Jefferson
School of Population Health

The Economics of Personalized Medicine and Genomics

Robert D. Lieberthal, PhD
Assistant Professor,
Jefferson School of Population Health

Disclosures—JSPH Research Projects

- I have worked on projects at the Jefferson School of Population Health funded by
  - Abbott Laboratories (Abbott Molecular division)
  - Genomic Health (Onco*type* DX®)

JSPH Academic Projects

Learning Objectives

1. Assess genomic approaches from the point of view of a patient and a population

2. Critique current approaches to assessment of personalized medicine

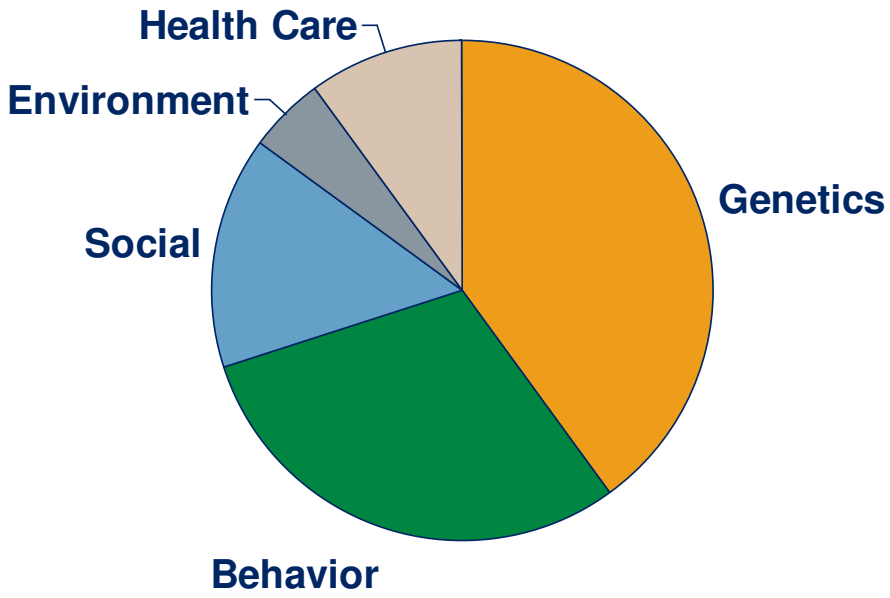
3. Evaluate the economic outcomes of genomic medicine for different populations

Connections to Colloquium Sessions

- **Carolyn Buck-Luce, MBA**
  - Global Pharmaceutical Sector Leader, Ernst & Young, New York, NY
  - The Importance of Innovation for Life Sciences
  - Tuesday, 2/28, at 11am

- **Chris McFadden**
  - Managing Director, Health Evolution Partners, New York, NY
  - Closing Keynote: Healthcare Investment Trends
  - Wednesday, 2/29, at 8:15am

Genetics is a major determinant of population health outcomes



- Source: *Population Health,* Ch. 10
- Behavior is number 1 at 40%
- Genetics is high at 30%

Genetics versus Genomics

- **Genetics**
  - "Study of genes and their roles in inheritance"
  - Genetic diseases: Cystic fibrosis, Huntington's disease, and phenylketonuria (PKU)

- **Genomics**
  - "Describes the study of all of a person's genes (the genome)"
  - Complex diseases: heart disease, asthma, diabetes, and cancer
  - Combination of genetic and environmental factors
  - "Genomics is offering new possibilities for therapies and treatments for some complex diseases, as well as new diagnostic methods."

Source: National Human Genome Research Institute, National Institutes of Health; genome.gov

Diagnostics as the first step toward Genomic Medicine

- We have mapped the whole human genome
- Reasonable first step: relate that map to known illnesses
- Genomic diagnostics
  - Predictive genomic tests—Onco*type* DX® (Genomic Health)
  - Genomic therapies—Vysis ALK FISH test (Abbott Molecular) and crizotinib (Pfizer)

Population health purposes for Genomic Diagnostics

- Research
  - This is where we are now
- Improvement
  - Future medicine—combine data from success of drugs with multiple genomic tests
  - Refine treatment for subpopulations
- Accountability
  - Definitely not yet
  - Examples: herceptin—HER2 breast cancer

Genomic tests sort people out

- Think about oncology drugs
  - Traditional chemotherapy
  - Novel, targeted, molecular therapies
- How much would a test be worth that separated responders from non-responders?
  - Direct valuable healthcare resources towards those most likely to benefit
- Value of test depends on population level variables
  - What percent of people are expected to succeed and fail?
  - Test validity is crucial and dependent on the scenario

Genomic diagnostics can help choose between existing options

- Genomics can show commonalities within groups
  - Genetic background
  - Gene-environment interaction
  - Special mutations
- Genomics is about classification
  - Which similarities matter clinically—go beyond disease diagnosis
  - What worked in the last patient that will work with this patient?
- Diagnostic genomics is an emerging field
  - Familiar challenge—making bench science into clinical therapy
  - New challenge—find which common markers that are already known are valuable

Examples of genomic diagnostics
Oncotype DX®

- Genomic Health
- Risk score for breast and colon cancer
- Stage 1 or 2 estrogen receptor-positive, lymph node-negative breast cancer
- Combines assay of 21 genes with "scoring" algorithm
- Generates recurrence score between 0-100
- Behavior change potential
  - Determine recurrence probability
  - Evaluate likely benefit from chemotherapy

Source: "The Economics of Genetic Testing for Women with Breast Cancer" (2012). Working paper, Jefferson School of Population Health.

Examples of genomic diagnostics—Vysis ALK Break Apart FISH Probe Kit

- Abbott Molecular
- Non-small cell lung cancer
- FISH test—genomic test to map genes
- ALK—a gene implicated in many types of cancer
- Predicts response to specific drug—crizotinib
- FDA approved, marketed as Xalkori® by Pfizer
- Behavior change potential
  - Evaluate benefit from a targeted molecular therapy that benefits a minority of patients

Source: FDA News Release, "FDA approves Xalkori with companion diagnostic for a type of late-stage lung cancer" www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm269856.htm

Targeted therapies aren't for everyone

- Successful genomic therapies often look great
  - From a clinical point of view
  - Ignoring the fact that we have to figure out how to assign treatment
- Successes and failures will tend to fall in groups
  - Can we identify those groups ahead of time?
  - If not, how rigorous are our post-hoc analyses?
- The main point
  - What looks great to a single patient doesn't always look great on a population level

Personalized Medicine means recognizing and using options

- Conventional therapies
  - Has the richest evidence base
- Novel therapies
  - Therapies that are often costly and/or require special training
- Alternative/complementary therapies
- Watchful waiting and/or palliative care
  - Not everything is curable (or even treatable)
  - A legitimate therapy for many conditions
  - Doctors may have the most work to support patients in this option
  - The outside option in most cases

New treatments complicate Personalized Medicine

- Complications for study design
  - More options to evaluate
  - More subgroups to consider
- Complications for creating an evidence base
  - Evidence-based medicine is based on matching condition and treatments
  - Personalization makes it harder for clinicians to look at the right "cell" in the evidence database
- Complications for economic analysis
  - Economics depends on the marginal choice
  - It's harder to identify the "marginal choice" for each patient
  - Where will policymakers get their data?

Regulatory "Wild West"

- FDA does not regulate laboratory developed tests
- Direct-to-consumer tests are available
  - Navigenics, 23andMe, and Decode Genetics
  - These companies have called for greater regulation
- Potential issues
  - Quality control
  - Reimbursement
  - Lack of development of FDA and other expertise
- Can personalized medicine succeed without regulation?

Billing for genomic tests is complicated

- No stand-alone CPT codes
  - ICD 10 may address this issue
- Example: ResponseDX CPT codes
  - Lung ® : 88323, 88381, 88313, 83907, 83891, 83902, 83898, 83896, 83912, 83900, 83901
  - Colon ® : 88323, 88381, 88313, 83907, 83891, 83902, 83898, 83896, 83912
  - Gastric ® : 88323, 88381, 88313, 83907, 83891, 83902, 83898, 83896, 83912
  - Melanoma ® : 88323, 88381, 88313, 83907, 83891, 83898, 83896, 83912
- ***Can personalized medicine succeed if we can't bill for it?***

Contemporaneous approval of therapy and diagnostic

- FDA is pushing for contemporaneous approval of therapy and diagnostic
- Two oncology approvals in 2011
  - Vemurafenib (melanoma) and cobas 4800 BRAF V600 Mutation Test
  - Crizotinib (lung cancer) and Vysis ALK Break Apart FISH Probe Kit
- Personalized medicine issues
  - Do those who “fail” the test get the drug?
- Economic issues
  - Evaluate the two simultaneously
  - Impossible to separate the comparative effectiveness of the test from the drug under current regulations
  - Back to the question: how do we value the test?
  - Answer to personalized medicine issue dictates the setup of economic evaluation

An economic perspective is needed

- The marginal value of extra information
  - Not how good is genomics
  - How much more good does it provide?
  - Value could be financial, clinical or humanistic
- Getting homogenous subpopulations is the point of personalized medicine
  - Not just on observable characteristics
  - Estimate what variation is unobserved
  - Maximize the value of all information
  - That describes the techniques for observational studies in economics research

Economics is about Value

	Low non-monetary costs	High non-monetary costs
Low monetary cost	Potentially high value treatment	High clinical/humanistic cost
High monetary cost	High financial cost	Potentially low value treatment

- All cells require assessment of benefits
- All cells require additional comparative effectiveness analysis

Genomics doesn't have to be fancy and expensive

- Clinicians already collect a lot of data—i.e. oncology
  - Sex and gender
  - Race and ethnicity
  - Age
  - Cancer stage
  - Cancer histology
- Usually cheaper to collect data by asking people than by running assays
- The promise of genomics is getting beyond the plainly observable
- Genomics imposes many costs to get additional data
  - Vysis ALK FISH test requires a tumor sample

Value of genomics depends on modality of practice of medicine

- Whose outcomes are we maximizing?
  - The patient
  - The statistical patient
  - Population health
- Do we personalize as much as we can?
  - We take into account as much data and experience as possible
  - Then we still have lots of partially informed choices—possibly with equally proven outcomes
  - How should payers choose between me-too drugs and me-too therapies?
- The answers could make genomics more or less valuable

Minimizing societal costs

- Economic perspective
- The value per average person
- This will make a test worth less or zero if there are too few or TOO MANY successes for our hypothetical drug
- Think of Vysis ALK FISH test
  - Too few predicted responders—the test identifies few new treatments
  - Too many predicted responders—we are harming people by charging for the test when we should just give everyone crizotinib!
  - Despite the heavy cost of inappropriate treatment for those non-responders

U.S. perspective on who bears the cost

- Treatment failures (or their insurers) pay a cost and get no benefit
- Treatment successes (or their insurers) pay a cost and get a benefit
- Different rule
  - If Onco*type* DX® test result changes treatment path, it was more valuable for that patient than average
  - You could charge successes once the test comes back, or charge everyone upfront and rebate the failures (VBID/risk sharing/other)

Universal health care systems perspective on who bears the cost

- Societal perspective
- Individuals accept that the payer may pay for treatments that don't benefit them
- The whole point is that we can easily identify the beneficiaries—more so than in many other types of medicine
- Equity issue—are those who don't benefit from the test left out?

Some people may be harmed by new technology

- Common problem in U.S., universal systems
- Some may pay for a test that doesn't directly benefit them
- Some who would have benefited from the old drug get the new drug
- Economics: how could we balance these harms?

Place of health policy is to raise these issues and make sure no one is harmed too much

- Genomics in personalized medicine
  - It's a science
  - Health policy can't change science
- The rationale and implications of the economic approach
  - Lots of studies involve modeling
  - We want to cut down to binary choices through the marginal approach
- Policy approach
  - Balance outcomes for populations and existing patients
  - Consider intended and unintended consequences
  - Decide how much weight to put on observational studies
  - Benefit the population

Summarizing the economic approach to Personalized Medicine

- Economic evaluation depends on
  - The practice of medicine
  - Regulator behavior
  - How medical science evolves
  - Population versus patient focus
- Test gives valuable information on whether to proceed with investment (expensive new treatment)
- Price discrimination may help access but hurt equity
- VBID/risk sharing arrangements—“no outcome, no income”!

Learning Objectives—Review

1. Genomic approaches
   a) Patient wants personalized treatment
   b) Population dictates how much variation we can observe
2. Assessment of personalized medicine
   a) Regulators have some expertise but limited say
   b) Payers can't find some treatments in their claims data
   c) Some may resist evidence-based medicine, and EBM may not be informed for every group
3. Evaluate the economic outcomes
   a) Some RCT evidence
   b) More observational studies/modeling
   c) Policy on how technology is deployed dictates how it should be studied