



# **Incidence-based Mortality Method to Partition Tumor-Specific Mortality Trends: Application to Non-Hodgkin Lymphoma Cancer**

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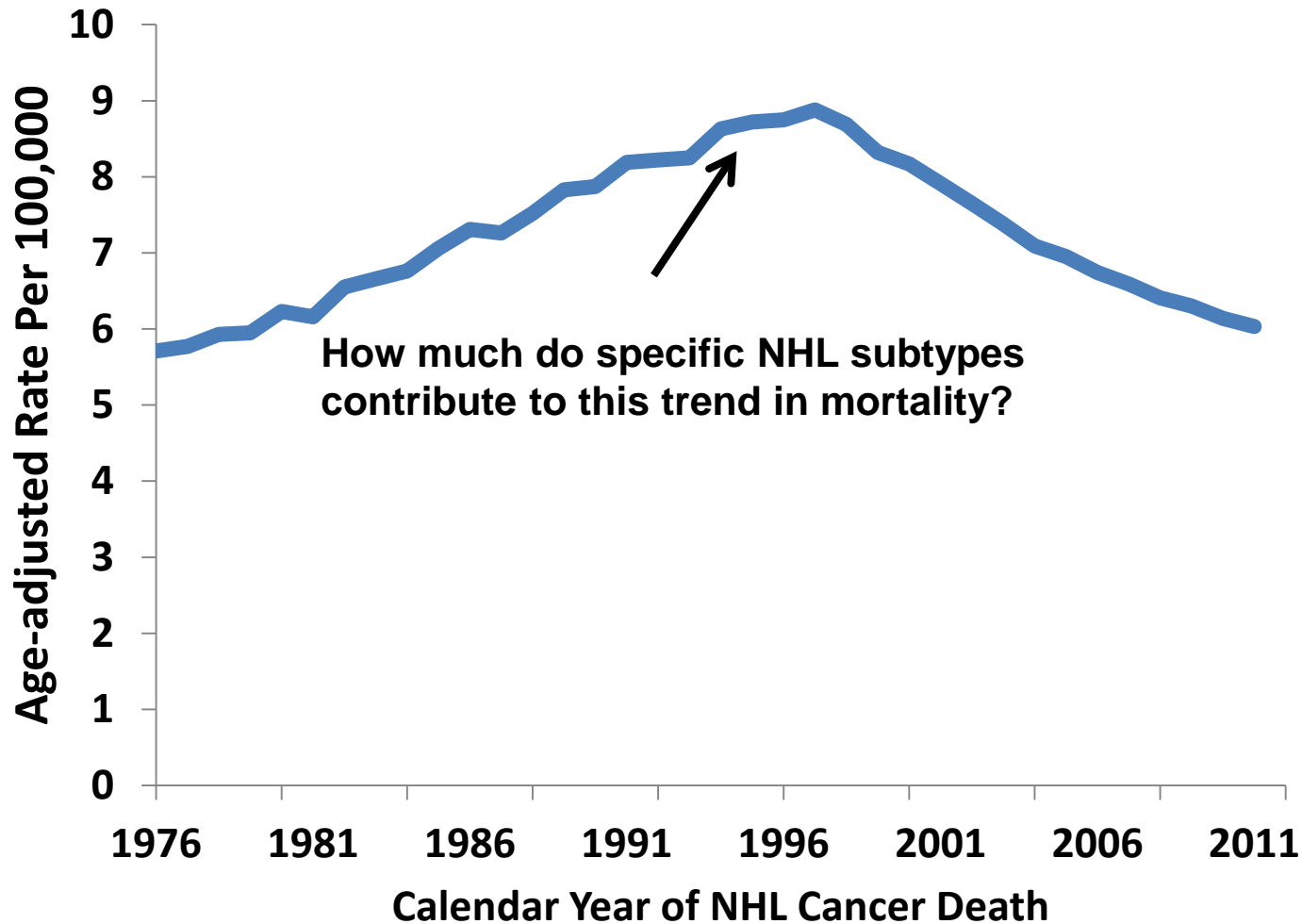
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# Overview

# NHL Mortality Rate: US General Population



Source: National Center for Health Statistics (NCHS Mortality, U.S.)  
NHL = Non-Hodgkin Lymphoma

# Background

# Non-Hodgkin Lymphoma (NHL)

- **Heterogeneous group of cancer malignancies**
  - Arises from lymphoid tissue and has varied clinical and biological features
- **NHL has many subtypes**
  - Based on cell type
- **Main subtypes are derived from either B-cell or T-cell**
- **Three main B-cell subtypes:**
  - Diffuse large B-cell lymphoma (DLBCL)
  - Follicular
  - Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)
- **Common T-cell subtype:**
  - Peripheral T-cell lymphoma (PTCL)

# Non-Hodgkin Lymphoma (NHL)

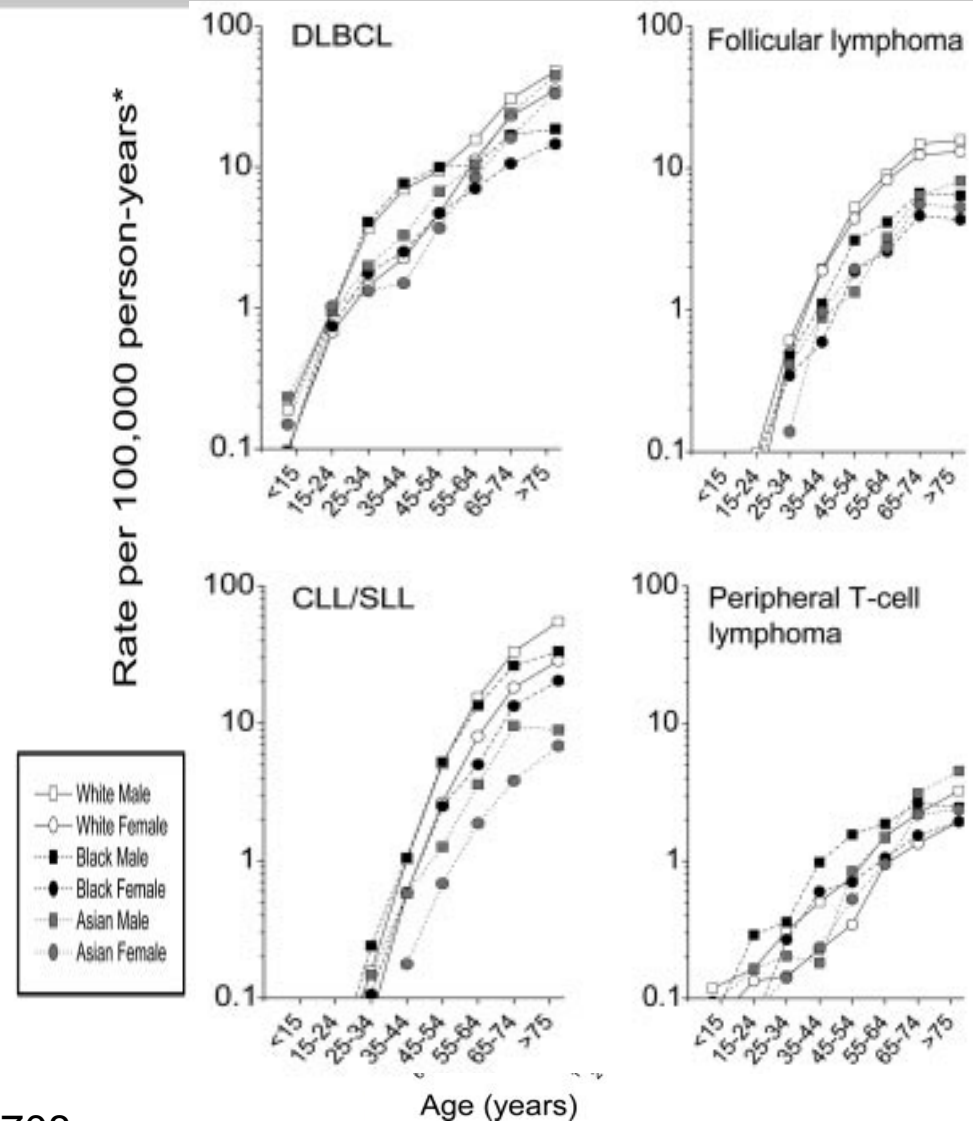
- Together these 4 subtypes represent ~70% of NHL cases

- 29% DLBCL

- 15% Follicular

- 22% CLL/SLL

- 4% PTCL



# NHL Incidence and Mortality Trends

- **Hypothesized that NHL mortality trends vary by tumor subtypes**
  - **Incidence and survival trends vary by tumor subtypes**
  - **Treatments improved in some subtypes but not all**
  - **1980s HIV epidemic contributed to the NHL incidence trends**

# Study Aims



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- **Assess contributions of population-level NHL mortality attributed to each main NHL subtypes over time**
- **Assess contributions of long term incidence and survival patterns to trends in mortality by tumor subtypes over time**

# Methods

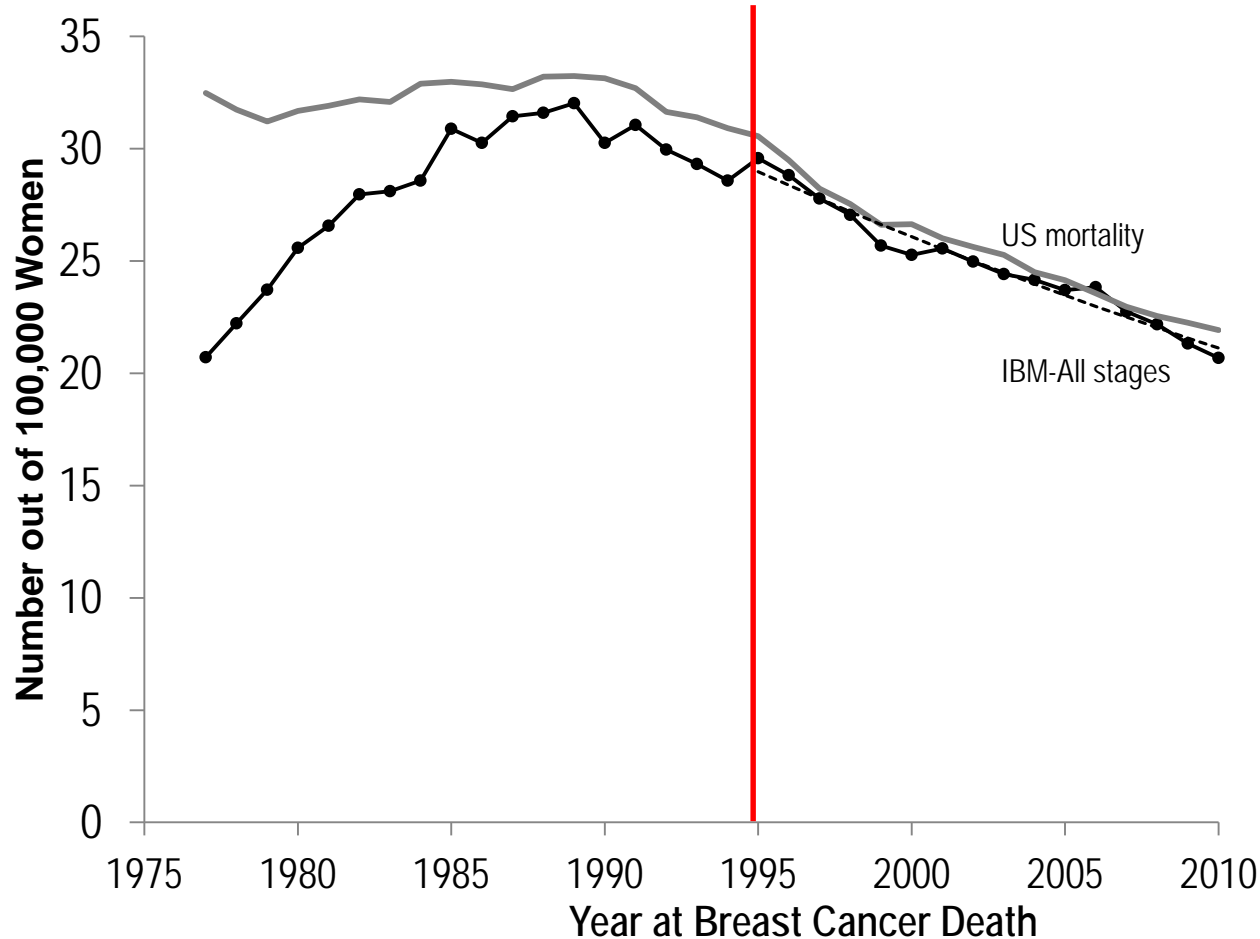
# Methods

- **Incidence-based mortality method (IBM)**
- **Adult (age 20+) NHL cases diagnosed in SEER-9 areas (1975-2011)**
- **Four main NHL subtypes (based on WHO classification)**
- **NHL cases of only or first invasive cancer for appropriate mapping of causes of death (COD)**
- **Excluded death certificate or autopsy**

# Mortality versus IBM

<b>Mortality</b>	<b>Incidence-based Mortality (IBM)</b>
<b>NCHS Mortality</b>	<b>SEER Incidence cases linked with NCHS Mortality</b>
<b>Entire US</b>	<b>SEER (e.g., SEER-9 covers 9% of the US population)</b>
<b>Deaths from 1950+</b>	<b>Deaths from cases diagnosed 1975+</b>
<b>By sex, age at death, year at death, geography</b>	<b>By factors related to cancer diagnosis (e.g, histology, stage at diagnosis, biomarkers)</b>
<b>Complete mortality over any period of time</b>	<b>Complete mortality depends on aggressiveness of the tumor</b>

# Example: Mortality versus IBM



Cho H, Mariotto AB et al. JNCI Monographs, 2014.

National Cancer Institute

# IBM Method: NHL 4 Main Subtypes

- Incidence-based mortality (IBM)

$$\text{IBM rate} = \frac{\text{Death among SEER incident cases}}{\text{SEER Population at risk at the time of death}}$$

- COD<sup>1</sup> included in IBM Rate
  - Hodgkin lymphoma, plasma cell, or leukemia in addition to NHL cancer deaths, if they linked to a SEER NHL case
- Require 15 years of data on incident cases prior to each year of mortality data
- Joinpoint to assess IBM trend changes over time

<sup>1</sup> SEER COD recode for detail ICD codes: <http://seer.cancer.gov/codrecode/>

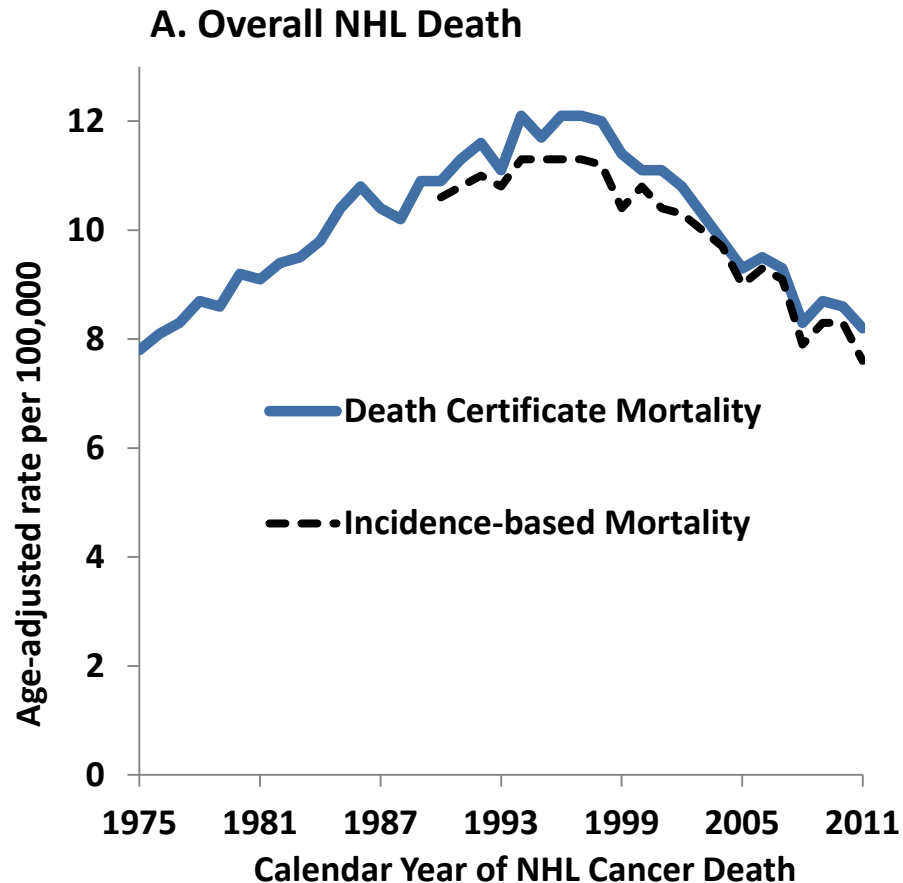
# Methods: Incidence and Survival

- **Age-adjusted incidence rates by 4 main subtypes over time (1975-2011)**
  - Adjusted for reporting delay
  - Due to lack of specific coding, PTCL trends are presented over a shorter period of time
- **Joinpoint to assess incidence trend changes over time**
- **Finally, calculated 5-year cancer-specific survival by 4 main subtypes over time (1975-2006)**

# Results

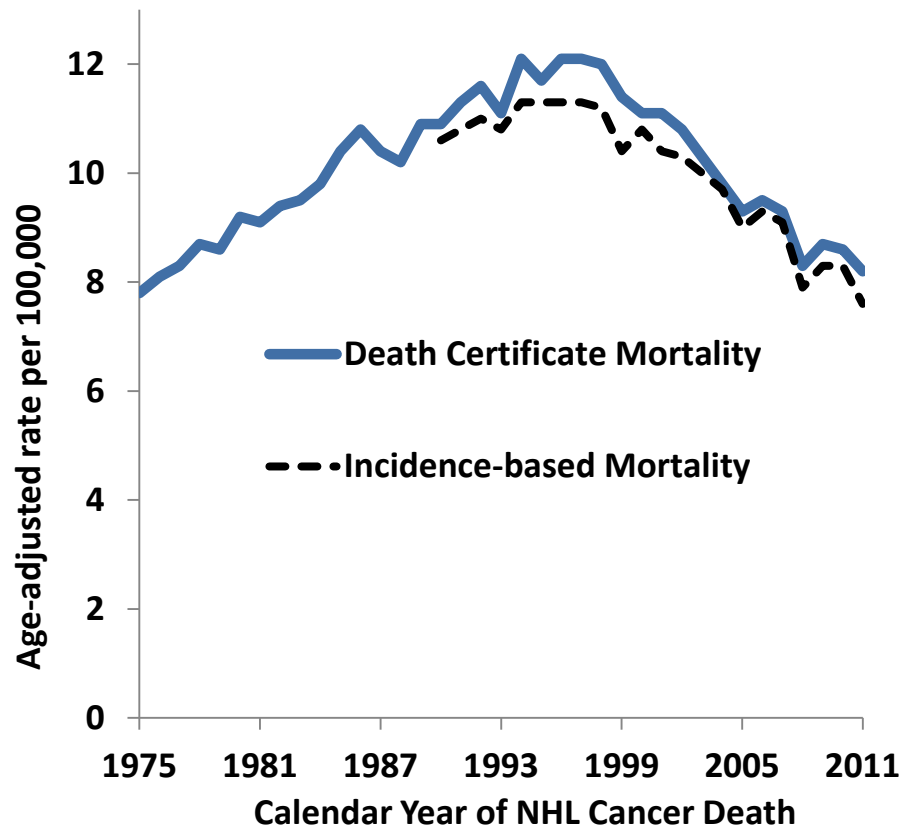


# Overall NHL Mortality & IBM, SEER-9

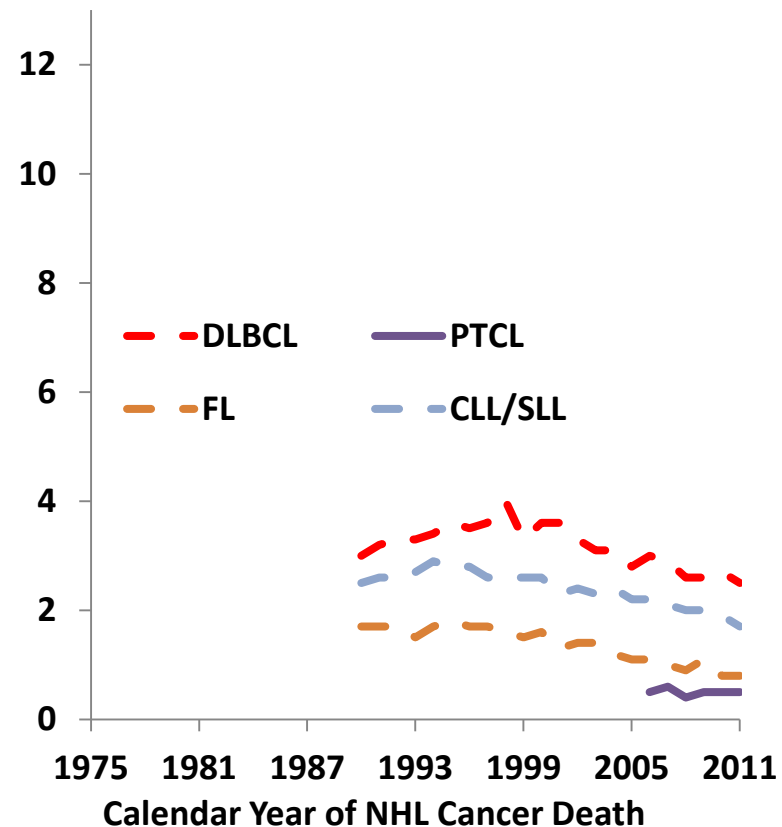


# Overall NHL Mortality & IBM Rates By Subtypes, SEER-9

A. Overall NHL Death



B. NHL Death By Tumor Subtypes

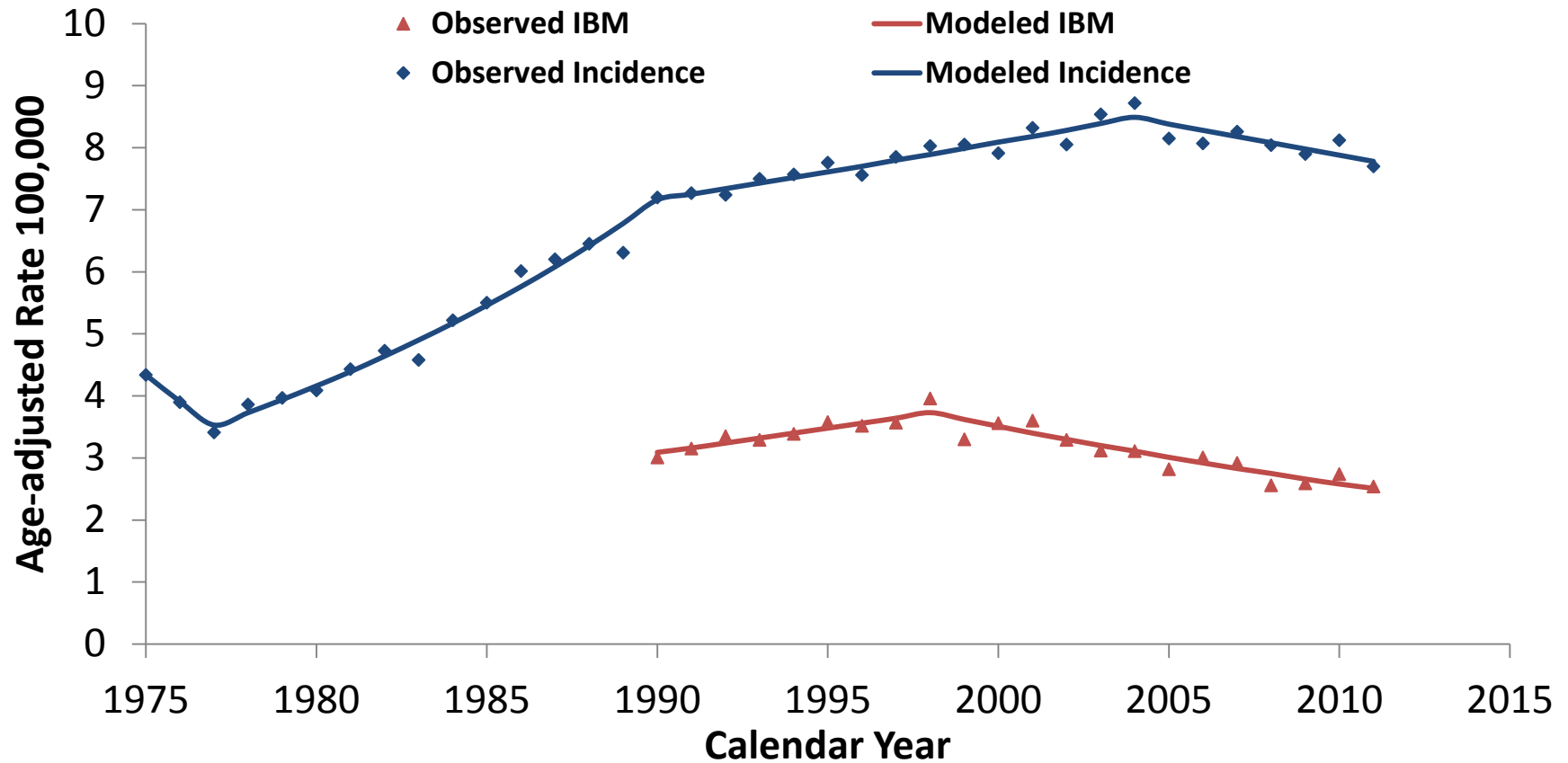


# Proportion of NHL Deaths by Subtypes. SEER-9, 2011\*

Subtypes	%
DLBCL	33
CLL/SLL	22
FL	11
PTCL	7

\* Other NHL subtypes contributed 27% of deaths.

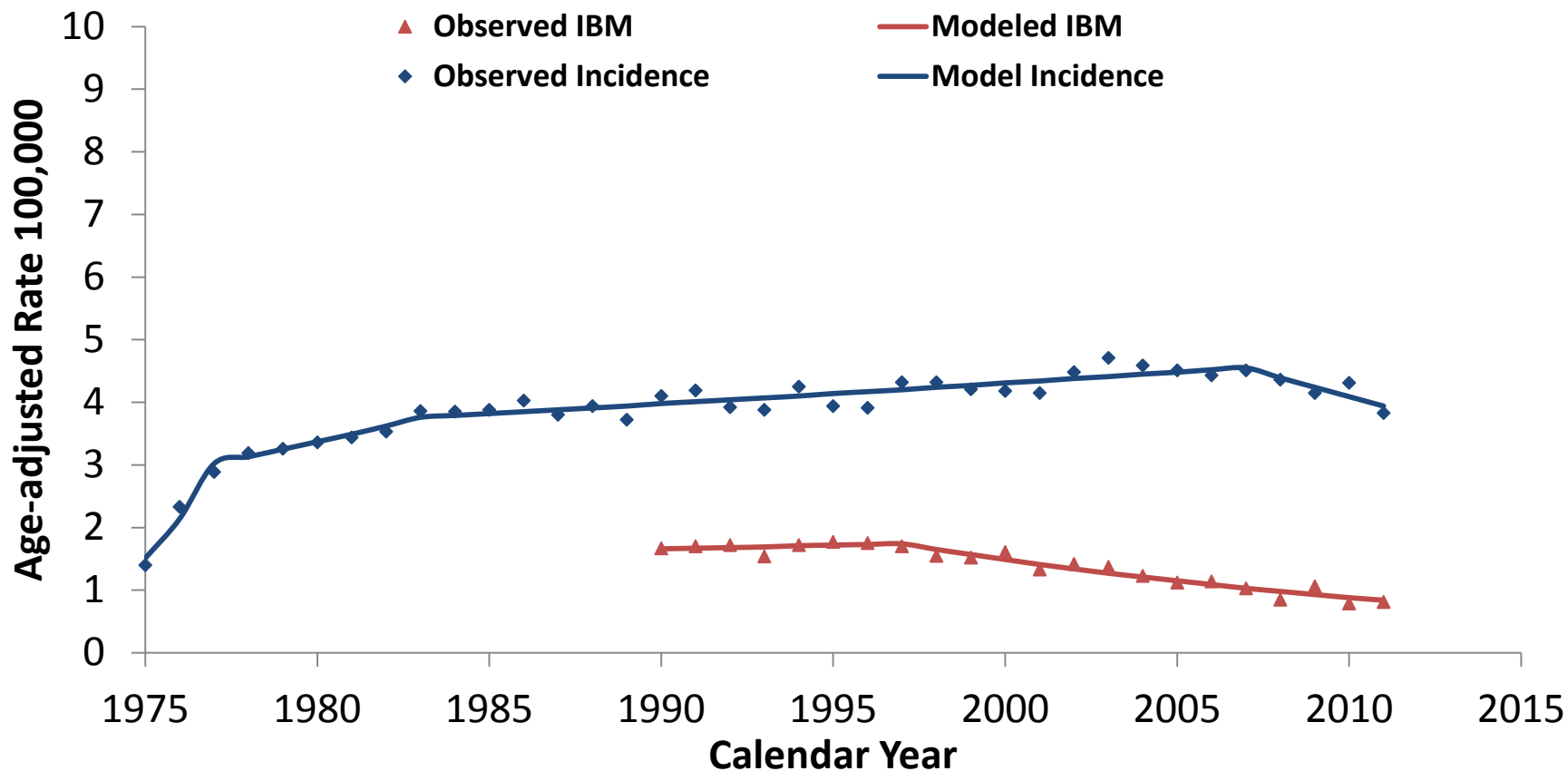
# DLBCL: Incidence, IBM, & Survival Trends, SEER-9



Percent surviving DLBCL cancer 5 years after diagnosis

1975	1981	1987	1993	1999	2005
40%	45%	52%	51%	55%	67%

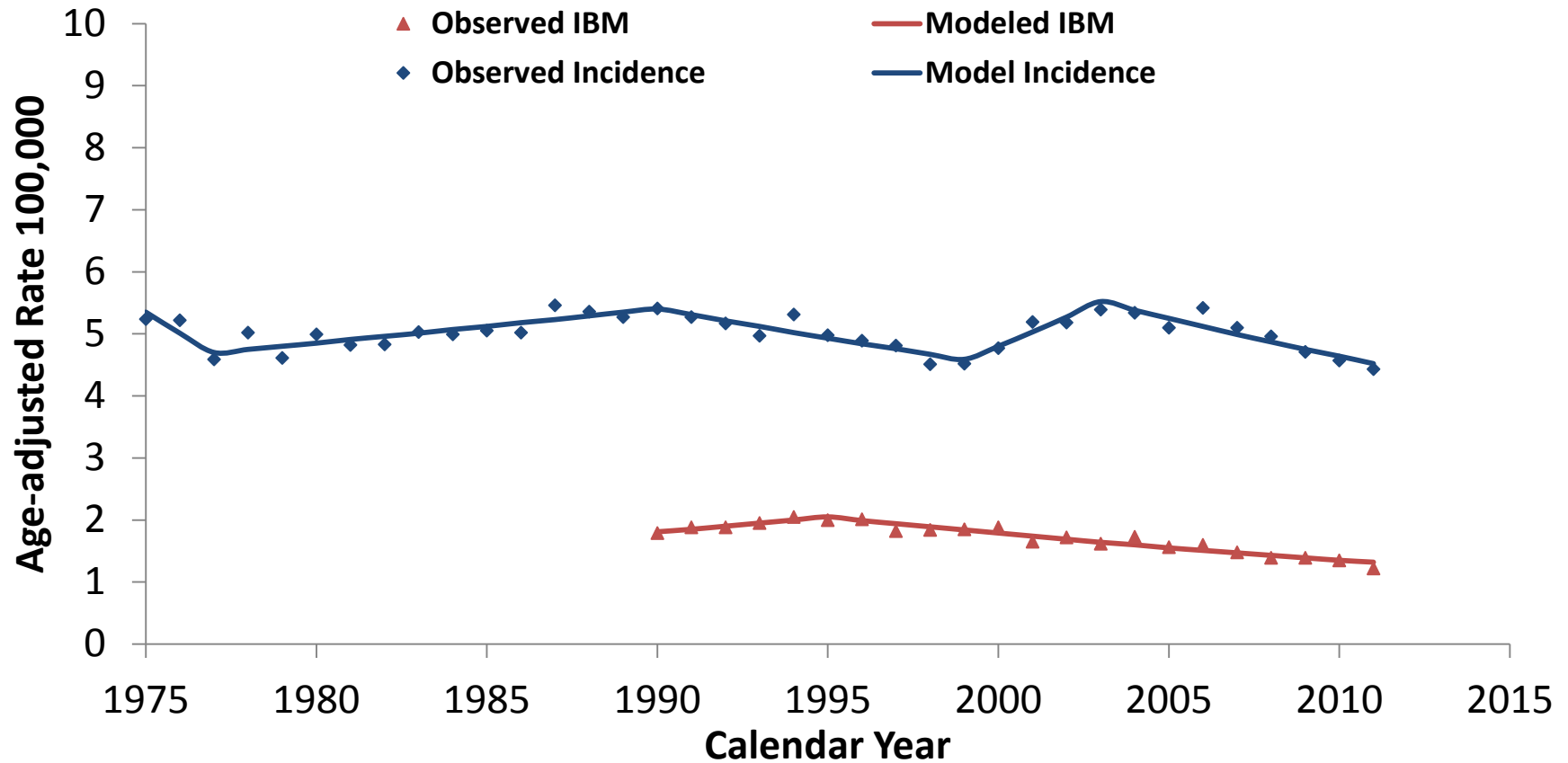
# Follicular: Incidence, IBM, & Survival Trends, SEER-9



Percent surviving FL cancer 5 years after diagnosis

1975	1981	1987	1993	1999	2005
75%	68%	71%	76%	78%	86%

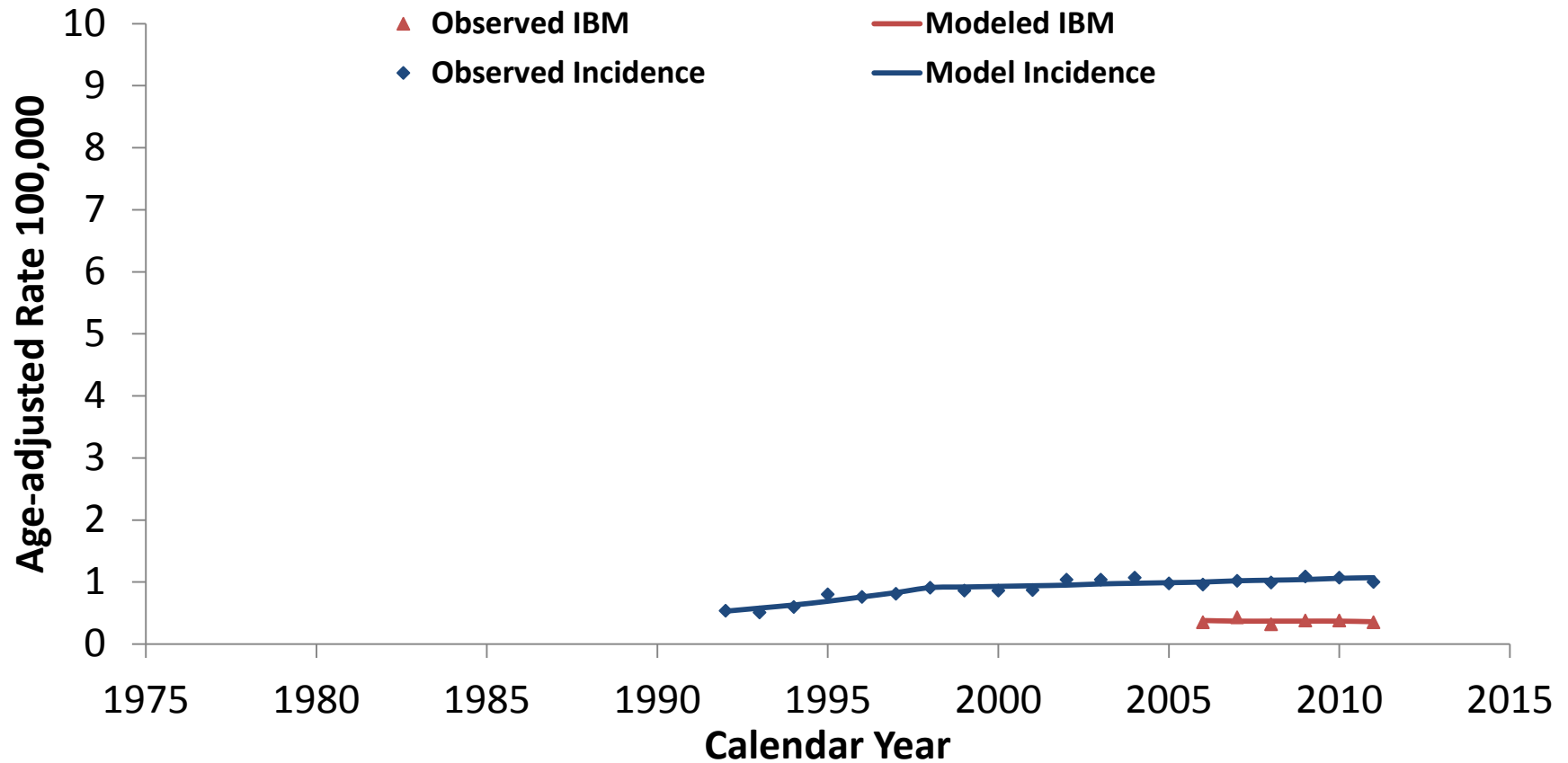
# CLL/SLL: Incidence, IBM, & Survival Trends, SEER-9



**Percent surviving CLL/SLL cancer 5 years after diagnosis**

1975	1981	1987	1993	1999	2005
69%	70%	74%	77%	76%	84%

# PTCL: Incidence, IBM, & Survival Trends, SEER-9



Percent surviving PTCL cancer 5 years after diagnosis

1975	1981	1987	1993	1999	2005
			65%	67%	64%

# Conclusions



# Conclusions

- **Mortality trends from B-cell tumor subtypes (DLBCL, FL, CLL/SLL) decreased before incidence decreased**
- **Survival improvement due to novel therapy**
  - Rituximab with CHOP (i.e., R-CHOP) for advanced stage disease among DLBCL and FL cases beginning 1998
  - Fludarabine, cyclophosphamide, and rituximab among CLL cases in 1990s
- **Mortality trends from PTCL remain unchanged**
  - Need better treatment

# Conclusions (Cont'd)

- **Better diagnostic tool may explain some increase in incidence trends, but not all**
  - **Known risk factors (e.g., HIV/AIDS for DLBCL) may contribute to the trends**
  
- **Novel method to partition mortality by subtypes**
  - **Strength: address misclassifications in COD by use of broad definition of COD**
  - **Limitation: IBM rates could be underestimated due to under-ascertainment of hematologic cases (e.g., CLL) in registries<sup>1</sup>**

<sup>1</sup> Penberthy L et al. Cancer Causes a & Control 2012

# Conclusions (Cont'd)

- **Survival benefit from these novel treatments were demonstrated in clinical trials**
- **First study to show large reduction in mortality in particular tumor subtypes at population level**
- **IBM methods should be valuable for assessing mortality trends for other tumor subtypes**

# More Information

# More Information

- **“Contributions of Subtypes of Non-Hodgkin Lymphoma to Mortality Trends”. Manuscript under preparation**
- **Next step to investigate how HIV epidemic contributed to subtype-specific mortality trends in US general population**

## Contact Information

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# Useful Reference for IBM

- **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.**
- **Hur C et al. Trends in esophageal adenocarcinoma incidence and mortality. Cancer 2013.**
- **IBM tutorial in surveillance research program website:  
<http://surveillance.cancer.gov/statistics/ibm/>**

**Thank you!**

# Extra Slides



# IBM: Numerator Definition

	SEER Incident Case	
NCHS COD	NHL	Non-NHL
NHL	A	B
Non-NHL	C	D

- **Cell A: Contributes**
- **Cell B: Does not contribute**
  - Breast cancer case die from NHL COD
- **Cell C: Does not contribute**
  - NHL case die from Non-NHL COD (e.g., heart disease)
- **Cell D: Does not contribute**
  - Lung cancer case die from lung cancer

NCHS= National Center for Health Statistics  
COD= Cause of Death

# Number of Years Required for IBM to be within 10% Death Certificate Mortality

<b>Organ</b>	<b>Years</b>
Brain and central nervous system	3
Breast (female)	8
Colon, rectum	5
Kidney	4
Lung (males or females)	3
Melanoma	10
Ovary	5
Prostate	8
Stomach	2
Thyroid	11
Uterus, corpus	6

Chu et al. J Clin Epi, 1994