

# Big Data, Health and COVID-19

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*August 4th, 2021*



Conflicts: Personalis, Genapsys, SensOmics, Qbio, January, Filtricine, Mirvie, Protos

# Medicine

## Presently



- Focus on **Illness**
- Reactive
- Measure very few things
- Infrequent
- Population based



## Should be

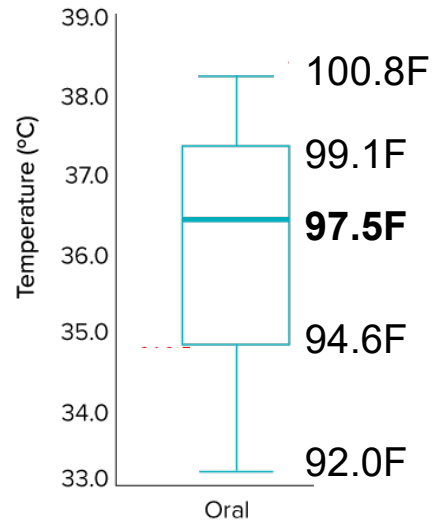


- Focused on **Health**
- Proactive
- Measure many things
- Frequent?
- Individual based

## Precision Health

# Importance in Individual Variation from “Normal”

Oral temp in 2749 healthy individuals



# Health Is a Product of Genome & Exposome

Genome



Exercise



Pathogens



Food

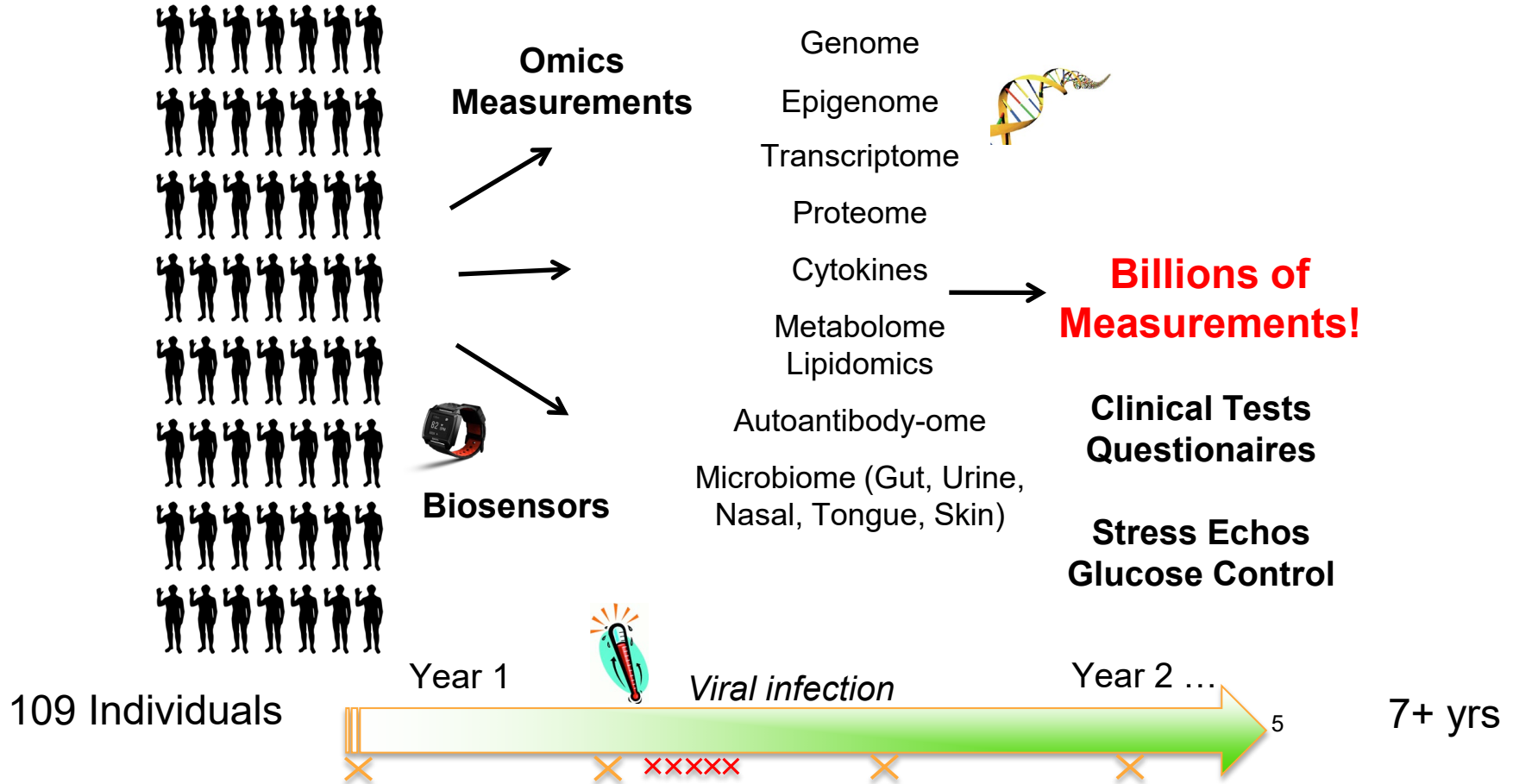


Environmental Exposures



Stress

# Longitudinal Personal Omics Profiling



# 49 Major Health Discoveries

## Metabolic

- 1 MODY mutation (gene)
- 1 ABCC8 Mutation (gene)
- 14 New Diabetes

## Cardiovascular

- 6 Carotid Plaques (imaging)
- 1 Atrial Fib. (wearable)
- 1 RMB20 mutation (gene)
- 1 Reduced LVEF/GLS (imaging)
- 3 Dilated L. Atrium (imaging)
- 1 Pharmagenomic (gene)

## Other

- 1 Sleep Apnea (wearable)
- 1 SLC7A9 mutation (cystinuria risk)
- 2 Macroalbuminuria

## Heme/Onc

- 7 Oncologic Risk Genes (Thyroid Cancer in 1)
- 1 Lymphoma (Imaging)
- 1 MGUS (IgM)
- 1 Smoldering Myeloma (IgM)
- 1  $\alpha$  Thalassemia (Clinical)
- 1  $\beta$  Thalassemia (Gene/Clinical)
- 1 Pros1 Mutation (gene)

## Infectious

- 1 Lyme Disease (wearable)

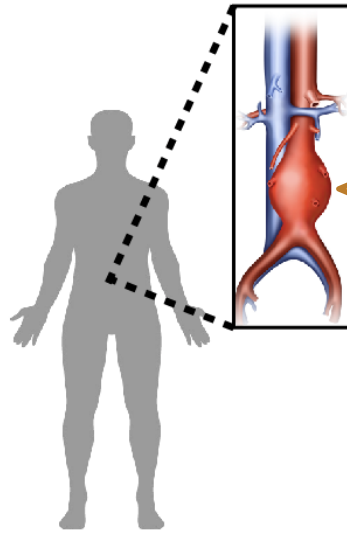


# Genome Sequencing – First 70 People

- Twelve have important pathogenic mutations:
  - **SDHB (2X): high freq. of neuroendocrine tumors<sup>^</sup>**
  - **APC (2X): Colon cancer**
  - **BRCA1: Breast & ovarian cancer**
  - **MUTYH: Colon cancer**
  - SLC7A9: Cystinuria
  - RBM20: Dilated cardiomyopathy<sup>^</sup>
  - CHEK2: Breast cancer
  - PROC: Affects coagulation
  - HNF1A: MODY mutation<sup>^</sup>
  - ABCC8: Hyperinsulinemic hypoglycemia
- All have reportable carrier mutations and/or pharmacogenetic variants



# Abdominal Aortic Aneurysm: High Prevalence and Mortality



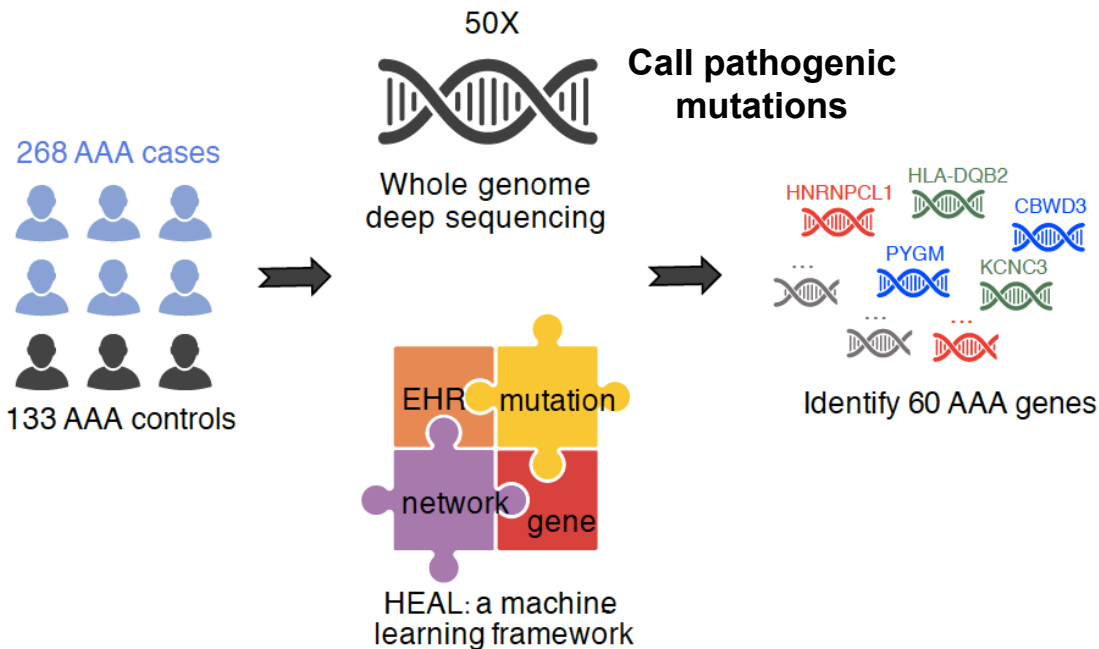
aneurysm

## Facts

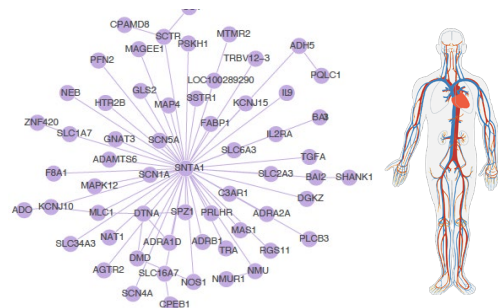
1. affecting 10% of the aged population
2. the 13<sup>th</sup> leading cause of death (U.S.)
3. asymptomatic as it grows
4. irreversible
5. >90% mortality rate upon rupture



# Identifying Genes Associated with AAA

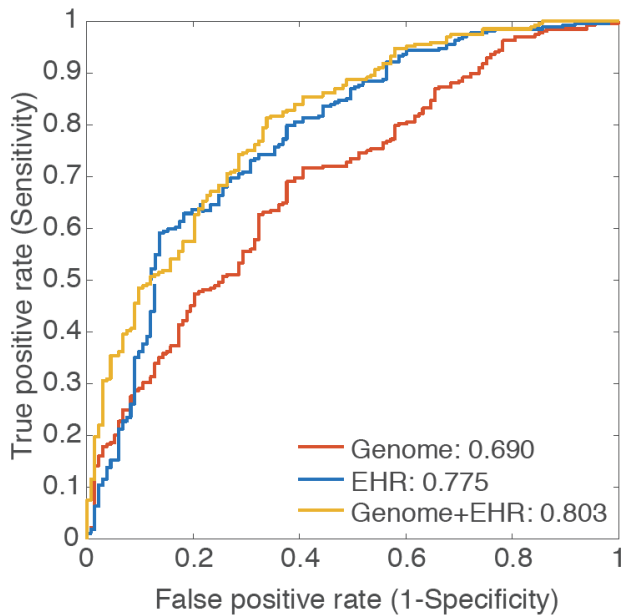
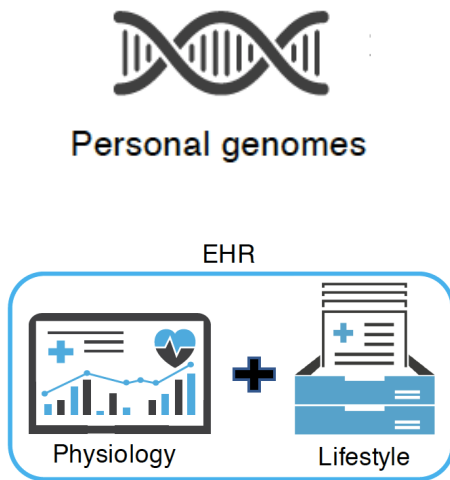


Blood Circulation, Blood Pressure, Cardiomyopathy

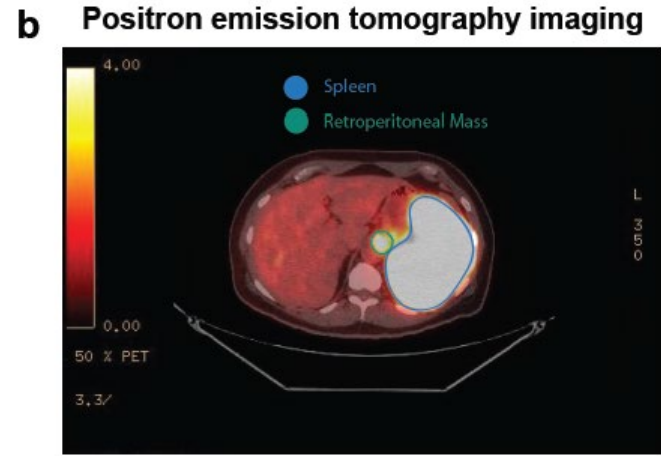
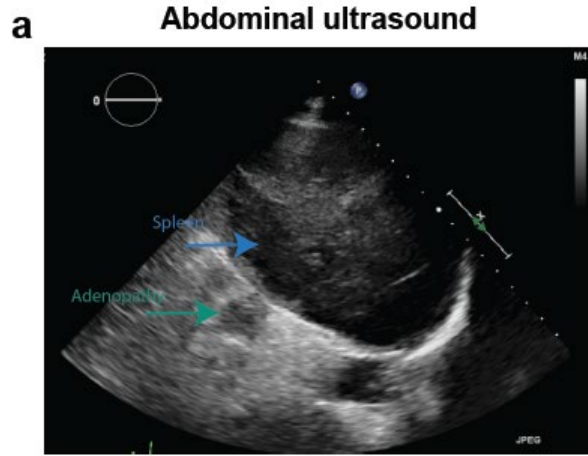


Jingjing LI, Cuiping Pan, Sai Zhang .. Phil Tsao, Cell 2018

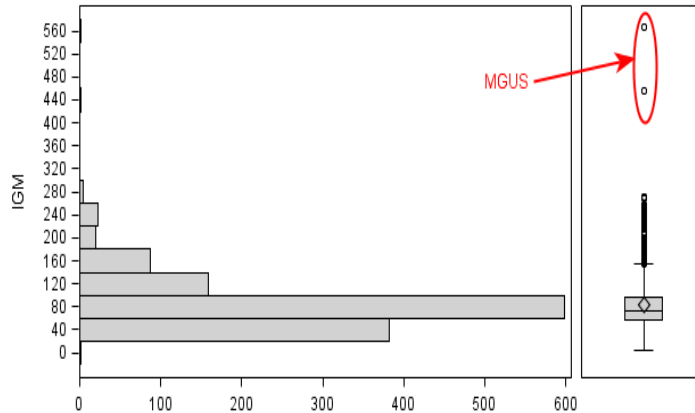
# Predict AAA Using Personal Genomes and Lifestyles



# Discovery of B-Cell Lymphoma

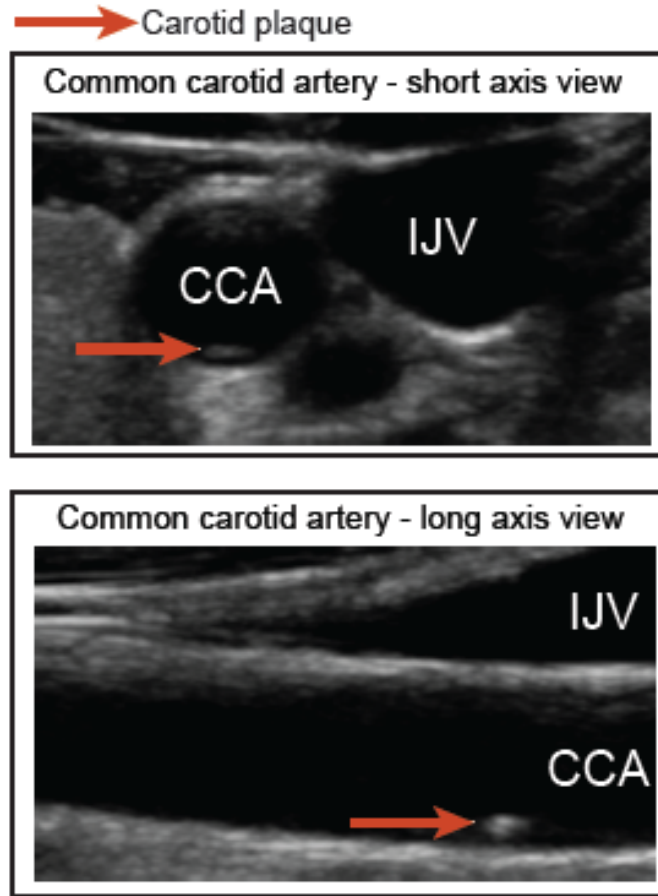


**MGUS**  
**PreCancer:**  
**High IgM**

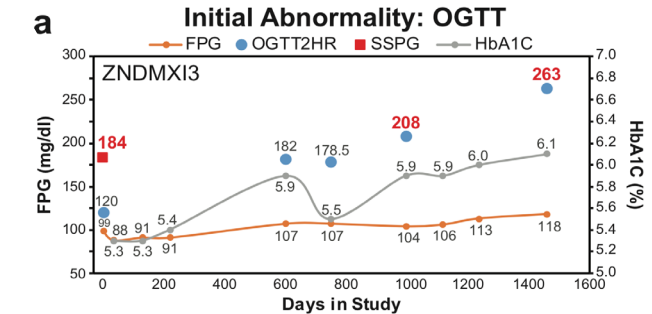
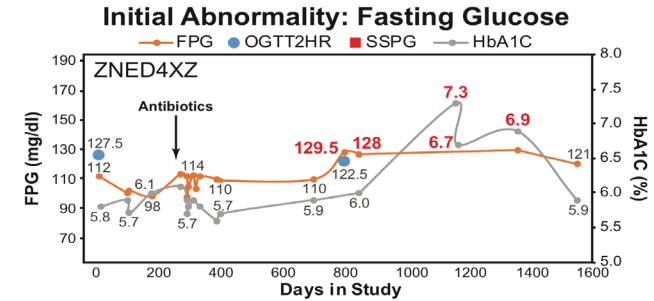
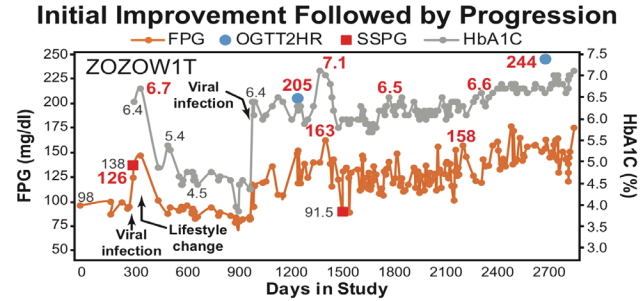
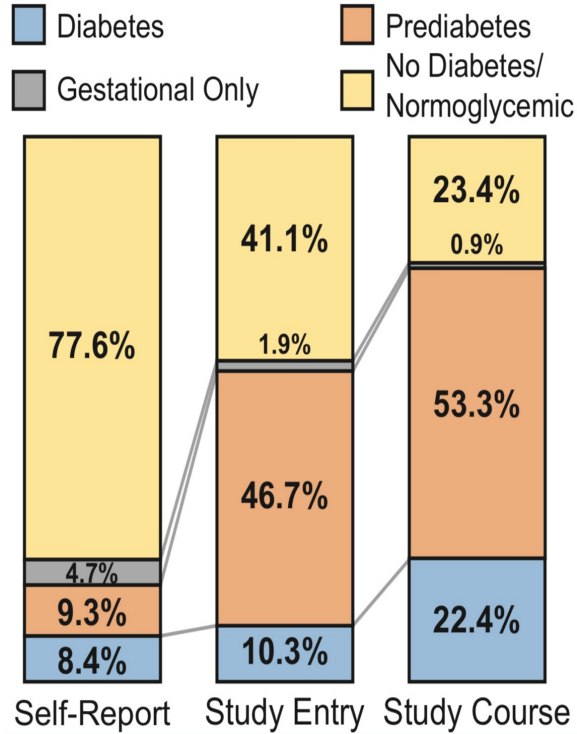


Rose, Contrepois et al.  
Nat. Medicine 2019

# 6 people with Carotid Plaque

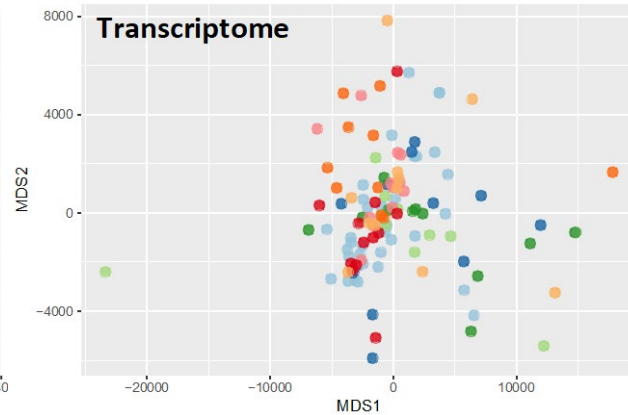
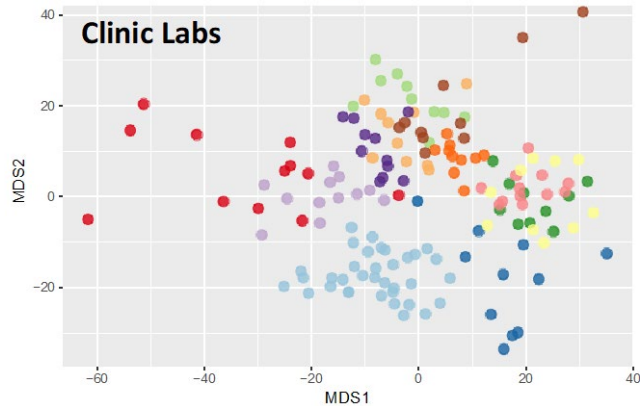
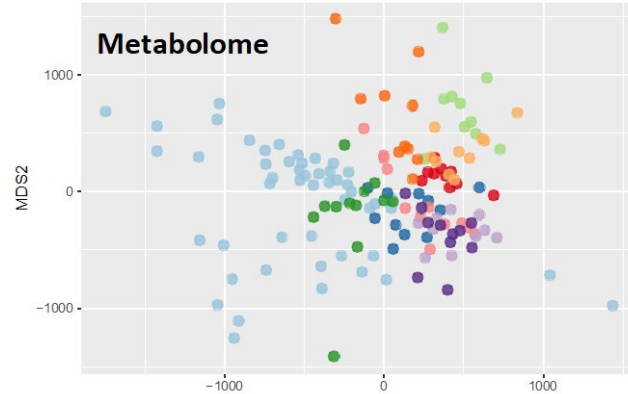
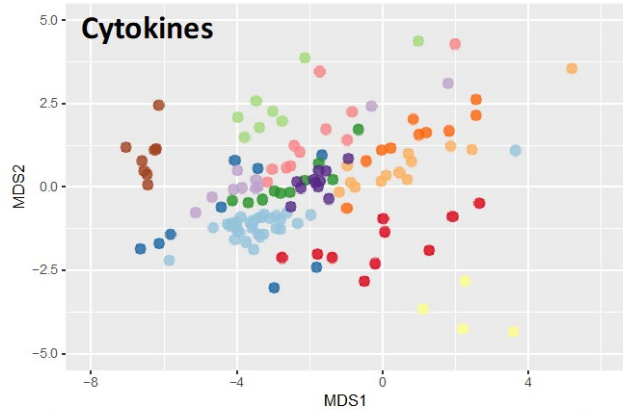


# Transitions in DM status

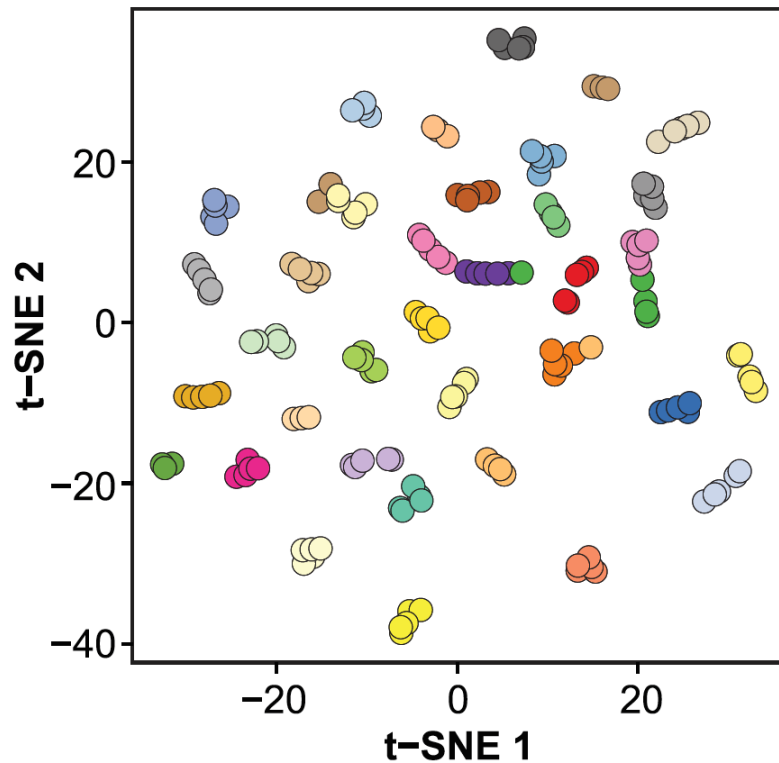


# Strong Personal Characteristics

MultiDimensional Scaling for 12 subjects with at least 10 healthy baseline visits



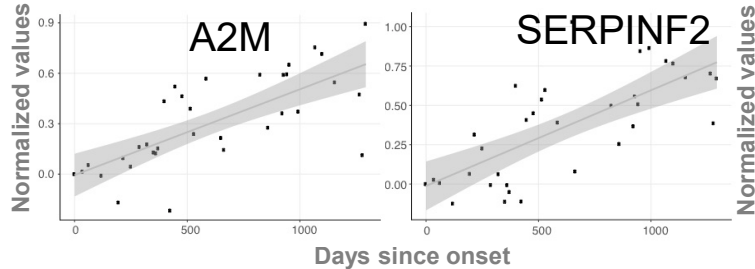
# Individual molecular profiles are more different than the changes induced by acute exercise



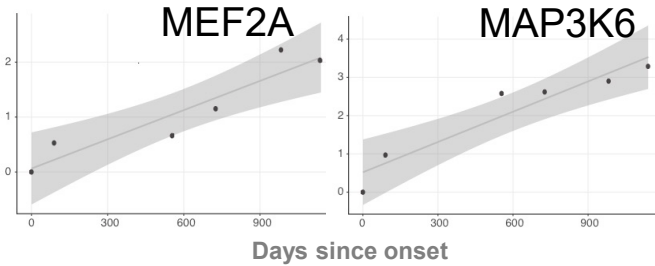
# Personal Aging Molecules and Pathways



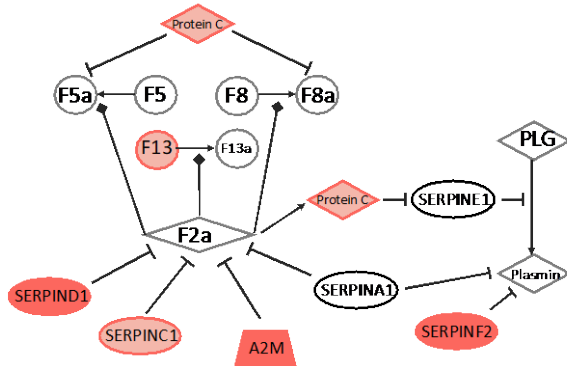
Person 1



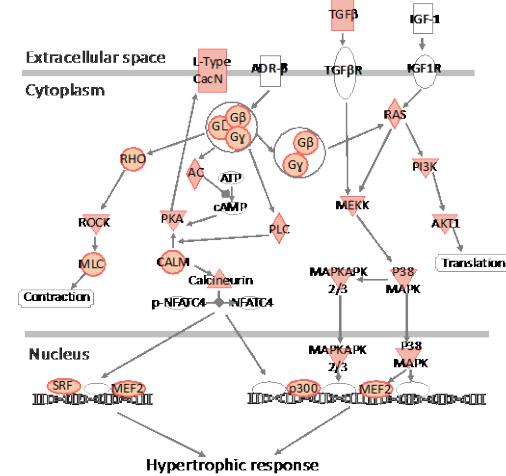
Person 2



Coagulation System

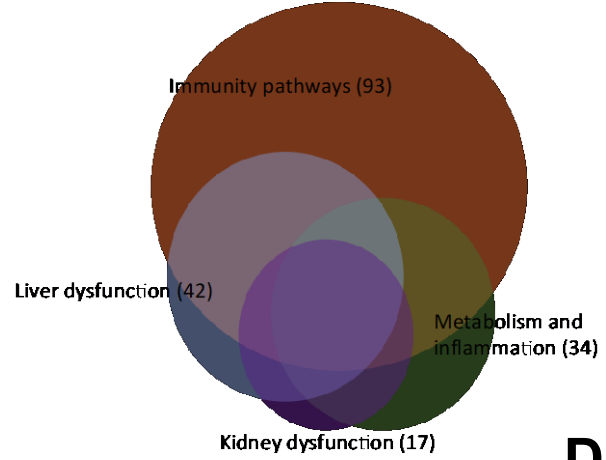


Cardiac Hypertrophy Signaling

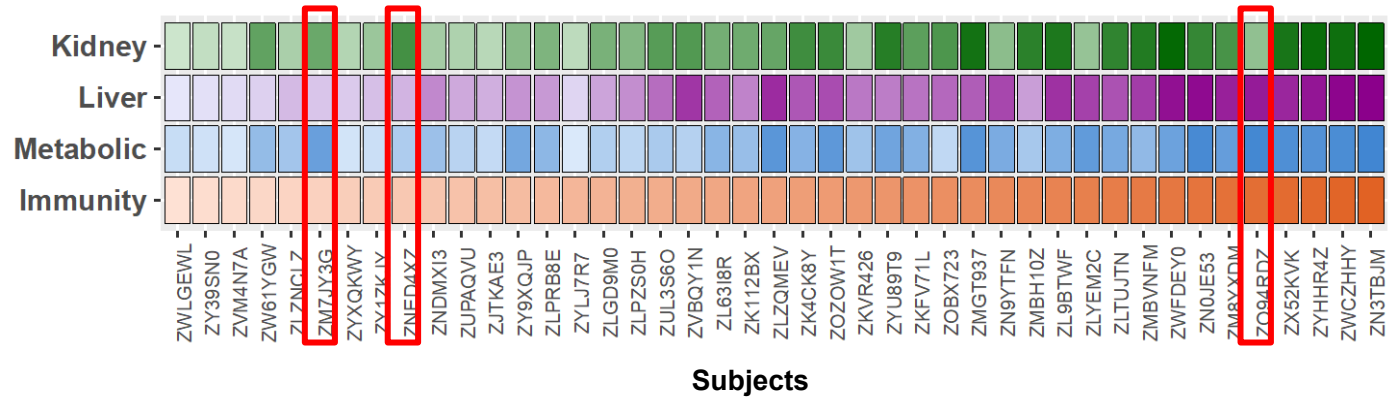




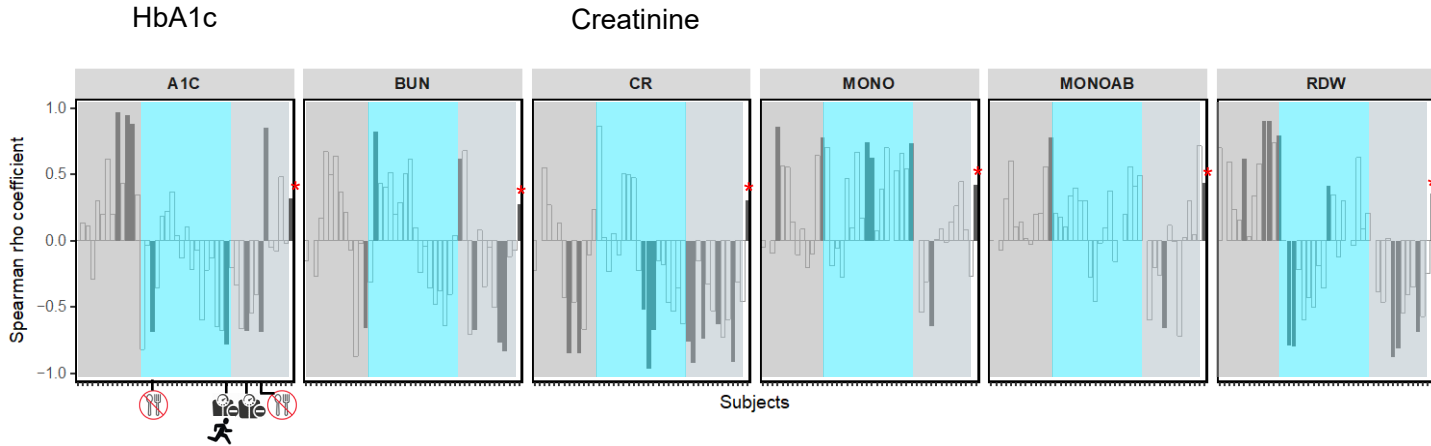
# Four General Classes of Aging Molecules







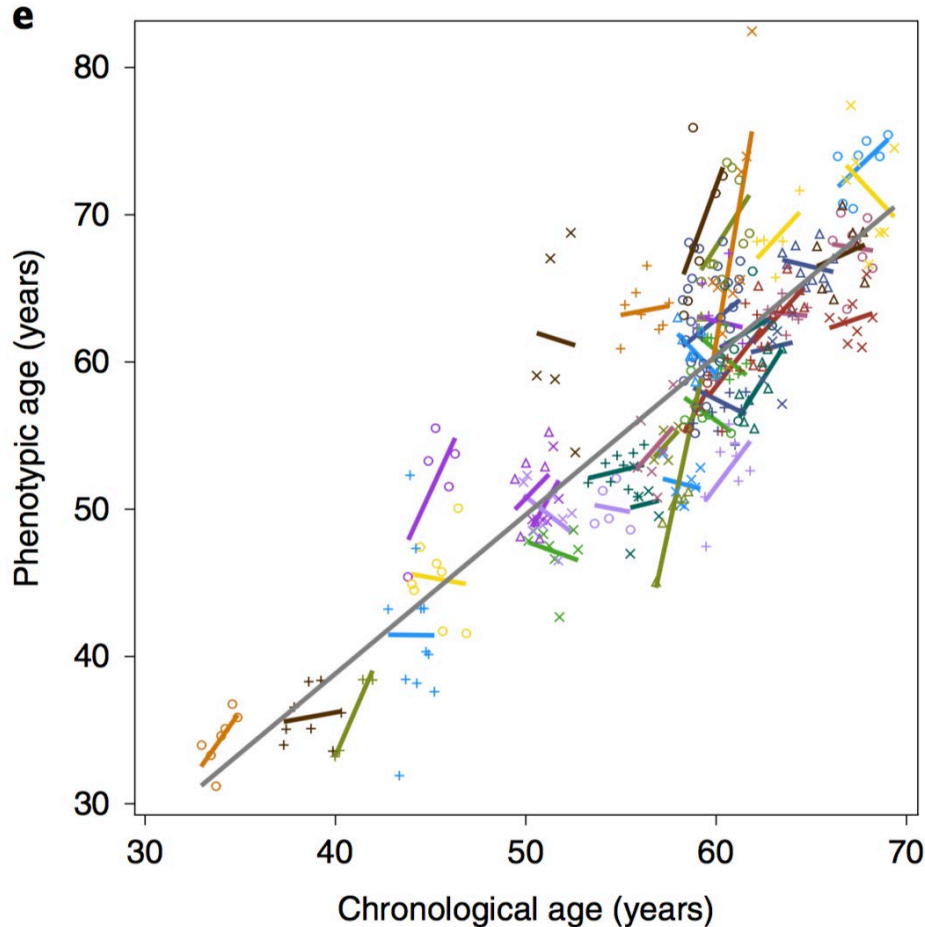
## Different People Have Different Ageotypes




# Personal Aging of Clinical Markers



-  Diet restriction
-  Exercise
-  Statin intake
-  Weight loss



## A new aging measure captures morbidity and mortality risk across diverse subpopulations from NHANES IV: A cohort study

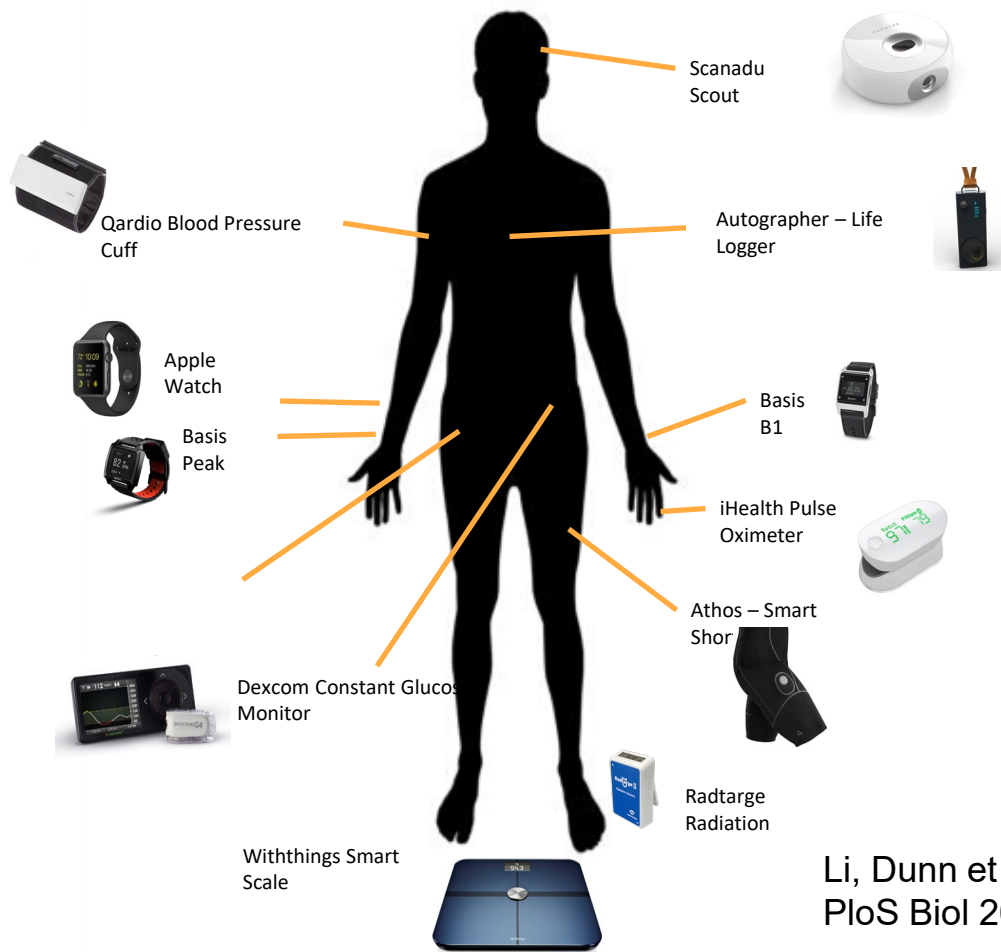
Zuyun Liu, Pei-Lun Kuo, Steve Horvath, Eileen Crimmins, Luigi Ferrucci, Morgan Levine 

Published: December 31, 2018 • <https://doi.org/10.1371/journal.pmed.1002718>

### *Phenotypic age:*

Chronological age and nine biomarkers, including albumin, creatinine, glucose, log (C-reactive protein), lymphocyte percent, mean cell volume, RDW, ALKP and white blood cell count

# Wearable Sensors: Over 900 Devices

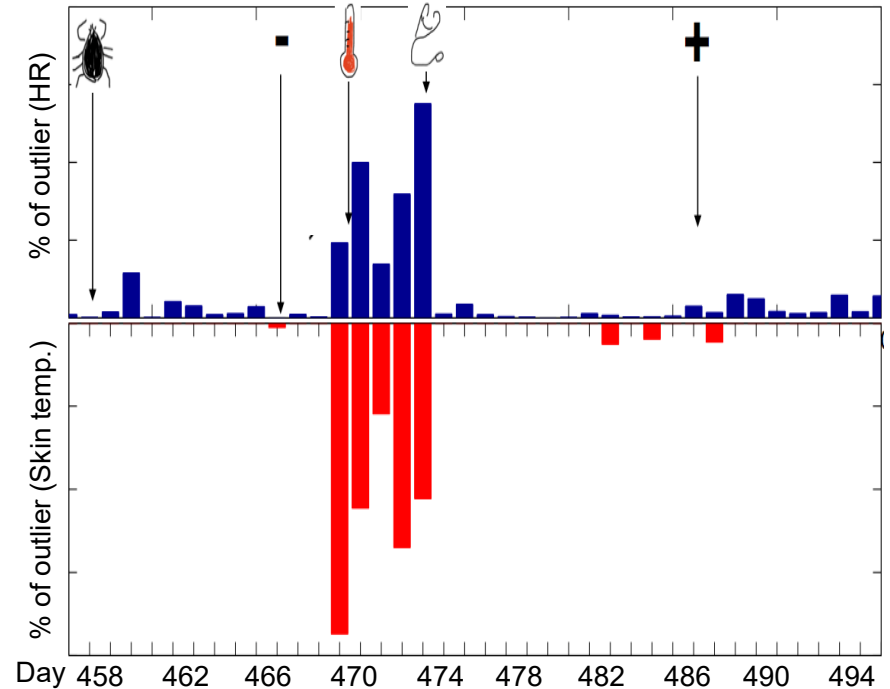
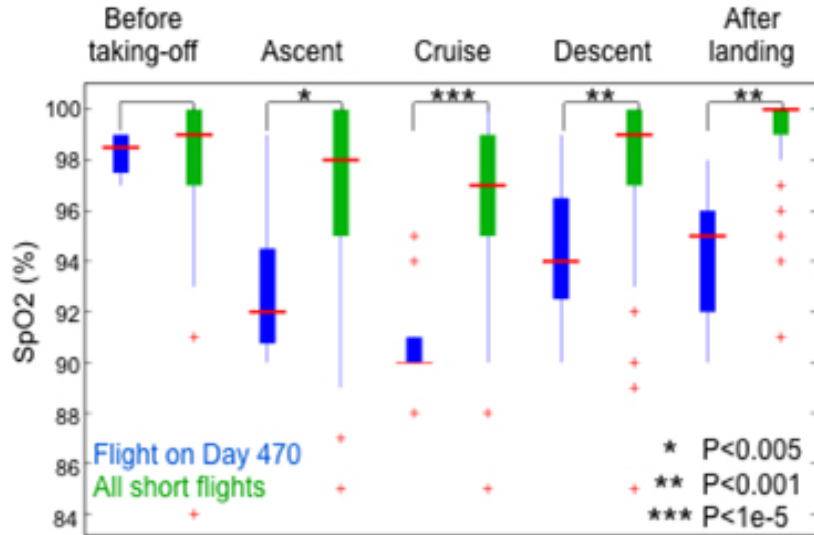


- Worn by millions of people (20% of US)
- Make 100Ks of measurements each day
- Wearables can track many things: HR, HRV, Respiration Rate, SpO2, Skin Temp, Blood Pressure

Li, Dunn et al.  
PloS Biol 2017



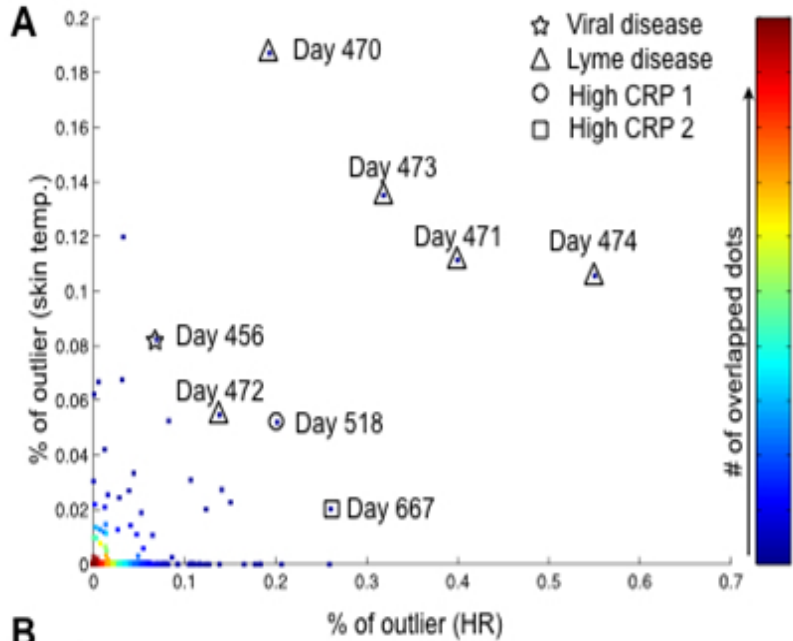
# Early detection of Lyme disease



## Digital Health: Tracking Physiomes and Activity Using Wearable Biosensors Reveals Useful Health-Related Information

Xiao Li , Jessilyn Dunn , Denis Salins , Gao Zhou, Wenyu Zhou, Sophia Miryam Schüssler-Florenza Rose, Dalia Perelman, Elizabeth Colbert, Ryan Runge, Shannon Rego, Ria Sonecha, Somalee Datta, Tracey McLaughlin, Michael P. Snyder 

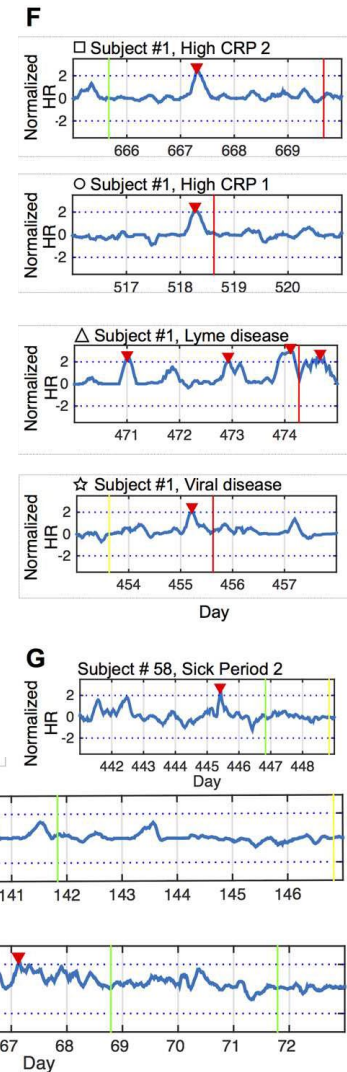
# Detects All Days of Illness



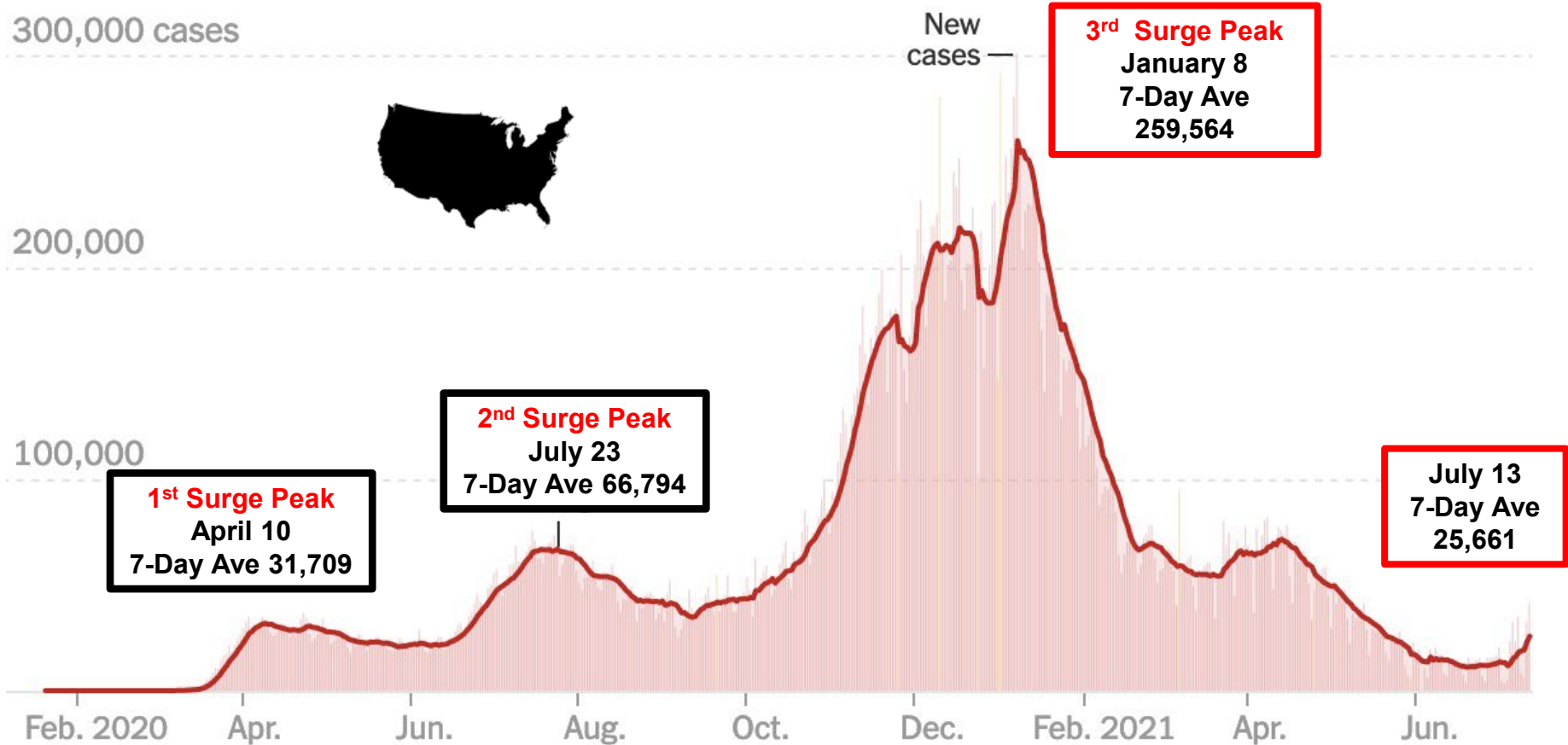
**R**

Li, Dunn et al. PloS Biol 2017

# Change-of-Heart Algorithm



# United States COVID-19 Cases/Day



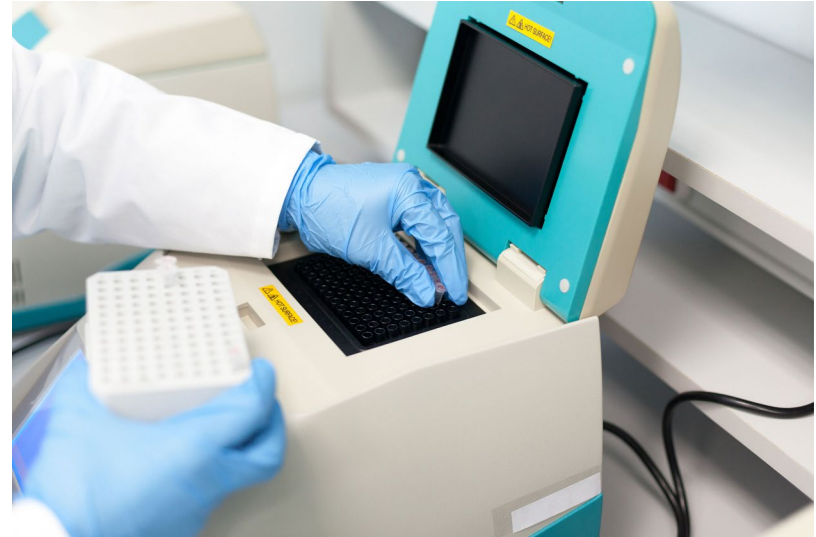
# Current Tests

## Thermometer



Does it work?

## PCR



Slow (1-2 days), Cost, Stochastic



# COVID-19 Infectious Disease Study

## Wearables Data Study

We are trying to find out if information from wearable devices, like Fitbit and Apple Watch, can be used to track infectious diseases like COVID-19. We hope to be able to predict the onset even before any symptoms start.

Healthcare workers and high-risk individuals are especially encouraged to enroll in the study.

**Enroll** >

Study email: covid19\_wearables@lists.stanford.edu  
Participants' rights questions: 1-866-680-2906

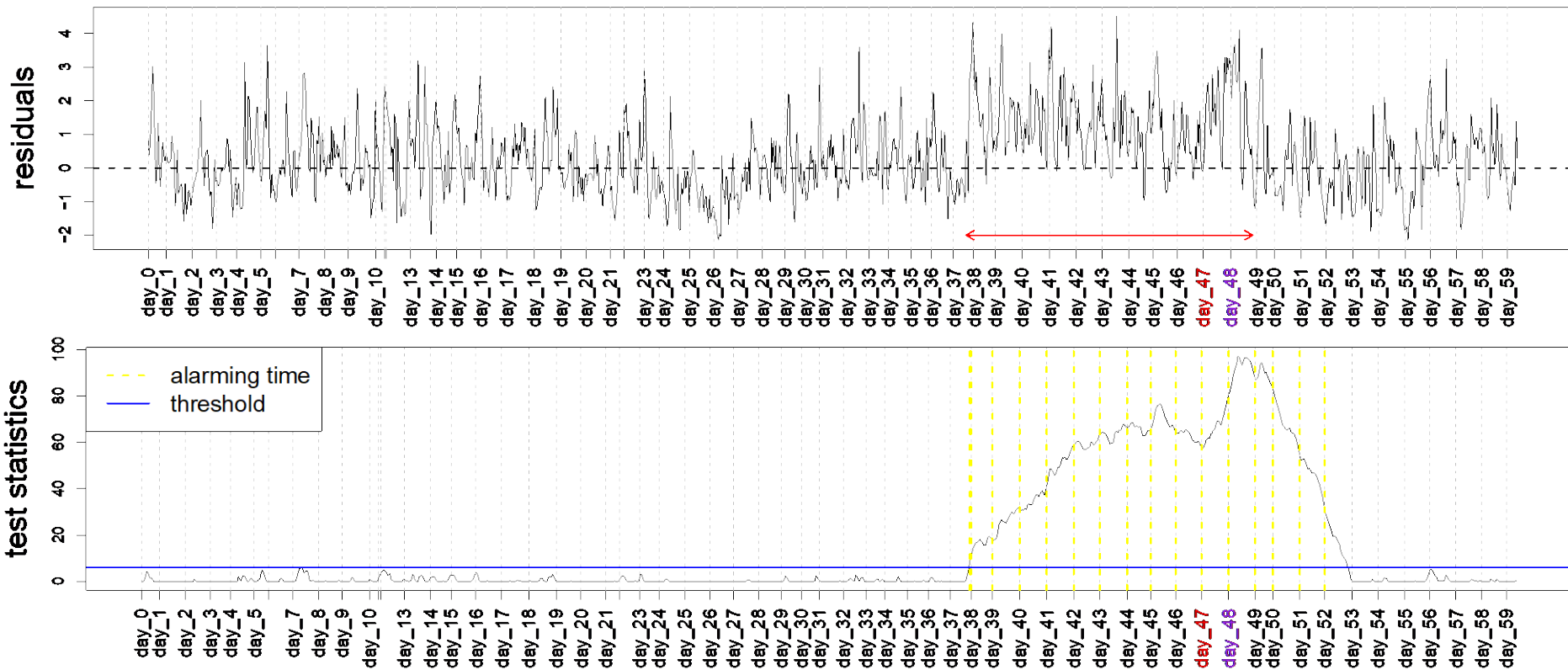


**Launched IRB  
Approved  
Study**

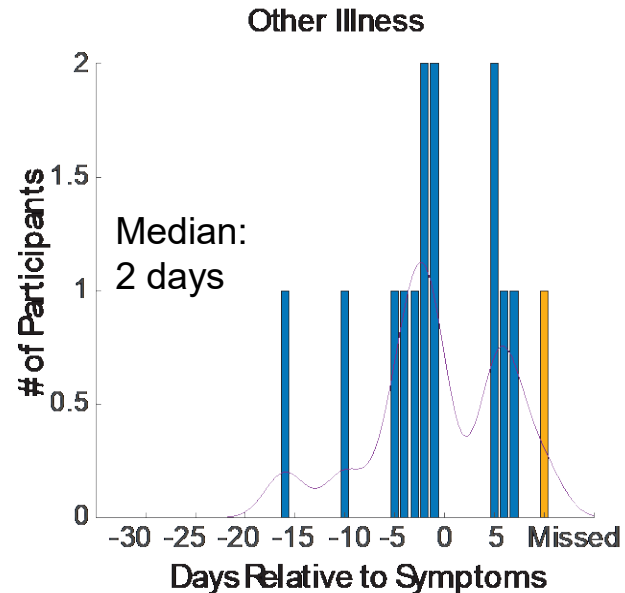
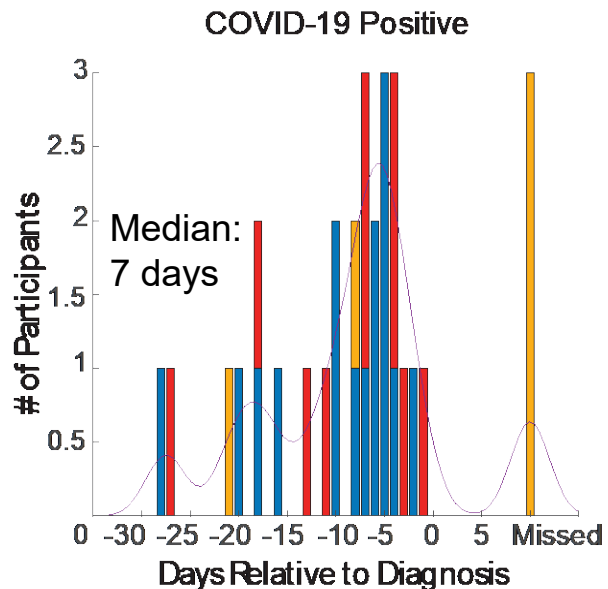
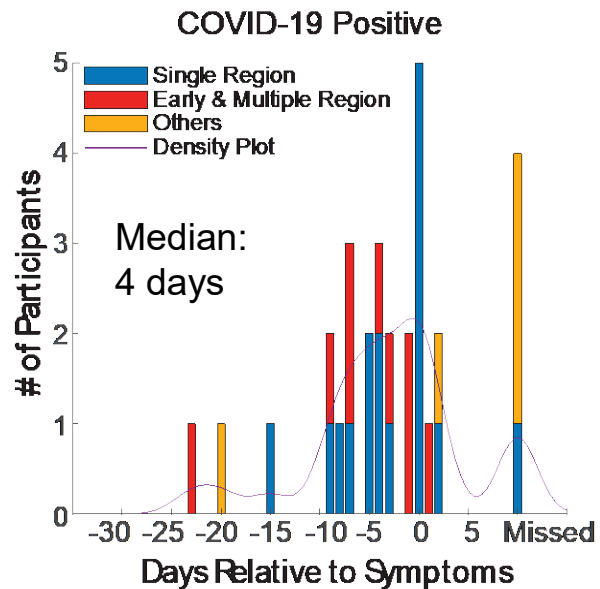
**Partnering with  
Leading Companies  
E.g. Fitbit, Garmin**

**>5000 Enrolled  
>30 COVID-19  
Positives (Golden  
dataset)**

# Identifying COVID-19 at early stage



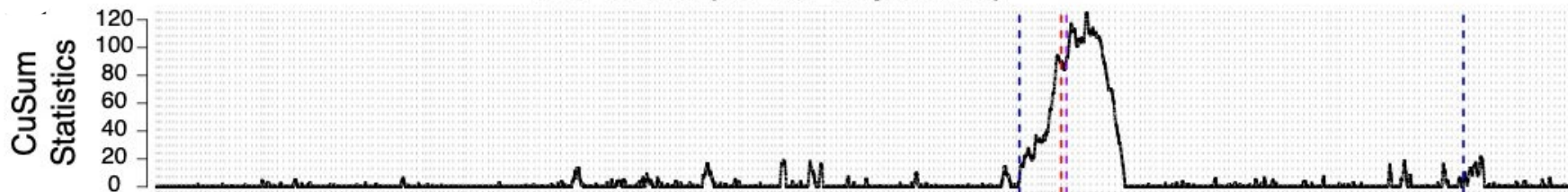
# Summary of Early Detection



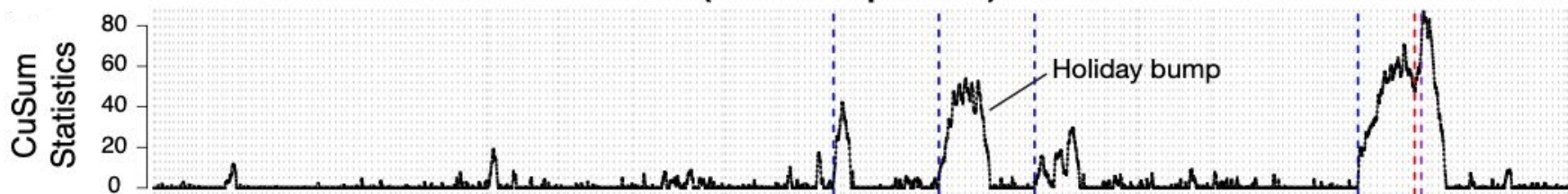
**Elevated Heart Rate: 7 Beats/Min**

## Phase 2: Online Real-Time Detection - CuSum

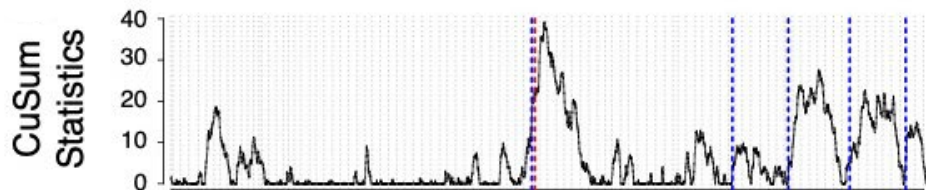
### ASFODQR (COVID-19 positive)



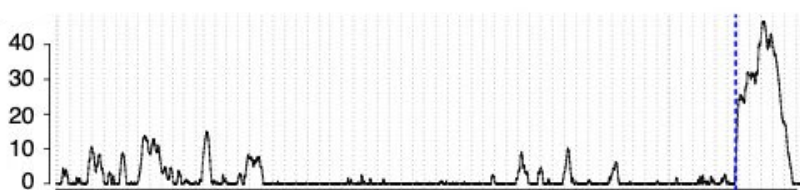
### AJWW3IY (COVID-19 positive)



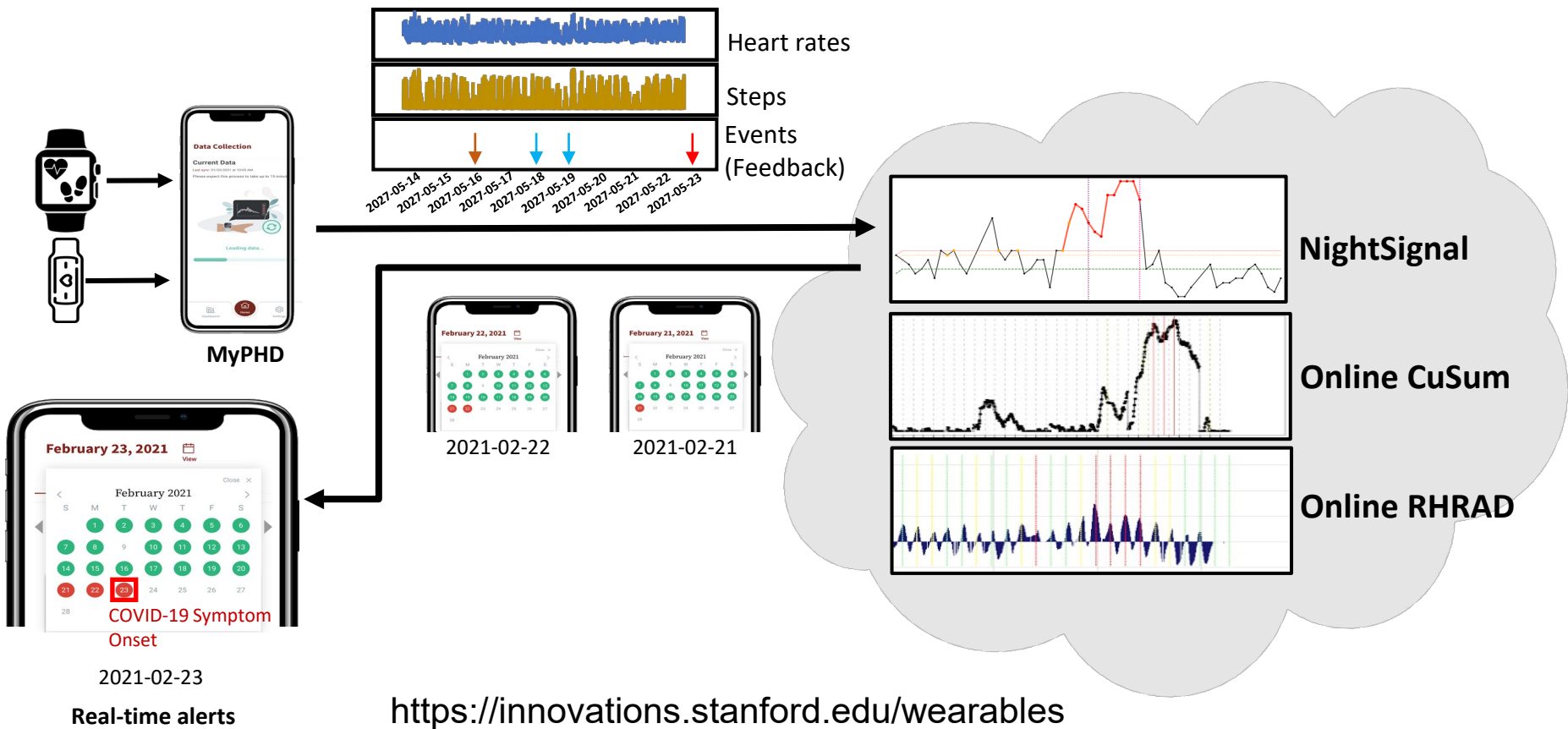
### AR4FPCC (Other illness)



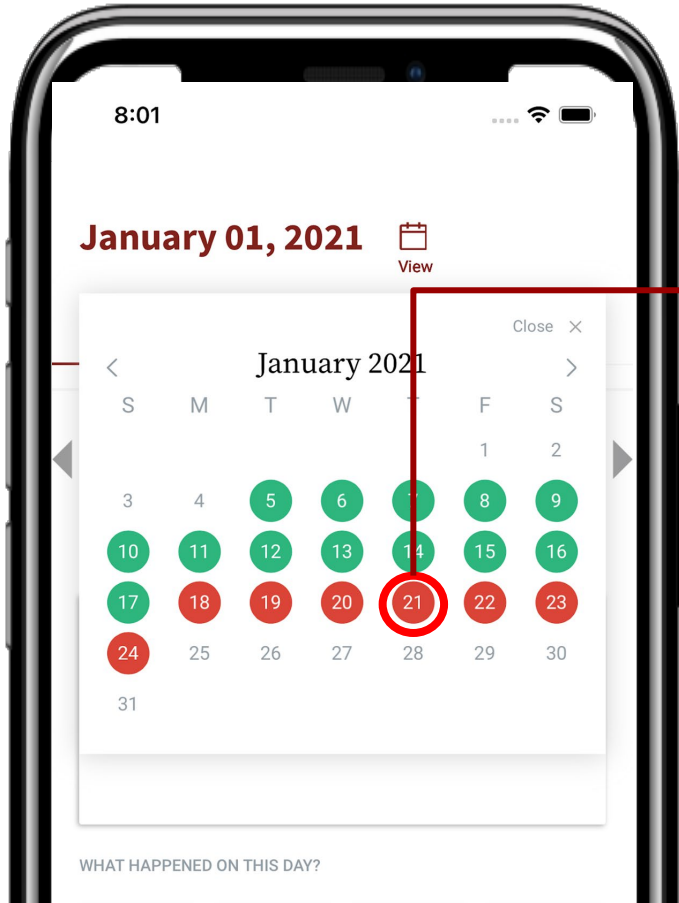
### AFEFA29 (Healthy)



# Real-time Alerting Overview



# Online Alerting System



**Real Covid positive case:**

Symptom Onset \*

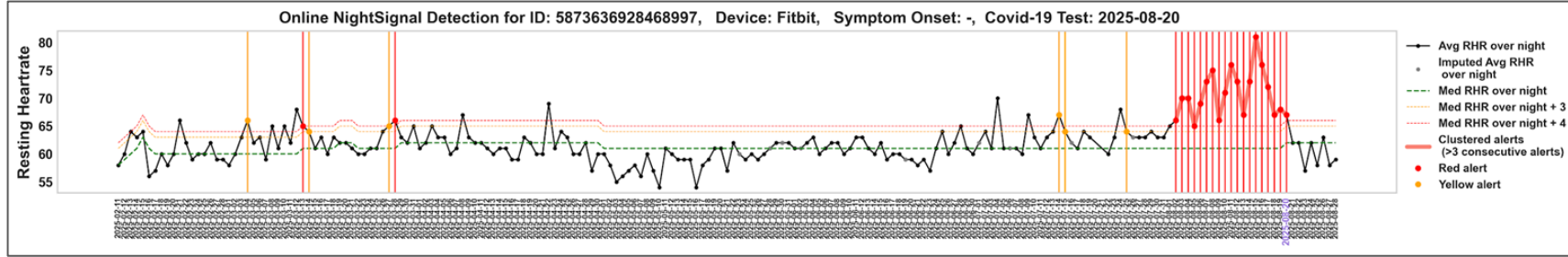
**Total = 78% (53/68) of cases**

\* For privacy reasons, actual dates have been slightly shifted

# Asymptomatic Detection Examples

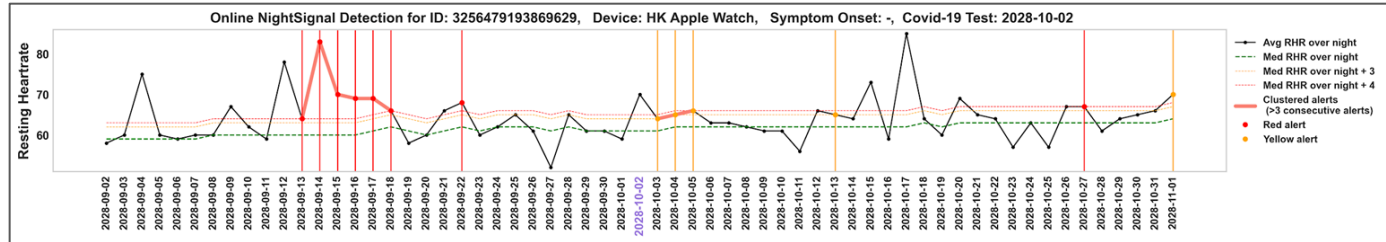
FitBit

NightSignal

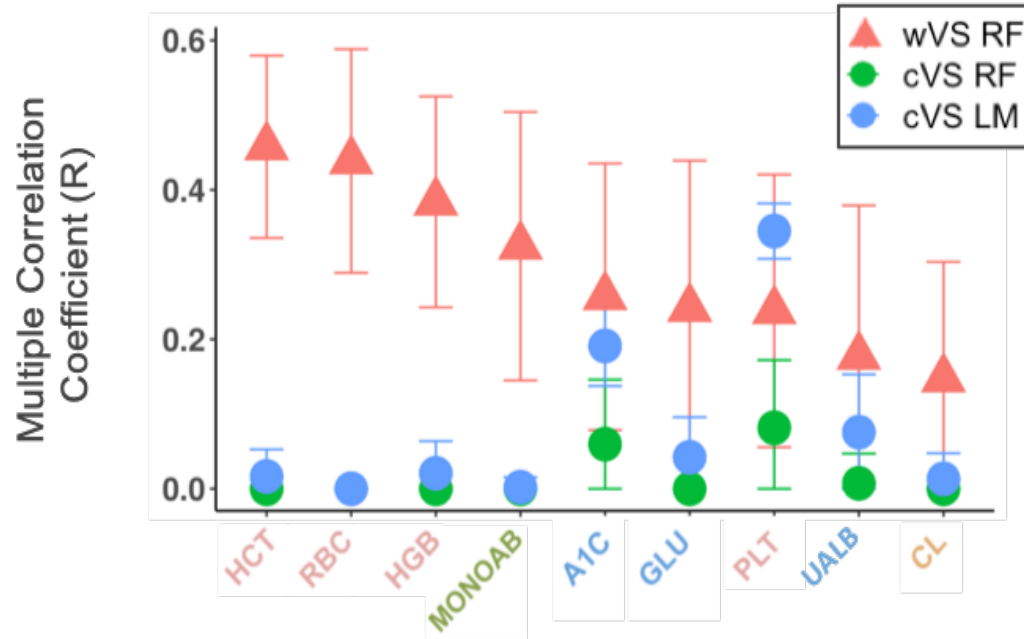


Apple Watch

NightSignal

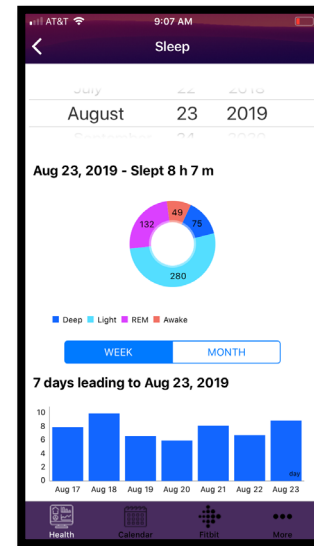
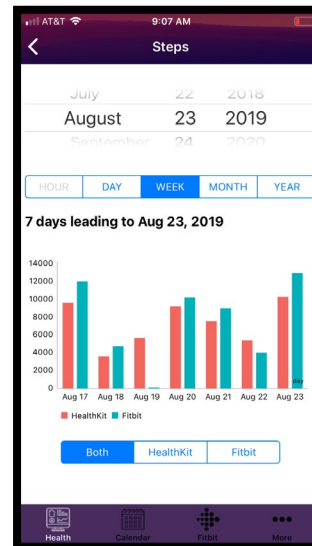
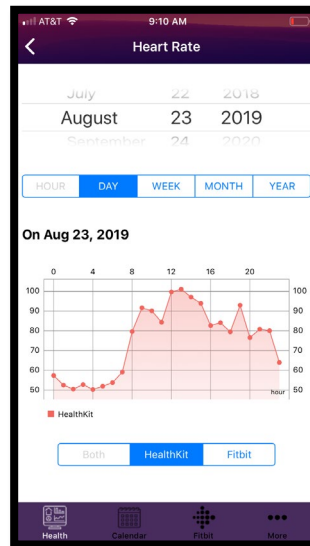
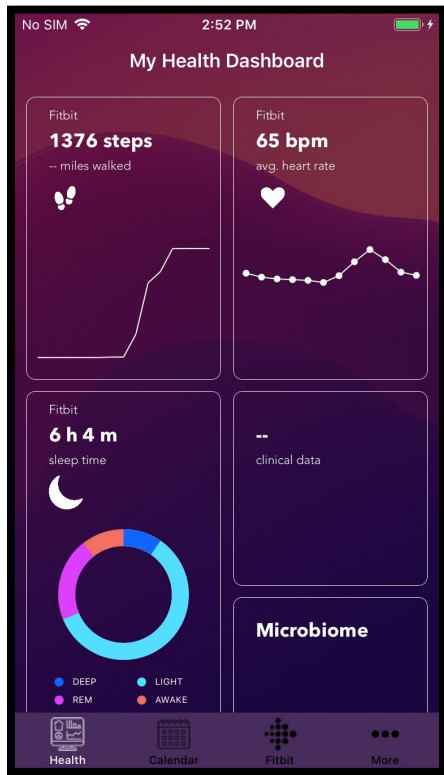


# Prediction of Other Clinical Biomarkers From a SmartWatch



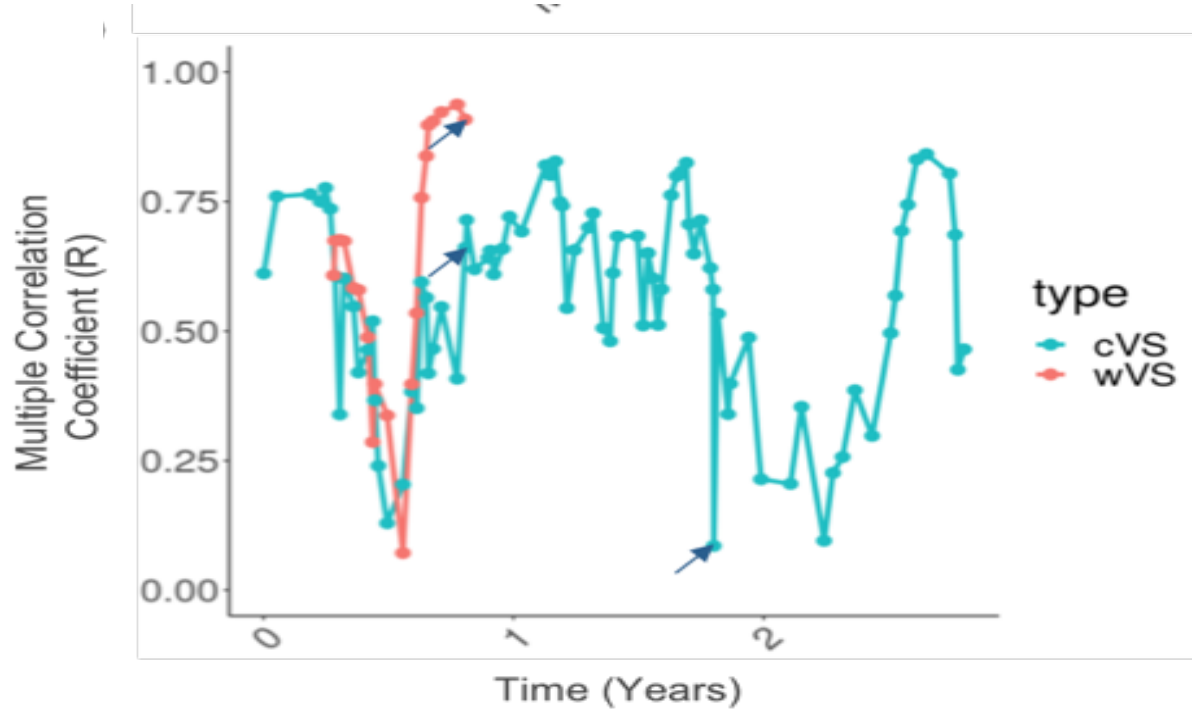


# My Health Dashboard UI



- Visualize and monitor your health data at different resolutions

# Personal Monitoring of Health Using AI and a SmartWatch



Dunn et al, 2021, Nat. Medicine.

# Share Information With Physician



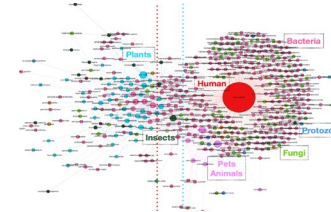
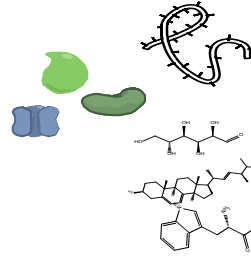
# The Future?

## Genomic Sequencing



```
GGTTCCAAAAGTTTATTGGATGCCG  
TTTCAGTACATTTATCGTTTGCTTT  
GGATGCCCTAATTAAAAGTGACCCT  
TTCAAAC TGAAATTCATGATACACC  
TTGGATATCCTTAGTCGATAAAAT  
TTGGGAGTACTTTCAAAGCCAAATG  
TAATTATCTATGGTAGACAAAACAT  
TACCAATTCATATCGATCCTCCT  
TATTATTTGGCGTTAGACACAGTT  
TATATTTA...
```

## Omes & Sensors: Personal Devices



1. Predict risk
2. Early Diagnose
3. Monitor
4. Treat



Amanda Mills

# Acknowledgements

## Snyder Lab

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Hannes Rost  
Varsha Rao  
Liang Liang  
Tejas Mishra  
Christine Yeh  
Hassan Chaib  
Eric Wei  
Monica Avina

Jon Bernstein

## Weinstock Lab

George Weinstock  
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Shana Leopold  
Daniel Spakowicz  
Blake Hanson  
Eddy Bautista  
Lauren Petersen  
Lei Chen  
Benjamin Leopold  
Sai Lek  
Purva Vats

## McLaughlin Lab

Tracy McLaughlin  
Colleen Craig  
Candice Allister  
Dalia Perelman  
Elizabeth Colbert



## Personal Health Dashboard

Amir Bahmani  
Arash Alavi  
Thore Buerger  
Audrey Haque  
Ming Nyguen  
Keith Bettinger

## Exposome

Chao Jiang  
Xin Wang  
Jingga Inlora  
Ting Wang  
Xiyan Li

## AAA

Jinjing Li  
Sai Jiang  
Phil Tsao

## Wearables

Xiao Li  
Jessie Dunn  
Denis Salins  
Sophia Rose  
Heather Hall

# Team



Xiao  
Li



Amir  
Bahmani



Tejaswin  
i Mishra



Ben  
Rolnik



Alessandr  
a Celli



Emily  
Higgs



Arash  
Alavi



Meng  
Wang



Andy  
Brooks



Ahmed  
Metwally



Thore  
Buergel



Ziyue  
Xing



Minh  
Nguyen



Josh  
Payne



Diego  
Celis



Pramod  
Kotipalli



Lisa  
Liao



Srinath  
Anan-  
thakrishnan



Sushil  
Upadhyayula



Audrey  
Haque



Ghazal  
Mazaheri



Ankit  
Mathur



Gireesh  
Kumar



Jason  
Li



Katherine  
Van  
Winkle



Camille  
Berry



Dan  
Gillespie



Qiwen  
Wang



Qinyi  
Yao



Kexin  
Cha



Tao  
Wang



Keith  
Bettinger



Wenyu  
Zhou

<https://innovations.stanford.edu>

