Influenza among older adults in the Netherlands

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Introduction

- Individuals with comorbidities have both increased risk of influenza and higher vaccine uptake
- When estimating vaccine effectiveness of influenza vaccines, it is therefore important to adjust for comorbidities
- However, this information is often not available for the whole population

Aim

To estimate vaccine effectiveness (VE) of the influenza vaccine among older adults (≥65 years) in the Netherlands, comparing Cox regression using calendar time on the whole cohort with test negative design (TND) in a sub-population with of influenza-like-illness (ILI) symptoms

Methods

Study population and design (figure 1)

- Cohort with older adults (≥65 years) in the Netherlands, 2012-2013
- Self reporting of ILI symptoms -> home visit
  - Virology samples and testing for influenza
  - Questionnaire, including comorbidity information
- Random selection healthy controls: home visit, questionnaire and sample

Imputing comorbidity status on non visited participants

- Logistic regression with age, sex and vaccination status as covariates and comorbidities as outcome was fitted to data from the randomly selected healthy controls
- For non-visited participants probability of comorbidity was calculated
- 1000 imputed datasets with comorbidity drawn from a binomial distribute based on participant-specific calculated probabilities

Estimating of vaccine effectiveness

- Outcome: laboratory confirmed influenza infection
- Negative control outcome: other laboratory confirmed infections
- Cohort Design: hazard ratio estimates based on Cox regression using calendar time
- Test Negative Design: odds ratio based on logistic regression
- Covariates: Vaccination status univariately and adjusted for comorbidity

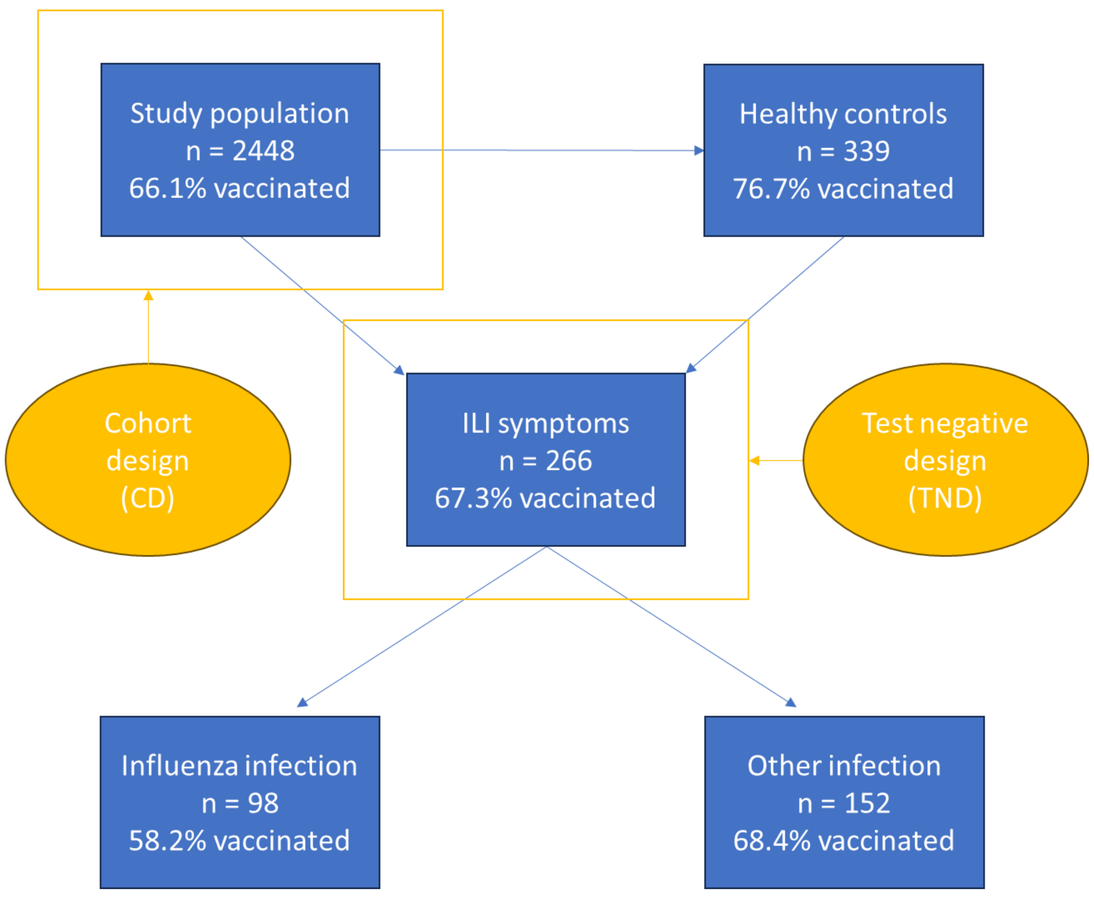

Figure 1: Overview of study design, including number of older adults (≥65 years) included (n) and proportion who received the influenza vaccine. In yellow: population used for VE estimates

Results

- Figure 2 gives an overview of random healthy sampling (red), sampling with ILI symptoms (blue) and cumulative incidence of influenza positive tests (black line).
- Figure 3 shows the distribution of predicted comorbidity status against true comorbidity status for ILI cases based on logistic regression model on data from the baseline visit.
- The VE against influenza infection was 26.7 (-9.7 – 51.0%, green) in the unadjusted and 34.0 (-1.0 – 56.0%, red) in the comorbidity adjusted Cox model (figure 4)
- The VE against non-influenza ILI was 2.0 (-43.0 – 32.0%, red) using adjusted Cox regression, compared to 39.2 (-2.9 – 64.1%, blue) in the adjusted TND (figure 4).

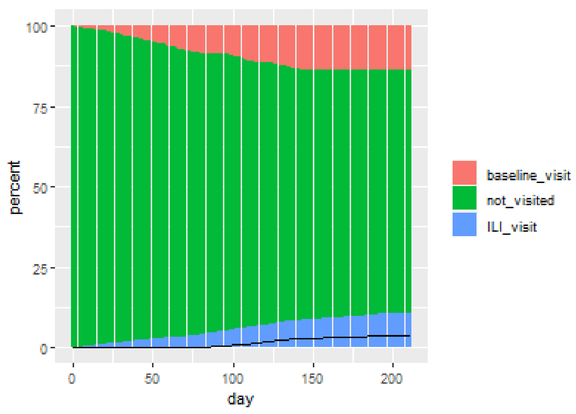

Figure 2: Cumulative ILI and baseline visit over time. Black line indicate cumulative influenza cases.

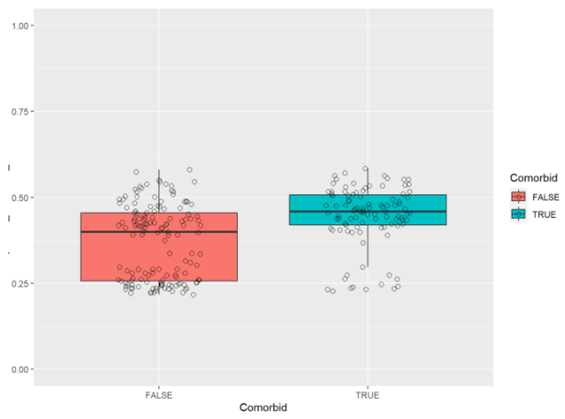

Figure 3: Predicted comorbidity status on ILI-visit population based on logistic regression model on data from baseline visit population

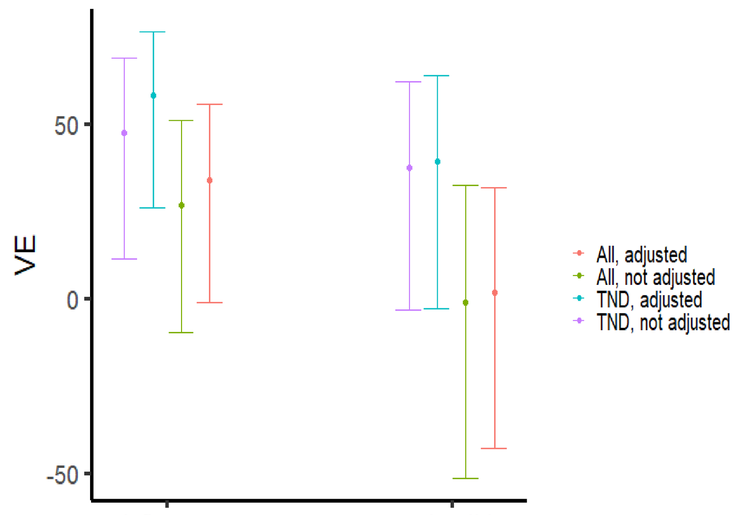

Figure 4 : Effectiveness of influenza vaccine, univariately and adjusted for imputed comorbidity against Influenza and as a negative control against other ILI. (TND: test negative design)

Conclusions

- The VE against non-influenza ILI (negative control outcome) was closer to zero using the cohort study with Cox regression than with test negative design. This suggests more residual confounding when using test negative design
- We show that a smaller subpopulation can be utilized to impute missing values of important confounders

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