

Future Challenges to Health Technology Assessment: Data Requirements for High Cost, Targeted Therapies

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Today's Discussion

- Where Are We Now & What Is Coming?
- 4 Key Challenges & Opportunities
- 4 Key Insights



2006 to 2011: What's New is Old; What's Old is New

- 2006 Conference: *“What Does the Future Hold for Targeted Therapies”?* (Prof Ross McKinnon)
- Rapid growth in high cost biologicals
- Increasing evidence that patients respond differently to drugs based on genetics
- “PGx is here?”



2006 Conference Outcomes

Medicines Australia and Dept of Health and Ageing agreed to undertake further dialogue and collaborative work:

- a. Explore how genomics and diagnostics will impact on the targeting of new medicines to the right patient and the impact of this on health technology assessment.
- b. Explore the impact of marketing issues in creating expectations in a climate where medicines become increasingly targeted within sub-groups of disease populations.



2008 Conference Outcomes

- Development of targeted therapies presents challenges to the way in which the various aspects of an integrated care model are managed and delivered.... On occasion, PBAC recommends medicines for PBS subsidy that require patients to undertake certain medical tests.... If the required test has not been evaluated by MSAC for cost effectiveness, access to the therapy could be hindered.
- The Department and the PBAC will work with MSAC to strengthen linkages between these two advisory bodies



2010 Symposium: New and Emerging Cancer Therapies: From Hype to Reality

- Genetic testing rarely parallels drug development
- Reimbursement of genetic tests and drugs is disconnected
- Evidence-based medicine is new in non-pharmaceutical world and evidence for efficacy of genetic tests is often ambiguous
- Hospital laboratories do not have infrastructure for genetic testing and there is high degree of QC variability
- Different payers for tests make it hard for patients to navigate the system
- Limited evaluation of the way in which medicines perform in routine care



Is Personalized Medicine Just Hype?

- Yes hype - but inevitable trend towards greater stratification & targeting
 - Knowledge of human genomics & molecular basis of disease
 - Emphasis on safety
 - High drug costs
 - Consumer directed care
 - Use of IT & ER
 - Comparative effectiveness research & focus on heterogeneity
 - *Inevitable that will change landscape of health care*



The Time is Now

2006

“In 20 years we will have ‘predictive, personalized, preemptive’ health care.”

Elias Zerhouni, Director of the National Institutes of Health (NIH)

2008

NIH names “translational issues in pharmacogenomics” among top 6 challenges for funding

2011

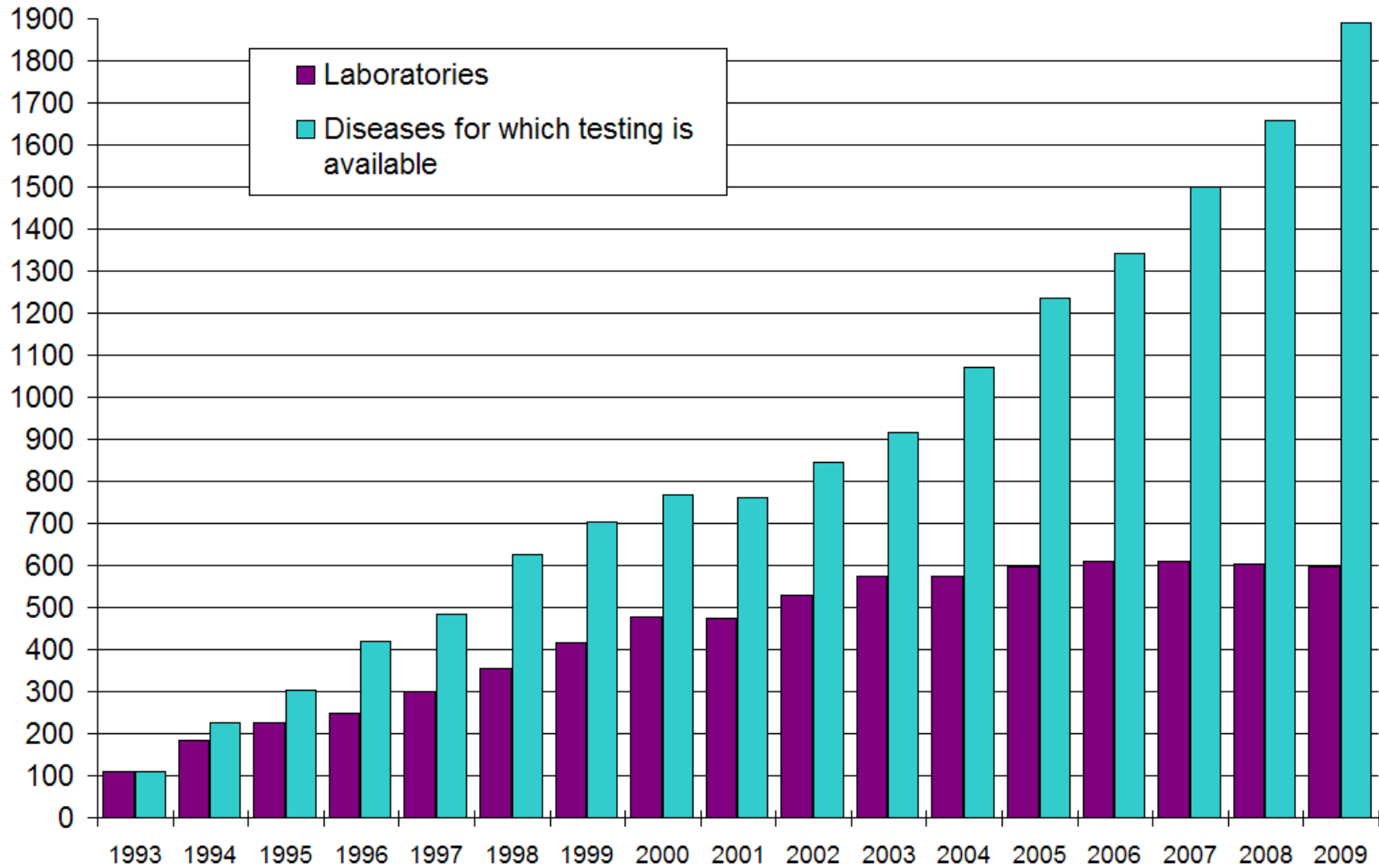
~200 clinically relevant genetic tests for cancer, coronary heart disease, psychiatric illness, AIDS, diabetes, asthma

➤ 100 cancer tests - 67% increase in 4 years



Growth in Testing

GENETests: Growth of Laboratory Directory





University of California
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The Center for Translational and Policy Research on Personalized Medicine



TRANSPERS is Born - 2008



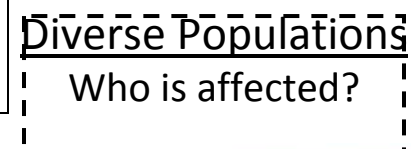
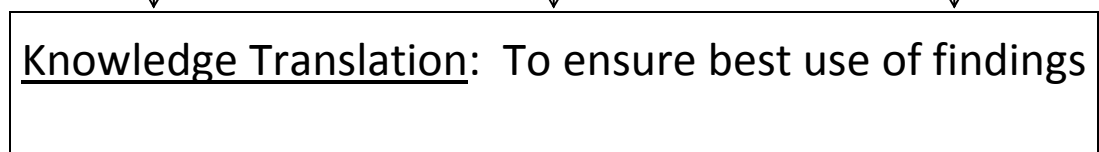
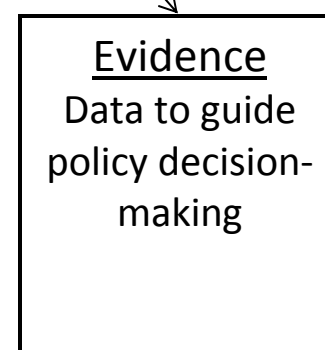
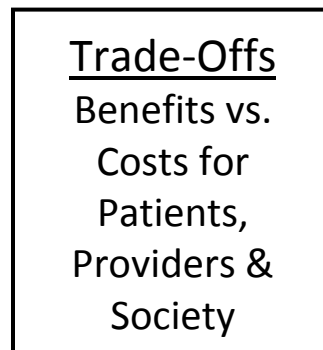
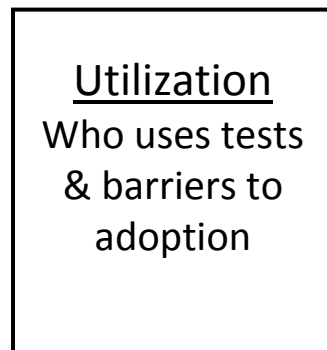
- **Objective:** Apply *real-world evidence* to determine how personalized medicine can be *effectively* and *efficiently* disseminated into clinical practice and health policy
- **Focus:** Cancer & cross-disease technologies
- **Approach:** Objective, cross-disciplinary & cross-perspective
- **Funders:** National Cancer Institute (P01); Aetna Foundation; Blue Shield Foundation of California; Department of Veterans Affairs



Translational Research & TRANSPERS Center



Policy Research on personalized medicine requires...



4 Challenges/Opportunities for Personalized Medicine

Negotiating Shifting
Industry Paradigms

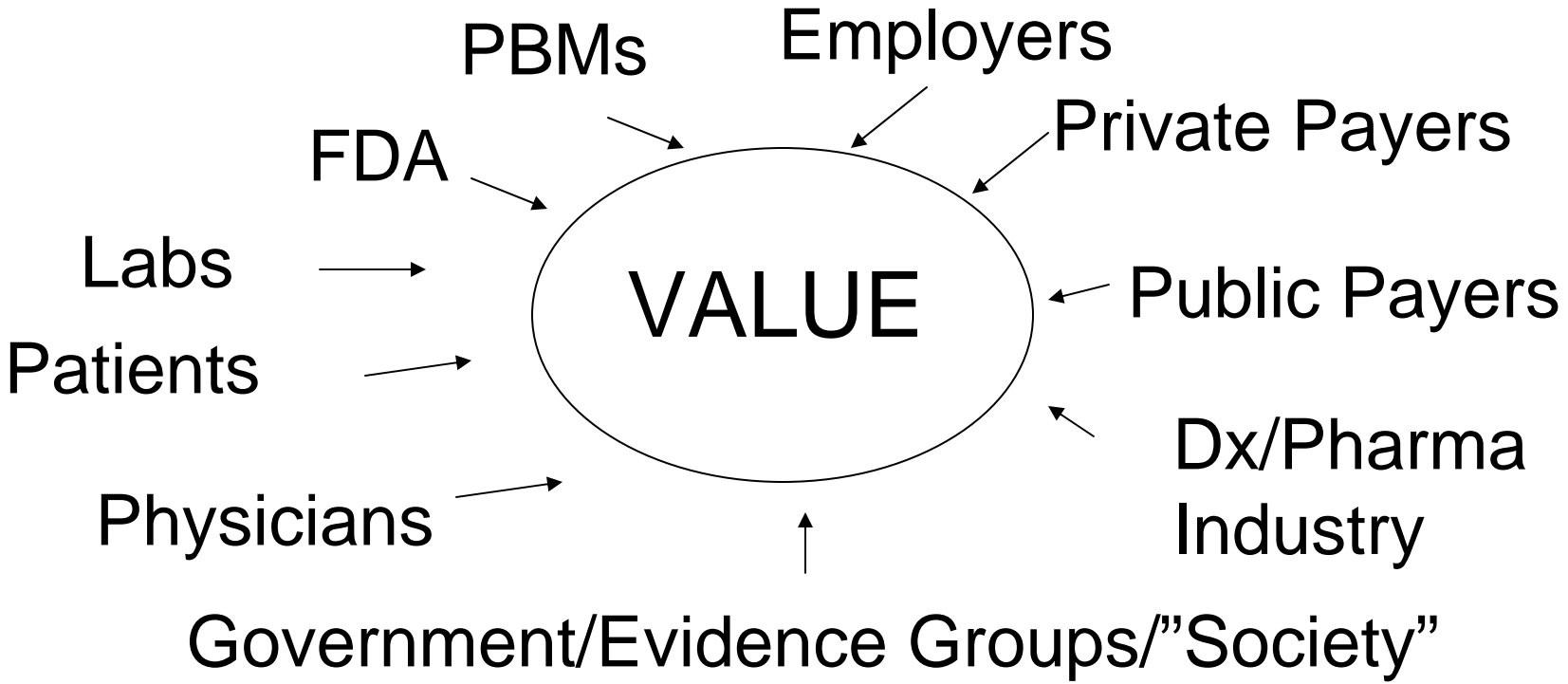
Building Evidence
Base

Balancing Innovation
& Regulation

Determining Value &
Reimbursement



“Value” is in Eyes of Beholder



Challenges to Establishing Value

- Value includes but is broader than cost-effectiveness
- Often little data on clinical utility of diagnostics – actual impact on provider & patient decisions & patient outcomes
 - If not effective, then not cost-effective
- Still relatively few economic analyses
- Just because it's a cool new intervention does not mean someone should or will pay for it



Challenges to Establishing Value

- Targeting does not necessarily provide greater value
 - Conceptually yes, in actuality no
 - May have small absolute or incremental benefits
 - E.g., prevention paradox, genetic testing for statins
- Linking targeting to improved outcomes is complex
 - Testing then treatment then outcomes
 - Impact on family members (if inherited)
- Targeting inadequately analyzed
 - Many analyses do not evaluate targeting method & accuracy
 - Concepts of test validity & utility poorly understood



4 Key Insights



1. Lack of evidence on the testing continuum—
from initial access to acting on results—hinders
evaluation of new technologies

2. Understanding actual practice patterns and
cost-effectiveness is critical to developing
appropriate policies

3. Patient and family member preferences for
care will increasingly drive results & outcomes

4. Context matters



Huge Progress in Personalized Medicine for Breast Cancer - But Evidence/Translation Gaps Remain

- Many genetically different breast cancers & tx are toxic, ineffective, & expensive
- ~30% of women with breast cancer are HER+ & can benefit from Herceptin
- Gene expression profiling (Oncotype*Dx*, Mammaprint) assesses who will benefit from chemo



TRANSPERS Studies on Breast Cancer

- Utilization in actual practice
 - Literature synthesis
 - Aetna & UnitedHealthcare data
- Cost-effectiveness of:
 - HER2/neu testing approaches
 - Impact of risk stratification (GEP)
- Factors influencing adoption
 - Private payer coverage decisions



Research on HER2/neu Testing for Herceptin Cancer

Clinical Practice Patterns and Cost-Effectiveness of HER2 Testing Strategies in Breast Cancer Patients.

Phillips KA, Marshall DA, Haas JS, Elkin EB, Liang SY, Hassett MJ, Ferrusi I, Brock JE, Van Bebber SL

JAMA[®]

The Journal of the American Medical Association

COMMENTARY

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Closing the Evidence Gap in the Use of Emerging Testing Technologies in Clinical Practice

Kathryn A. Phillips, PhD

There is no consensus about optimal testing methods.
Guidelines recommend using either immunohistochemis-



Other Relevant Publications

- Tradeoffs of Using Administrative Claims and Medical Records to Identify the Use of Personalized Medicine for Patients With Breast Cancer
- Liang, Phillips, Wang, Keohane, Armstrong, Morris, Haas



– Economic Evaluation of Targeted Cancer Interventions: Critical Review and Recommendations

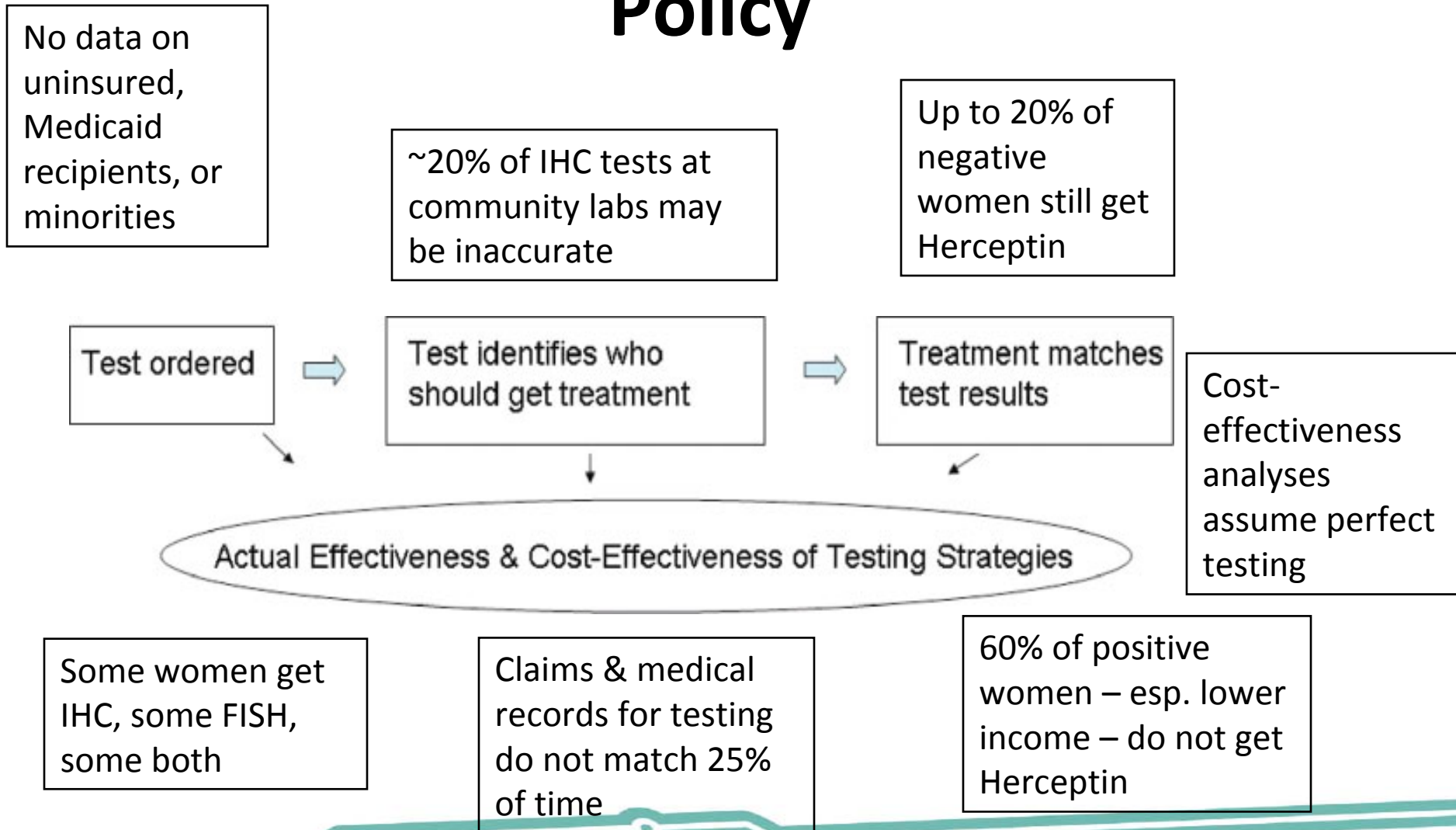
- Elkin, Marshall, Kulin, Ferrusi, Hassett, Ladabaum, Phillips (in press)
- 

Evidence/Translation Gaps Remain that Portend Future Challenges


- HER2 testing should be done prior to Herceptin treatment
- Herceptin a clinical success BUT:
 - Gaps in *evidence* on use of testing & treatment
 - Lack of evidence on *translation* of testing into care



Translating HER2 Testing to Practice & Policy



Gene Expression Profiling Tests: Interest & Controversy

- Measure activity of many genes simultaneously to create global picture of cellular function
 - Use proprietary algorithm to combine & interpret complex info
 - Increasingly used in cancer care
 - Breast, colorectal, lung, prostate
 - Concerns about
 - High cost (\$4000 for OncotypeDx)
 - Accuracy/reliability
 - Concordance & redundancy among tests
 - Patient & provider uses of information
 - Appropriate regulation and health policies
- 

TRANSPERS Studies on GEP

- Utilization & outcomes
- Cost-effectiveness
- Coverage & reimbursement decisions
- Role of GEP w/in care pathways
- Generalizability of GEP for breast cancer to other conditions & complex tests
- Use of private health plan data



Using Health Plan Data

- Great need to expand use of data from private health plans for CER & other uses
- Challenges/Opportunities
 - Understanding different approaches to data access
 - How to link testing, results, & outcomes
 - How to link databases: lab, registries, survey data
 - Developing analytical approaches
- Studies with Aetna, UnitedHealthCare, & Humana



Understanding Coverage & Reimbursement Decisions

- Reimbursement & Policy Board since 2007
 - Senior executives from 6 of 7 largest US plans, leading regional plans, PBMs, thought leaders representing industry, government, and Medicare perspectives



Long Adoption Curve for Plan Coverage for *OncotypeDx*

- *OncotypeDX* took *four years* to be adopted by all payers
 - Payers considered same evidence but weighted factors differently
 - Tipping points:
 - How clinical evidence interpreted
 - Health care system factors (patient & provider demand, Medicare coverage, guidelines)
 - Implications for other new technologies?




Variation in Health Technology Assessments Used by Payers

	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	# of payers
BCBS TEC	●	●	●	●	●	●	●	●	●		●	10
USPSTF	●	●	●	●	●	●	●	●	●			9
ICER	●	●	●	●	●	●	●					7
Hayes	●	●	●	●						●		5
EGAPP	●	●	●	●				●				5
ECRI	●		●							●		3
UP-TO- DATE	●	●										2
Total per payer	7	6	6	5	3	3	3	3	2	2	1	



Use of GEP Based on Health Plan Data

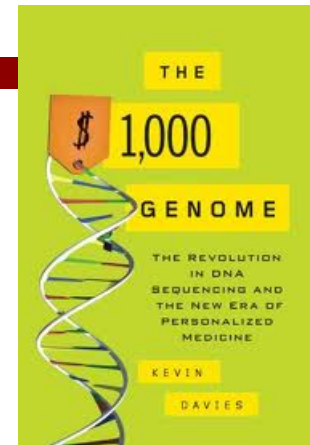
- Some studies suggest testing does change risk classification & use of chemo
 - But limited evidence about use in actual practice & about impact on adverse events & costs
 - Using national health plan data, we examined whether GEP use is associated with:
 - Use of chemotherapy
 - Occurrence of serious chemotherapy-related adverse effects
 - Costs of care
 - Used propensity scores to adjust for confounding
 - Age, comorbidity, year of diagnosis, tumor size, grade, nodal status, hormone receptor status, HER2 receptor status
- 

Sum of Findings - & Challenges

- GEP testing associated with overall decrease in chemo (adjusted)
 - But shift towards more chemo in low risk group & less chemo in high risk group
- Did not find differences in adverse events or charges
- CER requires data from actual practice
 - But high data costs & small N's, challenges in adjustment for selection bias, delayed timeframe



The Future: Whole Genome Sequencing



- Technology is (again) outpacing our ability to use the info
 - Likely to produce vast amounts of info that is not useful or unusable
 - Issues about how to model & allocate costs & benefits
- Developing study on how patients & physicians interpret info & make trade-offs (conjoint analysis) & how cost-effectiveness models can be developed to analyze WGS

Conclusion: Where Are We Going?

- Inevitable trend towards greater individualization of care
- Adoption of emerging technologies requires evidence & value proposition
- Potential to improve quality & decrease costs – but can it be realized?

“There’s a wonderful rule of thumb for American health care: Shift happens”

Uwe Reinhardt

