Panel 1: Key Unaddressed Evidence Gaps in Implementing Genomic Medicine

Genomic Medicine VIII

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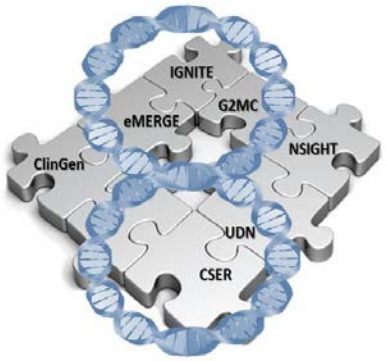
June 8-9, 2015
Rockville, Maryland



Panel Members

- Geoff Ginsburg
  - Director, Duke Center for Applied Genomics & Precision Medicine
  - G2MC, IGNITE
- Jonathan Berg
  - Department of Genetics, UNC Chapel Hill
  - Clinical Cancer and Adult Genetics
  - ClinGen, NCGENES, NC NEXUS
- Pierre Meulien
  - President and CEO, Genome Canada
  - G2MC
- Gurvaneet Randhawa
  - Medical Officer, Division of Health IT, Center for Evidence and Practice Improvement, AHRQ
  - EPC program (reviews and synthesizes evidence)
  - PCORI dissemination and training

Go Duke !

In the news

A Crisis at the Edge of Physics

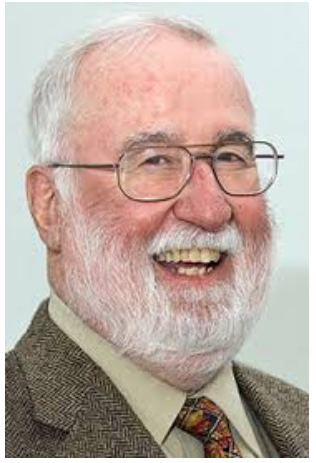
New York Times - 2 days ago

Does **science** always need empirical evidence?

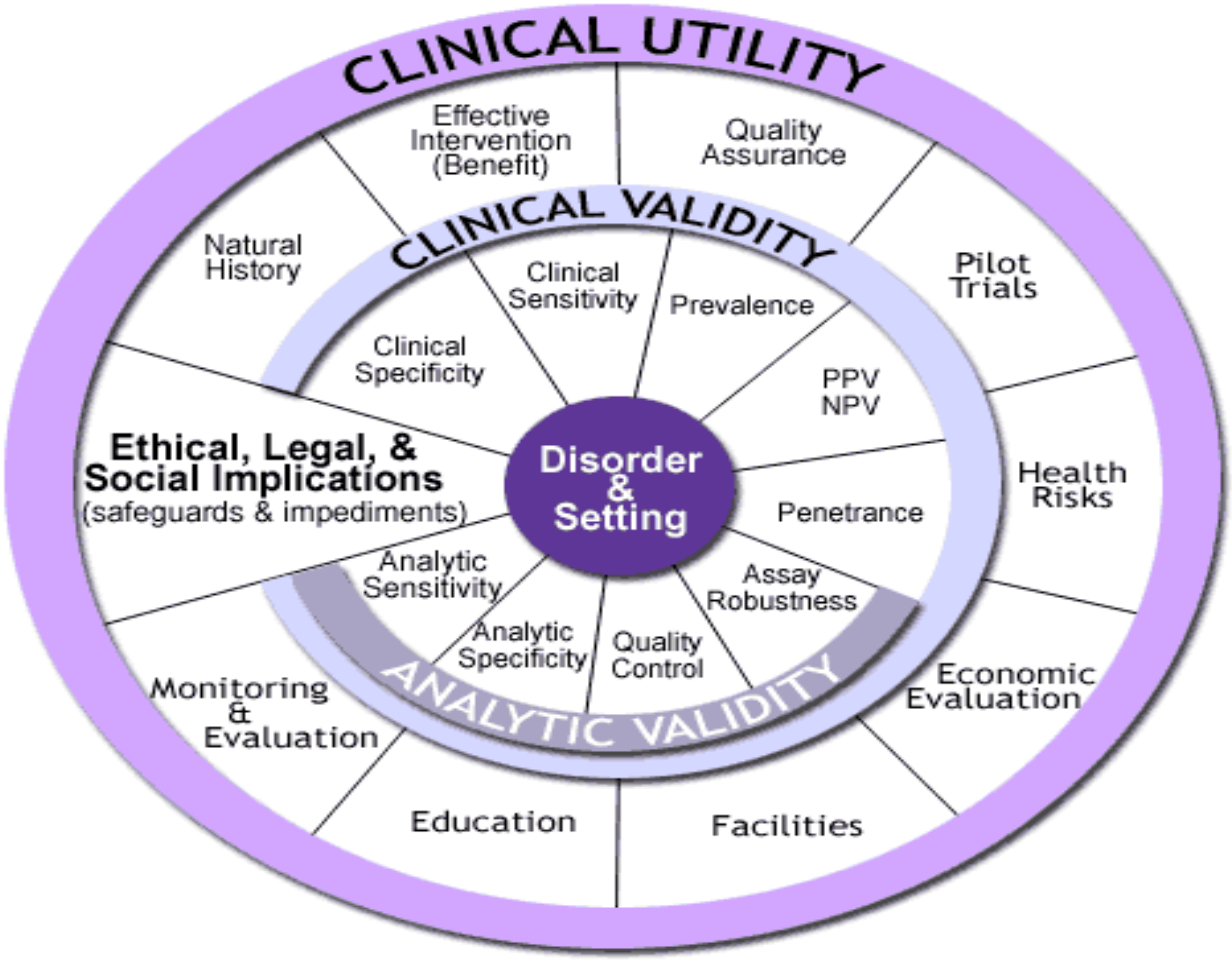
"Today, our most ambitious science can seem at odds with the empirical methodology that has historically given the field its credibility."

1. Why we need evidence: Importance and Impact for Genomic Medicine Implementation

- Clinical validity, clinical utility
- Guideline development
- Provider adoption
- Patient advocacy/adoption
- Regulatory approval
- Payer reimbursement
- Pre-implementation evidence gateway to broader evidence development and dissemination



An Evidentiary Framework for Genomic Medicine

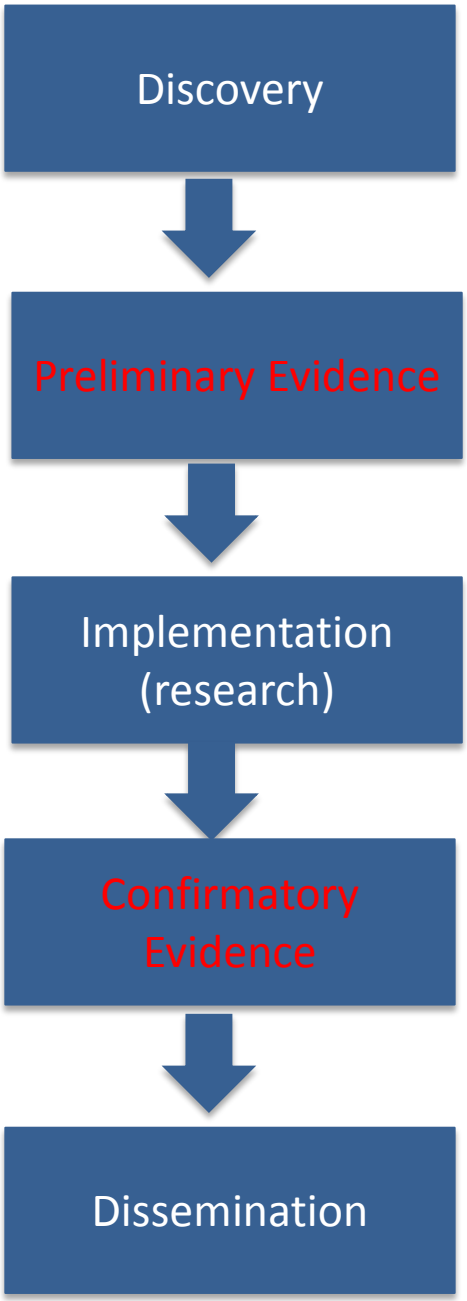


http://www.cdc.gov/genomics/gtesting/ACCE/

When do we need evidence and what level is required for

a) Implementation ?
b) Dissemination ?

Who makes these decisions?



Some Evidence Questions

- What are the types of evidence are required to support the use in a particular context?
- How can we align expectations?
  - Evidence “generators” (scientists)
  - Evidence “evaluators” (evidence-based reviewers)
  - Evidence “users” (regulatory agencies/payers, providers, patients, health systems executives?)
- What is the role of “personal utility” and how are patient-centered outcomes taken into account?

Clinical Decisions: Matching Evidence to Context

- Screening in populations (high bar)
- Therapy to improve survival, potentially for many years (high bar)
- Strategies to improve adherence to medications or lifestyle recommendations (lower bar)
- Optimizing pain control to improve quality of life for days to weeks (low bar)

An evidence matrix for patients, providers, systems

	Patient	Provider	System
Clinical	• Laboratory Result • Symptoms • Medication Use • Vital signs / BMI	• Disease Goals • Referrals • Adverse Events • New diagnoses	• % @ High Risk • % w/complications • % at goals • Visit length
Molecular	• Interest in /understanding of genetic testing	• Appropriate test ordering • Understanding of results	• Testing available • Clinical decision tools used
Behavioral	• Activity scores • Dietary record • Medication adherence	• Appropriate screens • Discussion of risk • Discussion of prevention	• % screened • % at goals • % adherent
Emotional	• Quality of life • Readiness to change • Satisfaction	• Satisfaction • Knowledge • Concurrent with decision support	• Staff satisfaction • Retention • Absenteeism
Financial	• Visit costs • Medication costs	• Medications ordered • Screening tests used	• Utilization • ER visits

Leveraging Clinical Data Infrastructure For Evidence Generation

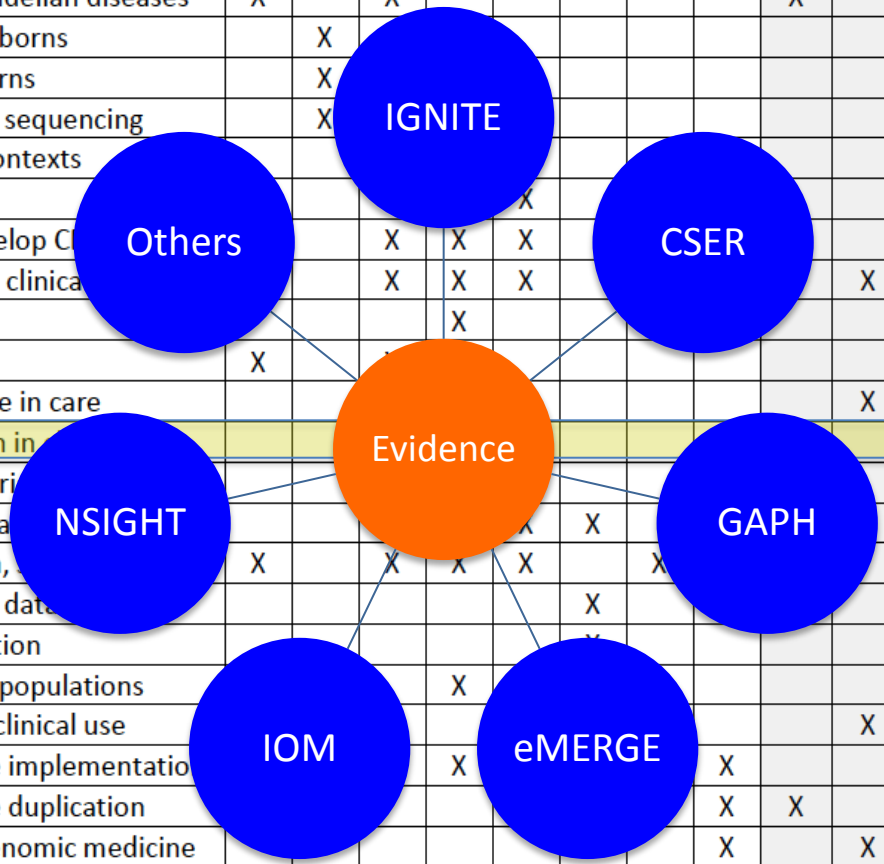
- Rapid adoption of health IT has enabled data-driven clinical care and real-time decision support
- Increased patient participation and use of PROs as part of the evidence base
- Gather and use health care information (eg EHR data) to build the evidence base
  - Learning health system
  - Genomic information integrated into the EHR

2. Who is addressing this topic? – Related Research Programs

- IGNITE
  - Implementation and outcomes programs in PGx, FHH, risk variants
- eMERGE
  - Implementation and outcomes programs in PGx
- IOM WG/AC
  - Genomics enabled learning health system
  - DIGITIZE
- GAPH (Genome Canada)
  - Broad programs to inform decision making re: effectiveness of drugs, adverse drug reactions, intervention strategies and disease management; economic analyses
- CPIC
  - Evidence synthesis for PGx
- NSIGHT
  - Evaluating evidence for sequencing newborns

Genomic Medicine Evidence Space

	Focus Programs								Related Programs							
	UDN	NSIGHT	CSER	eMERGE	IGNITE	ClinGen	GM Mtgs	G2MC	CMG	CPIC	GA4GH	GAPH	IOM	ISCC	LSAC	PAGE	PhenX
Improve genomic diagnostic methods	X	X	X						X								
Facilitate research in undiagnosed and/or Mendelian diseases	X		X						X								
Expand scale of genomic data available in newborns		X															
Advance understanding of disorders of newborns		X															
Research ethical/legal/social issues in genome sequencing		X											X				
Interpret sequence data in variety of clinical contexts																	
Integrate sequence data into patient care					X								X				
Incorporate actionable variants into EMR, develop Cl			X	X	X								X				
Educate clinicians and patients on genomics in clinica			X	X	X					X			X	X			X
Develop electronic phenotypes				X													X
Identify variants related to complex traits	X											X			X	X	
Characterize pharmacogenetic variants and use in care										X							
Assess outcomes of using genomic information in												X					
Assess penetrance of potentially actionable vari																	
Translate implementation outside highly specia					X	X											
Define and share processes of implementation,	X		X	X	X		X						X				
Share genotype/phenotype info through open dat						X					X						
Standardize clinical annotation and interpretation																	X
Improve understanding of variation in diverse populations				X												X	
Assess action ability of genes and variants for clinical use										X							
Identify, address barriers to genomic medicine implementatio				X				X									
Promote interaction and collaboration, reduce duplication								X	X		X		X	X			
Serve as clearinghouse, knowledge base for genomic medicine								X		X							
Use genomics to enable new drug development												X	X				
Create genomics-enabled learning health care systems				X	X								X				
Develop evidence base for clinical use of novel diagnostics												X					



3a. Gaps, Barriers and Opportunities

- For implementation you need evidence, and for evidence you need implementation
- *Effectiveness* evidence is needed
  - anticipated benefits from *efficacy* studies don't pan out in real-world
- Clinical validity and utility
  - ensuring study design and power
- Fragmentation of systems
  - Health systems (USA), ethics boards, tech assessment cmtes
- Health information technologies
  - tools and infrastructure
- Healthcare professional capacity (education)

3b. Gaps, Barriers and Opportunities

- Misalignment of payers, opinion leaders, patients, regulatory bodies etc
- Sub optimal health technology assessments and propositions based on “value” to the system (leading to reimbursement decisions)
  - Defining what evidence will be required for ROI
- The data infrastructure(s) and standards required to gather evidence in the context of clinical trials and clinical care
- EHR integration and interoperability
- QI (often not published) and evidence
  - Are they one and the same? Role of the learning health system?

Footnote:
Evidence and Drug Discovery Research

- Genomic Medicine is also about how drugs get developed enabled by genomic understanding
- Key issue: Articulate how to move from a gene signal to a full understanding of mechanism/development of a drug development hypothesis
- Collecting more information/data to go from GWAS/sequencing variant to a validated drug target
- High-throughput, non-invasive strategies to study function of alleles/genes in a system suitable for drug discovery linked to measurable quantitative biomarkers
- Developing the human genome KO collection

4. Possible Synergies Across Programs

- Common measures of outcomes
- “Implementation Commons” with key lessons learned
- Create/enhance evidence databases/warehouses
  - clinicaltrials.org and in clinicaltrialsregister.eu
  - Produce and update a catalog of these trials
  - ClinGen
- Joint publications across programs
- Ensure that programs are known to federal agencies (CMS, FDA, AHRQ, ONC) and non-profits (PCORI, RWJ etc.)
- Joint workshops with payers, regulators

5. Training Opportunities

- Translational genomic skills – what are the core competencies ?
  - Genomic medicine T32 NHGRI
- Fellowships linked to IGNITE, eMERGE or other programs
- Collaborative training with Genome Canada
- Development of tools and education materials to increase the understanding of the evidence for and uptake of genomic applications in health care and disease prevention (the genomic medicine “toolkit”)

6. Some Discussion Questions

- How can regulators, payers, researchers, developers, *and patients* come together to create an "end to end" solution ?
  - Should projects and programs incorporate the expectations the stakeholders to inform study design? If so, how to orchestrate?
- Should we/can we create partnerships among the programs?
  - Can we harmonization of data and outcomes measures across programs and projects? Coordination of coordinating centers?
  - To create/enhance evidence databases/warehouses?
- How do we define and agree to the evidentiary thresholds for pilot implementation? for dissemination?
- How do we incentivize health care systems to embed genomic information into their EHRs and workflows? To embrace Genomic Medicine? What is the ROI? Can we take a leadership role in the value proposition?