IT Infrastructure Required to Scale Personalized Medicine

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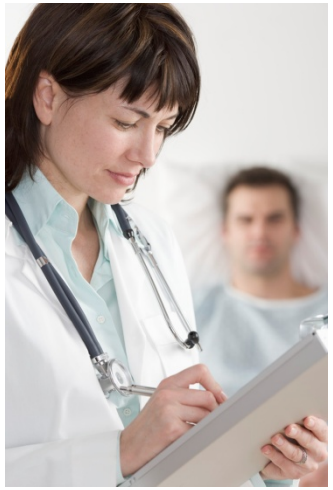
Our Goal

To build information infrastructure that improves patient care by enabling clinicians to effectively leverage increasing amounts of genetic and genomic data

Genetics in Current Clinical Practice

Clinician Identifies Clinical Concern



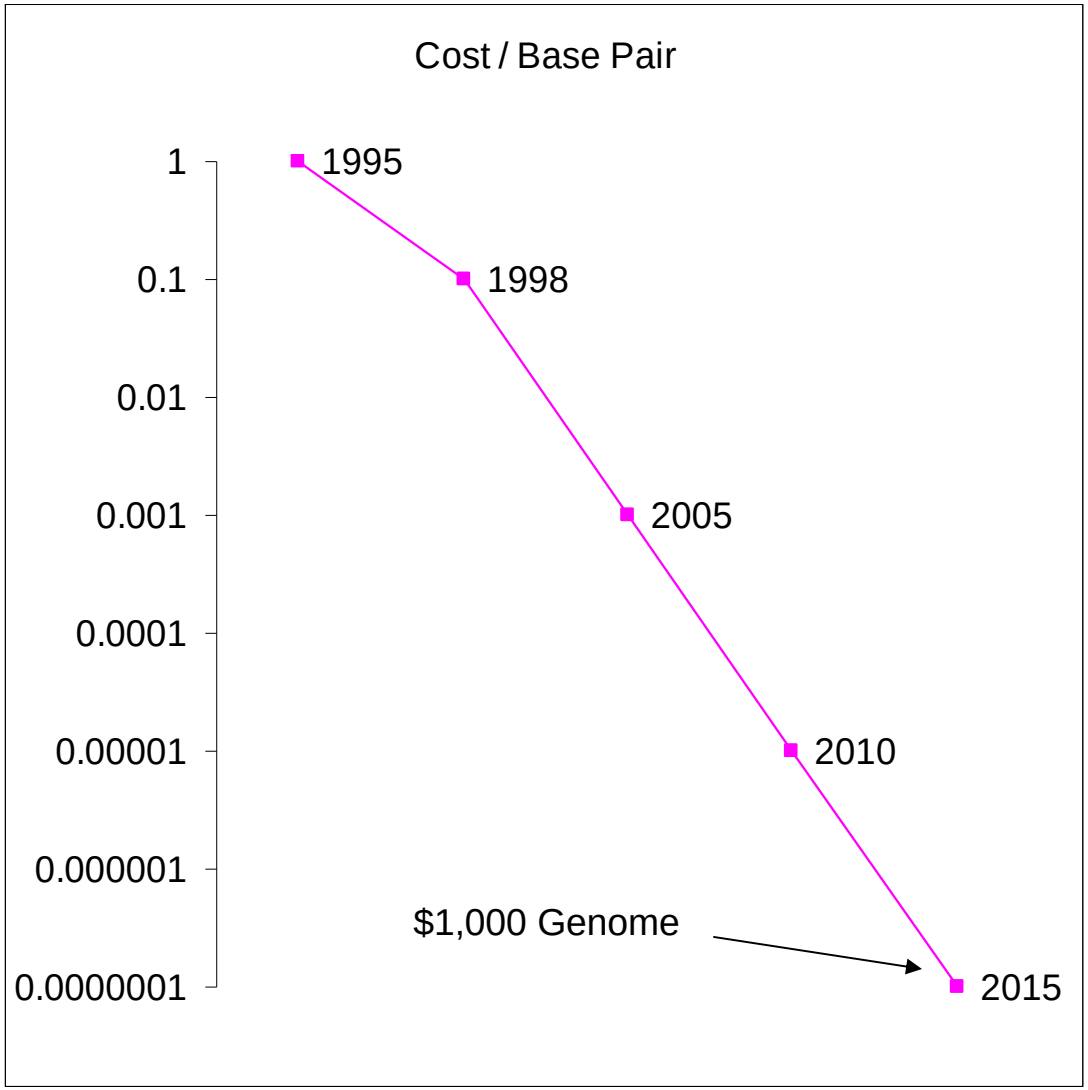
Specific Genetic Test Ordered

Targeted Genetic/Genomic Test Conducted

Medical Professional Writes Report Interpreting Result

Clinician Reviews Report and Applies Content to Clinical Decisions

Cost of DNA Sequencing



Data adopted from:

Mutation Research 573 (2005) 13–40

ww

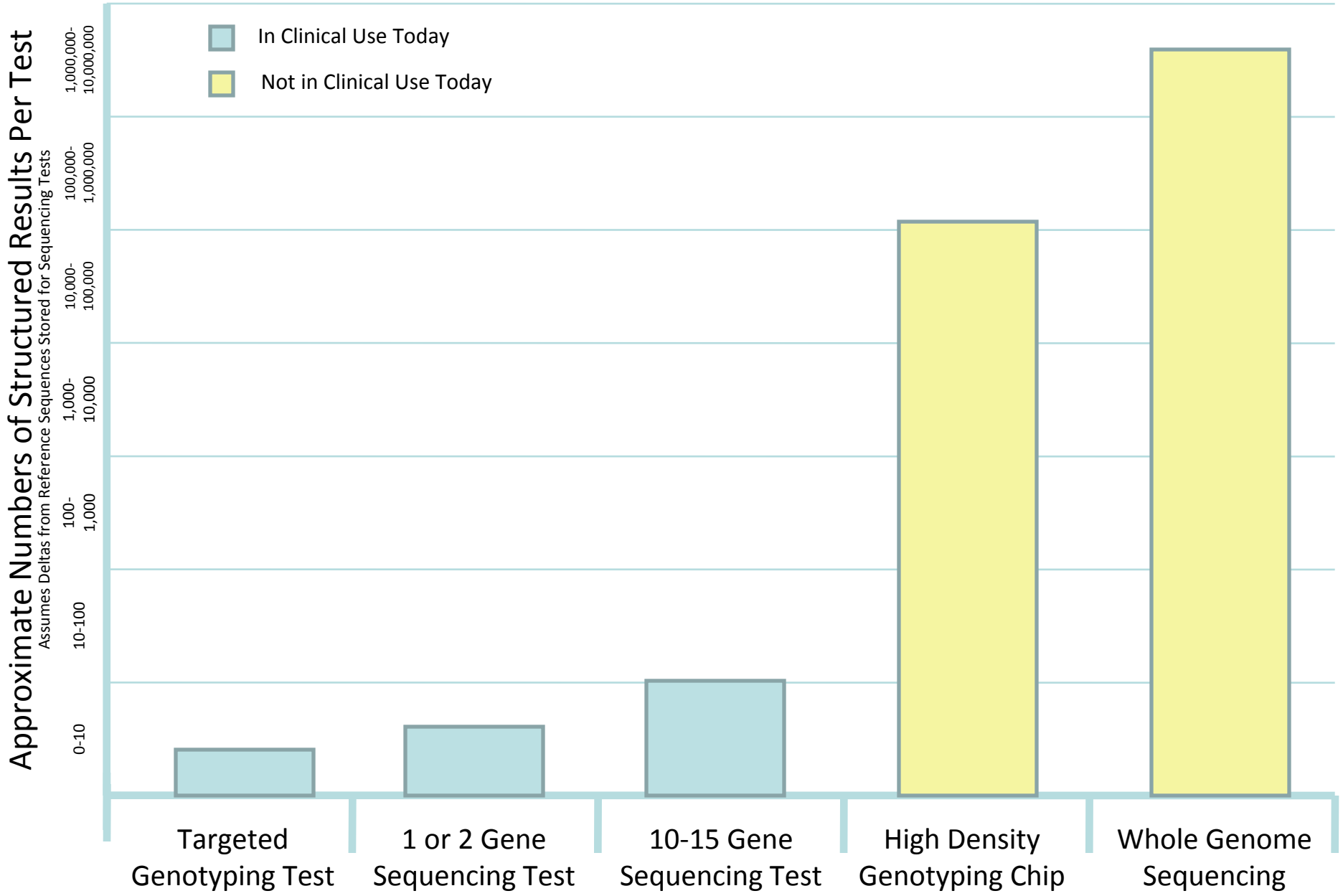
Community address: wv

Review

Advances in sequencing technology

Eugene Y. Chan *

Evolution of Genomic Technologies

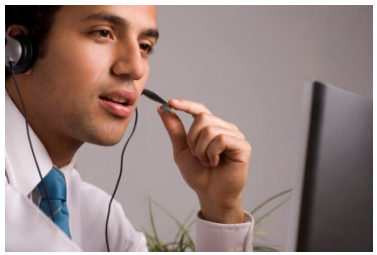


Broad Spectrum Genotyping Model (Not Current Clinical Practice)

Broad Spectrum Test Ordered for General Use

Large Portions (or all of) Patient's DNA Sequenced / Genotyped

Hundreds of Thousands to Millions of Variations for Each Patient Stored in a Repository



Repository Routinely Accessed to Understand Implications of Patient's Genome

Will be Challenging to Properly Support in the Clinic

4 – 5 Million

Estimated Number of Differences Between Each Person's DNA and a Universal Reference Sequence

(Levy S, Sutton G, Ng PC, Feuk L, Halpern AL, et al. (2007) The diploid genome sequence of an individual human. PLoS Biol 5(10): e254. doi:10.1371/journal.pbio.0050254)

9,582

OMIM Entries Either Added or Updated in 2007

(OMIM Website)

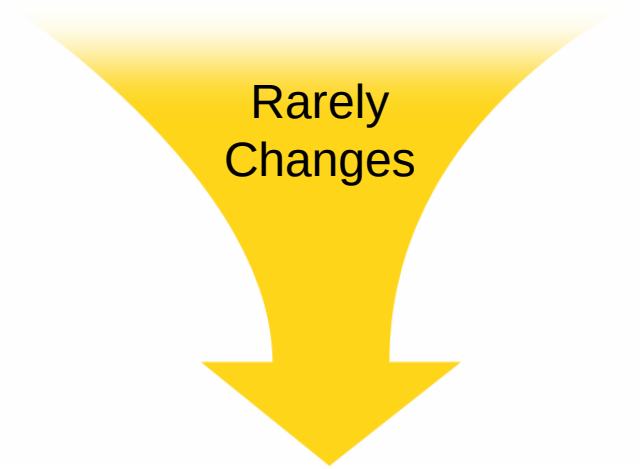
14.7 Minutes

The Medium Amount of Time a Clinician Has to Spend with Each of Their Patients

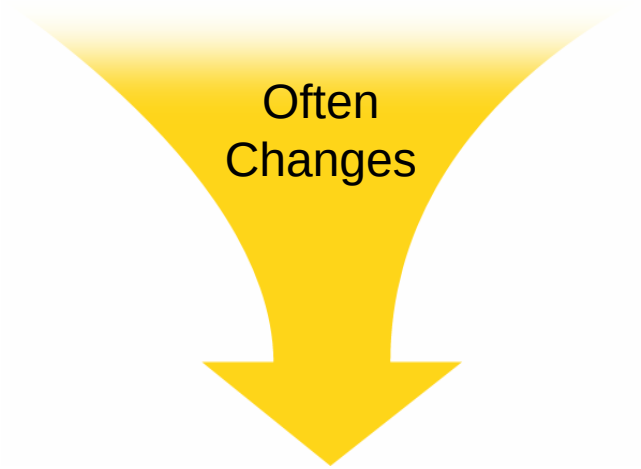
(Middleton KR, Hing E. National Hospital Ambulatory Medical Care Survey: 2004 outpatient department summary. *Adv Data. Jun 23 2006(373):1-27.)*

Genomic Contributions to Clinical Decision Making

What Genetic Variations Are Present in this Patient?

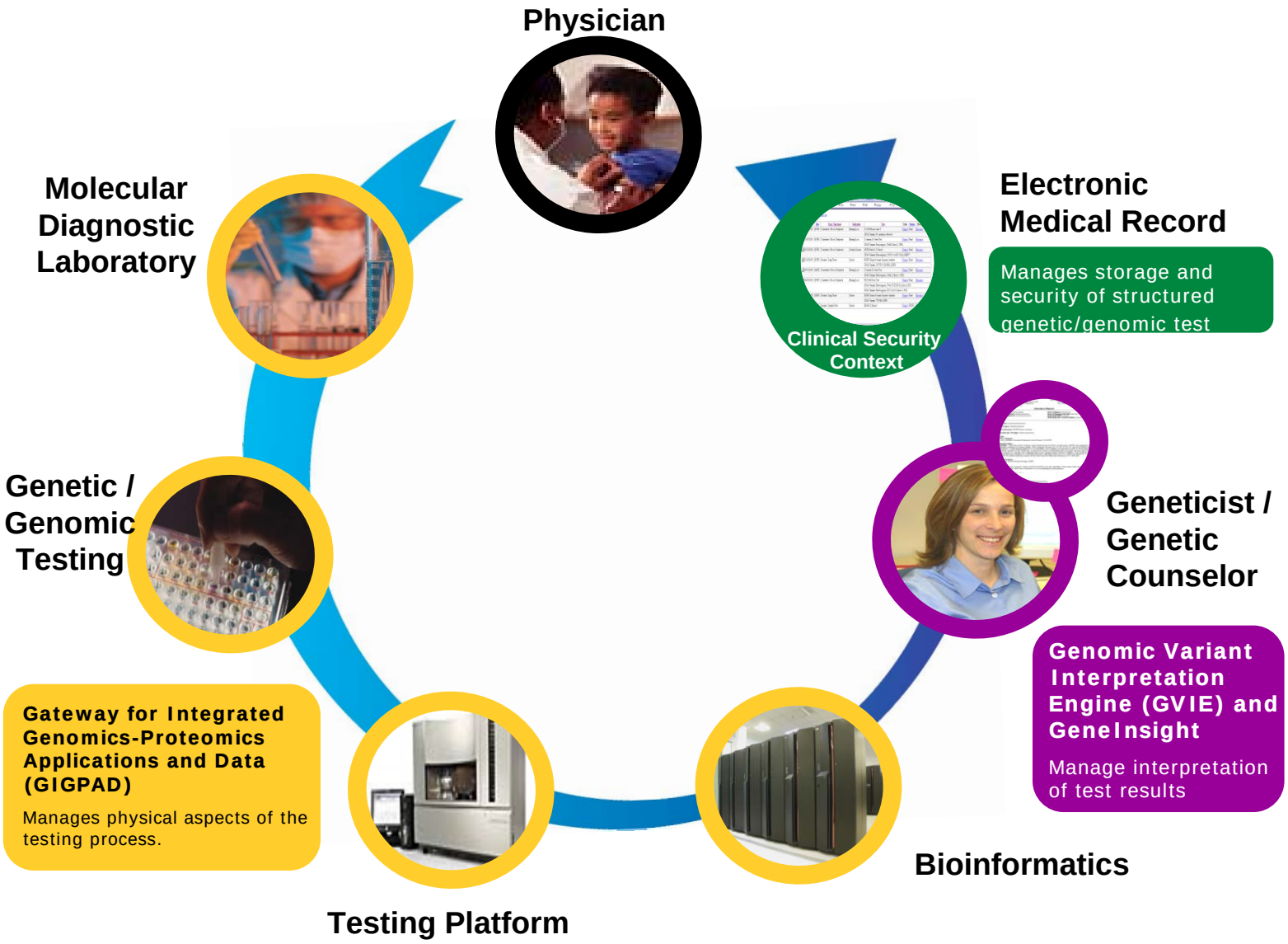


What is the Significance of the Variants Identified

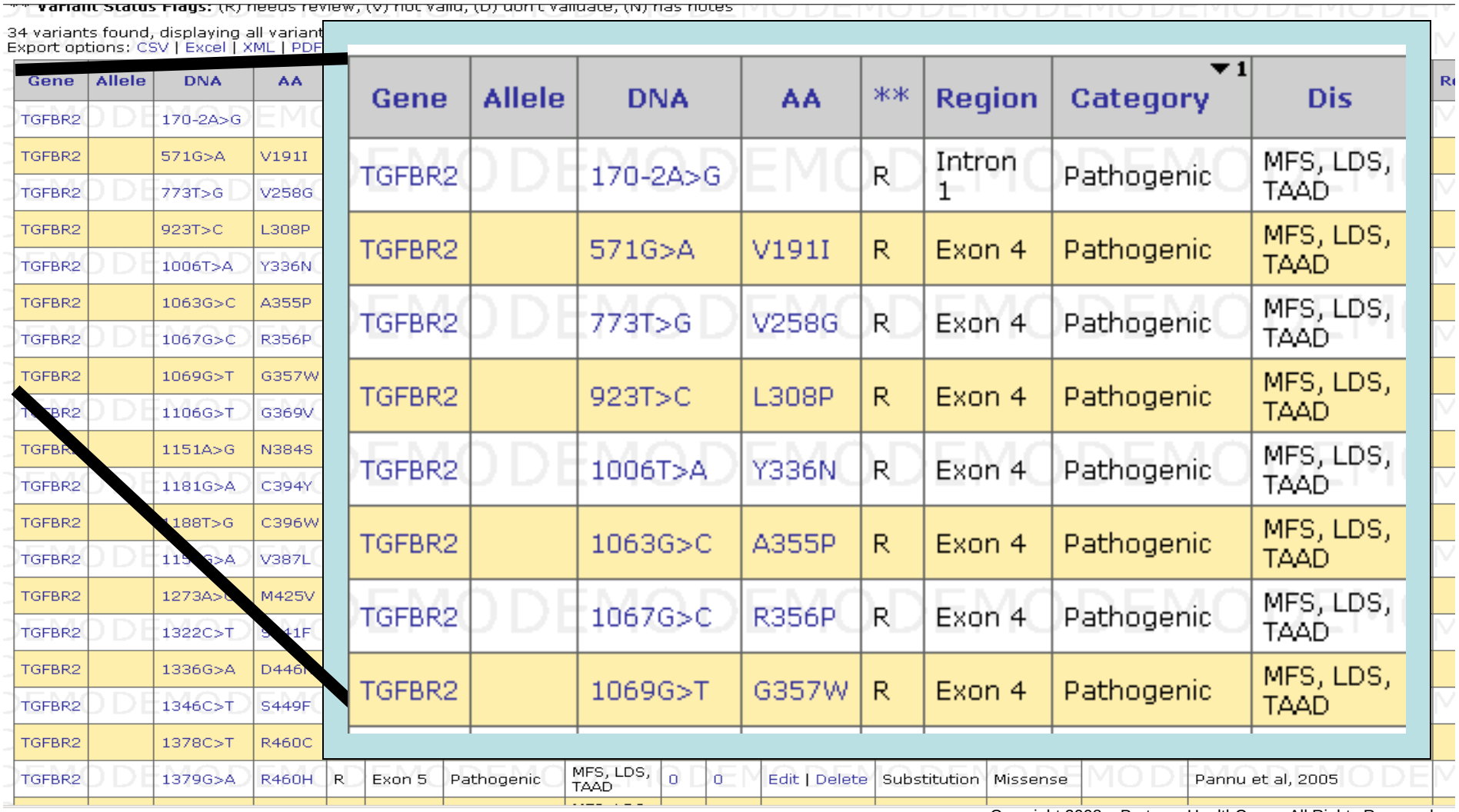


Genetically Informed Decision Making Process

Supporting the Current Clinical Model



GeneInsight - DNA Variant Knowledgebase



GVIE

Variants Identified In Patients

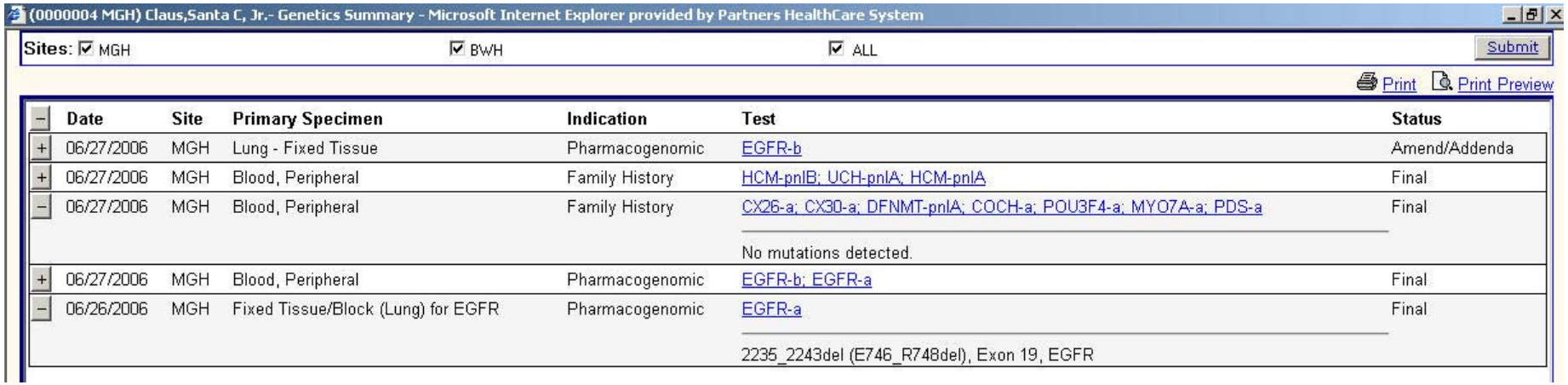
GVIE

Laboratory for Molecular Medicine
Center for Genetics and Genomics

MOLECULAR DIAGNOSTICS REPORT

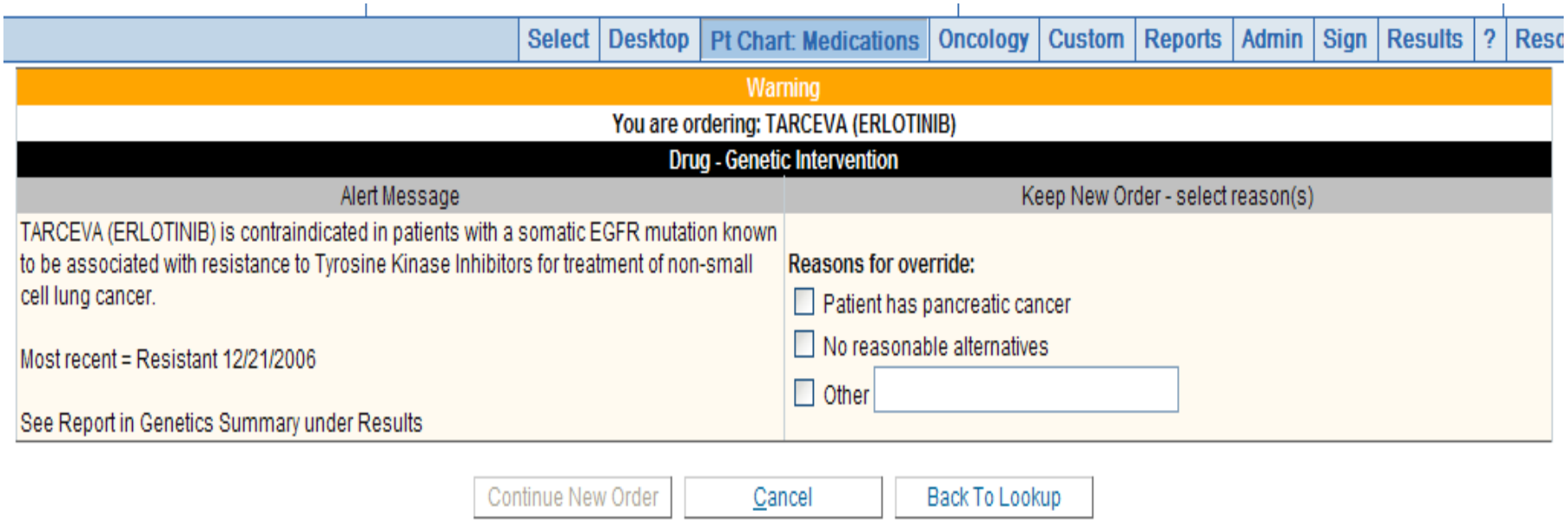
Gene	Allele	DNA	AA	**	Region	Category	Dis
TGFBR2		170-2A>G		R	Intron 1	Pathogenic	MFS, LDS, TAAD
TGFBR2		571G>A	V191I	R	Exon 4	Pathogenic	MFS, LDS, TAAD
TGFBR2		773T>G	V258G	R	Exon 4	Pathogenic	MFS, LDS, TAAD
TGFBR2		923T>C	L308P	R	Exon 4	Pathogenic	MFS, LDS, TAAD
TGFBR2		1006T>A	Y336N	R	Exon 4	Pathogenic	MFS, LDS, TAAD
TGFBR2		1063G>C	A355P	R	Exon 4	Pathogenic	MFS, LDS, TAAD
TGFBR2		1067G>C	R356P	R	Exon 4	Pathogenic	MFS, LDS, TAAD
TGFBR2		1069G>T	G357W	R	Exon 4	Pathogenic	MFS, LDS, TAAD

EHR

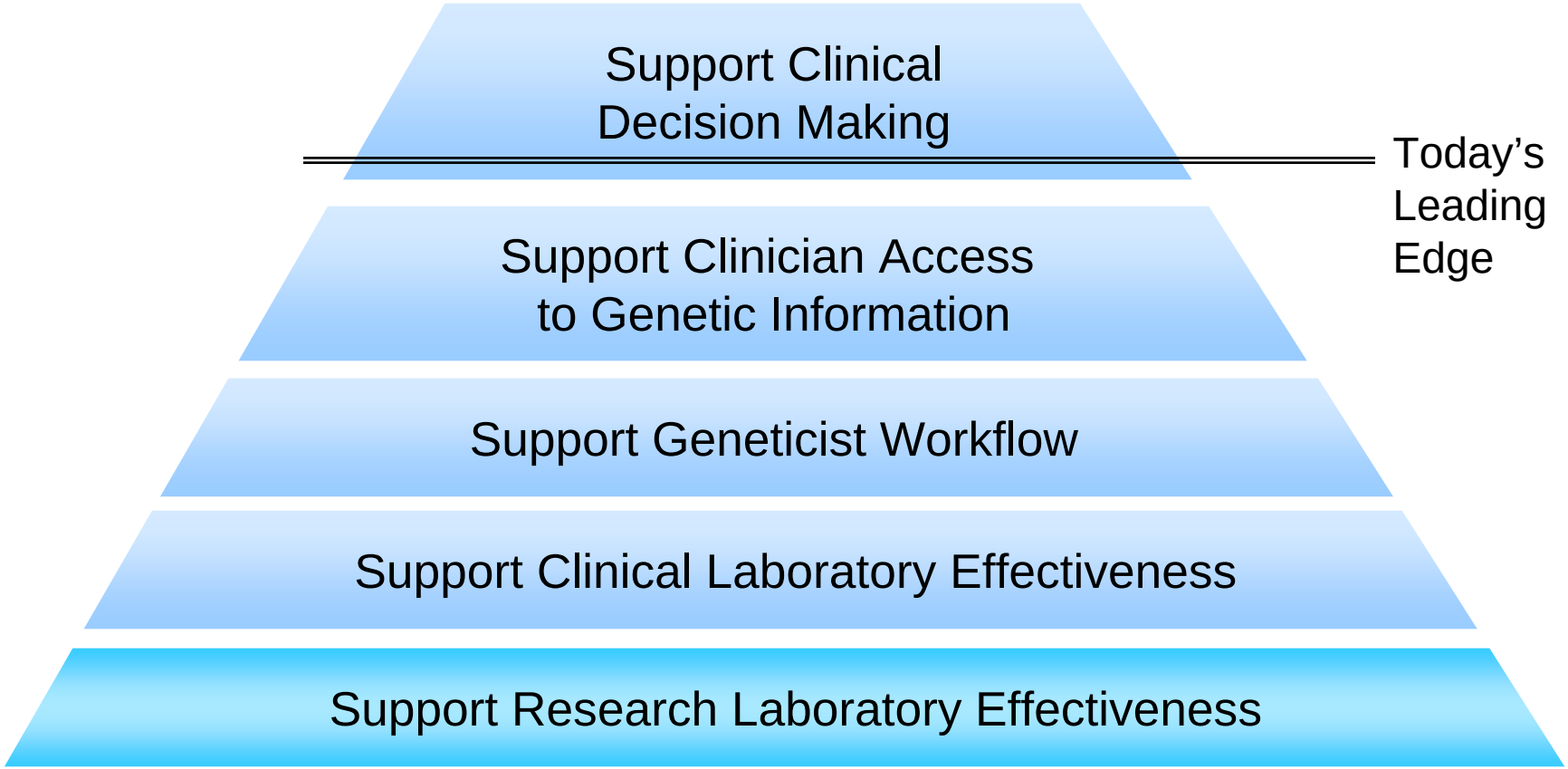


	Date	Site	Primary Specimen	Indication	Test	Status
+	06/27/2006	MGH	Lung - Fixed Tissue	Pharmacogenomic	EGFR-b	Amend/Addenda
+	06/27/2006	MGH	Blood, Peripheral	Family History	HCM-pnlB; UCH-pnlA; HCM-pnlA	Final
−	06/27/2006	MGH	Blood, Peripheral	Family History	CX26-a; CX30-a; DFNMT-pnlA; COCH-a; POU3F4-a; MYO7A-a; PDS-a	Final
					No mutations detected.	
+	06/27/2006	MGH	Blood, Peripheral	Pharmacogenomic	EGFR-b; EGFR-a	Final
−	06/26/2006	MGH	Fixed Tissue/Block (Lung) for EGFR	Pharmacogenomic	EGFR-a	Final
					2235_2243del (E746_R748del), Exon 19, EGFR	

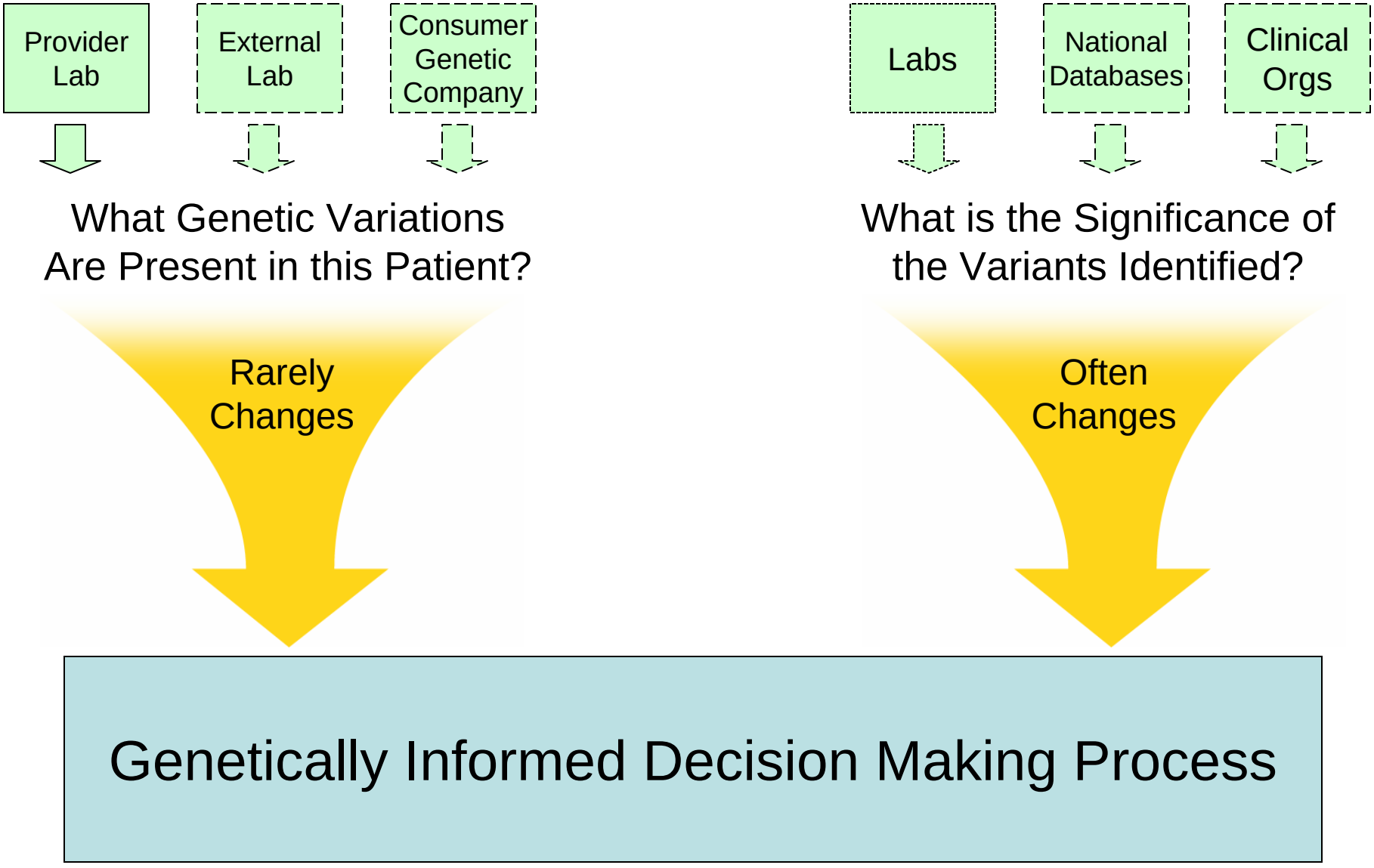
CDSS



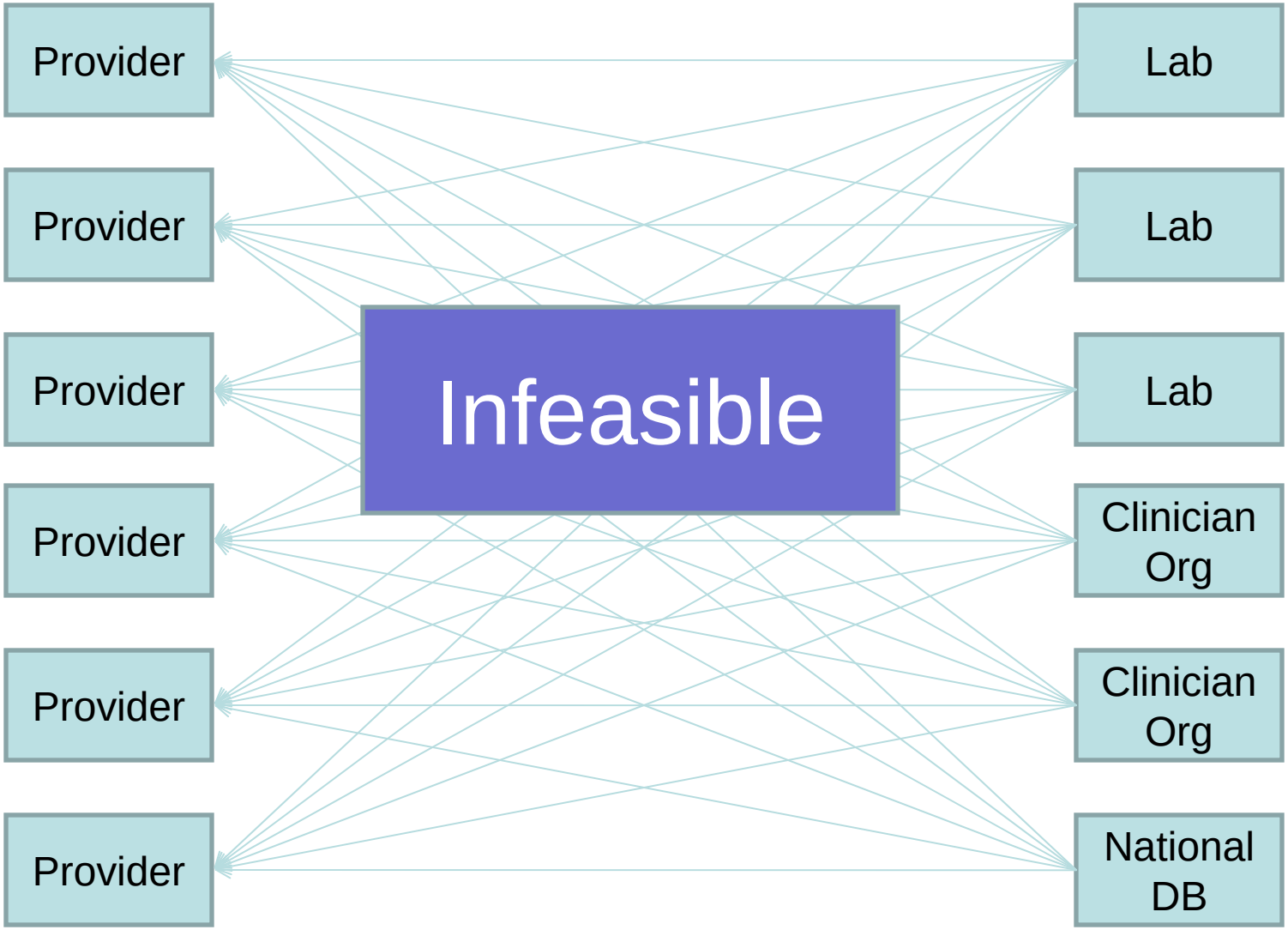
IT Support for the Clinical Practice of Genetic/Genomic Based Personalized Medicine



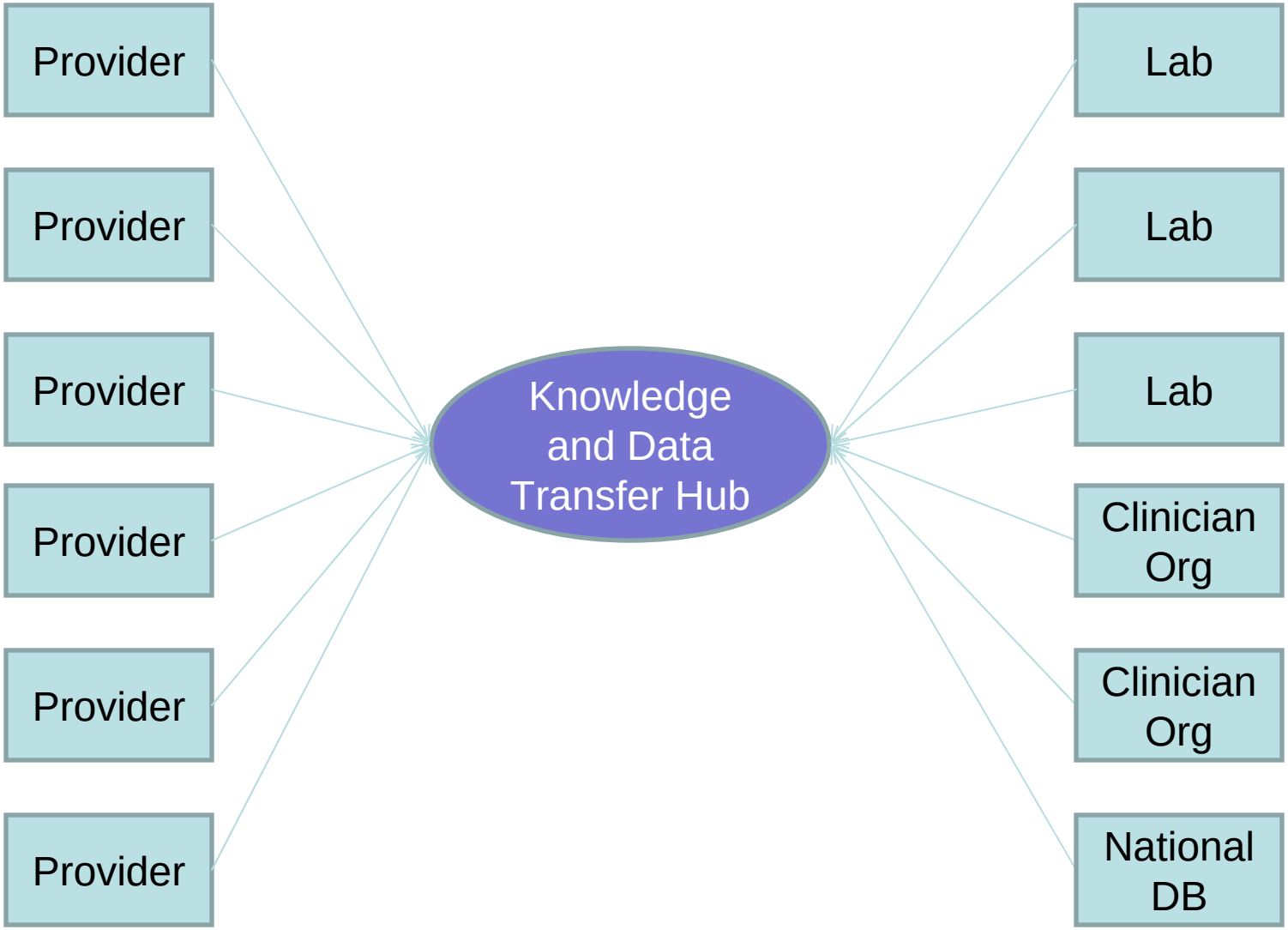
Information is Dispersed



The Many to Many Problem



The Hub Concept



GeneInsight Vision