RARE PATIENT ADVOCACY SYMPOSIUM

A partnership of
Penn Medicine Orphan Disease Center
and Global Genes

Global Genes®
Allies in Rare Disease

the orphan disease center

Sheraton University City Hotel

Saturday, May 19, 2018

7:00 am – 4:30 pm

Why and How Should We Expand the Data in Our Registry

Ben Shaberman

Senior Director of Communications

Foundation Fighting Blindness

Mary Drake

CEO

Innoven

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FOUNDATION FIGHTING BLINDNESS

My Retina Tracker
A Patient-Driven Registry for Inherited Retinal Degenerations

Presenter: Ben Shaberman, Senior Director of Science Communications
Contact: Brian Mansfield, PhD, Deputy Chief Research Officer
bmansfield@blindness.org

Mission:
Provide preventions, treatments, and cures for people affected by retinitis pigmentosa, macular degeneration, Usher syndrome, and the entire spectrum of retinal degenerative diseases

MY RETINA TRACKER™

Track Your Vision. **Drive the Research.**

Home | Understanding Your Participation FAQs | Login | Help | For Clinicians

Contact Us | Who We Are

Build a Retinal Health Profile

and

Help Accelerate the Advance

of

Sight Saving Research

Register Now

Login

Username

bmansfield

Password

••••••••••

Login

Forgot login?

My Retina Tracker™

My Retina Tracker is a free on-line registry provided by the Foundation Fighting Blindness as part of its mission to drive the research that will provide preventions, treatments and cures for people affected by retinitis pigmentosa, macular degeneration, Usher syndrome and the entire spectrum of inherited retinal degenerative diseases.

Orphan Inherited Retina Diseases (IRD)

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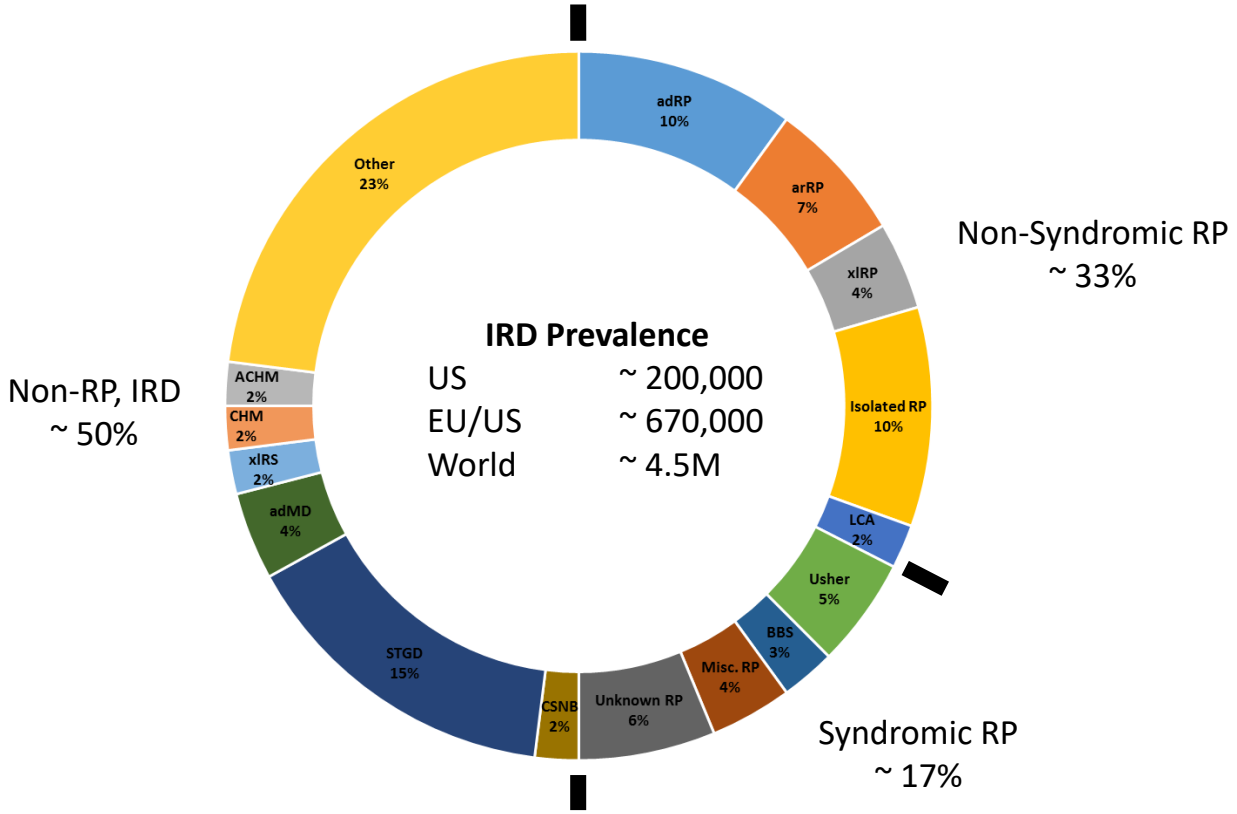

The IRD consist of many orphan diseases, each predominantly monogenetic. Over 260 different genes are implicated

Past and Present Registries:

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1992 – 2014

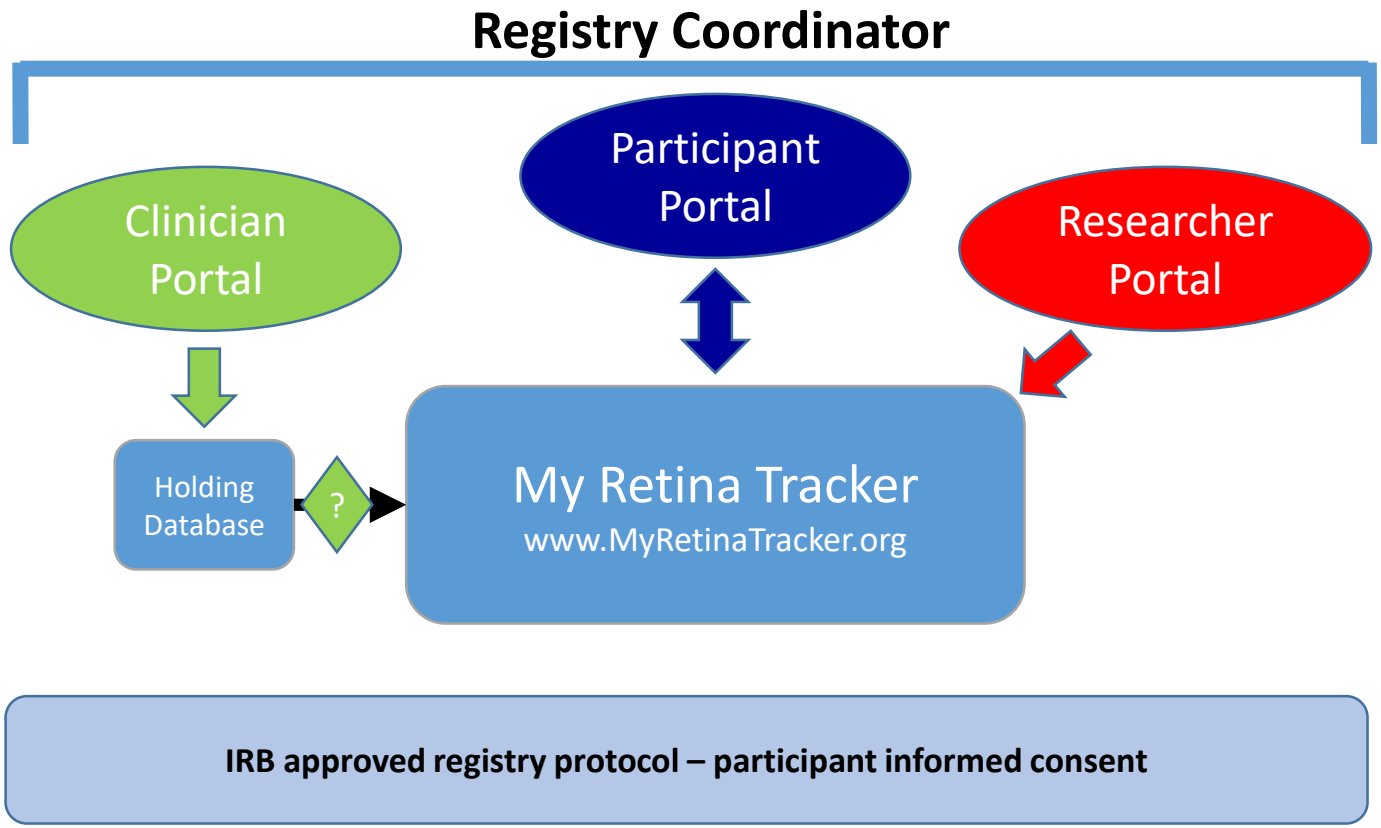
- Paper-based registry – lack of awareness
- Contact information
- Little – no disease information
- No informed consent
- No formal privacy policy
- Member has no direct control of data
- No longitudinal engagement
- No member benefits
- Not publicly
- Data expires – address, phone, email, deaths
- Size – ~11,000 names

2014 – Present **My Retina Tracker®**

- On-line registry – brand recognition
- Professional software and security
- Accessibility software reader compatibility
- Patient has direct control of own data
- IRB-approved protocols
- Informed consent
- Strict privacy policies – patient in control of data sharing
- Subjective patient perspective of disease
- Objective clinical data of disease
- Genetic information
- Longitudinal engagement
- De-identified data publicly accessible

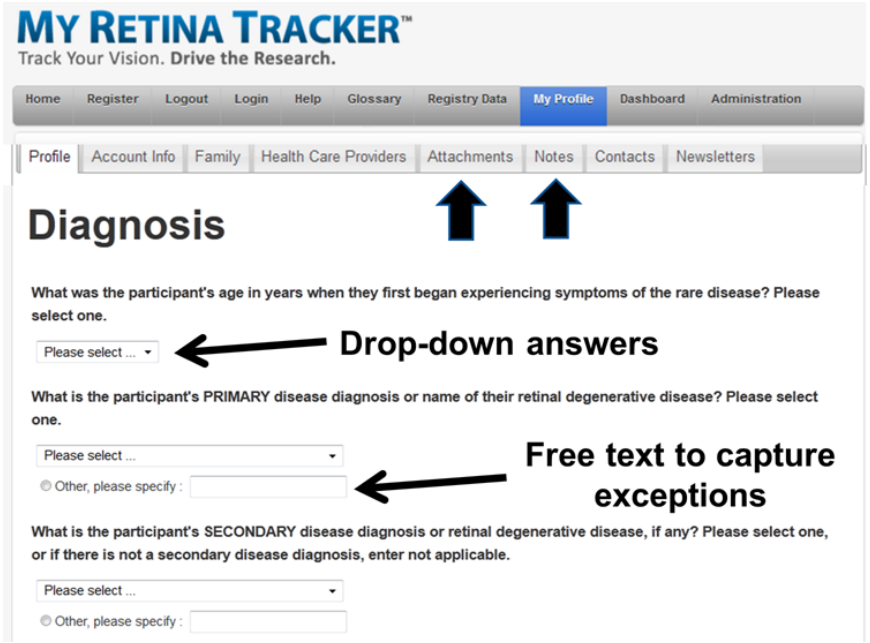
Registry Structure

MY RETINA TRACKER®
Track Your Vision. Drive the Research.



Member Survey Questions

- Diagnosis
- Genetic Testing – Genetic Profile
- Family History
- General Health
- Other Related Conditions
- Vision Evaluation
  - Objective
  - Subjective
- Driving
- Medications
- Research Study Participation
- Clinical Trial Participation
- Demographics



Easy data entry, controlled vocabulary,
compatible with assistive reading technologies

Clinician Entered Data

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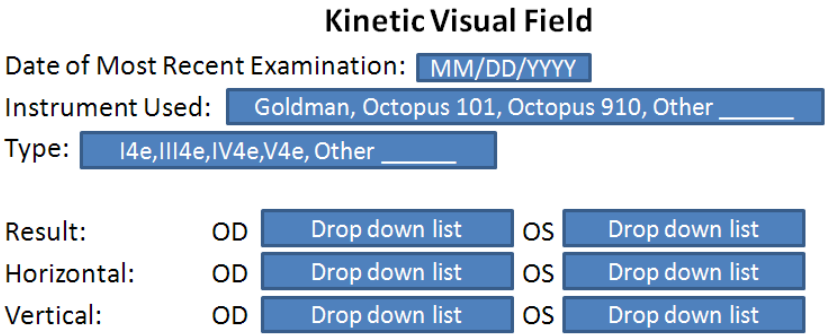
- Physician identification
- Clinical diagnosis and related conditions (Req'd)
- Visual acuity (Req'd)
- Genetic diagnosis
- Static visual field
- Kinetic visual field
- ERG data
- mfERG
- Light-dark adaptation
- Biosamples
- Review



No Username, no password, menu-driven, drop down data entry, controlled vocabulary

Connecting Participants and Researchers

MY RETINA TRACKER®
Track Your Vision. Drive the Research.

- Research portal provides access to de-identified data
- Only Registry staff can connect ID to the member contact information
- To engage members researchers must submit an application to the Foundation
- Foundation reviews application with advisors
- If approved, Registry staff decode and contact participant
- It is up to the member to decide if they are interested
- The Registry never shares any member identifying information

Patient controls privacy, chooses if to engage

My Retina Tracker Genetic Testing Study

- Membership benefit of My Retina Tracker
- IRB approved research study – clinician ordered
- Free genetic testing and genetic counseling
  - No insurance billing
  - No out of pocket expenses
- Clinician enters diagnosis and BCVA
- Two CLIA-certified, CAP-accredited labs contracted
  - >260 IRD-specific gene panel
  - May include CNV (deletion/duplication)
- Genetic counseling required
  - Local counselor
  - InformedDNA
- Genetic results entered into member's My Retina Tracker profile

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Track Your Vision. Drive the Research.

Blueprint Genetics

OCULAR GENOMICS INSTITUTE

InformedDNA
Genetics, Decoded.

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MY RETINA TRACKER

Track Your Vision. **Drive the Research.**

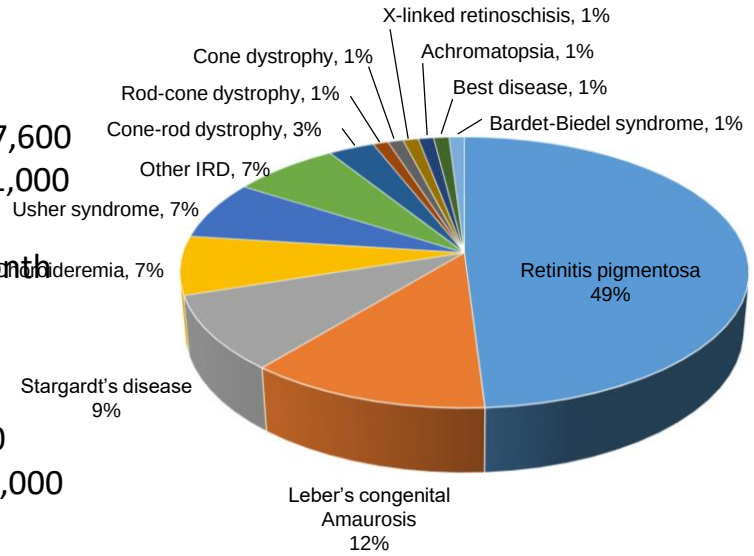
FOUNDATION FIGHTING BLINDNESS
CLINICAL RESEARCH INSTITUTE

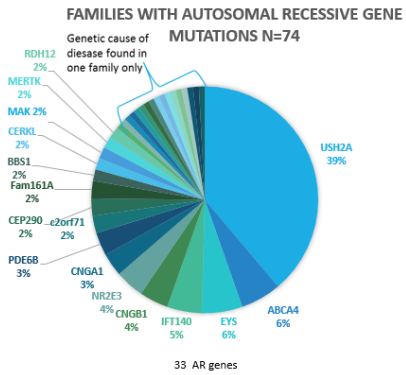
My Retina Tracker Enrolment

Membership	>18,840
Profiles	> 7,600
Profiles ex-US	1,000
Genetic data	30%
Growth	~300/month

Genetic Testing Study Participation

Enrolment to date	1,200
Reports returned	>1,000
Clinicians participating	>125
Sites participating	>85





International patient registry provides insights into prevalence, genetic diversity and progression of diseases

Uses of My Retina Tracker:

> 98 enquiries

- Understanding frequency of specific diseases at the gene and mutation level
- What target is a good “low hanging fruit?” – commercial target potential
- Guidance:
  - Developing patient reported outcomes
  - Designing natural history studies – longitudinal changes
- An efficient single resource to identify participants for:
  - Enrollment in natural history studies
  - Enrollment in clinical trials
  - Focus groups
  - Clinicians with specific groups of patients

Academic Researchers

Pharma Biotech

Contract Research Organizations

Challenges to Consider:

Labor

Cost

Critical Size

Informed Consent

Clinical Data

Engagement

- **Labor intensive**
  - Professional registry company for software, hosting and electronic security
  - Medical and Scientific advisory groups to design and improve surveys
  - Full time HIPAA compliant registry coordinator – IRB, curation, online and phone support
  - Full time registry assistant for studies and coordinating access enquiries
  - Communications team to maintain member engagement once they join
- **More expensive than it seems initially – substantial commitment**
- **Achieving a representative member population for an orphan indication is difficult**
  - Organic growth through chapter awareness not sufficient
  - If target is 25% of affected people - require proactive way to find affected people
- **Special needs for special groups – complete compatibility for assistive reading technology**
  - Exhaustive testing before launch to avoid frustration – impact acceptance
- **Informed consent slows / loses people during registration on-line**
  - Clinical coordinators help during clinical visits – cost
  - Phone-based support to assist registration over the phone
- **Collecting clinical data is difficult**
  - Provide incentives to clinicians to expend the extra effort to enter data
  - Provide added value studies – such as a genetic testing study
  - Provide alternatives – registry coordinator will enter clinical data if sent clinical report
- **Reward members to keep them engaged**
  - Pro-active communications package – newsletters, updates, richer content
  - Earlier access to breaking news, especially of clinical trials

Why and How Should We Expand the Data in Our Registry

Mary Dixon Drake

President & CEO

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How Should We Expand the Data in Our Registry?

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Global Genes®
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RARE PATIENT ADVOCACY SYMPOSIUM

THINK…….
Natural History Data

A Registry is not a Natural History dataset
But maybe it could be……

Outline

- What is Natural History (NH) Data?
- How can NH data be used in clinical trial setting?
  - Designing Trials
  - Trial Enrichment
  - Expediting Trial Execution
- How can NH data help address other unmet needs?
  - Diagnostic
  - Prognostic
  - Clinical Decision Support
- Example

I. Natural History data vs. Registry Data

What is NH data?

In medicine, a **natural history** study is a study that follows a group of people over time who have, or are at risk of developing, a specific medical condition or disease.

Example NH Dataset

- Demographics (Gender, Ethnicity, Race, DOB)
- Date of Diagnosis
- Relevant Medical History
- Family History
- Genetic Information
- Age of onset of critical symptom (where applicable)
- Disease Severity (if known)
- Longitudinal Data (solicited on timed cycle)
  - Lab data (efficacy or safety)
  - Vitals (where relevant to outcomes)
  - MRI or other imaging (where relevant to outcomes)
  - Symptoms (cognitive, physical, etc.)
  - Concurrent conditions/Comorbidities
  - Functional assessment (specific to indication)
  - Global assessment
  - Date of critical event(s)
  - Concurrent medications

Navigating Complex Issues

Privacy and Security

Consent and Trust

Preventing Misinterpretation or Misleading Secondary Analyses

“Just because you have massive amounts of data does not mean you have massive amounts of information.” - *Joe Blitzstein, Professor of the Practice in Statistics at Harvard University*

Consent and Trust

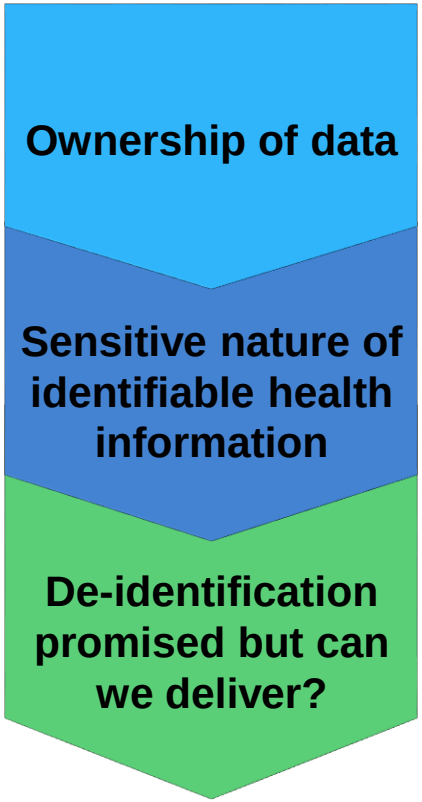
How do we provide patients with information and the right to consent to share their data while ensuring risks are clearly understood?

Establish Governance

Ensure there is a clear plan for how data will be used and a governance committee to oversee

Promises of De-identification

Even anonymized data can often be re-identified and attributed to specific Individuals. [2,3]



PHI

Patients may over or underestimate confidentiality protections[1]

1. Sankar et al., Patient Perspectives on Medical Confidentiality, JGIM (18) August 2003
2. Gymrek, et al., Identifying Personal Genomes by Surname Inference Science 2013; 339:321-4
3. Mailin et al, Technical and Policy Approaches to Balancing Patient Privacy and Data Sharing in Clinical and Translational Research. J Investig Med 2010:58:11-8

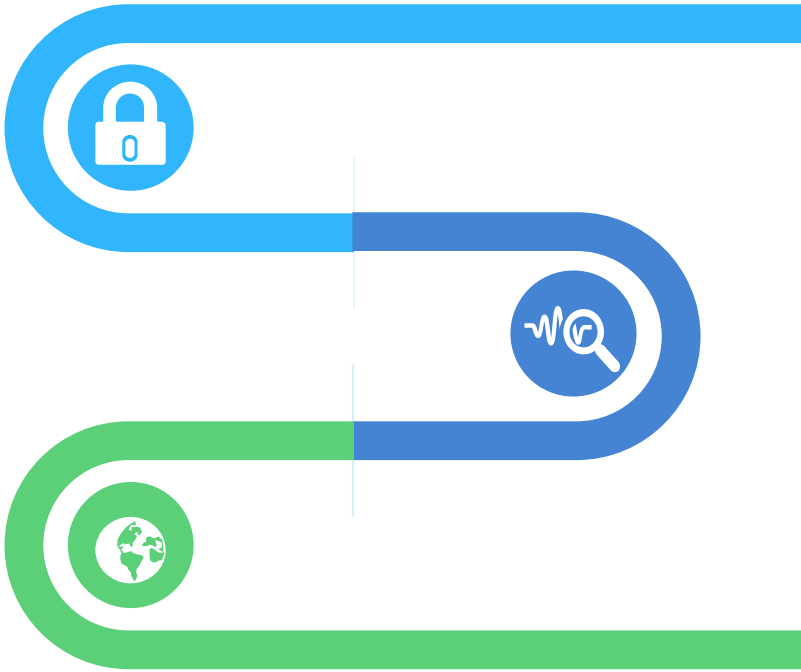
Database Security and Compliance

Privacy, Confidentiality, Process Integrity, Availability and Security

HITRUST
- Security Framework specific for ePHI and PHI data

SOC 2 auditing
- Access controls
- Two factor authentication
- Encryption
- Networking/applications firewalls
- Quality Assurance (QA)
- Performance monitoring
- Disaster recovery
- Security incident handling

General Data Protection Regulations (GDPR) – EU Law
- New enforcement May 25, 2018



Define Data Needed to Address Unmet Needs

What's wrong with me?

What's going to happen to me?

Which treatment?
When is the right time?
What dose?

Will the medication work for me?
Will I have side effects?

E-patient:

- Empowered
- Engaged
- Equipped
- Enabled

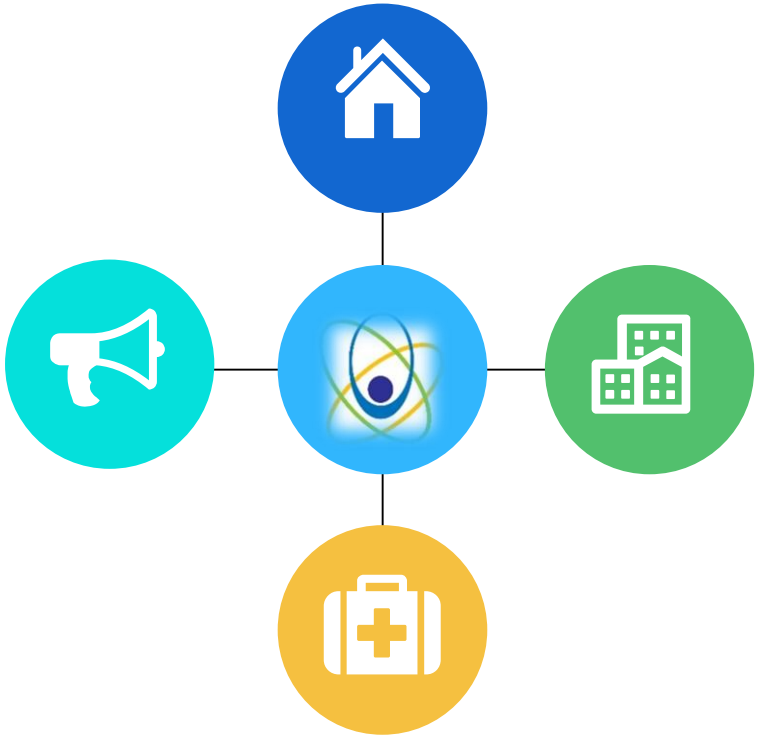
Explore physical, emotional & financial journey of patient through Social Listening, Ethnographic Research, and Market Research

Involve Critical Stakeholders

Designed Around Data Needed to Address Unmet Needs

Patients & Families

Advocacy Relationship & Influence



Industry/FDA Researchers

Health Care Providers

II. Using NH Data to Support Industry /Researchers

Designing Trials: Questions During Drug Development

- Who to enroll in studies?
- What is the clinical benefit objective?
- How to determine what doses to test?
- How to determine what dosing schedule to test?
- What intermediate assessments are useful?
  - Biomarkers? Clinical manifestation?
- How is the endpoint measured?
  - Develop a new measurement method?
- What is the duration of the study?
- How large is the study?

Poor choices due to inadequate knowledge can lead to program failure

Slide presented by M. Walton PMWC 2017

Trial Enrichment

- FDA biomarker qualification program
- Select patient subset to study (e.g., by phenotype or stage of disease)

Examples:

- Predictive biomarker to enrich for enrollment of a sub group of asthma patients who are more likely to respond to a novel therapeutic in Phase 2/3 clinical trials.
- Predictive biomarker to enrich trial with patients more likely to progress in period.

Learn more:
https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/BiomarkerQualificationProgram/ucm535922.htm#How_are_biomarkers_qualified_for_drug_development_

Approved Trial Enrichment Biomarkers

Mycoses Study Group	Serum/bronchoalveolar lavage fluid biomarker: Galactomannan	11/14/2015 Patient selection biomarker for enrollment in Invasive Aspergillosis (IA) clinical trials
Chronic Obstructive Pulmonary Disease (COPD) Biomarker Qualification Consortium (CBQC)	Plasma biomarker: Fibrinogen	9/14/2016 Prognostic biomarker for enrichment of clinical trials in Chronic Obstruction Pulmonary Disease (COPD)
Polycystic Kidney Disease Outcomes Consortium	Imaging Biomarker: Total Kidney Volume (TKV)	9/15/2016 Prognostic biomarker for enrichment of clinical trials in Autosomal Dominant Polycystic Kidney Disease

Expediting Trial Execution

- Historical Control
  - Diminish burden of placebo arm
    - **Uncommon to be suitable but FDA workshop this week gives hope for further evolution**
- Support Enrollment

III. Example

Consent

- Re-consent & ethics committee review
- Modified ICF expanded R&D objectives
  - **Data combined with other data from other studies/repositories**
  - Possibility of **new discovery**/development of additional solutions that may lead to **improvements in clinical care**
- Option to “Opt out” of data sharing
  - Not a requirement of participation (e.g., no undue coercion)
  - Risks associated with sharing data
- Withdrawal of consent at any time
- Specimen sample destruction if consent withdrawn

Disclaimer: For discussion purposes; does not represent language directly used in any informed consent

Clinical Decision Support Software

Imaging Analysis and Patient Following

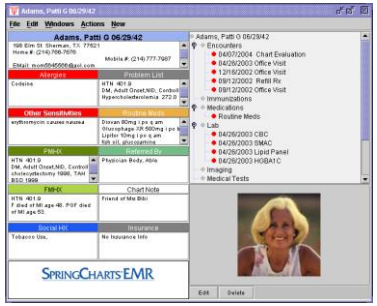
Patient data aggregation

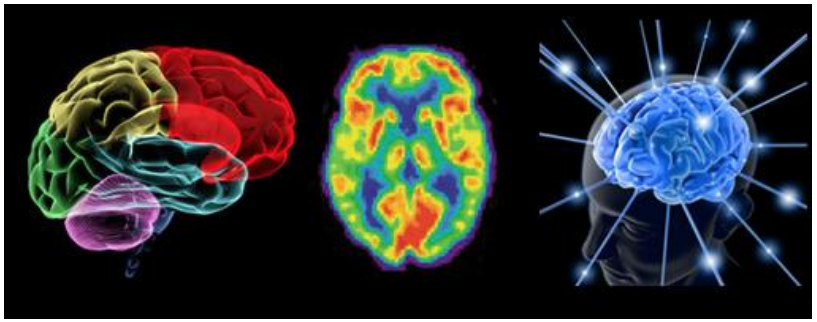
Automatic determination of organ characteristics

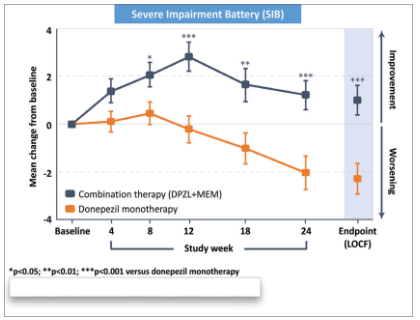
Web and mobile based

3-D rendition of organ

Patient specific, project progression, monitor change







- ✓ Designed and developed in compliance with device development standards (e.g., design control/QMS) and privacy and security requirements.
- ✓ Critical to have consent to use the data to develop new tools for disease management

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Reference Data
Secondary Use

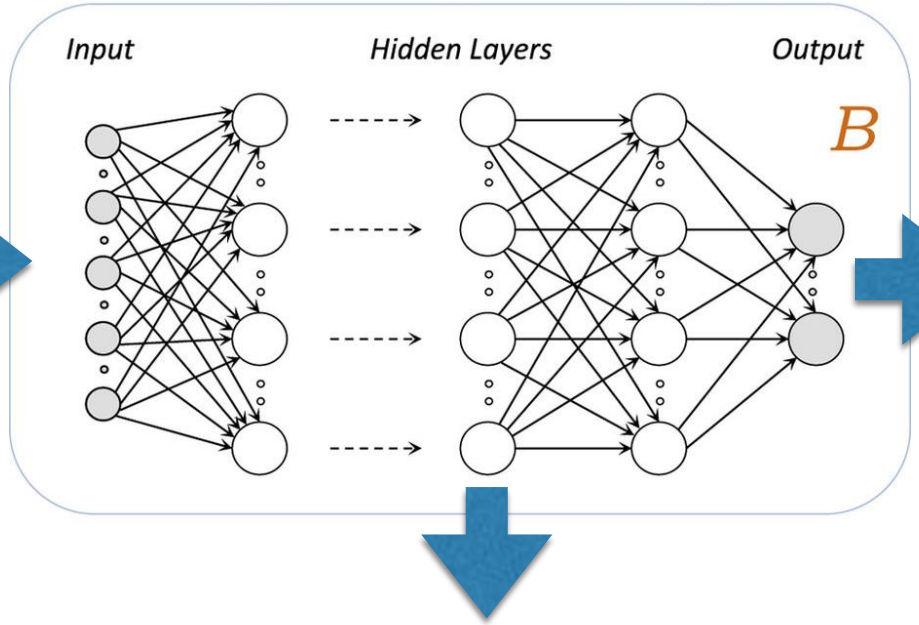
Clinical trial/
NH data

Imaging data

Clinician-facing

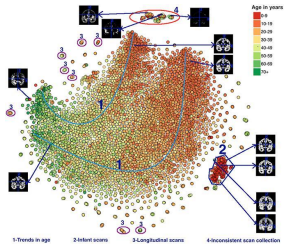
Patient-facing
(pending)

Panta SR et al. A Tool for Interactive Data Visualization: Application to Over 10000 Brain Imaging and Phantom MRI Data Sets. Frontiers in Neuroinformatics, 10(9), 2016.



Outcome (can be multi-factorial)

Deep representations



Similarity spaces as a function of outcome

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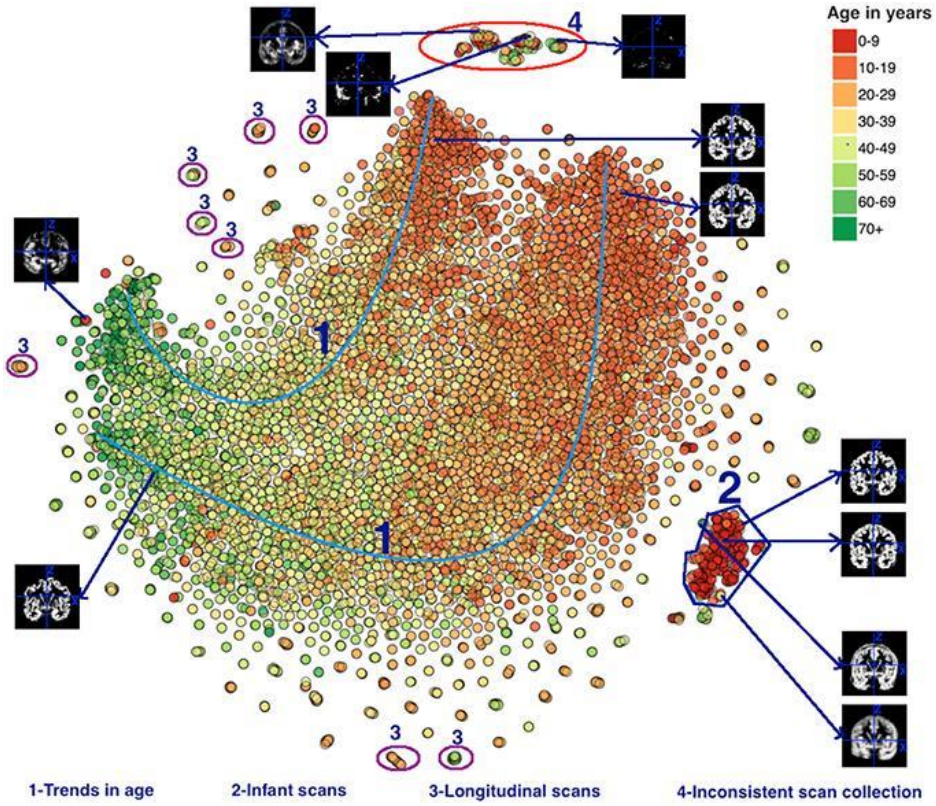
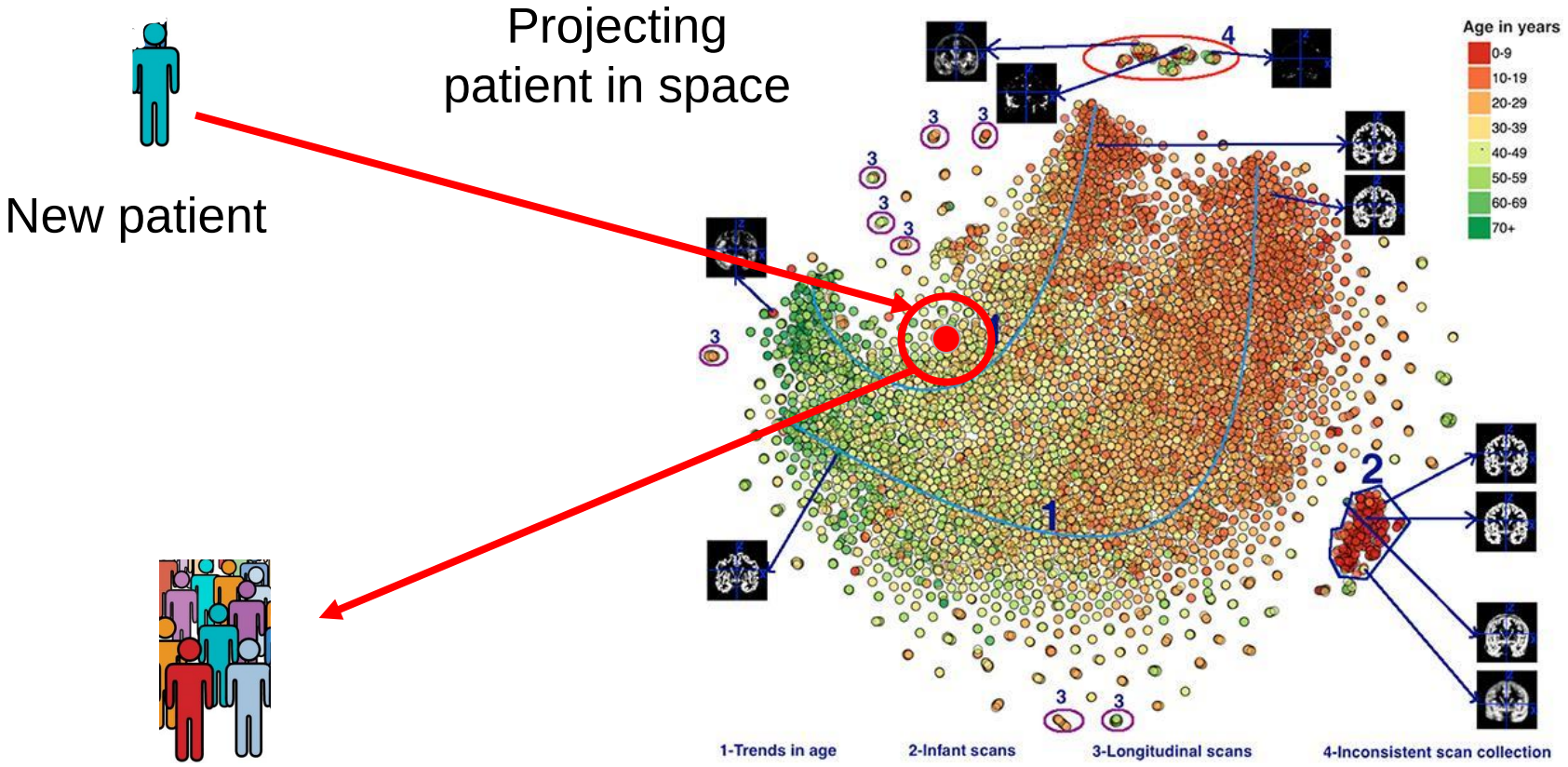
Using Machine Learning to Build Distributed Clinical Experience

Clinical trial data, EHR data, Imaging data



Building metric spaces from reference populations using deep representations (including genomic, radiomics, metabolomics, etc.)

Using Machine Learning to Build Distributed Clinical Experience



Real matching patients with complete clinical description, history, outcome

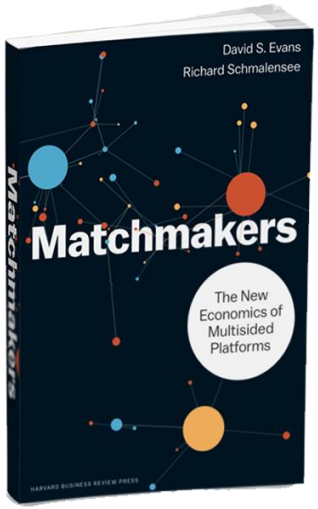
IV. Create Data Strategy

Create Data Strategy

Who needs the data? How we address their needs?

Industry

Early market insight, trial enabling, support development, reimbursement



Patients/Families

View personal data over time; support interactive health

Advocacy

Increase engagement and participation in fund raising

Health Care Providers

Drive Referrals. Visits, testing, outcomes

Payers

Early Diagnosis & Intervention to minimize care costs

Down stream providers

Collaborate to serve

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Considerations

- Work together to explore physical, emotional & financial journey of patient through:
  - Social Listening
  - Ethnographic Research
  - Market Research
- Define data needed to address these unmet needs
- Design, define and develop database(s) to address needs of patients and other stakeholders (e.g., pharma, HCPs, etc.):
  - Support Patient Journey
  - Enable Clinical Trials (biomarker for enrichment, trial design, enrollment)
  - Develop clinically relevant tools for diagnosis, prognosis, monitoring, etc.
- Provide hosting in a secure environment
- Secure data downloads, data integration, data traceability
- Manage reference database and data queries
- Manage application(s) of deep machine learning

Empower the voice of your patients by accumulating data and leveraging this data to address unmet needs

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