



# INTEGRATING GENETIC INFORMATION INTO ELECTRONIC HEALTH RECORDS

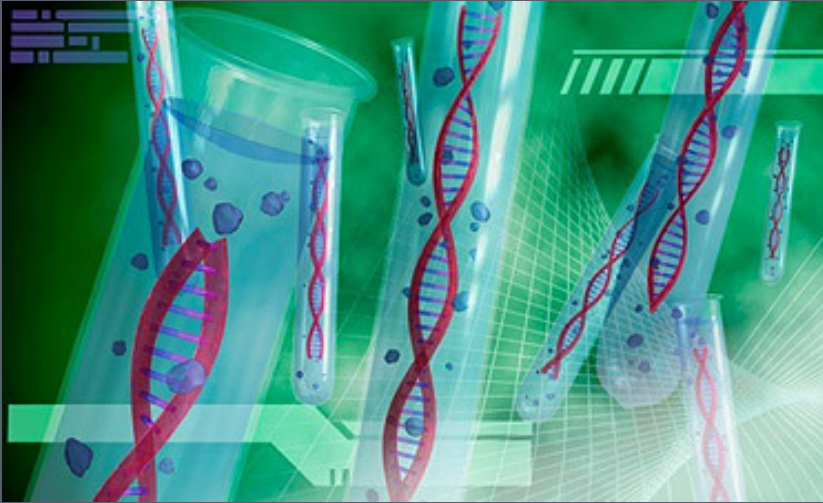
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# Integrating Genetic Information into EHRs



## Part 1: Market Overview

- Where is all of this genetic information coming from?
- Why so fast?
- What does it look like?



## Part 2: Clinical Integration

- How can we ensure that genetic information is available in a “clinically actionable” form?
- Are EHRs ready for genomic medicine?

# A Brief History of Molecular Diagnostics (“MDx”)

- Evolution Driven by Scientific Innovation
  - PCR and sequencing
  - Efficiency-focused innovations
    - High-throughput sequencing
    - Improved amplification methods
  - Now: Work-flow and multiplexing
    - Driven by efficiency, labor concerns, science



# MDx Innovation: A Virtuous Circle

## Research

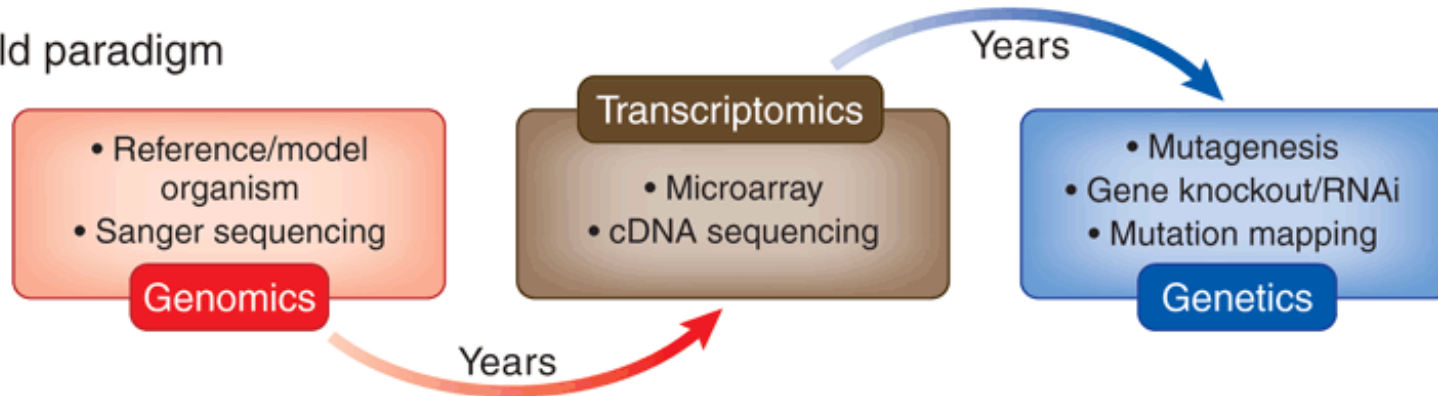
Identifies molecular marker (mutation, etc.) and clinical implications

## Test Development

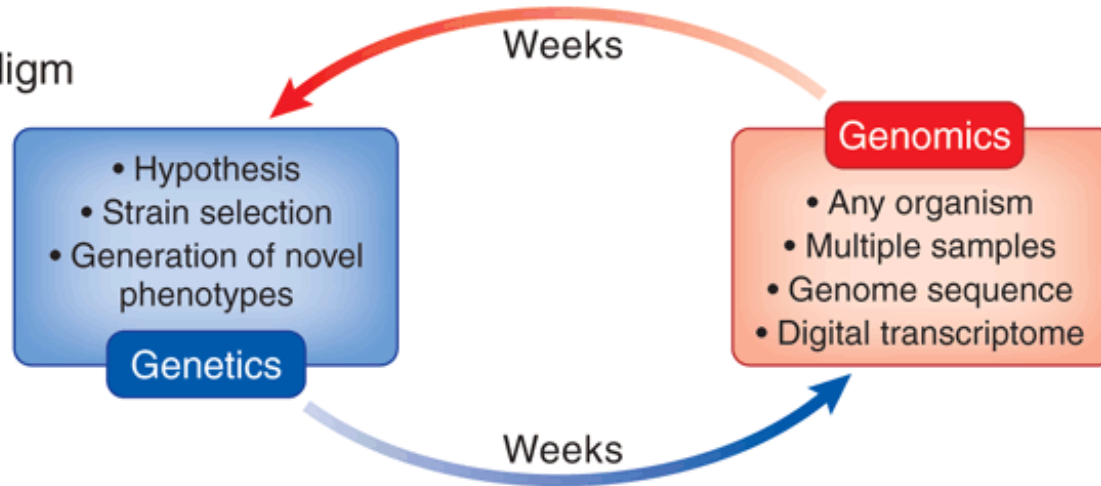
With demand comes need to improve test effectiveness and efficiency

# Paradigm Shift

## Old paradigm



## New paradigm



# In Vitro Diagnostics Lifecycle



Research Laboratory



Reference Laboratory



Central Hospital Laboratory



Decentralized Testing

# Molecular Diagnostics

## Methods

- Cytogenetics

- e.g., diagnosis of chromosomal breakage syndromes

- Fluorescence In Situ Hybridization (FISH)

- e.g., detection of oncogene amplification

- FISH Derivatives

- Spectral karyotyping imaging, comparative genomic hybridization, tissue microarray, chromogenic in situ hybridization

# Molecular Diagnostics

## Methods *(cont'd)*

- PCR
  - e.g., detect DNA sequence of interest
- PCR Derivatives
  - Nested PCR
  - Real-time PCR
    - e.g., HIV viral load
  - Reverse-transcriptase PCR
    - RNA → cDNA
  - Multiplex PCR
    - E.g., detect CFTR mutations in CF
  - Allele-specific oligonucleotides

# Molecular Diagnostics

## Methods *(cont'd)*

- Direct Sequence Analysis
- Southern Blot Analysis
- Variable Number Tandem Repeats
  - e.g., forensic applications, molecular pathology (microsatellites)
- Mutation Scanning
  - e.g., hereditary hemochromatosis
  - Types: DHPLC, SSCP, melting point analysis

# Molecular Diagnostics

## Methods *(cont'd)*

- Gene Expression Profiling
  - DNA (cDNA) microarray, DNA (oligo) chip
- Proteomics
  - Proteins as indicators of gene expression
- Loss of Heterozygosity
  - Sporadic and hereditary tumors
- Methylation Assays
  - Assess methylation status of region of DNA
  - e.g., tumor suppressor gene silencing in cancer

# Molecular Diagnostics

## Applications

- Clinical diagnosis
- Neonatal screening
  - PKU, congenital hypothyroidism
- Prenatal diagnosis
  - Trisomy 21
- Carrier testing
  - Tay-Sachs disease, thalassemia
- HLA typing
  - Transplant medicine, autoimmune diseases associated with specific HLA types

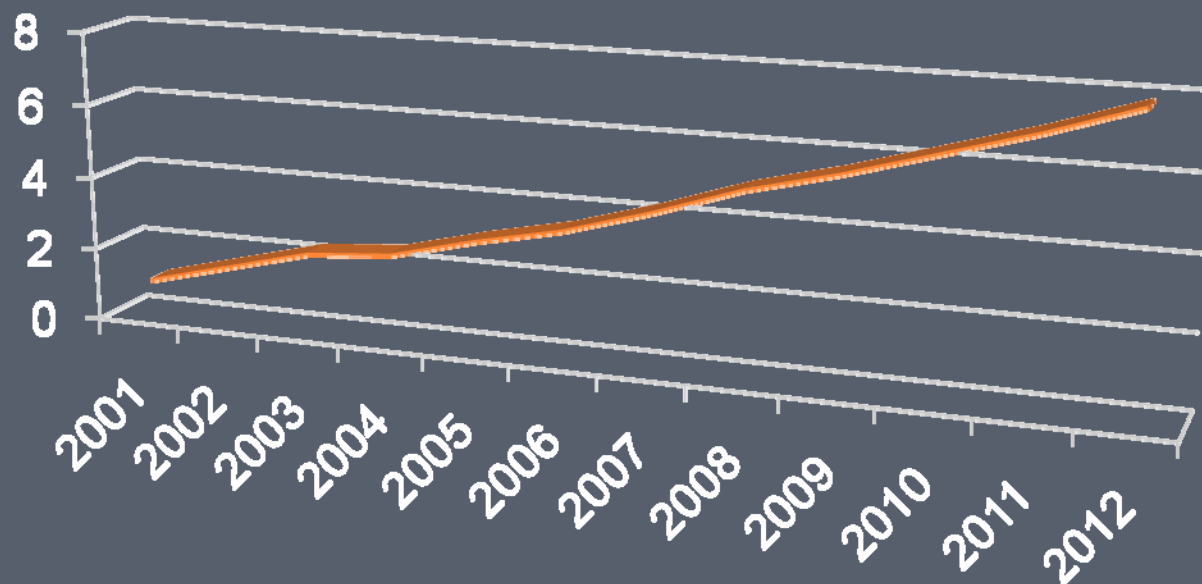
# Molecular Diagnostics

## Industry Trends

- Washington G-2 Reports estimates that the market for molecular diagnostics will grow by approximately 12% per year, compared to 5% growth for most other areas of laboratory testing
- An estimated 70 million molecular diagnostic tests will be conducted in the U.S. in 2009
- Molecular tests are becoming the standard of care...
  - FDA clearance, professional association guidelines, reimbursement
- ...But are still offered by only a fraction of clinical laboratories

# A Growing Global Market

- The global market for molecular diagnostics is expected to grow to approximately \$8 billion by 2012.



Source: Washington G-2 Reports

# Molecular Diagnostics in the Obama Era



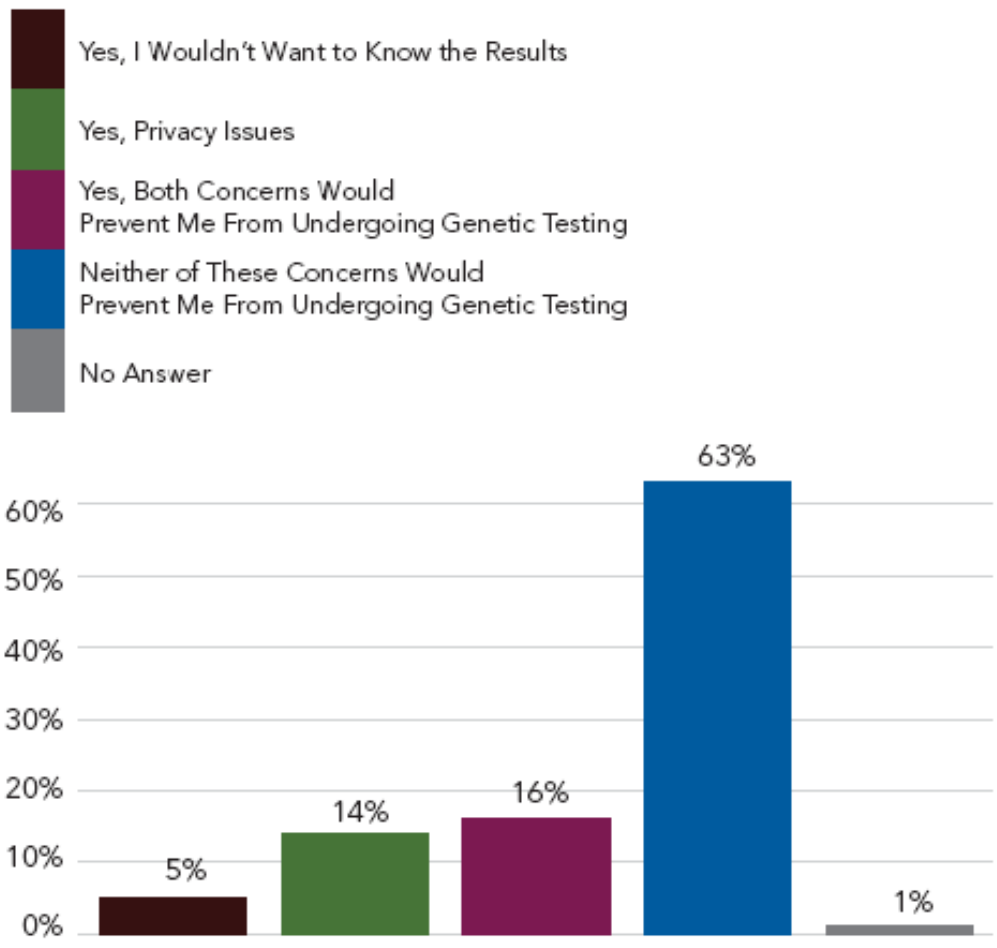
- Championing broad healthcare reform
- Particular interest in the development of genomic tests
- Environment ripe for increased regulation?
- Emphasis on improving healthcare quality, prevention, chronic disease management

# MDx: Market Drivers

- Hospitals working to streamline care and reduce testing costs
- Growing number and breadth of available tests
- Improved reporting of complex results
- New technologies that allow the necessary quality control and data capture from tests
- Rise of the MDx-savvy: scientist, clinician, vendor, media, patient



Some people say they won't undergo genetic testing because they would not want to know the results, while others say they wouldn't because of privacy concerns. What about yourself? Are either of these two concerns likely to prevent you from undergoing genetic testing?



Source: Burrill & Company and ChangeWave Research. *Personalized Medicine and Wellness Survey*, n=550 (May 2008)

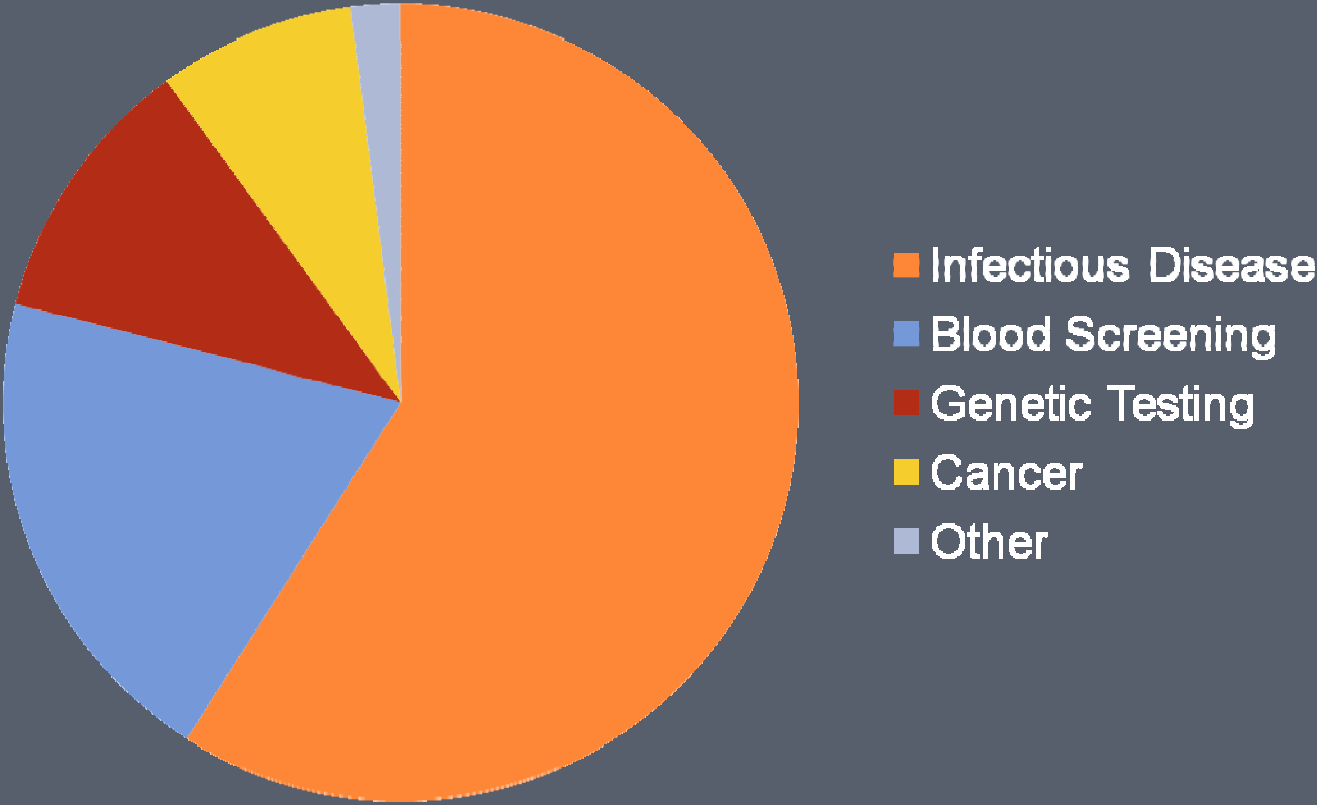


# A Technology-Driven Market

Molecular Diagnostics: A replacement and enabling technology

- PCR
  - Initially labor-intensive, manual process
- Automation, ease of use
- Expanded clinical applications
- Point-of-care orientation
- Multiplex testing
- Pharmacogenomics
- Whole-genome scanning?

# Global MDx Testing By Segment



Source: Washington G-2 Reports





# G-2's Molecular Diagnostics Survey

- The more than 100 U.S. clinical laboratories who participated in the survey predicted that in the next two years, MDx would account for an average of 19.1% of total lab revenue.
- Top tests: CT/NG, HPV, HCV, HIV
- Top tests planning to add: HSV, CF, HCV quantitative, CYP450



# Why MDx? And Why Not?

- Clinical impact
  - Effect on patient management
  - Sensitivity, specificity, and speed (better results)
- Practice guideline changes and regulatory decisions
- Potential savings
  - Decreased TAT
  - Decreased hosp. time
- Demand
  - Increasingly consumer-driven
- Ease of use
  - Lab in a box systems
  - Less invasive sample procurement
- Expensive
- Difficult to demonstrate potential savings
- Reimbursement
  - Lack of designated CPT codes
  - Royalty and licensure fees
- Staffing/Training
- Standardization
  - Quality control standards
- Market Education
  - Clinical utility
  - Applications
  - Availability
- Increased regulatory oversight imminent

# MDx Paradigm Shift

- MDx paradigm shift: more than just another test
- One sample, potential for many tests
  - Versatile: sample type, size
- Examples of cost savings
  - Decrease hospital stay
  - Establish duration of therapy
  - Discontinue ineffective therapy
  - Ability to identify high-risk patients

# Molecular Diagnostics

## Challenges

### ○ Personnel

- Shortage of laboratory personnel estimated to reach 100,000 by 2012 (U.S. Bureau of Labor Statistics)
- Training

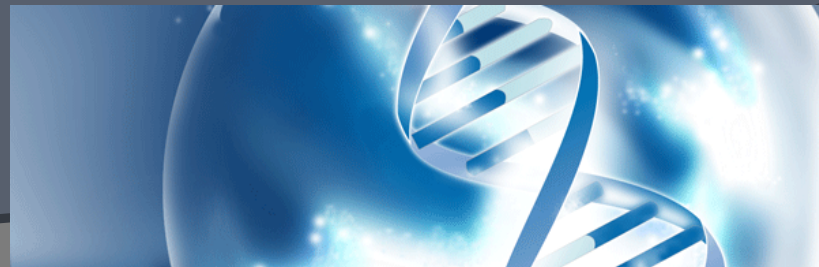
### ○ Need for technologies that make MDx easier to automate and less expensive



# Molecular Diagnostics

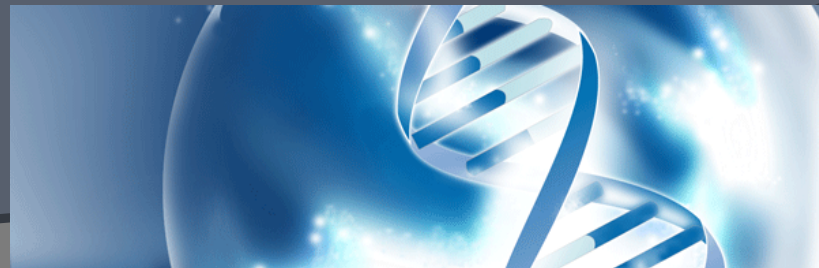
## Challenges

- Reimbursement
- Lack of standardization across platforms
- Limited quality control practices
- High expectations for accuracy (once-in-a-lifetime genetic tests)
- Inability to fully interpret test data



# Beyond a “yes” or “no” result...

- ⦿ ~ 25,000 human genes
- ⦿ ~ 150,000 - 200,000 splice variants
- ⦿ ? Regulatory RNA species
- ⦿ ~ 500,000 - 2,000,000 protein states
  - Post-translational modifications



# Pathwork Diagnostics Tissue of Origin Test - LDT Report

Tissue	Similarity Score	Low 0 5	High 100
Colorectal	88.2		◆
Pancreatic	4.4	◆	
Non-small Cell Lung	2.3	◆	
Breast	2.1	◆	
Gastric	1.2	◆	
Kidney	0.6	◆	
Hepatocellular	0.3	◆	
Ovarian	0.3	◆	
Soft Tissue Sarcoma	0.1	◆	
Non-Hodgkin's Lymphoma	0.1	◆	
Thyroid	0.1	◆	
Prostate	0.1	◆	
Melanoma	0.1	◆	
Bladder	0.1	◆	
Testicular Germ Cell	0.0	◆	

- Measures the gene expression of >1,500 genes
- Panel covers 58 different morphologies, consolidated into 15 tissue types
- ~90% of all solid tumors
- Accurate and robust results
- Reports which tissues are likely present (rule-in) and which are likely not present (rule-out)

\*In 352 formalin-fixed, paraffin-embedded (FFPE) specimens, the test demonstrated 89% positive percent agreement (akin to sensitivity) with available diagnoses, and greater than 99% negative percent agreement (akin to specificity) in specimens that had previously been identified with existing methods as being among the 15 tumor types on the panel



# Molecular Diagnostic Tests, Clinical Practice, and EHRs

- Clinicians not prepared to integrate genetic information into routine clinical practice
  - Collection, documentation, and interpretation of family history for risk assessment
  - Recommendation of risk-specific interventions
  - Knowing when to offer genetic tests

# Including Genomic/Genetic Data in EHRs Can Inform...



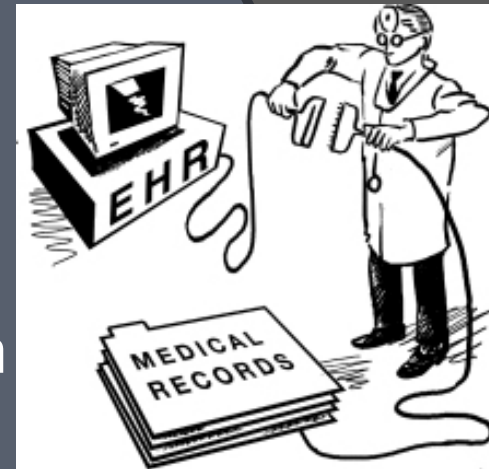
- Determination of disease risk
- Appropriate dosing to avoid adverse events
- Selection of effective treatment

## ...But Will Require:

- Broad access
- Appropriate privacy and security measures
- Data storage/transmission capabilities to

# American Health Information Community's Personalized Health Care Workgroup

- Informs policy on development of interoperable standards
- Vision: “A consumer-centric health system in which diagnostic, treatment, and management plans are customized based on a variety of factors, including culture, environment, preferences, personal and family health histories, and the individual’s unique genetic/genomic makeup.”
- Priorities: genetic/genomic tests, family health history, clinical decision support, privacy/security



# AHIC PHC Workgroup: What Data?

- Developing core dataset, including:
  - Demographic information
    - Name, unique identifier, race/ethnicity, occupation
  - Personal health information
    - History of specific disorders, relevant non-genetic lab test and pathology data, other clinical data (e.g., radiology), environmental exposure data, prior treatment for specific disorders
  - Family history information
    - Disorders of family members, ages of condition onset and/or death of various family members, environment exposure, relevant social data, pedigree in structure form



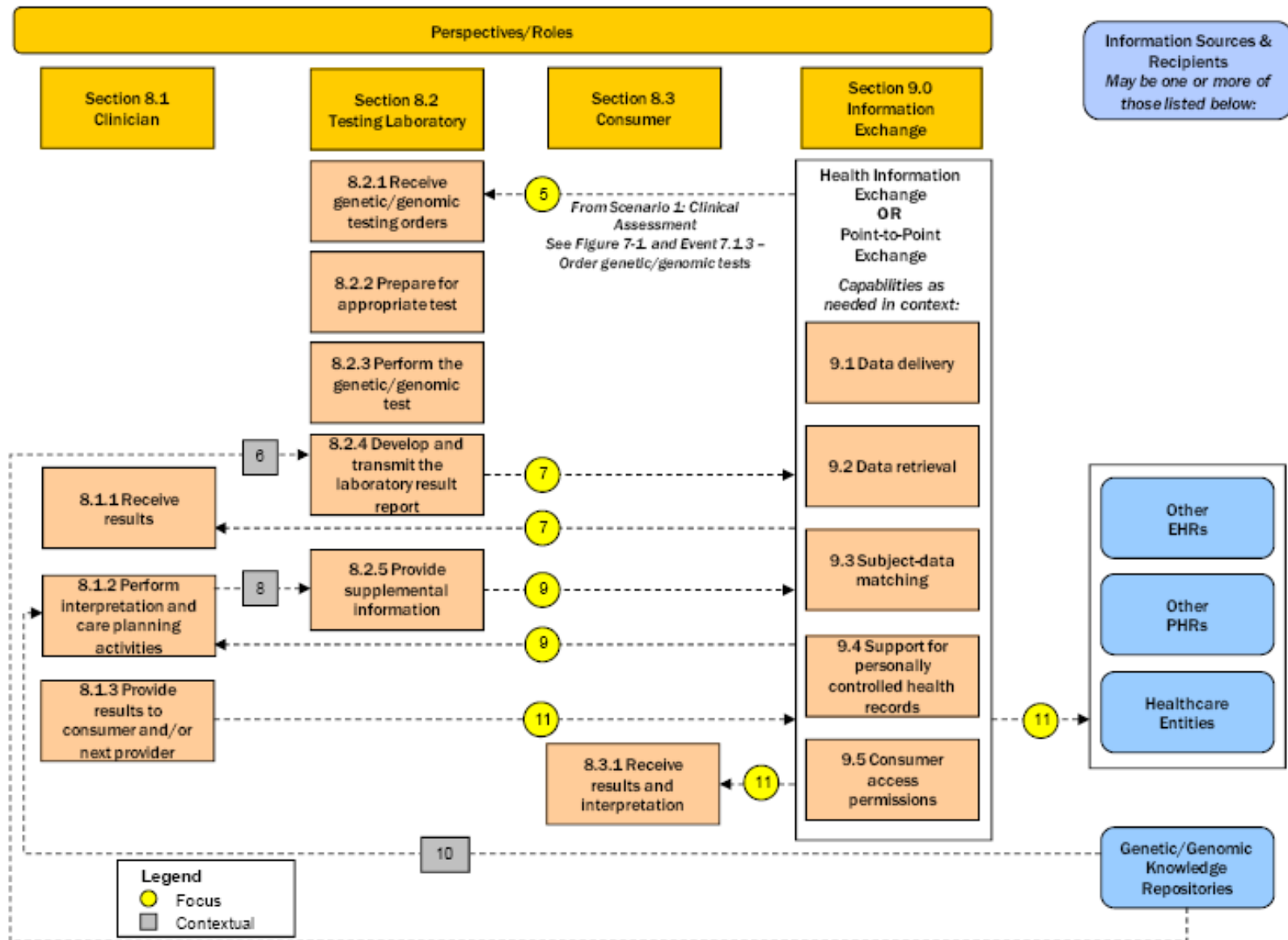
# AHIC PHC Workgroup: What Data?

- Personal genetic/genomic data
  - Prior genetic/genomic laboratory test results, prior genetic status for specific disease, full genome scan
- Family genetic/genomic information
  - Genetic/genomic data of family members, pedigree in structured form where appropriate, history of consanguinity, consent/access allowance information



# Scenario 2: Genetic Testing, Reporting, and Clinical Management

Figure 8-1. Genetic Testing, Reporting, and Clinical Management



# Are EHRs Ready for Genomic Medicine?

- What is the state of the art in EHR products regarding:
  - Documentation and organization of family history and genetic test information?
  - Related clinical decision support?
  - Needs and interests of key stakeholders regarding genetics/genomics content in EHRs?

➔ *Genetics in Medicine*. 2009;11(7): 510-517.



# EHRs and Genomic Medicine

- Survey of primary care clinicians (18), medical geneticists (16), genetic counselors (12), and EHR representatives (10)
- Core questions
  - Genetics/genomic content
    - Family history
    - Genetic test orders and results
  - Genetics/genomic issues
    - What are the barriers and challenges, if any, to including family history and genetic test information in EHRs?

# Clinician Respondents by EHR Type

EHR Type	Primary care, % (n=18)	Medical geneticists, % (n=16)	Genetic counselors, % (n=12)
Internally developed	22	50	25
GE Centricity	27	13	8
Epic	22	25	42
Practice partner	11	0	0
All Scripts	6	6	0
Cerner	0	6	17
Ecclypsis	0	0	8
SOAPware	6	0	0
Oasis	6	0	0

➔ *Genetics in Medicine*. 2009;11(7): 510-517.

# Genetics/Genomics Issues

- (*To EHR reps*) How has the market reacted to the increasing discussion of genetic/genomic medicine and has this translated to changes in data input or other requirements?
- (*To Clinicians*) Have EHR vendors/product managers responded to your genetic/genomic medicine needs, and what data elements or functionality would be most useful?
- What is the impact of EHRs and health information technology on genetic/genomic medicine, and how do you see that changing in the next five to ten years?
- What is the impact of genetic/genomic medicine on EHRs and health information technology, and how do you see that changing over the next five to ten years?

**Table 4.** Barriers and challenges relating to the integration of genetics/genomics content into the EHR

Response	Total, % (n = 56)	EHR representatives, % (n = 10)	Primary care, % (n = 18)	Medical geneticists, % (n = 16)	Genetic counselors, % (n = 12)
Time and resources required to enter family history, interrupts workflow, and lack of reimbursement to gather and input family history	55	30	78	56	42
Getting complete and accurate family history, concerns about patient-entered data, and reconciling conflicting family history	39	50	22	50	42
Clinicians do not understand how to use family history	30	30	39	25	25
Privacy concerns, concerns regarding genetic discrimination, and duty to warn at-risk relatives	29	10	6	25	83
Lack of demand for genetics content in EHRs	25	40	33	13	17
Lack of pedigree drawing capability or difficulty interfacing proprietary pedigree drawing programs with the EHR	25	20	6	31	50
Lack of standards for data elements, terminology, structure, interoperability, and clinical decision support rules	21	30	22	25	8
Ensuring adequate security of the data and determining access permission	21	10	11	13	58
A minority of patients take advantage of the patient portal, which could be used for family history data entry	18	20	6	38	8
Lack of incentives (e.g., from federal government, reimbursement); if they existed this would facilitate inclusion of genetics	18	0	33	19	8
Lack of available clinical decision support (e.g., for family history risk assessment, genetic test ordering, drug-gene interaction)	16	0	17	31	8
Limited adoption of the EHR (includes "technology phobia")	16	10	11	31	8
Presenting genetic test results in a meaningful way	13	40	11	6	0

**Table 5. EHR data elements or functionality relating to genetics/genomics that would be useful to clinicians**

Response	All clinicians, % (n = 46)	Primary care, % (n = 18)	Medical geneticists, % (n = 16)	Genetic counselors, % (n = 12)
Pedigree drawing capabilities	46	44	50	42
Clinical decision support for referential information, familial risk assessment, referral to genetics, genetic test orders and interpretation, or drug prescribing	39	61	38	8
Patient portal/patient-entered data	24	33	25	8
Standards for data elements, terminology, structure, interoperability, and clinical decision support rules	22	33	13	17
Family history better organized and more accessible (e.g., in one place in EHR)	20	22	13	25
Ability to update the family history in the EHR	17	17	13	25
Genetic tests better organized and accessible	17	22	0	33
Structured (detailed or granular) data format rather than text-only for clinical decision support and data queries	15	22	6	17
Ability to limit access permission (privacy concerns raised)	13	11	19	8
Efficient (branching, algorithmic, user-friendly) and flexible way (e.g., targeted or comprehensive) to enter and/or display family history	13	17	13	8
Ability to migrate/integrate medical or family history among EHRs of different family members	11	6	13	17
Reminding or requiring user to complete the family history	9	11	6	8
Do not know	2	0	6	0
Not answered/missing/other	15	6	19	25

EHR, electronic health record.

Participants could provide more than one response.

**Table 6.** The impact of health information technology and EHRs on genetic/genomic medicine

Response	Total, % (n = 56)	EHR representatives, % (n = 10)	Primary care, % (n = 18)	Medical geneticists, % (n = 16)	Genetic counselors, % (n = 12)
There is an impact	9	10	6	13	8
There is limited to no impact	11	10	22	6	0
There will be an impact in next 5 to 10 years	36	30	44	25	42
Will improve the ability to manage genetic information (e.g., improve data capture, display of information, sharing of data, and/or use of genetic data)	43	40	28	50	50
Will enable clinical decision-making (e.g., risk assessment, referral to genetics specialist or for genetic testing, treatment and prevention); Will provide clinicians with knowledge	39	30	33	44	42
Genetics will facilitate uptake/utilization of genetics in practice of genetics professionals or non-geneticists; genetics will be more available/accessible	25	20	17	25	42
Genetics/genomics can't be done without EHRs; information technology is essential/necessary	20	40	22	13	8
Will facilitate genomics research (i.e., our understanding of genetic basis of disease and/or disease risk, management and treatment); ambulatory offices will become a source of structured genetic data	18	40	11	25	0
Will raise ethical concerns around privacy, confidentiality, discrimination, and duty to warn regarding genetic information	11	0	0	0	50
Personal health records will be crucial to genetics/genomic medicine	2	0	0	0	8
Don't know	2	0	6	0	0
Not answered/Missing/Other	4	20	0	0	0

EHR, electronic health record.

Participants could provide more than one response.

# Molecular Diagnostics and EHRs

## What's Ahead

- Clinical decision support (CDS) as central part of care delivery
- Software tools that integrate multiple variables (e.g., test results, medical/medication history, patient preferences, family history)
- Genetic test reporting standards
- Integrating lab assays with informatics tools
- Integrate moderate complexity testing into clinical workflow
- Immunoassays and nucleic acid testing on same platform?



# MDx: What's Next?



- Integration with other areas of the laboratory while continuing to play a complementary replacement role
- Progress in full range of disease testing:
  - Diagnostics, screening, therapy response, risk/relapse prediction
- Specific diagnostic tests (particular disorders) → broader assays (variants)
- Focus on defining clinical significance of findings
  - Effects of single gene on common diseases generally small
  - Labs clarify how they will assist physicians with the complex interpretation of clinical data generated (particularly w/r/t pharmacogenomics)
    - What do genotypes mean? Will pharmacist be involved in final recommendation to physician?
- Moving to a point-of-care orientation
  - Simpler, faster platforms

QUESTIONS?

