

IT Infrastructure Required to Scale Personalized Medicine

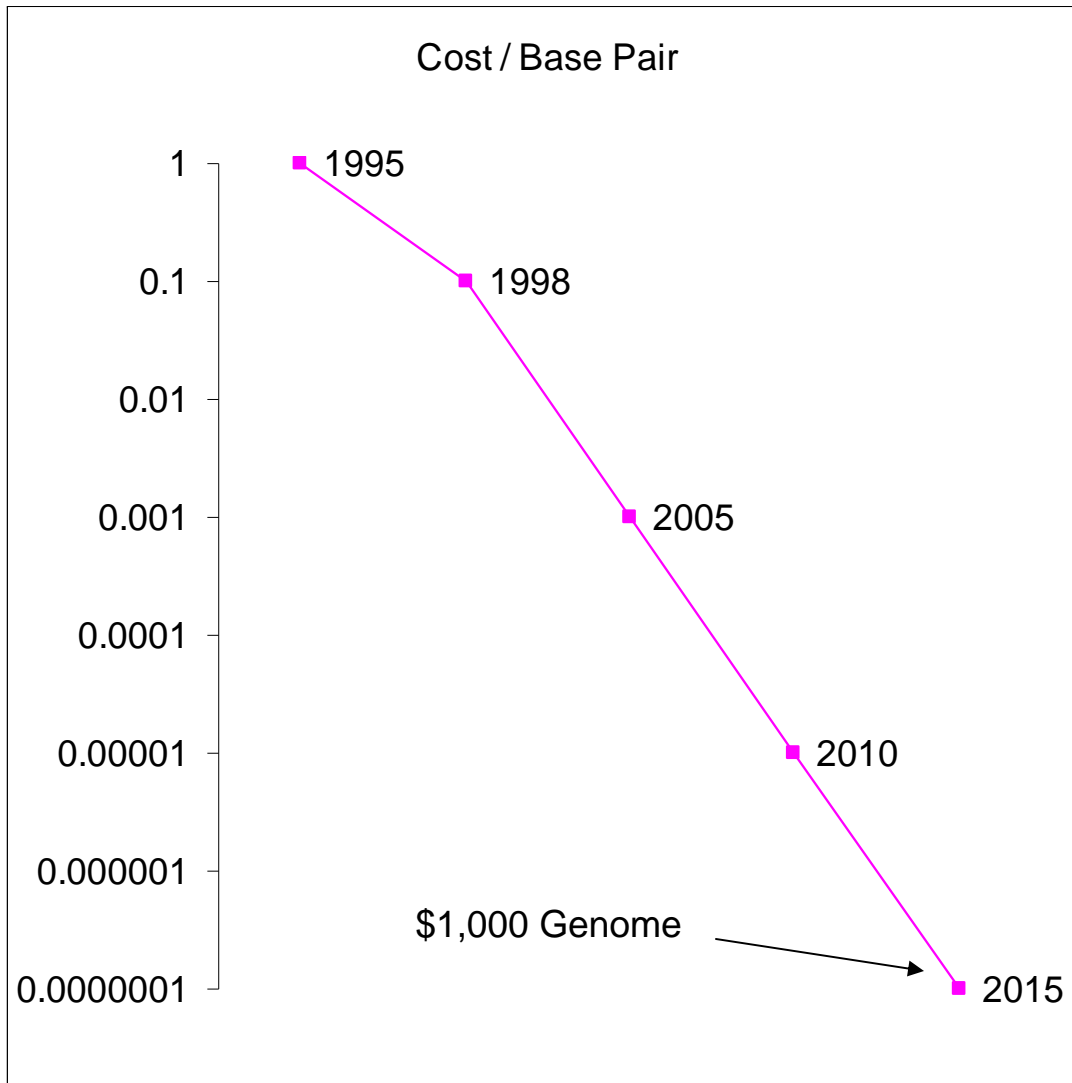
Sandy Aronson

Executive Director of Information Technology
Harvard Medical School – Partners HealthCare
Center for Genetics and Genomics

Our Goal

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

Cost of DNA Sequencing



Data adopted from:

Mutation Research 573 (2005) 13-40

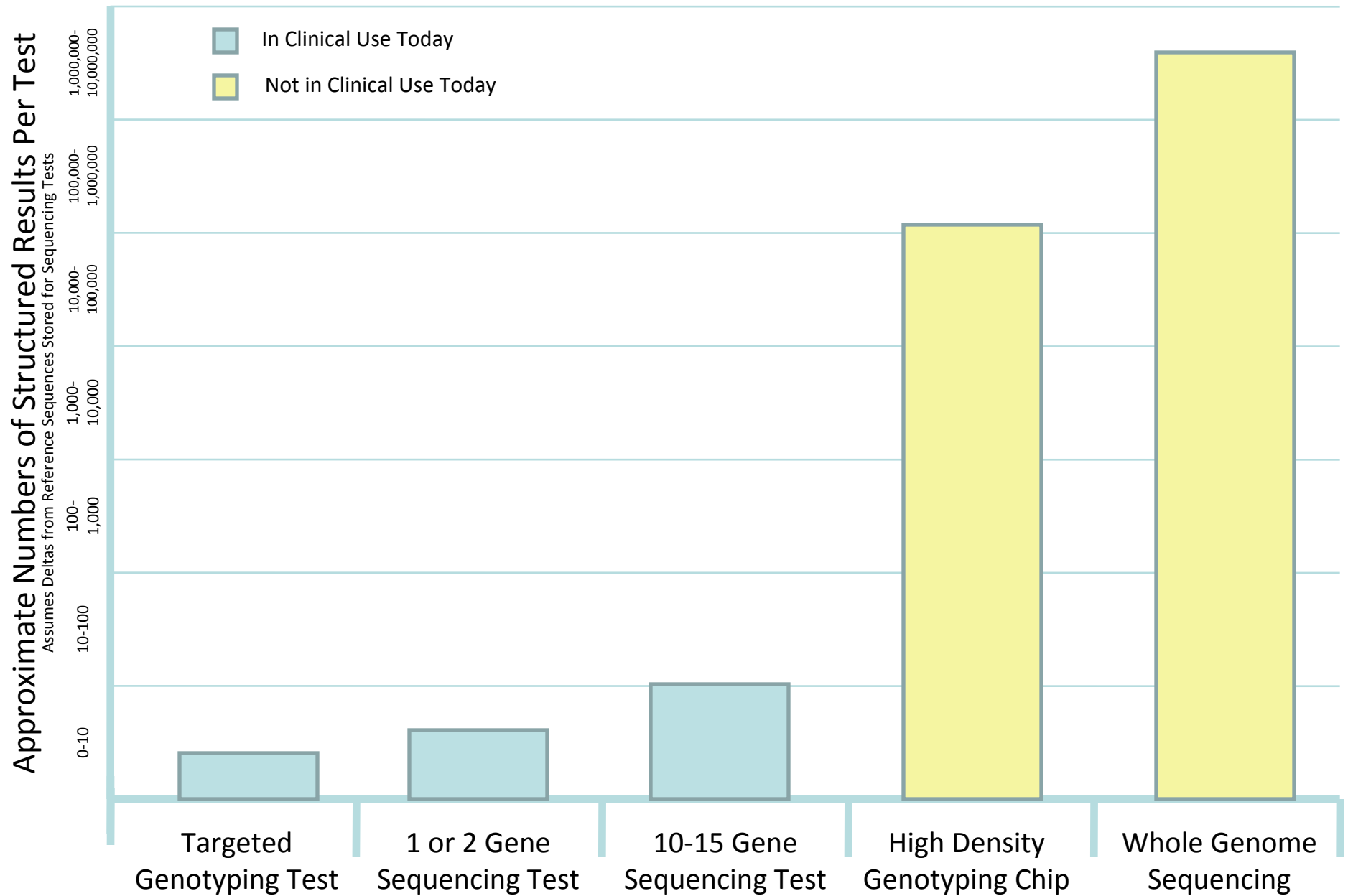
Community address: www

Review

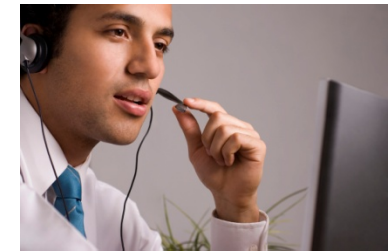
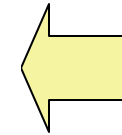
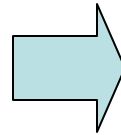
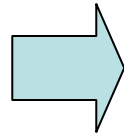
Advances in sequencing technology

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

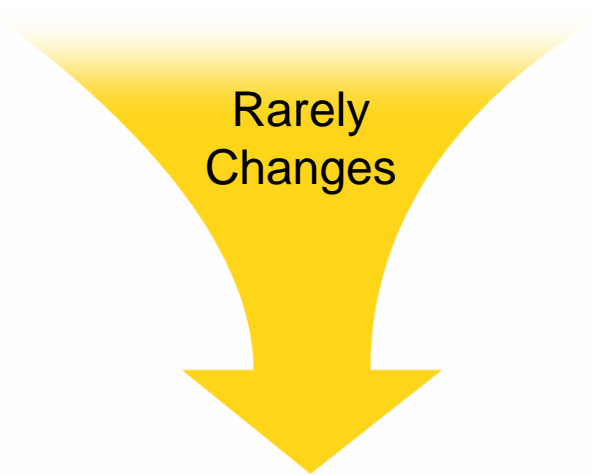
The Medium Amount of Time a Clinician
Has to Spend with Each of Their Patients

(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

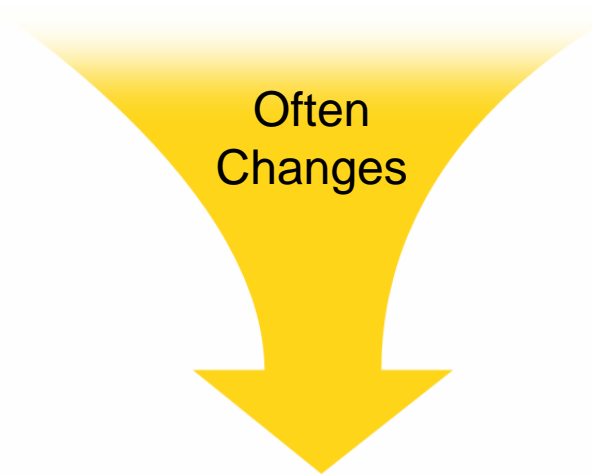
What Genetic Variations
Are Present in this Patient?

Rarely
Changes



What is the Significance of
the Variants Identified

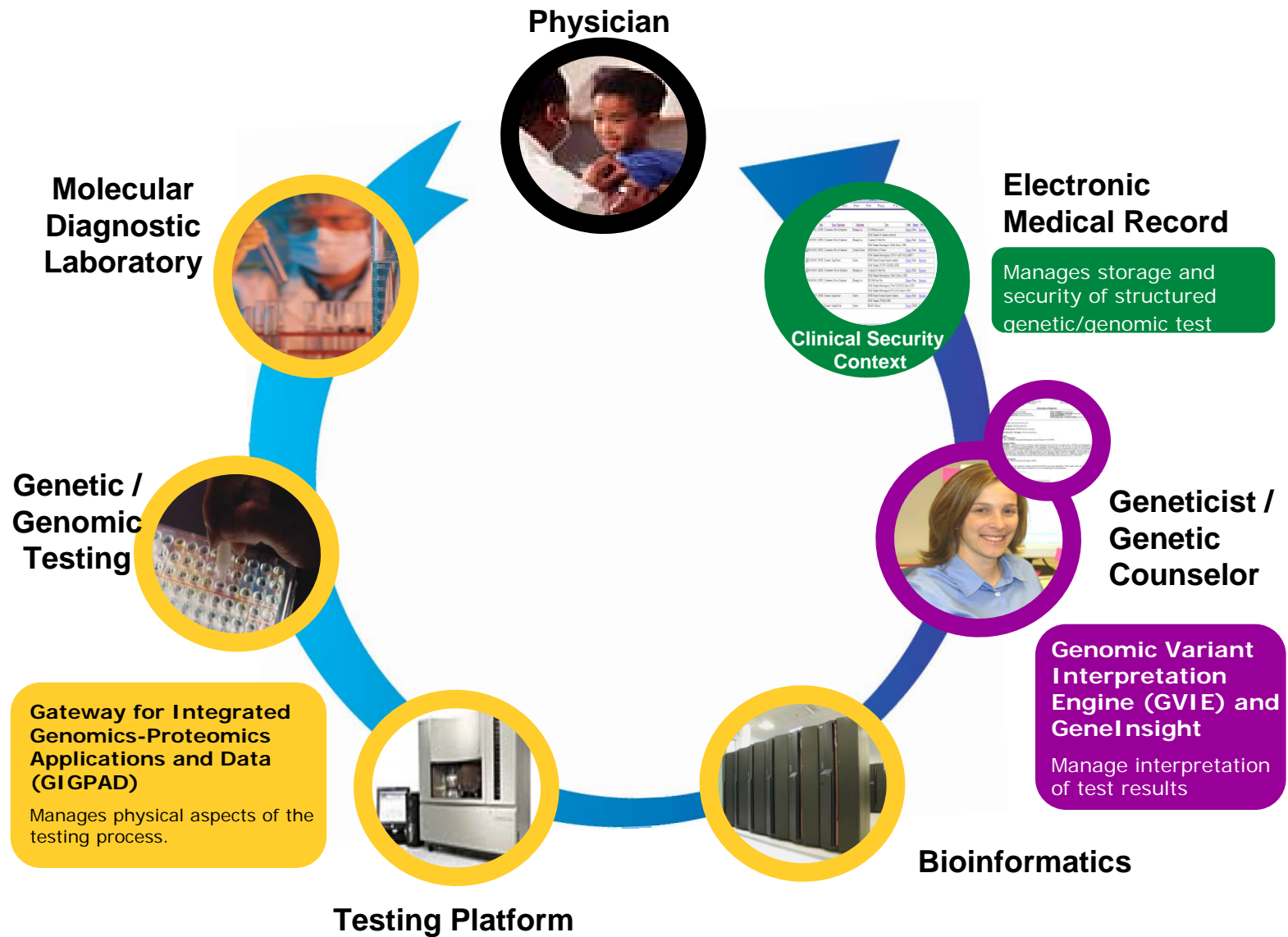
Often
Changes



Genetically Informed Decision Making Process



Supporting the Current Clinical Model



GeneInsight - DNA Variant Knowledgebase

Variant Status Flags: (R) needs review, (V) not valid, (D) don't validate, (N) has notes

34 variants found, displaying all variants
Export options: CSV | Excel | XML | PDF

| Gene | Allele | DNA | AA | ** | Region | Category | Dis |
|--------|--------|----------|-------|----|----------|------------|----------------|
| TGFBR2 | | 170-2A>G | | | | | |
| TGFBR2 | | 571G>A | V191I | | | | |
| TGFBR2 | | 773T>G | V258G | R | Intron 1 | 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 |
| TGFBR2 | | 1106G>T | G369V | R | Exon 4 | Pathogenic | MFS, LDS, TAAD |
| TGFBR2 | | 1151A>G | N384S | R | Exon 4 | Pathogenic | MFS, LDS, TAAD |
| TGFBR2 | | 1181G>A | C394Y | R | Exon 4 | Pathogenic | MFS, LDS, TAAD |
| TGFBR2 | | 1188T>G | C396W | R | Exon 4 | Pathogenic | MFS, LDS, TAAD |
| TGFBR2 | | 1195G>A | V387L | R | Exon 4 | Pathogenic | MFS, LDS, TAAD |
| TGFBR2 | | 1273A>G | M425V | R | Exon 4 | Pathogenic | MFS, LDS, TAAD |
| TGFBR2 | | 1322C>T | S441F | R | Exon 4 | Pathogenic | MFS, LDS, TAAD |
| TGFBR2 | | 1336G>A | D446E | R | Exon 4 | Pathogenic | MFS, LDS, TAAD |
| TGFBR2 | | 1346C>T | S449F | R | Exon 4 | Pathogenic | MFS, LDS, TAAD |
| TGFBR2 | | 1378C>T | R460C | R | Exon 4 | Pathogenic | MFS, LDS, TAAD |
| TGFBR2 | | 1379G>A | R460H | R | Exon 5 | Pathogenic | MFS, LDS, TAAD |

EHR

(0000004 MGH) Claus,Santa C, Jr.- Genetics Summary - Microsoft Internet Explorer provided by Partners HealthCare System

Sites: MGH BWH ALL

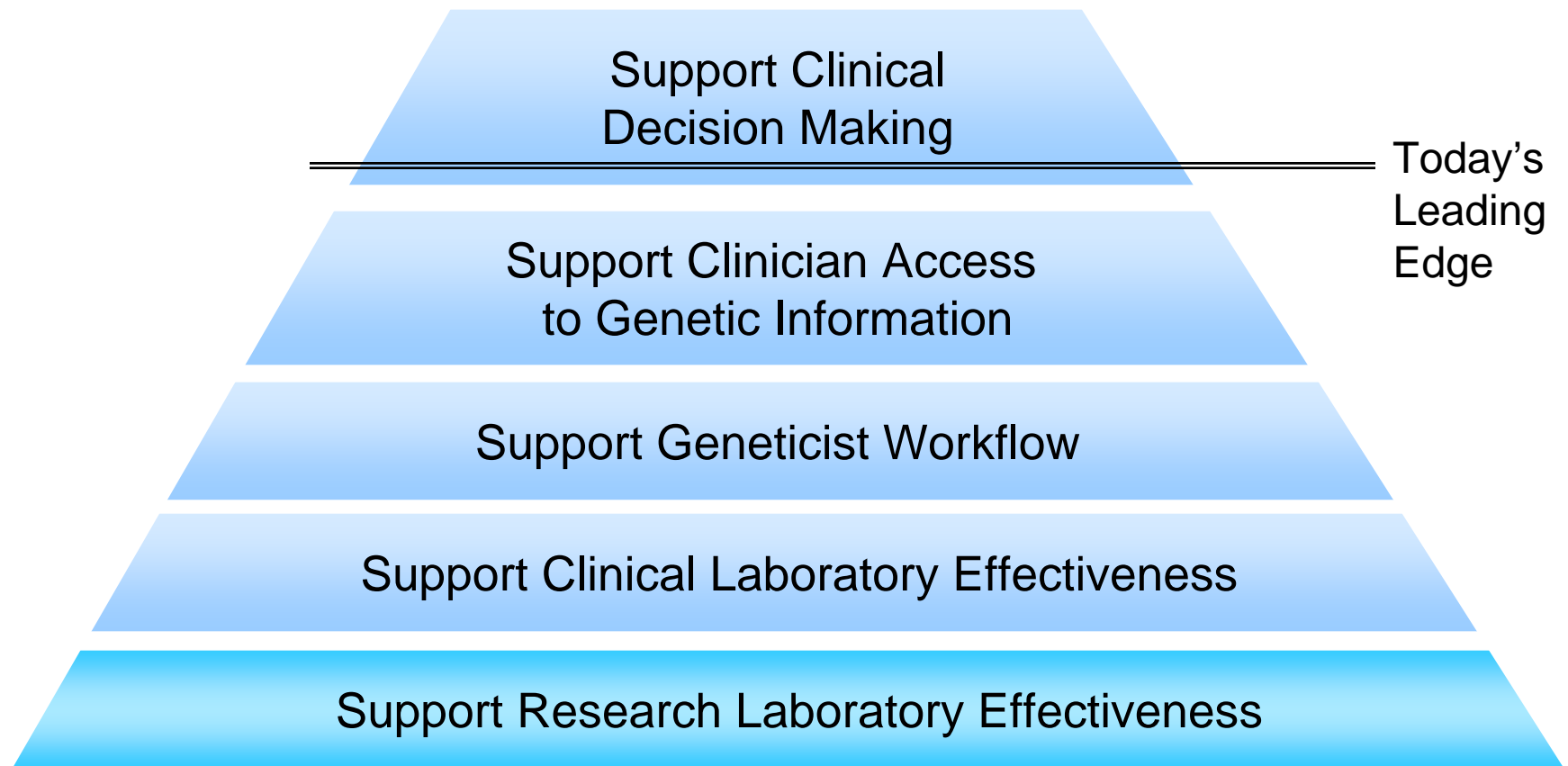
| - | Date | Site | Primary Specimen | Indication | Test | Status |
|---|------------|------|------------------------------------|-----------------|--|---------------|
| + | 06/27/2006 | MGH | Lung - Fixed Tissue | Pharmacogenomic | EGFR-b | Amend/Addenda |
| + | 06/27/2006 | MGH | Blood, Peripheral | Family History | HCM-pn1B ; UCH-pn1A ; HCM-pn1A | Final |
| - | 06/27/2006 | MGH | Blood, Peripheral | Family History | CX26-a ; CX30-a ; DFNMT-pn1A ; 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

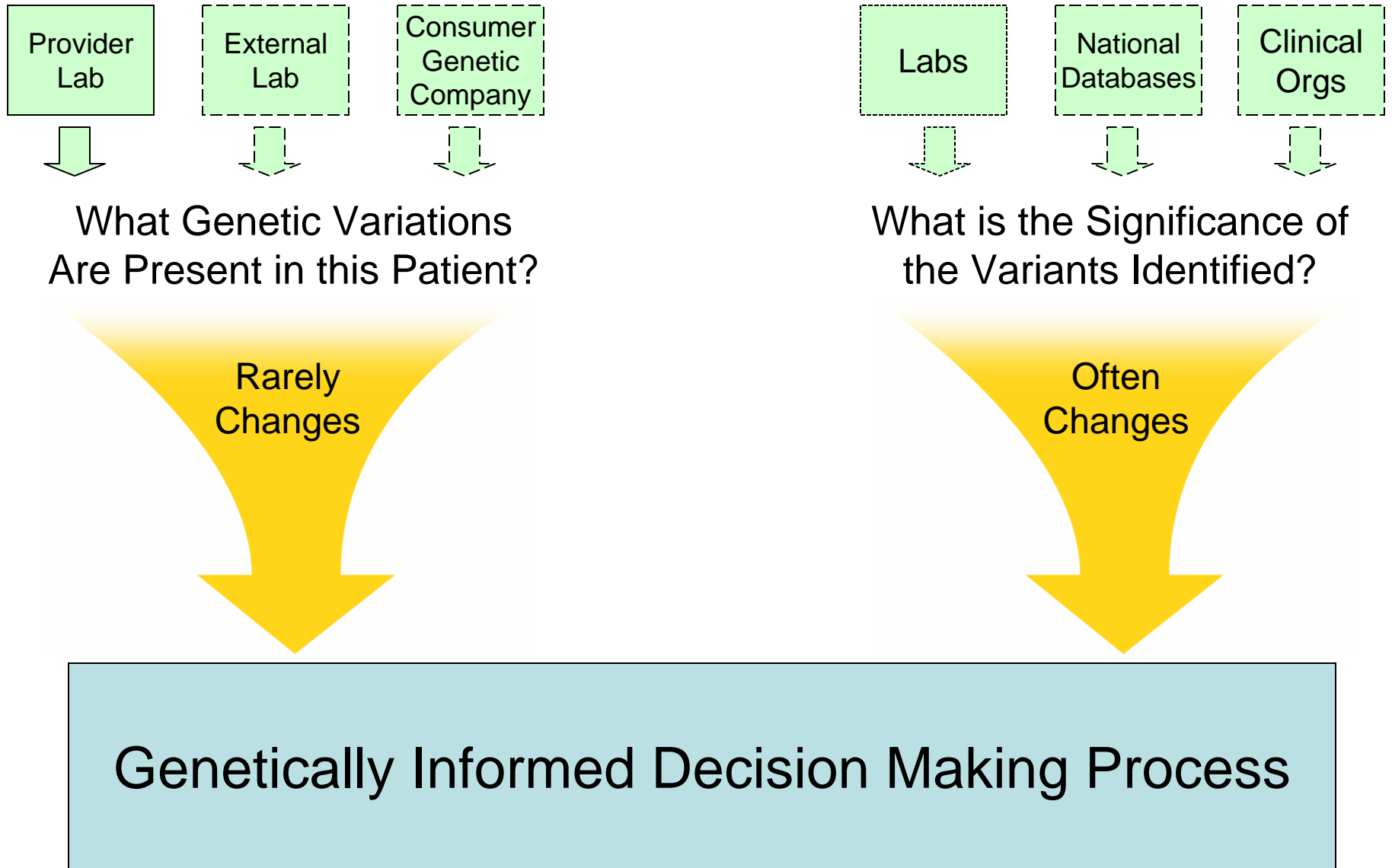
| | | | | | | | | | | |
|---|-------------------------|---------------------------------------|--------------------------|------------------------|--|-----------------------|----------------------|-------------------------|-------------------|----------------------|
| Select | Desktop | Pt Chart: Medications | Oncology | Custom | Reports | Admin | Sign | Results | ? | Resc |
| Warning | | | | | | | | | | |
| You are ordering: TARCEVA (ERLOTINIB) | | | | | | | | | | |
| Drug - Genetic Intervention | | | | | | | | | | |
| Alert Message | | | | | Keep New Order - select reason(s) | | | | | |
| TARCEVA (ERLOTINIB) is contraindicated in patients with a somatic EGFR mutation known to be associated with resistance to Tyrosine Kinase Inhibitors for treatment of non-small cell lung cancer. | | | | | Reasons for override: | | | | | |
| Most recent = Resistant 12/21/2006 | | | | | <input type="checkbox"/> Patient has pancreatic cancer | | | | | |
| See Report in Genetics Summary under Results | | | | | <input type="checkbox"/> No reasonable alternatives | | | | | |
| | | | | | <input type="checkbox"/> Other <input type="text"/> | | | | | |

[Continue New Order](#) [Cancel](#) [Back To Lookup](#)

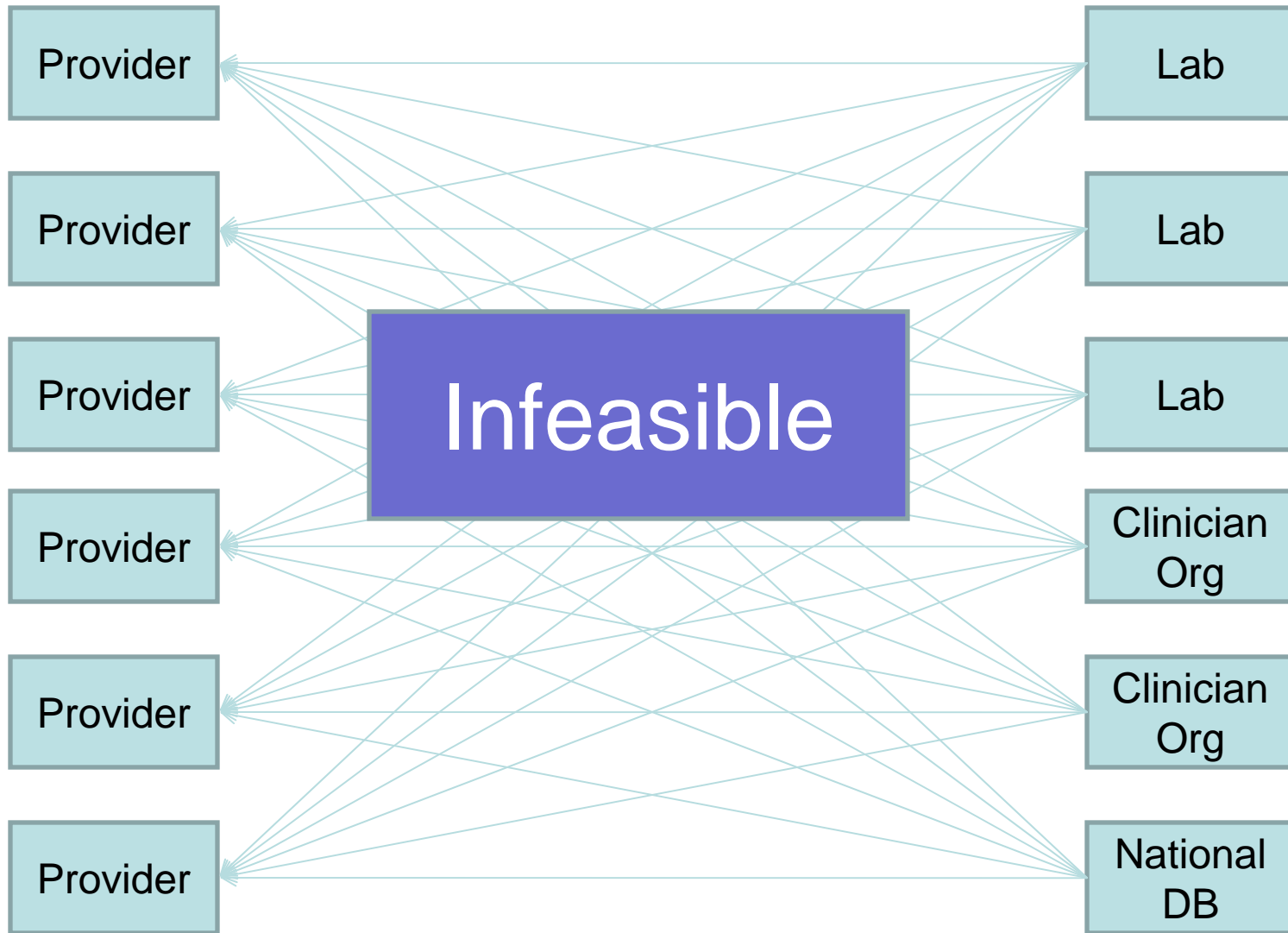
IT Support for the Clinical Practice of Genetic/Genomic Based Personalized Medicine



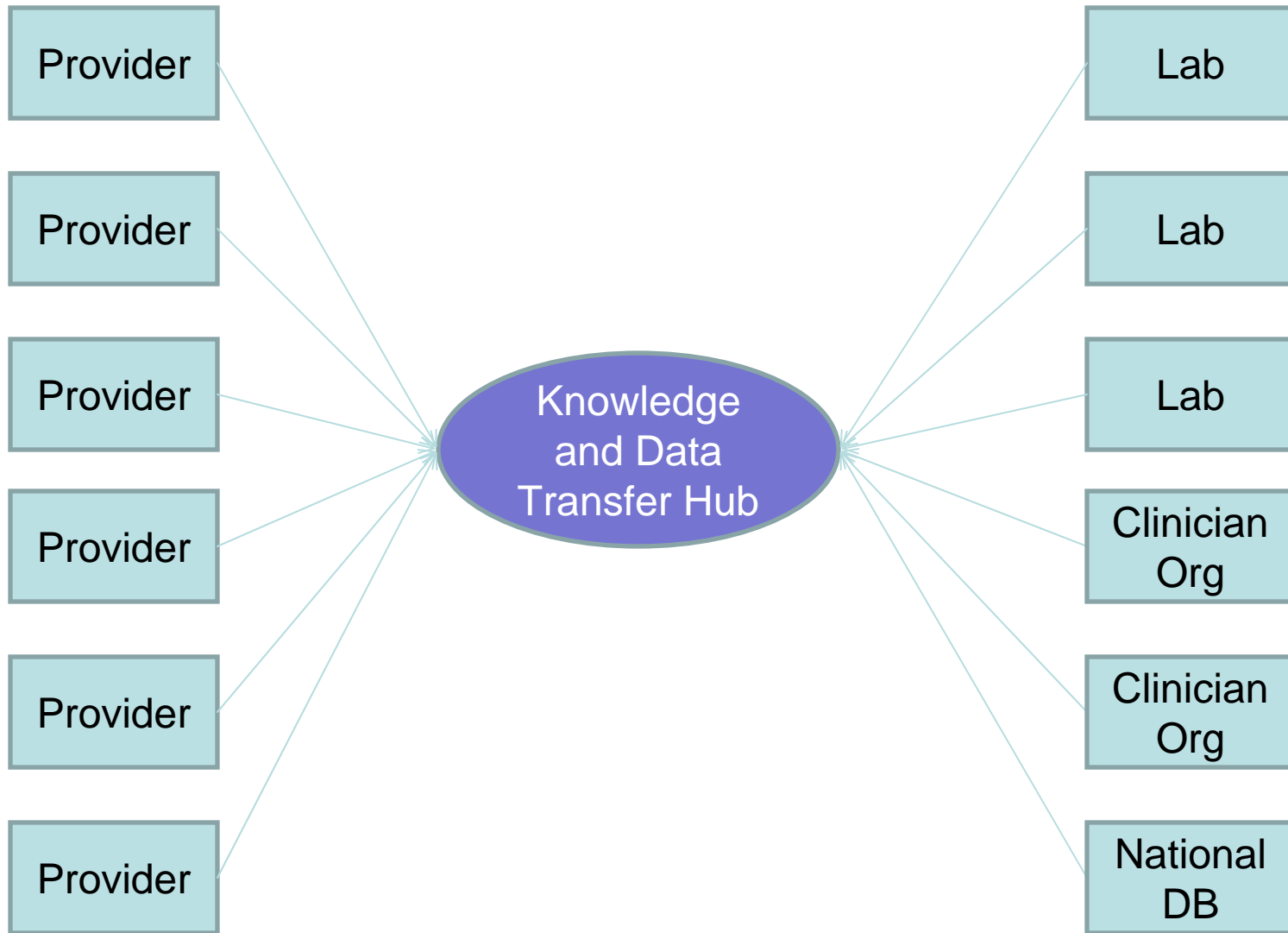
Information is Dispersed



The Many to Many Problem



The Hub Concept



GeneInsight Vision

