Influenza Vaccine Effectiveness Study in Ireland in 2010/2011

This newsletter presents the results of the influenza vaccine effectiveness study conducted in Ireland during the 2010/2011 influenza season. We would like to take this opportunity to thank all participating GPs for their valuable contribution.

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<th>Background</th>
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<td>• As influenza viruses constantly evolve and vaccines are reformulated every year, influenza vaccine effectiveness (IVE) needs to be estimated annually. Clinical trials can provide data on the efficacy of vaccines but they cannot be conducted yearly and are usually limited to healthy adults. Therefore observational studies are needed to estimate the IVE at population level.</td>
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<td>• Following the WHO recommendations for vaccine composition in February 2010, trivalent influenza vaccines were developed by manufacturers. In Ireland, the seasonal influenza vaccination campaign started on 6th October 2010 and two influenza vaccines were marketed. Both were non-adjuvanted.</td>
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<td>• To estimate the IVE in 2010/2011, we conducted a case-control study within the framework of the Irish College of General Practitioners (ICGP) influenza sentinel surveillance system.</td>
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<td>• This study was part of a European multicentre case-control study conducted within the I-MOVE network (I-MOVE: Influenza Monitoring Vaccine Effectiveness in Europe). The European study aimed to estimate the IVE in 2010/2011 using sentinel general practitioners (GP) surveillance networks from eight European countries.</td>
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<td>• This newsletter presents the results of the study conducted in Ireland.</td>
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<th>Objectives</th>
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<td>• <strong>Primary objective</strong> Estimate the trivalent influenza vaccine effectiveness (TIVE) in Ireland.</td>
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<td>• <strong>Secondary objective</strong> Estimate the TIVE:</td>
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<th>Methods</th>
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<td>• <strong>Design</strong></td>
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<td>• <strong>Timeline</strong></td>
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<td>• <strong>Study population</strong></td>
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<td>• <strong>Sampling strategy</strong></td>
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• Collected data
  - Nose and throat swab specimen sent to the National Virus Reference Laboratory (NVRL) for influenza testing
  - Questionnaire (paper or web-based):
    - Vaccination history (seasonal and pandemic influenza vaccine in 2010/11 and 2009/10 respectively)
    - Demographic, clinical symptoms, underlying medical conditions and related hospitalisations, pregnancy, functional status and antiviral treatment.

• Definition of cases and controls
  - Cases: ILI patients with a respiratory sample positive for influenza during the influenza season
  - Controls: ILI patients with a respiratory sample negative for all influenza viruses whose week of symptom onset was during or after the week of onset of the first laboratory-confirmed influenza case and prior to or during the week of onset of the last laboratory-confirmed influenza case.

• Exposure
  - Vaccination with the trivalent influenza vaccine in 2010/2011
  - Patients were considered as vaccinated if they had received one dose of vaccine >14 days before symptom onset.

• Trivalent influenza vaccine effectiveness (TIVE) = 1-OR [95% CI]

• Data analysis
  - Univariable analysis → Crude TIVE
  - Logistic regression → TIVE adjusted for potential confounders (provided that sample size is sufficient).

• Sample size calculation
  - 1,111 patients (556 cases and 556 controls) needed to detect a TIVE of 50% with a vaccine coverage of 20%, precision of 20%, power of 80% and alpha error 5%.
  - For an influenza outbreak duration of 8 weeks and a sampling frame of 5 patients per week per GP practice, 28 GP practices would have to participate (46% of all GP practices).

• Phylogenetic analyses
  - First positive specimen per week for influenza A(H1N1)2009 and influenza B
  - Nucleotide sequencing and phylogenetic analysis of the haemagglutinin (HA) gene.

### Results

**GP Participation**
- All 60 practices were invited to participate in the study
- 17 (28%) practices recruited at least one ILI patient
- GP practices recruited at least 2 patients per week in 28.5% of instances (given week and practice) between week 50 and week 9.

**Recruitment**
- 288 ILI patients recruited into the study
- No refusals notified.

**Exclusion of 97 patients**

- 288 patients
  - 32: Onset week before week 48-2010 or after week 12-2011
  - 17: > 7 days between symptom onset & swabbing
- 256 patients
  - 12: Missing information (lab result, onset date, date of swab, 2010-11 vaccination status or date)
- 239 patients
  - 1: Antiviral treatment before swabbing
- 227 patients
  - 35: Did not meet the EU ILI definition
- 226 patients
  - 191 patients
Finally, 191 patients were included in the analysis of the study. There were 85 controls and 106 (55.5%) influenza cases, of whom:
- 56 (52.8%) influenza A(H1N1)2009
- 47 (44.3%) influenza B
- 2 influenza A unsubtyped
- 1 influenza A(H3).

Distribution of ILI patients (N=191) and positivity rate by week of onset of symptoms and by virus subtype

Description of cases and controls
- Controls were more likely to have diabetes than cases (7.1% versus 0.9%, p=0.04)
- Influenza B cases were significantly younger than controls (median age: 12 years versus 31 years, p=0.001) whereas influenza A(H1N1)2009 cases had a similar age profile to controls (median age: 29 years versus 31 years, p=0.76)
- No significant differences for other baseline characteristics.

2010/2011 vaccination status
- Seven controls and one influenza case had received the vaccine more than 14 days before symptom onset
- The vaccinated case was confirmed as influenza B. This patient was a male aged 22 years old with chronic neurological disease.

Trivalent influenza vaccine effectiveness
- Crude TIVE against all influenza subtypes: 89.4% [95% CI: 13.8%; 99.8%]
- Crude TIVE against influenza A(H1N1)2009: 100% [-8%; 100%]
- Crude TIVE against influenza B: 77% [-90.0%; 99.5%]
- Multivariable and stratified analyses could not be performed because of the small number of vaccinated cases.

Phylogenetic analyses
- 18 specimens characterised (11 influenza A(H1N1)2009 and 7 influenza B)
- Specimen from the patient with vaccine failure could not be characterised
- All influenza A(H1N1)2009 isolates were similar to the vaccine strain A/California/7/2009
- All but one influenza B isolates were clustered as Victoria-like strains (similar to the vaccine strain B/Brisbane/60/2008).
Our results suggest that 2010/2011 influenza vaccines provided good protection against medically-attended laboratory confirmed influenza. This is consistent with phylogenetic analyses which demonstrated a good match between the vaccine and the circulating strain.

These results should be interpreted with caution given the wide confidence intervals and the fact that no adjustment for potential confounders could be performed due to the small sample size. However, cases and controls were similar for most baseline characteristics, suggesting that confounding did not appear to play an important role.

The main limitation was the power of the analyses due to a small sample size coupled with low vaccination coverage. The number of participating GP practices, number of patients recruited by week and vaccination coverage were all lower than expected. Moreover, a substantial number of recruited patients did not meet the inclusion criteria and had to be excluded from the analysis.

The issue of sample size was addressed by pooling of data with seven other European countries participating in I-MOVE. Preliminary results were published in March 2011 in Eurosurveillance:
http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19818

For coming influenza seasons, efforts should be made to increase sample size and vaccination coverage in order to obtain more precise IVE estimates for Ireland. We would need a much bigger sample size to be able to conduct multivariable and stratified analysis, and thus get a thorough understanding of influenza vaccine effectiveness.

The ICGP sentinel system is a unique network and opportunity to estimate the IVE at population level in Ireland. All sentinel GPs are encouraged to participate in this important research study in 2011/2012. Inclusion criteria could also be explained better and emphasised during the planning phase in order to optimise the recruitment strategy.