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

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NCI Analytic Tools SEERies

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NIH NATIONAL CANCER INSTITUTE

SEER

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 NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

The Effect of Advances in Lung-Cancer Treatment on Population Mortality

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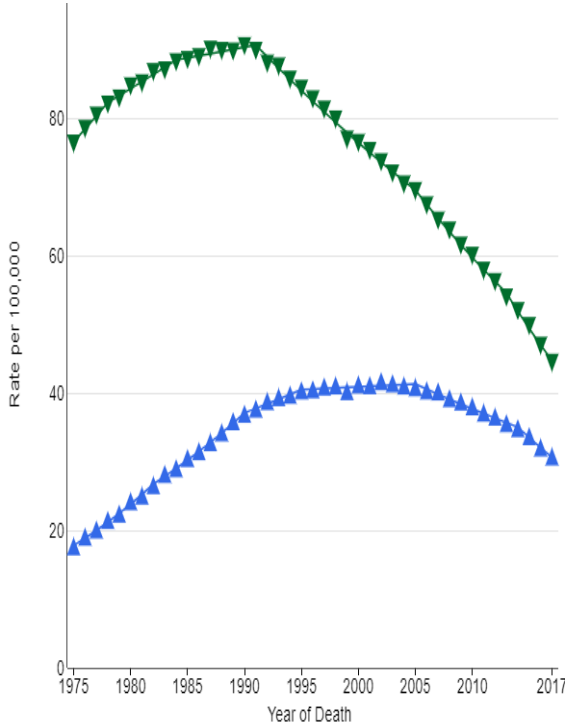
N ENGL J MED 383;7 NEJM.ORG AUGUST 13, 2020

Background

Background

Lung and Bronchus Cancer Mortality, US. 1975-2017



- 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

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- 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*

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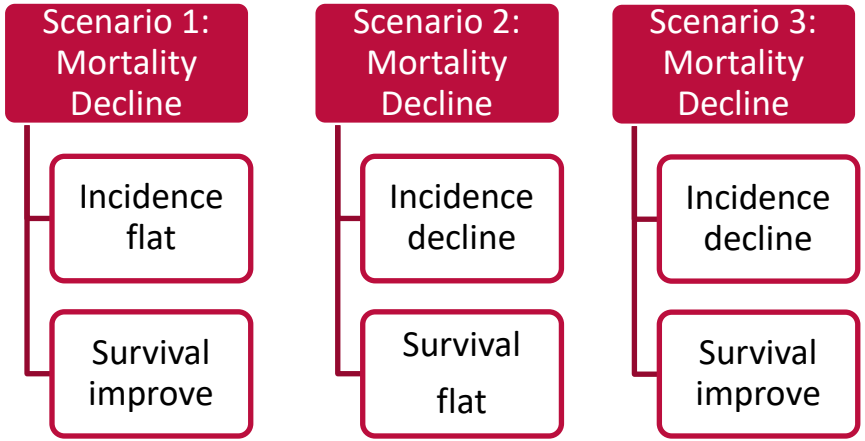


Study Design

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

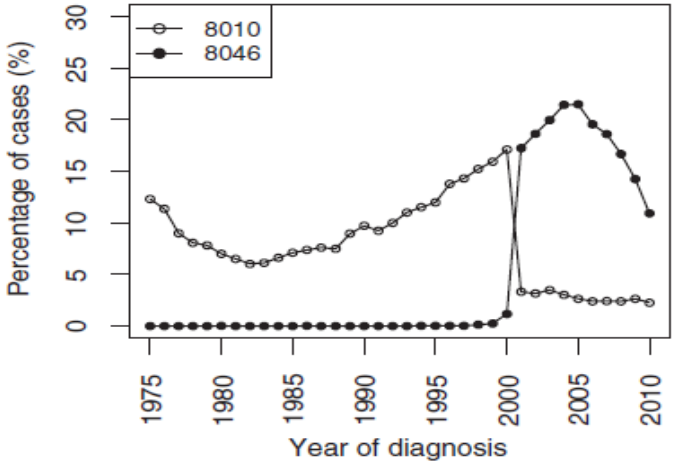
Lung Subtype Classification[1]

Histology	ICD-O codes
Small cell	8002, 8041-8045
Non-small cell	
Squamous and transitional cell	8051-8052, 8070-8076, 8078, 8083-8084, 8090, 8094, 8120, 8123
Adenocarcinoma	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
Large cell	8012-8014, 8021, 8034, 8082
Non-small cell carcinoma	8046
Other specified carcinomas	8003-8004, 8022, 8030, 8031-8033, 8035, 8200, 8240-8241, 8243-8246, 8249, 8430, 8525, 8560, 8562, 8575
Carcinoma, not otherwise specified (NOS)	8000-8001, 8010-8011, 8020, 8230

[1] Lewis et al. Cancer 2014

Challenges with Lung Subtype Classification[1]

Percent of lung cases coded as 8010 and 8046, SEER-9

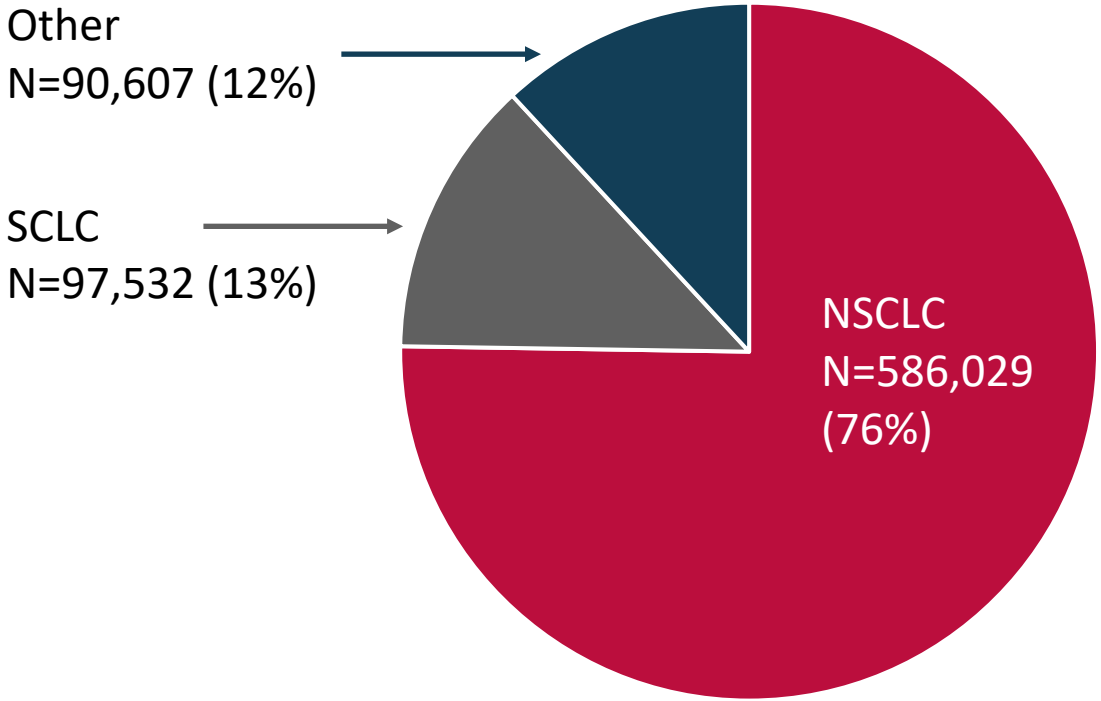


Code 8010 (Carcinoma NOS) was heavily used prior to 2001 to capture various types of NSCLC

- 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

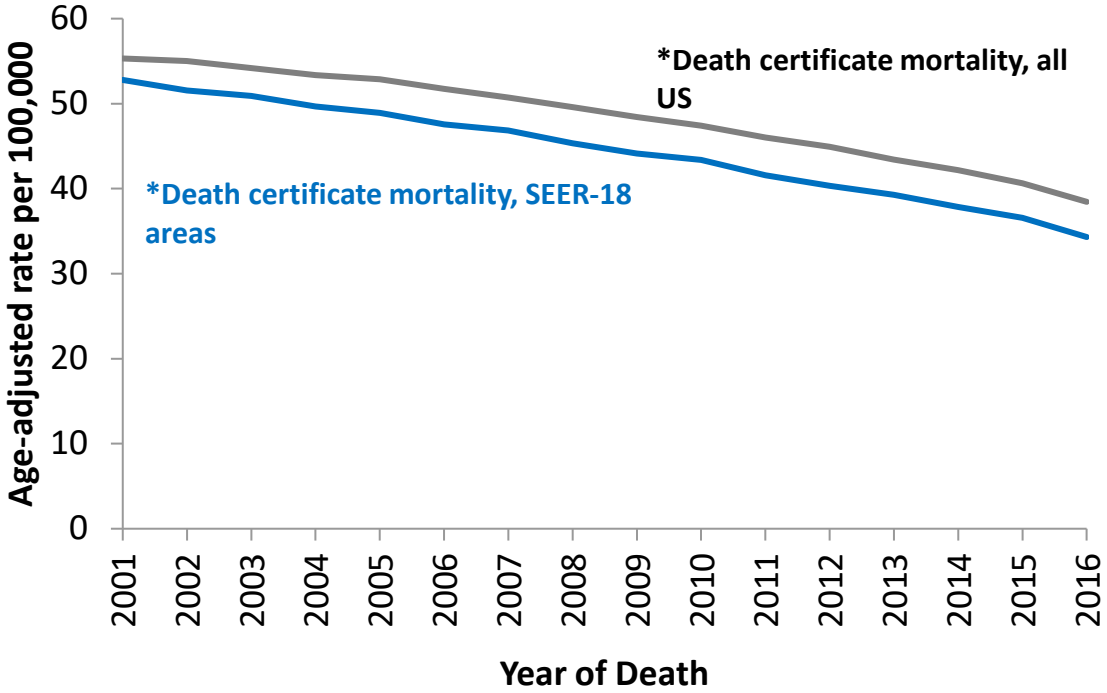
[1] Yu et al. CEBP 2014

Lung Cancer Cases: Distribution by Subtype (2001-2016)



Source: SEER-18

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



*Reported by NCHS= National Center for Health Statistics

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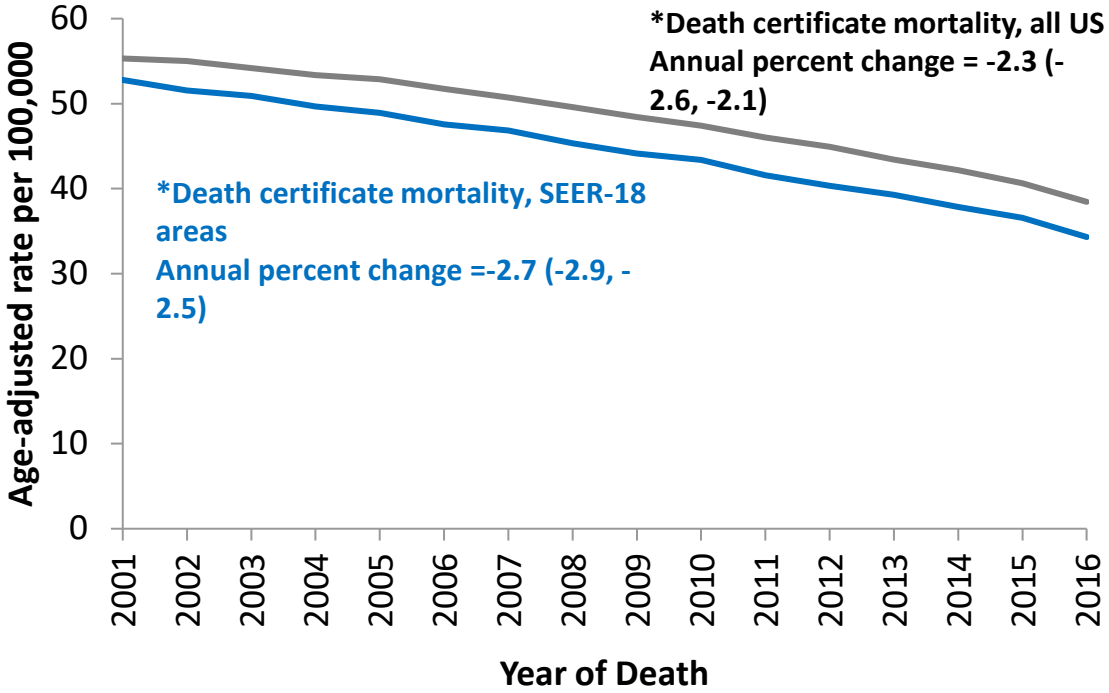


*Reported by NCHS= National Center for Health Statistics

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?

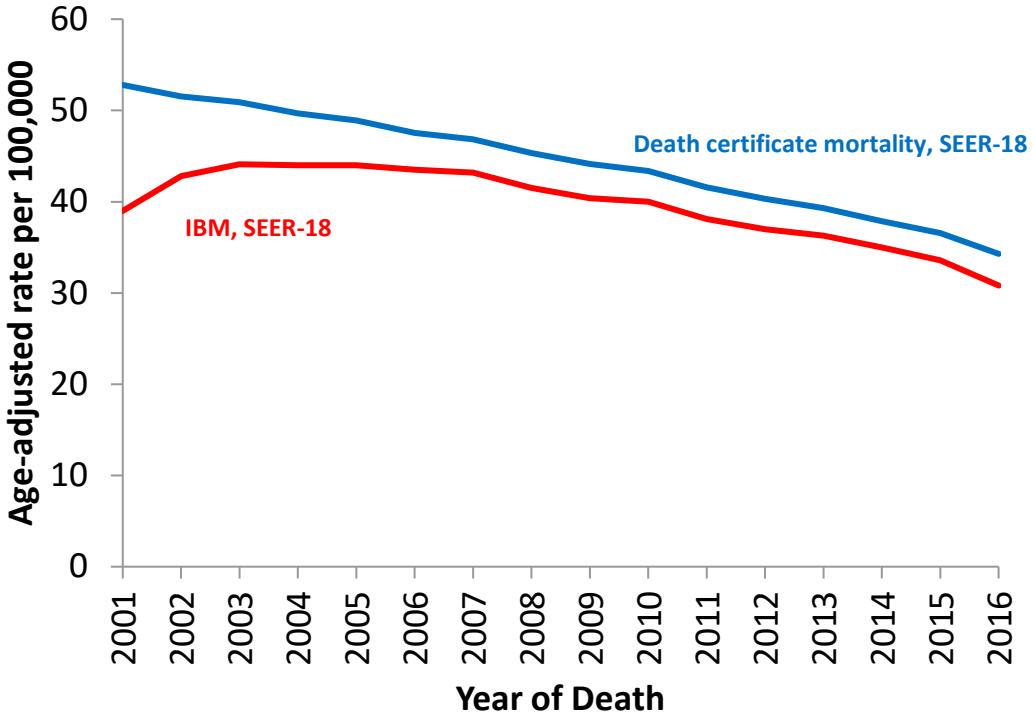
- IBM is a rate:

$$\frac{\text{Death among incident cases by subtypes in year 'x'}}{\text{General population in SEER areas in year 'x'}}$$

- 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



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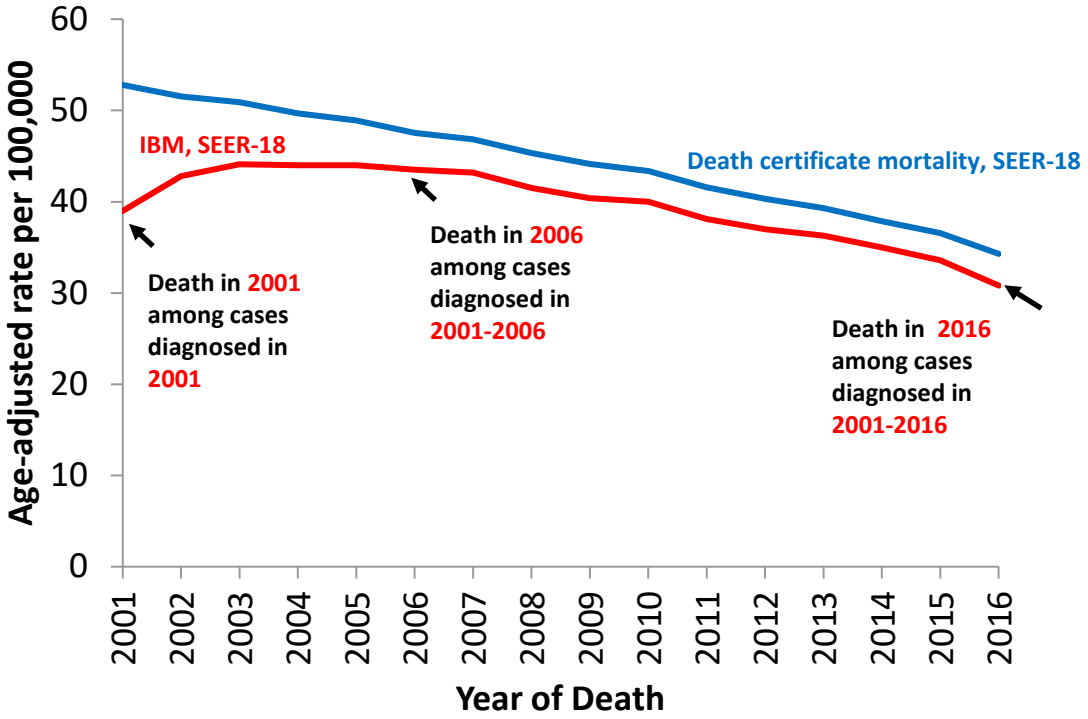

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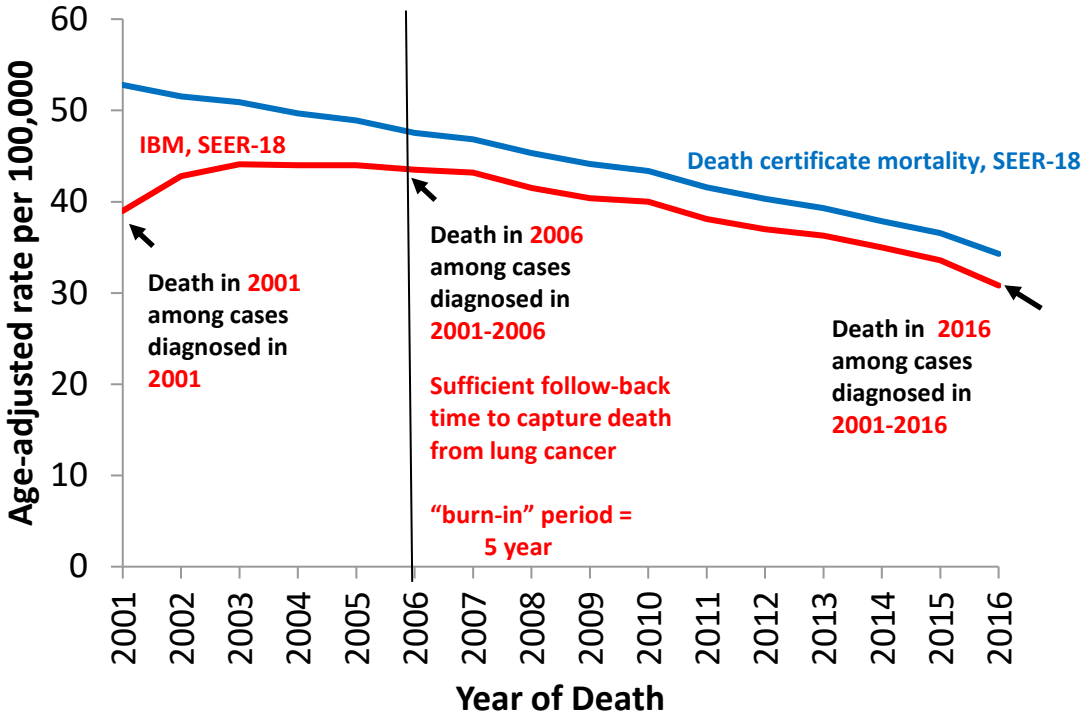
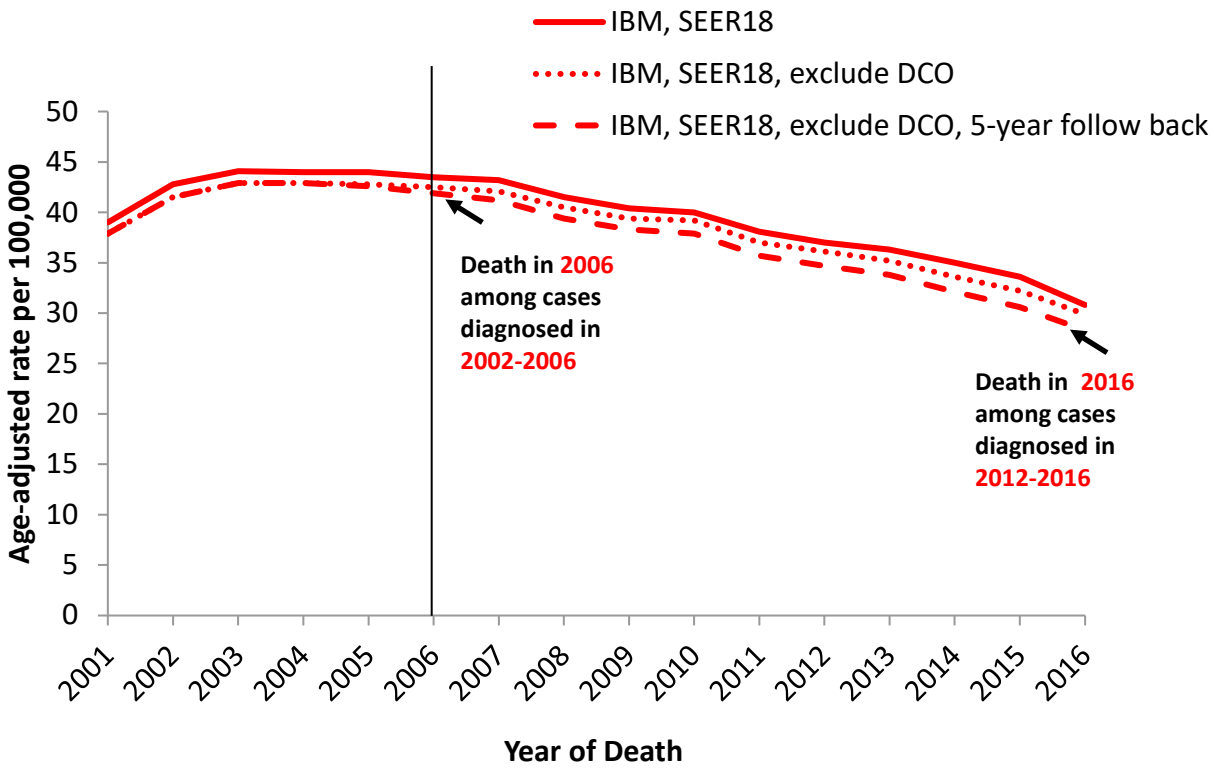
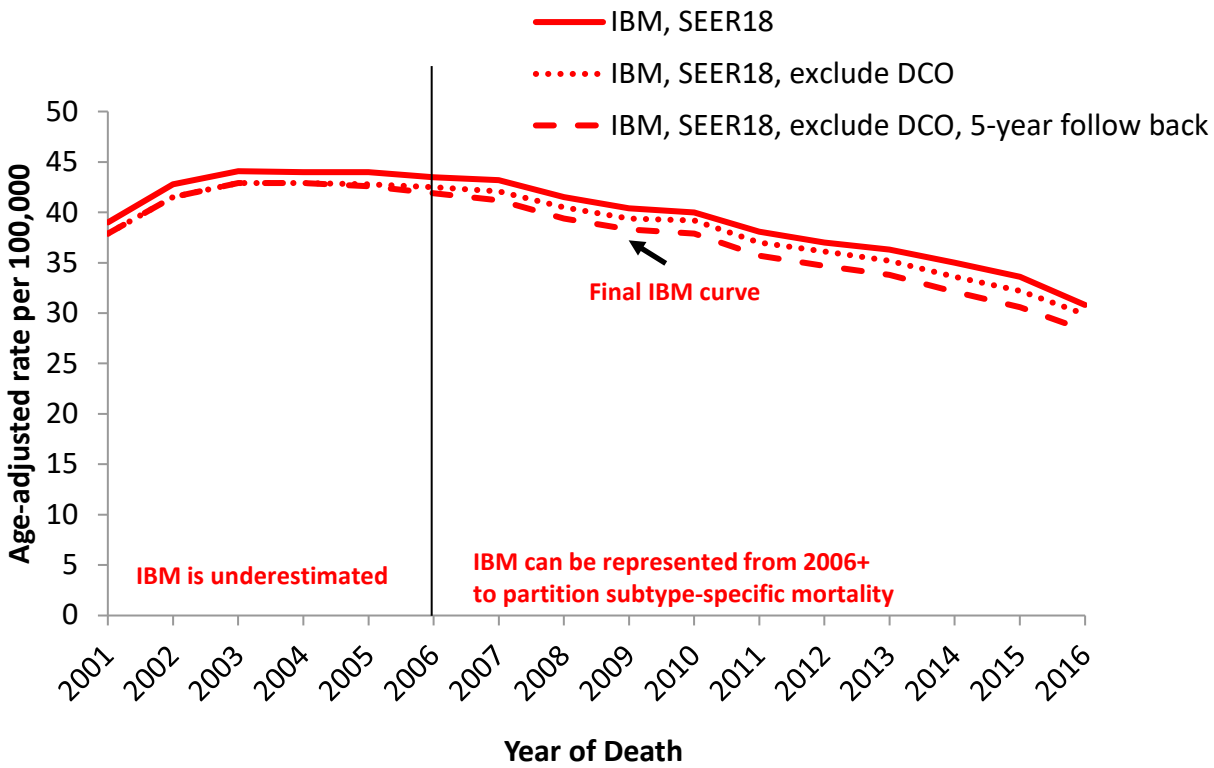


Final IBM: Lung and Bronchus



DCO: death certificate only; exclude 1.4% of cases

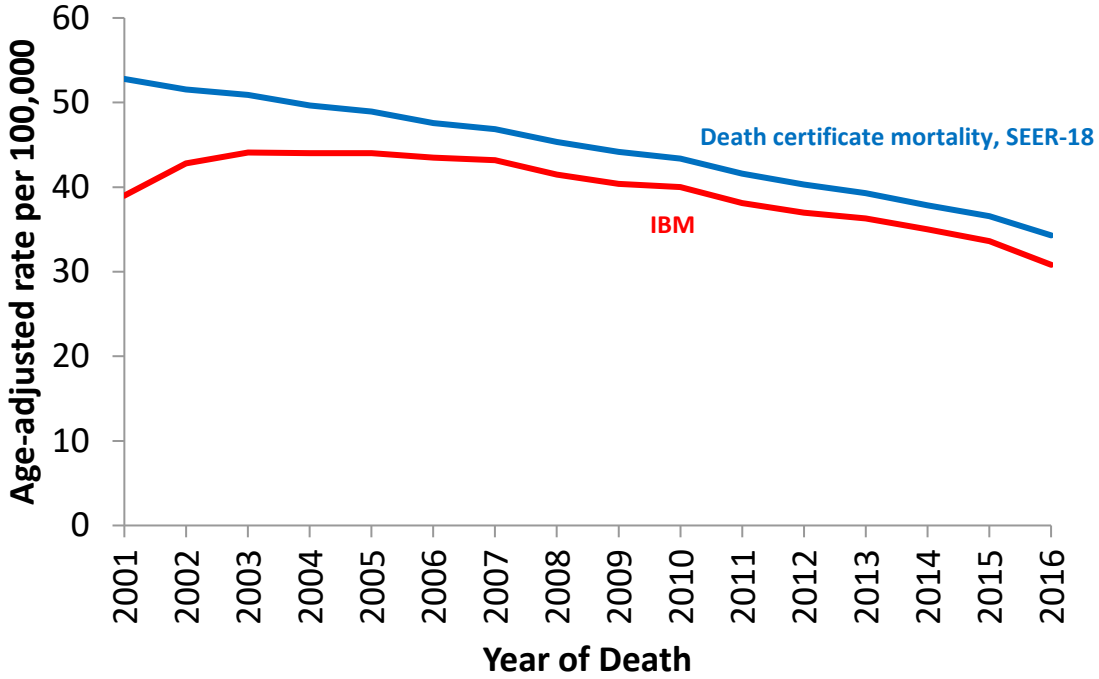
Final IBM: Lung and Bronchus

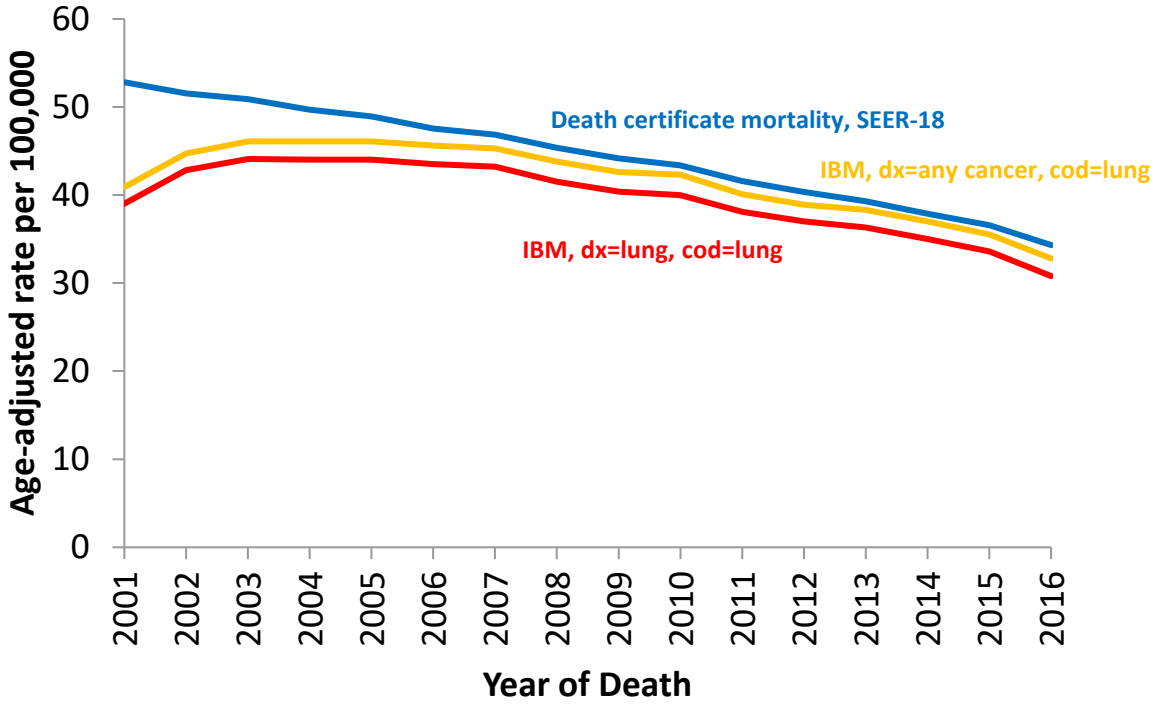


DCO: death certificate only; exclude 1.4% of cases

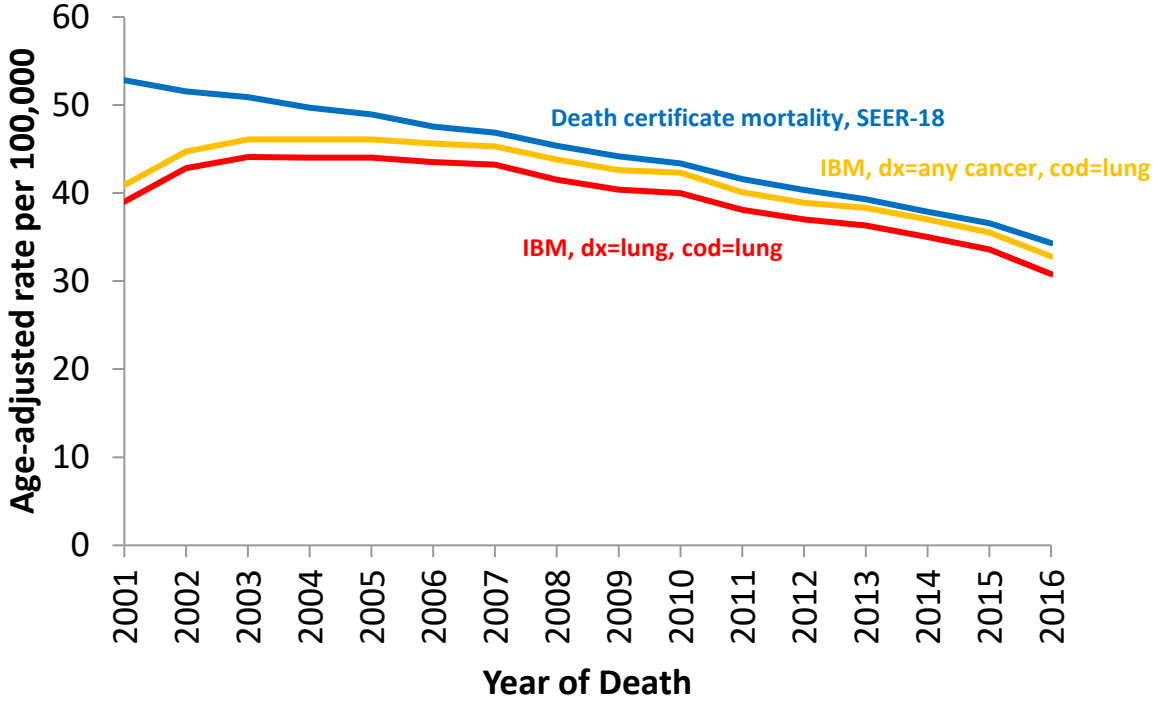
Why is there a Gap between the Lung Cancer Mortality Curves when we use Death Certificate Mortality vs. IBM?

Death Certificate Mortality vs. IBM: Lung and Bronchus




Age-adjusted rate per 100,000
60
50
40
30
20
10
0
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
Year of Death
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!

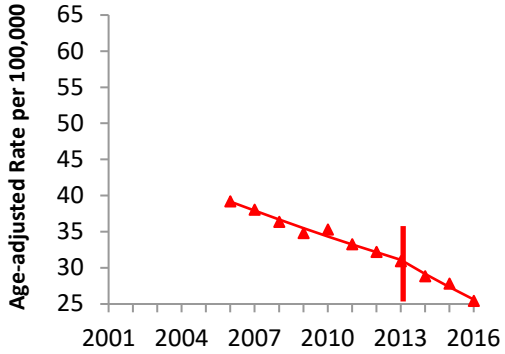


Results

Non-Small Cell Lung Cancer

NSCLC: IBM, Incidence, and Survival Trends, SEER-18

Males

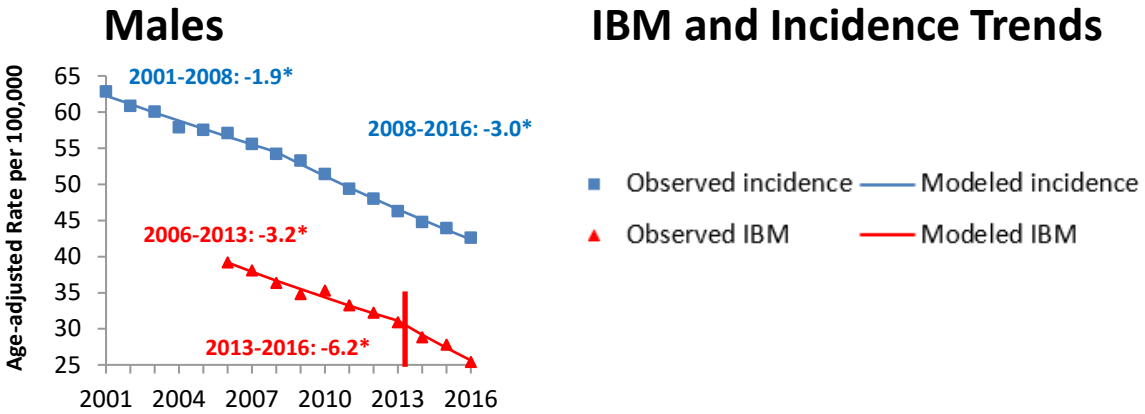


IBM and Incidence Trends

▲ Observed IBM — Modeled IBM

IBM decreased -3.2% from 2006-2013 then at -6.2% 2013-2016

NSCLC: IBM, Incidence, and Survival Trends, SEER-18



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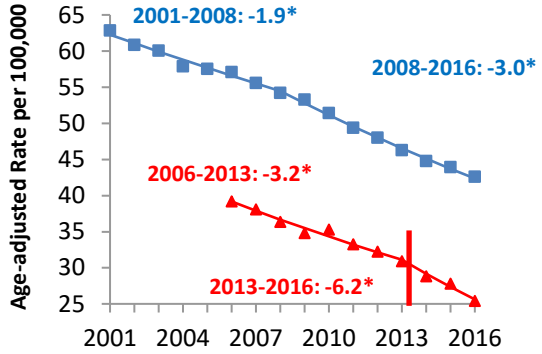
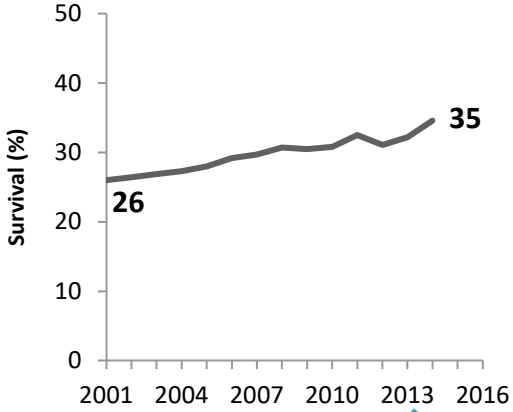
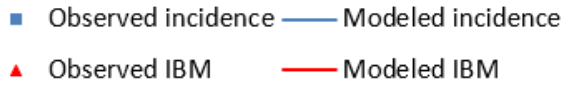




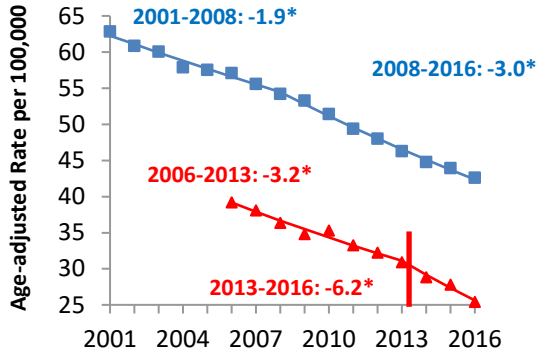
IBM and Incidence Trends

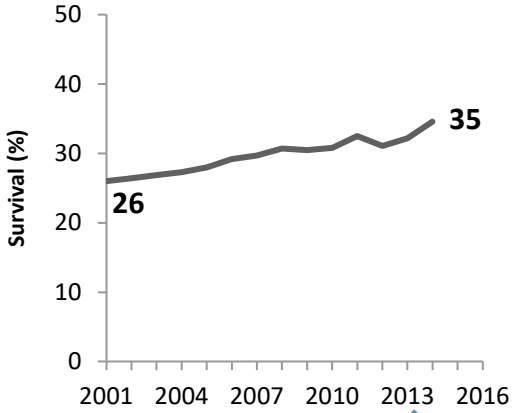


2- Year Lung Cancer Survival

NSCLC: IBM, Incidence, and Survival Trends, SEER-18

Males





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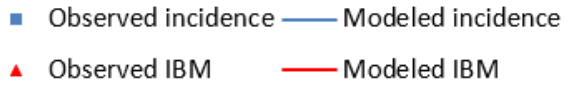
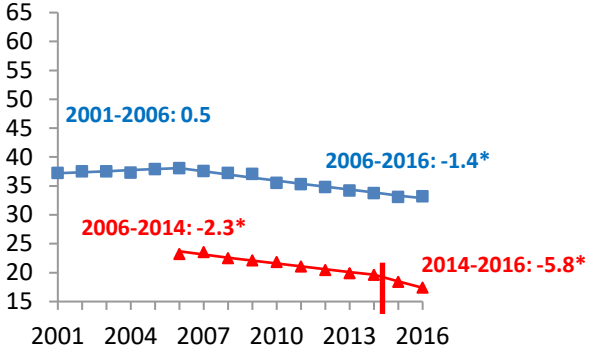
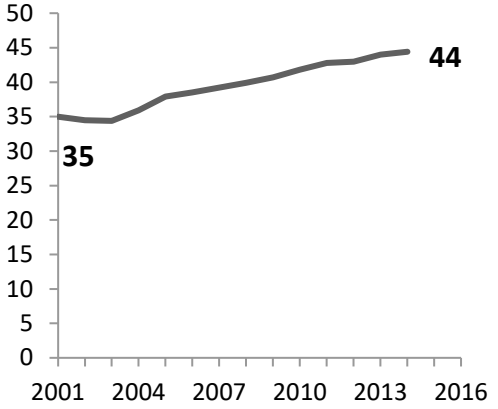


2- Year Lung Cancer Survival

Females

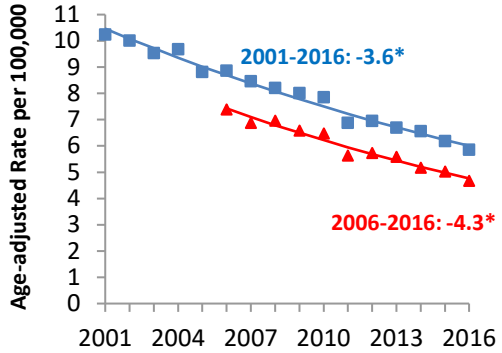




Small Cell Lung Cancer

SCLC: IBM, Incidence, and Survival Trends, SEER-18

Males

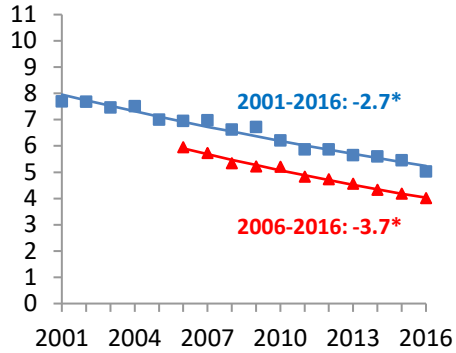


IBM and Incidence Trends

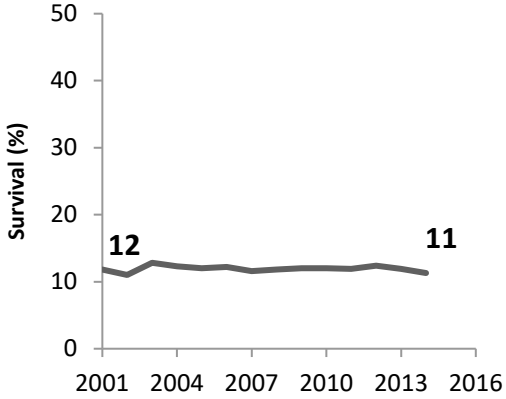
Observed incidence — Modeled incidence

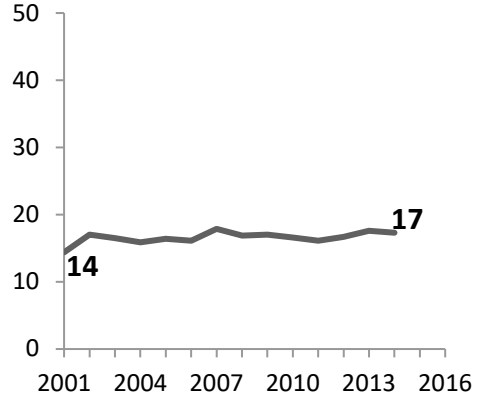
Observed IBM — Modeled IBM

Females



2- Year Lung Cancer Survival





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

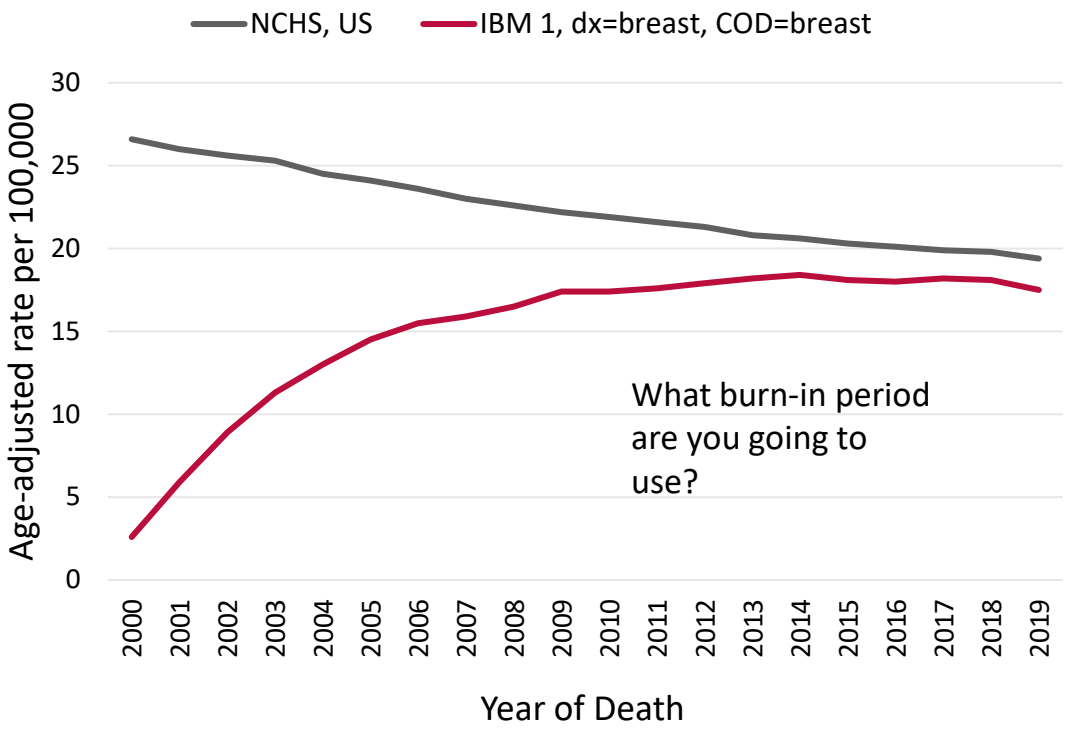
Nitty/Gritty of IBM

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

Breast Cancer, 2000-2019. SEER-17.



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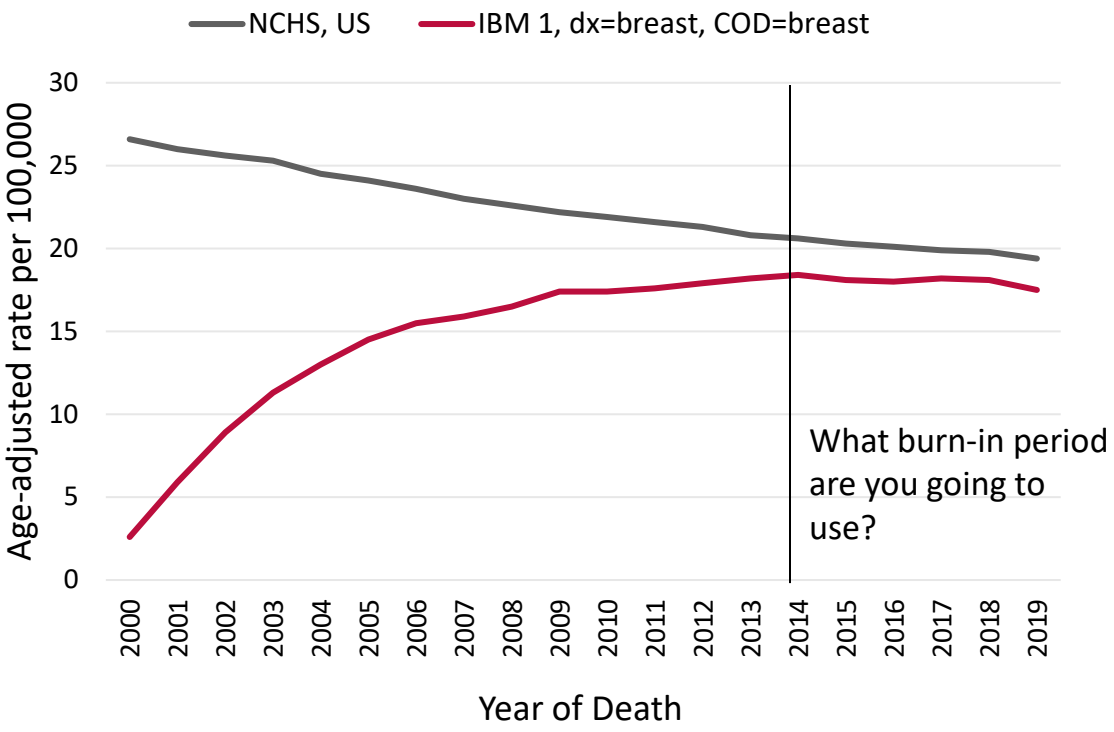
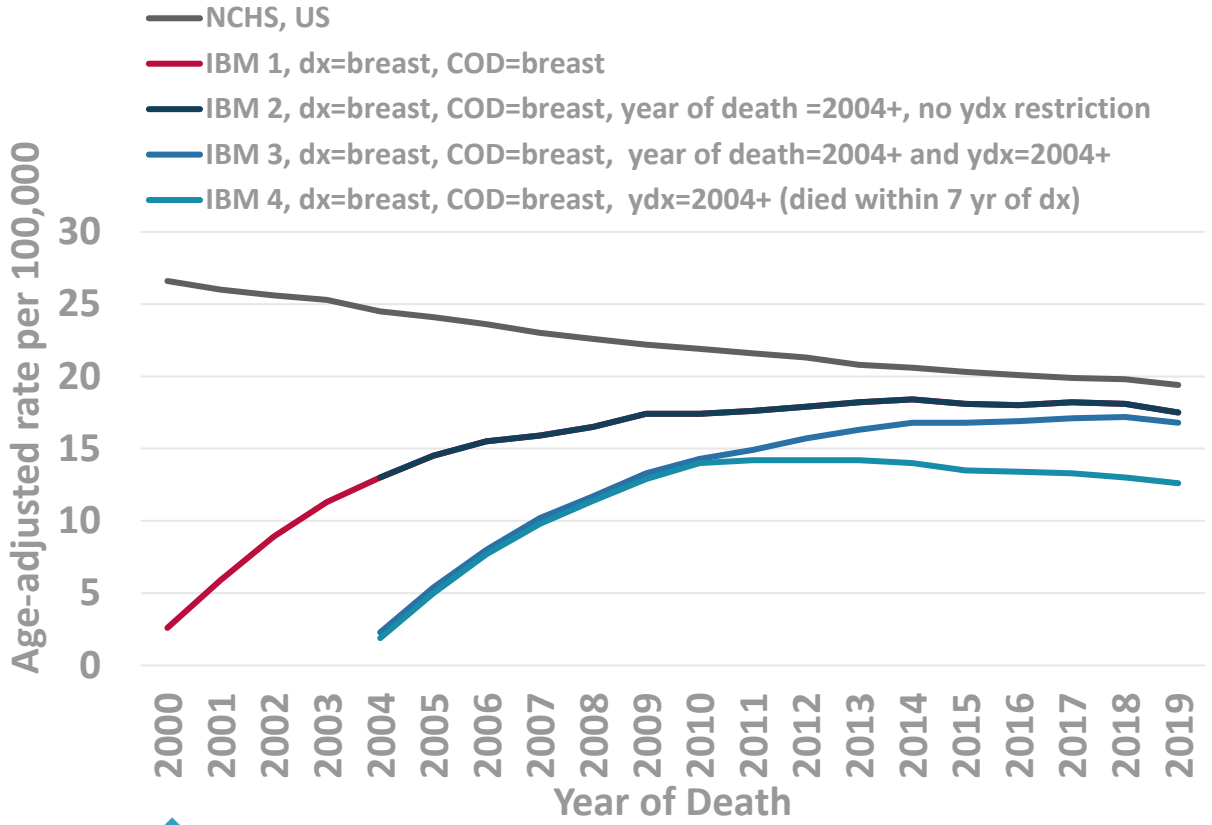


Things to consider

- 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+)

Breast Cancer, 2000-2019. SEER-17.

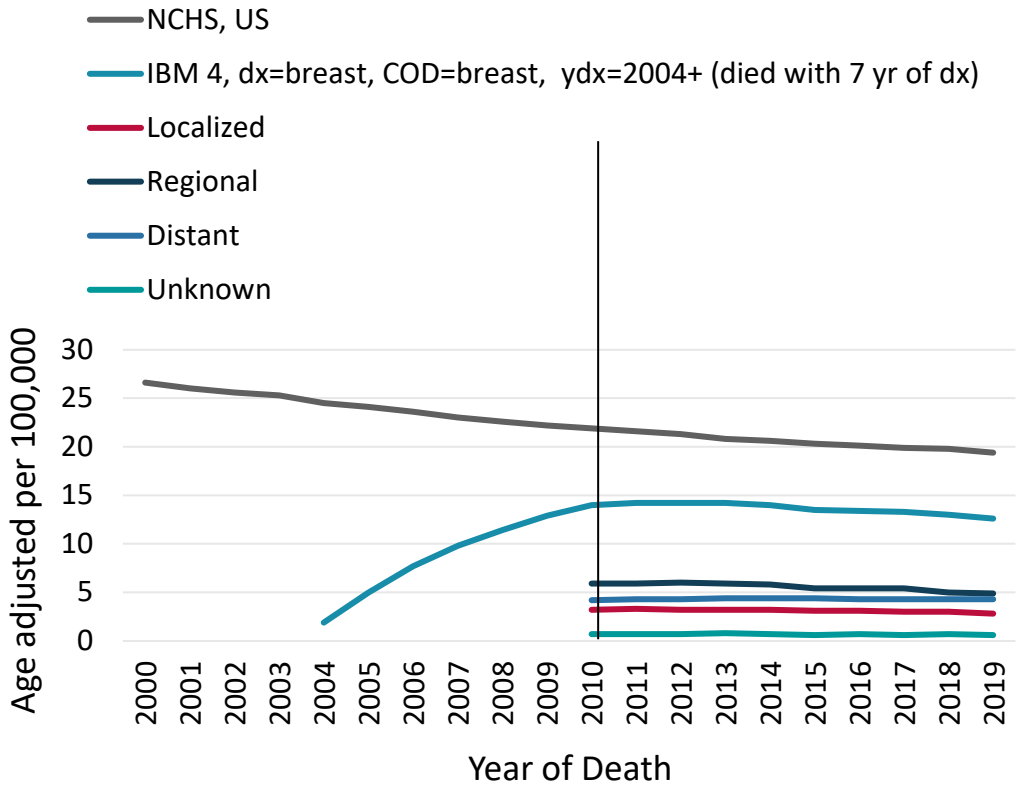


What burn-in period are you going to use?

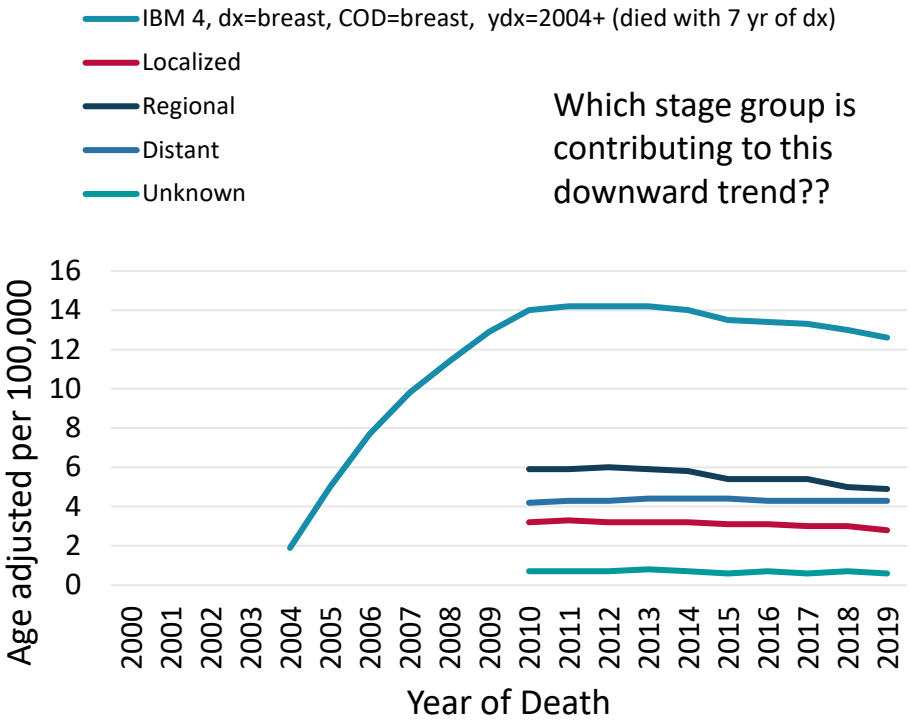
Things to consider

- 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

Breast Cancer by Stage, 2000-2019. SEER-17.



Breast Cancer by Stage, 2000-2019. SEER-17.



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 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

- Chu KC et al. A method for partitioning cancer mortality trends by factors associated with diagnosis. An application to female breast cancer. J Clin Epi 1994.

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

Few IBM Application References

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- Howlader N et al. Contributions of Subtypes to Non-Hodgkin Lymphoma Mortality Trends. CEBP 2016.
- Howlader N et al. Contributions of HIV to Non-Hodgkin Lymphoma Mortality Trends in the United States. CEBP 2016.
- Feuer EJ et al. Cancer surveillance series: interpreting trends in prostate cancer--part II: Cause of death misclassification and the recent rise and fall in prostate cancer mortality. JNCI 1999.

IBM Analysis in SEER*Stat

Thank you!

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