cycEVA:

Can we measure influenza vaccine effectiveness using a simple method?

Comparing two study designs using data from the Spanish Influenza Sentinel Surveillance System, 2008-9

C. Savulescu, S. de Mateo, M. Valenciano, A. Larrauri, and cycEVA study team*

ESCAIDE 2009
cycEVA: Background

- **Spanish Influenza Sentinel Surveillance System** aims to:
  - provide timely clinical and virological information on influenza activity

- Since **2002-3 season**: estimation of **Influenza vaccine effectiveness (IVE)** using the screening method

- **Season 2008-9**: case control studies part of “**I-MOVE: Monitoring IVE in European Union and European Economic Area**”
**cycEVA:** Case control studies

- **Objective:** estimate IVE in age group $\geq 65$ years old, in Spain

- **Cases:** medically attended influenza like illness (ILI), laboratory positive

- **Controls:** two control groups among GP patients:
  - **ILI negative:**
    - ILI - influenza laboratory negative
  - **non-ILI:**
    - non respiratory disease since beginning of season, matched 2:1 by week of swabbing / age group (65-74 and $\geq 75$)
**cycEVA:** Case Control studies: Data collected

- **Demographic:** age, sex, city, province
- **Clinical:** symptoms, date of onset, date of swabbing/consultation
- **Vaccination:** date
- **Laboratory data:** type and subtype of influenza

- **Confounding factors:**
  - Previous influenza vaccination
  - Pneumococcal vaccination
  - Smoking
  - Severity (previous hospitalizations)
  - Chronic diseases
  - Functional status


**cycEVA: Case control studies: Analysis**

- **Restriction** applied to the case - ILI negative control study:
  - After week 48 (recruitment of the first case)
  - Date of symptom onset – swabbing <4 days

- **Case control study:** crude and adjusted odds ratio (OR)

- **IVE calculation:**
  
  \[ \text{VE} = 1 - \text{OR} \]

- Statistical package **Stata v.10**
cycEVA: Screening method

- **Objective:** estimate IVE in age group ≥ 65 years old, in Spain

- **Cases:** ILI cases laboratory positive

- **Vaccination coverage:** GP catchment area

- **Analysis:** Farrington method*

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cycEVA: GP Participation

- Seven out 16 sentinel networks
- 164 / 219 sentinel GPs
  - 67(41%) reported cases
- Population under surveillance:
  - 46,461 people ≥65 years
  - 1.74% of ≥65 years
**cycEVA:** Results Case-Control Studies

**Cases and ILI negative controls (N=103) and ILI rates by week, season 2008-9, Spain**

- **ILI negative controls**
- **ILI positive cases**
- **ILI rate**

The graph shows the number of cases in the study and the ILI rates per 100,000 inhabitants by epidemiologic week for the season 2008-9 in Spain.

- **Number of cases in the study**
  - 0 to 40
- **ILI cases/100,000 inhabitants**
  - 0 to 250

The graph peaks around week 1, indicating a significant increase in ILI cases and rates.
Results Cases - ILI Negative Controls

restricted analysis (N=79)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases n (%)</th>
<th>Controls ILI negative n (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age</td>
<td>72.5±6.05</td>
<td>74.9±7.57</td>
<td>0.121</td>
</tr>
<tr>
<td>Sex: male</td>
<td>22/43 (51.2)</td>
<td>17/36 (47.2)</td>
<td>0.727</td>
</tr>
<tr>
<td>female</td>
<td>21/43 (48.8)</td>
<td>19/36 (52.8)</td>
<td>0.727</td>
</tr>
<tr>
<td>Vaccination 2008</td>
<td>26/43 (60.5)</td>
<td>33/36 (91.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Previous influenza vaccination</td>
<td>17/43 (39.5)</td>
<td>19/36 (52.8)</td>
<td>0.239</td>
</tr>
<tr>
<td>Pneumococcal vaccination</td>
<td>25/43 (58.1)</td>
<td>30/35 (85.7)</td>
<td>0.008</td>
</tr>
<tr>
<td>Any hospitalization</td>
<td>4/41 (9.76)</td>
<td>5/36 (13.9)</td>
<td>0.573</td>
</tr>
<tr>
<td>Smoker</td>
<td>10/43 (23.3)</td>
<td>8/35 (22.9)</td>
<td>0.966</td>
</tr>
<tr>
<td>Any chronic conditions</td>
<td>28/42 (66.7)</td>
<td>28/35 (80.0)</td>
<td>0.190</td>
</tr>
<tr>
<td>Poor functional status</td>
<td>2/43 (4.6)</td>
<td>3/36 (8.3)</td>
<td>0.503</td>
</tr>
</tbody>
</table>
## cycEVA: Results Cases – non-ILI Controls
Matched study (44 pairs)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases n(%)</th>
<th>Non-ILI Controls n(%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age</td>
<td>72.5 ± 5.98</td>
<td>73.9 ± 6.22</td>
<td>0.219</td>
</tr>
<tr>
<td>Sex: male</td>
<td>22 (50.0)</td>
<td>43 (48.9)</td>
<td>0.902</td>
</tr>
<tr>
<td>female</td>
<td>22 (50.0)</td>
<td>45 (51.1)</td>
<td>0.902</td>
</tr>
<tr>
<td>Vaccination 2008</td>
<td>27 (61.4)</td>
<td>71 (80.7)</td>
<td>0.033</td>
</tr>
<tr>
<td>Previous influenza vaccination</td>
<td>18 (40.9)</td>
<td>46 (52.3)</td>
<td>0.218</td>
</tr>
<tr>
<td>Pneumococcal vaccination</td>
<td>26 (59.1)</td>
<td>54 (61.4)</td>
<td>0.801</td>
</tr>
<tr>
<td>Any hospitalization</td>
<td>4/42 (9.5)</td>
<td>3 (3.4)</td>
<td>0.148</td>
</tr>
<tr>
<td>Smoker</td>
<td>10 (22.7)</td>
<td>33 (37.5)</td>
<td>0.087</td>
</tr>
<tr>
<td>Any chronic conditions</td>
<td>28/43 (65.1)</td>
<td>64/87 (73.6)</td>
<td>0.284</td>
</tr>
<tr>
<td>Poor functional status</td>
<td>2 (4.5)</td>
<td>3 (3.4)</td>
<td>0.747</td>
</tr>
</tbody>
</table>
cycEVA: Results Screening method

- Vaccinated cases: 26 (60.5%)

- Vaccination coverage
  - ILI negative controls: 91.7%
  - Non-ILI controls: 80.7%
  - GPs´catchment area: 65.3%
  - Spanish population ≥ 65 years: 66% (source: MoH)
cycEVA: Crude and adjusted IVE estimates by design

- Case-control ILI negative
- Case-control Non-ILI
- Screening Method
cycEVA: Limitations

Case control study

- Low number of cases
  - low number of GPs reporting cases
  - epidemic peak during Christmas holidays

Screening method

- No control for confounding factors
- GP attended cases compared with vaccination coverage of the whole catchment area
cycEVA:  Conclusions

- **Protective** effect of influenza vaccine against laboratory-confirmed influenza in *medically attended* Spanish population $\geq 65$ years

- VC differs in the various groups: *control group* representing the cases´source population?

- Limited sample size $\Rightarrow$ imprecise IVE for both methods

- Screening method uses available surveillance data only
  - cannot control for confounders
cycEVA: Season 2009-10

- More GPs included in the study
- Reinforced **training** of participating GPs
- Avoid disruption during Christmas holidays
- Take into account the **Influenza A(H1N1)v pandemic**:
  - GPs’ work overload
  - Swabbing increased (laboratory overload)
  - All age groups included
  - Laboratory negative controls and screening method
**cycEVA:** Study team*

- **Baleares:** A. Galmés Truyols, J. Vanrell Berga
- **Castilla y León:** M. Gutierrez Pérez, T. Vega Alonso
- **Cataluña:** A. Martínez Mateo, N. Torner Gracia
- **Extremadura:** J.M. Ramos Aceitero, M.C. Serraro Martin
- **Navarra:** M. García Cenoz, J. Castilla Catalán
- **País Vasco:** J.M. Altzibar Arotzena, J.M. Arteagoitia Axpe
- **La Rioja:** C. Quiñones Rubio, M.E. Lezaún Larumbe, M. Perucha González
- **CNM:** F. Pozo, I. Casas, P. Pérez Breña
- **CNE:** S. Jiménez, I. Salmeán
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cycEVA:

Thank you!