Pandemic influenza vaccine effectiveness in Europe in 2009-10

Results of I-MOVE multicentre case-control study

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Background: Pandemic vaccines

- **April 2009**
  - Emergence of 2009 pandemic influenza A(H1N1) virus
- **Pandemic vaccines developed and marketed in Europe**
  - Three vaccines authorised by the European Medicines Agency in October 2009
  - Additional vaccines authorised by national authorities
  - Adjuvanted / Non adjuvanted vaccines
- **Different target groups between countries**

Study frame

- **I-MOVE = Influenza Monitoring Vaccine Effectiveness in Europe**
  - European network established in 2007 by the European Centre for Disease Prevention and Control (ECDC)
  - Aims to measure the influenza vaccine effectiveness in the European Union (EU) and the European Economic Area (EEA)

- **2009-10:** 15 studies conducted in 10 EU countries
  - Three study designs (cohort, case-control, screening)

Objective

- **Objective of case-control study in 2009-2010**
  - Estimate the pandemic influenza vaccine effectiveness (PIVE) against medically-attended influenza-like illness (ILI) cases who were subsequently confirmed by laboratory as pandemic influenza

Study design

- **Multicentre case-control study**
  - Seven countries
  - Using sentinel general practitioners' (GPs) influenza surveillance networks

Study population and definitions

- **Patients consulting a participating sentinel GP for ILI**
  - EU ILI definition
    - Sudden onset of symptoms
    - At least one of the following systemic symptoms (fever, malaise, headache, myalgia)
    - At least one of the following respiratory symptoms (cough, sore throat, shortness of breath)
  - Nasal or throat swab <8 days after symptom onset
  - Systematic sampling of patients or all ILI patients
  - **Cases =** laboratory confirmed pandemic influenza
  - **Controls =** negative for any influenza virus

Study period

- **Start**
  - Symptom onset > 14 days after the beginning of vaccination campaigns in each country
- **End**
  - No confirmed pandemic influenza patient for two consecutive weeks

Data collection

- **Face-to-face interview by GP**
  - Country-specific standardised questionnaires

- **Data collected**
  - Vaccination status (seasonal and pandemic)
  - Demographic, clinical symptoms, chronic conditions and related hospitalisations, antiviral treatment, number of GP visits in previous 12 months
  - Laboratory results

- **Exposure**
  - Vaccination with pandemic vaccine > 14 days before symptom onset

Data analysis

- **Comparison of characteristics of cases and controls**
  (Fisher's exact or Mann-Whitney test)

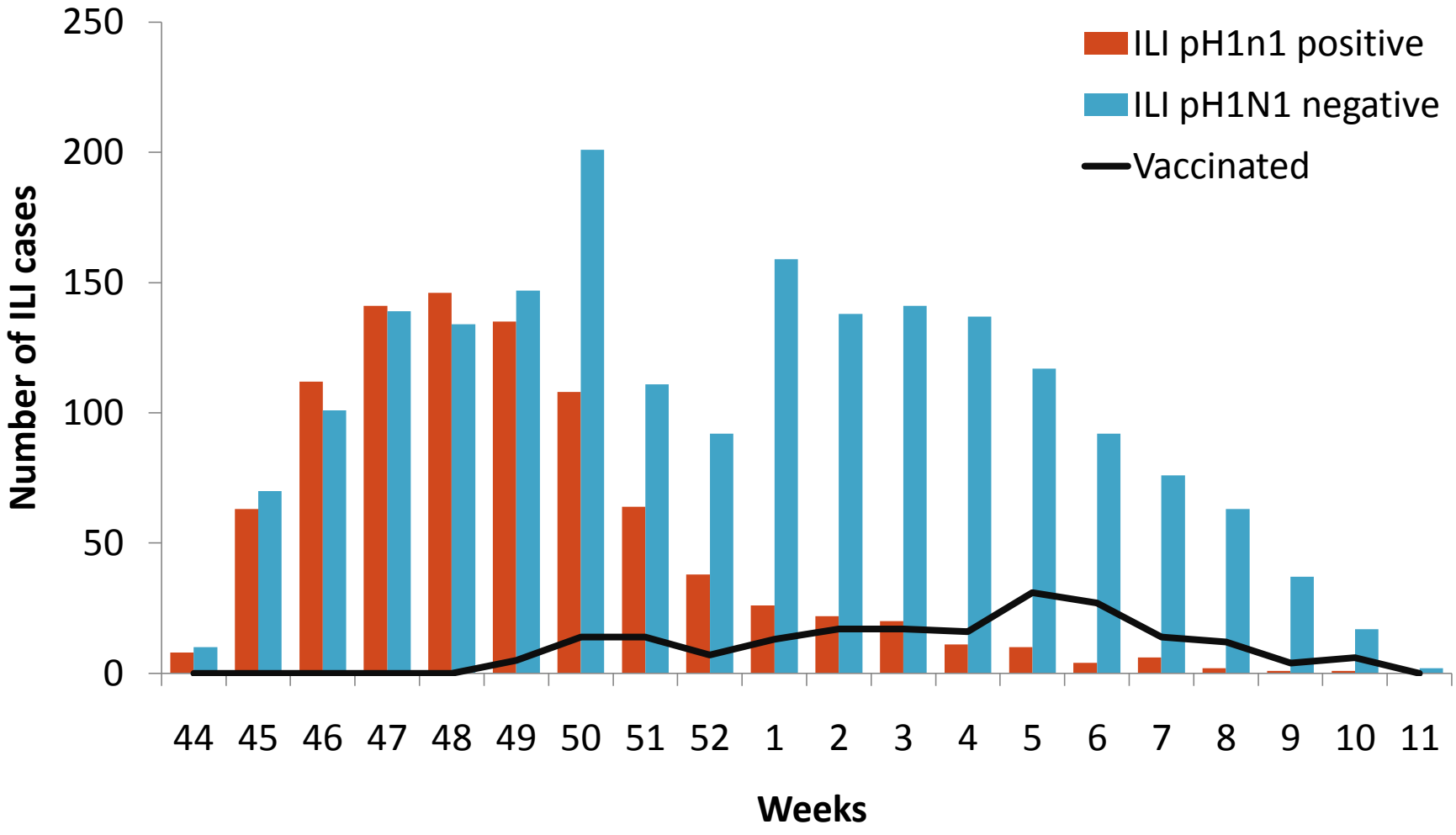
- **Multiple imputation of missing data by chained equations**

- **Pooled one-stage model**
  - Study site as fixed effect
  - Logistic regression
  - PIVE = 1 – OR [95% CI]

Descriptive results

- **699 GPs recruited at least one ILI patient**
- **2902 ILI patients included in the analysis**
  - 2728 (94%) swabbed <4 days after symptom onset
  - 918 H1N1 cases (31.6%) / 1984 controls
  - 197 vaccinated patients
  - 1,400 patients (48.2%) with missing value for at least one variable

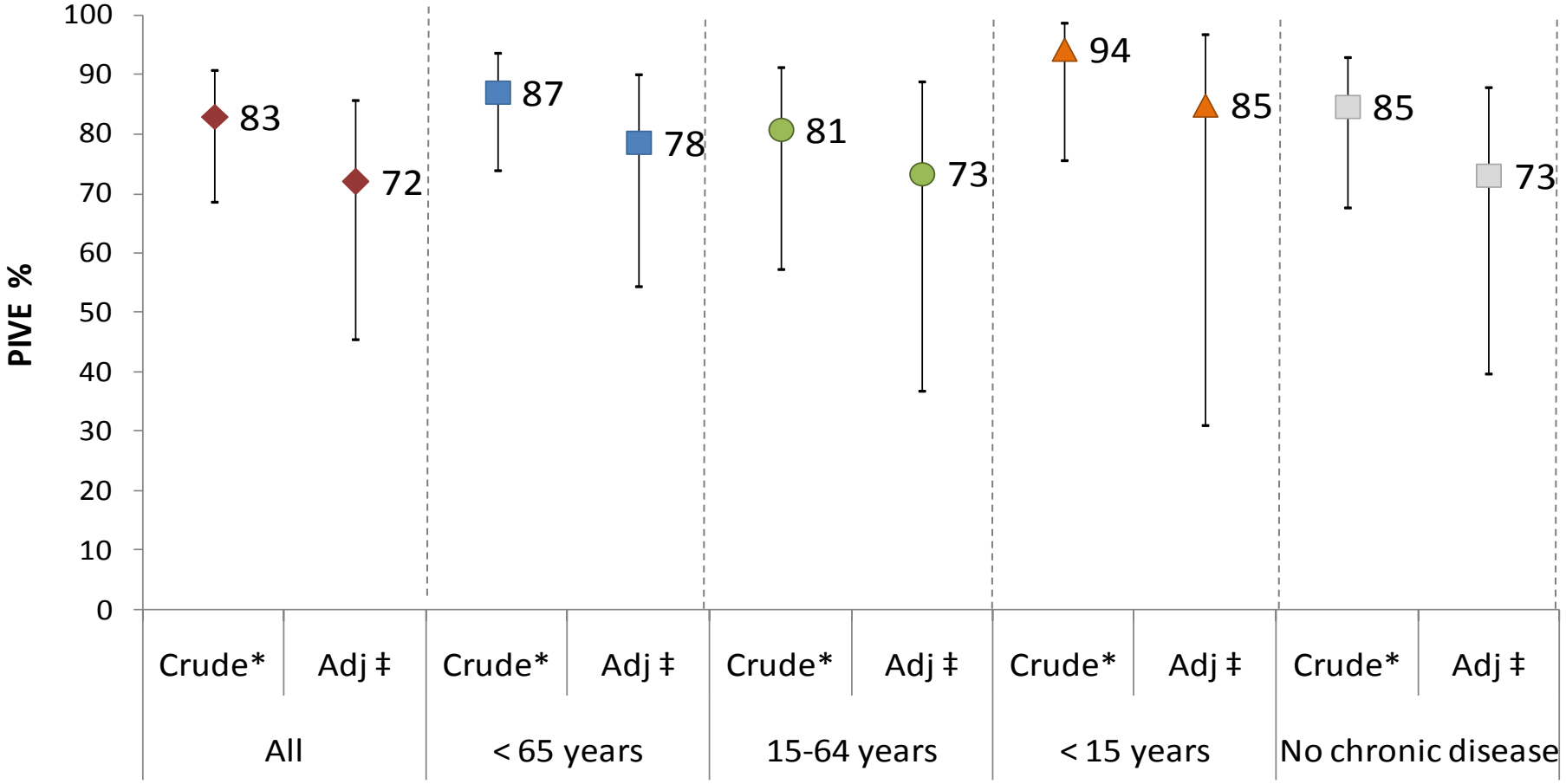
Recruitment by week of symptom onset (N=2902)



Comparison of cases and controls

Characteristics	H1N1 Cases (n=918)		Controls (n=1984)		P value
Median age (year) (min- max)	12 (1 mth- 85 yrs)		27 (2 mths- 96 yrs)		<0.001
	n	**%**	**n**	**%**	
At least one chronic condition	94	13.8	354	21.4	<0.001
Pandemic vaccination	12	1.3	185	9.5	<0.001

Pandemic influenza vaccine effectiveness (PIVE) – Imputed dataset



* Study site in model as a fixed effect

‡ adjusted for age-group, sex, month of onset, chronic diseases and related hospitalisations, smoking, seasonal influenza vaccinations and number of practitioner visits in the previous year

Discussion

- **All PIVE point estimates > 70%**

- **Small number of vaccinated cases**
  - Late start of pandemic vaccination campaigns
  - Low vaccination coverage
  - Good protection of pandemic vaccines

  → Limited statistical power for stratified analysis (e.g. by vaccine brand)

- **Natural immunity before the study started**

  → Overestimated PIVE if different between vaccinated and unvaccinated

Conclusions (1)

- **Suggest that pandemic vaccines conferred good protection**
  - Consistent with immunogenicity studies,
    other observational studies and
    good match between vaccine and circulating strain

- **Important adjunct to clinical trials**
  - To guide vaccination policies
  - For recommendations on influenza vaccine composition for use during the 2010-2011 season

Conclusions (2)

- **Added value of I-MOVE network**
  - Based on existing surveillance networks
  - Provided early and precise overall PIVE
  - Excellent collaboration between countries
  - Similar protocol and methods
  - Documentation of many potential confounding factors

- **Ongoing case-control study to estimate the effectiveness of the seasonal trivalent vaccine**
  - 8 countries (additional country: Poland)

Co-authors and acknowledgements

- **Co-authors**

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More information on I-MOVE at http://sites.google.com/site/epiflu/