Influenza vaccine effectiveness estimates from the I-MOVE multicentre case-control studies in Europe, 2011-12 to 2012-13: is there evidence of waning of vaccine-induced immunity?

Esther Kissling on behalf of the
I-MOVE multicentre case control study team

Introduction

Decrease of vaccine effectiveness (VE) over time suggested in European influenza studies in 2011-12 (UK, I-MOVE, Navarra)

- Higher early vs. late season VE; lower VE by days since vaccination

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Hypothesis: Virological changes may be greater later in season.

- Decrease in VE with more days since vaccination in early season more likely attributable to waning of immunity?

Methods

- I-MOVE multicentre case control study data
  - 2011-12 for A(H3N2); 2012-13 for influenza B: seasons of greater sample size
- Test-negative design: Patients consulting GP for ILI/ARI
  - Case Influenza A(H3)/B positive
  - Control Influenza negative
- Early/late influenza phase based on equal numbers of cases
- VE=(1-OR)*100
- Logistic regression, adjusting for age, onset week, sex and presence of chronic conditions
  - VE overall and early/late phase

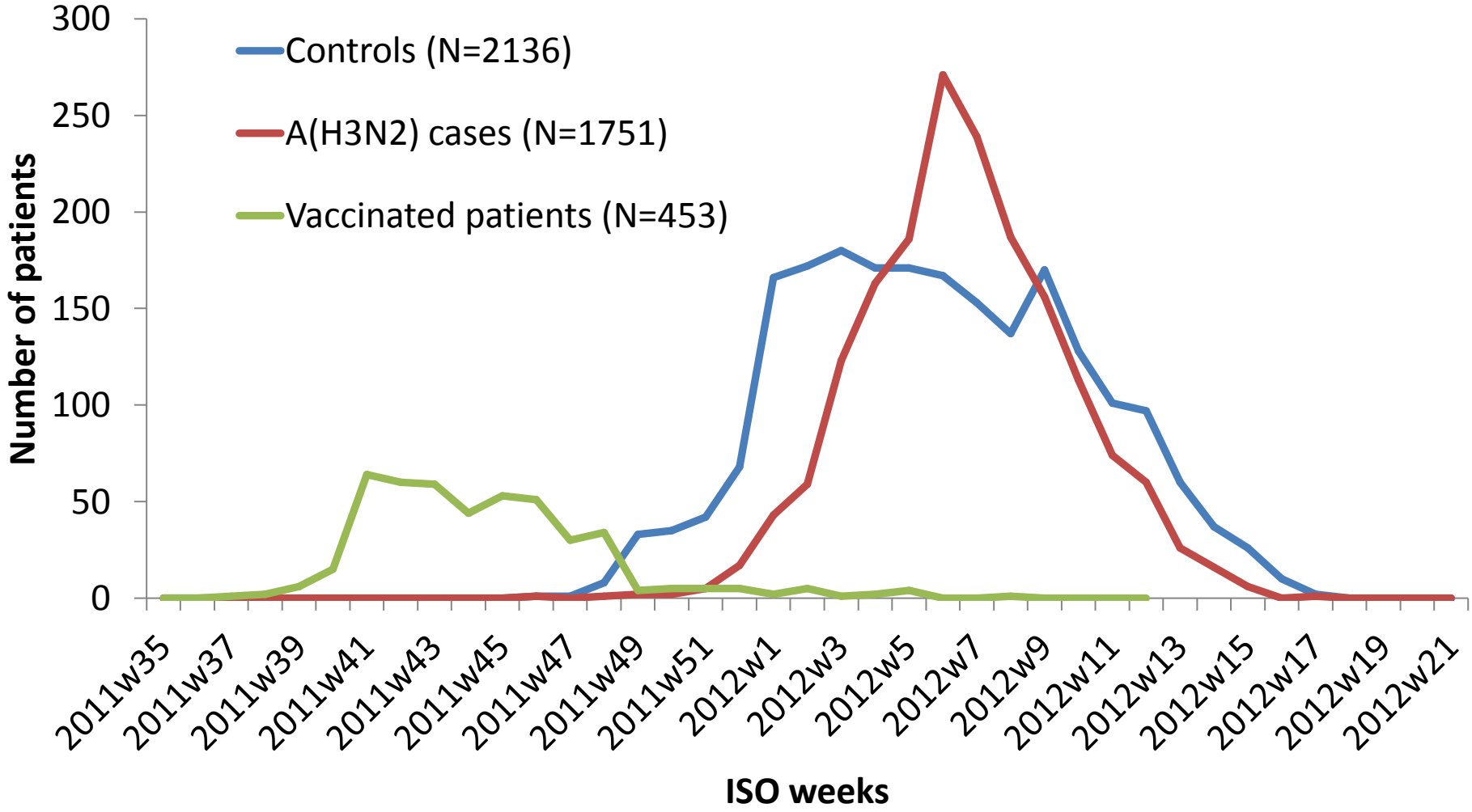
Methods

- Time since vaccination:
  - days between date of vaccination and onset of ILI symptoms

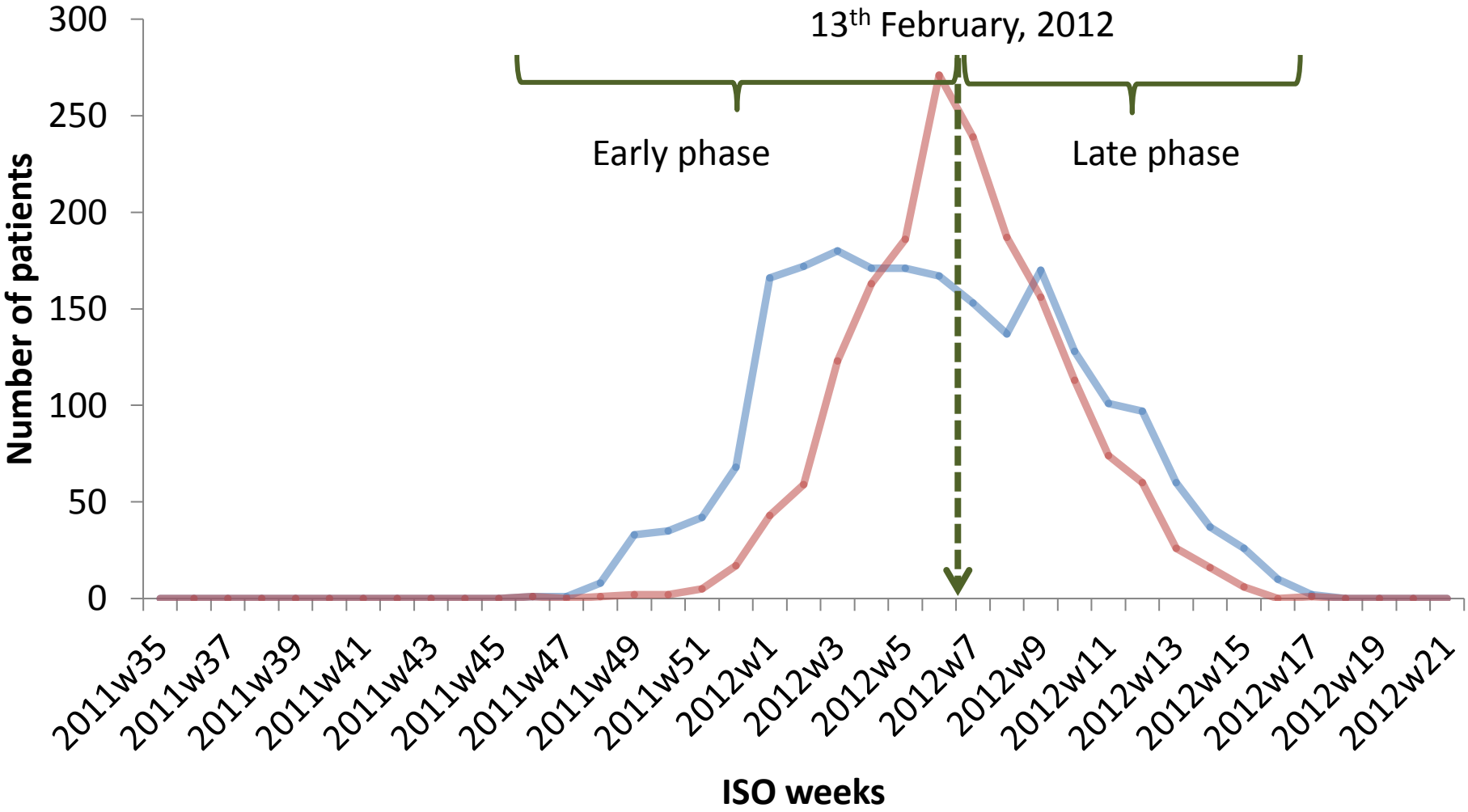
- Binary cutoff (Before/after: 3 months ~93 days)
- Model days since vaccination as restricted cubic spline
  - Segments of polynomials fitted together as curve
  - 3 or 4 knots depending on sample size
  - Knots at 0, 15 days (a priori) and then at 75th or 40th and 90th centile
  - Calculate adjusted VE by day since vaccination

RESULTS

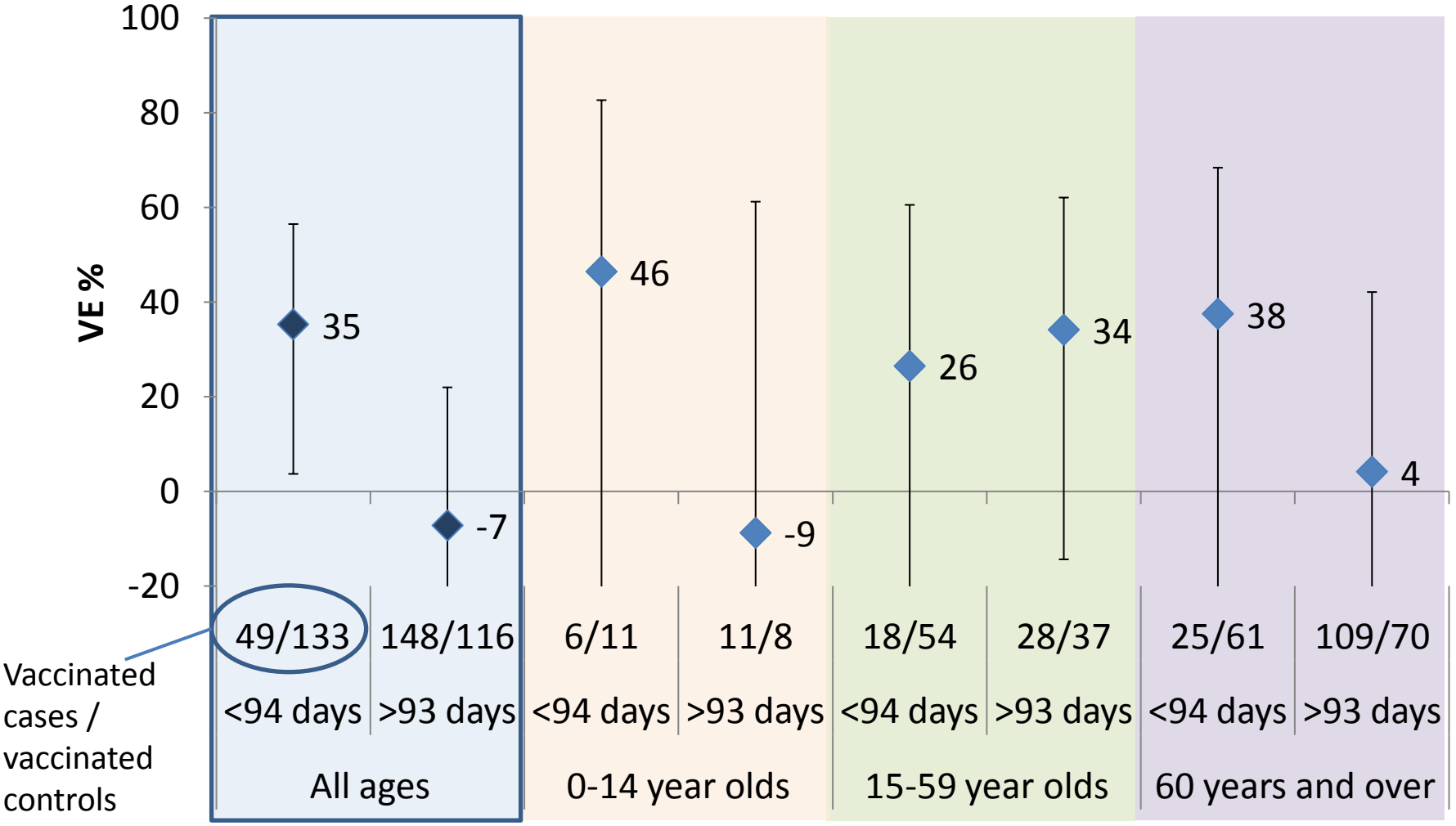
Number of ILI vaccinated by week of vaccination, A(H3) cases and controls by week of symptom onset, I-MOVE multicentre case control study, EU, 2011-12



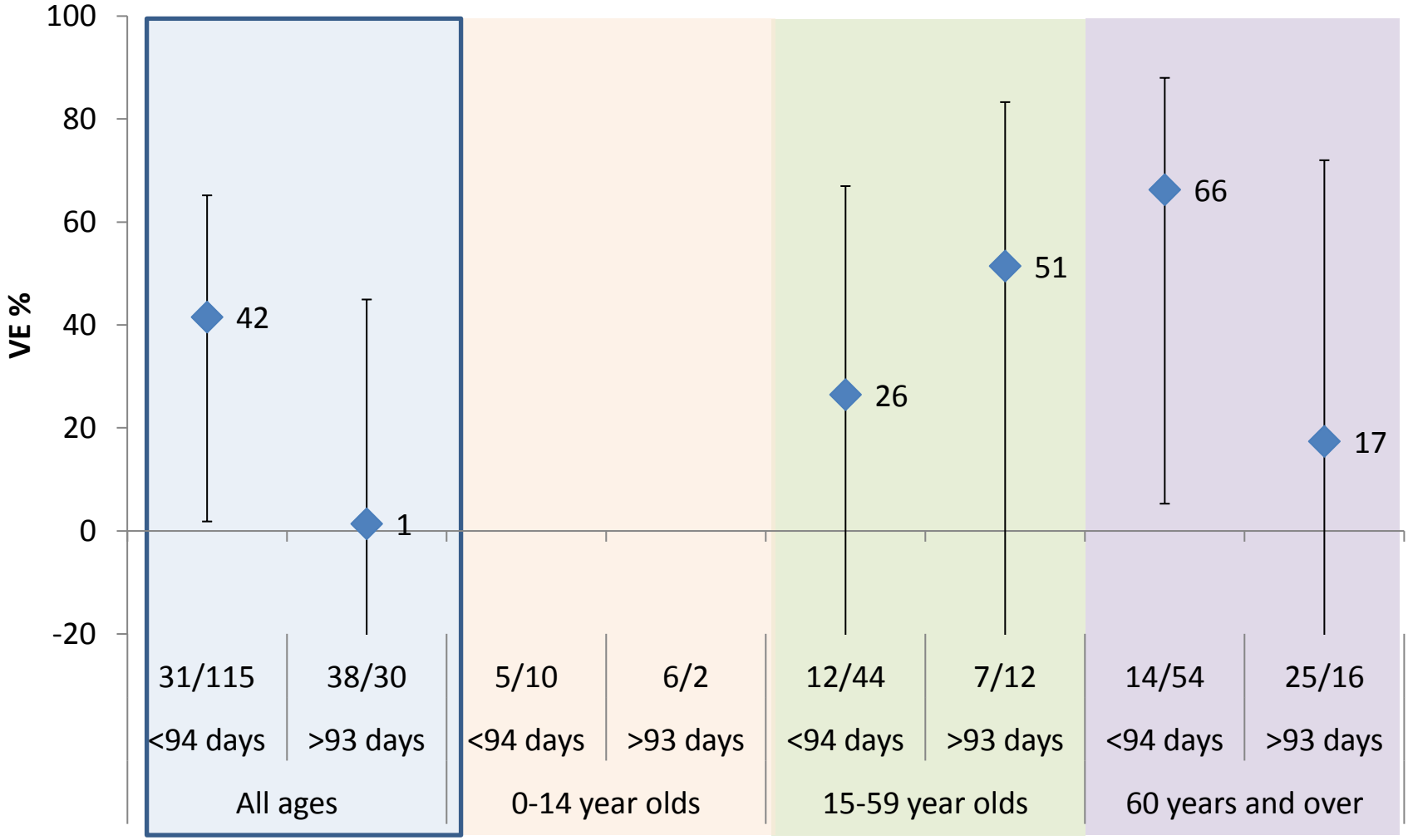
A(H3) cases and controls by week of symptom onset, I-MOVE multicentre case control study, EU, 2011-12



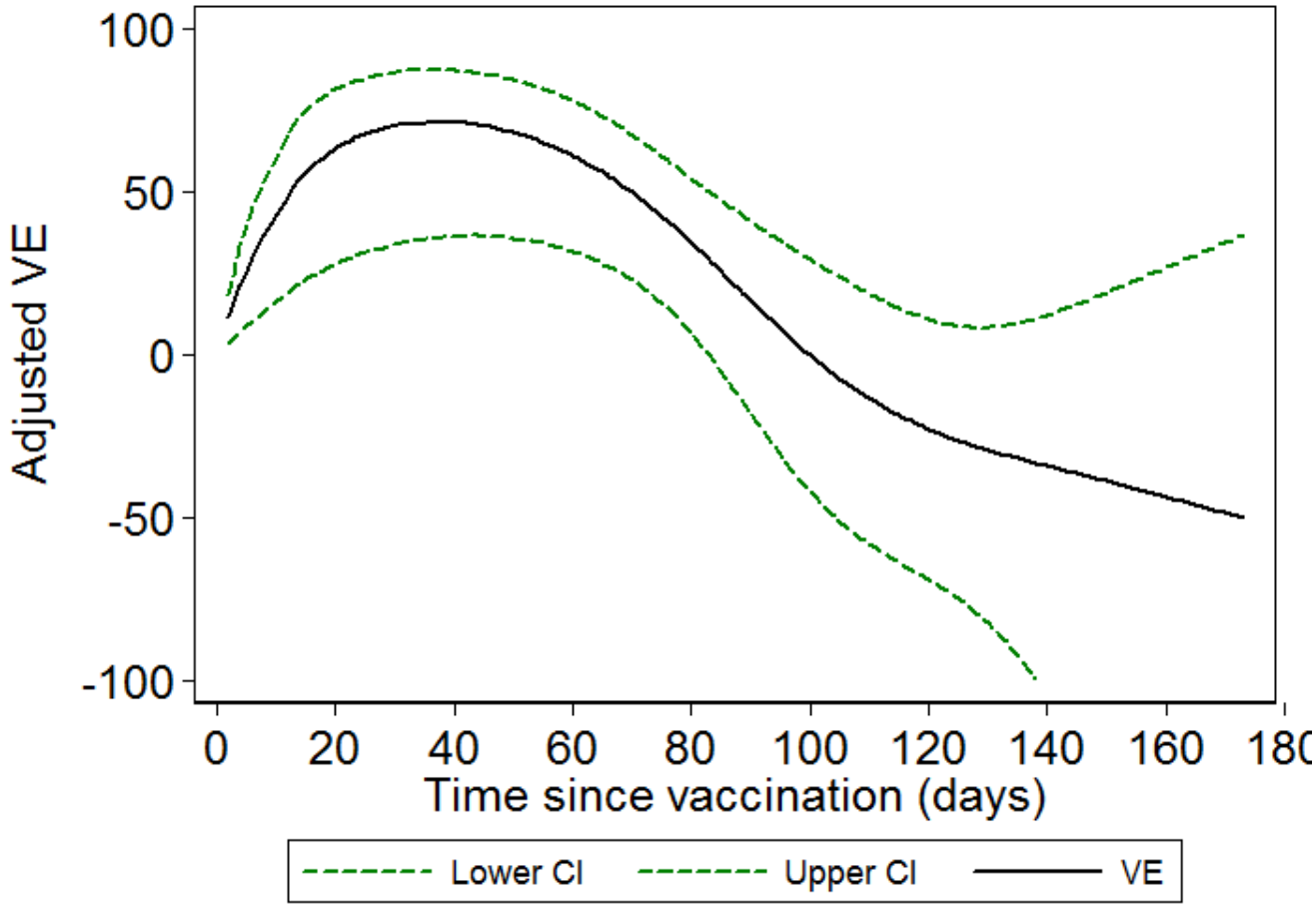
Adjusted VE against influenza AH3N2 by time since vaccination, by age group, I-MOVE multicentre case control study, EU, 2011-12



Adjusted VE against influenza AH3N2 by time since vaccination, by age group, early influenza phase, I-MOVE multicentre case control study, EU, 2011-12

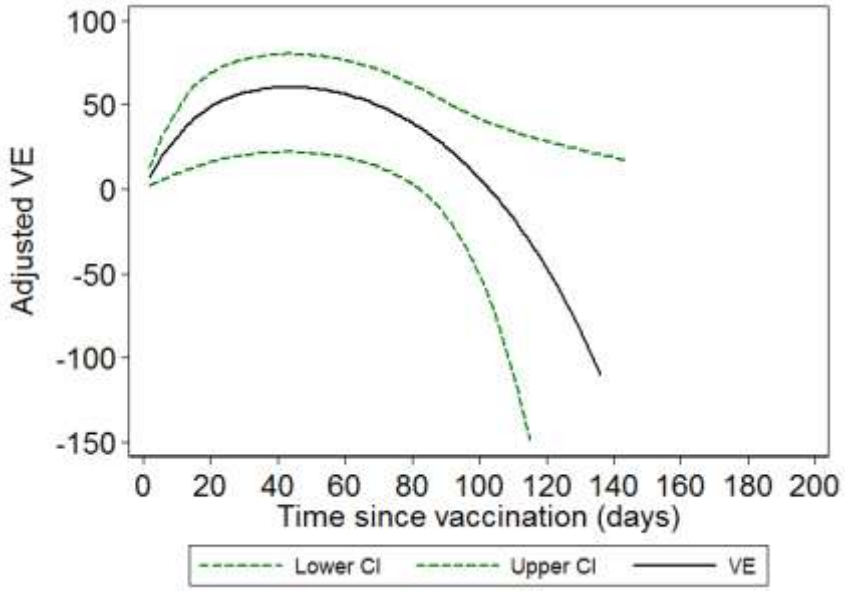


Adjusted VE against A(H3N2) by days between vaccination and onset of symptoms, I-MOVE multicentre case control study, season 2011-12

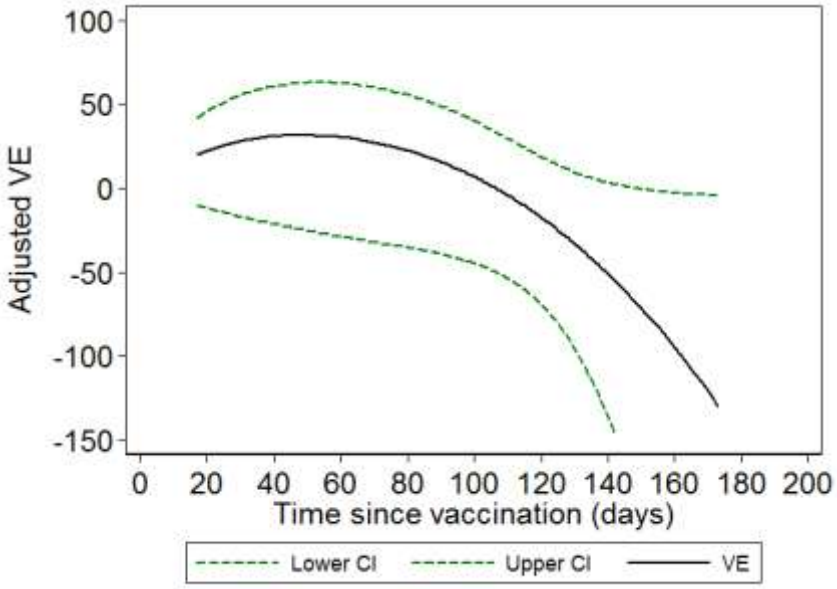


Note: data truncated at -100

Adjusted VE against A(H3N2) by days between vaccination and onset of symptoms, early and late phase, I-MOVE multicentre case control study, season 2011-12



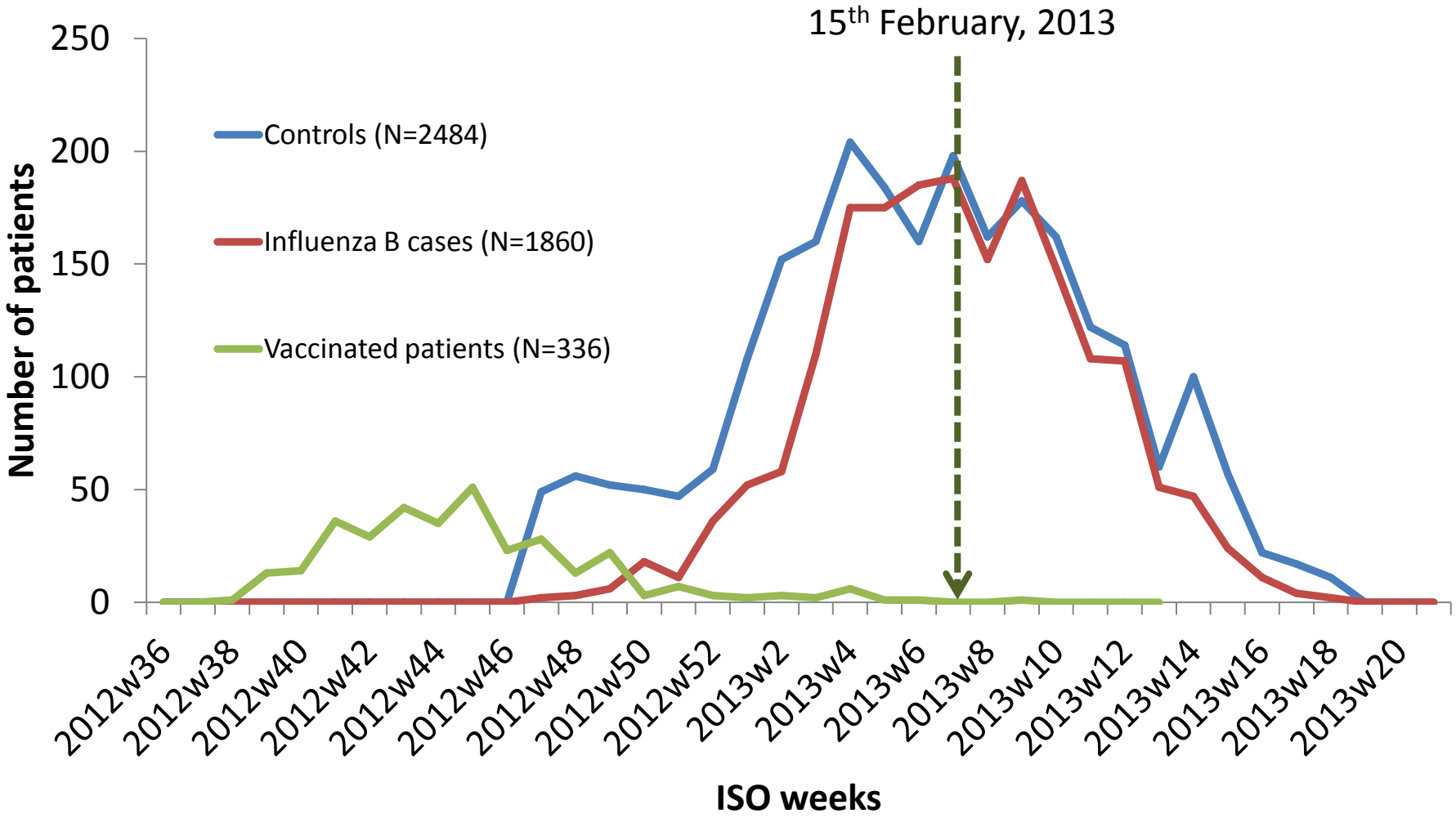
Early phase



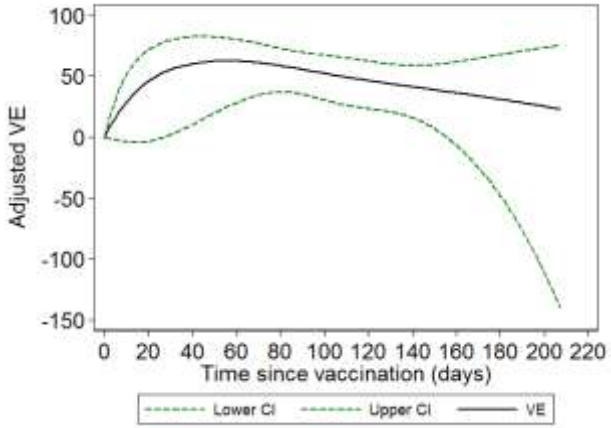
Late phase

Note: data truncated at -150

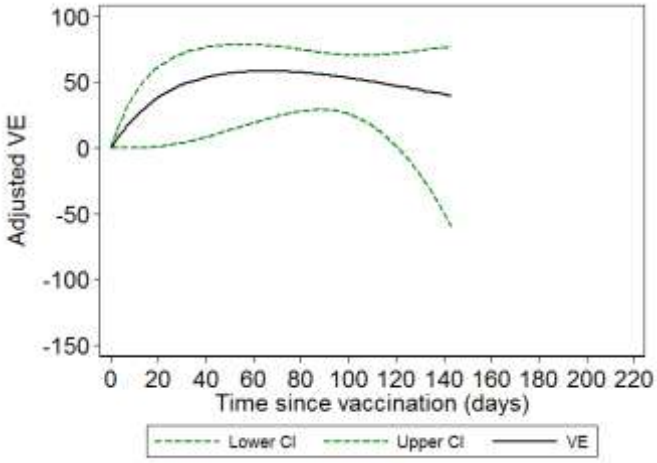
Number of ILI vaccinated by week of vaccination, influenza B cases and controls by week of symptom onset, complete case analysis, I-MOVE multicentre case control study, EU, 2012-13



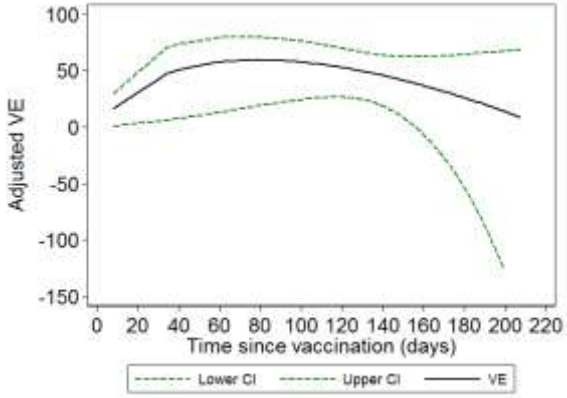
Adjusted VE against influenza B by days between vaccination and onset of symptoms, all ages, overall, early and late influenza phase, I-MOVE multicentre case control study, season 2012-13



Overall season



Early season



Late season

Note: data truncated at -150

Discussion

- Analysis suggests in 2011/12 decline in VE by time since vaccination for A(H3N2) for all ages
  - Peak VE at 31-43 days (71%)
  - Lower VE in late phase suggesting virological changes
  - Decline seen also in early phase, suggesting possibility of waning immunity

Discussion

- Analysis suggests in 2012/13 mild decline in VE by time since vaccination for influenza B for all ages
  - Small sample sizes overall do not exclude no decline
  - Peak VE at 54-55 days (63%)

Discussion

- Low number of vaccinated and vaccinated cases brings uncertainty into models
  - Greater sample sizes needed for conclusions
- Loss of information when using binary cutoffs
  - Modelling of time since vaccination as a continuous variable recommended
- Careful when partitioning early/late influenza phase and +/- 3 months since vaccination in a multicentre study:
  - Different epidemic timing and vaccination campaigns by country may bias results if heterogeneity between countries

Conclusions

- Waning of immunity may be a real phenomenon, but greater sample size needed to obtain precise results by age group and influenza type/subtype
- Individual detailed virological data in VE studies are needed to disentangle changes in immune response from virological changes over time

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- EpiConcept

Backup slides

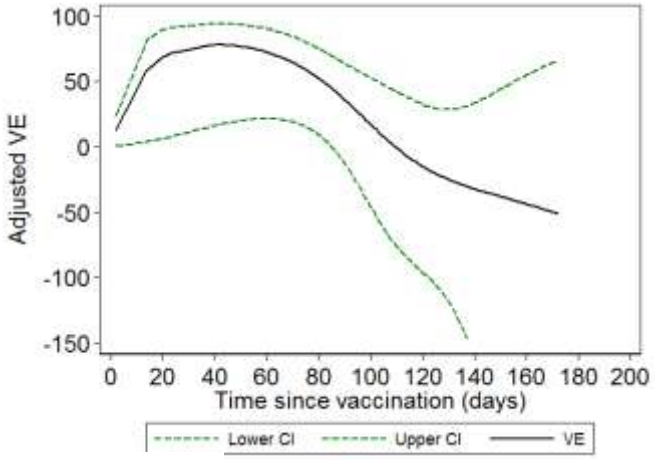
Decline in VE 2011-12

- UK multicentric, Spanish and Navarra (Spain) TND study show lower VE in later influenza phase 2011-12
  - UK: Early influenza phase: 43% (95% CI: -34 to 75), late influenza phase: 17% (95% CI: -24 to 45)
  - Navarra: Early influenza phase: 37% (95% CI: -18 to 67), late influenza phase 19% (95% CI: -176 to 76)
  - Spain: Early influenza phase: 52% (95% CI: 4–76), late influenza phase: 28% (95% CI: -124 to 77)

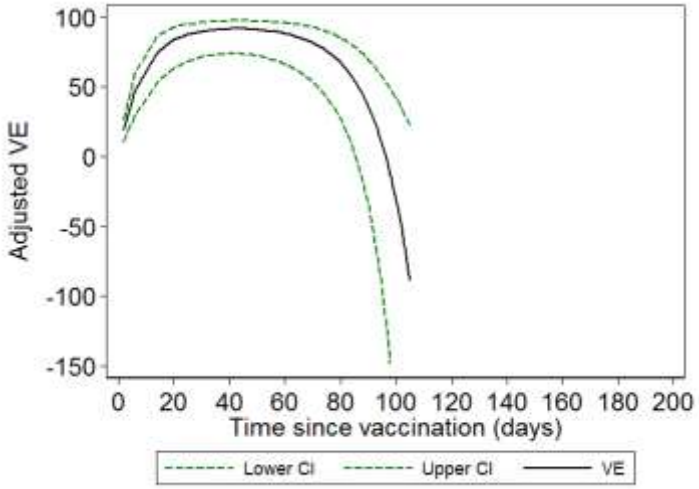
Decline in VE 2011-12

- UK multicentric, Spanish and Navarra (Spain) TND study show lower VE in later influenza phase 2011-12
  - UK: VE 53% (95% CI: 0 to 78) <3 months after vaccination, VE 12 % (95% CI: -31 to 41) 3 or more months after vaccination
  - Navarra: VE 61% (95% CI: 5 to 84) in the first 100 days after vaccination, 42% (95% CI: -39 to 75) between 100 and 119 days, and zero thereafter
  - Spain: persons ≥65 years VE 85% (95% CI, 18-97) < 3 months after vaccination, null estimate > four months after vaccination

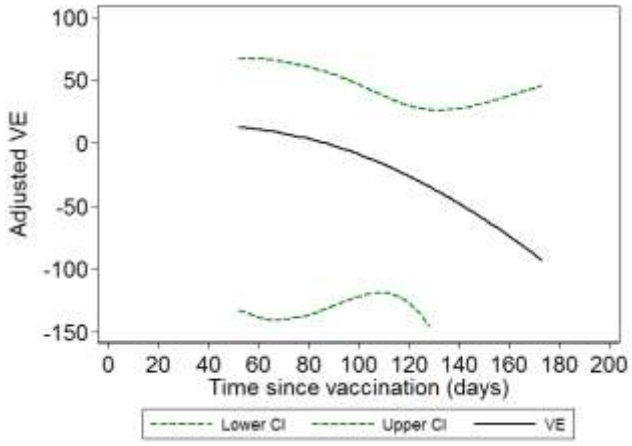
Adjusted VE against A(H3N2) by days between vaccination and onset of symptoms, among those aged 60 and older, overall, early and late phase, I-MOVE multicentre case control study, season 2011-12



Overall phase



Early phase



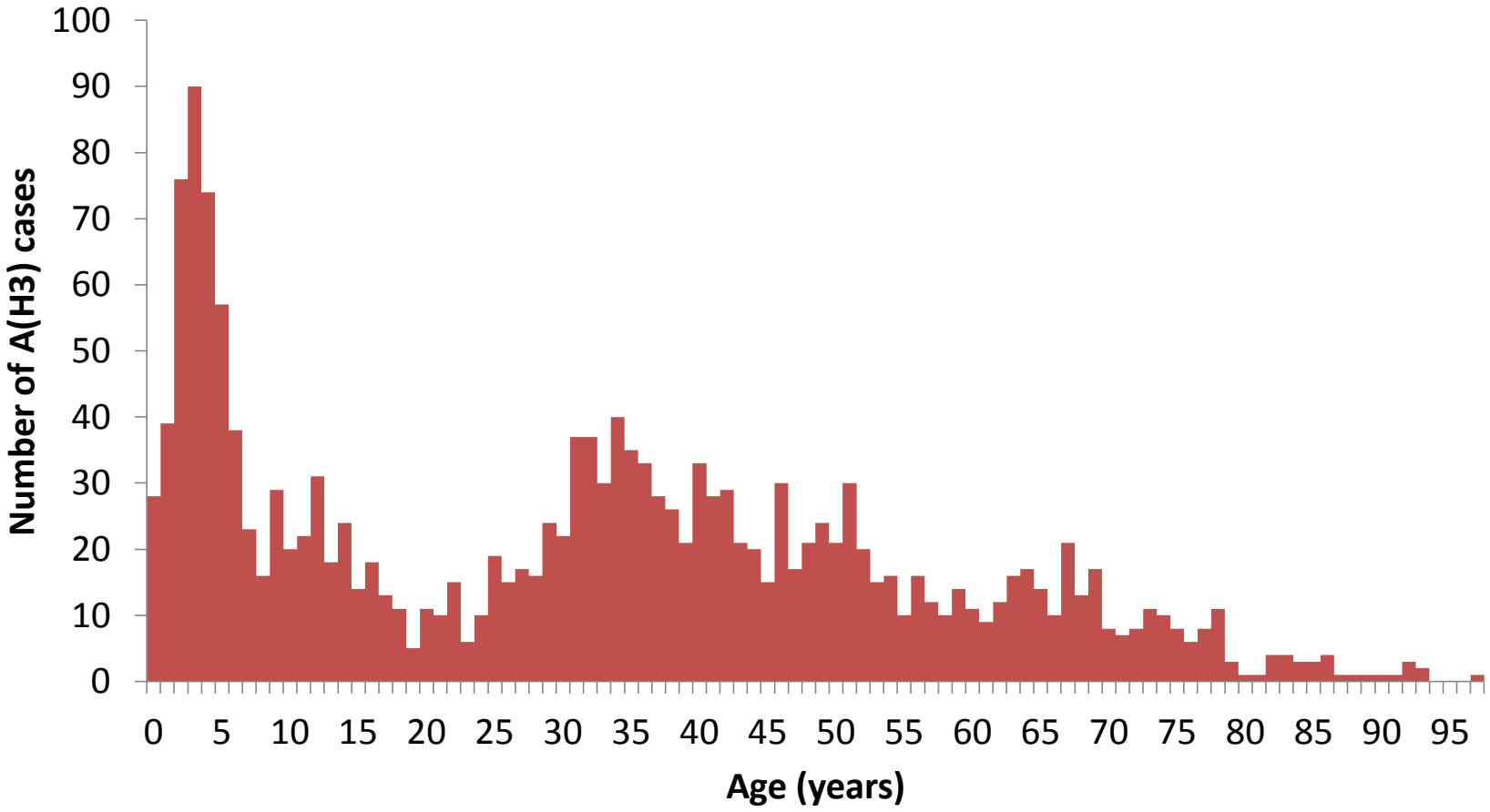
Late phase

Note: data truncated at -150

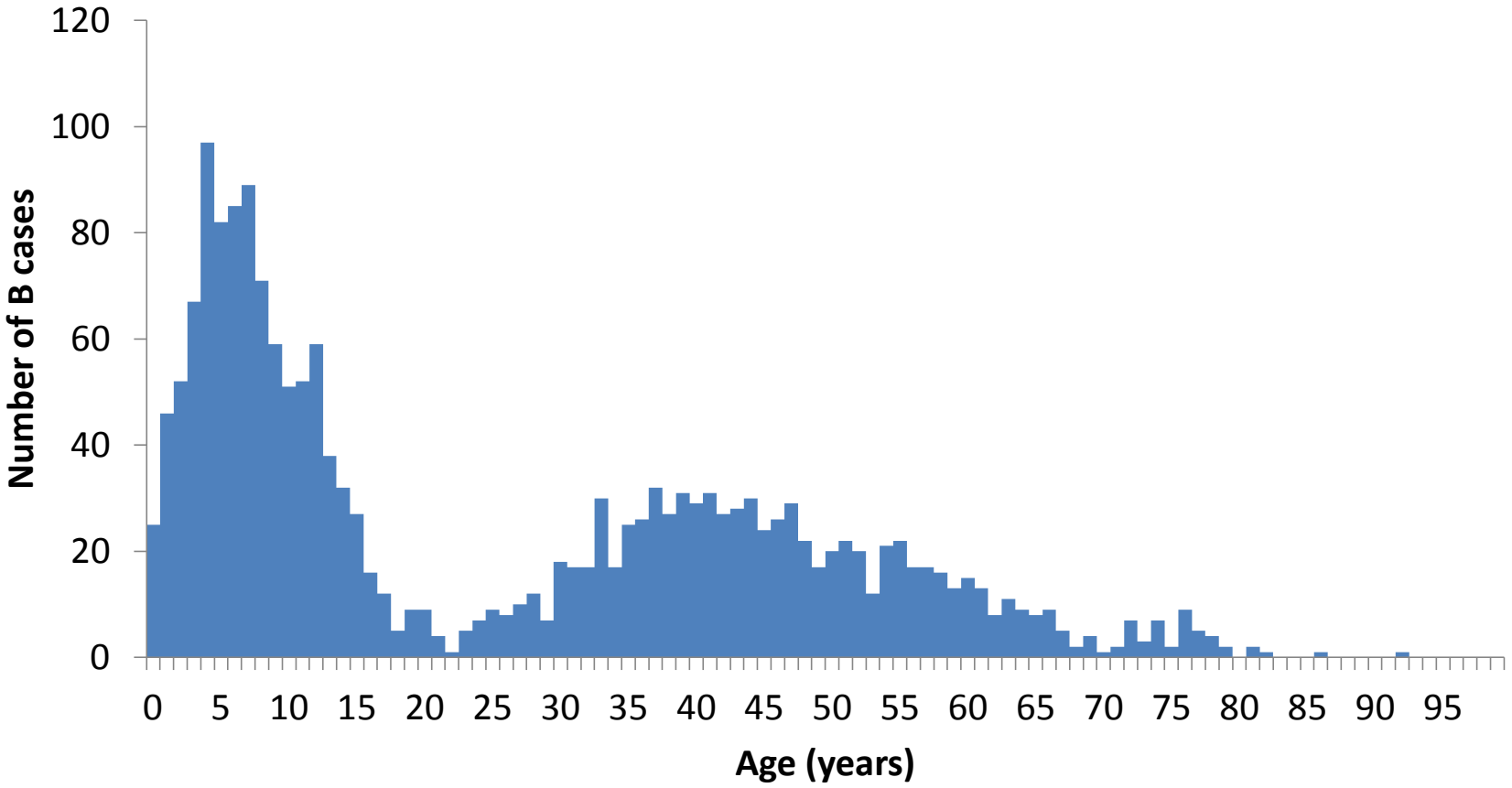
Introduction

- Duration of vaccine-induced immunity against influenza complex and debated, may be lower among elderly
- However antibody response studies show high seroprotection rates for A(H1N1) and A(H3N2) after 4 months, less consistency for B
- But do antibody response studies correlate with vaccine effectiveness (VE)?
- If waning of immunity within a season is real
  - Later begin of vaccination campaigns
  - 2nd dose of vaccine for some target groups

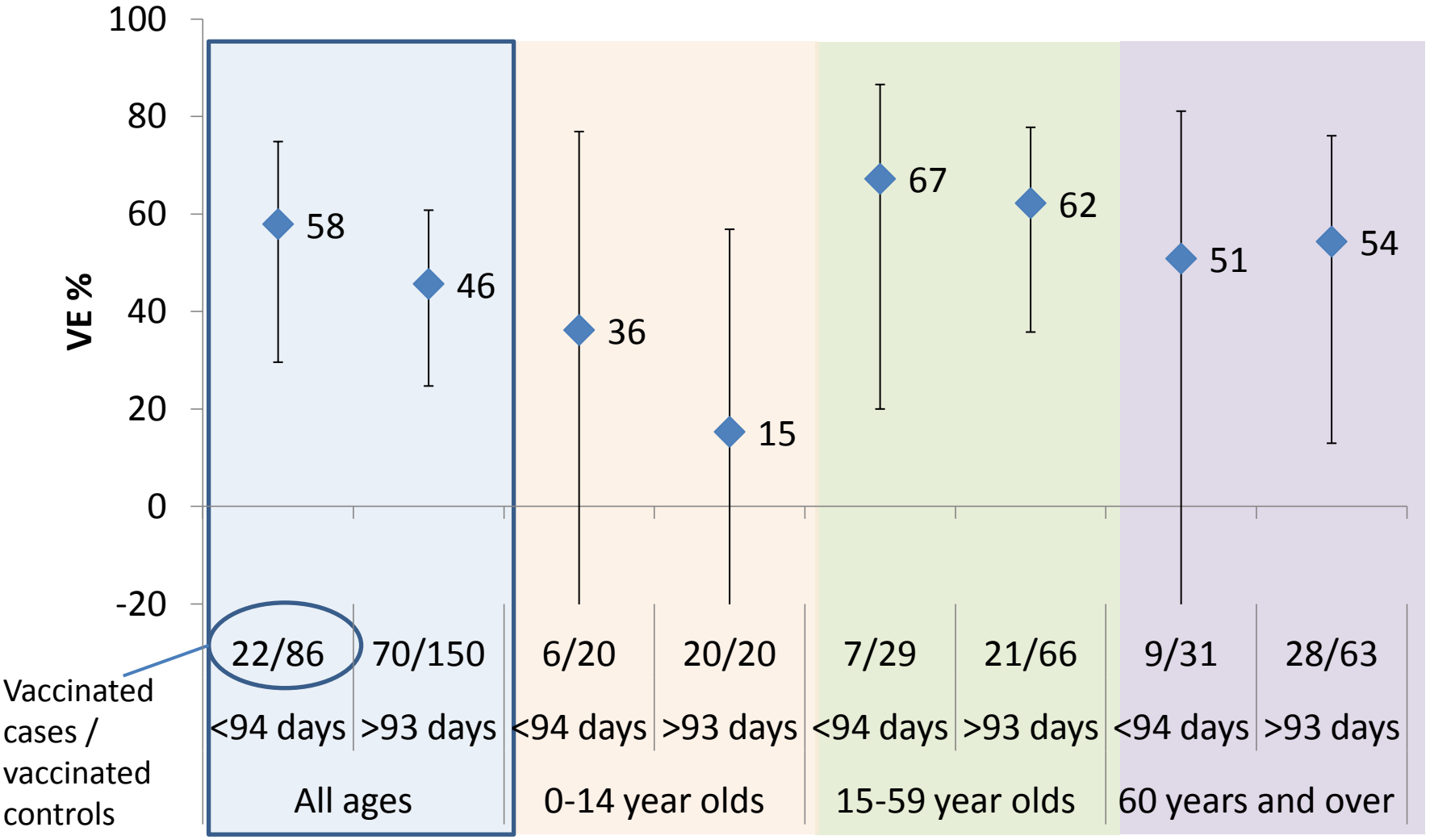
Number of A(H3) cases by year of age, I-MOVE multicentre case control study, EU, 2011-12



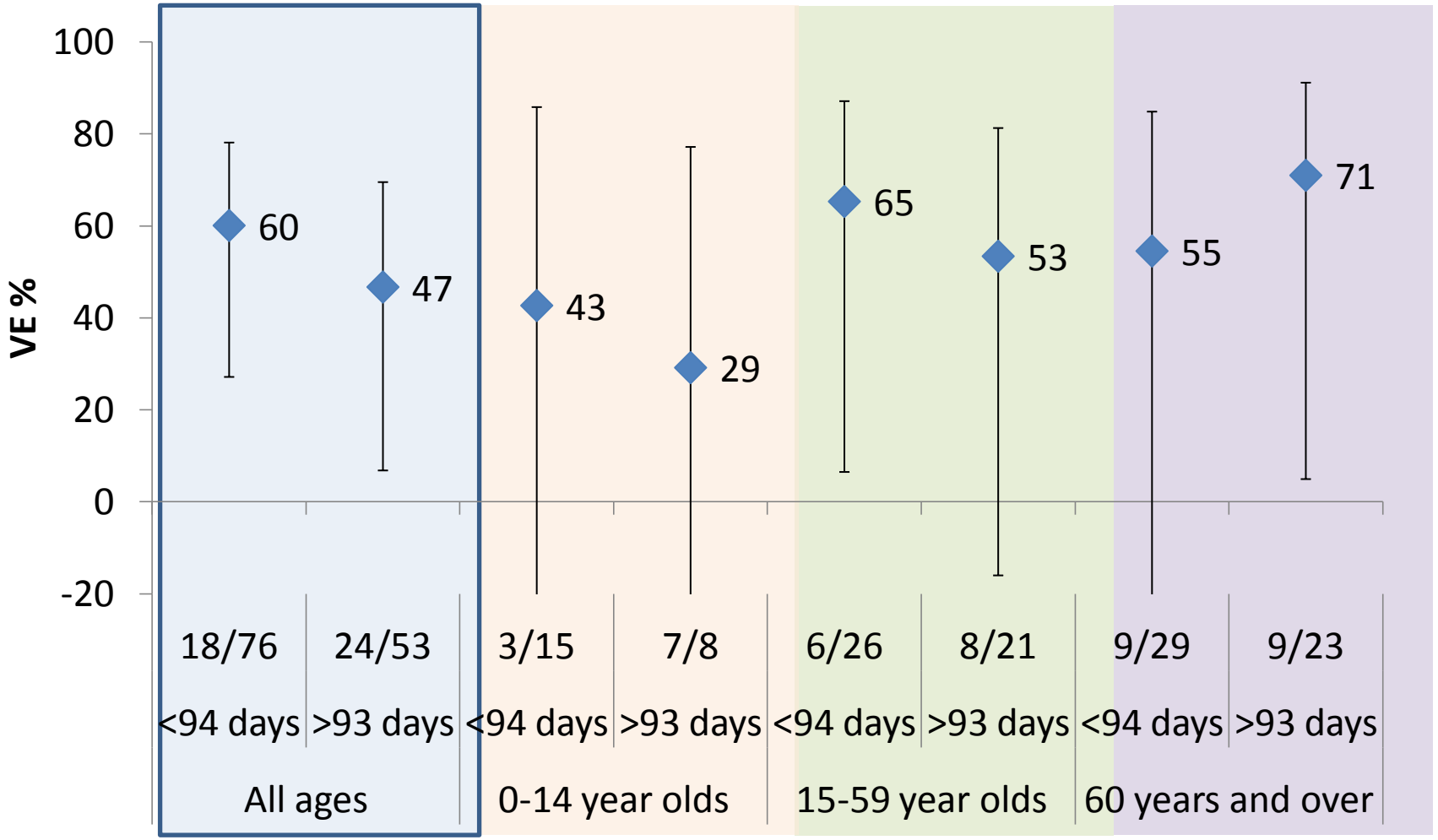
Number of influenza B cases by year of age, I-MOVE multicentre case control study, EU, 2012-13



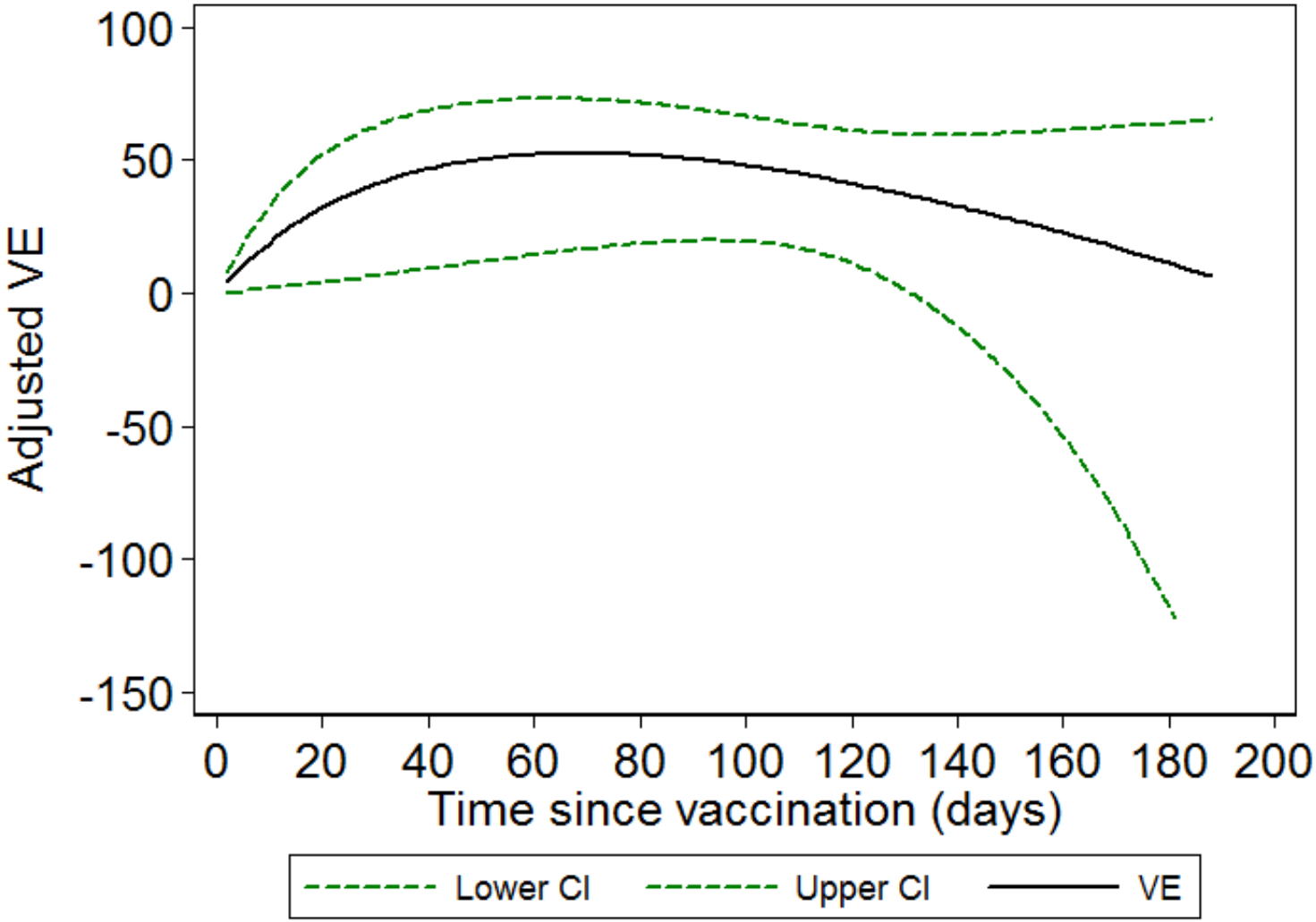
Adjusted VE against influenza B by time since vaccination, by age group, I-MOVE multicentre case control study, EU, 2012-13



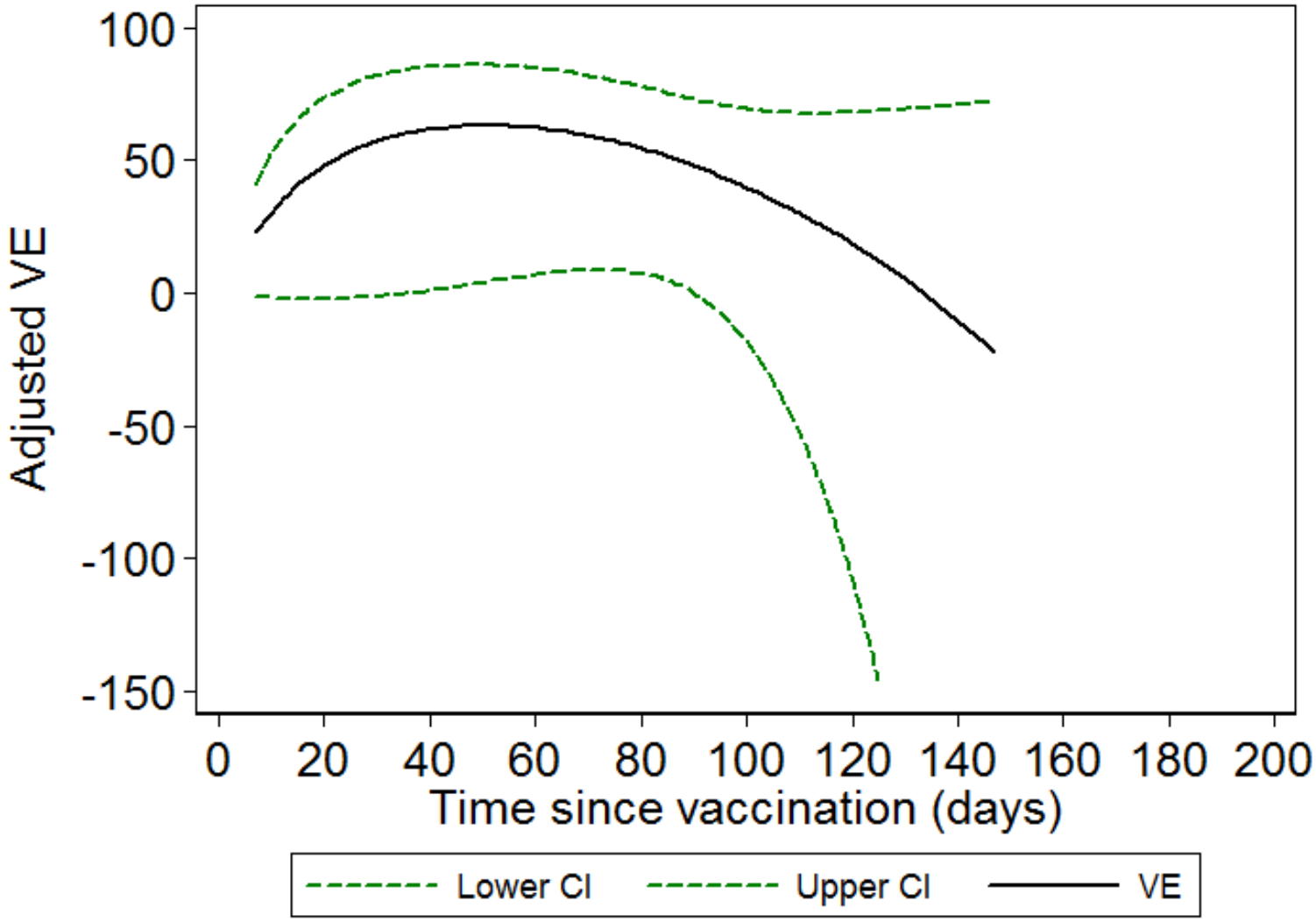
Adjusted VE against influenza AH3N2 by time since vaccination, by age group, early influenza phase, I-MOVE multicentre case control study, EU, 2011-12



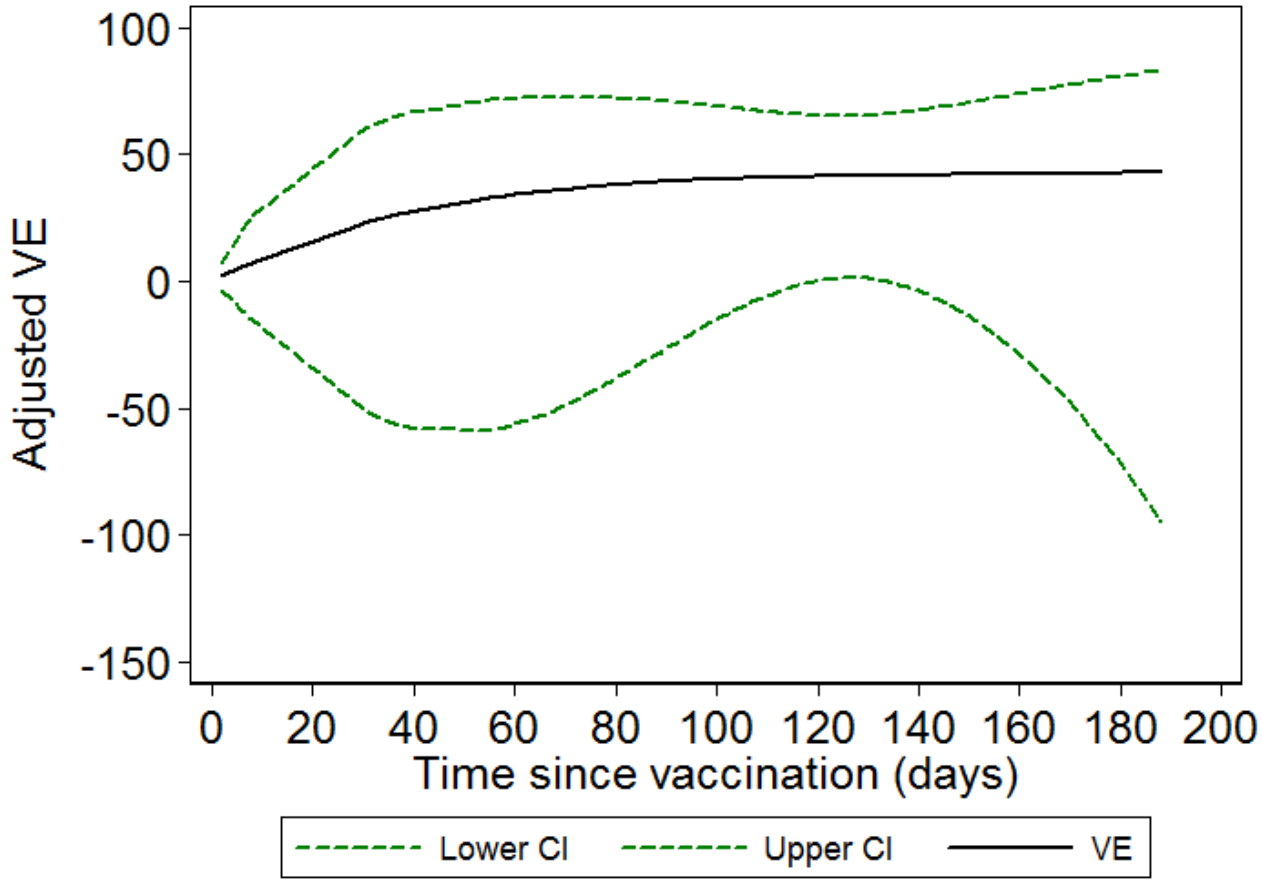
Adjusted VE against A(H3N2) by days between vaccination and onset of symptoms, total influenza season, I-MOVE multicentre case control study, season 2012-13



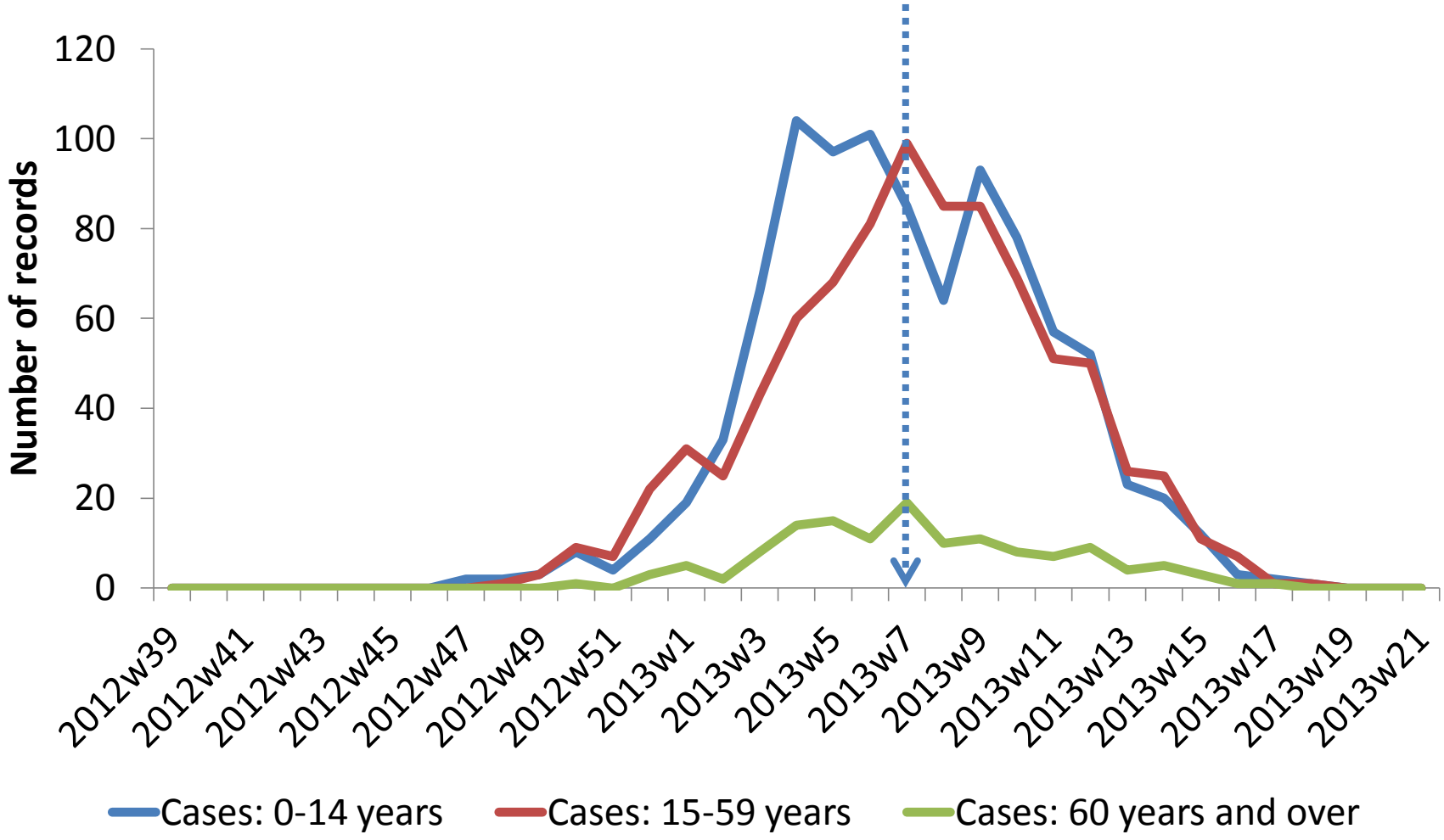
Adjusted VE against A(H3N2) by days between vaccination and onset of symptoms, early influenza season, I-MOVE multicentre case control study, season 2012-13



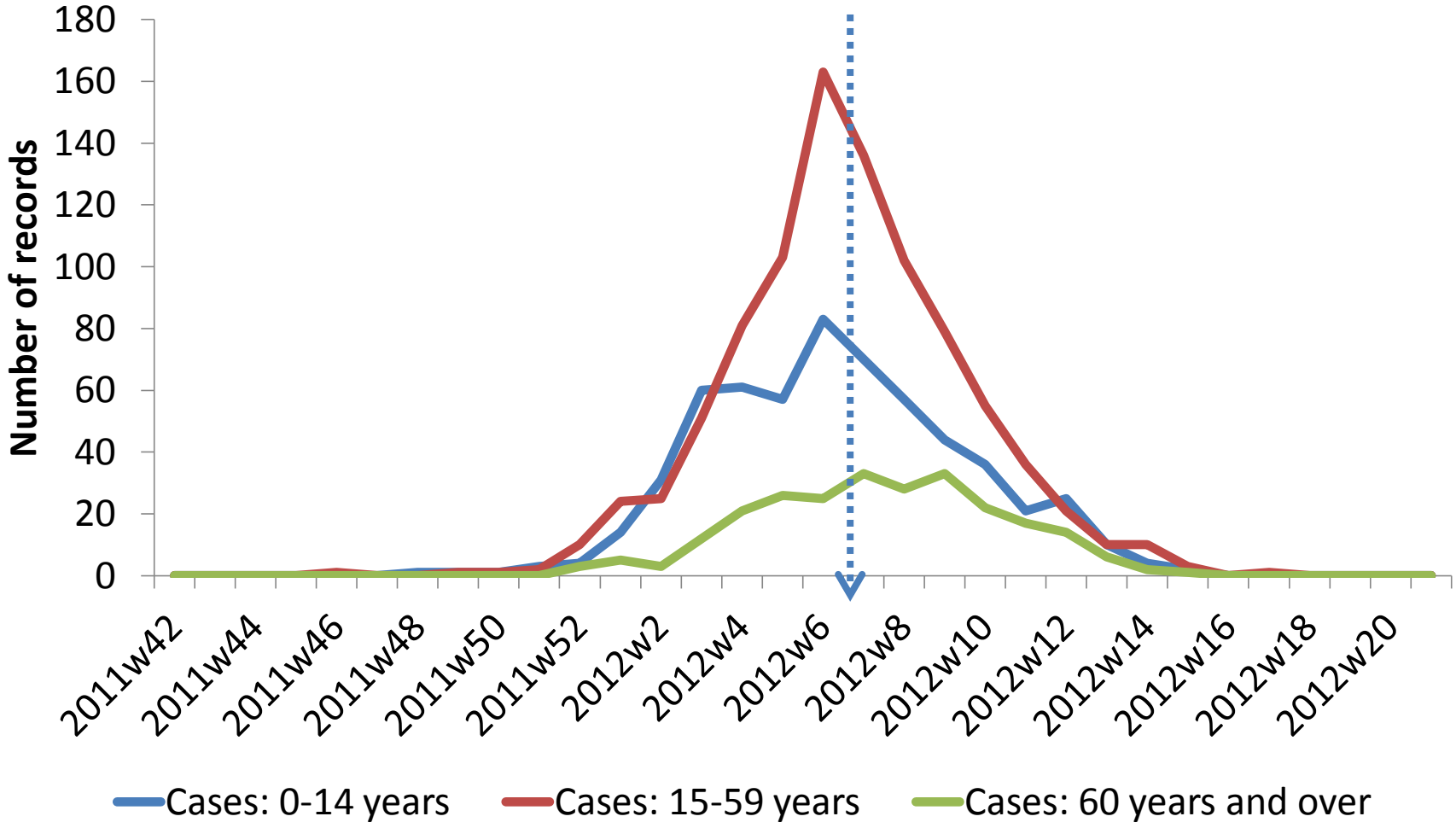
Adjusted VE against A(H3N2) by days between vaccination and onset of symptoms, late influenza season, I-MOVE multicentre case control study, season 2012-13



Number of cases by week of symptom onset and age group for influenza B, I-MOVE multicentre case control study, season 2012-13



Number of cases by week of symptom onset and age group for influenza A(H3N2), I-MOVE multicentre case control study, influenza season 2011-12



Proportion of vaccinated controls by early/late influenza phase, I-MOVE multicentre case control study, influenza seasons 2009/10 to 2012/13