Monitoring Influenza Vaccine Effectiveness in Europe, the I-MOVE network

I-MOVE network

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I-MOVE objectives
(Influenza monitoring VE in Europe)
ECDC tender 2007

- To identify and **pilot test methods** to measure seasonal and pandemic influenza VE 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 network 2008/9 – 2012/13

**Partners**
- 26 institutes
- 17 MS EU / EEA MS

**Studies in 14 sites**
- national case-control based on sentinel networks
- multicentre case-control
- cohorts based on primary care computerised registers with nested case control
- screening
I-MOVE cohort studies with nested case control

England, Scotland, Navarra region
I-MOVE cohort studies

Methods

- Large electronic GP databases
  - **England** 1,005,132; **Scotland** 200,000; **Navarra** 604,595
  - All ages

- Outcomes
  - ILI
  - all respiratory illness
  - hospitalisations
  - death
  - *laboratory confirmed (nested case-control)*

- Adjustment for + and - confounding

- Analysis
  - Poisson/Time dependent, Cox regression
  - Logistic regression (case-control)
I-MOVE cohorts: Preliminary IVE (end of March 2011) against MA-ILI

<table>
<thead>
<tr>
<th>Country/Region (Population Size)</th>
<th>Statistical Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>England (873,289) - Poisson regression</td>
<td>Crude 21</td>
</tr>
<tr>
<td>Scotland (93,380) - Cox</td>
<td>Adjusted 35</td>
</tr>
<tr>
<td>Navarra (604,595) - Cox</td>
<td>Crude 38</td>
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<tr>
<td></td>
<td>Adjusted‡ 64</td>
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<tr>
<td></td>
<td>Crude 27</td>
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<tr>
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<td>Adjusted‡ 64</td>
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Country /region (population size) - Statistical method
### Feasibility of pooling cohort databases

**Combined Model, VE against ILI consultations (2010/11)**

<table>
<thead>
<tr>
<th></th>
<th>VE %</th>
<th>LCL</th>
<th>UCL</th>
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</thead>
<tbody>
<tr>
<td><strong>Combined</strong></td>
<td>25.9</td>
<td>19.8</td>
<td>31.6</td>
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<tr>
<td>(three data sets together)</td>
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</tr>
<tr>
<td><strong>Random Effects</strong></td>
<td>26.1</td>
<td>19.9</td>
<td>31.8</td>
</tr>
<tr>
<td>(pooling of separate analysis in each country)</td>
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<tr>
<td><strong>Fixed Effects</strong></td>
<td>26.1</td>
<td>19.9</td>
<td>31.8</td>
</tr>
<tr>
<td>(pooling of separate analysis in each country)</td>
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</tbody>
</table>
Screening method

Italy, Portugal, Spain, England, Scotland
Screening method: pandemic vaccine effectiveness against laboratory confirmed influenza by age-group, Spain, 2009-10

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

Courtesy Dougas Fleming
I-MOVE case-control studies

2008/9
5 study sites: DK, SP, HU, PT, RO (elderly)

2009/10
7 study sites: SP, FR, IE, IT, HU, PT, RO

2010/11, 2011/12
8 study sites: SP, FR, IE, IT, HU, PO, PT, RO

2012/13
6 study sites: DE, SP, IE, PO, PT, RO
Methods: Multicentre case-control study

- Sentinel networks (> 1000 GPs)
  - interview and swab of ILI patients

- Reference laboratories
  - cases: ILI positive for influenza
  - controls: ILI negative (test-negative)

- Vaccination status
  - vaccinated: vaccine > 14 days before ILI onset

- Pooled 1-stage model
  - study as fixed effect
  - covariates to adjust for + and - confounding
Multicentre case-control
Strengthening methods along the seasons

Study sites, population, sample size
- Pilot season  5 study sites, elderly (N= 327)
- 2011/12     8 study sites, all population (N=4747)
- 2012/13     6 study sites, all population (N=4853)

EU ILI case definition
- Pilot season  4/5
- 2012/13     6/6

ILI patients swabbed
- All elderly
- Other age groups: a systematically selected sample

Data quality
Influenza VE by age and risk groups, type/subtype
Multicentre case control study, I-MOVE, 2007-12, EU

Adjusted vaccine effectiveness (%)
Adjusted VE of seasonal vaccine against A(H3), vaccination target group, by early and late phase and time since vaccination I-MOVE multicentre case control study, EU, 2011-12

Adjusted for age (10 year bands), sex, week of onset, chronic diseases and related hospitalisations and number of practitioner visits in the previous year.

* Adjusted for age (10 year bands), sex, week of onset, chronic diseases and related hospitalisations and number of practitioner visits in the previous year.
Late season & low VE (particularly in late season)
- Concordance with virological surveillance showing virus changes towards end of season
- Antigenic drift + waning of vaccine effect?

Lower VE with more time since vaccination in early influenza phase
- Waning of vaccine effect?
  ➔ Currently working on retrospective analysis of change in influenza vaccine effectiveness across the season, with a focus on possible waning of immunity
Early estimates 2012-13
Early 2012-13 influenza VE estimates against laboratory confirmed influenza, by virus type, subtype, study site (US, Canada, UK, I-MOVE MCC, Navarra, Spain, the Netherlands)
Highly motivated study teams

Continuous exchanges between I-MOVE members and with European and international experts
  – during the season teleconferences, workshops
  – annual meeting
  – website [https://sites.google.com/site/epiflu/Home](https://sites.google.com/site/epiflu/Home)
The I-MOVE network

Communication
- 35 articles published
- Scientific conferences (national and international)
- I-MOVE results included in meta-analysis
- Since 2009/10
  - preliminary results communicated to EMA, WHO, ECDC

Funding
- 2008/9-2011/12
  - study sites
  - ECDC
- 2012/13
  - study sites
  - WHO/Europe contributed to 2 study sites
  - EpiConcept (coordination)
Conclusions

- 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, target population
- Contributes to
  - strengthen influenza surveillance
  - better understand complexities of influenza VE
I-MOVE will continue

Research projects undergoing

Challenge
  – Long term funding....
  – Sample size

“While other countries, such as Australia, Canada, and the United States support similar influenza vaccine effectiveness studies, the EU is the acknowledged leader in defining and addressing the issue of effectiveness with the current HA-head vaccines.”

Osterholm et al, CIDRAP report, October 2012
Patients

Influenza Sentinel networks

Study sites I-MOVE

- Denmark: A Mazick, K Molbak (2008-9)
- England, Wales RCGP: D Fleming, H Durnall
- France OpenRome / GROG: JM Cohen, A Mosnier, I Daviaud
- Germany, RKI: A Reuss, U Buchholz
- Hungary, NCE, : B Oroszi, K Horvath
- Ireland, HSE: AS Barret, J Rebolledo, J O’Donnell
- Italy, ISS: C Rizzo, A Bella, MC Rota, S Erlich
- Poland National Institute of Public Health: I Paradowska-Stankeiwicz, M Fluchowska, P Stefanoff
- Portugal, Inst Nac Saude Dr Ricardo Jorge: B Nunes, A Machado, J Marinho Falcão, R Guiomar
- Romania, Cantacuzino Institut: V Alexandrescu, D Pitigoiti, E Lupulescu,
- Scotland, HPS: J McMenamin, C Robertson
- Spain, CNE, ISCIII: A Larrauri, S Jiménez, S De Mateo
- Spain, Navarra Public Health Institute: J Castilla, I Martínez
- UK, HPA: R Pebody, N Andrews, P Hardelid, G Kaftatos

ECDC: B Ciancio, P Kramarz, A Nicoll

EpiConcept: E Kissling, A Moren, M Valenciano
C Savulescu, T Seyler, A Halm, V Nancey, N Colombo, G Jeannerod

Other partners Institutes

- Belgium IPH
- Finland. THL
- France, InVS
- France, Sentinel
- Greece, KEEPNO
- Norway, FHI
- The Netherlands, RIVM
- The Netherlands, Erasmus University
- Sweden, SMI

Thanks
BACK UP SLIDES
### I-MOVE multicentre cas control studies, ILI patients included in 2008-13

<table>
<thead>
<tr>
<th>Season</th>
<th>ILI * included</th>
<th>% influenza positive</th>
<th>Percentage virus type /subtype among cases</th>
<th>VC **</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td>A(H1N1)</td>
<td>A(H1N1)2009</td>
</tr>
<tr>
<td>2008/9 (elderly)</td>
<td>327</td>
<td>42%</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>2009/10</td>
<td>2902</td>
<td>32%</td>
<td>0%</td>
<td>100%</td>
</tr>
<tr>
<td>2010/11</td>
<td>4410</td>
<td>47%</td>
<td>0%</td>
<td>58%</td>
</tr>
<tr>
<td>2011/12, all Targeted for v.</td>
<td>4362</td>
<td>48%</td>
<td>0%</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>1033</td>
<td>43%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2012-13 early Entire season</td>
<td>1161</td>
<td>37%</td>
<td>0%</td>
<td>34%</td>
</tr>
<tr>
<td></td>
<td>10000?</td>
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</tbody>
</table>

* Influenza-like illness
** Vaccine coverage
Number of ILI vaccinated* by ISO-week of vaccination (N=372), ILI cases by onset week (N=1033), A(H3) database, vaccination target group, I-MOVE multicentre case control study, EU, 2011-12

* Regardless of interval between vaccination date and date of onset of symptoms
Adjusted VE of seasonal vaccine against A(H3), vaccination target group, by early and late phase I-MOVE multicentre case control study, EU, 2011-12

Adjusted for age (10 year bands), sex, month of onset, chronic diseases and related hospitalisations and number of practitioner visits in the previous year.
Early 2012-13 influenza VE estimates against laboratory confirmed influenza, by virus type, subtype, population, study site (US, Canada, UK, Denmark, I-MOVE MCC, Navarra, Spain, the Netherlands)
Early 2012-13 influenza VE estimates against laboratory confirmed influenza A(H3N2) by population, study site (US, Canada, I-MOVE MCC, Netherlands, Denmark)
Early 2012-13 influenza VE estimates against laboratory confirmed influenza, by virus type, subtype, population, study site (US, Canada, UK, I-MOVE MCC, Navarra, Spain, the Netherlands)