

EMR Integration of Genomic Results and Automated Decision Support

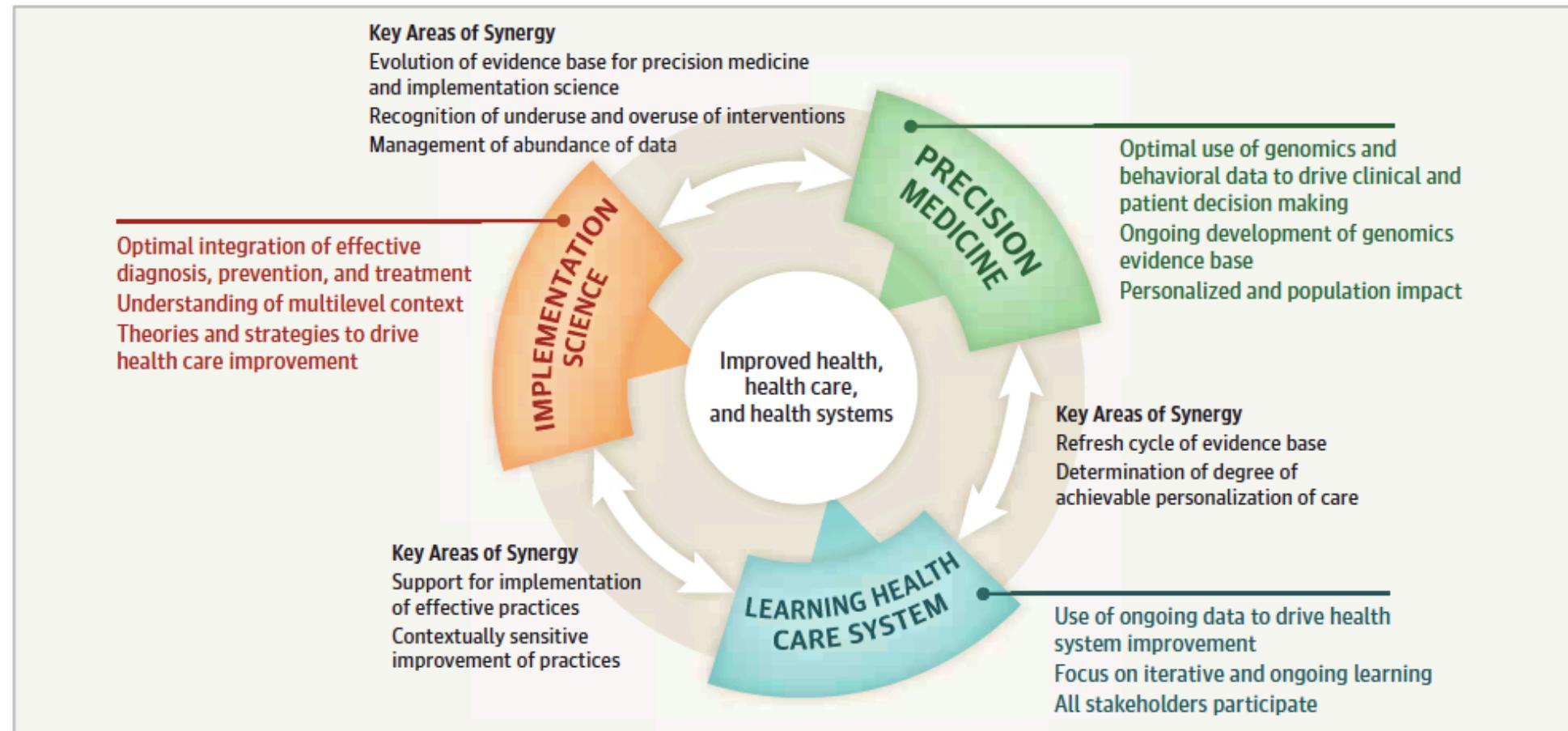
Sandy Aronson & Casey Overby Taylor

eMERGE EHR integration working group co-Chairs

eMERGE & Beyond: The Future of Electronic
Medical Records (EMR) and Genomics
October 30th, 2017
Rockville, MD

Research and clinical practice co-exist to enable ongoing learning and evidence development

Figure. Contributions of Implementation Science, Learning Health Care System, and Precision Medicine



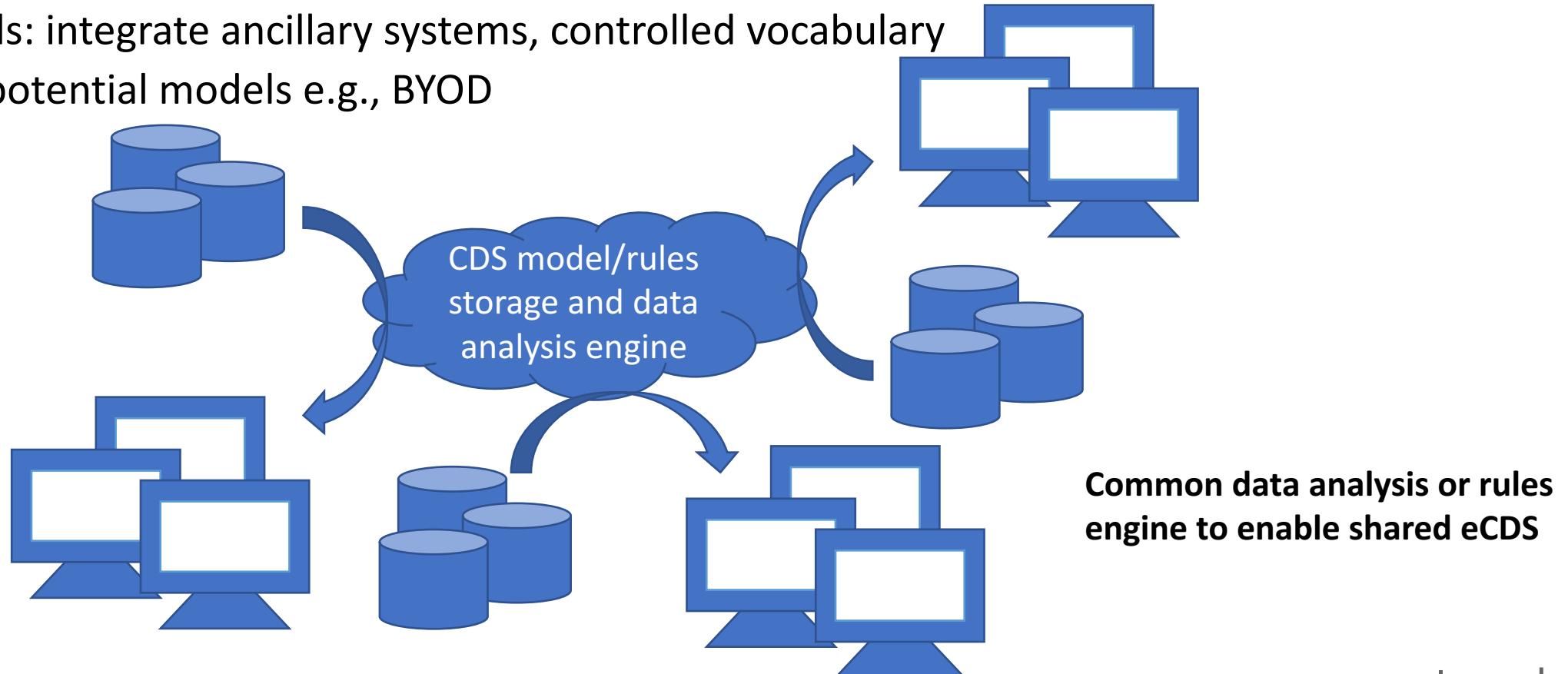
(Chambers, Feero, Khoury. JAMA. 2016)

Clinical and translational informatics challenges in a learning healthcare system

- Reproducibility
 - CDS at multiple institutions
- Timing & data quality
 - Upstream patient risk screening
- Diversity
 - Digital strategies to recruit populations while also minimizing sample disproportionality
- Replicability
 - Genomic variant interpretations may change
 - Clinical guidelines may change

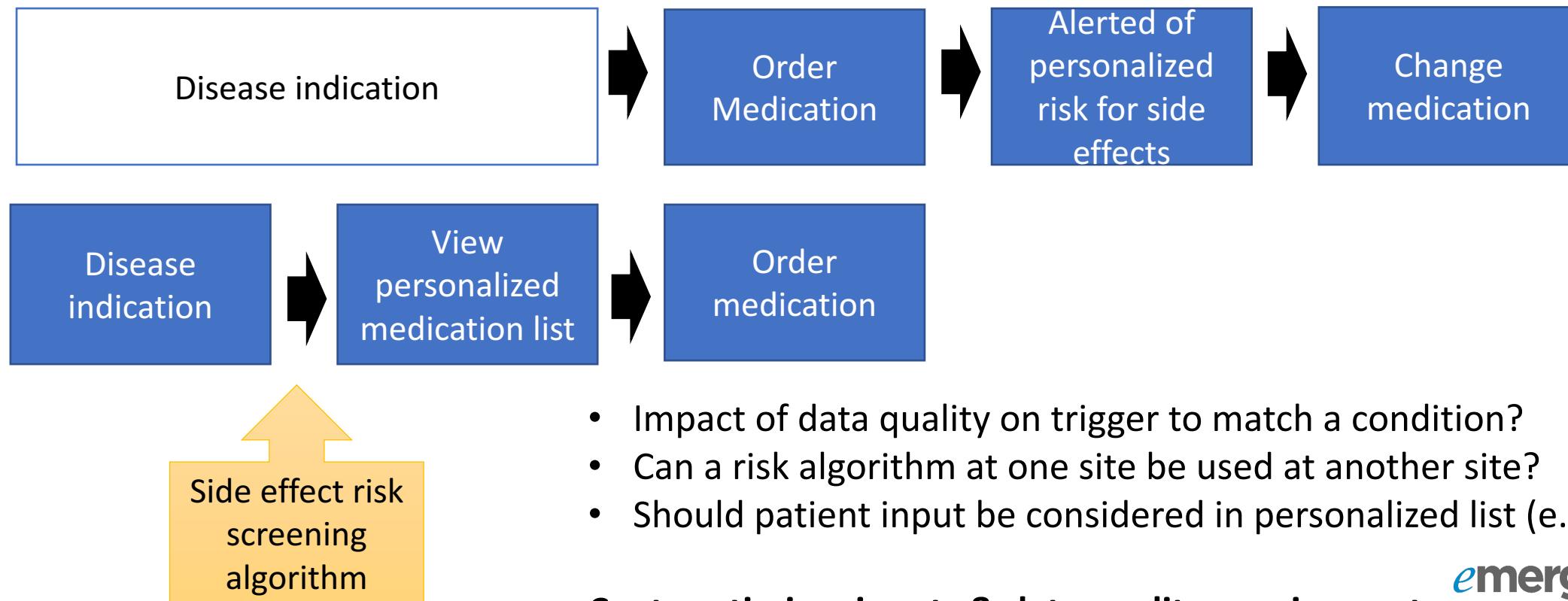
Reproducibility: implications for clinical and research practice

- CDS at multiple institutions
 - Data is already in the EHR and ancillary systems and can potentially be acted upon
 - Standards: integrate ancillary systems, controlled vocabulary
 - Several potential models e.g., BYOD



Timing, inputs & data quality: implications for clinical and research practice

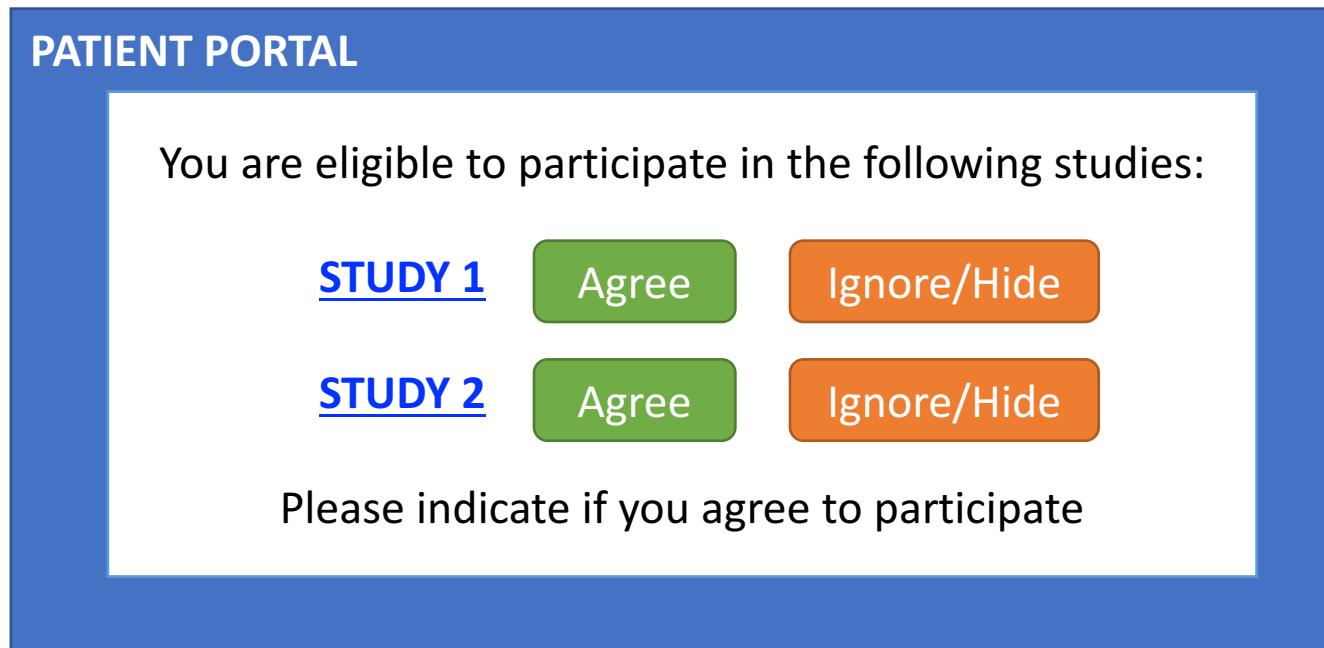
- CDS differ in timing that support is provided (before, during and after the clinical decision is made)
- Upstream patient risk screening with clinical decision support



Capture timing, inputs & data quality requirements

Diversity: implications for clinical and research practice

- Digital strategies to recruit populations while also minimizing sample disproportionality



- Who are we missing?

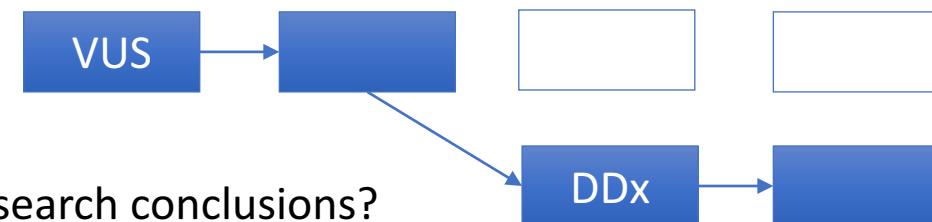
Support a range of recruitment strategies and multiple levels of health literacy

Replicability: implications for clinical and research practice

- **Clinical use example:** A 43-year-old female patient with a personal and family history of breast cancer undergoes sequencing analysis of BRCA1 and BRCA2. A missense VUS is reported in BRCA1 and reported as a VUS. Therefore **it is not recommended that testing for this variant be used to determine risk in relatives of this patient. Nine months later, a revised laboratory report reclassifies the variant as pathogenic based on additional evidence. The EHR is updated to now follow the recommendations found in Diagnostic and Actionable categories.**

eMERGE II & CSER (*Shirts et al. 2015*)

- What changes have occurred?
- When were changes made?
- How do changes influence retrospective data analyses?
- What is the impact of changes on the patient and on research conclusions?



Tools to track provenance are needed

Clinical & Translational Informatics Scope Considerations

Dimension	Nature of Scope	Ways to Limit Scope
Reproducibility	Creating CDS for use at multiple sites	Agreed upon standards and controlled vocabularies to integrate data from EHRs and ancillary systems Agreed upon model to enable using the same CDS at multiple sites
Timing, inputs & data quality	Upstream patient risk screening	Specify timing for CDS Specify inputs & data quality requirements for the use of EHR phenotypes for risk screening
Diversity	Using digital strategies to enable the recruitment of diverse populations	Support a range of digital strategies based upon site needs
Replicability	Accounting for evidence changes when replicating previous research or clinical interpretations	Choose standards & services that can be accessed across the network and that document provenance

These considerations are not new. Existing approaches should be assessed to determine if they are sufficient, should be improved, etc

Disclosure

Sandy Aronson works for Partners HealthCare which receives royalties on the sale of GeneInsight software which performs functions similar to some of the functions described in this presentation.

Sandy Aronson's team also receives funding from Persistent Systems to develop an open source Health Innovation Platform as well as open source SMART on FHIR apps that run on the platform.

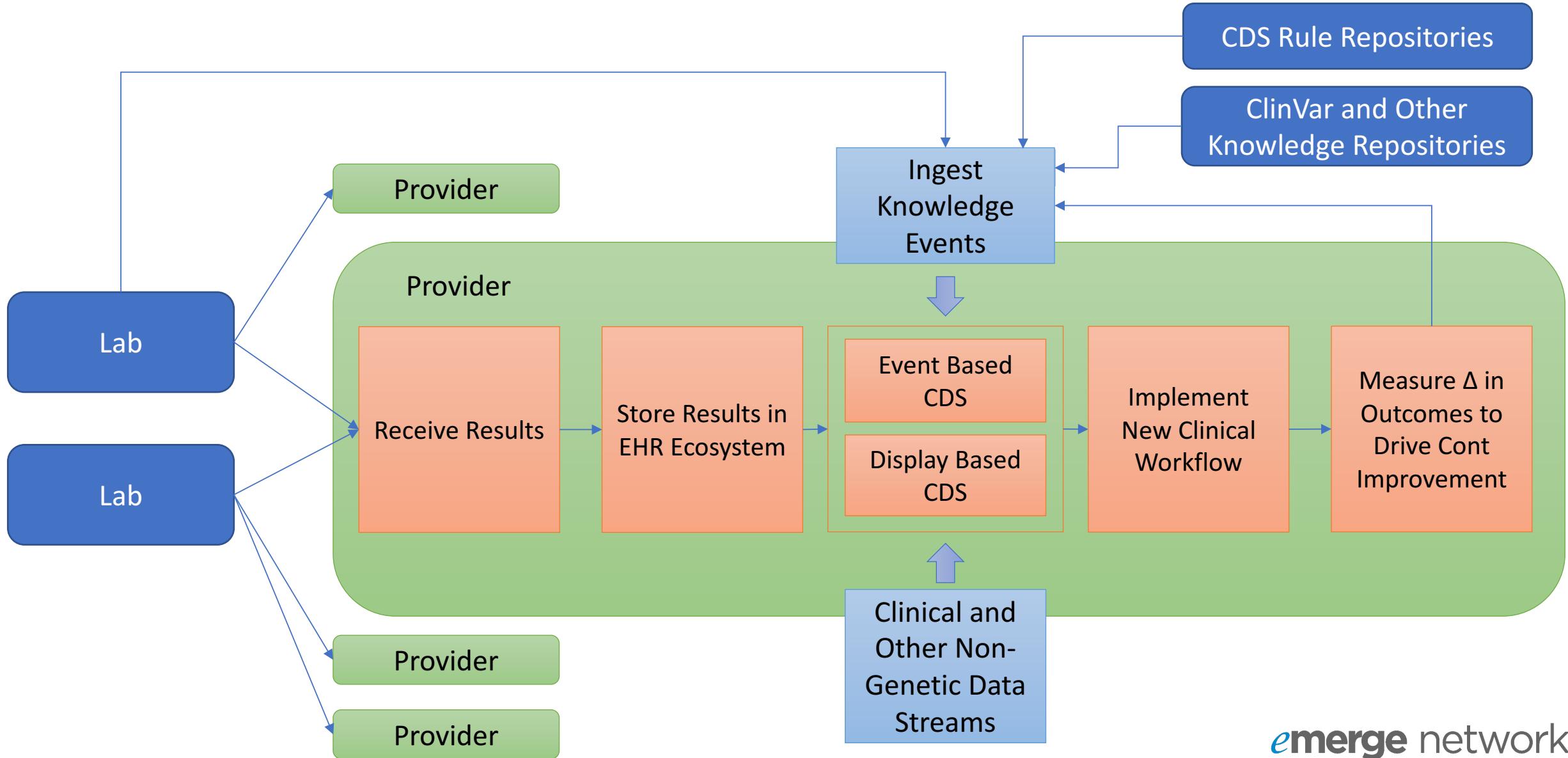
Core Contentions

- Demonstrating uses of genetics that produce clinical and/or economic value are important to the clinical genetics community
- Electronic Clinical Decision Support (CDS) will be a critical to the widespread adoption, use and safety of many clinical genetic techniques
- eMERGE could greatly accelerate the development and deployment of genetic aware CDS

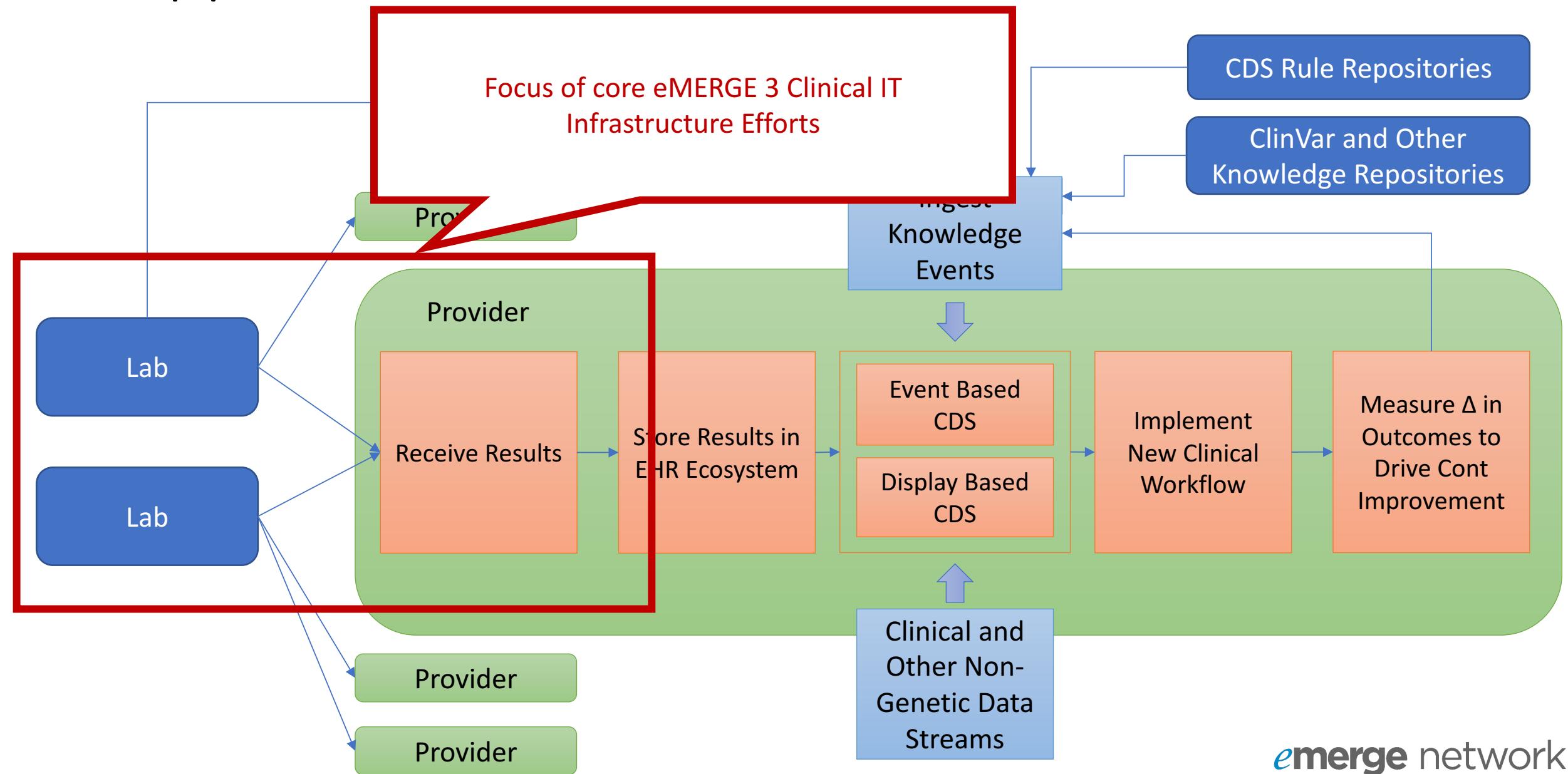
However

- Development and deployment of CDS is very different than developing research IT infrastructure
- If eMERGE chooses to pursue CDS, appropriately focusing resources will not only be important for success but also for patient safety and ensure we “do no harm”
- There are many options for focused resource deployments that could be helpful

IT Support for Clinical Genetic Workflow Refinement



IT Support for Clinical Genetic Workflow Refinement



Considerations for eMERGE 4

- Display based (SMART on FHIR) vs Event Based (CDS Hooks) eCDS
- Generalized Genetic vs Clinical Condition Specific Functionality
- Site Specific Objectives vs Network Based Objectives
- Foundation Building vs End-to-End Value Focused

Event Based Clinical Scenario Specific eCDS

The image displays two consecutive screens from a clinical decision support system (eCDS) named "Discern".

Top Screen (PGEN TESTING):

- Title:** PGEN TESTING
- Text:** TPMT genotype test is recommended before using a thiopurine (mercaptopurine, thioguanine, and azathioprine). A TPMT genotype test does not appear to have been ordered for this patient.
- Alert Action:**
 - cancel
 - continue
- Add Order for:**
 - TPMT Genotype -> T.N, Collect Now, Blood, DNCE
- Buttons:** History, Add Info, OK

Bottom Screen (WARNING):

- Title:** WARNING
- Text:** Based on the genotype result, this patient is predicted to have intermediate TPMT activity. The patient is at risk for myelosuppression with normal doses of 6-mercaptopurine. Consider starting 6-mercaptopurine doses at 30 - 70% of the normal dose. Please consult a clinical pharmacist or review the pharmacogenetics tab for more information.
- Alert Action:**
 - Cancel entry
 - Dose altered accordingly
 - Modify
- Buttons:** History, Add Info, OK

Genetic Specific Display Based eCDS

ClinGen EHR App - Interpretations of patient reported variants

Doe, Jane 62yr, Female, 1/1/1954

NM_007294.3(BRCA1):c.5503C>T (p.Arg1835Ter) FINDINGS

Source	Disease	Zygosity/Inheritance	Significance (reviewed)
GeneDx	Hereditary breast and ovarian cancer syndrome	Heterozygous	Pathogenic (5/17/16)
ClinVar ★★★★☆	Hereditary breast and ovarian cancer syndrome	Autosomal dominant	Pathogenic (4/22/16)

NM_000179.2(MSH6):c.3632T>C (p.Leu1211Pro) FINDINGS

Source	Disease	Zygosity/Inheritance	Significance (reviewed)
Ambry Genetics	Lynch syndrome 1	Heterozygous	<u>Uncertain significance</u> (8/20/15)
ClinVar ★★★★☆	Lynch syndrome 1	Autosomal dominant	Pathogenic (11/24/15)

UNMATCHED VARIANTS

Variant	Disease	Zygosity	Significance (reviewed)
NM_170707.3(LMNA):c.1303C>T (p.Arg435Cys)	Hutchinson-Gilford progeria syndrome	Heterozygous	Likely pathogenic (4/20/13)
NM_004004.5(GJB2):c.670A>C (p.Lys224Gln)		Heterozygous	Uncertain significance (11/25/15)

KEY

- Match
- Potential discrepancy
- Discrepancy (underlined)
- Additional details

Prototype Developed by
Partners HealthCare and
Geisinger Teams

Condition Specific Display Based eCDS

Platelet App v0.10.0

Select Patient Home Administration Signout

Patient [REDACTED]
DOB [REDACTED] Age [REDACTED] Sex [REDACTED]
MRN [REDACTED]
ABO RH Type A Positive
Last Platelet Count 4 K/uL Today @ 09:30
Threshold 10k Changed my mind
[CHANGE THRESHOLD](#)
[History](#)

cPRA (anti HLA-A/B only) 99.2% [REDACTED]

HLA Type [REDACTED]
Alleles [REDACTED]
AB Screening Date [REDACTED]
anti-HLA-A [REDACTED]
anti-HLA-B [REDACTED]
Unacceptable Platelet Antigens [REDACTED]

Blood Bank Inventory 0 Matches

Match Quality	Platelet Unit#	ABO RH	HLA Type	Expires (023:59)	Status
-	W120217403475	PBT100	[REDACTED]	[REDACTED]	IN
-	W120217403477	A NEG	[REDACTED]	[REDACTED]	IN
-	W120217403477	A NEG	[REDACTED]	[REDACTED]	IN
X	W120217403485	A POS	[REDACTED]	[REDACTED]	IN
X	W120217403451	B POS	[REDACTED]	[REDACTED]	IN
X	W120217403451	B POS	[REDACTED]	[REDACTED]	IN
X	W120217403451	B POS	[REDACTED]	[REDACTED]	IN

Platelet Count & Procedures Last Platelet Count 4 K/uL Today @ 09:30

Views: 1 Week 1 Month 3 Months 6 Months 1 Year Prior Year

Platelet Count (K/uL)

08-26 10-24 09-14 10-22 09-59 07-04 12-03 07-46 13-29 09-47

■ Platelet Counts ■ Transfusions ■ HLA Antibody Screen

Whiteboard

Enter note here... [POST](#)

Pt is getting XM'd pts instead of HLA mx'd

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Acknowledgements View Demo

Bill Layne
Rick Kauffman
HIP Development Team

Specific Options

Option	Benefit
Develop Open Source SMART on FHIR App for Genetic Results Maintenance and Implement Across Multiple Sites	<ul style="list-style-type: none">Drive development and adoption of clinical genetic result and knowledge standards.Get genetic data into the EHR ecosystem in structured form for use in other forms of eCDSAddress the problem of keeping clinicians up to date as genetic knowledge evolves
Implement DIGITizE Guide Rules Across Multiple Sites	<ul style="list-style-type: none">Demonstrate capabilities of genetic aware event based eCDSImprove patient safety in specific clinical areas
Develop Display Based CDS for a Specific Clinical Area	<ul style="list-style-type: none">Demonstrate ability to integrate genetic data into decision making within a specific clinical areaBuild support that facilitates new clinical workflowLikely more amenable to clinical and economic outcome studies
Build de-identified case and/or knowledge exchange network to support any of the above	<ul style="list-style-type: none">Further drives standards developmentOpens possibility for cross site continuous learning

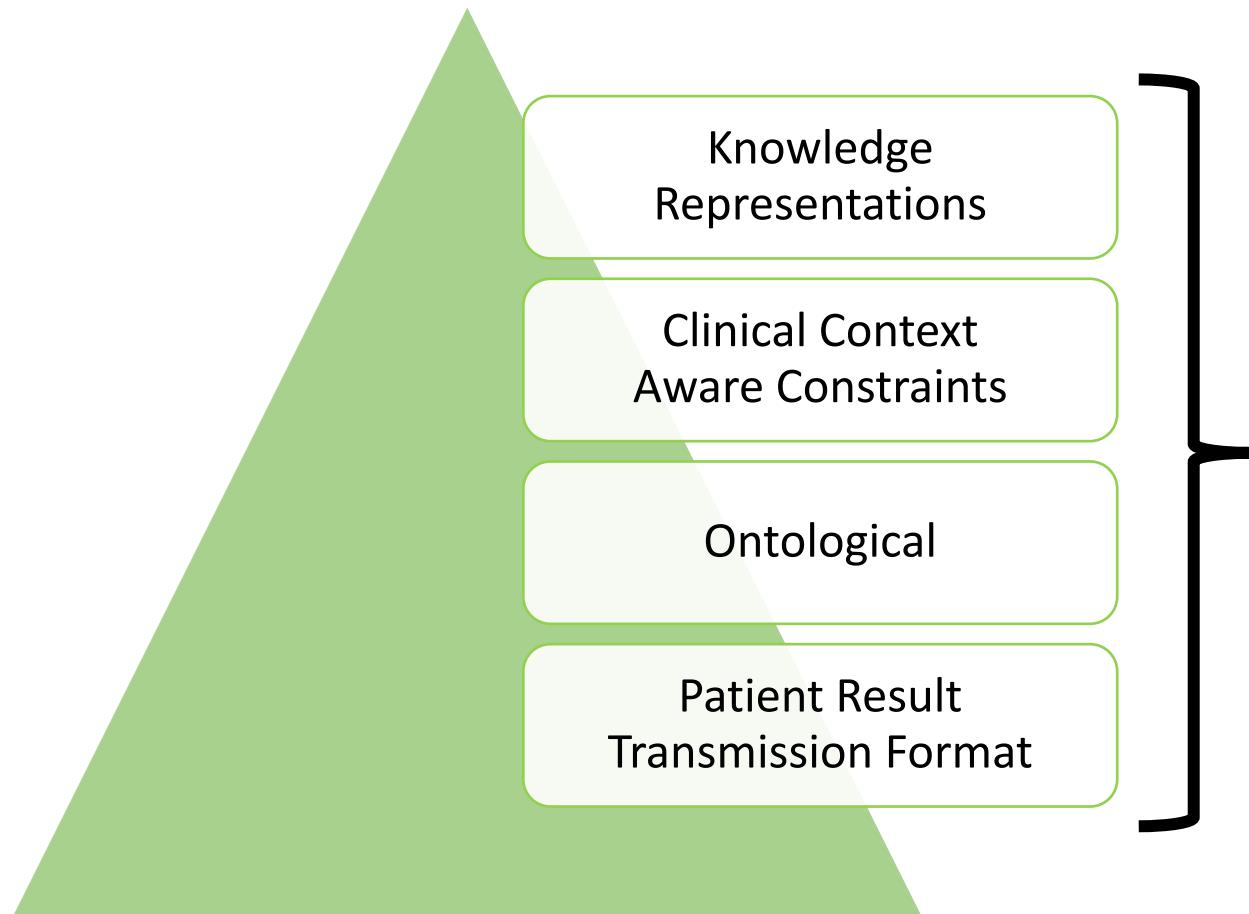
End to End IT Support for Clinical Genetic Workflow Involves Enormous IT Scope

Reproducibility, data quality, diversity, and replicability will be key considerations to generate usable data for CDS

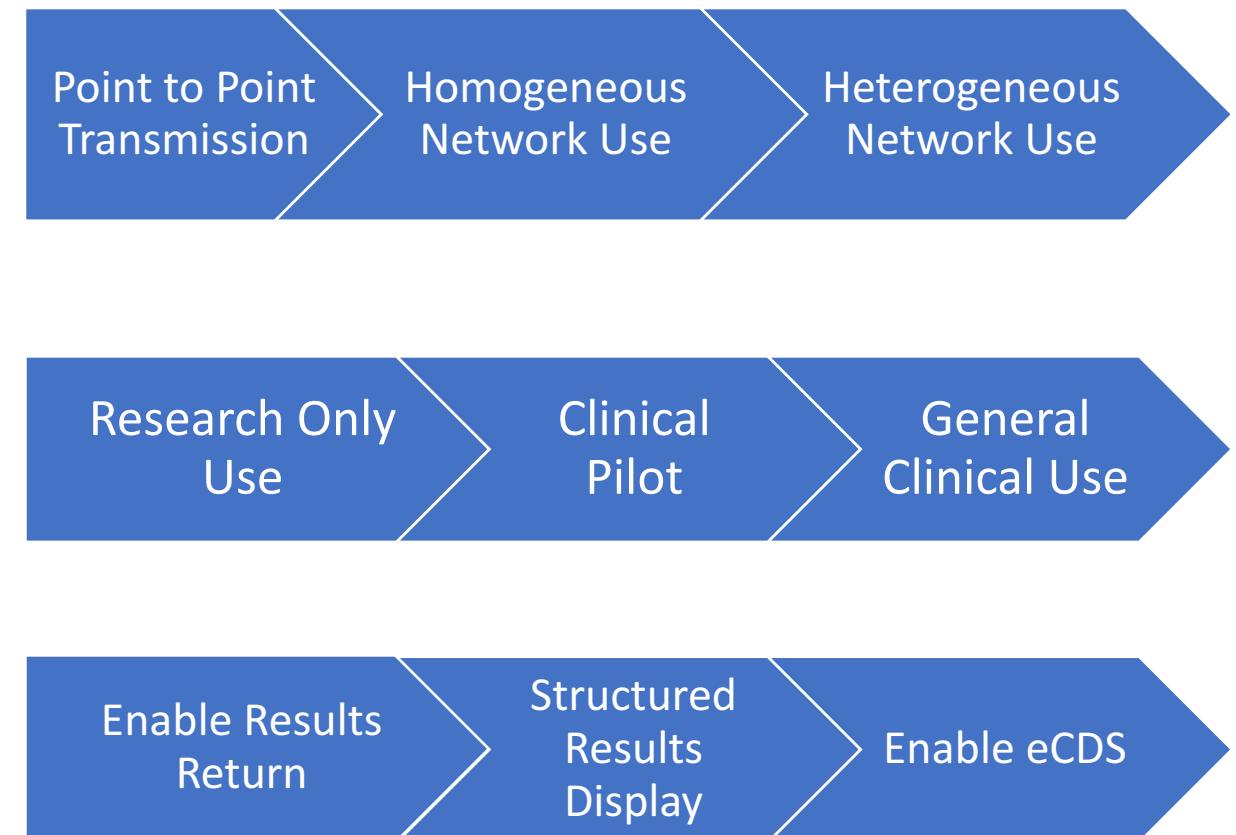
It will be critical for eMERGE IV to focus its resources on the scenarios and processes it would most like to support.

Backup

Standards



Levels of Refinement



Why is eCDS Deployment So Resource Intensive?

Issue	Implication
Clinicians resist functionality that does not fit their workflow like a glove	Lots of User Experience design expertise and iteration required
Corner cases can harm patients	Lots of validation required
The clinical data logic depends upon often not readily available	Often requires support from IT groups throughout the enterprise
Usually requires enterprise integration	Integrating with multipurpose enterprise systems creates support and enhancement complexity