiate medical products



It’s time for some polling Q&A!

Please type your questions for speakers into the Q&A feature while the polling questions load

Question 1

Have you launched a drug where payers wanted more info about patient functioning?

- Yes
- No

Question 2

Are you incorporating digital measures into your RWE plans?

a) Already doing it
b) Plan to do in future
c) No plans

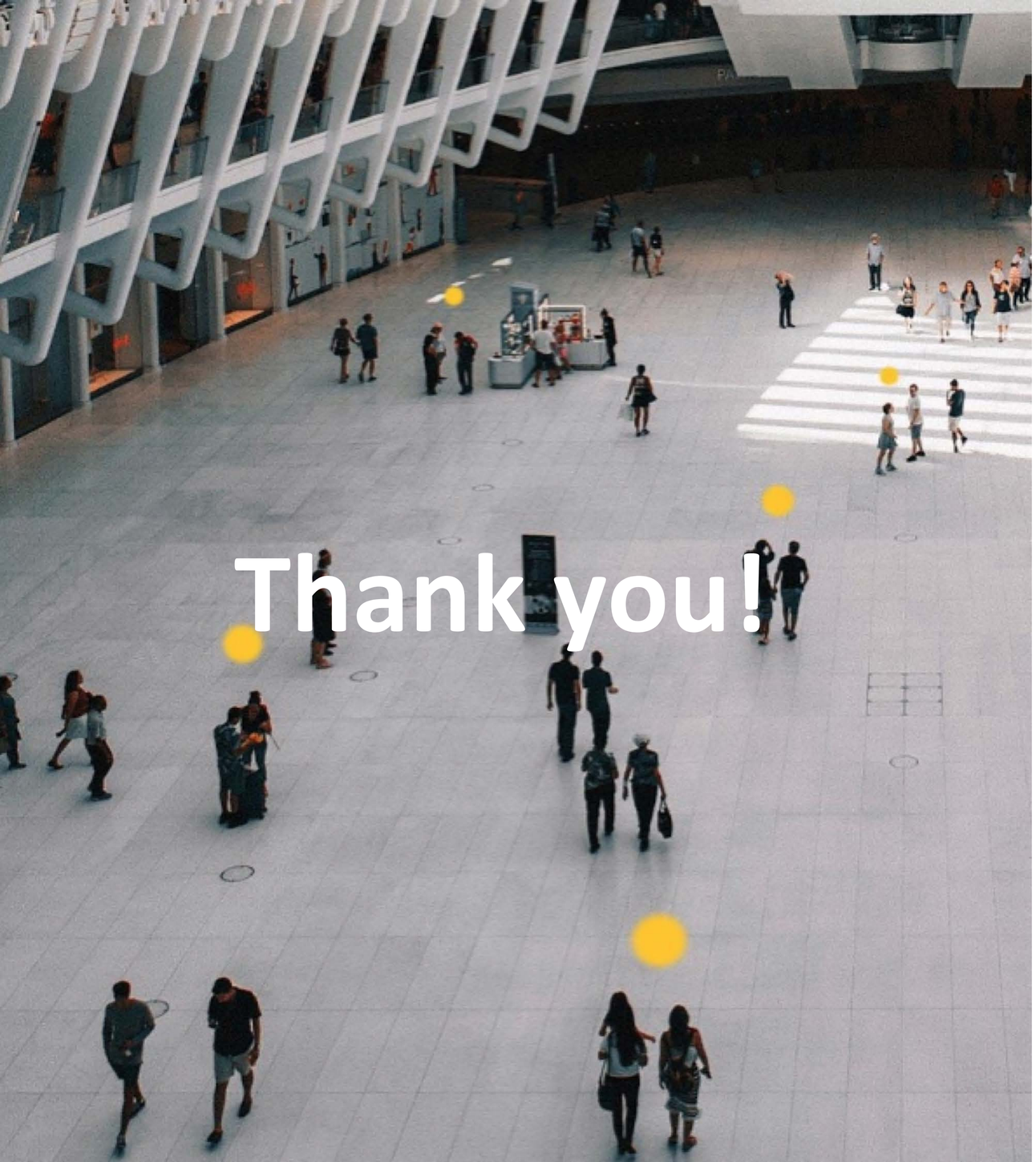
e

Question 3

Which barriers if any have you faced internally to including digital measures in your evi gen plans?

a) None
b) Funding
c) Culture not open to innovative approaches
d) Not incorporated early enough in evidence generation plans
e) Clinical or operational feasibility


Questions for speakers?



Join our Twitter chat continuing the conversation immediately after this workshop: **@evidation**
#PGHDinRWE

For any further questions, please email: bpatricklake@evidation.com