Pandemic influenza vaccine effectiveness in Europe in 2009-10

Results of I-MOVE multicentre case-control study

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On behalf of the I-MOVE case-control team

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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**
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 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
• 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

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>H1N1 Cases (n=918)</th>
<th>Controls (n=1984)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median age (year)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(min- max)</td>
<td>12 (1 mth- 85 yrs)</td>
<td>27 (2 mths- 96 yrs)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>At least one chronic condition</strong></td>
<td>94 13.8</td>
<td>354 21.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><em>Pandemic vaccination</em></td>
<td>12 1.3</td>
<td>185 9.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Pandemic influenza vaccine effectiveness (PIVE) – Imputed dataset

<table>
<thead>
<tr>
<th>Age Group &amp; Condition</th>
<th>Crude*</th>
<th>Adj ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>83</td>
<td>72</td>
</tr>
<tr>
<td>&lt; 65 years</td>
<td>87</td>
<td>78</td>
</tr>
<tr>
<td>15-64 years</td>
<td>81</td>
<td>73</td>
</tr>
<tr>
<td>&lt; 15 years</td>
<td>94</td>
<td>85</td>
</tr>
<tr>
<td>No chronic disease</td>
<td>85</td>
<td>73</td>
</tr>
</tbody>
</table>

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
• 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
  Marta Valenciano, Esther Kissling, Jean Marie Cohen, Beatrix Oroszi, Caterina Rizzo, Baltazar Nunes, Daniela Pitigoi, Amparo Larrauri, Anne Mosnier, Judit Krisztina Horvath, Joan O´Donnell, Antonino Bella, Raquel Guiomar, Emilia Lupulescu, Camelia Savulescu, Bruno Ciancio, Piotr Kramarz, Alain Moren

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