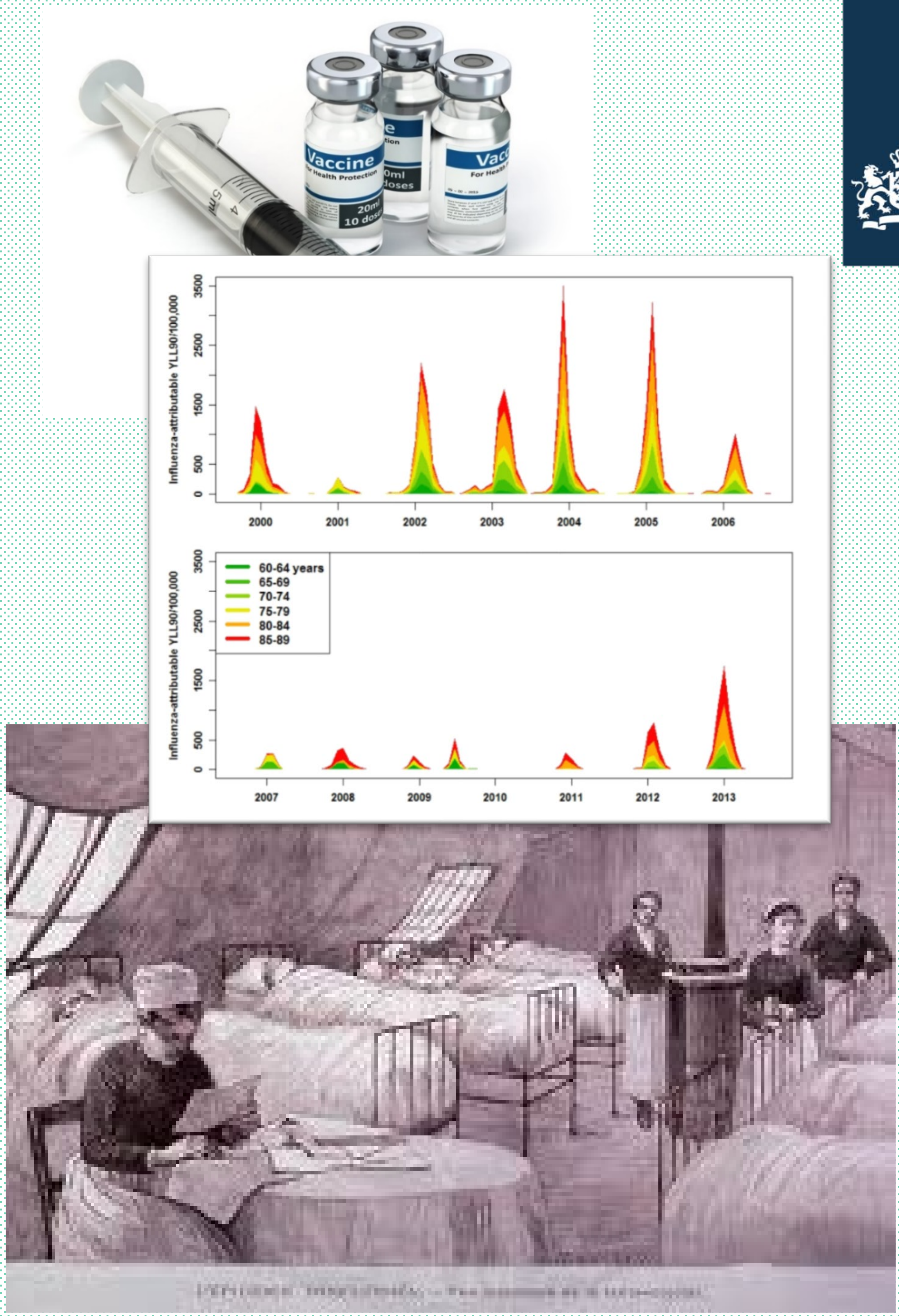

National Institute for Public Health
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Ministry of Health, Welfare and Sport

Computing the burden of infectious diseases in an ageing population: Accounting for competing mortality risks

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Motivation & objectives

In an ageing population, the mortality burden due to infectious diseases is challenging to measure

- Higher prevalence of co-morbidities in the elderly affects risk of mortality from non-infectious causes, and thus remaining life expectancy
- This is the classic competing mortality risk situation: eg. *dying of influenza precludes dying from another condition, and v.v.*
- Standard approaches for computing Years of Life Lost (YLL) could lead to **overestimation of burden** attributable to the infectious disease

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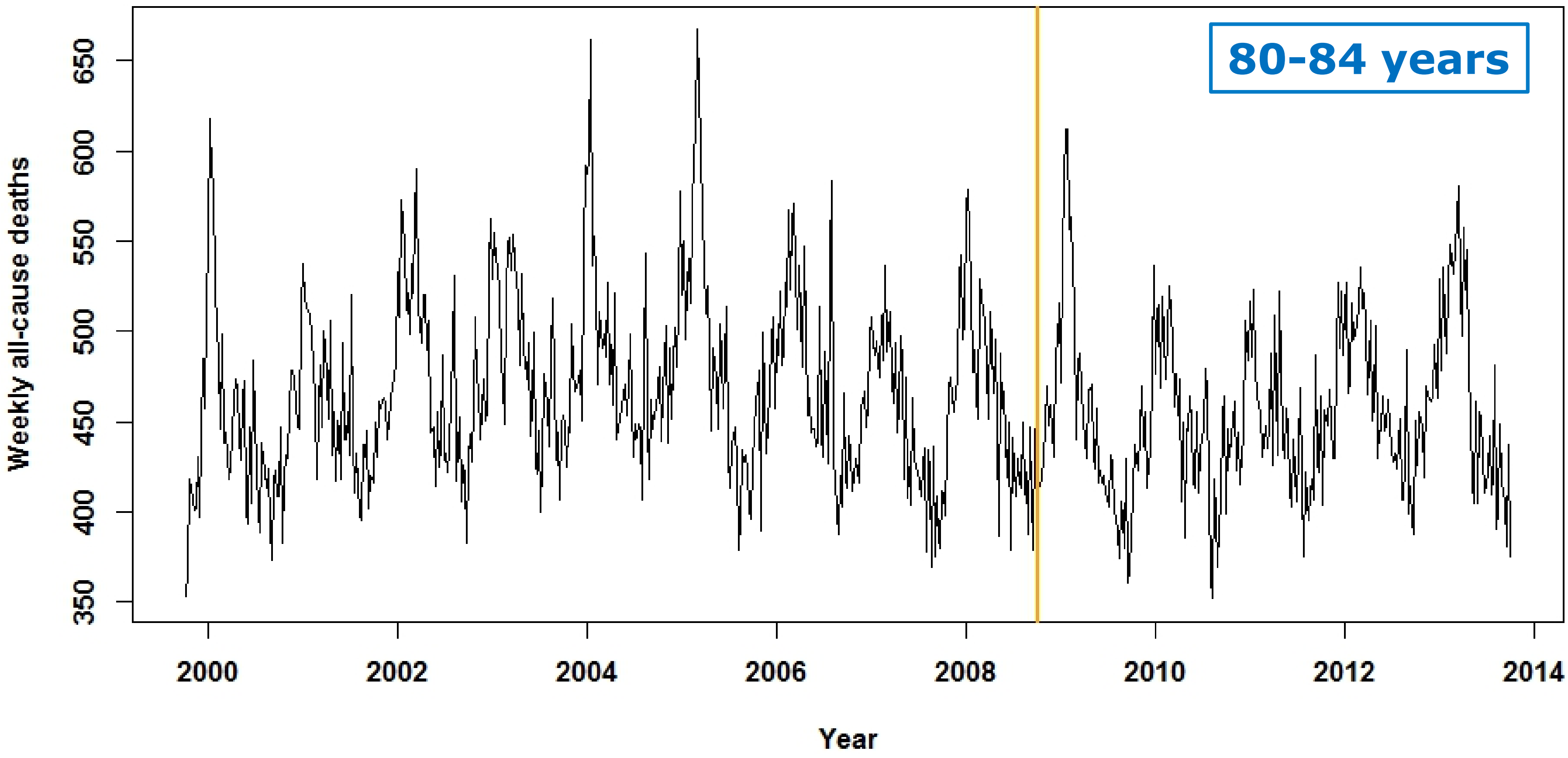
How can we avoid overestimation, and thus also the problem of 'double-counting' disease burden?

Proposed approach

- Step 1: estimate influenza mortality (a challenge in itself!)
  - **a:** estimate weekly **influenza-attributable** mortality, per age-group (60 to 85+ yrs), from all-cause mortality data using established additive regression approaches
  - **b:** estimate **burden** of premature mortality, as the 'standard' YLL measure

- Step 2: estimate **cause-specific mortality burden** while accounting for competing risks

Main data source: NL all-cause mortality data

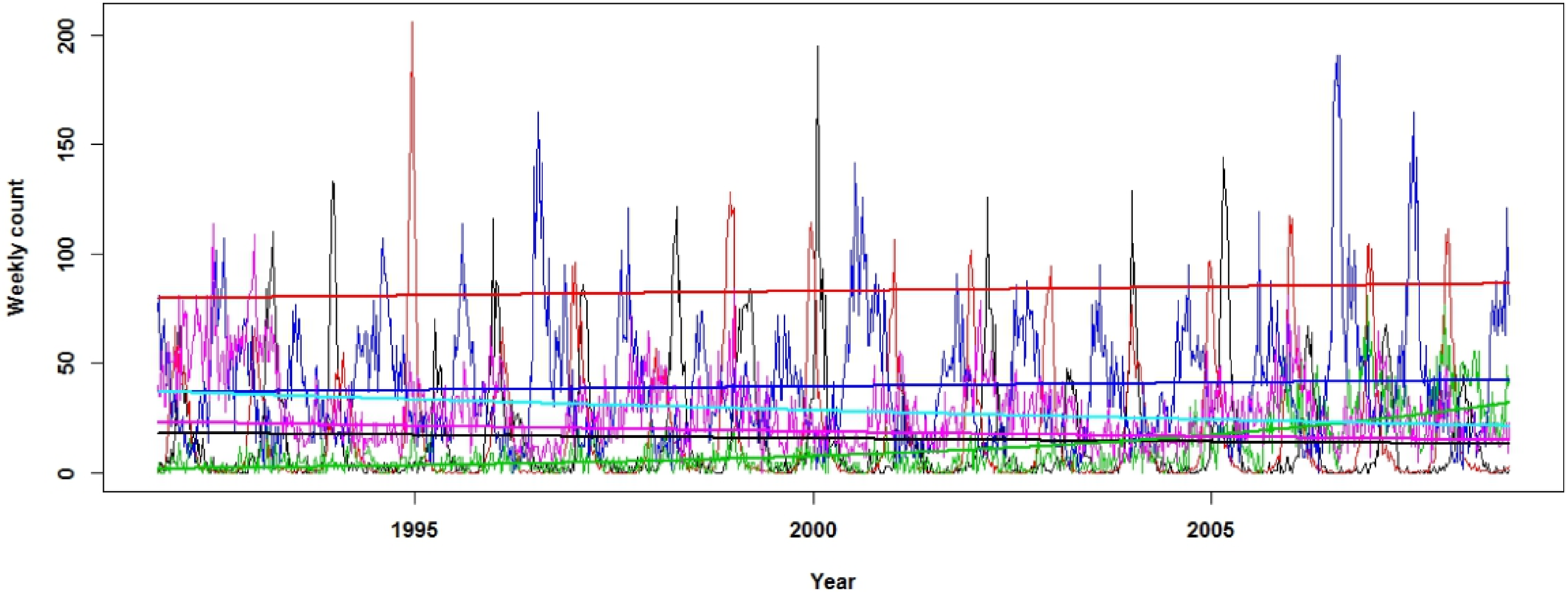


Methods

- Step 1a: estimate weekly **influenza-attributable** mortality using co-circulating respiratory pathogen positive tests (eg. influenza A, B, RSV) and extreme temperatures as covariates
  (eg. van Asten et al., 2012, J Infect Dis)

Methods: step 1a

- Model weekly **influenza-attributable** deaths using additive Poisson regression with co-circulating respiratory pathogen positive tests from weekly lab surveillance as covariates



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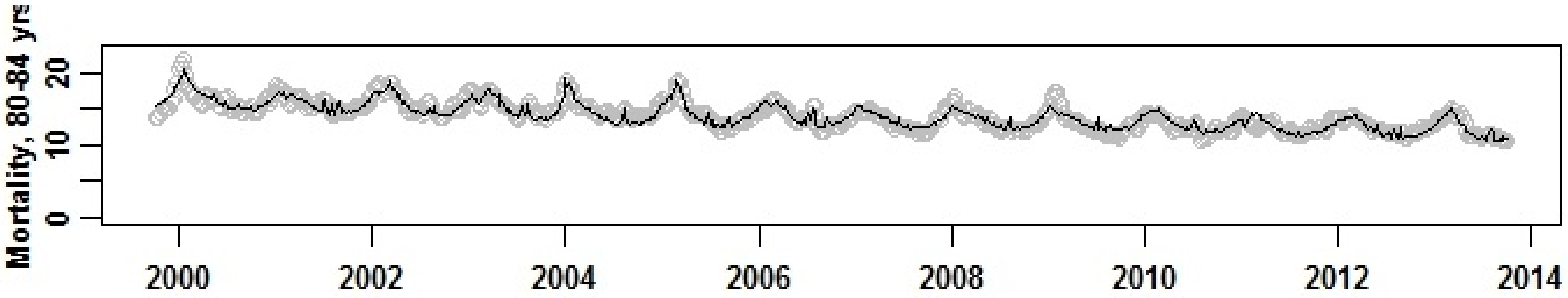

Methods: step 1a

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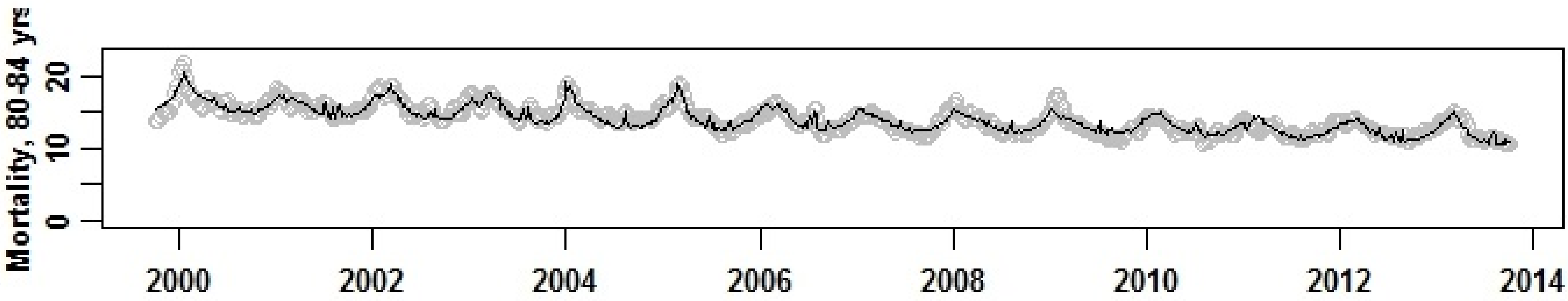


Annual influenza-attributable deaths (60+ yrs): **40 to 3330** per season
Aggregating over seasons: **1.3%** of all deaths in 60+ yrs

Methods: step 1b

- Estimate mortality burden, per 5-year age-group
  - YLL goes beyond influenza-attributable deaths; allows **extent of premature mortality** to be taken into account
  - We calculate YLL to assess the extent of overestimation **not accounting** for competing risks (based on Kaplan-Meier survival)

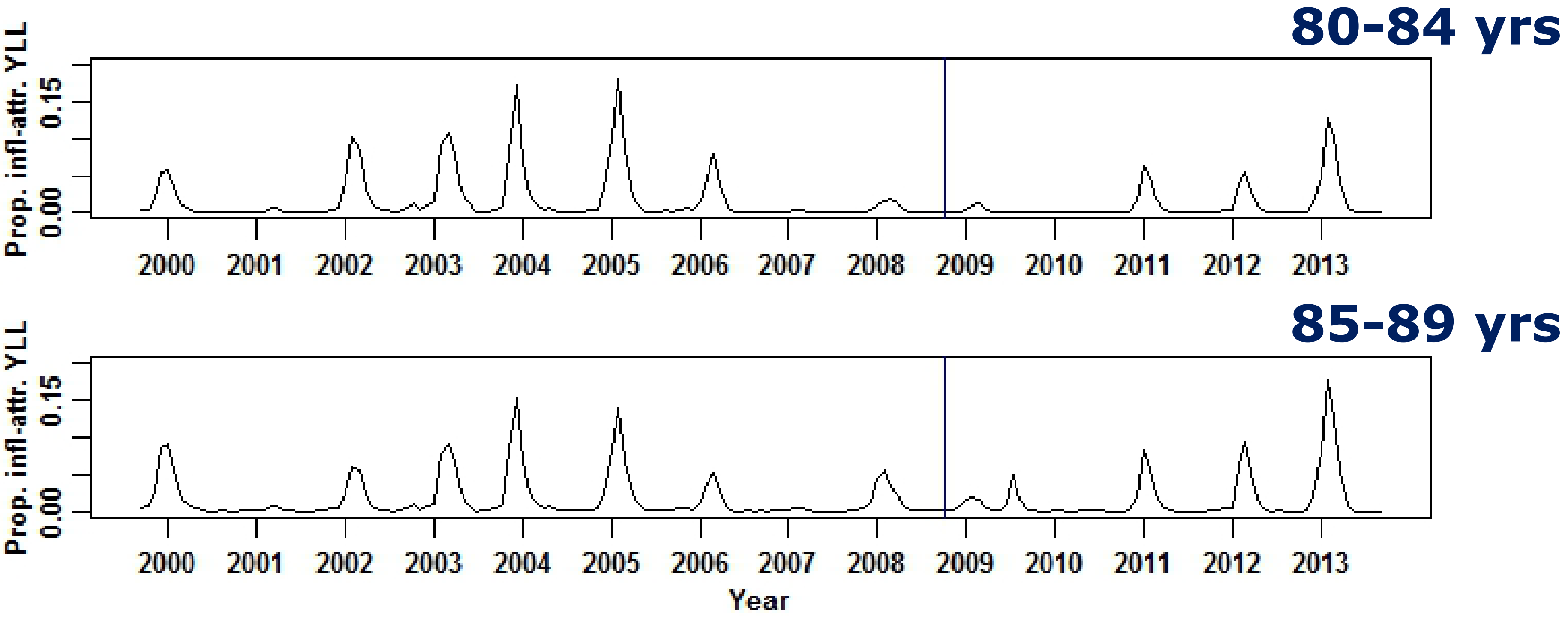
Methods: step 2

- Estimate **cause-specific burden** while accounting for competing risks
  - Implicit assumption when estimating mortality burden of a single cause is that removing this cause from the population does not affect probability of dying from other causes
  - Intuitive that this issue is most important for the oldest age-groups

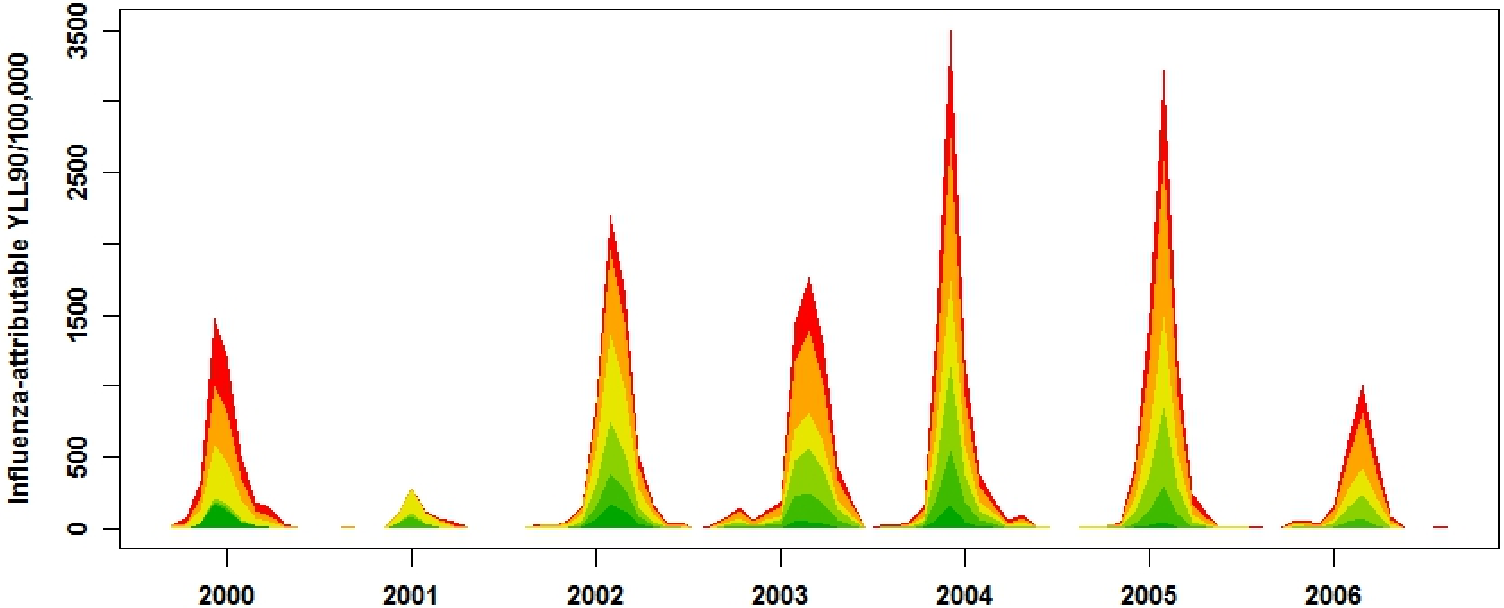
Methods: step 2

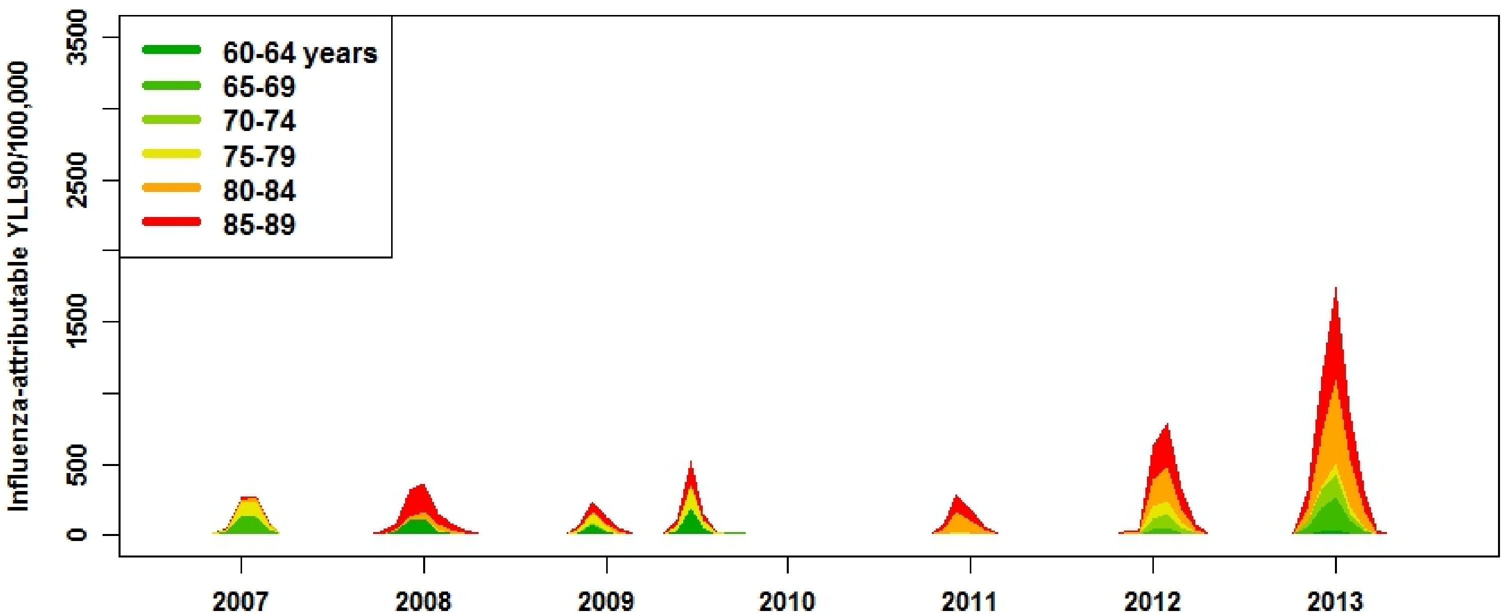
- Estimate **cause-specific burden** while accounting for competing risks
  - Implicit assumption when estimating mortality burden of a single cause is that removing this cause from the population does not affect probability of dying from other causes
  - Intuitive that this issue is most important for the oldest age-groups
  - We compute **YLL90**, where 90 years is [arbitrarily] assumed to be the maximum attainable age, using restricted mean lifetimes survival analysis (Anderson, 2013, Stat Med)
  - Requires cumulative mortality risk per age-cohort to be estimated, by changing to 'cohort' view of data using Lexis expansion and simulation methods (van Wijhe et al., 2016, Lancet ID)

Influenza-attributable YLL90, 2 example age-groups



YLL90 per 100,000 (adjusting for population size)





Importance of competing risks approach?

Age-group (years)	Influenza-attributable YLL90 (competing risks method)	YLL90 per 100,000 (95% UI)	Influenza-attributable YLL (Kaplan-Meier survival)
60-64	488	62 (44-82)	502
65-69	573	86 (64-108)	607
70-74	1070	186 (157-218)	1167
75-79	1141	246 (210-283)	1343
80-84	1348	423 (377-472)	1783
85-89	842	345 (305-389)	1852
All 60+	5472	177 (166-190	7278

Importance of competing risks approach?

- Comparing approaches taking and not taking (Kaplan-Meier method) competing mortality risks into account:
  - Small overestimation of mortality burden for 60-64 years: **3.5%**
  - Greatest extent of overestimation in 80-89 years age-group: **82%**

Summary

- Highest mortality burden (YLL90 per 100k) in 80-84 years, despite more influenza-attributed deaths in 85+ years age-group
- 'Standard' YLL measure overestimates burden, compared with YLL90, as does not take competing mortality risks into account
- Most relevant for **fatal infectious diseases** among the oldest segment of the population, who have a higher prevalence of co-morbidities
- Implications for **disease burden ranking and prioritisation** for treatment/prevention measures
- Population ageing implies that the competing risk issue will become increasingly important for disease burden estimation

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