Monitoring Influenza Vaccine Effectiveness, a long term approach

The “I-MOVE” ECDC network

E. Kissling, A. Moren, M. Valenciano, on behalf of the I-MOVE network
Presentation overview

- Why monitoring influenza vaccine effectiveness?
- I-MOVE: Influenza Monitoring VE in Europe,
  - methods
  - results 2007/10
- I-MOVE long-term perspectives
Monitoring influenza vaccine effectiveness in EU: why?

- Not a very good vaccine but recommended in all EU MS
- Evaluate influenza vaccination programme
- Maintain confidence in vaccination programmes
- Influenza VE (IVE) varies from year to year
  - clinical IVE cannot be predicted based on antigenic distance
  - IVE varies by age, subgroups, suptype
- Detect variations in effectiveness due to
  - changes in the target population
  - changes in the epidemiology of disease
  - poor virus-vaccine match
  - special field conditions
Monitoring influenza vaccine effectiveness in EU: why?

- Trigger other public health measures
  - use of antivirals

- For new vaccines IVE should be incorporated as component of post-licensure surveillance

- ILI /ARI incidence does not predictably decrease with increased vaccination coverage
  - VE cannot be inferred from surveillance data

- Trigger research on more effective vaccines
  - mode of administration
    - adjuvanted vs non-adjuvanted
    - dosages
I-MOVE objectives
(Influenza monitoring VE in Europe)

- To identify and pilot test methods to measure seasonal and pandemic IVE in EU and EEA

- To develop a system to monitor on a routine and real-time basis IVE in EU and EEA
  - have early estimates during the influenza season
  - have a system ready to assess and monitor IVE in a pandemic
I-MOVE

- ECDC
- 20 EU & EEA Member States
- Coordination, EpiConcept

- Collaboration with
  - Australia
  - Canada
  - USA

- Smittskjødssnstituet, Stockholm, Sweden
- Statens Serum Institut, Copenhagen, Denmark
- Scottish Centre for Infection and Environmental Health (CIEH)
- Istituto Superiore Di Sanita, Rome, Italy
- Greece, National Institute of Health
- Royal College of General practitioners Birmingham Research Unit, UK
- Instituto Nacional de Saude Dr. Ricardo Jorge, Lisboa, Portugal.
Influenza VE studies in EU, 2008/11

2010-11 Case control
- Spain
- Romania
- Hungary
- Portugal
- Ireland
- Italy
- France
- Poland
- Valencia, Spain Hospital CC study

2010-11 Cohorts & Nested case control
- England, UK
- Scotland, UK
- Navarre, Spain

2010-11 Screening method
- Italy
- France
- Spain
- Portugal
- England
- Scotland

Studies I-MOVE partners
2008-9: 7 ECDC/MS pilot
2009-10: 11 ECDC/MS funded, 4 EVM, 3 MS funding
2010-11: 11 ECDC/MS funded, 2 private funding
I-MOVE multicentre case-control Methods

- VE case-control studies
  - 2008-9  5 studies (*elderly*)
  - 2009-10  7 studies
  - 2010-11  8 studies

- Recruitment: influenza surveillance sentinel networks

  Systematic swabbing ILI patients (all study sites in 2010-11)

  **Cases:** ILI patients positive for influenza

  **Controls:** ILI patients negative for influenza

- Common covariates to adjust for + and - confounding

- Very similar protocols ➔ pooled analysis
  - EU ILI with symptom onset – swab delay of < 8 days
I-MOVE multicentre case control
Methods

Evaluation of heterogeneity
– Qualitative and statistical

Pooled
– 1-stage model (2008-9, 2009-10, 2010-11)
– 2-stage model (2010-11)

Logistic regression
– complete case analysis
– multiple imputation, chained equations (2009-10, 2010-11)

Adjustment for all covariates
Seasonal IVE 2008-9, pooled analysis pilot season (elderly) – 5 study sites

**Vaccine effectiveness (%)**

<table>
<thead>
<tr>
<th></th>
<th>Crude</th>
<th>Full model</th>
<th>65 - 74</th>
<th>75+</th>
<th>Influenza A only</th>
<th>Influenza AH3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall sample size N</td>
<td></td>
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</tbody>
</table>

* Study site in model as a fixed effect
‡ adjusted for sex, chronic diseases and related hospitalisations, smoking, previous seasonal influenza vaccination, functional status,
Pandemic IVE 2009-10, imputed dataset, pooled analysis – 7 study sites

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

Overall sample size N = 2902
Seasonal 2010-11 IVE, by influenza subtype, imputed dataset, pooled analysis – 8 study sites

Overall sample size N = 4411
I-MOVE cohort studies

Methods

Large electronic GP databases
- England: 873,289; Scotland: 93,380; Navarra: 604,595
- All ages

Outcomes
- ILI
- all respiratory illness,
- hospitalisations
- death

Adjustment for + and - confounding

Poisson/Time dependent Cox regression
(person-time analysis)
Cohorts: Preliminary (end of March) IVE 2010-11 against MA-ILI

Country (population size) - Statistical method

<table>
<thead>
<tr>
<th>Country</th>
<th>Population</th>
<th>Method</th>
<th>Crude</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>England</td>
<td>(873,289)</td>
<td>Poisson</td>
<td>21</td>
<td>35</td>
</tr>
<tr>
<td>Scotland</td>
<td>(93,380)</td>
<td>Cox</td>
<td>52</td>
<td>38</td>
</tr>
<tr>
<td>Navarra</td>
<td>(604,595)</td>
<td>Cox</td>
<td>27</td>
<td>64</td>
</tr>
</tbody>
</table>
IVE 2010-11 against MA-ILI and lab confirmed influenza in pop with chronic conditions, Navarra

Cohort study to evaluate the IVE in preventing MA-ILI

Test negative case-control study to evaluate the IVE in preventing laboratory-confirmed influenza

* Euro Surveill 2011;16(7):pii=19799.
Screening method: pandemic IVE vaccine effectiveness by age group 2009-10 season, Spain

Courtesy Amparo Larrauri
MA-ILI – 2010-11, preliminary Screening IVE (end of March) Effectiveness by week, England

Courtesy Dougas Fleming
I-MOVE 2007-10

- A consolidated network for measuring IVE
  - estimates from several countries, designs
  - laboratory confirmed outcome
  - control for positive / negative confounders

- Early estimates in seasons or pandemics

- IVE by age group, subtype

- Contribution to strengthen influenza surveillance
  - case definition
  - systematic sampling

- Excellent scientific exchanges
  - within Europe
  - with international experts
I-MOVE future

- Multicentre case-control study
  - increase sample size by study site
  - estimates by vaccine brand, subgroups

- Electronic cohort studies
  - validation laboratory subset
  - validate data

- Screening
  - adjust at least for age-groups
I-MOVE future

- To monitor influenza VE against severe outcomes

- Network of EU hospitals
  - similar protocol ➔ pooling
  - can be used for other diseases

- ECDC EVER project
  - collect, analyse, communicate data and information on immunisation programmes in EU
  - bring under same umbrella activities previously covered by different projects
  - integrate the elements of vaccine preventable disease surveillance programme: disease surveillance, vaccine effectiveness, vaccination safety and vaccination coverage
Gracias

- **Sentinel networks**
- **Partners conducting studies in 2010/11**
  - **England and Wales, RCGP**: Douglas Fleming, Haylay Durnall,
  - **France, OpenRome / GROG**: Jean-Marie Cohen, Anne Mosnier, Isabelle Daviaud
  - **Hungary, NCE**: Beatrix Oroszi, Krisztina Horvath, Marta Melles, Agnes Csohan
  - **Ireland, HSE**: Anne-Sophie Barret, Joan O’Donnell, Darina O’Flanagan, Aidan O’Hora,
  - **Italy, ISS**: Caterina Rizzo, Paolo Dancona, Antonino Bella, Maria Cristina Rota
  - **Portugal, Inst Nac Saude Dr Ricardo Jorge**: Baltazar Nunes, José Marinho Falcão, Raquel Guiomar
  - **Romania, Cantacuzino Institut**: Viorel Alexandrescu, Daniela Pitigoiti, Emilia Lupulescu,
  - **Scotland, HPS**: Jim McMenamin, Chris Robertson, Arlene Reynolds
  - **Spain, ISCIII**: Amparo Larrauri, Silvia Jiménez, Salvador De Mateo
  - **Spain, Navarra Public Health Institute**: Jesús Castilla, Iván Martínez
  - **Poland, National Institute of Public Health**: Iwona Paradowska-Stankeiwicz, Malgosia Fluchowska, Pawel Stefanoff
  - **UK, HPA**: Richard Pebody, Nick Andrews, Pia Hardelid

- **ECDC**: Bruno Ciancio, Piotr Kramarz, Angus Nicoll
- **EpiConcept**: A Moren, M Valenciano, E Kissling, C Savulescu, T Seyler, A Halm, V Nancey, N Colombo, G Jeannerod
- **Other Partner Institutes**
  - **Belgium, IPH**
  - **Denmark, SSI**
  - **Finland, THL**
  - **France, InVS**
  - **France, Sentinelles**
  - **Italy, Campobasso, Catholic University**
  - **Greece, KEEPNO**
  - **Norway, FHI**
  - **Spain, Valencia CSISP**
  - **Sweden, SMI**
  - **The Netherlands, RIVM**
  - **The Netherlands, Erasmus University**