

# Leveraging Real-World Data in Rare Diseases: Longitudinal Data Sets as “Virtual Natural History”

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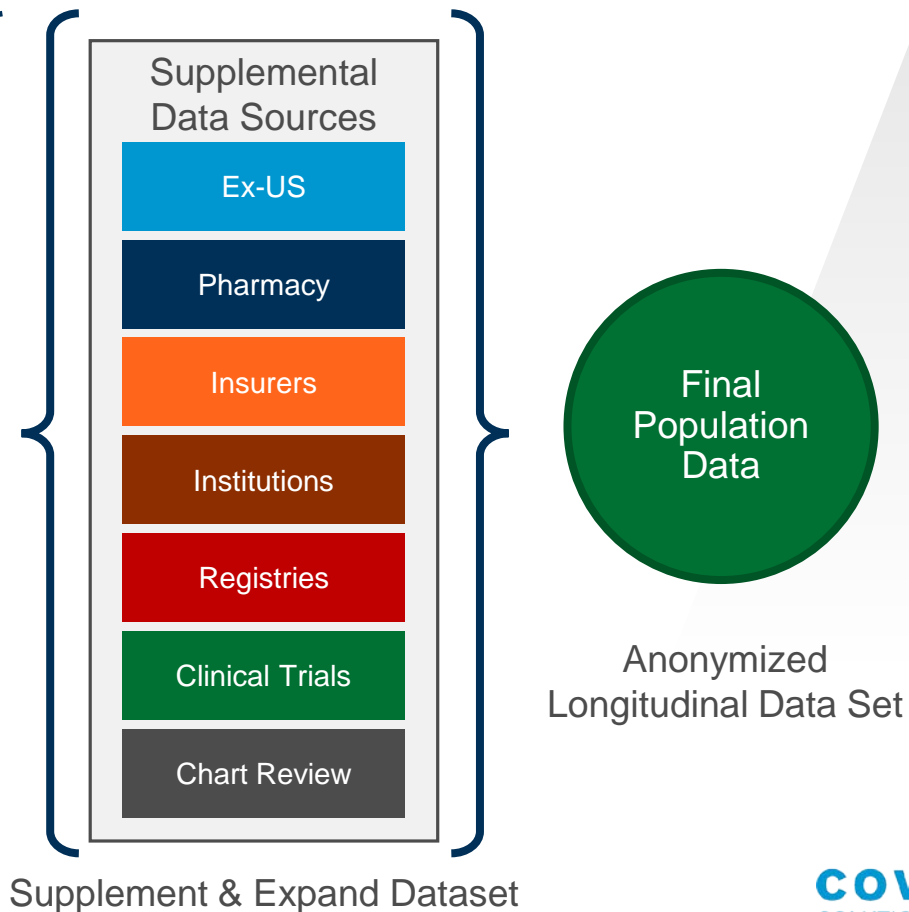
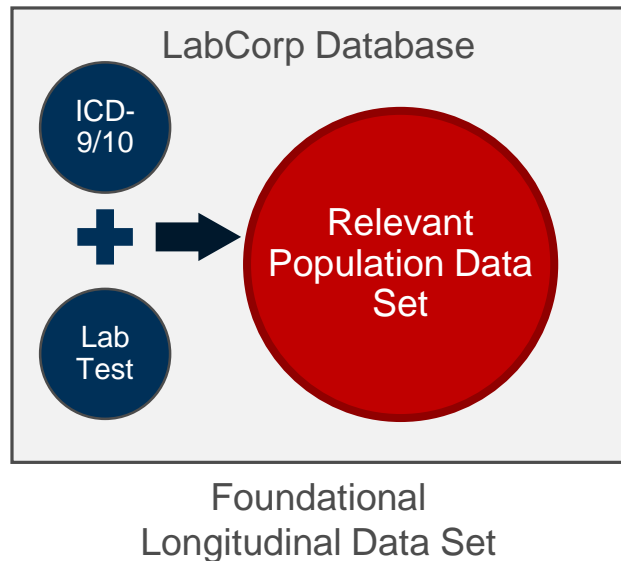
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# Data Set Development

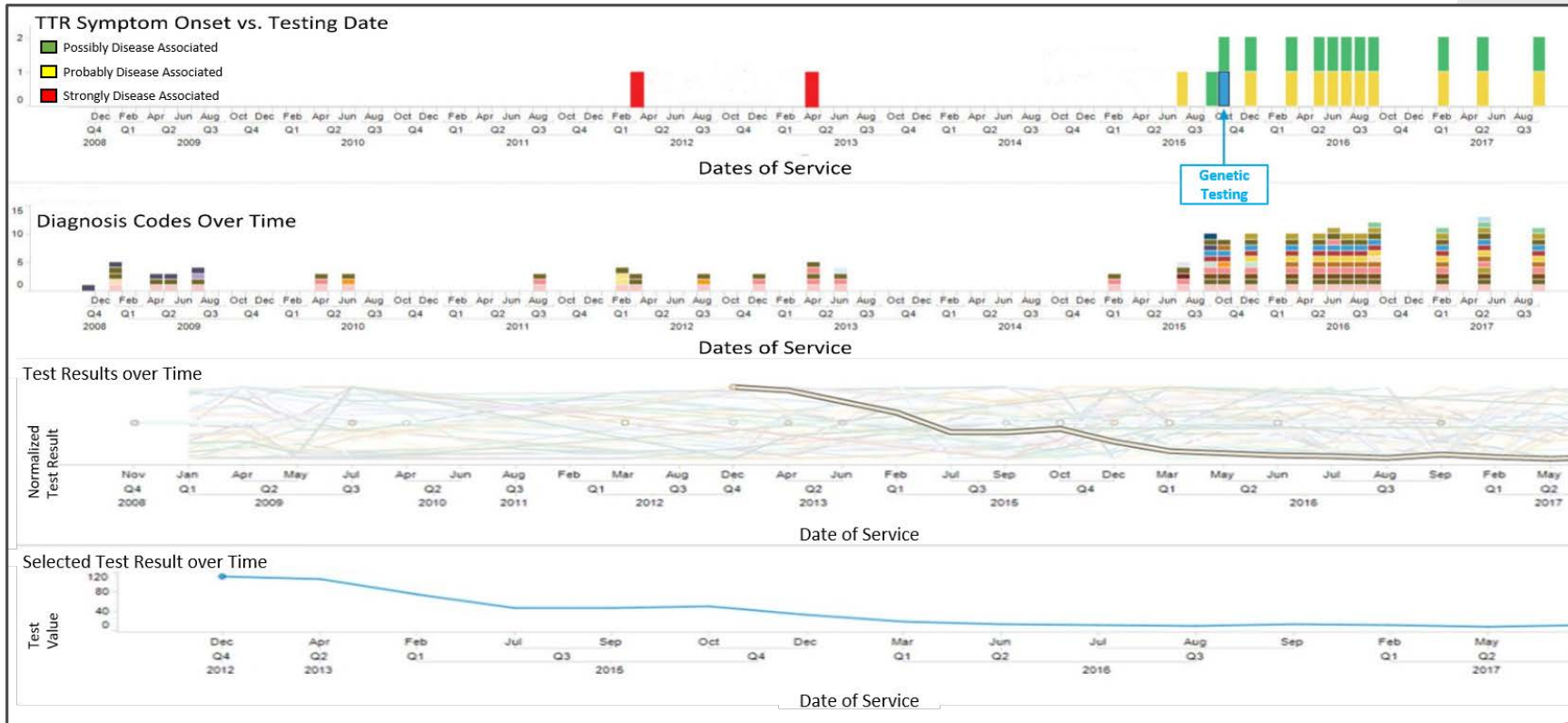


# Longitudinal Results for a Single c.424g>a Patient



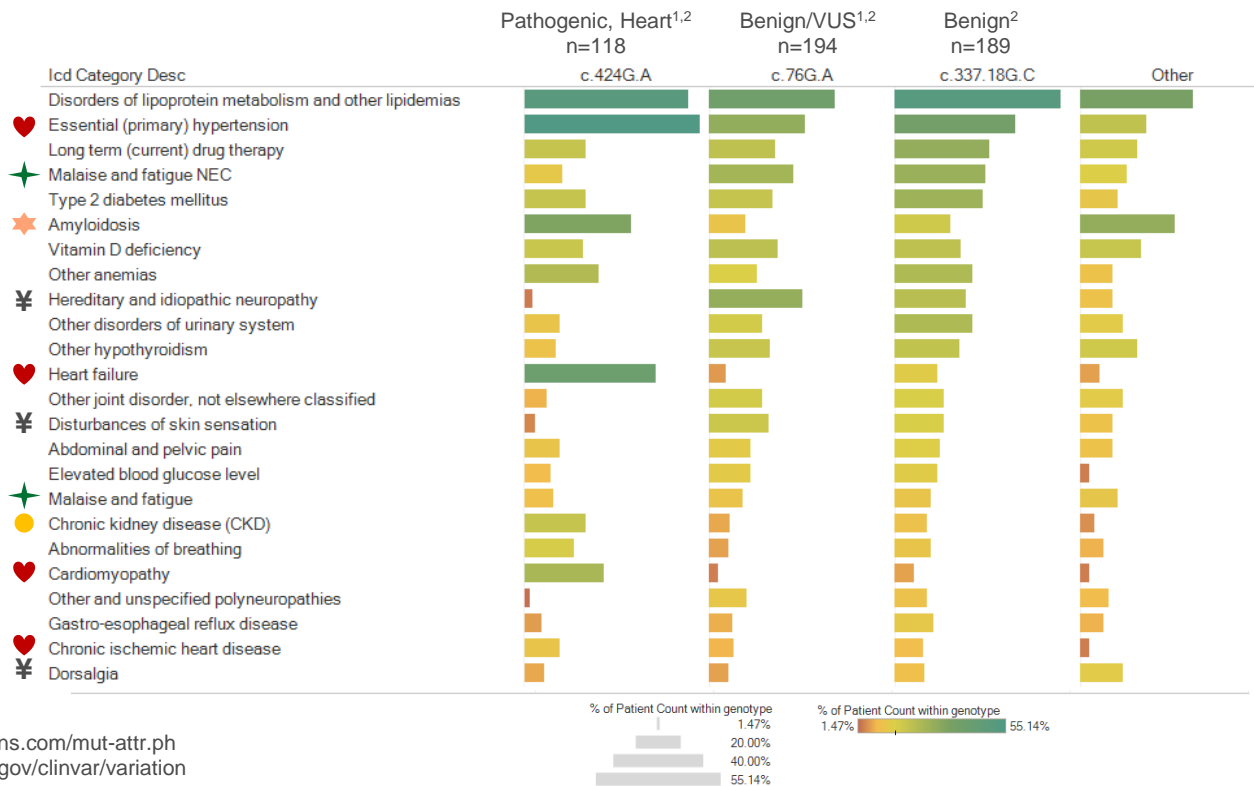
# Longitudinal RW Data - Individual Patient

## aTTR Patient with c.424G>A



# Genotype-Phenotype Insights

- ★ Amyloidosis
- ♥ Cardiac
- ⚡ Neuropathy
- Renal
- ✦ Fatigue



1. <http://amyloidosismutations.com/mut-attrib.ph>  
 2. <https://www.ncbi.nlm.nih.gov/clinvar/variation>

# Impact of I/E Criteria on Patient Pool

## 26% Reduction in Eligible Patients

853 Patients between 10/2010 and 10/2018 with transthyretin variant by genotyping

801 Patients between 18 and 82 years old.

796 Without HIV, Hep B, Hep C

787 Without Malignancy, Autoimmune disease, or other neuropathy

786 Without primary amyloidosis

776 Without liver transplant

642 With creatinine < 6 mL/min/1.75

635 With Platelets < 125 x 10<sup>9</sup>L

627 With ALT and AST > 1.9 ULN

**The protocol inclusion / exclusion criteria is applied to the patient pool and then matching patients are geo-located on the map.**



# Longitudinal Data as a Control

## Retrospective “Synthetic” Control Arm

- ▶ Integrate historical past clinical trial datasets: Covance Labs, Sponsor clinical data (EDC)

## Retrospective “Contemporary” Control Arm Study using RWE

- ▶ Integrate real-world datasets, identify patients in historical RWD who meet study criteria
- ▶ Outcome analysis to:
  - Define an index event (e.g., start of control treatment)
  - Define the observation period
- ▶ Analyze outcome (incidence rates, Kaplan-Meier analysis, etc.)

## Prospective “Synthetic” Control Arm Study

- ▶ Collect study data, including direct from patient through surveys, ePRO, mHealth apps
- ▶ Integrate direct from patient data with EHR / Labs and other data sets for analysis

## Real-World Comparative Safety Study

- ▶ Compare adverse events (AEs) rate of lab testing and clinical outcomes determined by diagnosis codes of Product X to the rate experienced by currently available products

# Real-World Evidence: Bridging the Gaps

- ▶ Unbiased by trial selection/recruitment process
- ▶ Leverages multiple, existing data sources
  - More robust, more rapid
  - Potential to unify fragmented data
- ▶ Enables identification / diagnosis of target population
  - Characterize the patient journey
- ▶ More effectively characterize genotype-phenotype
- ▶ Hypothesis test
- ▶ Protocol modeling

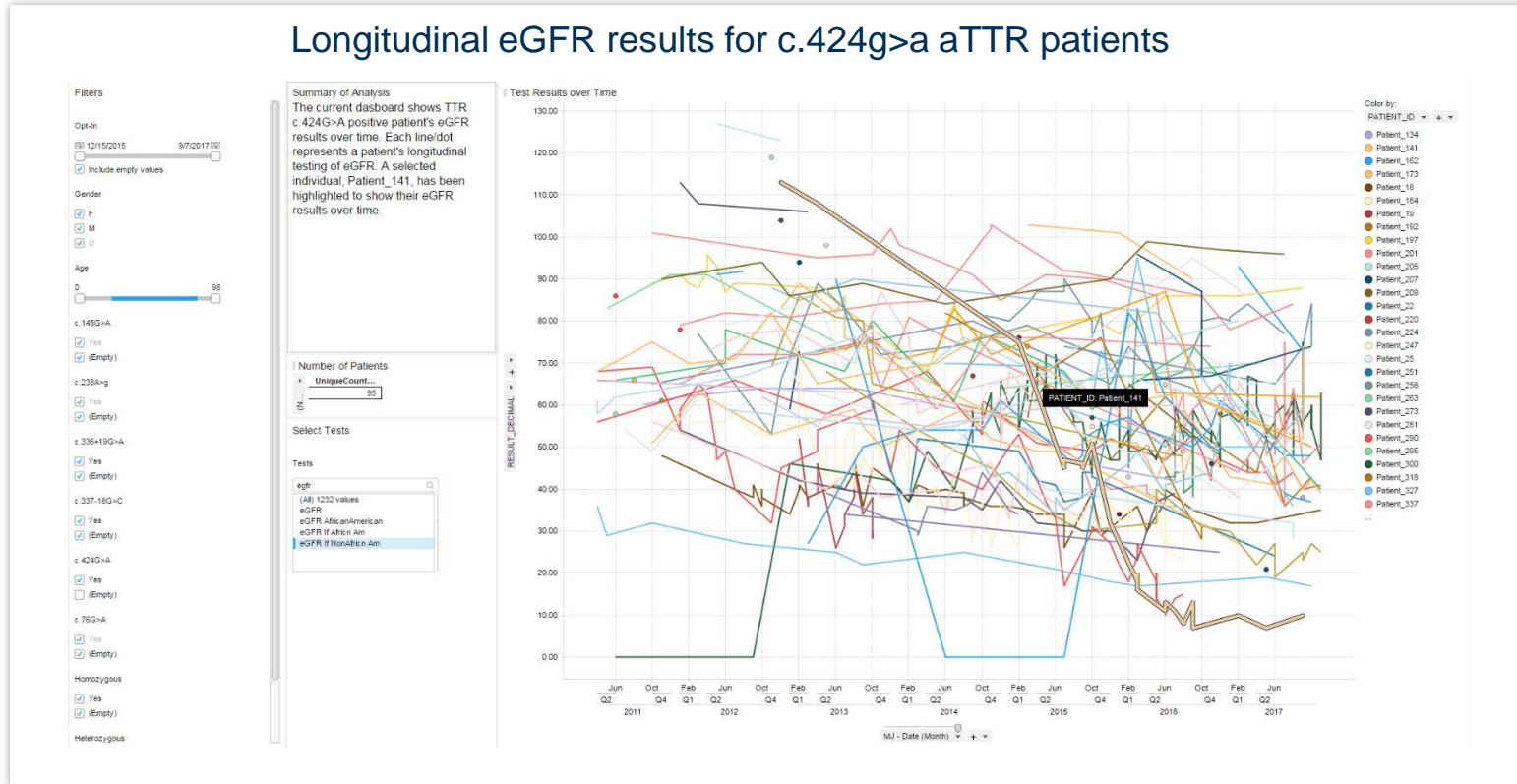
TRANSFORMING DATA INTO INSIGHTS



# Back-up

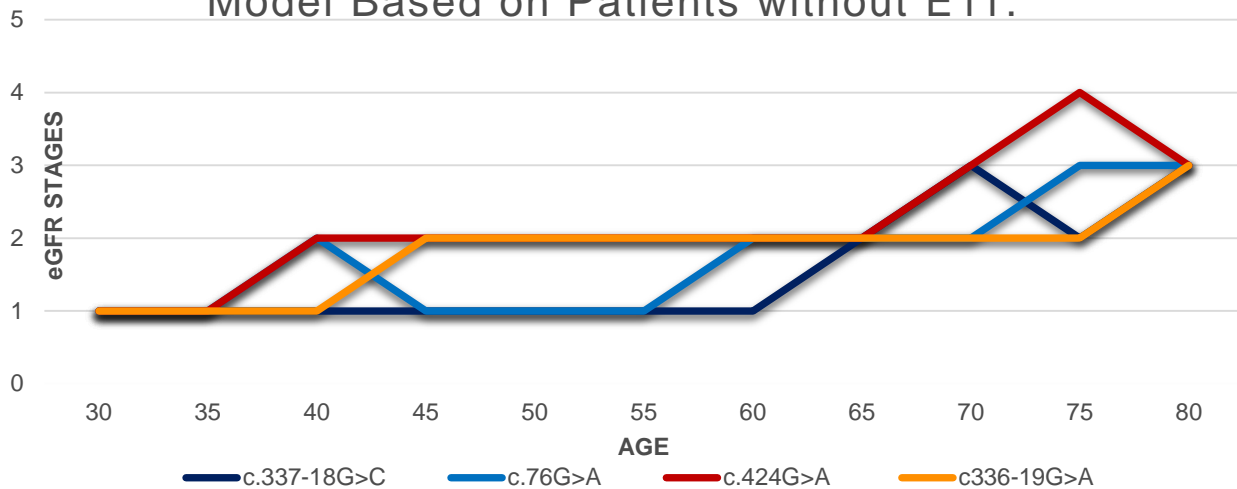
# “Virtual Natural Histories” – Longitudinal RW Datasets

## Longitudinal eGFR results for c.424g>a aTTR patients



# Exploring Predictive Modeling: eGFR & Age by Mutation

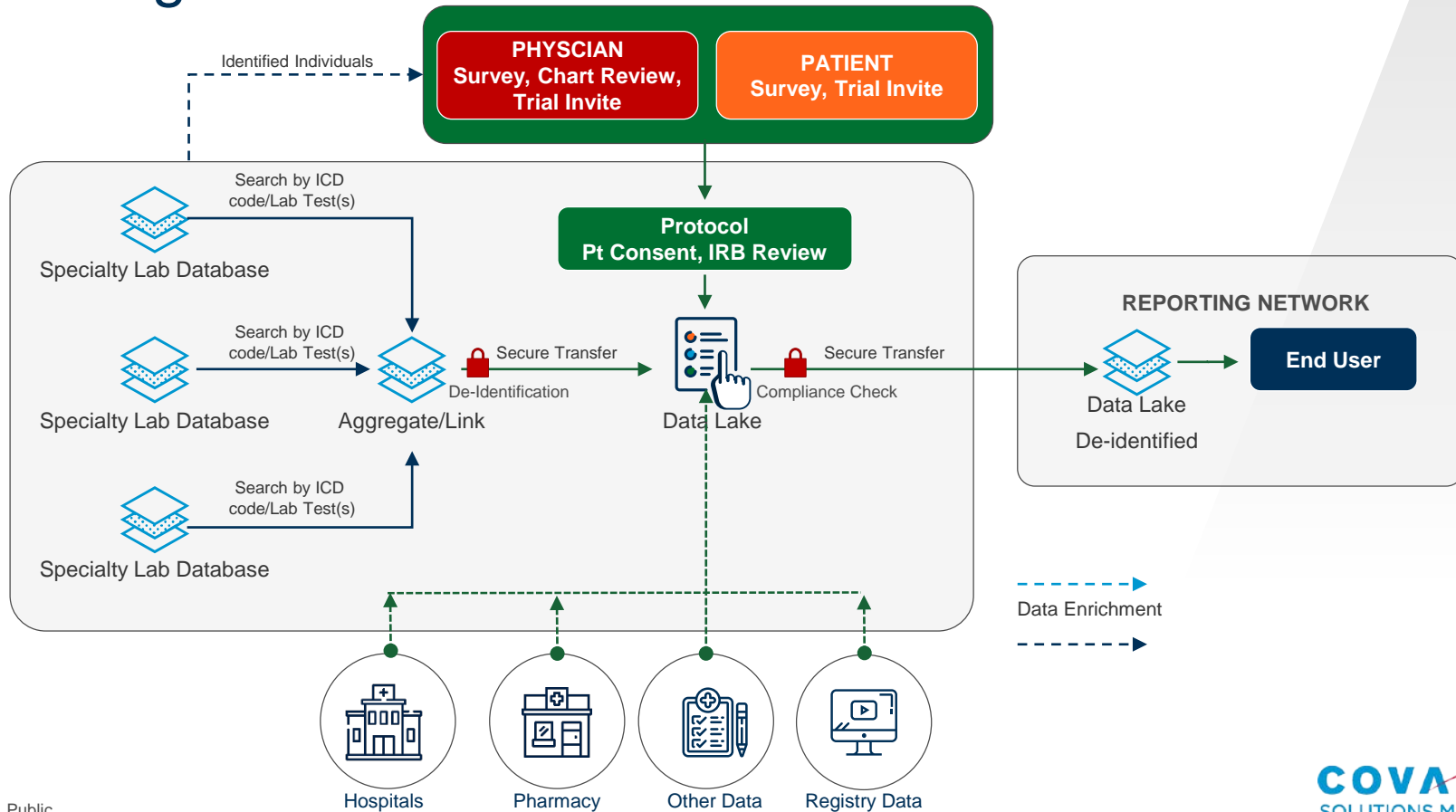
**eGFR Longitudinal Analysis**  
Model Based on Patients without E11.\*



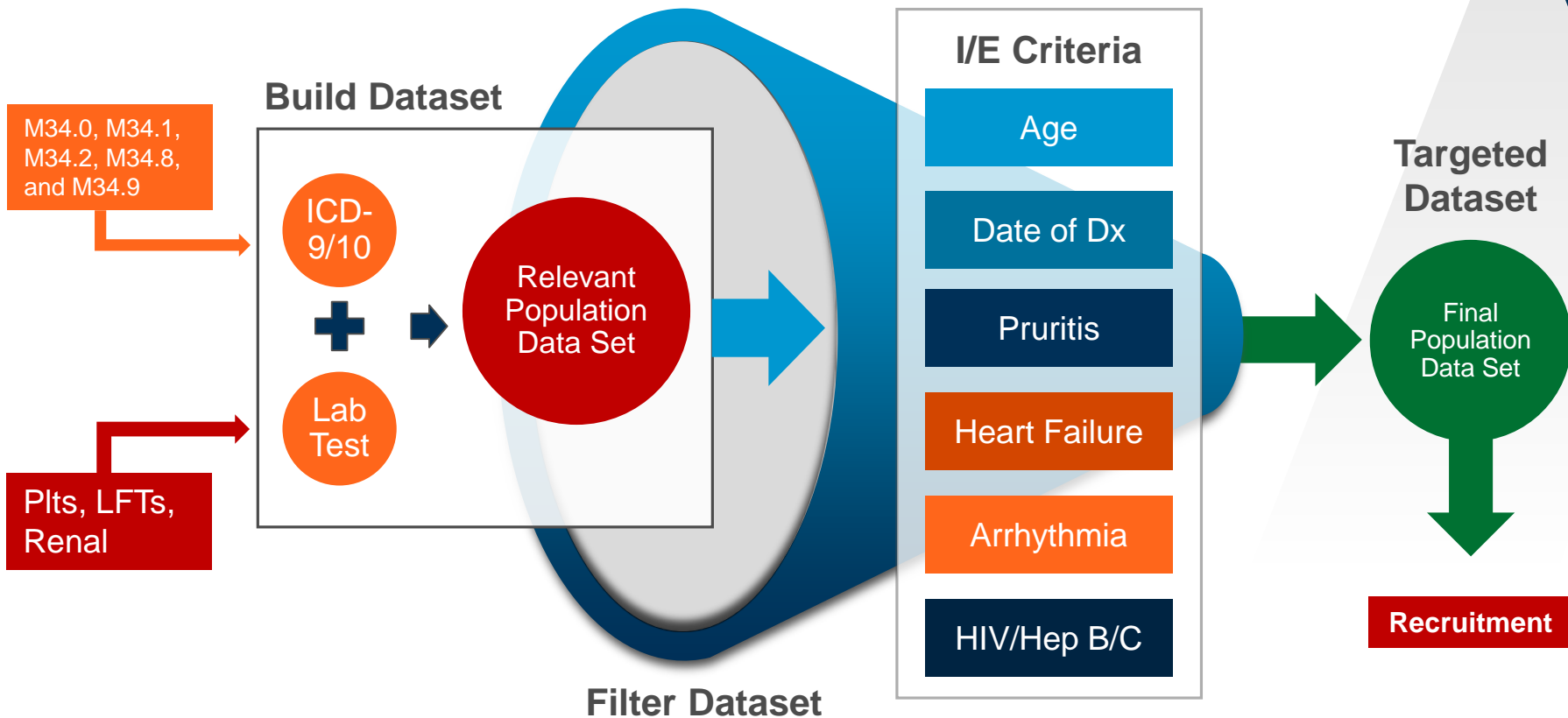
Stage	Kidney Disease	GFR
1	Normal	> 90 mL/min
2	Mild CKD	= 60-89 mL/min
3	Moderate CKD	= 30-59 mL/min
4	Severe CKD	= 15-29 mL/min
5	End Stage CKD	<15 mL/min

Mutation type	c.337-18G>C Intronic	c.76G>A Gly6Ser (Likely benign)	c.424G>A Val122Ile (Pathogenic)	c.336-19G>A Intronic
Patient Count #	142	125	94	61

# Creating a Data Lake



# Development of a Dataset: Protocol Considerations



# Patient Care Data in Rare Diseases



## PATIENTS

## BRIDGING THE GAP

## DRUG DEVELOPERS

Delayed diagnosis

Multiple physicians

Uncertainty of disease progression

Complexity of clinical trials

Need for approved therapies

Address several key challenges for both patients and drug developers

Longitudinal objective laboratory data and physician diagnostic coding in patient care setting

Advance approaches for data analysis

Established data quality assurance procedures, understanding data limitations, exploring novel methods

Optimize protocol design and connect patients to clinical trials

Patient identification

Identification of treating physicians

Lack of natural history data

Understanding of patient perspective

De-risk clinical development

# Leveraging Our Data Assets

## Patient Data Privacy and Security

- ▶ Protecting the privacy and security of patient information is of paramount importance to LabCorp's business and key to maintaining trust of patients, study participants, and clients
- ▶ With respect to the use and disclosure of LabCorp patient data for clinical research purposes, our company is committed to compliance with all applicable federal, state, and local privacy laws, including HIPAA

### Better Together Patients

- ▶ Through Better Together, patients voluntarily authorize LabCorp to disclose their lab data and demographic information to Covance for the purpose of identifying and being contacted about clinical research opportunities
- ▶ Patients provide authorization through the LabCorp | Patient™ portal or such other secure means that allow for the verification of the individual's identity
- ▶ Authorization can be revoked by the patient at any time
- ▶ Covance reviews lab data for Better Together patients, and may contact patients directly about clinical studies
- ▶ Through survey outreach, patients also provide feedback and insights on their clinical trial experiences and the burden of disease, allowing for more optimal protocol design and patient-centric approaches to study recruitment and participation

### Other LabCorp Patient Data

- ▶ Outside of Better Together, LabCorp shares de-identified lab data with Covance, allowing for analysis of diseases/conditions of potential interest to study sponsors
- ▶ As a healthcare provider and HIPAA covered entity, LabCorp's use and disclosure of protected health information (PHI) is subject to HIPAA
- ▶ Any outreach by LabCorp to other healthcare providers/patients regarding clinical research that involves the use of PHI is done in accordance with the HIPAA Privacy Rule

# Frederick J. Derosier, D.O.

- ▶ D.O. from the New York College of Osteopathic Medicine; 10 years of private practice experience as an internist
- ▶ 17 years of experience, primarily in neuroscience and rare diseases, in the pharmaceutical and biotechnology industry; joined Covance in 2017
- ▶ Co-chairs the Covance pan-enterprise Advanced Therapies, Drugs, and Devices Development group which supports the development advanced therapeutic technologies,
- ▶ Executive Director, Covance Rare Diseases and Pediatrics Team, focusing on strategic considerations for patient-centric drug development within rare diseases.
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