INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

Board on Health Sciences Policy
Roundtable on Translating Genomic-Based Research for Health

Evidence Generation for Genomic Diagnostic Test Development: A Workshop

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Roundtable on Translating Genomic-Based Research for Health

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Current Healthcare Environment

- US healthcare costs are 17% of US GDP
- US healthcare system delivers poorest outcomes of any developed nation
- Demand for cost-effectiveness and better outcomes of US healthcare system

The Hope of the Human Genome Project

- Understand human genetic variations and their relation to health and disease
- Predict disease risks for prevention & earlier intervention
- Refine disease diagnosis by underlying molecular mechanisms
- Treat based on molecular mechanism
- Improve health and healthcare outcomes

Genetic Tests

- Focus on single gene genetic tests
- IVD industry not focused on small market with poor reimbursement
- Genetic tests developed by clinical laboratories
  - Based on published genotype-phenotype correlation,
  - Using standard molecular biology methods, and
  - Set of patient & control samples,
  - Under CLIA without FDA approval/clearance
  - Predominantly for diagnosis of disease
- Concern about quality, potential harm and clinical validity/utility (ELSI, SACGT, SCAGHS) & cost

Genomic Tests

- Complex testing algorithms of multiple genetic variants, multiple genes, or gene expression patterns
- Used for diagnosis, therapeutic selection, dosing, prognosis and residual disease detection
- Companies using CLIA pathway instead of FDA
- Little evidence of improved health outcomes from use of genomic tests

Clinical Validity/Utility Evidence for Genomic Tests

Genetic Test	Source	Conclusion
Thrombophilia tests	AHRQ/EGAPP	**No direct evidence** for improved outcomes
HER2 testing in breast cancer	AHRQ	**Weak evidence** relating test result to treatment outcomes
Gene expression profiles for breast cancer	AHRQ/EGAPP	**High quality** retrospective clinical utility data for Oncotype DX
UGT1A1 genotyping for CRC patients	EGAPP	**Insufficient evidence** for or against testing
Genetic testing for HNPCC	EGAPP	**Limited evidence** that MMR mutations cause family members to have increased screening
CYP450 for non-psychotic depression	EGAPP	**Paucity of good quality evidence** that testing useful for SSRI outcomes
Genomic tests for ovarian cancer	EGAPP	**No evidence** that tests impact outcomes in asymptomatic women

Conclusion:
Health outcomes data lacking for most genetic/genomic tests

Usual List of Barriers

- Different type/level of evidence needed by different stakeholders (doctors, patients, FDA, payers, evidence-review groups, etc)
- No funding for RCTs for genomic tests
- RCTs take too long
- High cost of archiving specimens from therapeutic clinical trials
- Lack of access to annotated clinical specimens
- Etc, etc, etc

Need to define the evidence needed & mechanisms to generate that evidence for genomic tests to realize the hope of the human genome project

The Purpose of the Workshop

- What evidence is needed by different stakeholders?
- Are there innovative ways to generate higher quality evidence more efficiently?
- Are there barriers to using the innovative ways to generate the evidence and how can the barriers be overcome?

Think Outside Your Box!

Meeting Agenda

- Stakeholder perspectives on evidence
- New models for evidence generation
- Overcoming the barriers
- Strategies for moving forward

Success = identifying one or more specific actions to facilitate evidence generation for genomic tests