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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The Keck Center of the National Academies

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
- Diagnose disease by molecular mechanism
- Treat based on molecular mechanism
- Improve health and improve healthcare outcomes

Current Healthcare Environment

- US healthcare costs are 17% of US GDP
- US healthcare system delivers poorest outcomes of any developed nation
- Global economic crisis demands fiscal responsibility
- Driving demand for cost-effectiveness and better outcomes of healthcare system

History of Genetic Tests

- Initial 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)

Today's Genomic-based 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 genetic 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:
Evidence lacking for the impact of most genetic/genomic tests on health outcomes

Need to figure out better mechanisms to generate health outcomes evidence for genomic-based tests in the future

Usual List of Barriers

- Different type/level of evidence needed by different stakeholders (doctors, patients, FDA, payers, evidence-review groups, etc)
- Lack of funding for RCTs for genomic tests
- Length of time for RCTs for genomic tests
- Cost of archiving specimens from therapeutic clinical trials
- Lack of access to annotated clinical specimens
- Etc, etc, etc

The Purpose of 2010 Workshop

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

2010 Meeting Agenda

- Hearing from the different stakeholders
- New models for evidence generation
- Overcoming the barriers
- Strategies for moving forward

Success = identifying one or more specific actions

Strategies for Moving Forward

EVIDENCE

- The FDA is our friend – safety & efficacy requirements lower than payer requirement of health outcomes evidence
- Close the gap between FDA & payers evidence requirements?
- Analysis of cost-effectiveness of “analytic framework” process vs single good clinical trial
- Must define adequate, not perfect, evidence that gets us to 85% ”B grade” certainty

Strategies for Moving Forward

COVERAGE & REIMBURSEMENT

- Discuss new economic models (reimbursement) that value tests which prevent therapy when not useful
- Implement system that does not pay for treatment if not supported by prognostic/predictive test

Strategies for Moving Forward

MEDICAL PRACTICE

- Determine if safety & efficacy is enough for clinical use of new genomic tests, in the context of medical practice
- Medical process ignores EBR recommendations because they can; no checks on medical practice
- Perception that EBR groups don't understand the biological variability of individual patients in clinical practice