

# Making use of our genome for life: strategic opportunities and challenges

Marylyn D. Ritchie, PhD

Department of Genetics

Institute for Biomedical Informatics

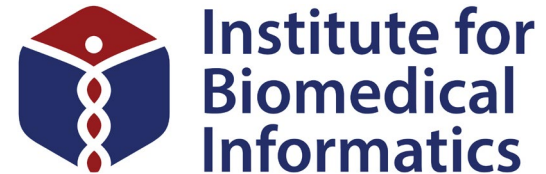
University of Pennsylvania

<http://ritchielab.org>

 @MarylynRitchie

 @theCALMpodcast

<http://marylynritchie.com/podcast>



# Past paradigm for using genetics in clinic\*



\* Different from prenatal/newborn screening

# Future paradigm for using genetics in clinic



**Physician develops  
prevention strategy  
for patient based on  
genetic testing  
results**

**If patient  
develops illness,  
treatment based  
on genetic  
testing**



- ▶ Identify patients “at risk” for follow-up, deeper evaluation, and phenotyping
- ▶ Identify patients for genotype-guided clinical trials
- ▶ Return information to patients about their genetic risks

# Future paradigm for using genetics in clinic

- For this to become reality, we need to have access to sequence information across a patient's lifetime.

## Mendelian Disease Risk Genes

Current ACMG/AMP guidelines:

Pathogenic			
Supporting	Moderate	Strong	Very strong
Missense in gene with low rate of benign, missense variants and pathogenic missenses common - PP2	Mutational hot spot or well-defined functional domain without benign variation - PM1		

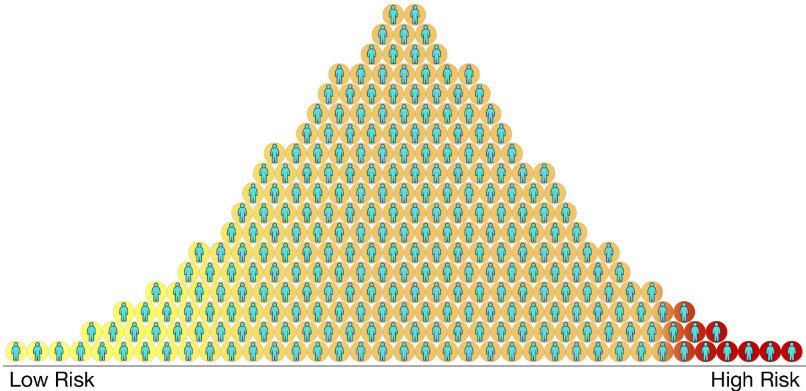
Proposed adapted ACMG/AMP guidelines:

Pathogenic			
Supporting	Moderate	Strong	Very strong
Non-truncating variant in gene or protein region with $0.8 \leq EF < 0.9$ PM1_supporting	Non-truncating variant in gene or protein region with $0.9 \leq EF < 0.95$ PM1_moderate	Non-truncating variant in gene or protein region with $EF \geq 0.95$ PM1_strong	

## Pharmacogenomics



## Polygenic Risk Scores



<https://www.genome.gov/Health/Genomics-and-Medicine/Polygenic-risk-scores>

# Opportunities for Clinical Informatics

- ▶ EHR systems are starting to build capacity for storing genetic information as structured data
  - Example: Epic Genomics Module

☒ Filters ☒ Hide Canceled

Medications and orders also exist in active treatment plans: [ONCOLOGY SUPPORTIVE CARE PLAN](#)

Date	Description	Status
Recent		
Yesterday	CPD ORDER	Final result
07/09/2019	PENN PRECISION MEDICINE TESTING CNS	Final result
07/08/2019	PENN PRECISION MEDICINE TESTING GYN	Pending
06/27/2019	PENN PRECISION MEDICINE TESTING HEAD AND NECK	Ordered
06/21/2019	PENN PRECISION MEDICINE TESTING HEAD AND NECK	Ordered
06/21/2019	PENN PRECISION MEDICINE TESTING CNS	Ordered
06/10/2019	PENN PRECISION MEDICINE TESTING - RECTAL CANCER	Ordered
06/10/2019	PENN PRECISION MEDICINE TESTING HEAD AND NECK	Ordered
04/15/2019	PENN PRECISION MEDICINE TESTING GU	Pending
03/12/2019	PENN PRECISION MEDICINE TESTING GU	Pending
02/21/2019	PENN PRECISION MEDICINE TESTING GU	Pending
1 Year Ago		
04/25/2018	PENN PRECISION MEDICINE TESTING CNS	Ordered
04/25/2018	PENN PRECISION MEDICINE TESTING CNS	Ordered
04/25/2018	PENN PRECISION MEDICINE TESTING CNS	Ordered
04/25/2018	PENN PRECISION MEDICINE TESTING CNS	Ordered
03/22/2018	PENN PRECISION MEDICINE TESTING NSCLC	Ordered

## Results

CPD ORDER [CPDORDER] (Order 397921)

### Result Information

Status: Final result (Resulted: 7/16/2019)

### Patient Information

Patient Name Sex DOB  
Zzzepic, DAD (330009978) Male 10/5/1959

### Order-Level Results - 07/10/2019:

[Scan on 7/17/2019 10:38 AM by Thai, Mark: Genetic Testing - Final Report](#)

### Result Read / Acknowledged

[Acknowledge result](#)

No acknowledgement history exists for this order.

### 7/17/2019 10:38 AM - Thai, Mark

### Additional Information

Specimen ID	Specimen Source		Bill Type	Client ID	
	BLOOD [30]				
Specimen Date Taken	Specimen Time Taken	Specimen Received Date	Specimen Received Time	Result Date	Result Time
				Jul 16, 2019	

### Lab and Collection

CPD ORDER (Order: 397921) - 7/16/2019

© 2020 Epic Systems Corporation. Used with permission.



# Opportunities for Clinical Informatics

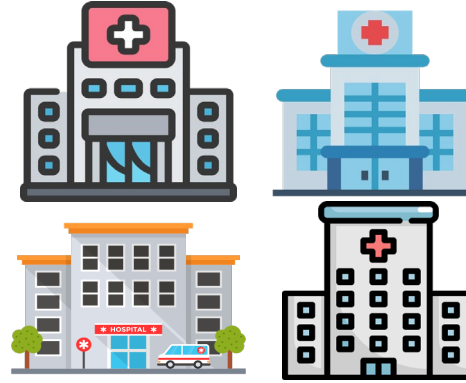
- ▶ EHR systems are starting to build capacity for storing genetic information as structured data
  - Example: Epic Genomics Module
- ▶ With Clinical Decision Support (CDS) built to disseminate the relevant genetic sequence information, healthcare providers across the system can find and use the information
  - Enormous potential to use genetic information outside of Medical Genetics Clinics
  - More on this topic in “Challenges”
- ▶ Through Health Information Exchanges (HIE), this relevant genetic information can be shared across health systems → following the patients wherever they go
  - More on this topic in “Challenges”
- ▶ As more knowledge is gained in Genomic Medicine, informatics systems can push annotation updates to patient records based on the genetic sequence data stored
  - More on this topic in “Challenges”

# Challenges to overcome



## Clinical Decision Support

- Need to build individual genomic indicators with CDS
- Need to update regularly
- Need to educate providers across the system (current medical education does not cover genetics extensively)



## Health Information Exchange

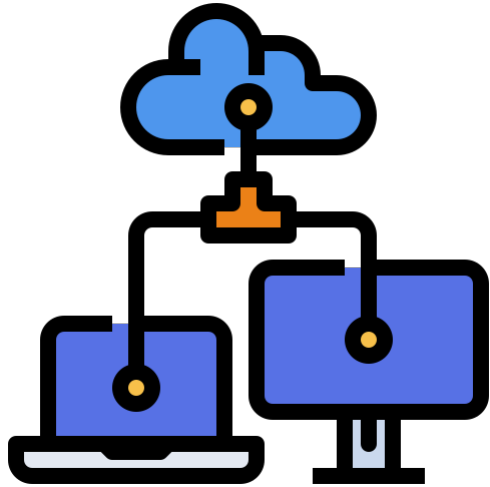
- This \*could\* provide the infrastructure to have important genetic information follow patients throughout their healthcare journey
- Need genetic data to be shared- currently not always part of HIE
- Need to educate providers across systems



## Genome Annotations

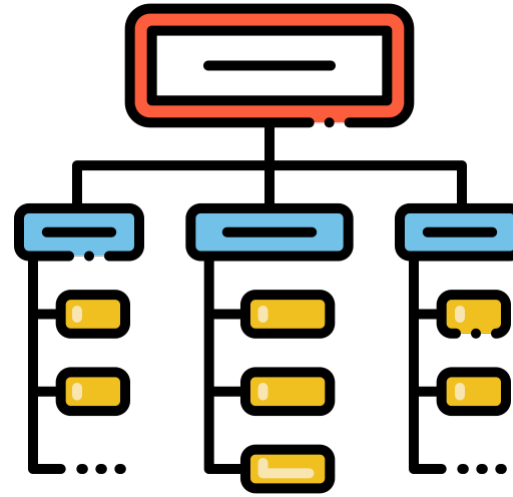
- Knowledge about genome function changes regularly
- Need to update annotations and interpretations
- Need infrastructure to alert providers

# Challenges to overcome



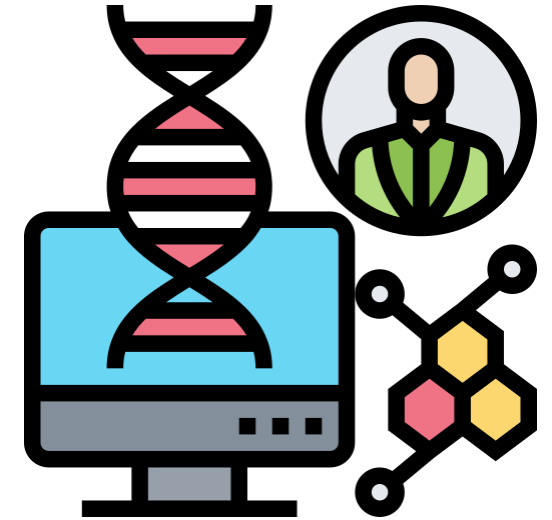
## Compute limitations

- Cloud storage costs and egress costs are high
- These costs may exacerbate health disparities



## Phenotype ontology/standards

- HPO (or any ontology) is not well supported in EHR
- Broad ontology adoption is lacking



## Genomic annotation standards

- There are great standards for genomics (e.g., GA4GH)... but they are poorly adapted to broad clinical standards yet
- Similarly true for functional annotations

# Future Needs: A strategy to address gaps and barriers

Chart Review

Encounters Labs Imaging Procedures Cardiology Medications Precision Medicine Other Orders Episodes Letters Notes Media LDAs Referrals Misc Reports

Preview Refresh (10:39 AM) Select All Deselect All Review Selected Lab Flowchart Flowchart Apply Default Sorting Route Load Remaining Add to Bookmarks Immune Health Report

Filters Hide Canceled

Medications and orders also exist in active treatment plans: ONCOLOGY SUPPORTIVE CARE PLAN

Date	Description	Status
Yesterday	CPD ORDER	Final result
07/09/2019	PENN PRECISION MEDICINE TESTING CNS	Final result
07/08/2019	PENN PRECISION MEDICINE TESTING GYN	Pending
06/27/2019	PENN PRECISION MEDICINE TESTING HEAD AND NECK	Ordered
06/21/2019	PENN PRECISION MEDICINE TESTING HEAD AND NECK	Ordered
06/21/2019	PENN PRECISION MEDICINE TESTING CNS	Ordered
06/10/2019	PENN PRECISION MEDICINE TESTING - RECTAL CANCER	Ordered
06/10/2019	PENN PRECISION MEDICINE TESTING HEAD AND NECK	Ordered
04/15/2019	PENN PRECISION MEDICINE TESTING GU	Pending
03/12/2019	PENN PRECISION MEDICINE TESTING GU	Pending
02/21/2019	PENN PRECISION MEDICINE TESTING GU	Pending
1 Year Ago		
04/25/2018	PENN PRECISION MEDICINE TESTING CNS	Ordered
04/25/2018	PENN PRECISION MEDICINE TESTING CNS	Ordered
04/25/2018	PENN PRECISION MEDICINE TESTING CNS	Ordered
04/25/2018	PENN PRECISION MEDICINE TESTING CNS	Ordered
03/22/2018	PENN PRECISION MEDICINE TESTING NSCLC	Ordered

Results

CPD ORDER [CPDOORDER] (Order 397921)

Result Information

Status: Final result (Resulted: 7/16/2019)

Patient Information

Patient Name: Zzepic, DAD (330009978) Sex: Male DOB: 10/5/1959

Order-Level Results - 07/10/2019:

Scan on 7/17/2019 10:38 AM by Thai, Mark Genetic Testing - Final Report

Result Read / Acknowledged

Acknowledge result

No acknowledgement history exists for this order.

7/17/2019 10:38 AM - Thai, Mark

Additional Information

Specimen ID	Specimen Source	Bill Type	Client ID
	BLOOD [B0]		

Specimen Date Taken	Specimen Time Taken	Specimen Received Date	Specimen Received Time	Result Date	Result Time
				Jul 16, 2019	

Lab and Collection

CPD ORDER (Order: 397921) - 7/16/2019

© 2020 Epic Systems Corporation. Used with permission.

