

Re-Imaging Framingham Heart Study Today

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NASEM

**Precision Medicine in Neuroscience: Tools, Translation, and
Implementation: A Workshop**

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Disclosures

Signant Health
Novo Nordisk

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Alzheimer's Disease Data Initiative
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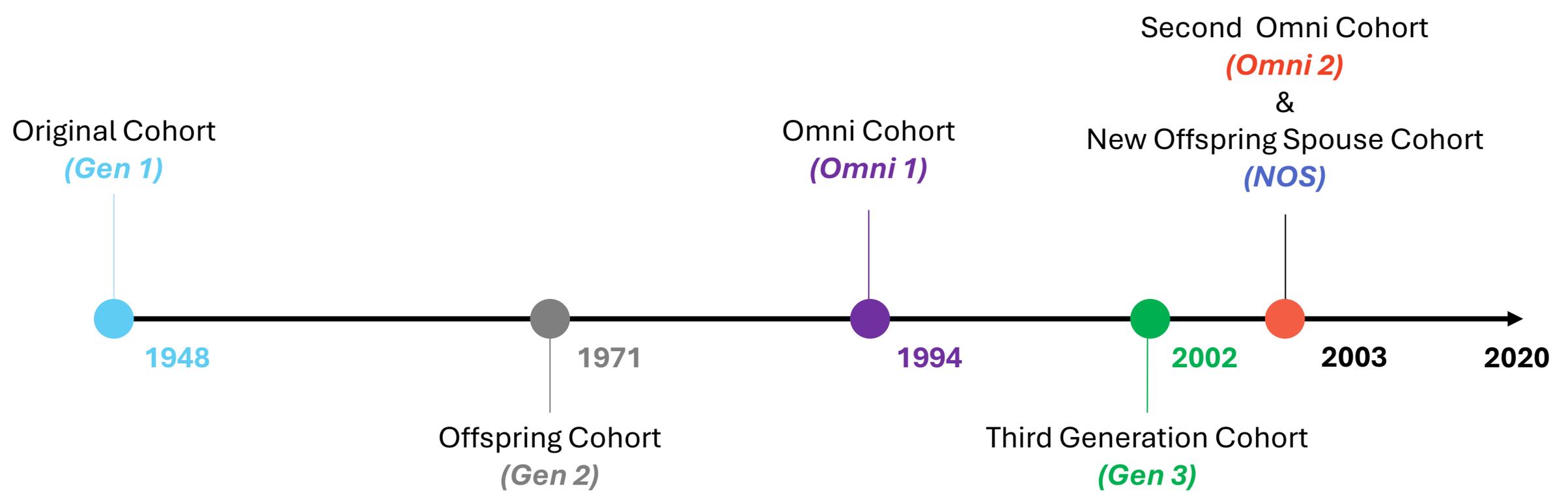
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Global Research and Imaging Platform

Framingham Heart Study (FHS) Cohorts



 International Journal of Epidemiology 2015, 44(1):1-12
doi:10.1093/ije/dy127
Cohort Profile 

Cohort Profile

Cohort Profile: The Framingham Heart Study (FHS): overview of milestones in cardiovascular epidemiology

Establishing the Concept of Risk



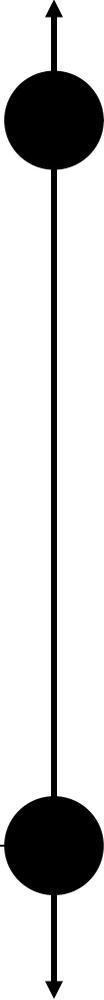
[Ann Intern Med. 1961 Jul;55:33-50. doi: 10.7326/0003-4819-55-1-33.](#)

Factors of risk in the development of coronary heart disease--six year follow-up experience. The Framingham Study

W B KANNEL, T R DAWBER, A KAGAN, N REVOTSKIE, J STOKES 3rd

PMID: 13751193 DOI: 10.7326/0003-4819-55-1-33

1961



1957

[Am J Public Health Nations Health. 1957 Apr;47\(4 Pt 2\):4-24. doi: 10.2105/ajph.47.4_pt_2.4.](#)

Coronary heart disease in the Framingham study

T R DAWBER, F E MOORE, G V MANN

PMID: 13411327 PMID: PMC1550985 DOI: 10.2105/ajph.47.4_pt_2.4

FHS Risk Scores Used in Clinical Practice Today



> *Stroke*. 1991 Mar;22(3):312-8. doi: 10.1161/01.str.22.3.312.

Probability of stroke: a risk profile from the Framingham Study

P A Wolf ¹, R B D'Agostino, A J Belanger, W B Kannel

Affiliations + expand

PMID: 2003301 DOI: 10.1161/01.str.22.3.312

> *Circulation*. 1998 May 12;97(18):1837-47. doi: 10.1161/01.cir.97.18.1837.

Prediction of coronary heart disease using risk factor categories

P W Wilson ¹, R B D'Agostino, D Levy, A M Belanger, H Silbershatz, W B Kannel

Affiliations + expand

PMID: 9603539 DOI: 10.1161/01.cir.97.18.1837



1991

1998

2009

> *Lancet*. 2009 Feb 28;373(9665):739-45. doi: 10.1016/S0140-6736(09)60443-8.

Development of a risk score for atrial fibrillation (Framingham Heart Study): a community-based cohort study

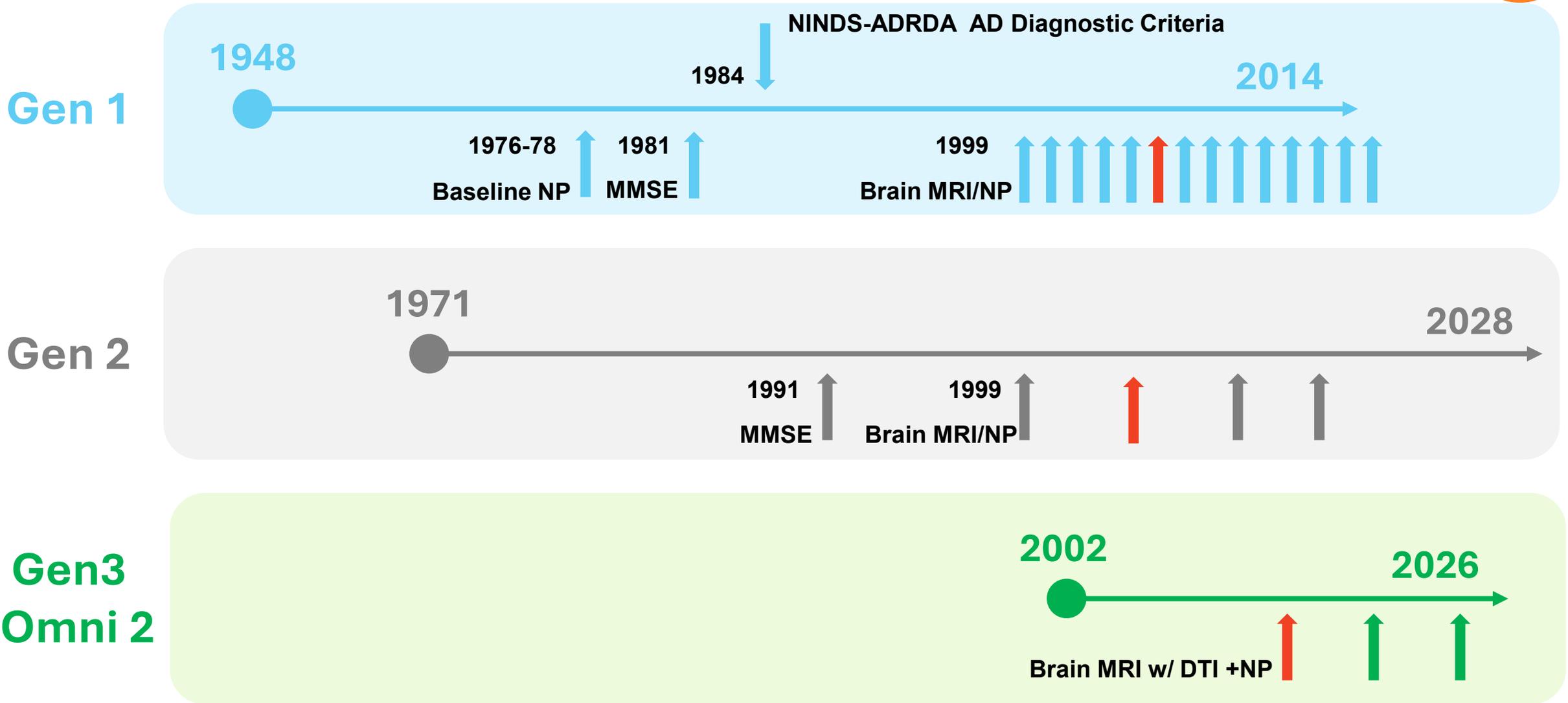
Renate B Schnabel ¹, Lisa M Sullivan, Daniel Levy, Michael J Pencina, Joseph M Massaro, Ralph B D'Agostino Sr, Christopher Newton-Cheh, Jennifer F Yamamoto, Jared W Magnani, Thomas M Tadros, William B Kannel, Thomas J Wang, Patrick T Ellinor, Philip A Wolf, Ramachandran S Vasan, Emelia J Benjamin

Affiliations + expand

PMID: 19249635 PMCID: PMC2764235 DOI: 10.1016/S0140-6736(09)60443-8



FHS Brain Aging Program (FHS-BAP)



↑ Start of digital data collection

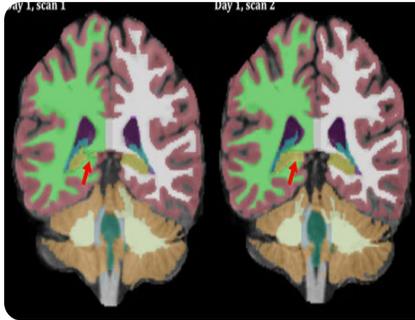
FHS-Brain Aging Program Clinical Data



Cognitive Assessment



Neurological Exam

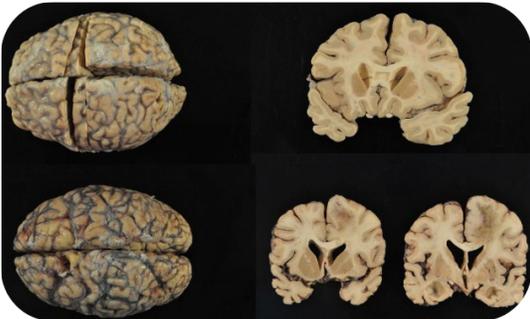


Brain MRI

- LEGEND**
- Right cerebral WM
 - Left cerebral WM
 - Lateral ventricles
 - Hippocampus
 - Choroid plexus
 - Cerebral cortex
 - Cerebellum WM
 - Cerebellum cortex
 - Fourth ventricle
 - WM hypointensities



Dementia Diagnosis



Post-Mortem Brain Tissue

FHS Digital Data



Digital Voice



Digital Voice Transcripts



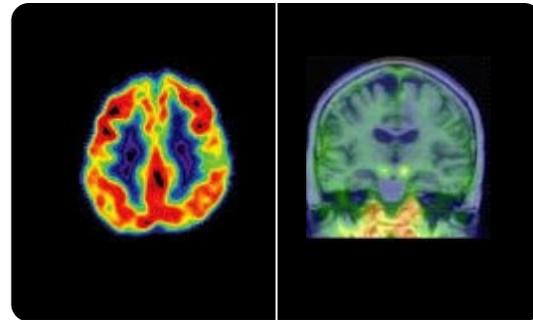
Digital Clock



Digital Pen



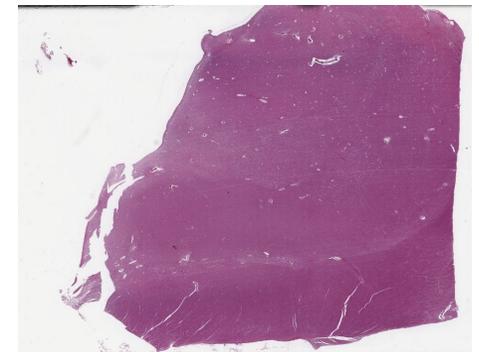
Smartphone Tasks



PET Amyloid & Tau



Brain & Cardiac MRIs



Digital Neuropathology Slides

FHS Digital Exposome



Technology



...Coming Soon

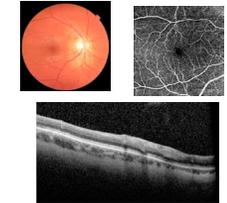
Measures



Steps



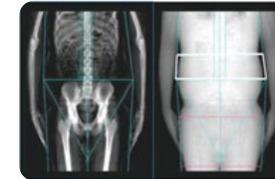
Sleep



Optical vascular metrics



Blood Pressure



Bone Mineral Density



Heart Rate

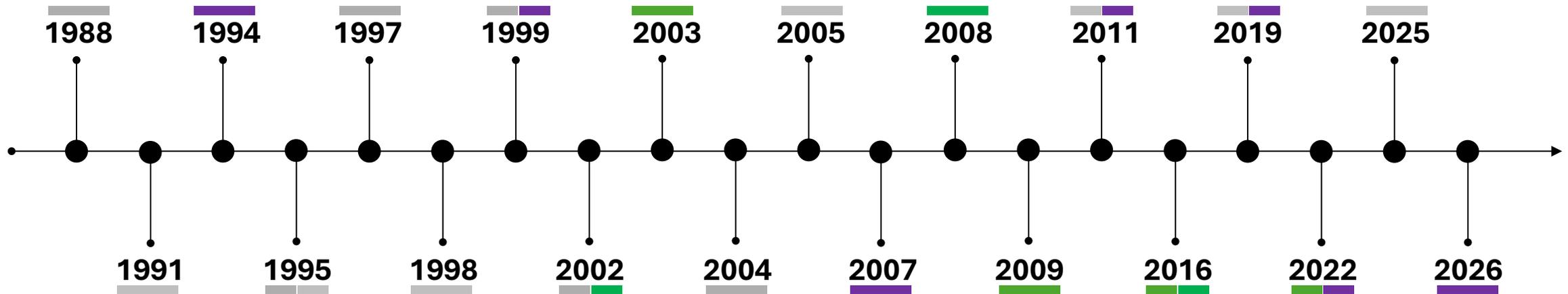


Physical Activity

Longitudinal Blood-Digital Resource

Cohort: Gen 1 Gen 2 Gen 3 Omni 1 Omni 2

Blood Samples for AD biomarkers (n~22,263 + 5,970 + 6,548)



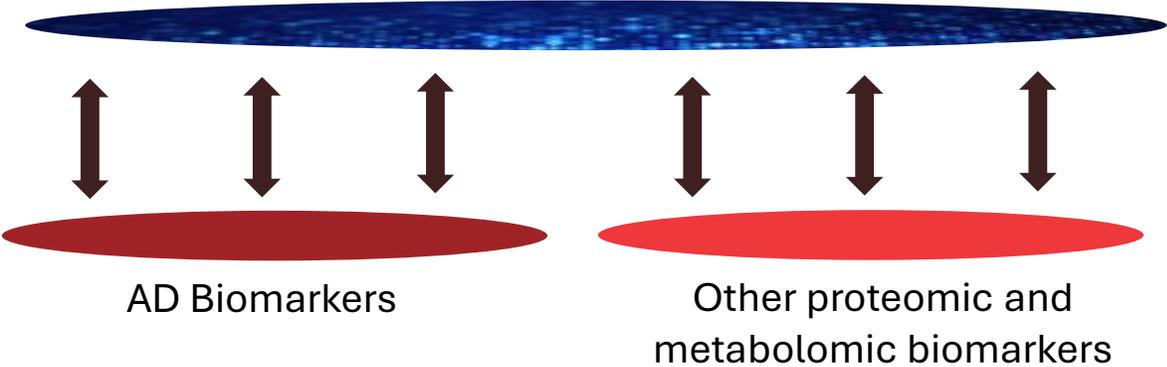
Digital data (audio, pen, smartphone, wearables; n= 18,000+)



FHS AD Precision Medicine at Scale



Digital data



Gen 1

Gen 2

Omni Gen 1

Omni Gen 2

Gen 3

NOS

Starting a FHS Today

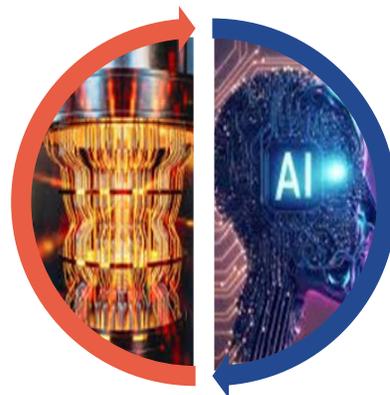
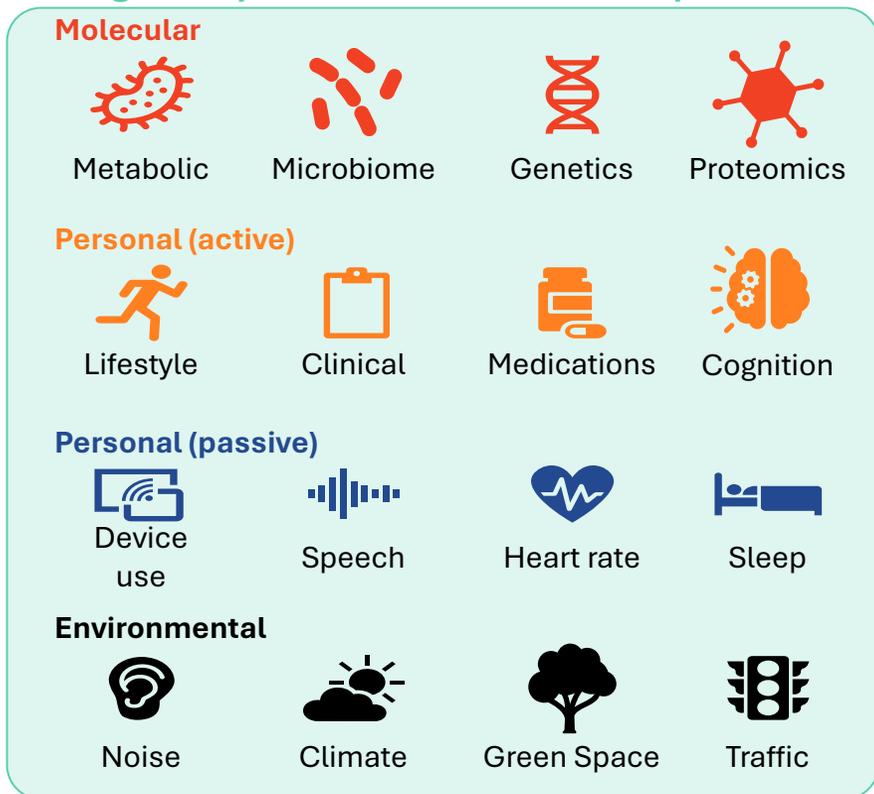
Embracing the Complexity of the Brain



Collection Methods



Digital Representation of Human Exposome



Drug development



Clinical trials



Predictive algorithms



Preventative interventions



Diagnostic models



Digital biomarkers

Entire pipeline to be conducted within a QMS



8+ Billion Population Scale Gap

1 Inaccessible, expensive, invasive, biased research methods

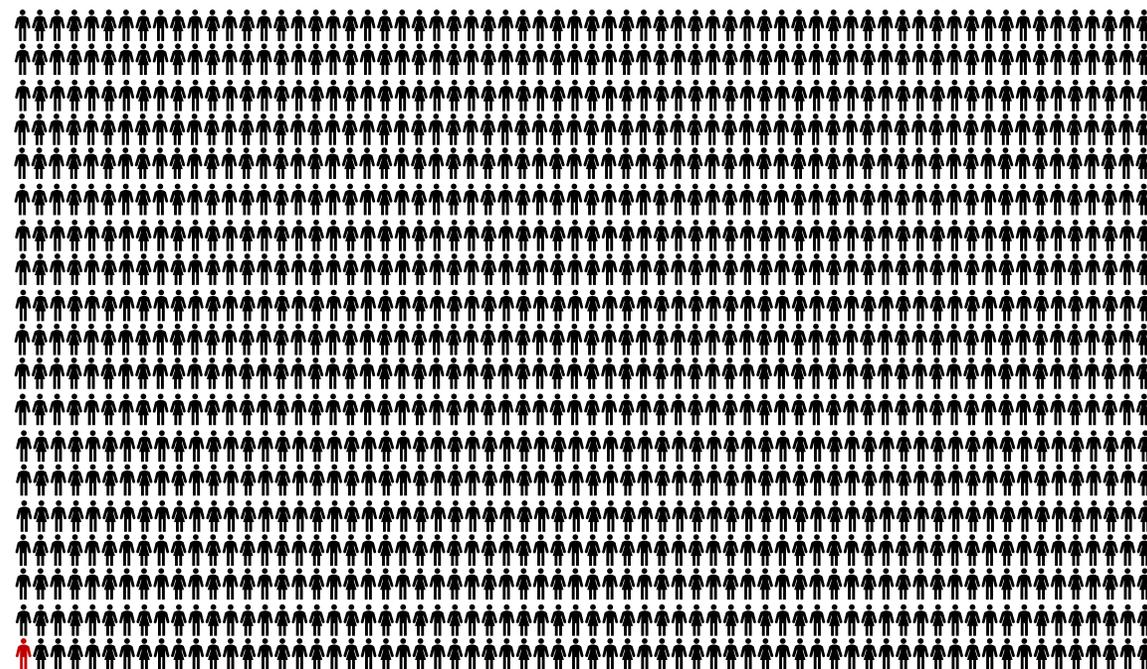
- Inaccessible research methods
 - Required on site imaging devices
 - Limited availability
 - High out-of-pocket costs
- Reliance on biased tests
 - Created largely in western countries
 - Require examiner interface

2 Homogenous Participants

- Participants with high socio-economic standing
 - Primarily western cultures
 - Non-diverse samples
 - Large portions of the globe missing

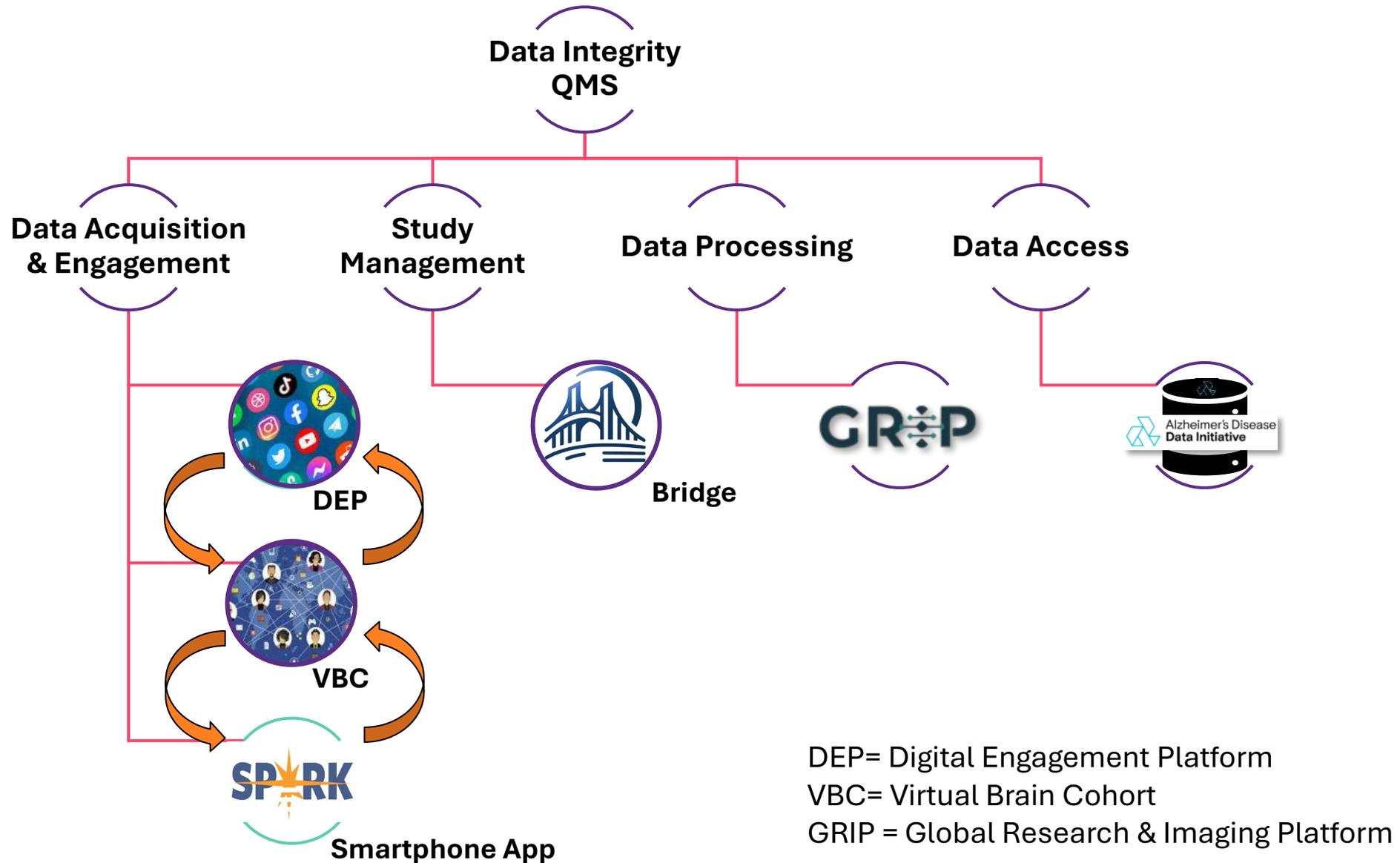
3 Limited Interoperability

- Research infrastructure designed, built, and conducted in silo



Studies are performed in the hundreds and thousands, not representing the global population and inhibiting discovery

End-to-End Solution



Quality Management System (QMS)

To increase the utility of data collected from observational studies to aid in device or drug development

Currently undefined with regulators for observational and academic studies

Open-source materials to be shared with the greater scientific community

QMS to cover:



General quality practices



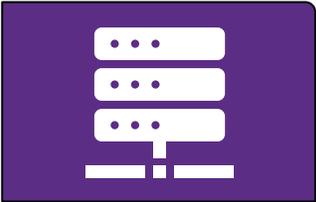
Human subject studies



Digital health technologies



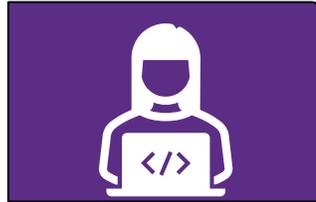
Data collection, processing, and analysis



System lifecycle management



Security



Software development

Front End for Data Acquisition and Engagement



Digital Engagement Platform

- “Facebook for Brain Health”
 - Builds community
 - Sustains interest



Virtual Cohort

- “Take All Comers”
 - Family, Friends, Word of Mouth
 - Converts Screen-fail to screen-enroll
- Prolong involvement
 - Changes enroll-end to enroll-continue



Smartphone App

- Multimodal self-administered data collection
 - Cognitive tasks, voice recording, and surveys
- Centralized Coordinating Center
 - Connecting IoT devices

Backend Infrastructure Partners



Bridge Platform

Study Management



Data Processing



**Alzheimer's Disease
Data Initiative**

**Federated Data
Sharing Appliance
(FDSA)**

**AD
Workbench**

Data Access

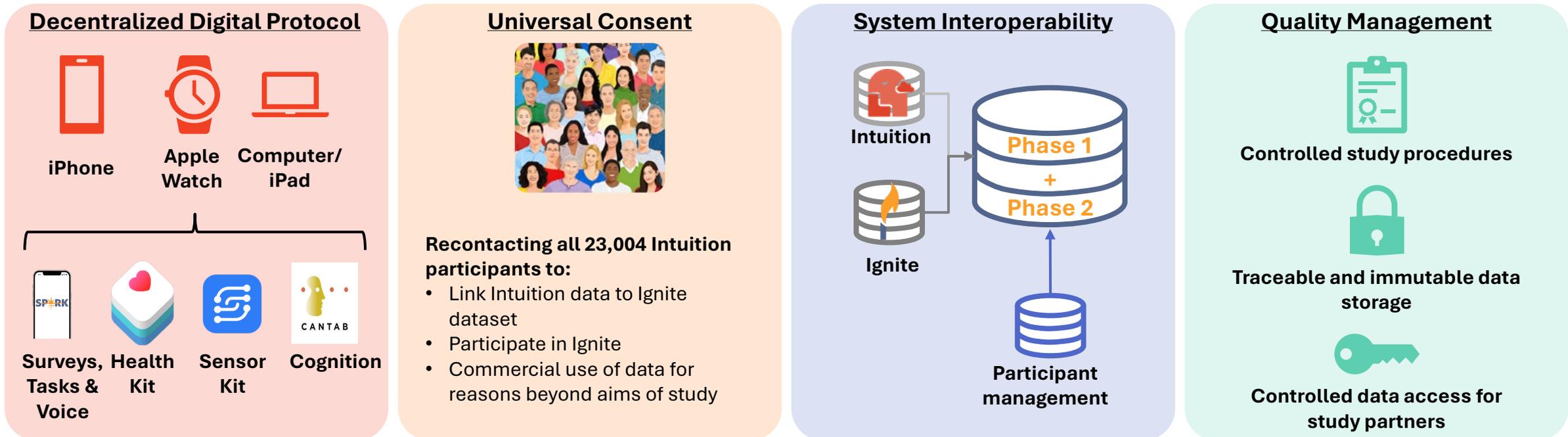
A Place to Start: Ignite Study



The Ignite study is resurrecting the Apple-Biogen Intuition study's collection of multi-modal behavioral data from continuous normal usage of an iPhone and Apple Watch for 6-18 months (Phase 1).

The Ignite study (Phase 2) aims to re-enroll the Intuition cohort to the extent possible and replicate much of the Intuition data collection methods.

The Ignite Study addresses:



Building a Longitudinal Data Resource

Sep 2021



Sep 2023

2027



2032

Intuition Study (Phase 1 completed)

- Passive data streams
- Cognitive assessments
- Voice tasks
- Surveys
- 23,004 participants



Participant re-consent for
longitudinal data
connection

Ignite Study*

- Passive data streams
- Cognitive assessments
- Voice tasks
- Surveys
- Recontact all consenting 23,004 participants



Ensuring Reproducibility

Quality Management System

The **FDA** requires a Quality Management System (**QMS**) for the development of **regulated products**. A QMS is a structured framework of policies, procedures, and resources that organizations use to ensure their **products or services** consistently meet **participant** and **regulatory requirements** while **continuously improving** their operations.

A QMS establishes **traceability** and **reproducibility** of any product or service delivered by an organization. The **Ignite** study **will enhance** the value of **observational studies** by incorporating:



Major QMS Components



Controlled work instructions and records for all processes and decisions



Immutable and traceable data; Federated data access for partners



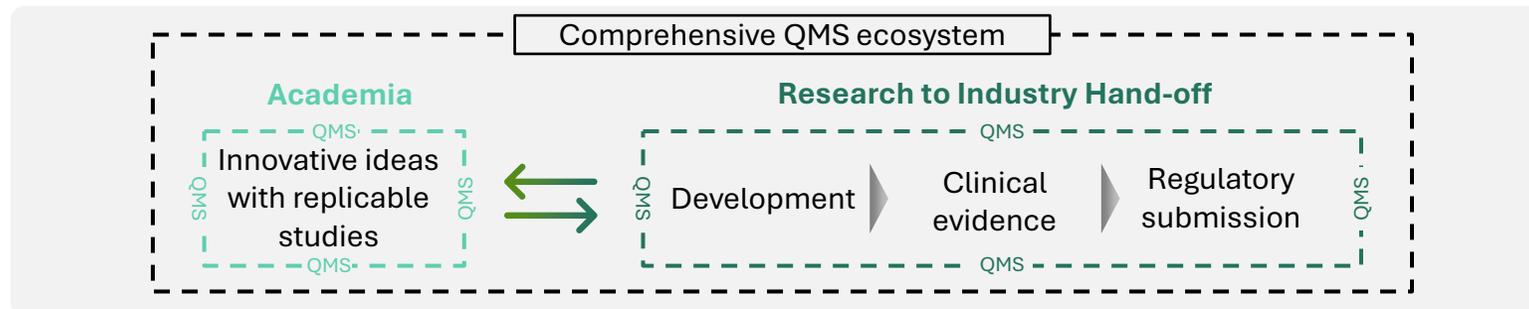
Predefined corrective and preventative action procedures



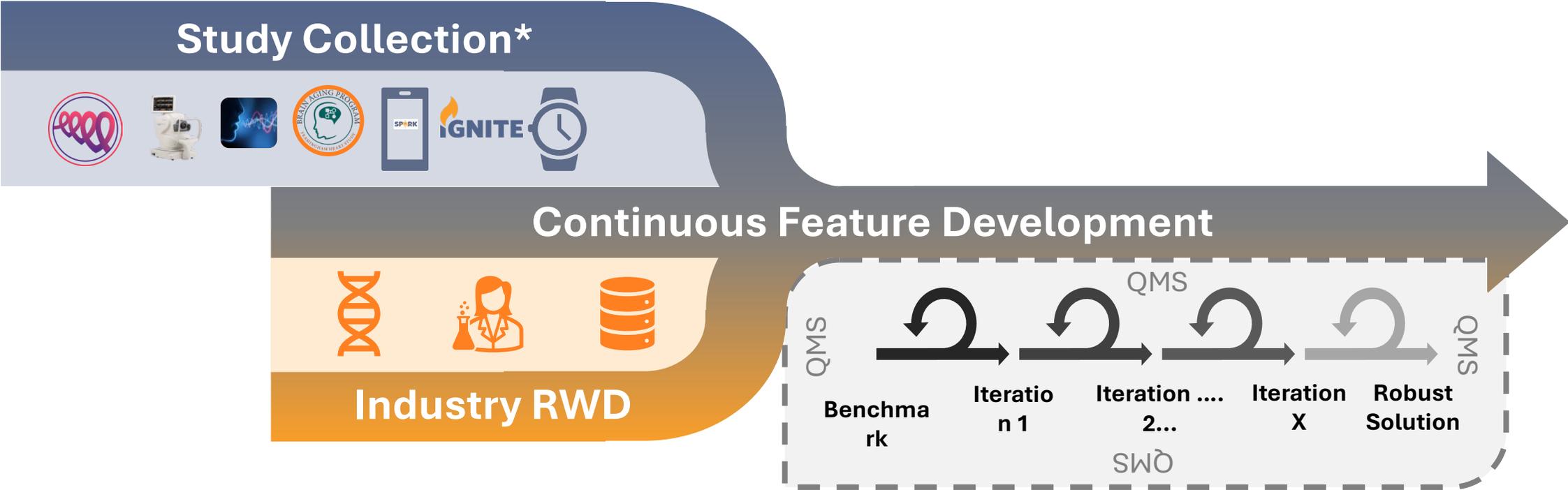
Participant compliance monitoring and continuous improvement

Product Development

Conducting NIH funded studies with a QMS will lead to findings that can be used as body of evidence for regulatory approval, accelerating the discovery to translation timelines.

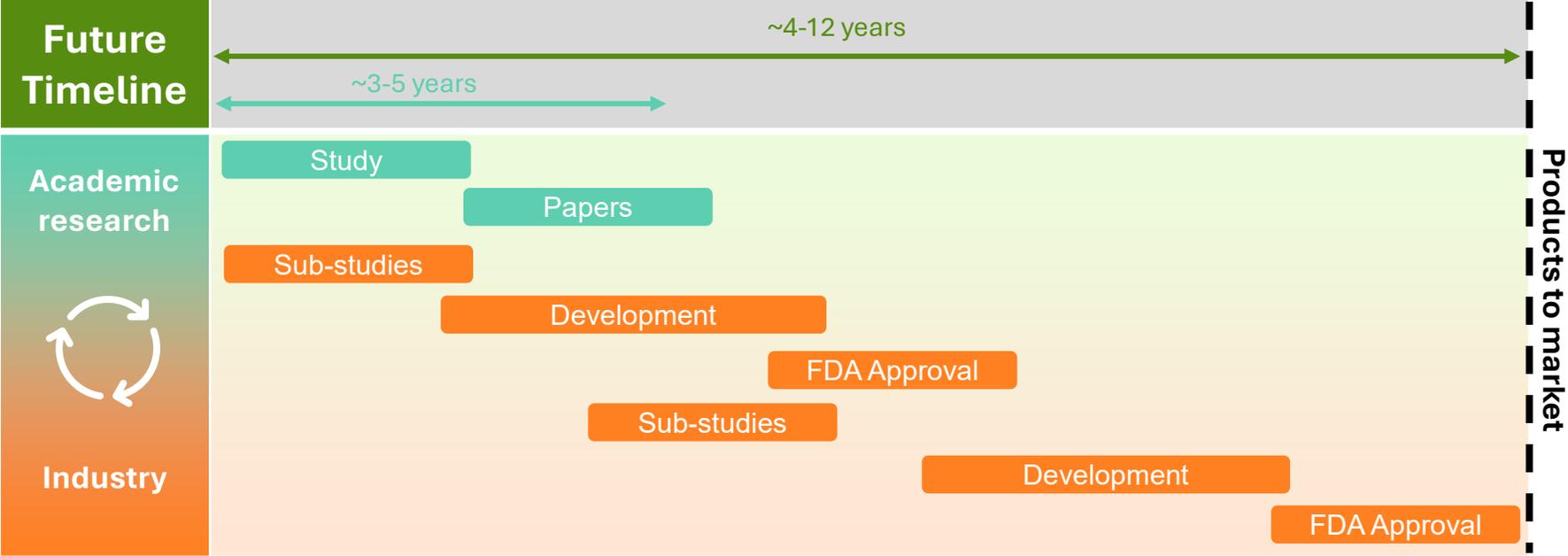
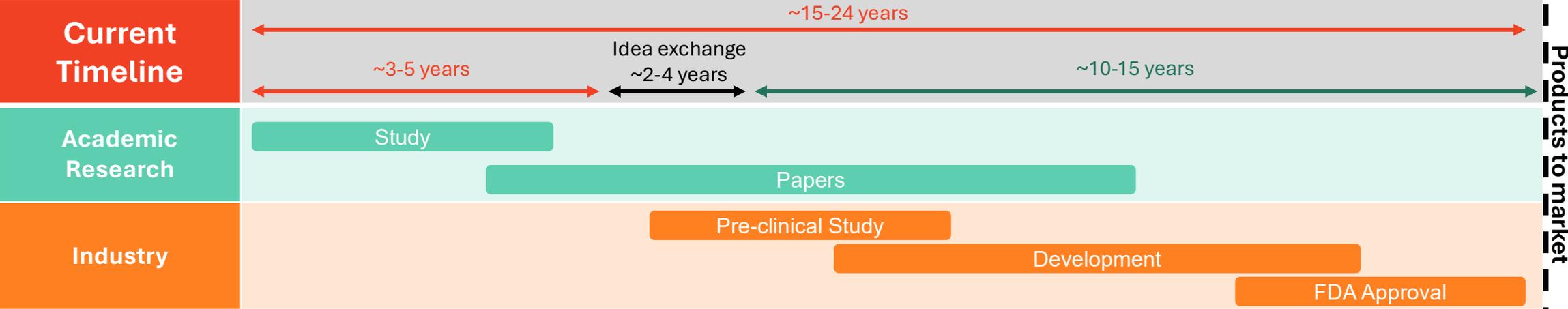


Enabling Trusted AI Solutions



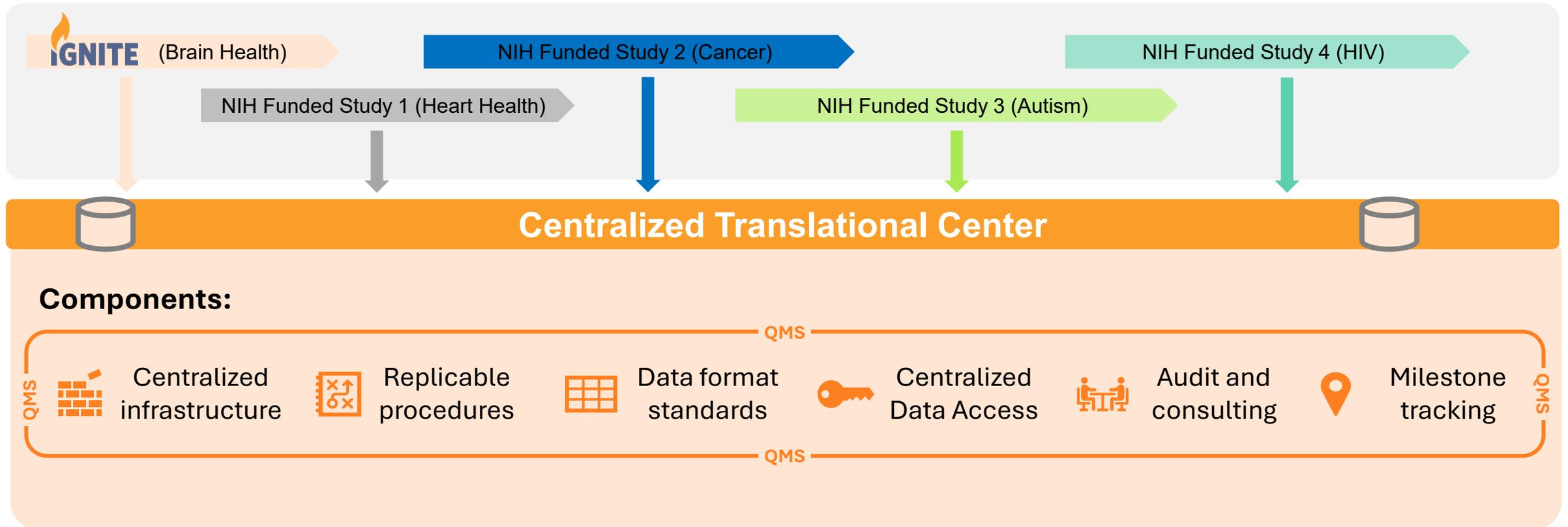
*Industry grade QMS protocol

Compressing Innovation Timelines



Translational Center Efficiencies Beyond Brain Health

A replicable minimum viable protocol can support an array of decentralized studies utilizing billions of IoT devices sharing common procedures, infrastructure, and study app.



“Igniting” a New Approach

Ignite

- 1 Proof of concept for large high frequency of collection, digital, remote (decentralized) studies
- 2 Testing ideal frequency and criteria to trigger continuous collection to reduce amount of collected data and participant/device burden
- 3 Develop regulatory compliant procedures for digital studies that can be replicated
- 4 Generic and repeatable framework for large-scale data collection
- 5 Testing white labeled study app for mass adoption
- 6 Testing participant engagement strategies
- 7 Necessary first step in digital biomarker development

Future NIH Studies



Longitudinal digital data at population scale



Trusted RWD for the generation of RWE*



Cross functional analysis of risk factors across diseases



Enable Industry partnerships

*real world evidence

Digital is the New Blood



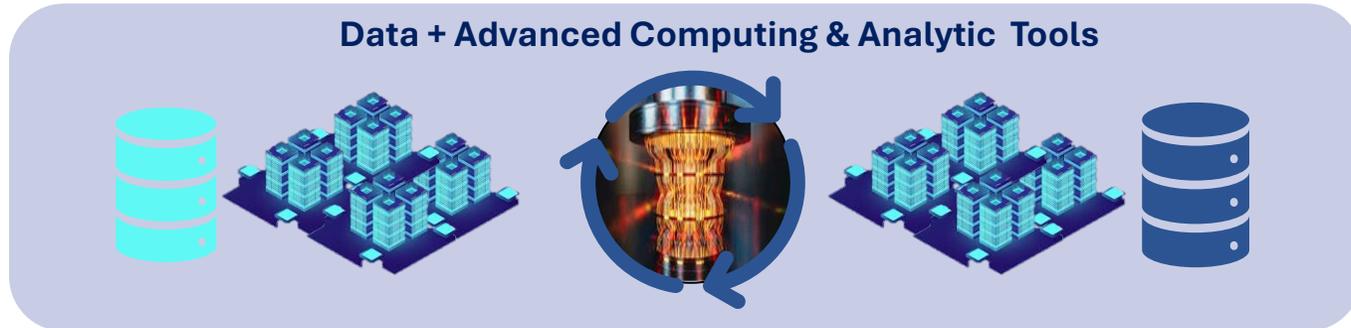
Population Digital Data



Clinical Data



Real World Data



Getting from Here

..... to There



Voice (acoustic, linguistic, paralinguistic)



Physical activity (step count, heart rate, intensity)



Sleep (duration, apnea, oxygen saturation)



Cognition (memory, executive function, attention)



Retinal Imaging (macular volume, thickness)





Thank You!