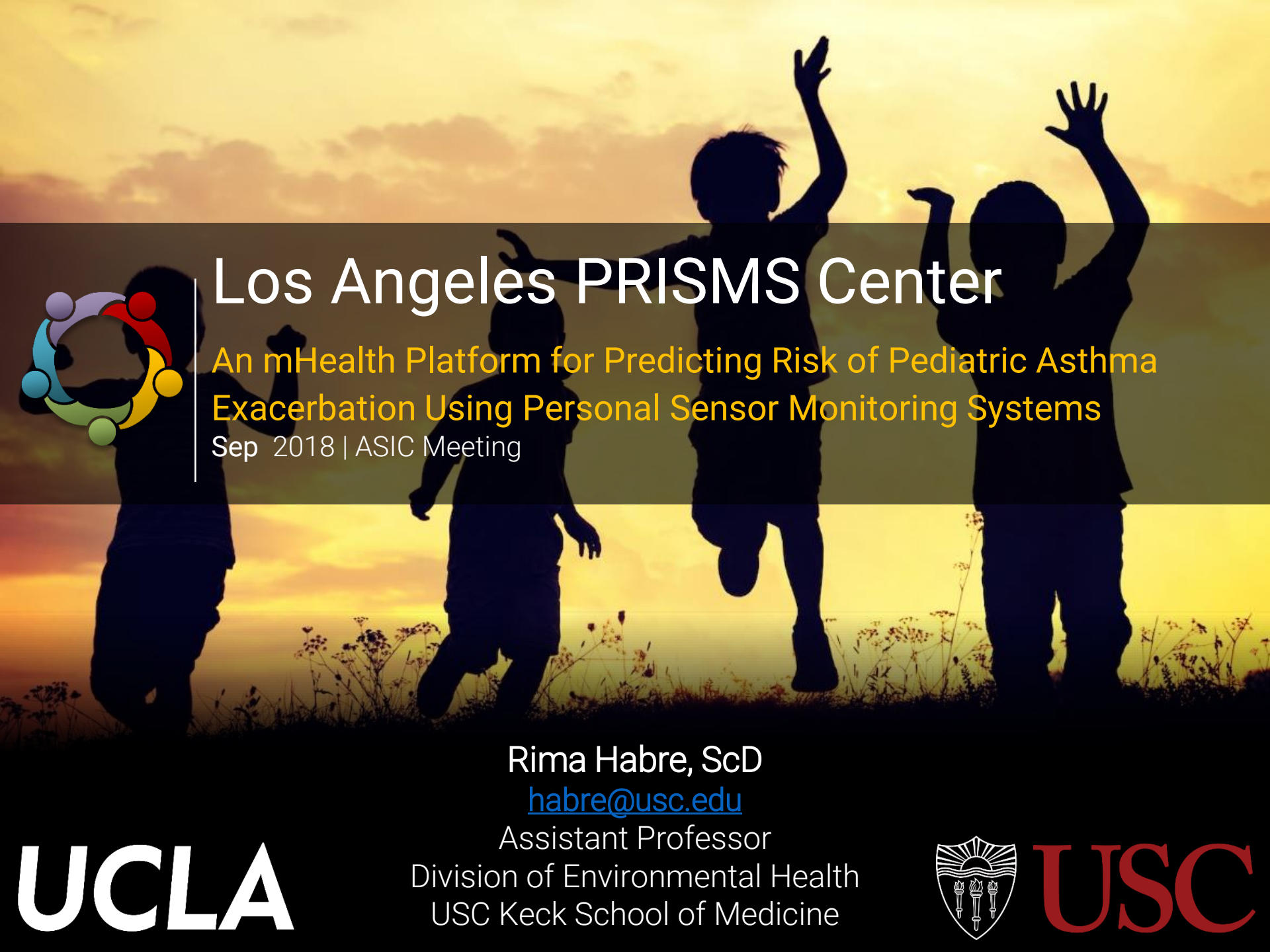


Los Angeles PRISMS Center

An mHealth Platform for Predicting Risk of Pediatric Asthma Exacerbation Using Personal Sensor Monitoring Systems

Sep 2018 | ASIC Meeting

Rima Habre, ScD
habre@usc.edu
Assistant Professor
Division of Environmental Health
USC Keck School of Medicine

UCLA

USC

Outline

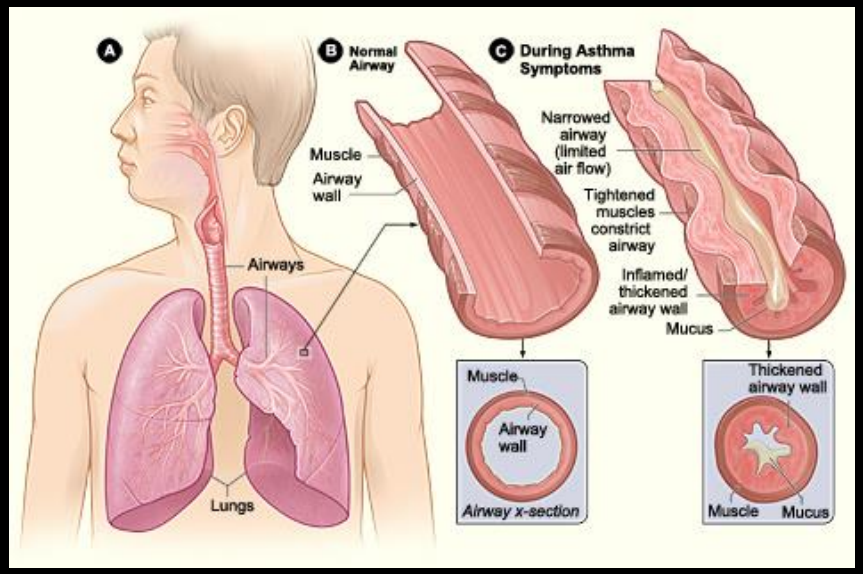
- Asthma
- Design of the platform
- Deployment of the platform
  - Preliminary pilot data

Air Pollution as an Underappreciated Cause of Asthma Symptoms

George D. Thurston, ScD
David V. Bates, MD

JAMA The Journal of the American Medical Association

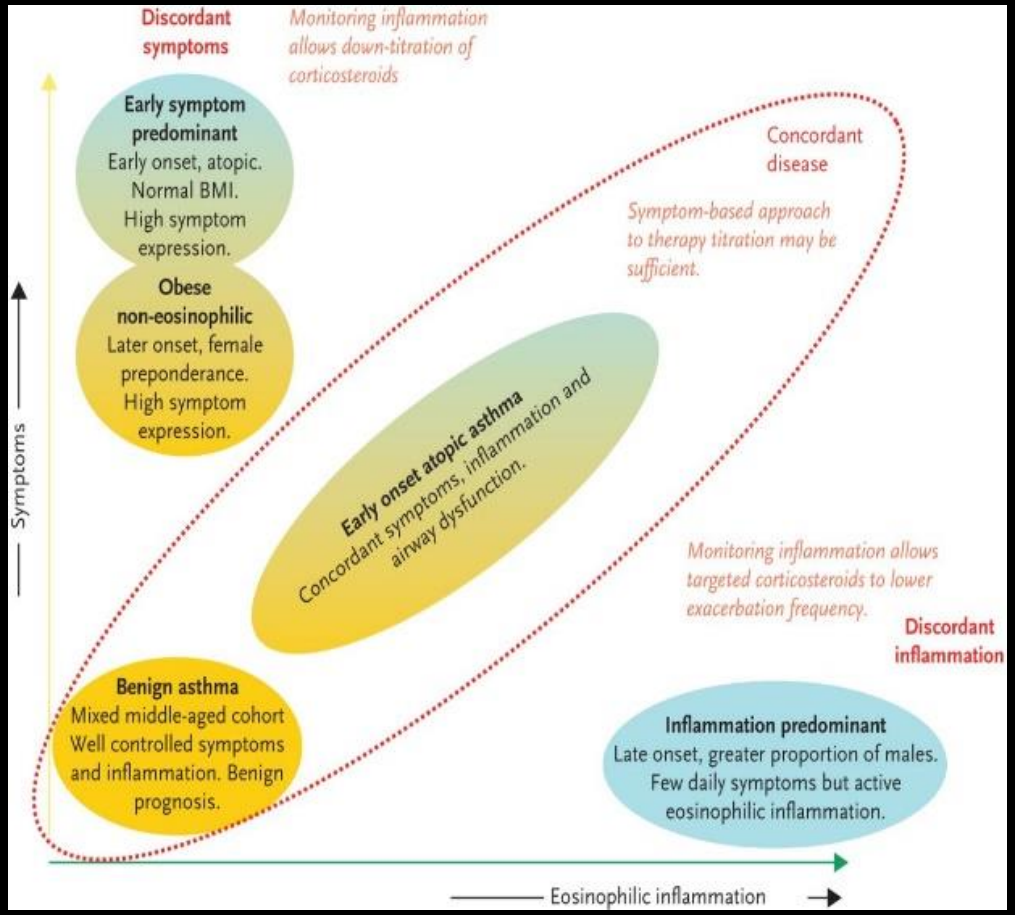
EDITORIALS

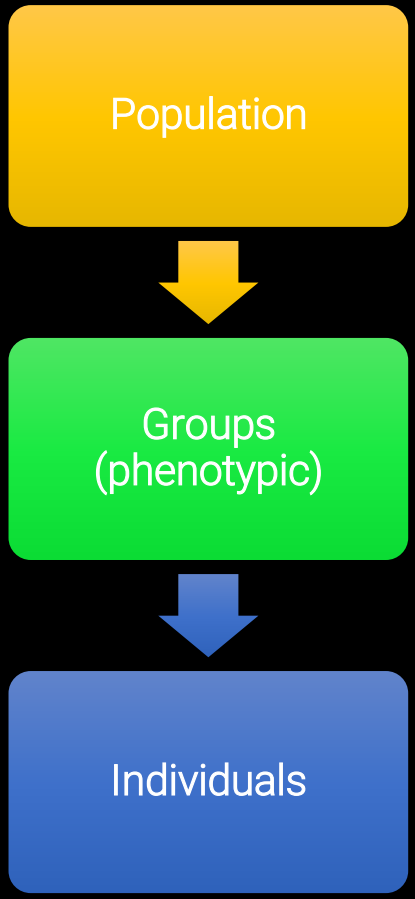


"While physicians no doubt recognize that they cannot do much about modern urban air pollution on an individual level, they can make recommendations to patients with asthma to help them avoid the potentially adverse effects of air pollution."

Thurston, G.D. and Bates, D.V., 2003. *JAMA*, *290*(14), pp.1915-1917.

Pediatric Asthma





Clementine Bostantzoglou et al., Clinical asthma phenotypes in the real world: opportunities and challenges. *Breathe* 2015;11:186-193

The Los Angeles PRISMS Center

Los Angeles PRISMS Center

PI Alex Bui (UCLA)

Project 3, Real-Time Air Pollution and Asthma Study

PIs Habre and Gilliland

What if you could predict ahead of time, for a given individual, an asthma attack, and mitigate if not prevent it?

The Los Angeles PRISMS Center

Los Angeles PRISMS Center

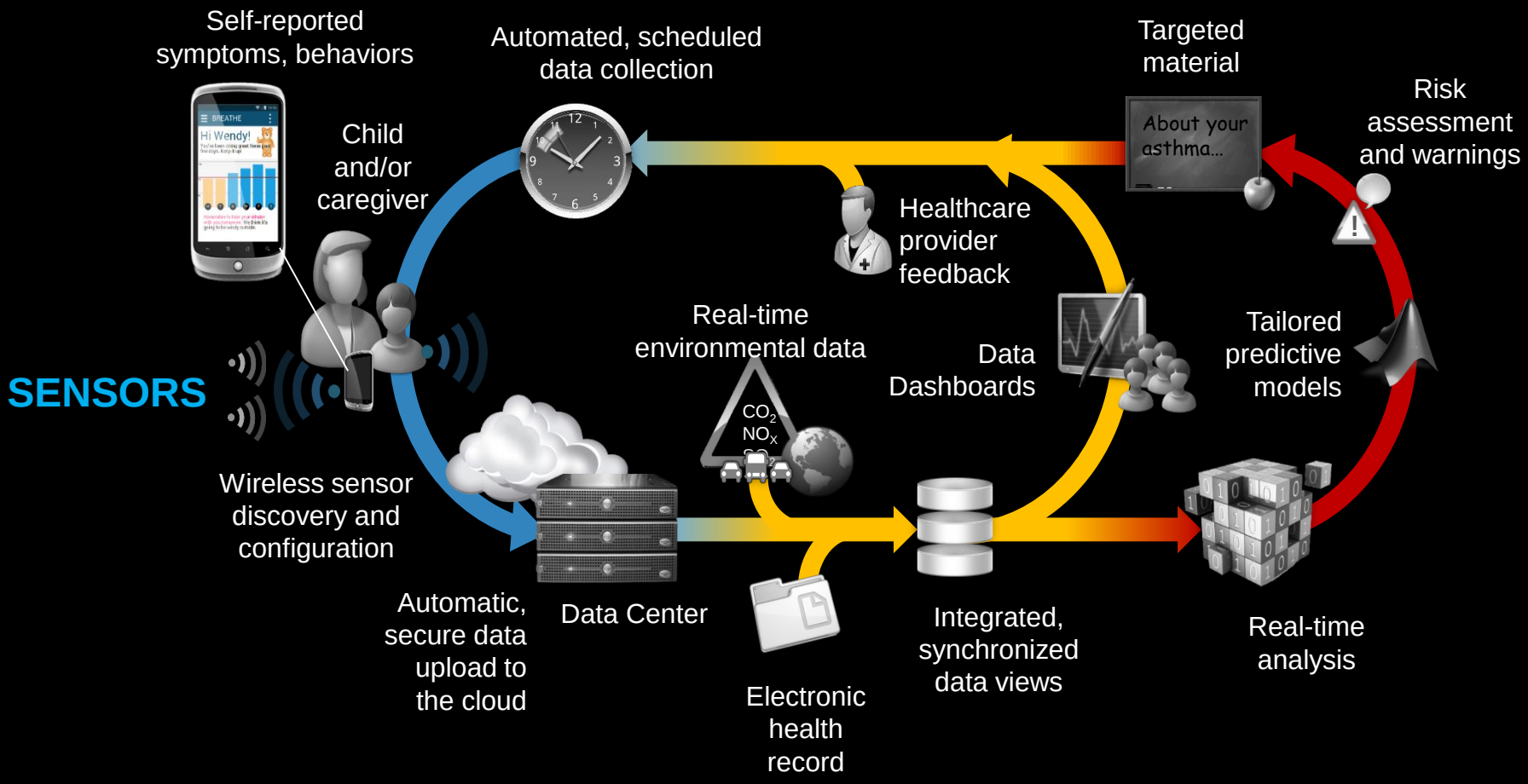
PI Alex Bui (UCLA)

Project 3, Real-Time Air Pollution and Asthma Study

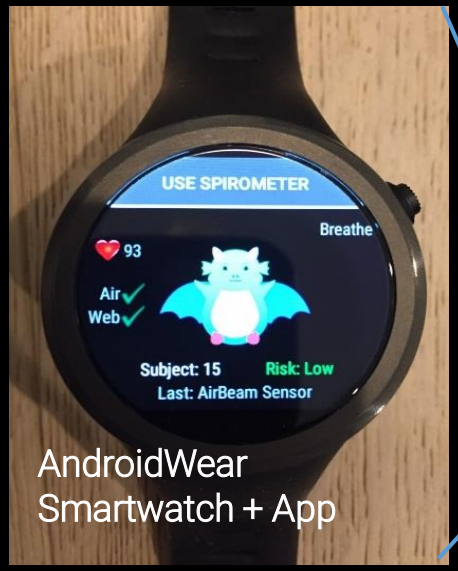
PIs Habre and Gilliland

- Build a secure, non-invasive, sensor-based informatics platform for pediatric asthma environmental health studies
- Enable individualized 'trigger discovery'
- Advance our scientific understanding of
  - Time lag between exposure and response
  - Relevant dose metrics for asthma (peak exposures vs average?)
  - Role of multiple exposures and behaviors in context
  - Variation in personal exposures and risk at short temporal and fine spatial scales

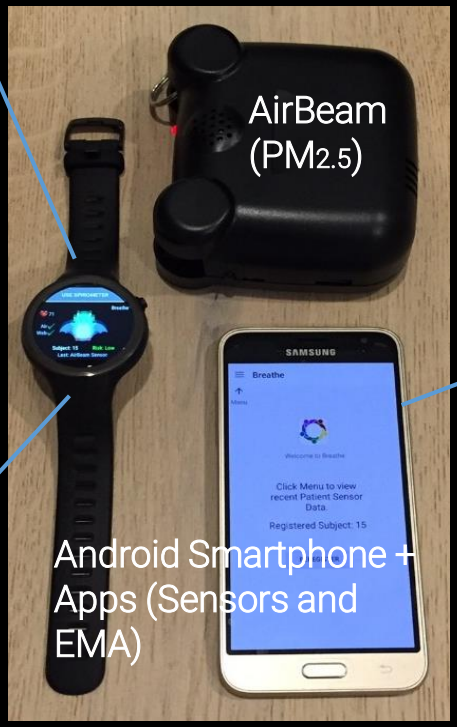
The Los Angeles PRISMS Center BREATHE Informatics Platform for Epidemiological Studies of Pediatric Asthma



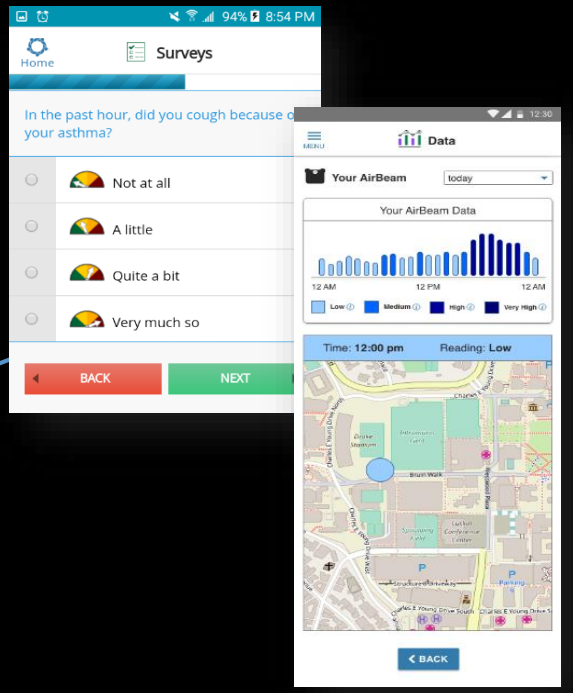
Breathe Kit



AndroidWear
Smartwatch + App



Android Smartphone +
Apps (Sensors and
EMA)



Ecological Momentary
Assessment (EMA) Surveys
+ mobile dashboards

Inhaler

Spirometer

BREATHE Kit: Biomedical REAl-Time Health Evaluation

Data Integration

Sensors

- GPS
- Spirometry
- Inhaler usage
- Activity monitoring (accelerometry to classify lying, sitting, standing, walking, running, etc.).
- Environmental measures (PM, NO_2, etc.)

Self-reported measures

- Ecological momentary assessment (EMA) for asthma symptoms, stress
- Questionnaires (health status, physical activity, etc.)

Geospatial data

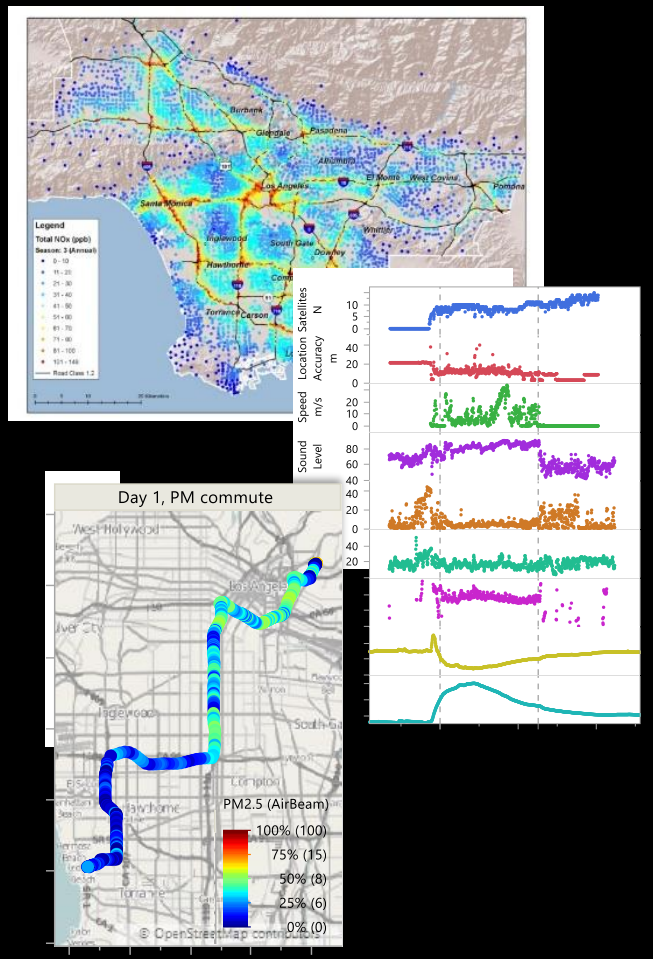
- Weather
- Pollen
- Air quality indices
- Nearby traffic volumes
- Indoor/outdoor metrics

Electronic health record

- Demographics, vitals
- Medications
- Allergies and documented triggers
- Health status and comorbidities
- Pulmonary function tests, other labs
- Past exacerbations (e.g., ER visits)

U01 Sensors (2019)

- Black/brown carbon MA200 (Columbia)
- Particle sensor (UW)
- Ozone and VOCs sensor (ASU)



High spatial and temporal resolution

Breathe Kit Deployment in Asthma Study

Today's talk
n=20, 1-week monitoring,
baseline Breathe Kit sensors

Starting 2019
n=40, 2-week monitoring,
integrating U01 sensors

Clinic-Based Recruitment

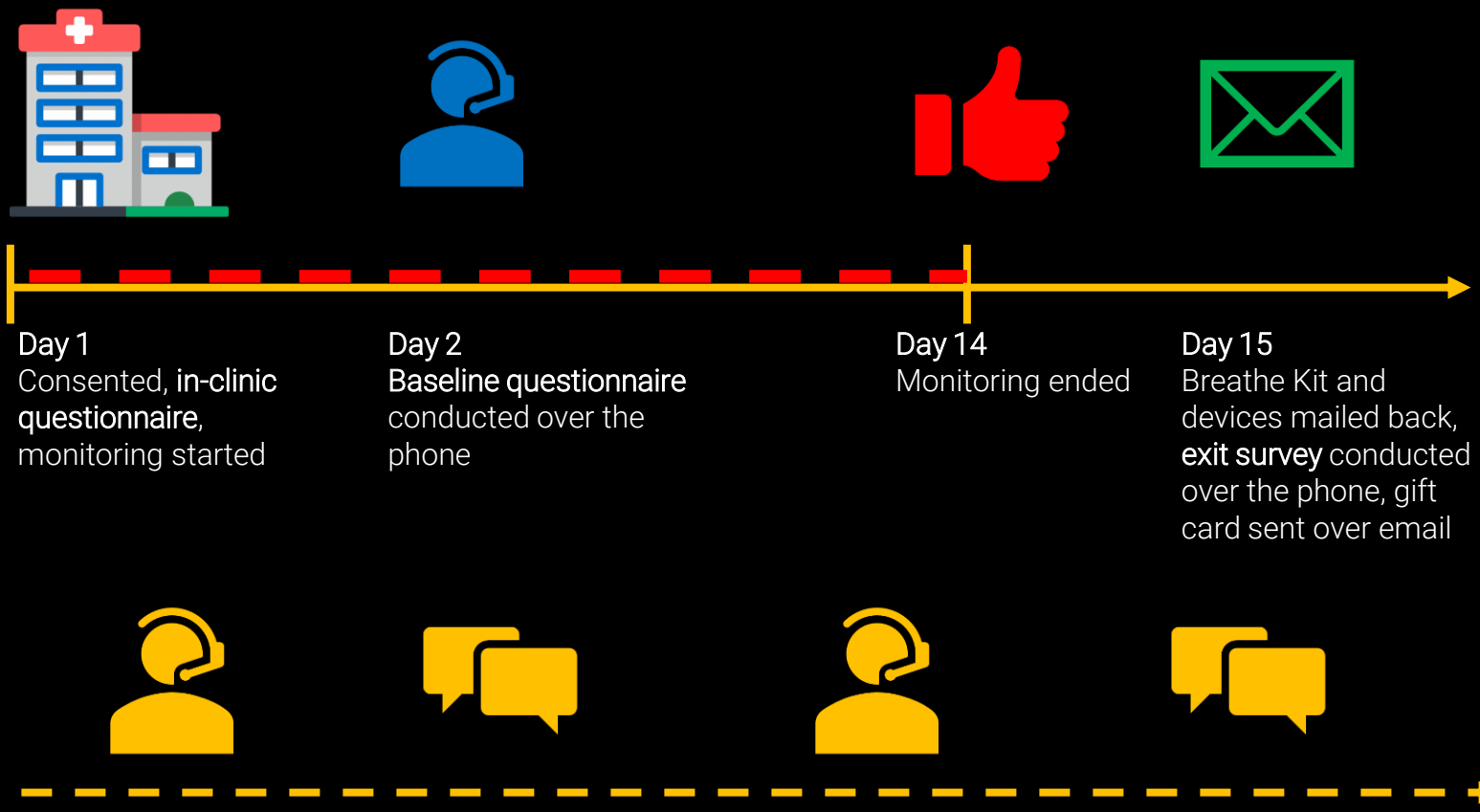
Study coordinator reviews medical records ahead of time to determine eligibility and medications. On day of appointment, recruitment, informed consent, in-clinic questionnaire and explanation of the study and the kit take place in the clinic during the doctor's visit.

UCLA MATTEL Childrens Hospital
Pediatric Pulmonology & Sleep Medicine

Dr. Sande Okelo

Two Pediatric Pulmonology clinic sites led by Dr. Sande Okelo
Westwood and **Santa Monica**

Participant Timeline



Day 1
Consented, **in-clinic questionnaire**, monitoring started

Day 2
Baseline questionnaire conducted over the phone

Day 14
Monitoring ended

Day 15
Breathe Kit and devices mailed back, **exit survey** conducted over the phone, gift card sent over email

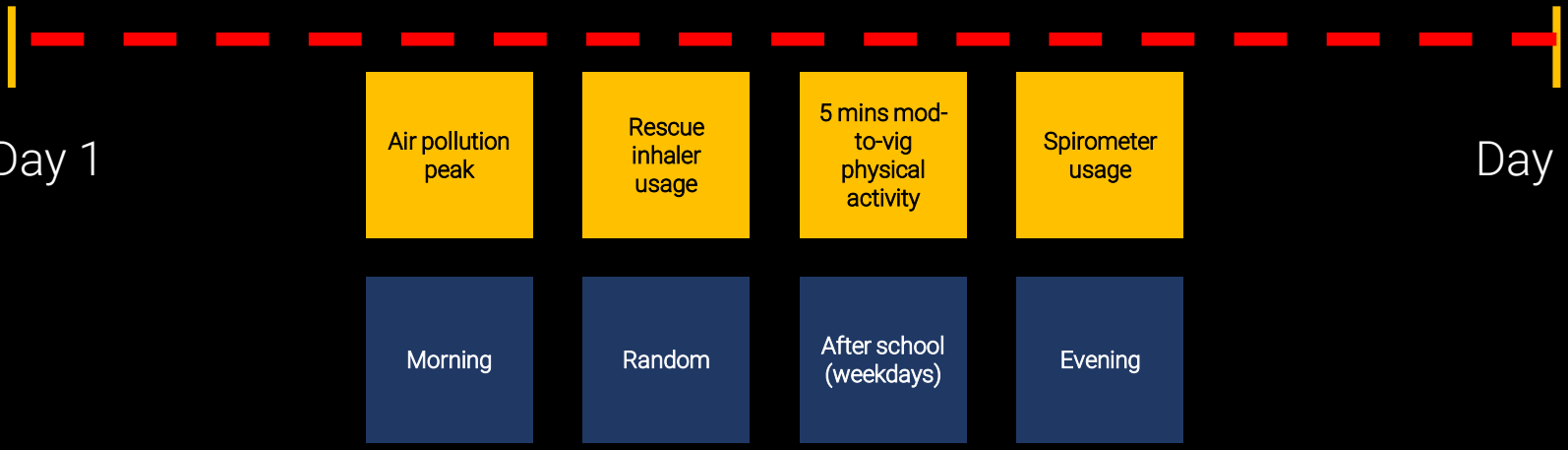
Throughout the monitoring period
Regular contact and verification of data flows through BREATHE researcher dashboards and 24/7 support on standby

Data Collection

Air pollution exposures, heart rate, respiration rate, physical activity, GPS, etc… streaming *continuously, in real time*

Controller and rescue medication captured *every use*

Spirometry measurements (FEV_1 and PEFR) *2x/day* (morning and evening)

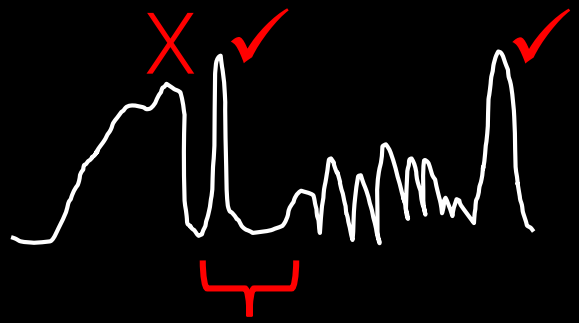


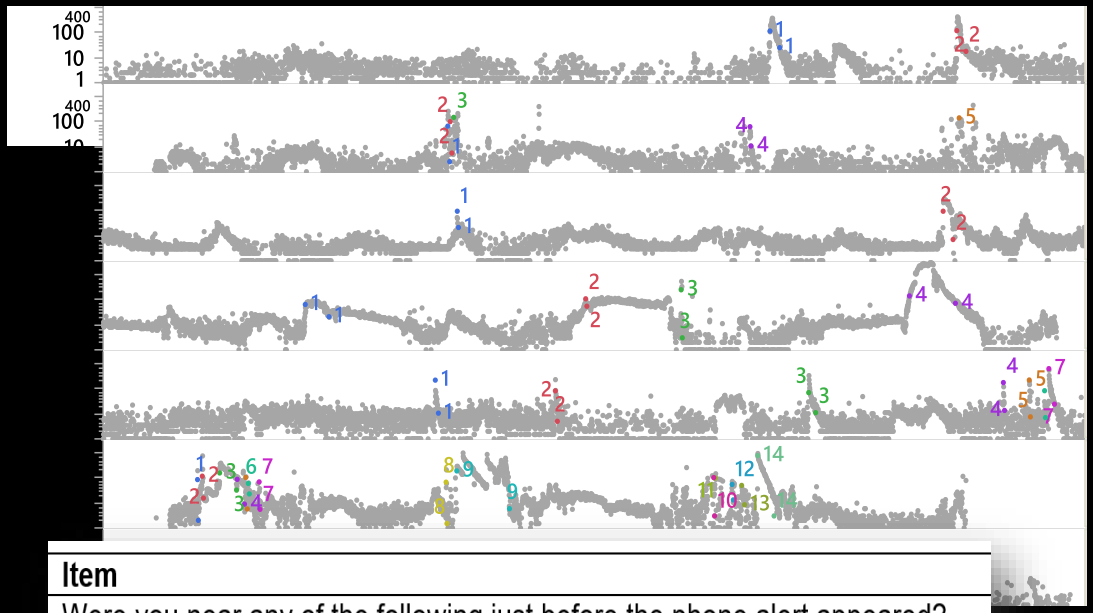
Symptoms, context, physical acitivity, etc.. with random and context-sensitive EMA surveys *5-8x/day* with tailored suppression logic and prioritization scheme to manage participant burden and select for suspected triggers ($PM_{2.5}$ peaks from primary combustion sources, high physical activity, etc..)

Context-Sensitive Data Collection

Capture exposures and behaviors in real time (proximal to outcome) and in context to formally evaluate as potential asthma triggers

eg, $PM_{2.5}$ peaks from primary combustion sources





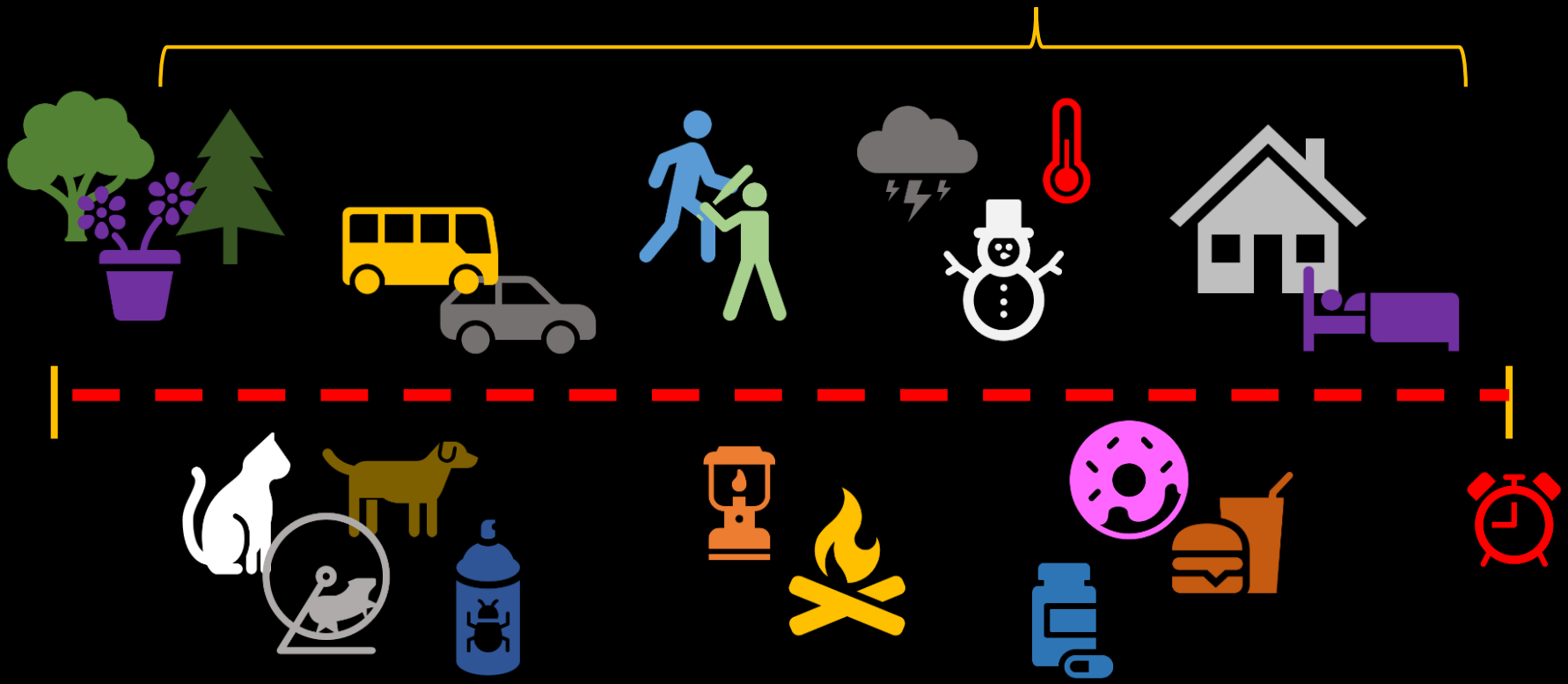
Item
Were you near any of the following just before the phone alert appeared?

Response Choices
Traffic (cars, buses or trucks)
Cigarette smoke
Vaping/e-cigarette vapor
Cooking or barbequing (BBQ)
Lit fireplace (burning wood or gas)
Space heater (burning fuel)
Burning candles or incense
Other smoke

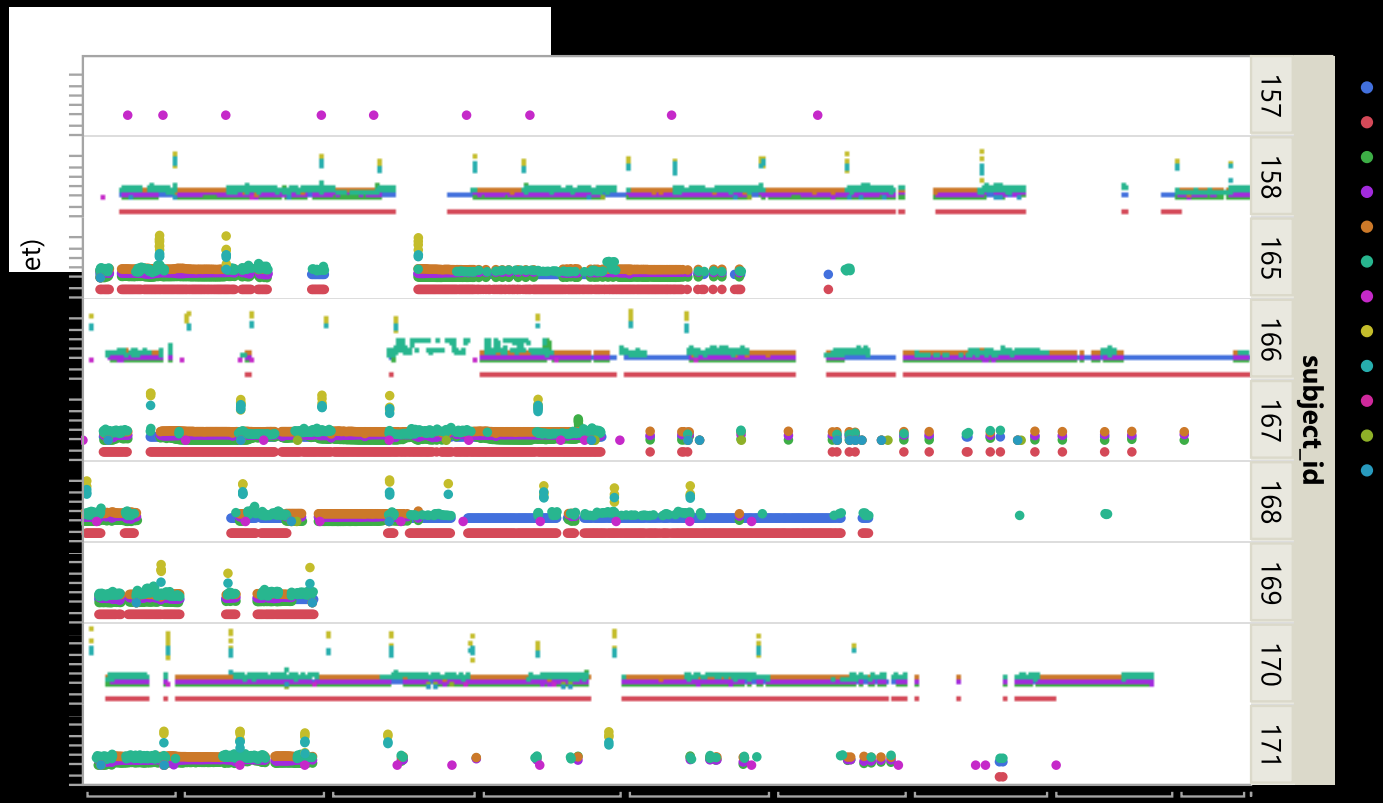
Between-person

Within-person (over time, eg. days)

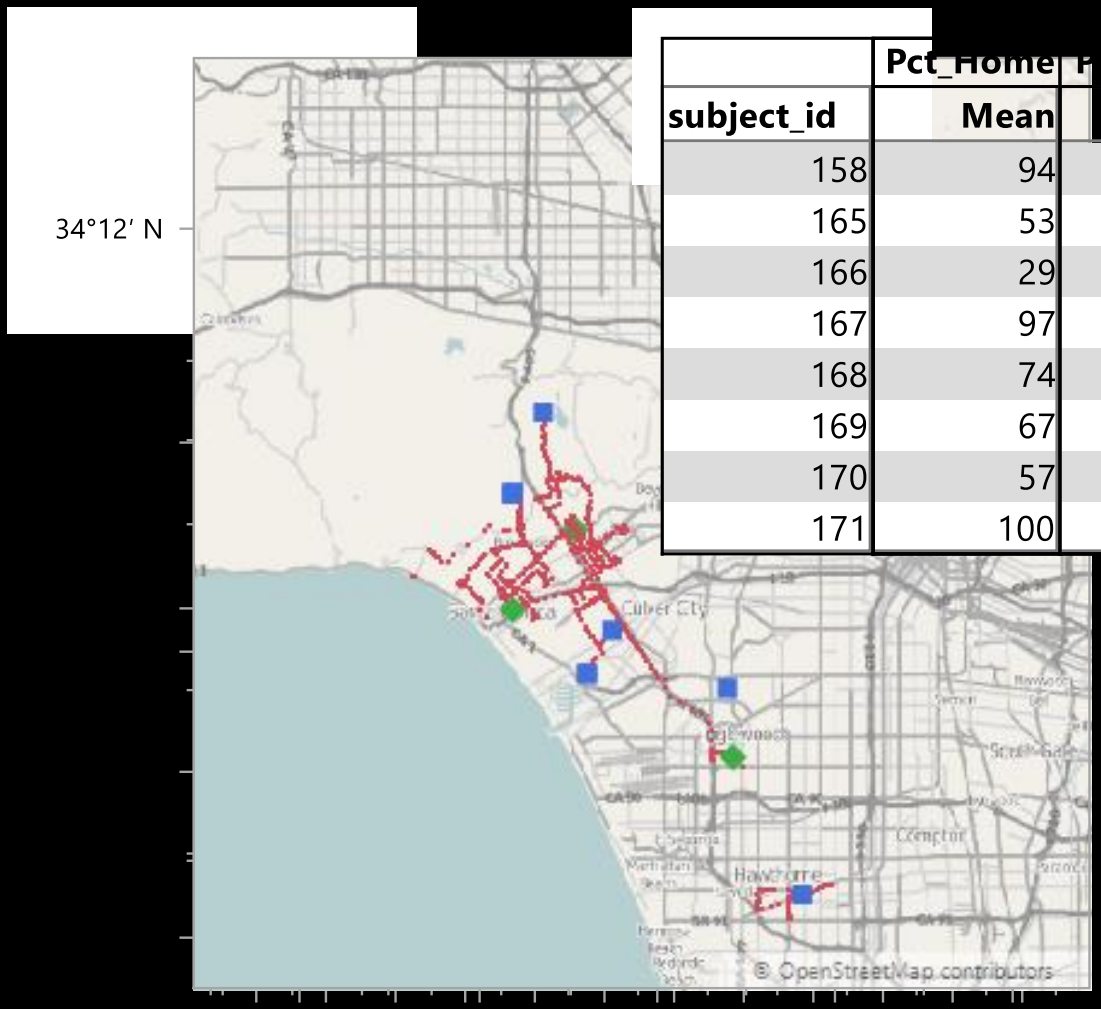
Within-day (within-person)



Preliminary Data Explorations (n=9)

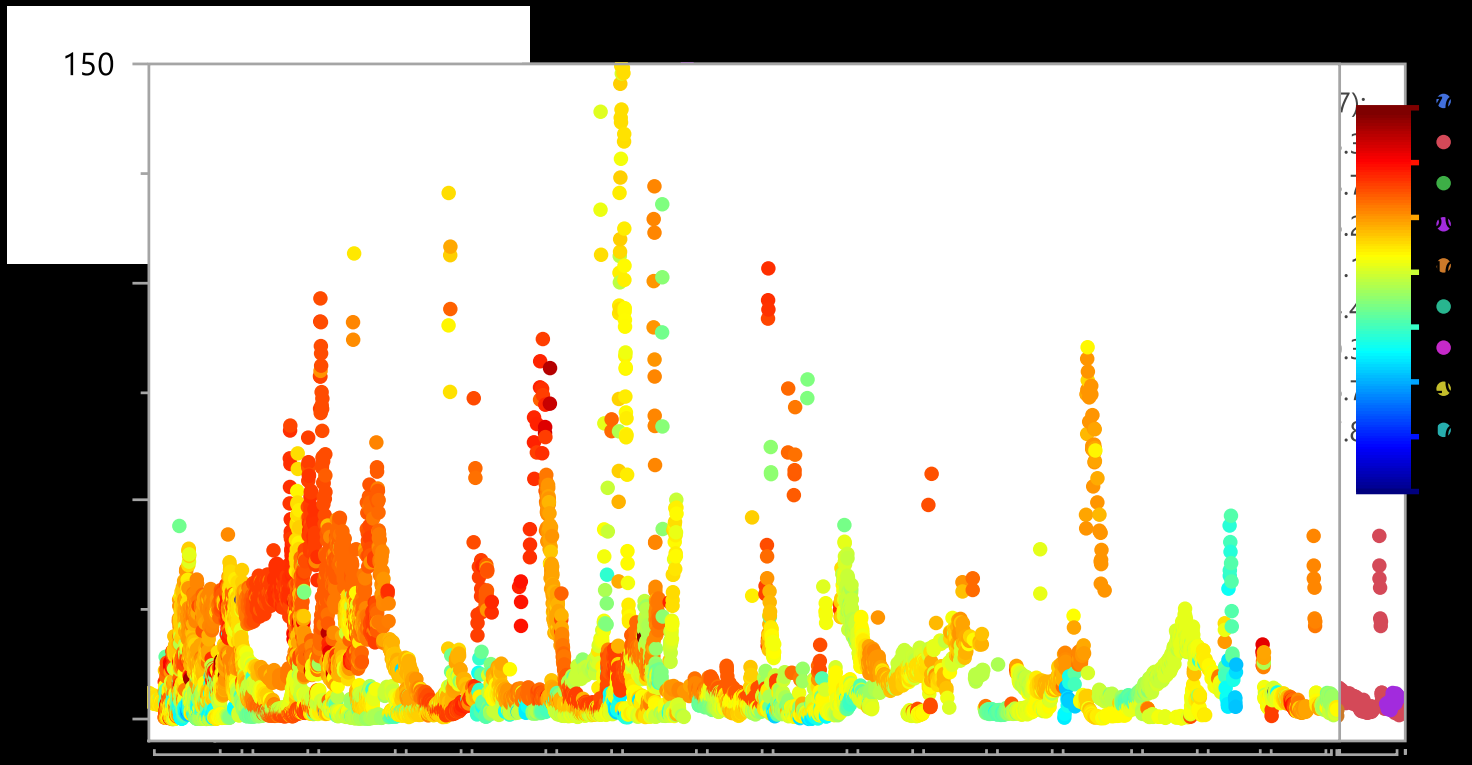


GPS



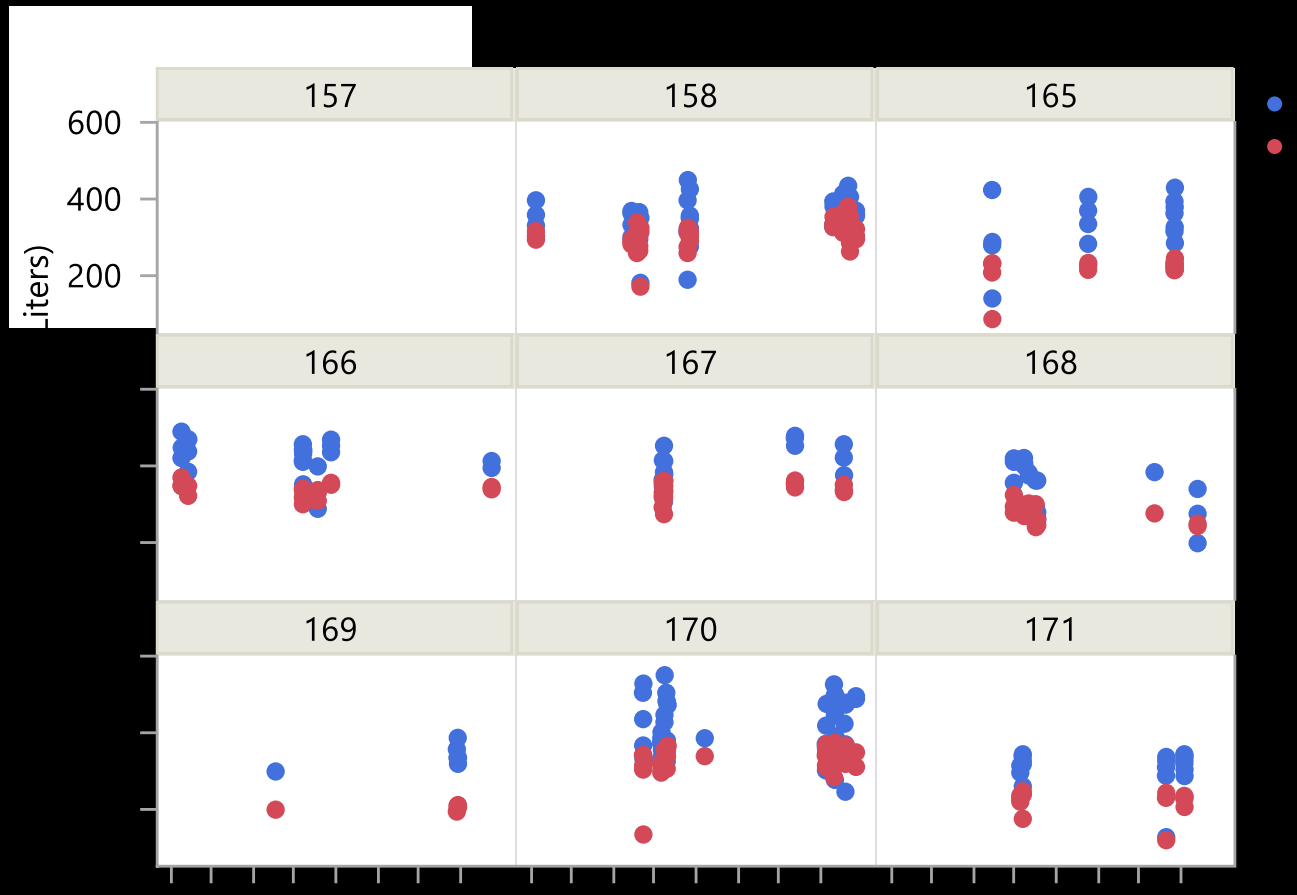
subject_id	Pct_Home Mean		
158	94	0	95
165	53	43	96
166	29	60	89
167	97	0	97
168	74	1	75
169	67	0	67
170	57	26	83
171	100	0	100

AirBeam, Personal $PM_{2.5}$

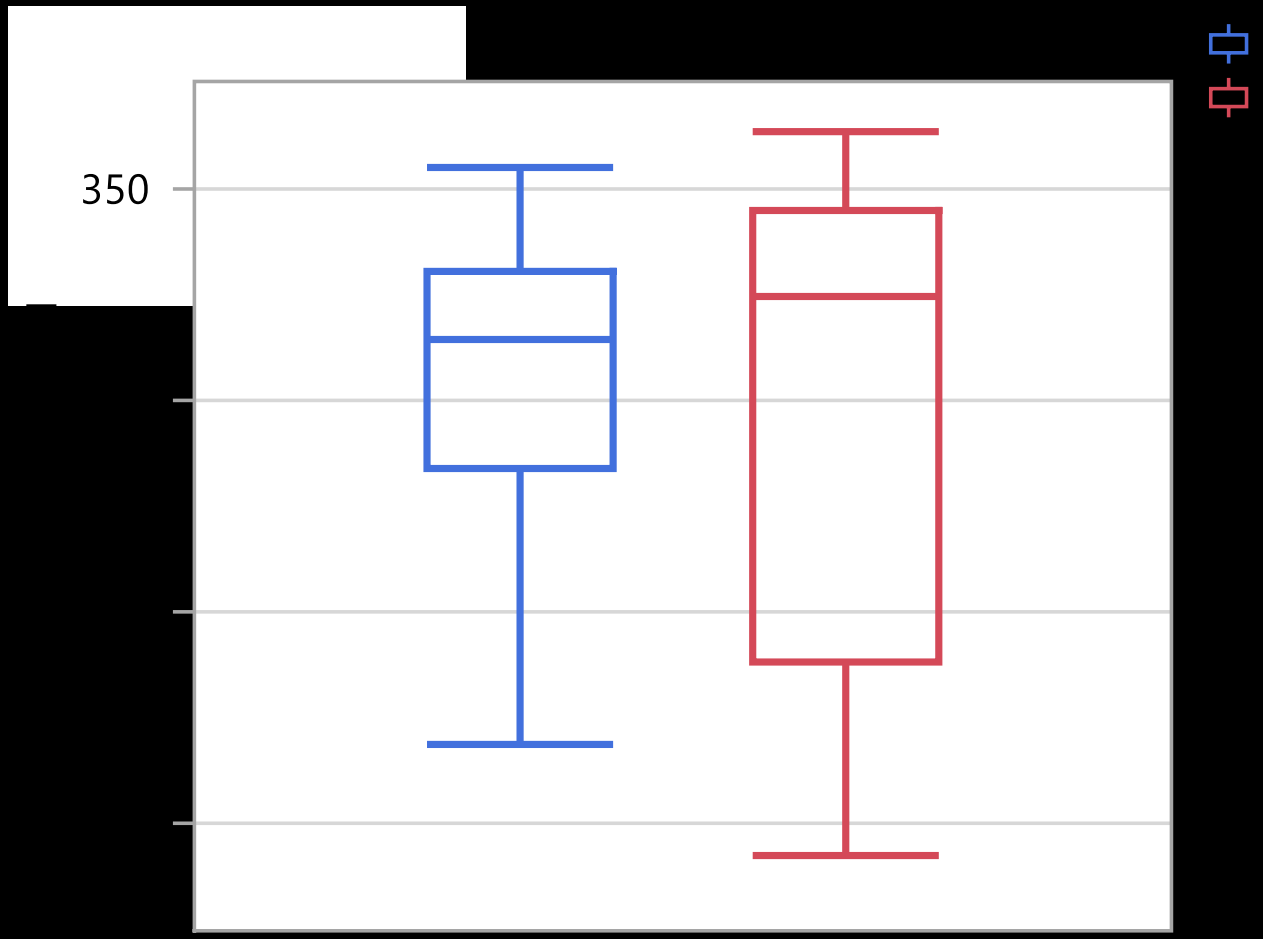


*NOT calibrated yet

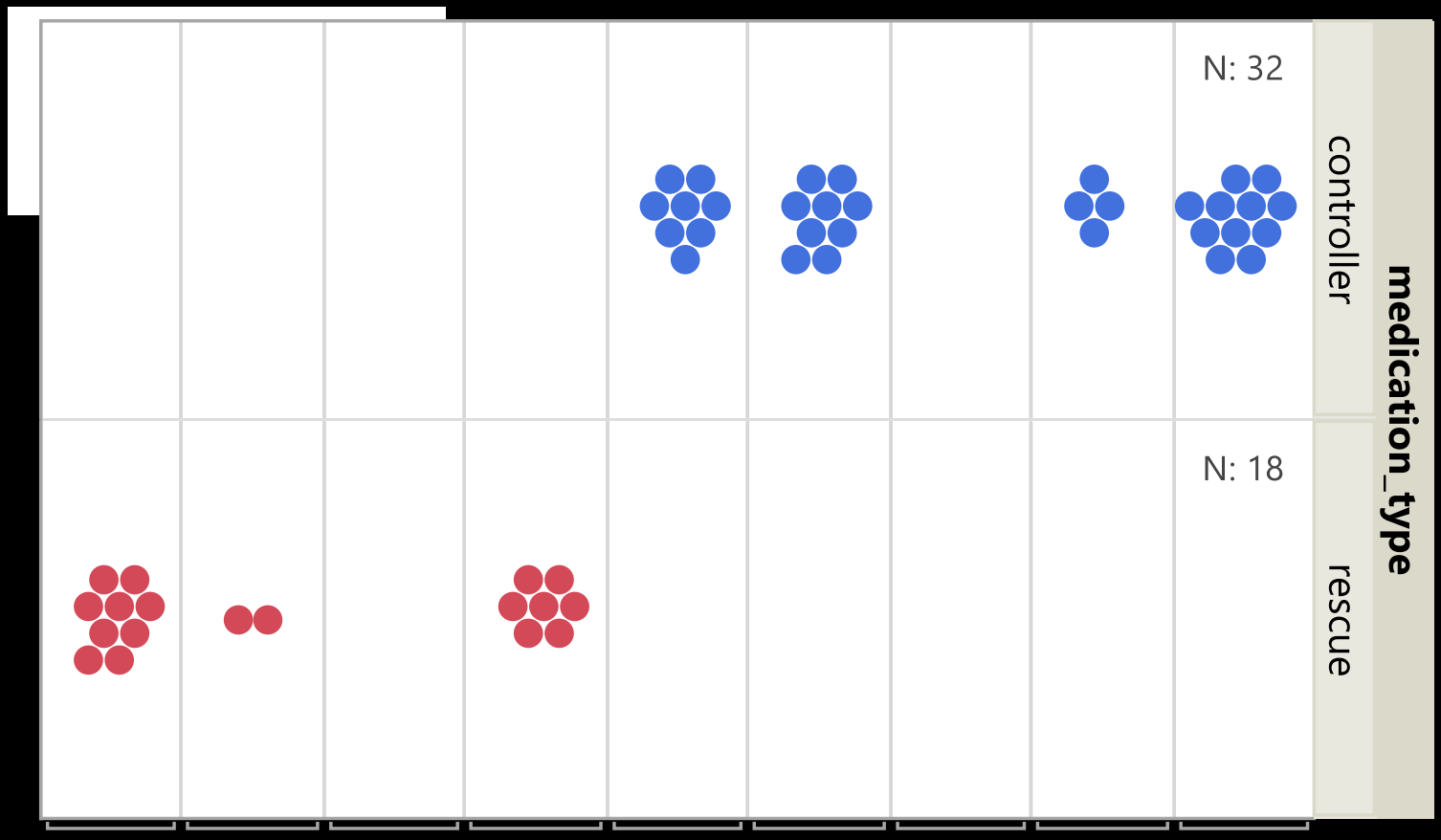
Lung Function



Diurnal Variability in Lung Function



Controller and Rescue Medication Use



Propeller sensors

Preliminary Health Models (n=9)

- Basic mixed effects model at day-level (j), random intercept for subject (i)

$$Y_{ij} = \beta_0 + \beta_i + X_{ij} + \varepsilon$$

- PEF lability or % diurnal variation as marker of airway responsiveness (Redell et al, BMJ. 1999; 319(7201): 45–47)

PEF Lability, n=13 person-days			
Effect	Est	Std Error	Pr > |t|
Intercept	-12.6052	5.3777	0.0661
lag_PM	**0.7834**	**0.4691**	**0.1459**

Please do not cite.

Preliminary Health Models (n=9)

- FEV_1 (PM, afternoon)

FEV1 (PM), n=25 person-days

Effect	Est	Std Err	Pr > |t|
Intercept	296.67	21.5493	<.0001
PM	**-0.9281**	**0.4526**	**0.0570**

- Cough Score

Cough, n=16 person-days

Effect	Est	Std Err	Pr > |t|
Intercept	-2.2467	1.7899	0.2777
lag_PM	**0.1750**	**0.1485**	**0.2659**

Cough, adjusted for % time spent indoors, n=16 person-days

Effect	Est	Std Err	Pr > |t|
Intercept	10.9610	29.3630	0.7337
lag_PM	**0.7172**	**0.3631**	**0.0765**
Pct_Indoors	-0.2214	0.3601	0.5524

Please do not cite.

Innovation for Pediatric Asthma Research

BREATHE: Biomedical REAl-Time Health Evaluation

- Very promising <u>early exploratory</u> findings with very limited, small sample size pilot data
- Individualized 'trigger discovery' at high time and space resolutions, looking at *multiple* environmental *exposures*, *behaviors* and *psychological* factors *in context*
- Need sensor-based health studies to answer research questions – minutes to hour scales
  - Need health outcomes assessment at matching time resolution!
  - Repeated measures designs are very powerful

Thank You

- Questions? habre@usc.edu
- Acknowledgements
  - The Los Angeles PRISMS Center team, led by Dr. Alex Bui (UCLA), NIH U54 EB022002
    - Majid Sarrafzadeh and Anahita Hosseini (P1)
    - Rose Rochio and the OIT Mobilize Team
    - Frank Gilliland, Sandrah Eckel, Genevieve Dunton and the USC team
    - Sande Okelo and the UCLA Pediatric Pulmonology team
    - http://www.mii.ucla.edu/research/projects/prisms/
  - The NIH/NIBIB PRISMS Program: Pediatric Research Using Integrated Sensor Monitoring Systems
    - https://www.nibib.nih.gov/research-funding/prisms

NIH/NIBIB PRISMS Program

Sensor Development (6)

Informatics Platforms (2)

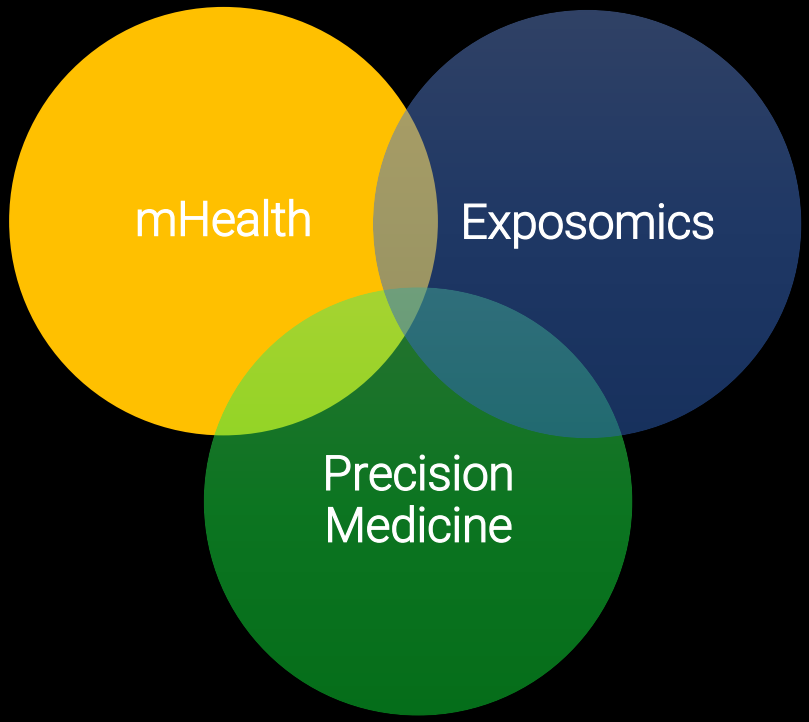
Data and Software Coordination and Integration (1)

- Nine research centers
- Data modeling working group
- Steering committee
- Independent expert committee

NIH National Institute of Biomedical Imaging and Bioengineering

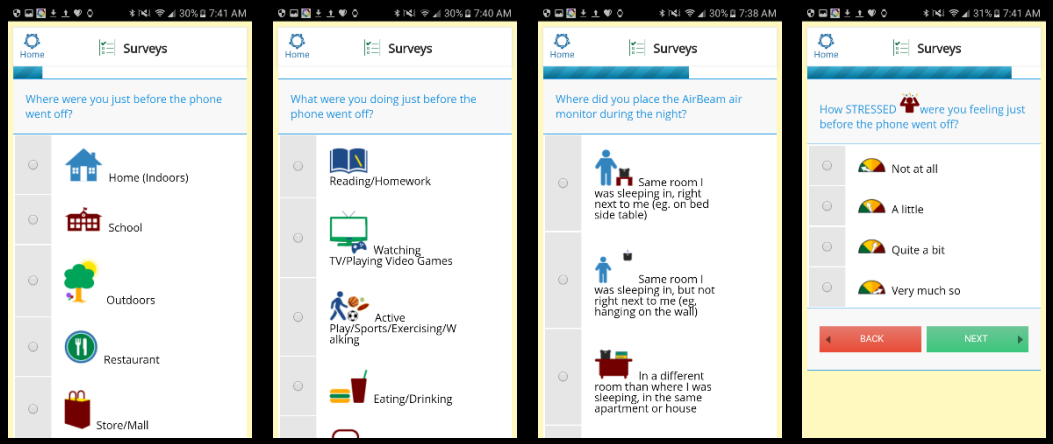
Creating Biomedical Technologies to Improve Health

"Personal" or "Individual"



Smartphone and Smartwatch Apps

Engage participants in data collection and track compliance

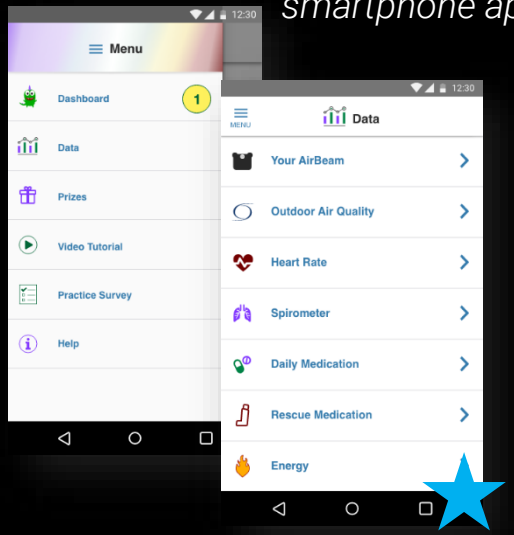


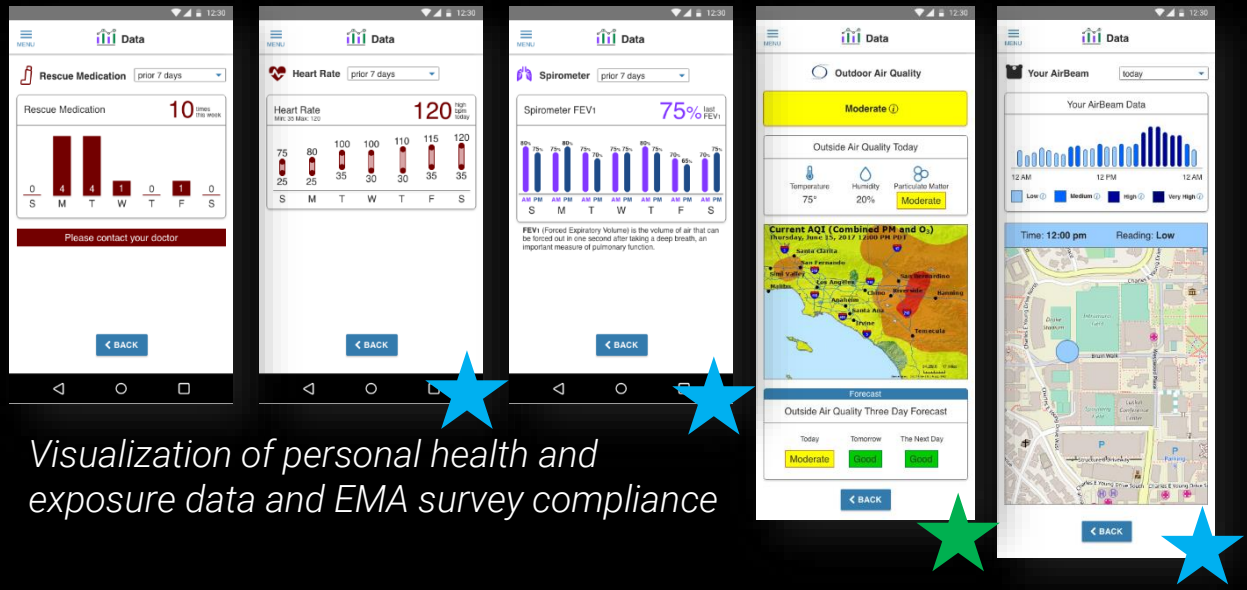
Smartphone app delivers EMA Surveys

View In Progress

View Completed

Mobile dashboards in smartphone app



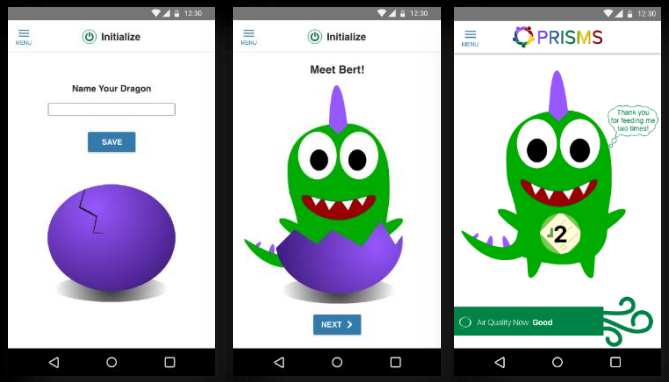


Visualization of personal health and exposure data and EMA survey compliance

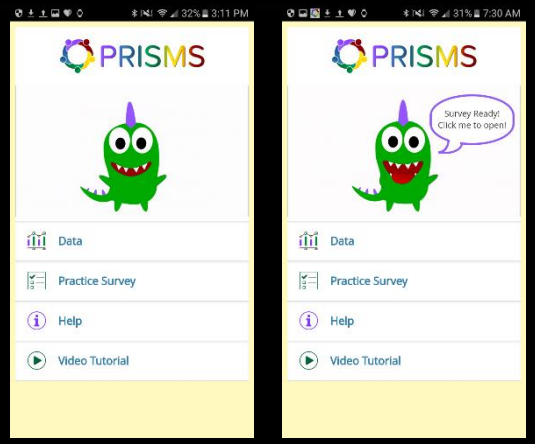
Rose Rocchio, Director MWS, and UCLA OIT Mobilize Team

Smartphone and Smartwatch Apps

Gamification for participant engagement in data collection



Animated pet dragon encourages survey completion



Rose Rocchio, Director MWS, and UCLA OIT Mobilize Team

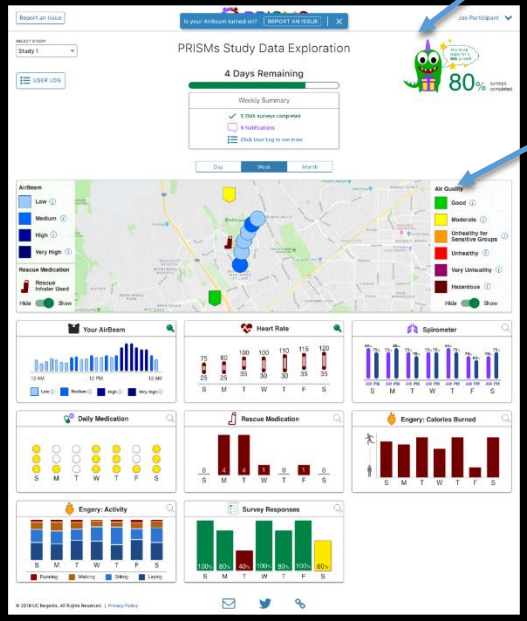
Smartwatch app communicates system status, animated dragon conveys risk of asthma attack based on underlying ML model

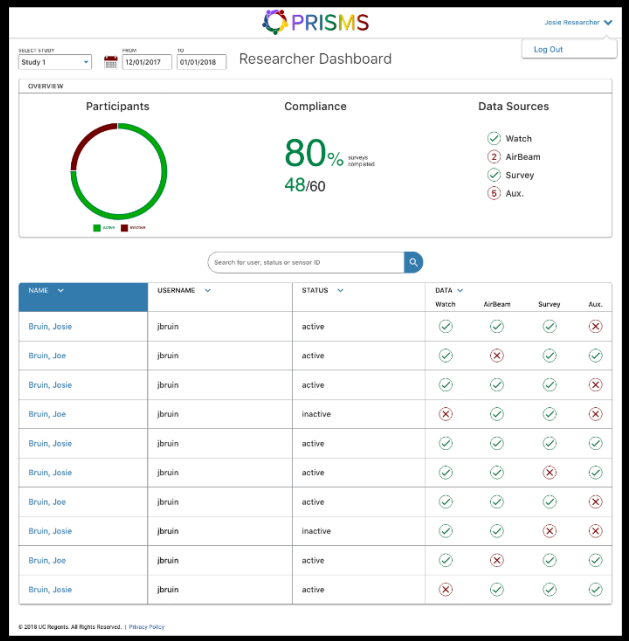
Majid Sarrafzadeh, PhD and Anahita Hosseini, UCLA Computer Science

User, Researcher and Clinician Web Dashboards

Gamified compliance

Visualize data in time and space





Researcher and study coordinator view to track and get notified in real time about any issues with data collection or compliance while study ongoing

Rose Rocchio, Director MWS, Nathan Jacobs, and UCLA OIT Mobilize Team

Preliminary Exit Survey Data

From seven participants

	N	% of Total
How satisfied is your child with their overall experience using the Breathe Kit?		
Very Dissatisfied	0	0%
Diassitsfied	0	0%
Satisfied	4	57%
Very Satisfied	3	43%
How easy or difficult was it for your child to use the Breathe Kit overall?		
Very difficult	0	0%
Somewhat Difficult	0	0%
Somewhat Easy	5	71%
Very Easy	2	29%
As a parent and caretaker, how satisfied are you with your child's overall experience using the Breathe Kit?		
Very Dissatisfied	0	0%
Dissatisfied	1	14%
Satisfied	3	43%
Very Satisfied	3	43%
Using the Breathe Kit was an enjoyable experience for my child.		
Strongly Disagree	0	0%
Disagree	1	14%
Agree	3	43%
Strongly Agree	3	43%

	N	% of Total
It was easy for my child to remember to use the Breathe kit as instructed (wear the air pollution monitor, wear the watch, do the lung function tests, and charge overnight).		
Strongly Disagree	0	0%
Disagree	1	14%
Agree	5	71%
Strongly Agree	1	14%
Using the Breathe Kit every day was burdensome (took too much time or effort) for my child.		
Strongly Disagree	2	29%
Disagree	3	43%
Agree	1	14%
Strongly Agree	1	14%
Carrying or wearing the Breathe kit every day was uncomfortable for my child.		
Strongly Disagree	1	14%
Disagree	4	57%
Agree	2	29%
Strongly Agree	0	0%
It was easy to get three 'good blows' every time my child tried to use the spirometer (or peak flow meter) to test their lungs.		
Strongly Disagree	0	0%
Disagree	0	0%
Agree	6	100%
Strongly Agree	0	0%

Preliminary Exit Survey Data

From seven participants

	N	% of Total
Using the app on the smartwatch to do a spirometry test was easy for my child.		
Strongly Disagree	0	0%
Disagree	0	0%
Agree	6	100%
Strongly Agree	0	0%
Responding to surveys on the smartphone was easy for my child.		
Strongly Disagree	0	0%
Disagree	2	33%
Agree	3	50%
Strongly Agree	1	17%
Responding to surveys on the smartphone often interrupted or disrupted my child's activities.		
Strongly Disagree	0	0%
Disagree	5	83%
Agree	1	17%
Strongly Agree	0	0%
On weekdays, there were too many surveys to respond to on the smartphone.		
Strongly Disagree	1	17%
Disagree	4	67%
Agree	1	17%
Strongly Agree	0	0%
On weekends, there were too many surveys to respond to on the smartphone.		
Strongly Disagree	1	17%
Disagree	5	83%
Agree	0	0%
Strongly Agree	0	0%

	N	% of Total
The surveys on the smartphone were too long.		
Strongly Disagree	1	17%
Disagree	4	67%
Agree	1	17%
Strongly Agree	0	0%
Using the new sensors attached to their rescue and control inhalers was easy for my child.		
Strongly Disagree	0	0%
Disagree	0	0%
Agree	4	67%
Strongly Agree	2	33%
Having a smartphone was distracting to my child.		
Strongly Disagree	1	14%
Disagree	5	71%
Agree	1	14%
Strongly Agree	0	0%
My child had technical difficulties using the Breathe Kit.		
Strongly Disagree	1	14%
Disagree	5	71%
Agree	1	14%
Strongly Agree	0	0%
It was easy to get help when my child faced technical difficulties using the Breathe Kit.		
Strongly Disagree	0	0%
Disagree	1	14%
Agree	4	57%
Strongly Agree	2	29%

Ongoing Pilot Study

Preliminary Feedback

- Very successful recruitment rate so far; only 2 out of 11 total approached declined to participate (1 case where parent thought this is too complicated for 8 year old child, another where child was not interested)
- Very positive responses in exit surveys so far (7 analyzed)
- Most were satisfied with their experience, thought it was somewhat easy for their child to use BREATHE overall
- Most thought it was very easy to get help when the child faced any technical difficulties
- Many requested more notifications rather than less (buzzing watch, having the dragon talk or make sounds)
- Many wanted more information/data/feedback on their 'data' or 'test results'. We will try to prompt for more details in future surveys…

Challenges/Lessons Learned

- First participant considered practice run for in-clinic protocols, no sensor data collected
- Deployed an earlier version of EMA app, lots of new and improved features by now (mainly around notifications and interaction)
- Some technical issues with Propeller inhaler sensors; resolved, quick support issued from Propeller
- One instance with BREATHE not connecting properly, switched out and monitoring time extended to compensate for lost days
- One challenging situation with one participant, problem identified and resolved for future deployments, parent was very understanding
- Lifecycle of hardware (constant servicing/replacement needs)
- Managed to recruit 3 in 1 day but very demanding, more chances for errors and technical issues arising…
  1 to 2 per day more reasonable.

Research Questions

Examples of within-day analyses

- Does exposure to air pollution (single or multiple pollutants, personal or ambient) increase the risk of asthma exacerbation?
- What is the time lag between exposures and observed health effects?
- What combination of factors, behaviors, and exposures triggers rescue inhaler use (or an asthma attack)?
- Is exposure to peaks of combustion-related $PM_{2.5}$ associated with increased asthma symptoms? Which metric is most relevant for health (peak level, cumulative dose, duration of peak)?
- Does the composition of $PM_{2.5}$ modify the effect of short-term peak exposures on asthma exacerbation risk? (eg, is PM from cooking less toxic than PM from traffic or smoking?)
- Is personal air pollution exposure reduced following experiencing adverse asthma events (avoidance behavior)?

Research Questions

Examples of within-day analyses adjusted for day-level predictors

- What are the major sources of air pollution, behaviors and time-activity patterns contributing to total personal $PM_{2.5}$ exposure? And how much do peaks contribute?
- Is spending time in certain microenvironments (eg, in-transit) associated with increased asthma symptoms?
- Is lack of adherence to prescribed control medication associated with increased symptoms?

Examples of day-level (or higher) analyses

- Does high pollution on the previous day(s) increase the risk of nighttime sleep disturbance due to asthma?
- Is reduced lung function in the previous day(s) predictive of asthma exacerbation?

Abstract

- Pediatric asthma is a complex and heterogeneous chronic disease that affects millions worldwide and results in significant morbidity and mortality. Studies have shown environmental exposures such as air pollution to be associated with risk of asthma attacks, but little is known about the time lag between exposure and response, the role of multiple exposures in context, and variation in personal risk at short temporal and fine spatial scales.
- As part of the Los Angeles PRISMS Center, the LA PRISMS Breathe (Biomedical Real-Time Health Evaluation) Kit is being developed as a non-invasive, secure end-to-end informatics platform that utilizes the latest in mHealth technologies to advance environmental health studies of pediatric asthma. The platform is based on a smartwatch/smartphone that securely and wirelessly communicates with a suite of personal environmental, physiological and health sensors in real time and collects self-report symptoms data and contextual information using Ecological Momentary Assessment methods. External environmental data such as meteorology, traffic and air quality is also collected based on time and location of the participant. Data is integrated and analyzed to build individualized exposure and asthma exacerbation prediction models and the information is fed back to asthmatics, caretakers and physicians to improve asthma management.
- This talk will present key components of the Breathe Kit and its deployment in environmental health research studies, including participant engagement, compliance and burden considerations. Data from preliminary pilot testing in a panel study of children with asthma recruited from the UCLA Pediatric Pulmonology clinic will be presented.
- The ultimate goal of the LA PRISMS Breathe Kit is to be able to predict a looming asthma attack in an individual so that early intervention methods can mitigate if not prevent the episode entirely.