Determinants and Outcomes of Mutation Testing in Cancer Treatment

CHRISTINA A. NGUYEN
HARVARD COLLEGE ’15

MENTORS:
PETER GROENEVELD, MD, MS
ANDREW EPSTEIN, PHD, MPP
MIRAR BRISTOL-DEMETER, MA

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Roadmap

- Significance
- Overall aims
- Background
  - Cancer in Pennsylvania
  - Somatic mutation tests
- Overview of projects
- Project descriptions
  - Aims, methods, findings, my role
- Policy implications
- Lessons learned
Significance

- Frequency of lung, colon, and breast cancers by county in Pennsylvania

- Philadelphia, PA
  - Lung cancer (n = 9,958)
  - Colon cancer (n = 5,406)
  - Breast cancer (n = 10,737)

Significance

Estimated Deaths in United States in 2013 by Cancer Type

1) Lung
2) Colorectal
3) Breast

= 61% of all deaths from cancer

3. American Cancer Society, Cancer Facts and Figures, 2013
Significance

Incidence and Mortality Rates*

Lung Cancer

Colorectal Cancer

* Rates are age-adjusted to the corresponding year’s US standard population

Overall Aims

For lung, colon, and breast cancer:

- **Advanced Stage Cancer**
- **Race**
- **Technical Challenges**

**PDS / IBC / Medicare & Medicaid**

1) PCR = Pennsylvania Cancer Registry
2) PDS = Penn Data Store
3) IBC = Independence Blue Cross
4) Medicare & Medicaid

**Mutation Testing**

- Chemotherapy
- Costs
- Survival
- Disparities

**No Testing**
3 somatic mutation tests used to help determine potential effectiveness of treatment

- **Epidermal Growth Factor Receptor (EGFR)**
  - Lung Cancer

- **KRAS**
  - Lung Cancer
  - Colon Cancer

- **Oncotype DX**
  - Breast Cancer
Background

Progression-Free Survival in EGFR Mutation +/- Patients

EGFR mutation positive
(261/437 = 59.7%)

EGFR mutation negative

Hazard Ratio (95% CI) = 0.48 (0.36, 0.64)
\( p < 0.0001 \)

Hazard Ratio (95% CI) = 2.85 (2.05, 3.98)
\( p < 0.0001 \)

KRAS mutation positive  
(167/394 = 42.3%)

Cetuximab plus best supportive care (n=75)  
Best supportive care alone (n=76)

Hazard Ratio (95% CI) = 0.99 (0.73, 1.35)  
p = 0.96

KRAS mutation negative

Cetuximab plus best supportive care (n=110)  
Best supportive care alone (n=105)

Hazard Ratio (95% CI) = 0.40 (0.30, 0.54)  
p < 0.001

Overview of Projects

1) **Validation of claims data** for somatic mutation testing

2) **Systematic review** of the suitability of using cytological specimens in somatic mutation testing for lung cancer patients
Claims Validation

Aims

Methods

Findings

My Role
Claims Validation

Through a validation of claims data for somatic mutation testing using data obtained from the Penn Data Store, verify that

1. eligible patients are receiving mutation testing

2. mutation testing can be identified in both the medical and administrative data records
Claims Validation

Targeted population:

- 40 years of age or older
- diagnosed between 2007 and 2010
- invasive lung, colorectal, or breast cancer in Pennsylvania
- diagnosed or treated at Penn Med
Case Report Form

Validating receipt of genetic testing

Clinical Information

- Study ID 397
- Was this patient treated at Penn for a cancer diagnosis? (yes, no, unsure based on record)
- Which of the following did the patient receive at Penn? (cancer diagnosis, cancer treatment, unsure based on record)
- Does this subject have insurance? (yes, no)
- Date of cancer diagnosis
- What type of cancer does the patient have? (Lung)
- NSCLC Subtype (Adenocarcinoma)
Claims Validation

EPIC Chart and Administrative Data

Luman, Harold
Male, 60 y.o., 03/02/1950
PCP: None
Allergies: Bee Venom, Cat Hair...

Chart Review
- Filtered
- Default filter

<table>
<thead>
<tr>
<th>Date</th>
<th>Type</th>
<th>Specialty</th>
<th>Department</th>
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<tr>
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</table>

Harold Luman
10/29/2010 10:28 PM
MRN: 207778
Provider: McQueenie, Diana, MD
Department: Emc Family Medicine

Patient Demographics and Encounter Information

Patient Demographics
- Patient Name: Mineral, Robert H
- Sex: Male
- DOB: 08/15/1939 (70 y.o.)
- SSN: xxx-xx-6638
- Address: 134 Elm Street
- Phone: 608-213-5808 (Home)
- Madison, WI 53706

Source: Penn KnowledgeLink Epic EMR Training
Lung CA patients at risk in PCR & PDS* (n = 2,719)

- Diagnosed in 2010 (n = 834)
- Had IBC Insurance (n = 1,164)
  - Screened (n = 365)
  - Treated or Diagnosed at Penn (n = 111)
  - Received Testing (n = 28)

* Diagnosed between 2007 and 2010
Claims Validation

Aims

Methods

Findings

My Role

Colon CA patients at risk in PCR & PDS* (n = 574)

Diagnosed in 2010 (n = 92)

Had IBC Insurance (n = 223)

Screened (n = 34)

Treated or Diagnosed at Penn (n = 10)

Received Testing (n = 2)

* Diagnosed between 2007 and 2010
# Claims Validation

**30/121 = 24.79%** received mutation testing

<table>
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<tr>
<th>EPIC Medical &amp; Administrative Records</th>
<th>Yes</th>
<th>No</th>
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<td></td>
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<tr>
<td>Claims: No</td>
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</table>

- **Sensitivity** = \( \frac{\text{Claim} + \text{EPIC} +}{\text{Claim} + \text{EPIC} +} \)
- \( \text{Sensitivity}_{\text{Lung}} = \frac{P}{28} \)
- \( \text{Sensitivity}_{\text{Colon}} = \frac{P}{2} \)

- **Specificity** = \( \frac{\text{Claim} - \text{EPIC} -}{\text{Claim} - \text{EPIC} -} \)
- \( \text{Specificity}_{\text{Lung}} = \frac{N}{83} \)
- \( \text{Specificity}_{\text{Colon}} = \frac{N}{8} \)
Claims Validation

- Data synthesis, and creation of tables and figures
- Literature reviews of overall aims and testing
- IRB protocol for subproject
- Case Report Form in REDCap
- Validation of claims data for testing in EPIC

Next steps:
- Cross data with claims
- Manuscript development
Assess the suitability of using cytological specimens to perform somatic mutation tests for individuals with lung cancer.

Cytological specimen obtained by EBUS-TBNA
Lung Cancer

Mutation Testing

No Testing

Outcomes
- Chemotherapy
- Costs
- Survival
- Disparities

Technical Challenges
Systematic Review

Incidence of Mutations Detected in Lung Cancer Patients

Mutation found in **54% (280/516)** of tumors completely tested (CI 50-59%)

6. Johnson et al., WLCC, July 2011
7. Kris et al., ASCO, June 2011
Inclusion criteria: original data on the sufficiency of cytological samples and the sensitivity of mutation testing

Unique articles in EMBASE and PubMed (n = 134)

Articles screened (n = 134)

Articles excluded (n = 99)

Articles added through citation review (n = 6)

Full-text articles assessed for eligibility (n = 41)

Articles excluded (n = 22)

Articles included in synthesis and analysis (n = 19)
Systematic Review

Overall Sufficiency of Cytological Specimens

Sizes of bubbles proportionate to sample size
Endobronchial ultrasound-guided transbronchial aspiration (EBUS-TBNA)
Systematic Review

EBUS-TBNA* Sufficiency of Cytological Specimens

- Esterbrook, 2013
- Navani, 2012
- Santis, 2011
- Nakajima, 2011
- Billah, 2011
- Sakairi, 2010
- Garcia-Olive, 2010
- Nakajima, 2007

* EBUS-TBNA = Endobronchial ultrasound-guided transbronchial aspiration
### Systematic Review

#### Aims

#### Methods

#### Findings

#### My Role

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**Sensitivity of EGFR Detection in Cytological Specimens**

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<tr>
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<th>Successful Procedures</th>
<th>Total Procedures</th>
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<tbody>
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<td>Patriella, 2013</td>
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<td>50</td>
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<td>Esterbrook, 2013</td>
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<td>Horiike, 2007</td>
<td>130</td>
<td>260</td>
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<tr>
<td>Nomoto, 2006</td>
<td>140</td>
<td>280</td>
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</table>

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**Number of Procedures**

0 25 50 75 100 125 150 175 200 225
Systematic Review

- Searches for and collection of relevant articles
- Review of studies
- Data extraction
- Production of tables and figures
- **Next steps:**
  - Data synthesis and analysis
  - Further development of tables and figures
  - Manuscript development
Policy Implications

- improvements in treatment and survival
- improvements in the quality of documentation of mutation testing and concordance with insurance claims
Policy Implications

- Racial disparities
- Costs

policies to improve access of genomic technologies to minority populations
Lessons Learned

This summer, I....

- completed an IRB protocol
- created a case report form in REDCap
- read and analyzed lab results, and chart and administrative records in EPIC
- discovered that obtaining data is a waiting game and uphill battle
- conducted a systematic review
- honed my Excel and Stata skills while synthesizing data
Special Thanks

- Peter Groeneveld, MD, MS
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- Andrew Epstein, PhD, MPP
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- Joanne Levy, MBA, MCP; SUMR Staff; and LDI
- Yu-Ning Wong, MD, MSCE
- Lin Yang, MS
References


7. Kris et al. on behalf of LCMC investigators (June 2011). ASCO, Abstract #CRA7506.
Questions?

Harvard University
CHRISTINA ANGIE NGUYEN
Harvard College, Class of 2015
A.B. Candidate in Sociology
Secondary Field in Global Health and Health Policy
Email: christinaangienguyen@college.harvard.edu