Incidence-based Mortality (IBM) Tool to Partition Tumor-Specific Mortality Trends Using Factors Related to Diagnosis

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1. Overview of IBM and application to a cancer site (Lung Cancer)
2. Nitty-gritty of developing IBM (Breast Cancer)
3. SEER*stat demo
The Effect of Advances in Lung-Cancer Treatment on Population Mortality

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Background
Background

Rapidly declining lung cancer mortality rates

ACS reported largest one-year drop in cancer mortality; decline in deaths from lung cancer drove the record drop

This captures overall trend from all subtypes combined

How much do specific lung cancer subtype contribute to this overall trend in mortality?

ACS = American Cancer Society
Study Aims
Study Aims

- How do the two major subtypes contribute to the overall mortality decline?
  - Small cell (SCLC) and non-small cell lung cancer (NSCLC)
- Is the decline in the mortality more related to incidence or survival?
  - Mortality is influenced by both incidence and survival
Study Aims

- How do the two major subtypes contribute to the overall mortality decline?
  - *Small cell (SCLC) and non-small cell lung cancer (NSCLC)*
- Is the decline in the mortality more related to incidence or survival?
  - *Mortality is influenced by both incidence and survival*
Study Design
Study Design: Analysis Cohort

- Lung and bronchus cancer cases in SEER-18 areas during 2001-2016
  - SEER-18 areas cover 28 percent of US population
  - SCLC and NSCLC defined based on Lewis et al.¹
  - Coding challenges with classification of subtypes

¹ Lewis et al. Cancer 2014
Study Design: Methods

- Use incidence-based mortality (IBM) technique to partition subtype-specific mortality trends
  - Because regular death certificate mortality do not have subtypes
  - Details to follow in a few slides
  - Joinpoint to assess IBM trend changes over time

- Assess incidence and survival trends to understand IBM trends
  - Estimate age-adjusted incidence rates by subtypes
    - Further adjusted for reporting delay
    - Joinpoint to assess incidence trend changes over time
  - Estimate two-year lung cancer-specific survival by subtypes
    - Relative survival approach
## Lung Subtype Classification

<table>
<thead>
<tr>
<th>Histology</th>
<th>ICD-O codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small cell</td>
<td>8002, 8041-8045</td>
</tr>
<tr>
<td>Non-small cell</td>
<td></td>
</tr>
<tr>
<td>Squamous and transitional cell</td>
<td>8051-8052, 8070-8076, 8078, 8083-8084, 8090, 8094, 8120, 8123</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>8015, 8050, 8140-8141, 8143-8145, 8147, 8190, 8201, 8211, 8250-8255, 8260, 8290, 8310, 8320, 8323, 8333, 8401, 8440, 8470-8471, 8480-8481, 8490, 8503, 8507, 8550, 8570-8572, 8574, 8576</td>
</tr>
<tr>
<td>Large cell</td>
<td>8012-8014, 8021, 8034, 8082</td>
</tr>
<tr>
<td>Non-small cell carcinoma</td>
<td>8046</td>
</tr>
<tr>
<td>Other specified carcinomas</td>
<td>8003-8004, 8022, 8030, 8031-8033, 8035, 8200, 8240-8241, 8243-8246, 8249, 8430, 8525, 8560, 8562, 8575</td>
</tr>
<tr>
<td>Carcinoma, not otherwise specified (NOS)</td>
<td>8000-8001, 8010-8011, 8020, 8230</td>
</tr>
</tbody>
</table>

1 Lewis et al. Cancer 2014
Challenges with Lung Subtype Classification

Code 8010 (Carcinoma NOS) was heavily used prior to 2001 to capture various types of NSCLC

- In 2001, a new histology code was added: Code 8046 – NSCLC NOS
- Code 8010 cannot be uniquely assigned as either SCLC or NSCLC
- We use the cohort from 2001 to get around this coding issue

1 Yu et al. CEBP 2014
Lung Cancer Cases: Distribution by Subtype (2001-2016)

- **NSCLC**
  - N=586,029 (76%)
- **SCLC**
  - N=97,532 (13%)
- **Other**
  - N=90,607 (12%)

Source: SEER-18
Is Lung Cancer Mortality for SEER-18 Areas Representative of that for the entire U.S.?

*Death certificate mortality, all US

*Death certificate mortality, SEER-18 areas

*Reported by NCHS = National Center for Health Statistics
Is Lung Cancer Mortality for SEER-18 Areas Representative of that for the entire U.S.?

*Death certificate mortality, all US
Annual percent change = -2.3 (-2.6, -2.1)

*Death certificate mortality, SEER-18 areas
Annual percent change = -2.7 (-2.9, -2.5)

*Reported by NCHS= National Center for Health Statistics
Incidence-Based Mortality (IBM)
Why Do We Need Incidence-Based Mortality (IBM)?

- Information on lung cancer subtypes not available on death certificate mortality data, but available from SEER data on incident cases.
- To provide a resource to address this limitation in death certificate mortality data, the SEER program has linked mortality records to SEER incident cases.
- Therefore, we can use information on deaths in SEER cases to reconstruct mortality curves using IBM.
- In fact to partition mortality trends by any factors associated with cancer onset we need to use IBM.
What Is IBM?

- IBM is a rate:

  Death among incident cases by subtypes in year ‘x’
  
  General population in SEER areas in year ‘x’

- IBM rates are valid for a shorter period of time than death certificate mortality rates

- Require ‘n’ years of data on incident cases prior to each year of mortality data to account for ‘burn-in’ period
Death Certificate Mortality vs. IBM: Lung and Bronchus

Death certificate mortality, SEER-18

IBM, SEER-18

Age-adjusted rate per 100,000
Death Certificate Mortality vs. IBM: Lung and Bronchus

Death in 2001 among cases diagnosed in 2001
Death in 2006 among cases diagnosed in 2001-2006
Death in 2016 among cases diagnosed in 2001-2016

Age-adjusted rate per 100,000

Year of Death


IBM, SEER-18
Death certificate mortality, SEER-18
Death Certificate Mortality vs. IBM: Lung and Bronchus

- Death in 2001 among cases diagnosed in 2001
- Death in 2006 among cases diagnosed in 2001-2006
- Death in 2016 among cases diagnosed in 2001-2016

Sufficient follow-back time to capture death from lung cancer

“burn-in” period = 5 year

Year of Death

Age-adjusted rate per 100,000

- IBM, SEER-18
- Death certificate mortality, SEER-18
Final IBM: Lung and Bronchus

Death in 2006 among cases diagnosed in 2002-2006

Death in 2016 among cases diagnosed in 2012-2016

DCO: death certificate only; exclude 1.4% of cases
Final IBM: Lung and Bronchus

IBM can be represented from 2006+ to partition subtype-specific mortality

IBM is underestimated

DCO: death certificate only; exclude 1.4% of cases
Why is there a Gap between the Lung Cancer Mortality Curves when we use Death Certificate Mortality vs. IBM?
Death Certificate Mortality vs. IBM: Lung and Bronchus

Year of Death

Age-adjusted rate per 100,000


IBM

Death certificate mortality, SEER-18
Death certificate mortality, SEER-18

IBM, dx=any cancer, cod=lung

IBM, dx=lung, cod=lung
IBM likely represent lung cancer mortality more accurately than using death certificate mortality!
Non-Small Cell Lung Cancer
IBM decreased -3.2% from 2006-2013 then at -6.2% 2013-2016
NSCLC: IBM, Incidence, and Survival Trends, SEER-18

Males

IBM and Incidence Trends

- Observed incidence
- Modeled incidence
- Observed IBM
- Modeled IBM
NSCLC: IBM, Incidence, and Survival Trends, SEER-18

IBM and Incidence Trends

Males

- 2001-2008: -1.9*
- 2008-2016: -3.0*
- 2006-2013: -3.2*
- 2013-2016: -6.2*

2- Year Lung Cancer Survival

- Observed incidence
- Modeled incidence
- Observed IBM
- Modeled IBM

Survival (%)
NSCLC: IBM, Incidence, and Survival Trends, SEER-18

**Males**

IBM and Incidence Trends

- 2001-2008: -1.9*
- 2008-2016: -3.0*
- 2006-2013: -3.2*
- 2013-2016: -6.2*

2- Year Lung Cancer Survival

- 2001: 26
- 2016: 35

**Females**

IBM and Incidence Trends

- 2001-2006: 0.5
- 2006-2016: -1.4*
- 2006-2014: -2.3*
- 2014-2016: -5.8*

2- Year Lung Cancer Survival

- 2001: 35
- 2016: 44
Small Cell Lung Cancer
SCLC: IBM, Incidence, and Survival Trends, SEER-18

**Males**

IBM and Incidence Trends

- Age-adjusted Rate per 100,000

2001-2016: -3.6*

2006-2016: -4.3*

**Females**

IBM and Incidence Trends

- Age-adjusted Rate per 100,000

2001-2016: -2.7*

2006-2016: -3.7*

2- Year Lung Cancer Survival

**Males**

- Survival (%)


2001: 12

2016: 11

**Females**

- Survival (%)


2001: 14

2016: 17
Conclusion
Conclusions

- We partitioned the lung cancer mortality decline in the U.S. by subtypes
  - SCLC: steady decline
  - NSCLC: initial period steady decline followed by rapid decline in 2013-2014
- Recent progress in mortality for NSCLC is driven by both declining incidence and improvement in survival
  - Potentially driven by dissemination of targeted therapies in the population for NSCLC (approved in 2013 for stage IV EGFR+ NSCLC as first line therapy)
  - The estimates suggest possible population level impacts of targeted therapies for NSCLC
- SCLC mortality decline explained entirely by decrease in incidence
  - Potentially attributable to reduced tobacco use
Nitty/Gritty of IBM
Nitty/Gritty of IBM (1)

- Because IBM rates are derived based on deaths linked to SEER incident cases from previous years, the follow-up of cases diagnosed in the past is required
  - Restricts how far back we can go to show the IBM trends
  - Depends on prognosis
  - Conditional survival

- Need to plot NCHS mortality and IBM over time to

What burn-in period are you going to use?
What burn-in period are you going to use?
Things to consider

- This is a simple IBM we constructed
  - did not put restriction on calendar year of diagnosis or death
  - cases are dying many years after diagnosis so the later trend maybe more biased than earlier trend
  - try to get rid off the long-term survivors so not to bias the ibm curves for later years compared to earlier years
- Goal is to partition total breast cancer mortality by summary stage 2000 (available for cases diagnosed in 2004+)

What burn-in period are you going to use?

Age-adjusted rate per 100,000

- NCHS, US
- IBM 1, dx=breast, COD=breast
- IBM 2, dx=breast, COD=breast, year of death =2004+, no ydx restriction
- IBM 3, dx=breast, COD=breast, year of death=2004+ and ydx=2004+
- IBM 4, dx=breast, COD=breast, ydx=2004+ (died within 7 yr of dx)
Things to consider

- We want to partition the deaths by stage which is available from 2004+
  - So we first restrict year of death 2004+ but no restriction on ydx (IBM 2, same as IBM 1)
  - However, stage is not available before 2004, now further restrict to ydx 2004+ (IBM 3 slightly lower than IBM 2 because kicked out cases ydx 2000-2003)
- When we look at IBM 3, it looks like we need 7 year of data for IBM to become parallel to NCHS
  - Restrict by using survival months = 0- 84 months
  - Exclude DCO cases

- NCHS, US
- IBM 4, dx=breast, COD=breast, ydx=2004+ (died with 7 yr of dx)
- Localized
- Regional
- Distant
- Unknown

Age adjusted per 100,000

Year of Death


Which stage group is contributing to this downward trend??
Nitty/Gritty of IBM (2)

- How one defines death due to cancer can impact IBM rates because misclassification in COD could be problematic
  - Start with same diagnosis and death, (e.g. diagnosis = breast cancer; death = breast cancer)
  - address misclassifications in COD by use of broad definition of COD\(^1\)

\(^1\) Howlader et al. *JNCI* 2010
SEER special COD variable: https://seer.cancer.gov/causespecific/
Nitty/Gritty of IBM (3)

- When assessing IBM by tumor subtypes, need to consider
  - Consistent coding of the subtypes by time and registry
  - If subtypes classification span over long period of time, assess reliability for translation of individual codes from different International Classification of Diseases for Oncology systems e.g., ICD-O-2 to ICD-O-3;
  - Review literature on expert versus nonexpert pathology review on concordance of subtypes
  - Need to consider lethality and survival by subtypes
Nitty/Gritty of IBM (4)

- In-migration or out-migration of cancer cases into the registry catchment area could also impact the IBM trends

  - E.g., case diagnosed in Seattle (inside SEER registry catchment area) dies in Florida (outside SEER registry catchment area) → IBM not impacted because of the NDI linkage, in other words that death is being found/reported

  - E.g., case diagnosed in Oregon (outside SEER catchment area) dies in Seattle (inside SEER catchment area) → IBM underestimated because not a SEER incident case

- However, these likely to cancel out and have a minor impact on IBM
IBM Method References


- IBM tutorial in surveillance research program website: http://surveillance.cancer.gov/statistics/ibm/
Few IBM Application References

IBM Analysis in SEER*Stat
Thank you!

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