PAYER PERSPECTIVES ON EVIDENTIARY STANDARDS

MOLECULARLY TARGETED THERAPIES FOR CANCER

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Presentation for the National Cancer Policy Forum

CENTER FOR MEDICAL TECHNOLOGY POLICY

ABOUT CMTP

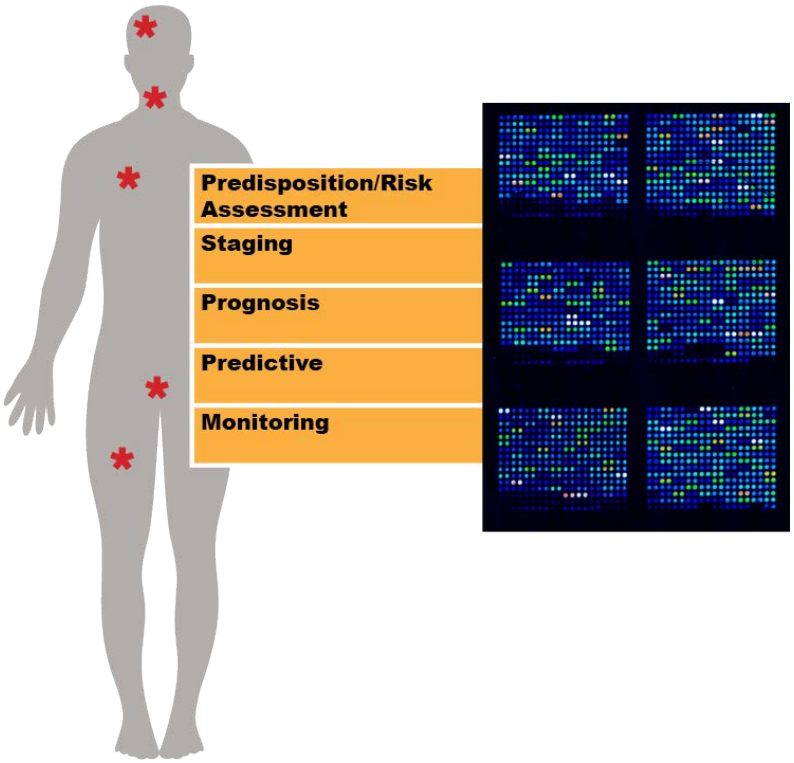
- The Center for Medical Technology Policy (CMTP) is an independent nonprofit seeking:
- **Better Evidence**
  - Research that meaningfully involves all key healthcare stakeholders
  - Evidence reflective of real-world patients and practices
- **Better Decisions**
  - Innovative, high-value technologies rapidly adopted and appropriately used in an increasingly resource-constrained environment
  - Evidence-based clinical advice delivered by health professionals and guideline committees
  - Coverage and reimbursement decisions based on value
- **Better Health**
  - Improved public trust in research
  - Less uncertainty in everyday healthcare

THE CHALLENGE: MDx TEST INTEGRATION

Molecular diagnostic (MDx) tests have the potential to transform oncology practice

But integration of MDx biomarkers into practice has been inefficient

1. Lack of evidence of clinical utility
2. Incomplete/flawed studies of clinical validity
3. Lack of shared evidentiary framework
4. Lack of clear and predictable methodological standards



THE CHALLENGE FOR PAYERS

- **Explosive growth** in number, complexity, cost of tests
  - In past 20 years, # of diagnostic tests of all kinds has doubled
  - Genetic testing available for >2,000 conditions*
- Rapid discovery of potentially useful new genetic variants
  - Since 2012 launch, over 144,000 submissions to ClinVar representing over 125,000 variants across thousands of genes
- Potential downstream consequences of wrong information/decisions
  - Unnecessary treatments, procedures, harms; missed opportunities for effective treatment
- **For payers, closer scrutiny needed even as tests proliferate**

*http://report.nih.gov/nihfactsheets/ViewFactSheet.aspx?csid=43

DISCORDANCE ACROSS COVERAGE POLICIES

- Payers can have differing policies for molecular diagnostic and multiplex tests because…
  - Serving different patient populations
  - Have differing financial/organizational models
  - Have not necessarily all reviewed the same evidence for each test
  - Differing corporate cultures, awareness, attitudes
- Level of discordance: differing coverage decisions for 5/49 tests among policies of 10 national payers reviewed (1)

(1) A. Hresko and S.B. Haga, Insurance Coverage Policies for Personalized Medicine. *J. Pers. Med.* **2012**, *2*, 201-216.

EVIDENCE-RELATED CONSIDERATIONS FOR COVERAGE (POLICIES TAKEN FROM PAYER WEBSITES)

A medically necessary test is one that will have a ***direct impact on clinical care***	Intended or actual changes in management not nec. enough…	Payers ask: what other clinical tools exist for same purpose?
• Disease is treatable and/or preventable, and • Test results will lead to change in the intensity of surveillance frequency and /or treatment	• Often want to see ***improvement in outcomes when test is used***	• If other tools, comparison to standard of care desirable • If no other tools <u>and</u> serious medical need, lower strength of evidence may be accepted – *but some evidence still needed*

DEMONSTRATION OF CLINICAL UTILITY: TYPES OF EVIDENCE CONSIDERED BY MOST PAYAERS

- Overall strength of evidence assessed
- Peer-reviewed studies published in medical journals
  - Tests not covered “tend to lack evidence from prospective, randomized clinical trials” (1)
- A review of available studies on a particular topic
  - e.g., AHRQ, BCBS TEC, Duke Evidence-based Practice Center
- Evidence-based consensus statements
  - Professional societies or other bodies
- Guidelines from nationally recognized health care organizations
  - NCCN, ASCO

DEMONSTRATION OF CLINICAL UTILITY: ADDITIONAL CONSIDERATIONS

- FDA cleared test, approved drug a plus, but not always…
  - e.g. UGT1A1 for toxicity/dosing of irinotecan in CRC. FDA-cleared, revised drug label with PGx info, but not covered (1,2)
- Expert clinical opinion; physician practice patterns (3)
  - Could be influential when evidence of utility is sparse, especially when medical need is great
- Cost effectiveness not mentioned in payer policy decisions (1)

(2) http://www.aetna.com/cpb/medical/data/700_799/0715.html
(3) Trosman, J.R.; van Bebber, S.L.; Phillips, K.A. Coverage policy development for personalized medicine: Private payer perspectives on developing policy for the 21-gene assay. *J. Oncol. Pract.* **2010**, *6*, 238–242.

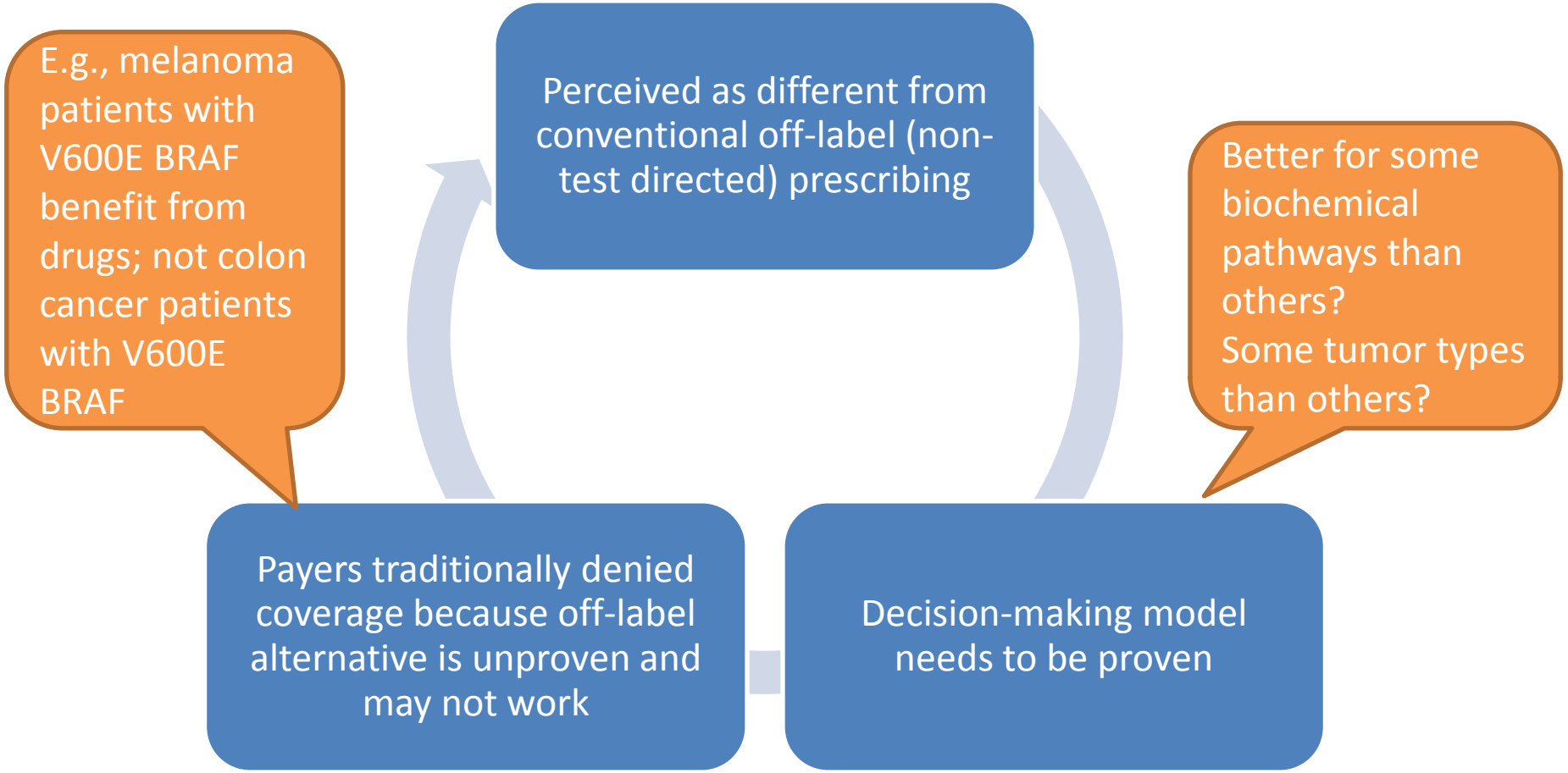
EVIDENCE OF CLINICAL UTILITY LACKING

2012 review of payer policies (1)

Study concluded…

"The low number of disease-related genomic tests considered for coverage by insurers is likely due to the few studies published demonstrating clinical utility, the often small role of genetics in complex diseases, and availability of alternative effective screening methods." (1)

PAYERS AND TEST-DIRECTED OFF-LABEL PRESCRIBING



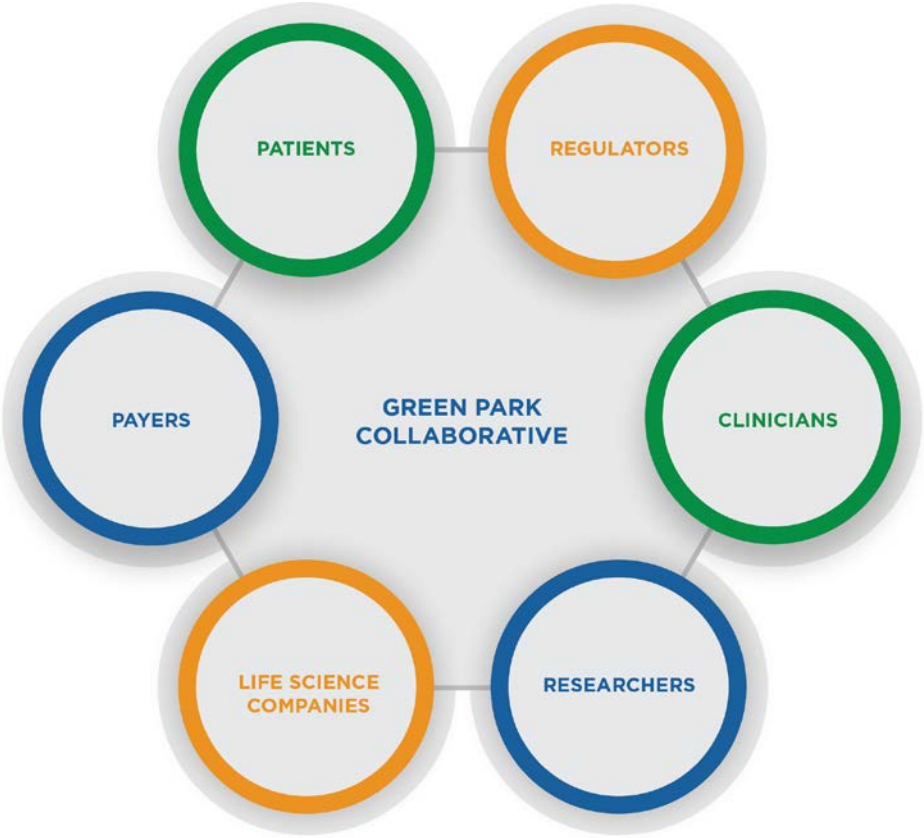
CHANGE IN THE AIR: CHANGING LANDSCAPE FOR POLICY DECISION-MAKING

- Priority Health revising policies, including:
  - Covered NGS for specific clinical situations
  - Covered test-directed off-label use of targeted therapies in some situations, i.e., in the context of clinical trials
    - ACA requires coverage for pts in trials
    - De facto coverage with evidence development
- Policies recognize possible benefits of multiplex testing for targeted therapy while still seeking clinical utility
- Palmetto MolDx: more emphasis on direct evidence or promoting collection through coverage with data devel.

HOW TO ACHIEVE CONSISTENCY, PREDICTABILITY IN EVIDENCE STANDARDS

The Green Park Collaborative - USA (GPC-USA)

- develops condition and technology-specific study design recommendations to guide the generation of evidence needed to inform both clinical and payment decisions
- GPC-USA includes a diverse mix of payers, life sciences companies, patients, clinicians, researchers, regulators and other stakeholders.



EFFECTIVENESS GUIDANCE DOCUMENTS

- Recommendations on specific study designs
- Multi-stakeholder process
- Analogous to FDA guidance
- Targeted to researchers
- **MDx guidance document:***
  - Recognizes cost, time to do RCTs
  - Strong emphasis on alternative methods

*http://www.cmtpnet.org/docs/resources/MDX_EGD.pdf

MOLECULAR DIAGNOSTICS EGD IN ADULT ONCOLOGY RECOMMENDATIONS: PHASE 4

PHASE 1	PHASE 2	PHASE 3	PHASE 4
Initial Test Performance & Assay Refinement	Test Validation & Generalizability	Components of Clinical Test Performance & Health Impacts	Comparison with Standard Care

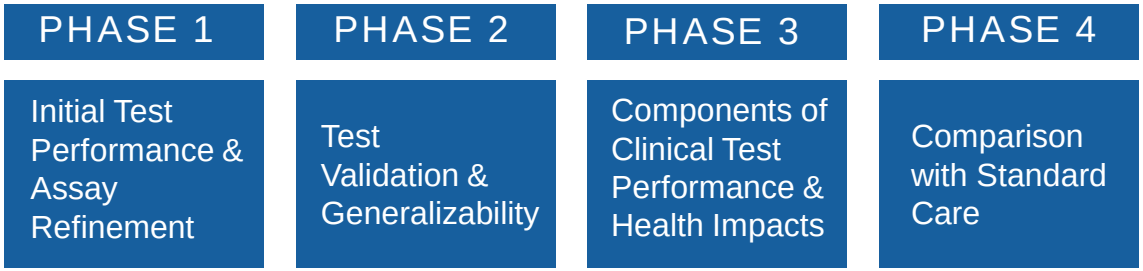
Determine the net impact on health outcomes & added value compared to current patient management without MDx testing (clinical utility)

Recommendation 6:
RCT design selection, OR

Recommendation 7:
Prospective-retrospective study, OR

Recommendation 8:
Single-arm study, OR

RECOMMENDATIONS: PHASE 4



Determine the net impact on health outcomes & added value compared to current patient management without MDx testing (clinical utility)

Recommendation 9:
Prospective observational study, OR

Recommendation 10:
Modeling techniques (e.g., decision-analytic)

NEXT UP: GREEN PART COLLABORATIVE PROJECT CLINICAL UTILITY OF NEXT GENERATION SEQUENCING

- Multi-stakeholder workshop July 7 2014 (summary available)
- Multi-stakeholder meetings thru June 2015 to create guidance on, e.g.:
  - **Panels:** What type of assessment needed?
  - Should "**interim standards**" be considered when information is lacking but patient need is great?
    - What standards? What conditions? What limits?
  - What is the role of **case reports** for rare or newly discovered biomarkers?
    - Stds for interpretation and integration w/other data?
  - Should standards be established for **reporting** coverage of sequencing and types of variants detected to payers?