Genome-friendly Connected Care

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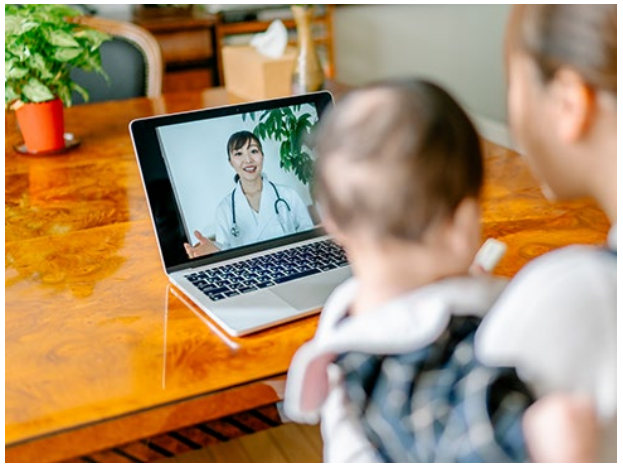

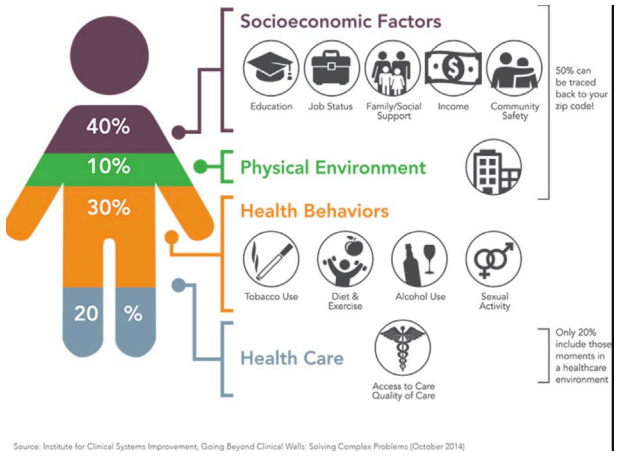

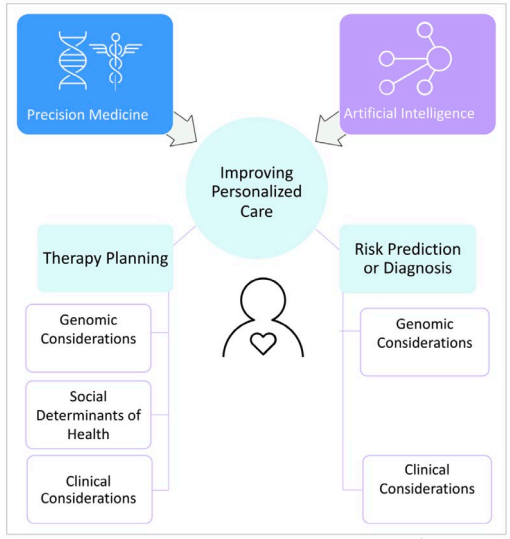

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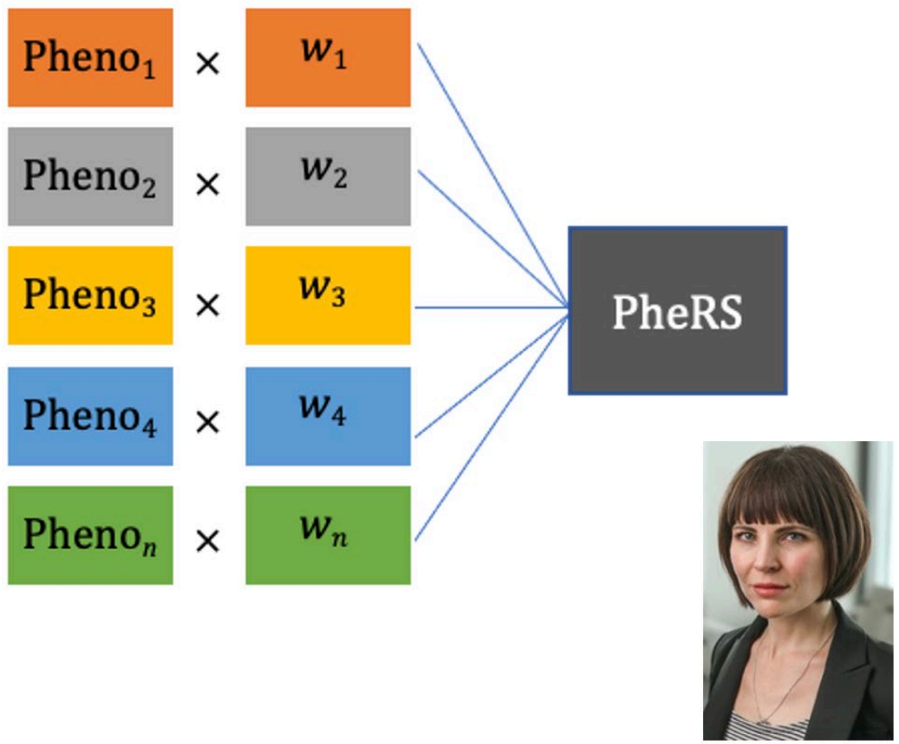
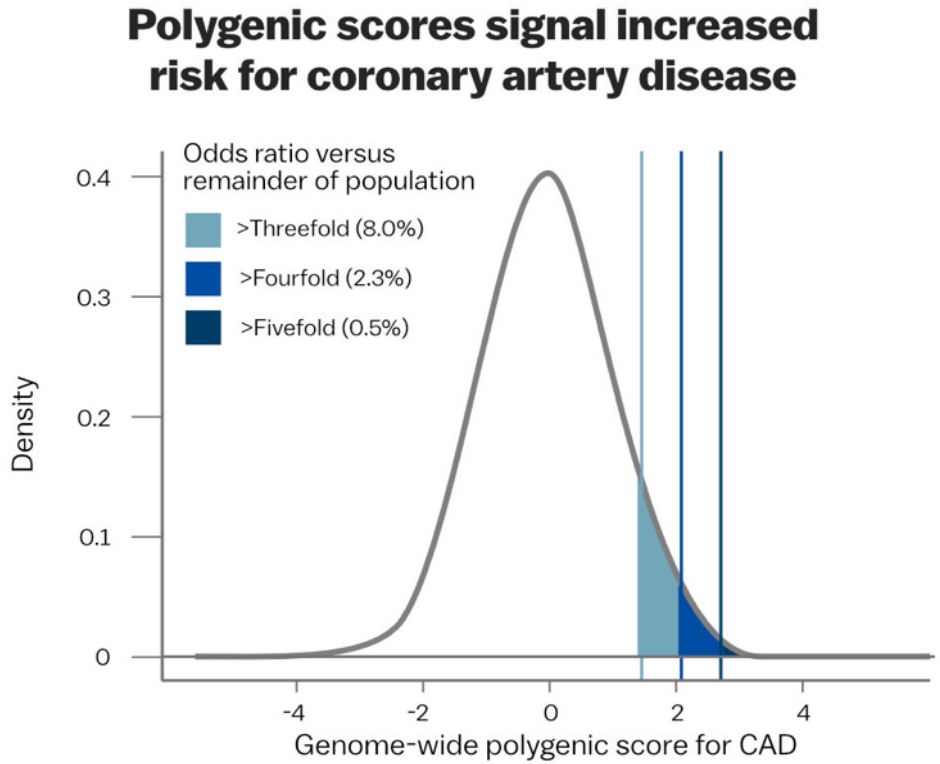
Where is Medicine Going?

Advances in Prediction



Science, 2018



Source: Nature Genetics

Khera et al, Nature Genetics, 2019

Literature Supporting Personalization

Proposed Healthy Adult Screening Program

Box 2 | Suggested Tier System for Genomics-Based Screening Programs

TIER 1

- Lynch syndrome-associated genes *(MLH1, MSH2, MSH6, PMS2, EPCAM)*
- Hereditary Breast and Ovarian Cancer (HBOC)-associated genes *(BRCA1, BRCA2)*
- Familial hypercholesterolemia (FH)-associated genes *(LDLR, APOB, PCSK9)*

TIER 2

- Genes with unknown or low penetrance
- Genes with a less well-established knowledge base
- Efficacious interventions available
- Follow-up confirmatory tests available
- Examples including but not limited to *PALB2*, hereditary hemochromatosis, malignant hyperthermia, hypertrophic cardiomyopathy, long QT syndrome, pharmacogenomic variants

SOURCE: PSWG Working Group, 2018.

Murray and Khoury, NAM 2018

Genomics sensitive preventative care workflows

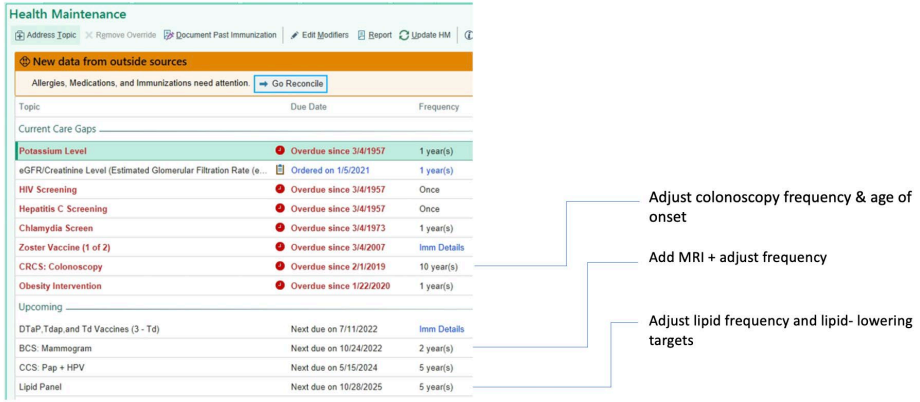
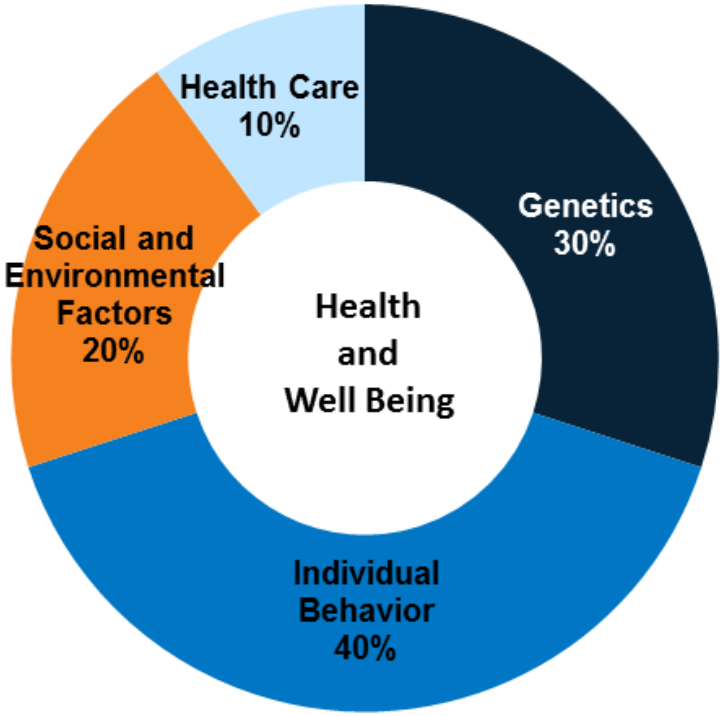


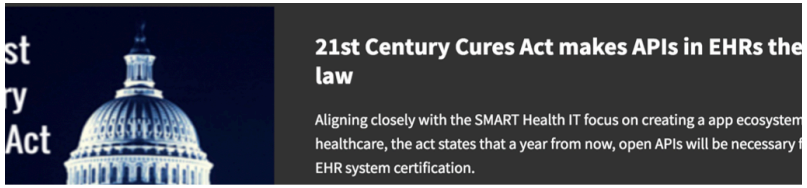
Figure 2

Impact of Different Factors on Risk of Premature Death



SOURCE: Schroeder, SA. (2007). We Can Do Better — Improving the Health of the American People. *NEJM*. 357:1221-8.

KFF
HENRY J KAISER FAMILY FOUNDATION



itle I: Innovation rojects

- $4.8 Billion to NIH for Precision Medicine ($1.45E Moonshot ($1.8B), Brain Initiative ($1.5B)
- $1B over 2 years for grants to states to suppleme abuse prevention and treatment activities

itle II: scovery

- Supporting Young Emerging Scientists
- NIH Strategic Planning
- Facilitating use of data for research

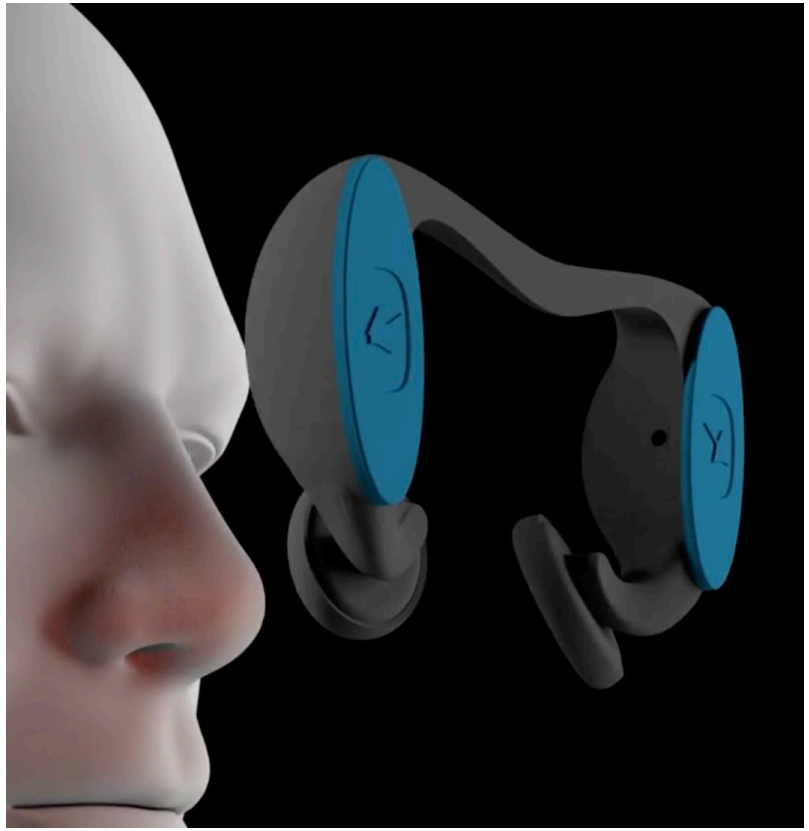
itle III: elopment

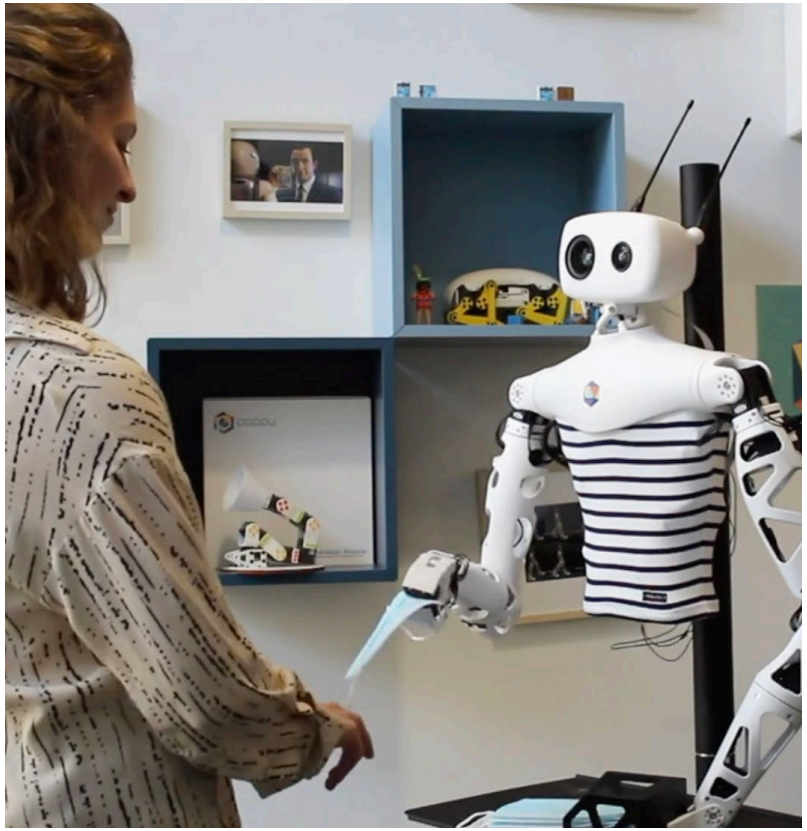
- Patient-focused drug development
- Patient access to Therapies and Information
- Modern trial design and evidence development
- Advancing new therapies

itle IV: elivery

- Interoperability
- Information Blocking
- Leverage EHR to support participatory medicine

https://www.nihcollaboratory.org/Pages,



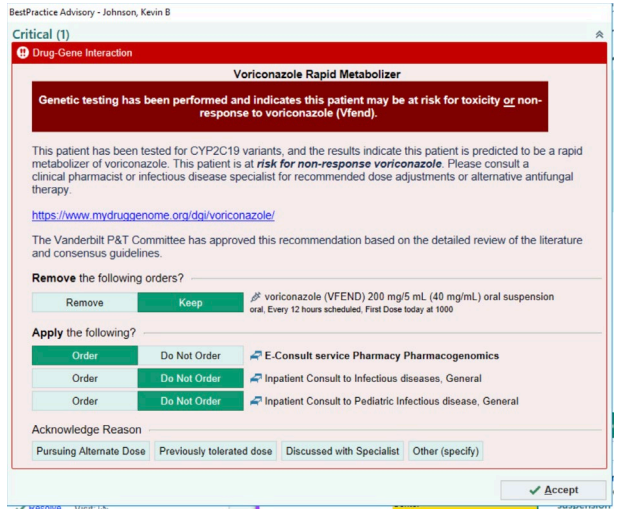


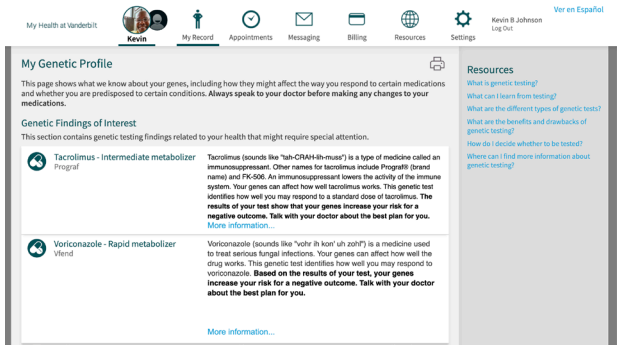
Enabling Platforms

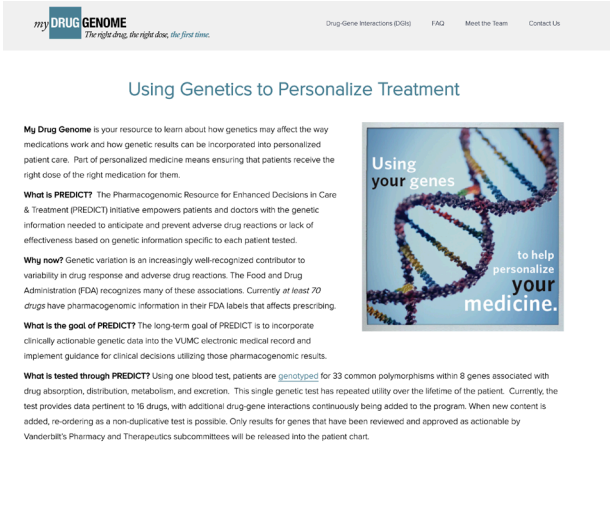
VUMC: Current Capabilities

Specific Drug Gene Interactions

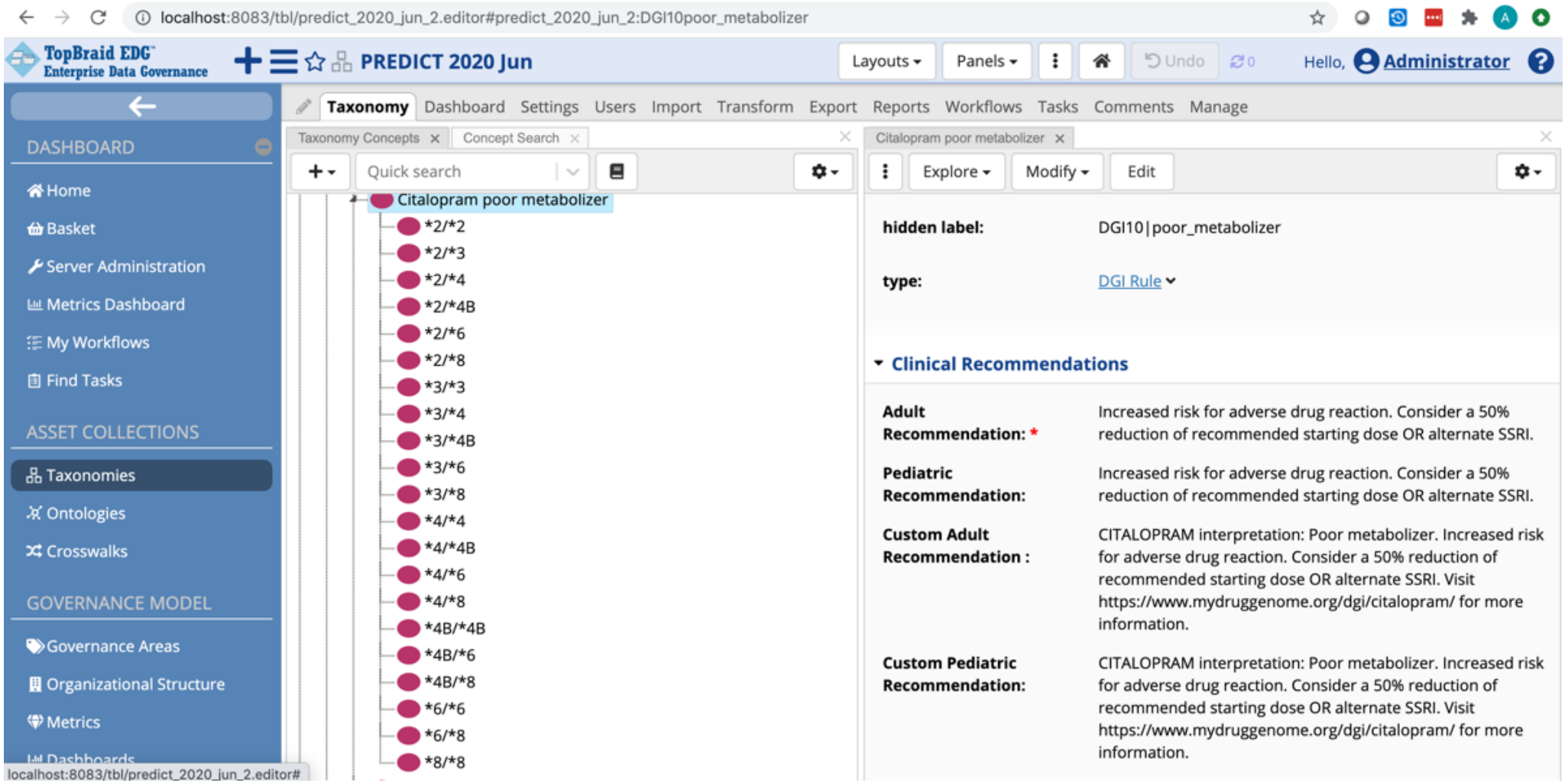
- Citalopram (Celexa) – CYP2C19
- Clopidogrel (Plavix) – CYP2C19
- Codeine – CYP2D6
- Escitalopram (Lexapro)- CYP2C19
- Fluvoxamine (Luvox) – CYP2D6
- Ondansetron (Zofran) – CYP2D6
- Paroxetine (Paxil)- CYP2D6
- Sertraline (Zoloft)- CYP2C19
- Simvastatin (Zocor) – SLCO1B1
- Tacrolimus (Prograf) – CYP3A5
- Thiopurine (Purinethol, Imuran, Tabloid) – TPMT
- Tramadol (Ultram) – CYP2D6
- Voriconazole (Vfend) – CYP2C19
- Warfarin (Coumadin) – CYP2C9 / VKORC1 / CYP4F2







Rules supporting clinical recommendations for *CYP2C19* Alleles - Citalopram



Escitalopram CDS in Adult with Actionable *CYP2C19*

CYP2C19 Phenotype

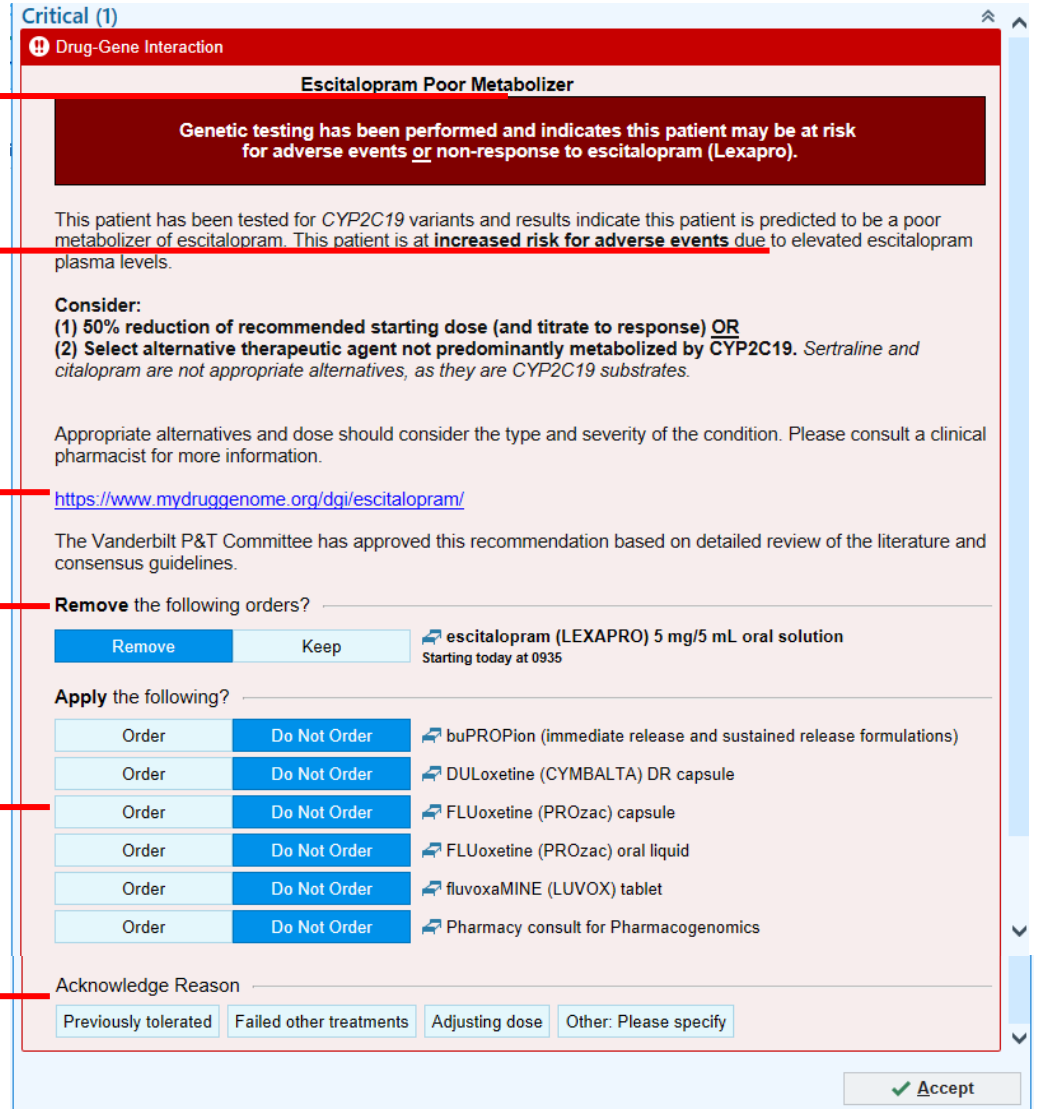
Associated Risk

Evidence Link

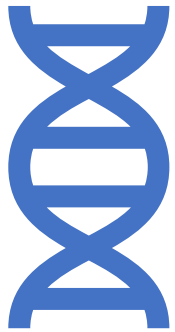
Remove orders

Apply orders

Acknowledgment



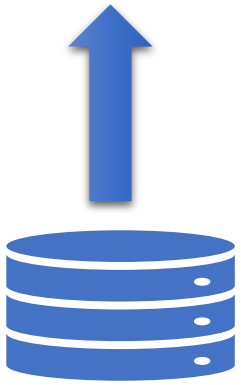
Epic Genomics Module



Genomics Laboratory

(pharmacogenomics, somatic, germline)

Genomics module



External Knowledgebase
(e.g., PREDICT, My Cancer Genome)

Discrete Result Storage

- Resulting
  - Provider
  - Patient
- Clinical Decision Support
  - Alerts
  - Health maintenance reminders
  - Registries
- Analytics

A Vision

Questions that we should anticipate

Which drug will be most effective in my patient?

Should I be considering genetic testing? If so, what test?

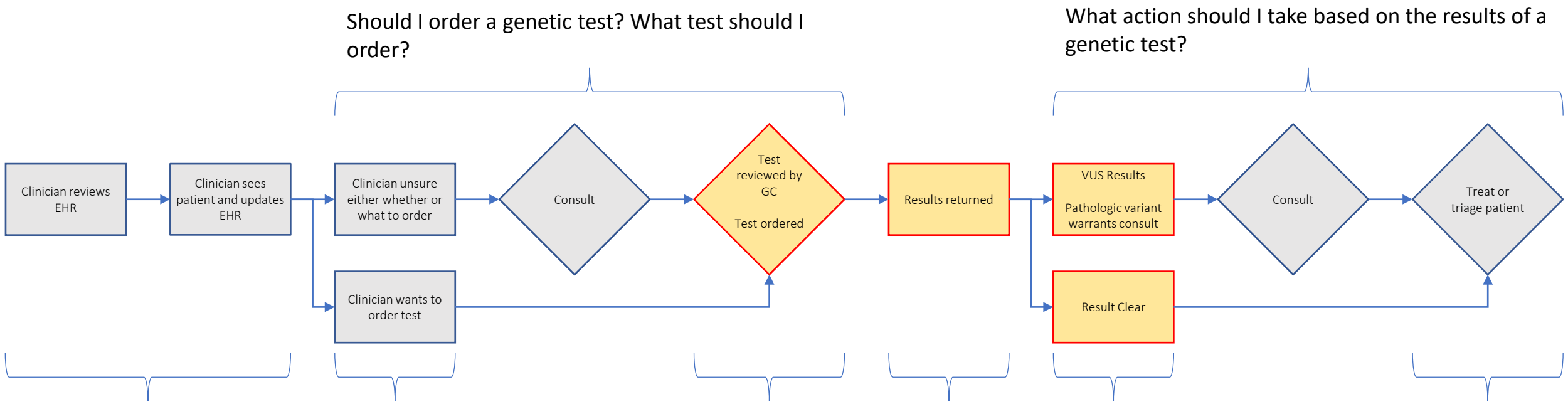
How do I interpret these test results? They don't have clinical meaning? What does indeterminate mean?

The literature isn't specific to my patient. What have other patients like her at Vanderbilt experienced with this condition and this treatment?

Is there a clinical trial for my patient out there?

What is the best way to treat my patient's tumor?

Workflow supported by technical foundation:



Additional panels in house

Scale Epic genomics module and Tempus

Expand E-consult launched

Case:

19 year-old woman evaluated in primary care after spontaneous pneumothorax with a heart murmur. The clinician suspects Marfan syndrome.

Translating PheRS or Related techniques

- Technical requirements:
  - Large, identified, full-text EHR
  - Syndrome features organized into an ontology
  - *Concept-indexed EHR documentation*

- Challenges:
  - Algorithm refinement to reduce manual review
  - Patients may not have appropriate clinical relationships established

Health System Challenges

- Interoperability / data flow
- Provider Knowledge
- Information Literacy
- ROI for Screening

- Computable data from outside labs
- Recontact as information changes

- Understanding the nomenclature
- Addressing family concerns

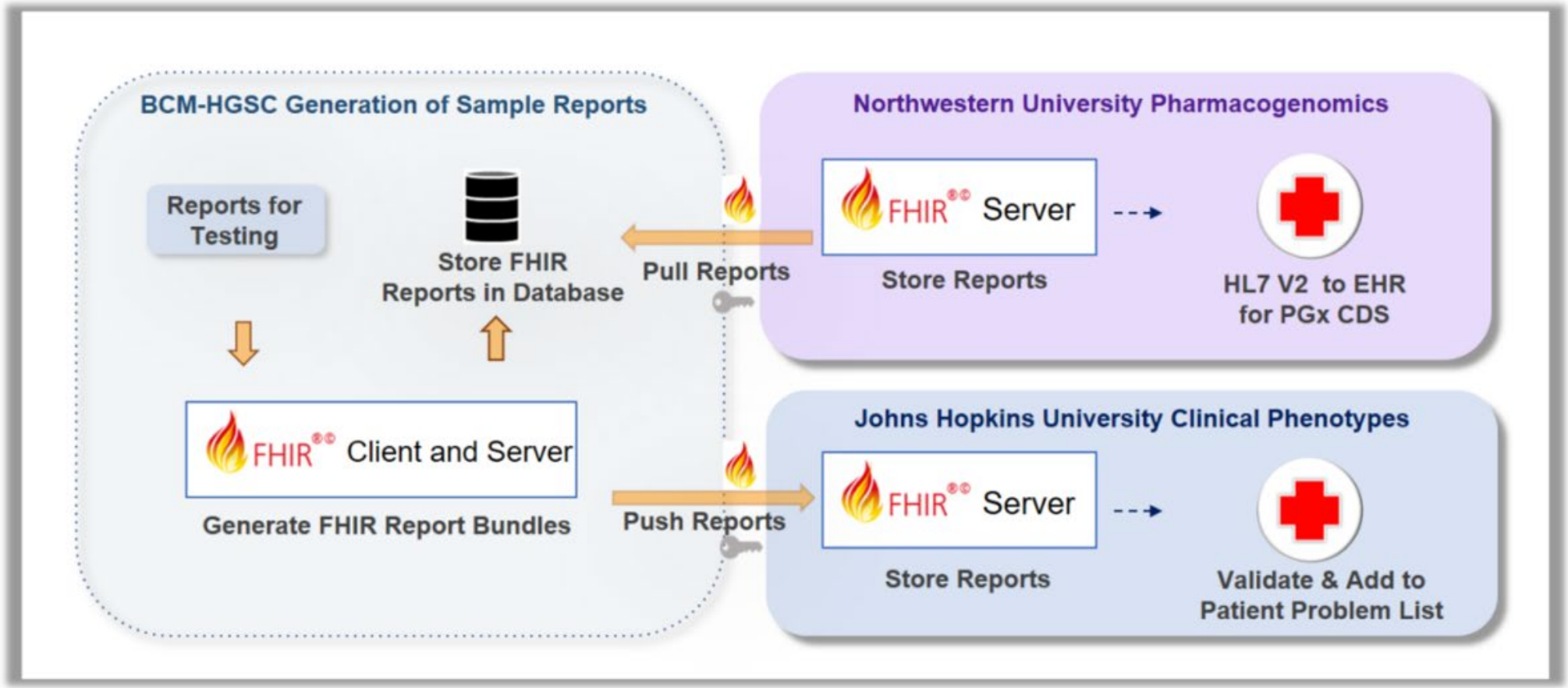
- Consistent knowledge representation
- Understandable to the lay public

- Quality evaluation studies
- Payor and self-insured party support

“Data in motion”: HL7 FHIR Genomics

Transmission standard for sequencing data

Figure 1: Baylor College of Medicine Human Genome Sequencing Center Demonstration Project



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Sync for Genes v3 Report for ONC, 2021

Daily Living Challenges

Equity

Literacy

Fear and Misinformation

Life Integration

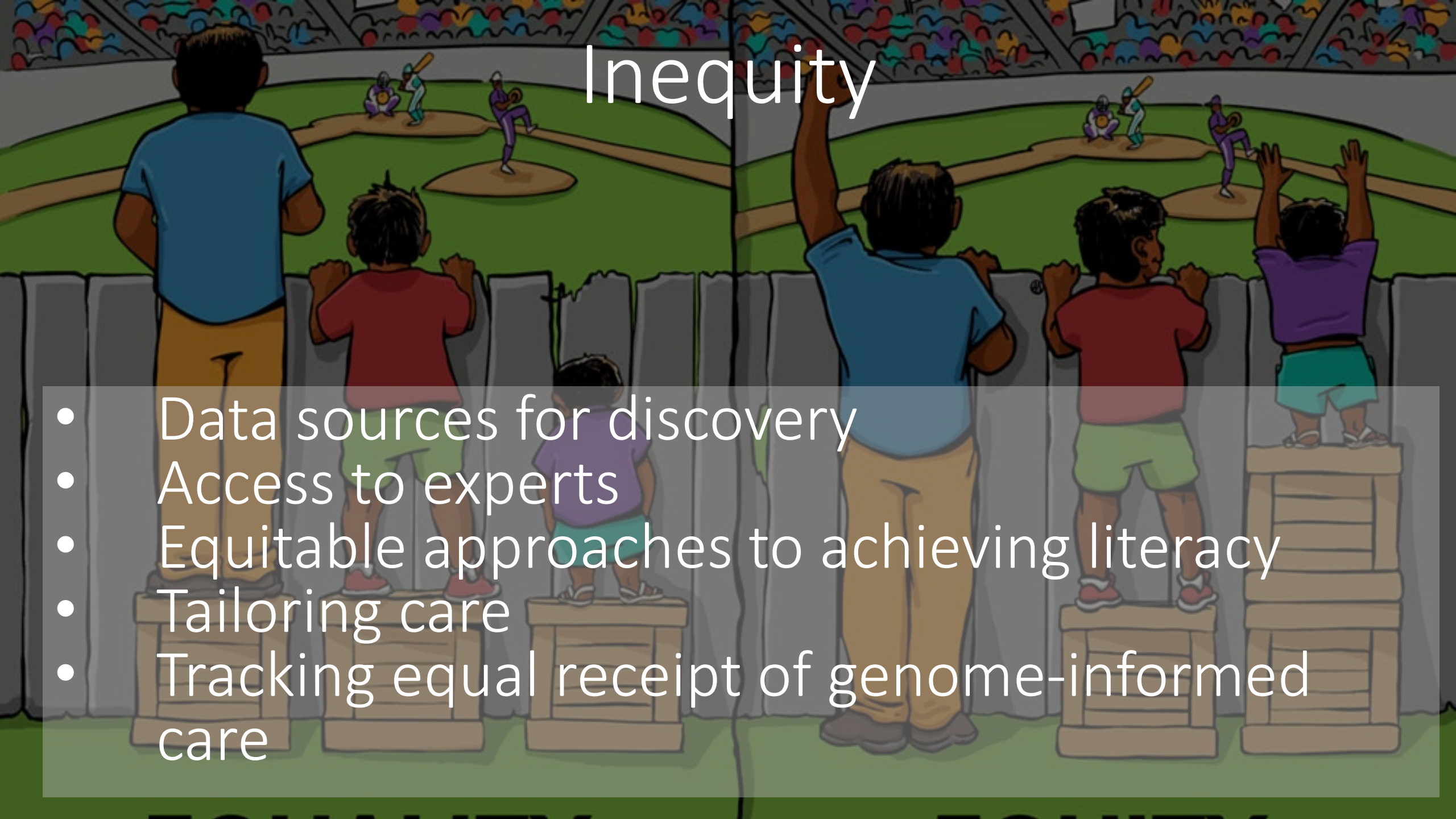
- Access to tailored care/ trial options
- Recontact as information changes
- Mitigating biases in data

- Understanding the nomenclature
- Addressing family concerns

- Concerns about experimentation
- Concerns about job retention and insurability

- Technology literacy
- Recontact over time

Inequity



- Data sources for discovery
- Access to experts
- Equitable approaches to achieving literacy
- Tailoring care
- Tracking equal receipt of genome-informed care

How Do We Lesson Genetic Discrimination Fears?

U.S. Equal Employment Opportunity Commission

MENU

Fact Sheet: Genetic Information Nondiscrimination Act

This guidance document was issued upon approval of the Chair of the U.S. Equal Employment Opportunity Commission.

OLC Control Number:	EEOC-NVTA-0000-4
Concise Display Name:	Fact Sheet: Genetic Information Nondiscrimination Act
Issue Date:	09-09-2014
General Topics:	ADA/GINA
Summary:	This document provides basic information about the Genetic Information Nondiscrimination Act, including the definition of genetic information under the law.

What Can/Should We Automate?

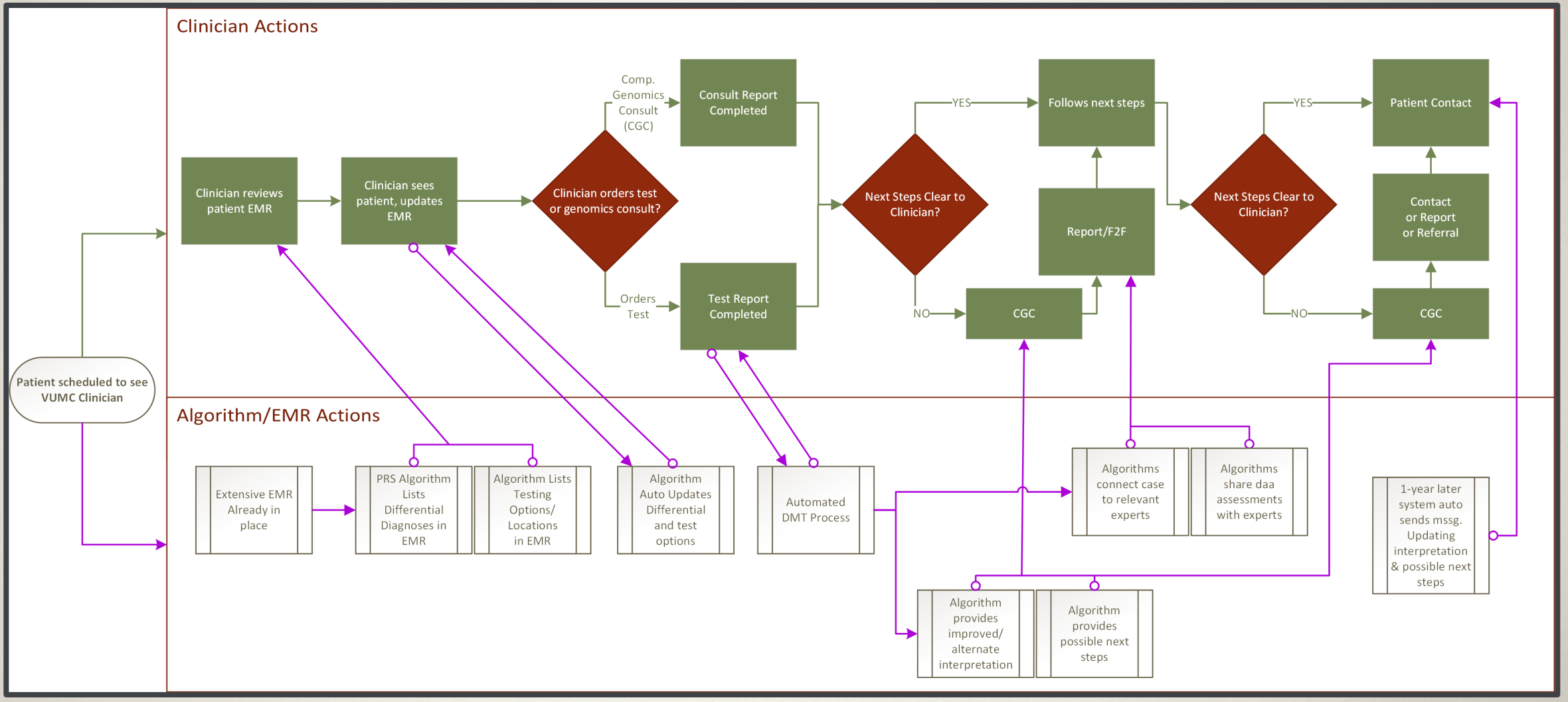
Summary: What Research/Development is Necessary

- Literacy
- Expanding ClinVar, dbGaP, EGA
- Standards for genomic interoperability from external labs into the EHR
- ROI for sequencing in support of both screening and diagnosis
- More experts available for clinicians

- Literacy
- Tools and pilots of innovation solutions
- Patient understanding of genomic medicine in general
- Patient understanding of genomic risk
- Equitable approaches to genomic literacy
- More expertise available for everyone else

"The future is here
– it's just not
evenly distributed"

William Gibson



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Future Tech

- Non-invasive prenatal testing over amniocentesis and CVS
- Expanded pediatric screening for genetic risk/protection variants