Clinical Evidence for Genomic Medicine Sustainability: State of Science and Gaps

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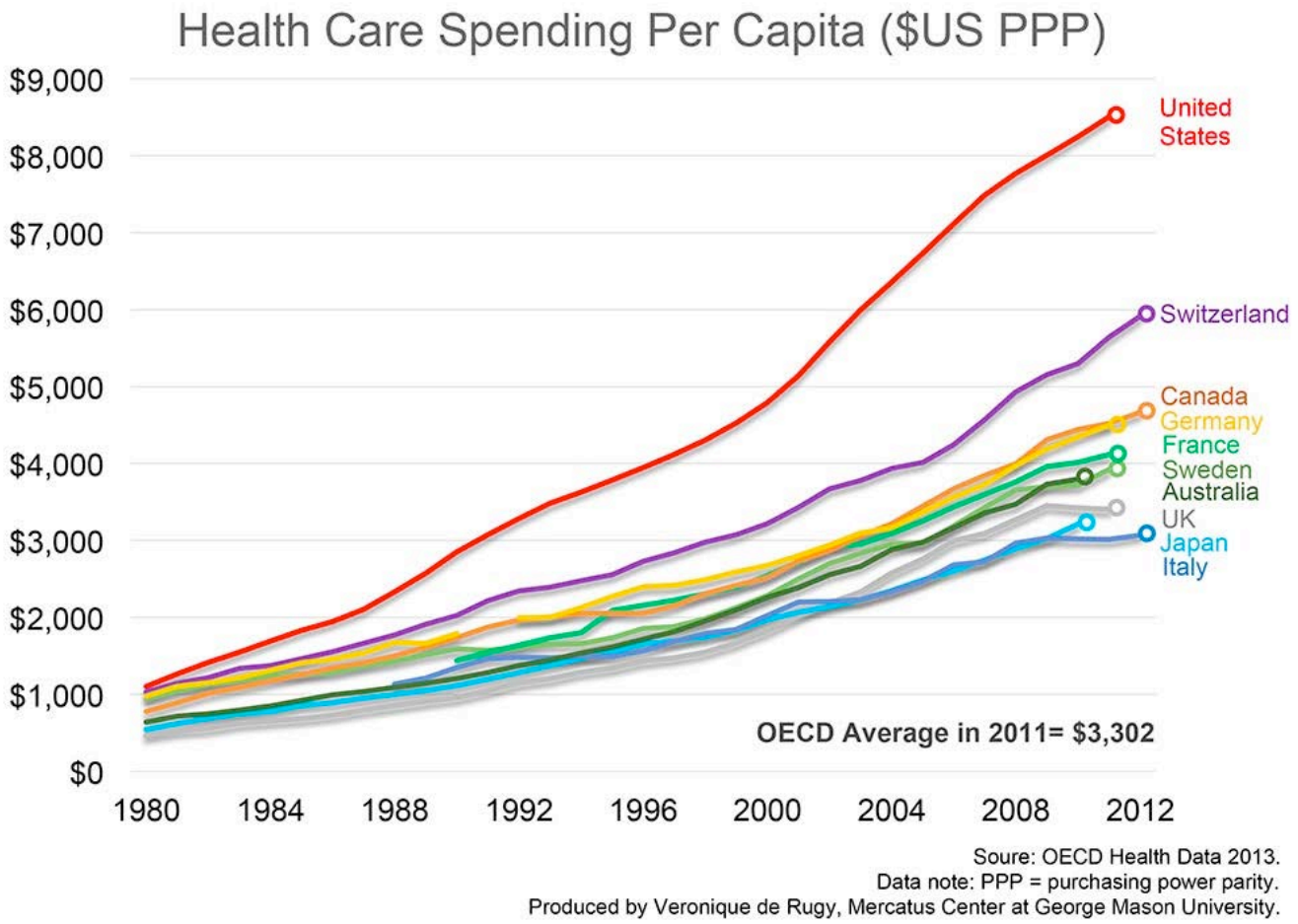
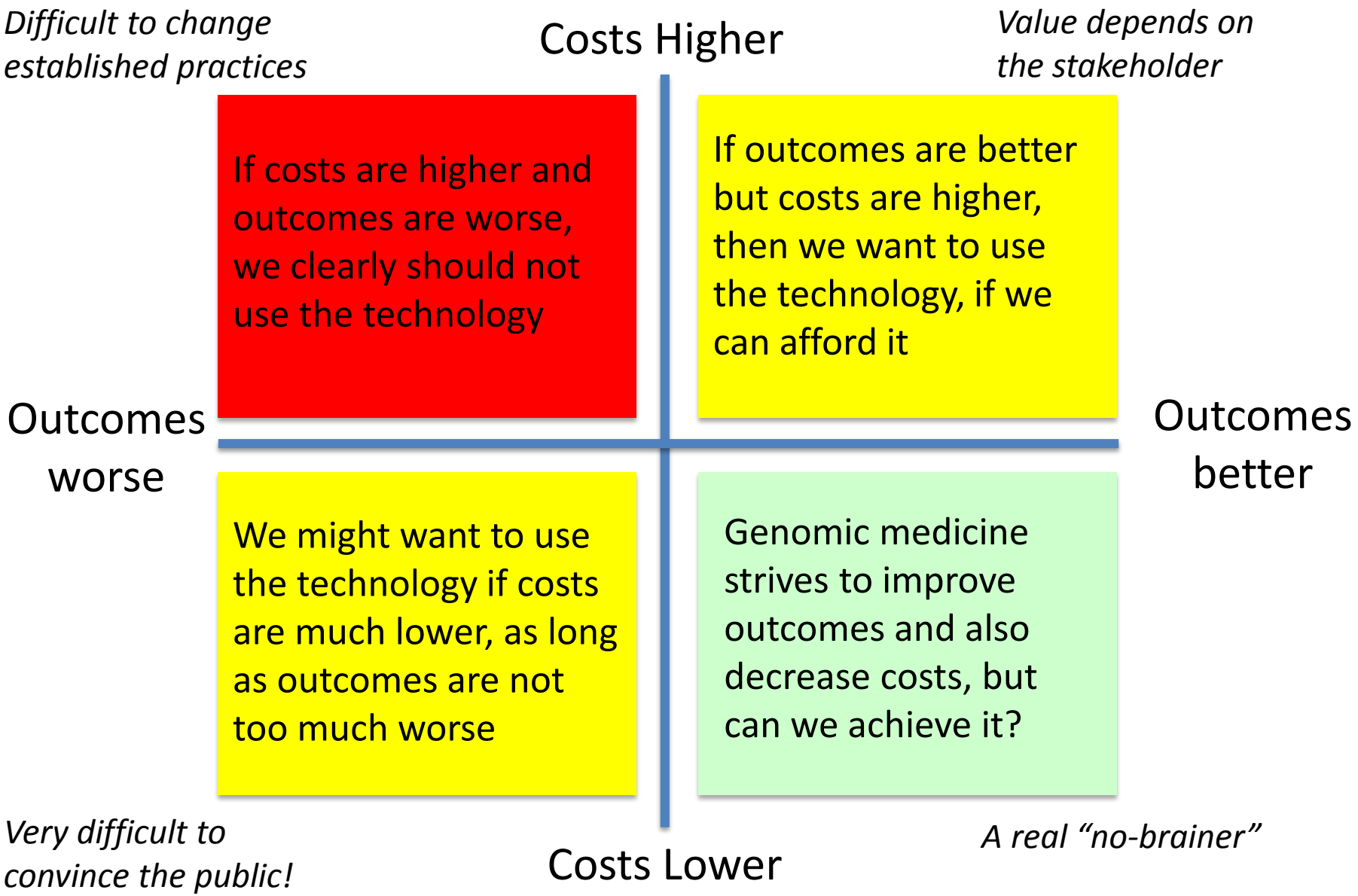
Rising cost of healthcare, rising pressure to reduce spending



http://mercatus.org/publication/us-health-care-spending-more-twice-average-developed-countries

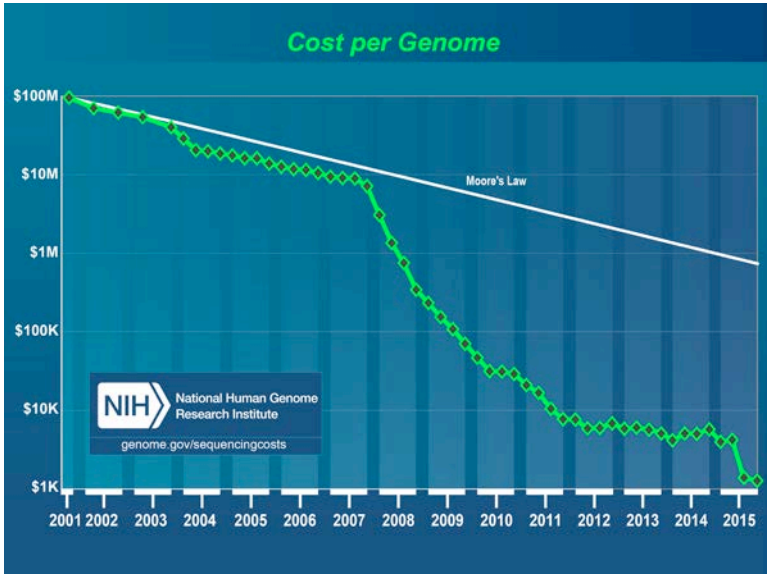
Technology and healthcare costs

- Much of the increase in healthcare costs is attributed to technology
- This perception, whether or not it is correct, is at least part of why 3rd party payers are so focused on evidence of utility and cost-effectiveness
  - We need to meet them in that space
  - Genetics cannot be exempt from evidence of utility



Modified from David Veenstra, IOM workshop presentation, July 17-18, 2012.

- We are so accustomed to the ubiquitous “cost per genome” graph that it seems obvious that genomic sequencing will be used widely in health care



- But we must address the cost/benefit:
  - Costs of interpretation (certainly not the $1 million genome hyperbole, but more than $0) ***and*** costs of downstream interventions (definitely not $0)
  - What are the **net** outcomes and cost effectiveness of achieving those outcomes?

Evidence for Genomic Medicine

- Depends on who you ask (Stakeholders)
  … Their perspectives (Values)
  … And how much certainty is required
- Implementation studies are necessary to understanding how to effectively utilize a new technology, *if it is proven to be useful*
- Sustainability depends on convincing third parties (healthcare systems, insurance providers, FDA) that genomics is effective

Public Health Genomics

Original Paper

Public Health Genomics 2011;14:59–67
DOI: 10.1159/000290452

Received: September 27, 2009
Accepted after revision: February 19, 2010
Published online: April 20, 2010

Stakeholder Perspectives on a Risk-Benefit Framework for Genetic Testing

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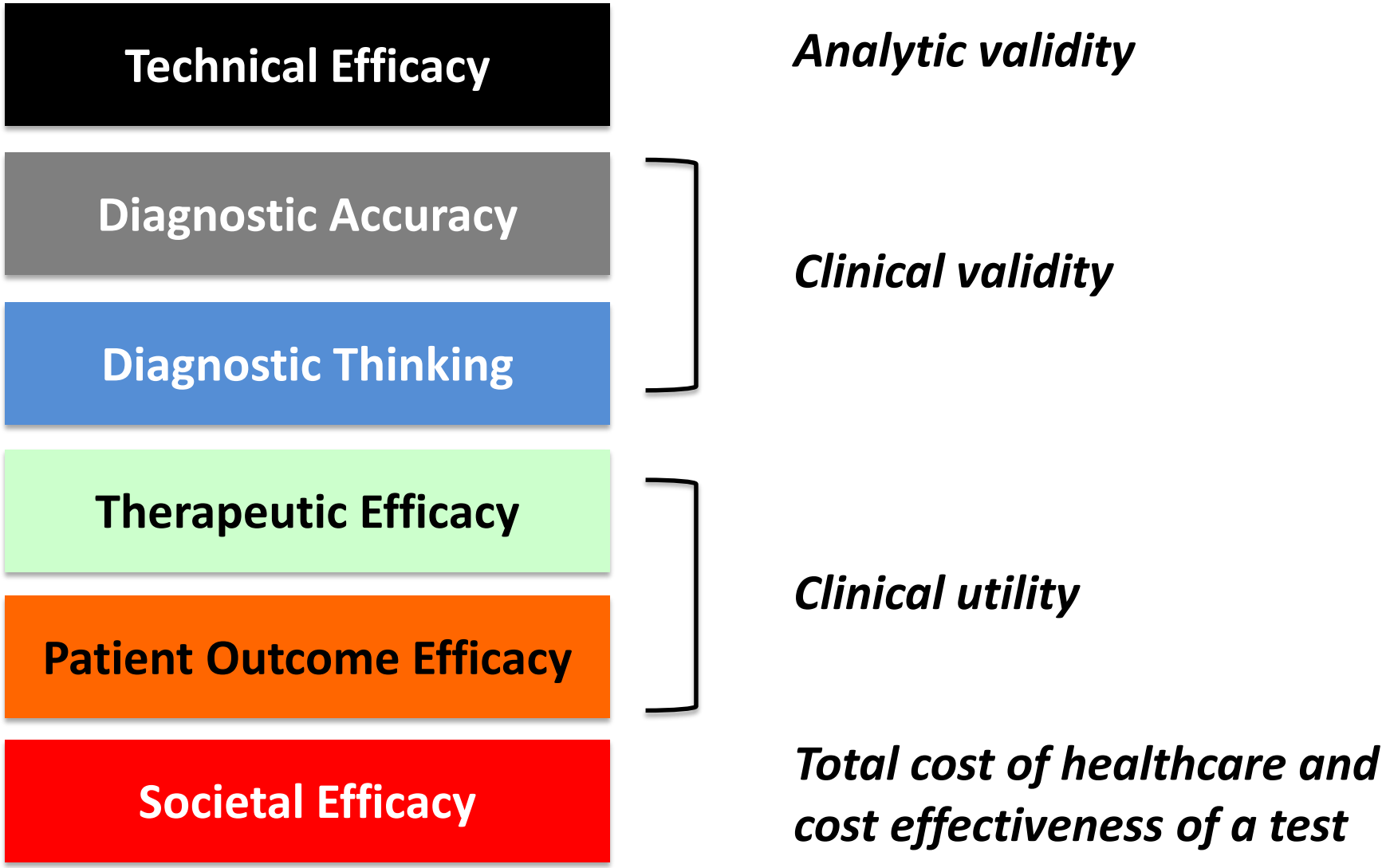
	High uncertainty	Moderate uncertainty	Low uncertainty
Favorable risk-benefit	Use with evidence development	Consider use in clinical practice	Appropriate for use in clinical practice
Neutral risk-benefit	Do not use, conduct additional research	Use with evidence development	Consider use in clinical practice
Unfavorable risk-benefit	Do not use, conduct additional research	Do not use	Do not use

Which outcomes matter?

- Ideally, direct health outcomes
  - Mortality, morbidity, healthcare utilization
- For physicians, improved management might be a reasonable expectation
  - Allowing use of best clinical judgment for the individual patient with a rare disorder
- For patients/families, simply having a diagnosis may have value
  - Including understanding recurrence risk

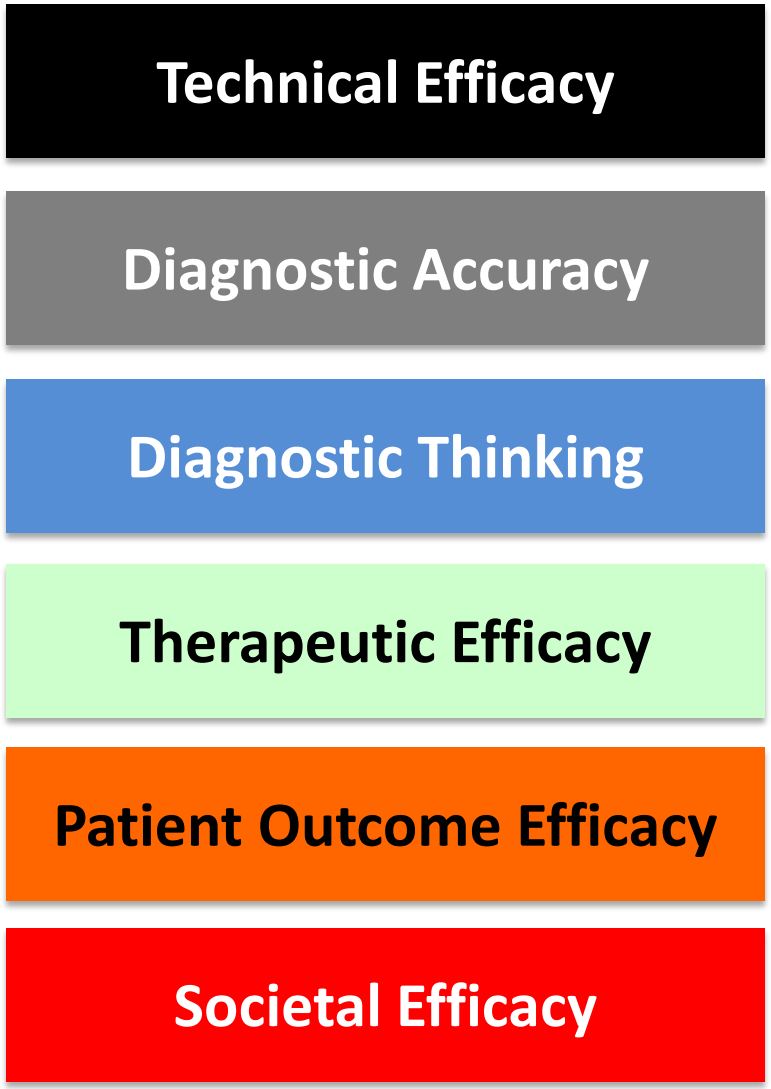
Fryback and Thornbury Hierarchical Model – Initially proposed for evaluation of imaging tests



Example: Diagnostic Testing

- Consider a patient with a clinical diagnosis of Cystic Fibrosis based on sweat chloride test
  - Is genetic testing needed?
  - If so, what test?
  - Should it be covered by insurance?

Example: Diagnostic Testing



- Clinical genetic testing modalities (genotyping, sequencing) are generally quite accurate and reliable
- Establishing the disease-causing variants (eg. homozygous F508del) would not affect diagnostic thinking…
- However, if the specific molecular defect enabled decisions about therapy (eg. Lumacaftor/Ivacaftor), it would alter therapeutic efficacy…
- And possibly patient outcomes…
- And conceivably the cost of caring for CF patients.

Example: Diagnostic Testing

- Is genetic testing needed?
  - Yes, to determine whether Lumacaftor/Ivacaftor is a possible therapy
- If so, what test?
  - Targeted genotyping? *CFTR* gene sequencing? Exome?
- Should it be covered by insurance?
  - It depends on the economics; the cost of the test / drug and the nature of the health outcomes
  - If outcomes are sufficiently improved (1/3 as many hospitalizations) and the costs are affordable ($259,000 / yr)

Example: Diagnostic Testing

- What about the reproductive implications?
  - Requires only that the test is analytically and clinically valid
  - There are no defined measures of “utility” in this context
    - Each family will have different uses for the information
- Each stakeholder will view this information differently
  - Making this a very difficult argument with payers

Where are the gaps?

- Stakeholder engagement
  - Conducted with respect to a defined clinical scenario (patient population, test, indication)
  - Establish the value that different stakeholders (patients, providers, healthcare systems, payers) place on relevant outcomes
  - Understand the evidence that stakeholders need to make decisions about use and coverage of genetic tests

Where are the gaps?

- Evidence generation
  - Studies designed with specific outcomes in mind, to provide evidence that directly addresses the requirements of stakeholders
  - Should not completely ignore other important scientific questions
    - Eg. how to deal with secondary findings
  - Genomic medicine researchers need to learn how to frame studies to convey results to different stakeholders

Where are the gaps?

- Evidence synthesis
  - Just as we need databases of genes and variants (eg. ClinGen/ClinVar), we need systematic collection, curation, and evaluation of genomic studies
  - Designed in collaboration with stakeholders to structure information that facilitates their review
  - Publicly available and curated by experts
  - So that we have transparency in the evidence that stakeholders are looking for, and studies can be designed for maximal impact

Take homes

- Technology and healthcare costs
- Stakeholders and what they value
- Context and outcomes matter
- Engage stakeholders to promote understanding and produce relevant evidence