Influenza vaccine effectiveness assessment in the UK

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Introduction

• In the UK trivalent influenza vaccine (TIV) has been used for many years in those aged 65 years and over, in clinical risk groups and health care workers.
• In 2009/10 the H1N1 adjuvanted monovalent influenza vaccine (MIV) (Pandemrix) was used targeted at risk-groups and all children <5 years.
• In 2014/15 introduction of live attenuated nasal vaccine programme for all 2-16 year olds is planned.
• Vaccine uptake across the UK for 2011/12 was 68-77% in those aged 65+ and 50-70% in risk groups.
Swabbing Schemes

- Swabbing is performed by GPs in five schemes across the UK
  - Royal College of General Practitioners – England (~100 GPs)
  - HPA Region Microbiology Network – England (45 GPs)
  - Health Protection Scotland (90 GPs)
  - Public Health Wales (44 GPs)
  - Public Health Agency of Northern Ireland (37 GPs)

- Total population covered by the GPs is about 2.5 million

- 2004/05 to 08/09
  - RCGP data used to estimate VE by test negative case control (TNCC)

- Since 2009/10:
  - Data pooled across the UK schemes for TNCC
  - Mid season estimates produced
  - RCGP /Scotland have done cohort studies.
  - RCGP also do within season screening assessment
Test-negative case-control design (TNCC)

- Started to be used for Influenza VE in about 2005 by various groups (UK, Canada)

- Individuals are tested for infection with a certain vaccine preventable disease. Vaccination history is also ascertained.

<table>
<thead>
<tr>
<th>Sample</th>
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<tbody>
<tr>
<td>Tested +</td>
<td>Tested –</td>
</tr>
<tr>
<td>Vaccinated</td>
<td>a</td>
</tr>
<tr>
<td>Unvaccinated</td>
<td>c</td>
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VE = 1 – (a/c)/(b/d)

Analysis is as with a classic case control study (logistic regression)
Influenza VE using the TNCC in the UK

Individual presents to GP with ILI

GP is part of a network of swabbing GPs

Oct-March: GP swabs all or a subset of ILI patients

Results and epi-data go into a database. For the RCGP scheme lab results coded back into GP database by GPs

Sample tested by PCR for flu (and type of flu). Also testing for other viruses (RSV)

Sample sent to National Laboratory along with a form with vaccination history, date of onset, age, gender and risk group.
Swab and instructions
Key Potential Confounding variables

- Age (certainly a confounder)
- Period (certainly a confounder)
- Region/country (possibly)
- Being in a risk group for vaccination (possibly)
Example of swabs taken in 2010/11

Timing of vaccine uptake in the general population
Description of swabs taken, 2010/11

Swabs taken per scheme 10/11

Age of patients 10/11

Interval from onset to swab 10/11

Vaccination Status 10/11
Results for 2010/11 (Pebody 2012*)

<table>
<thead>
<tr>
<th></th>
<th>H1N1</th>
<th>B</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccinated (&gt;14d)</td>
<td>81</td>
<td>58</td>
<td>604</td>
</tr>
<tr>
<td>Unvaccinated</td>
<td>1626</td>
<td>1064</td>
<td>3693</td>
</tr>
</tbody>
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Crude TIV VE for H1N1pdm(09) = 70%
Crude TIV VE for B = 67%

Crude estimates not too meaningful – adjustment for age and period makes the most difference

Adjusted TIV VE against H1N1pdm(09) = 56%, 95% CI (42-66%)
Adjusted TIV VE against B = 57% (42-68%)

Adjustment for risk group / scheme made very little difference to the estimates

We also looked at VE of monovalent pandemic vaccine in 2009/10 which was 72% (15-91%) in under 5 year olds and 10% (-36 to 41%) in over 5 year olds.

VE estimates against H1N1 by age–group, 2010/11
wide 95% CIs

Results since 2004/05
(except 2009/10 when TIV VE was 0% and MIV approx 70%)
Methodological Issues

• Bias from lack of sensitivity - Orenstein (IJE 2007) considered this and gave formulas.

• GP selection of ILI cases to swab. We ask for swabs irrespective of vaccination history. No reason to suspect biased selection and GP does not know test result when selecting who to swab.

• Should be good matching on propensity to consult.
Cohort studies

- Part of i-Move
- RCGP and Scotland using Primary Care data extracts
- ILI, LRTI, ARTI end points examined
- RCGP – swabbing results could also be used as laboratory results are written back into the GP record.
- Results show sensible VE against ILI but ARTI/LRTI not specific enough (VE 0 or negative).
- Issues of bias due to propensity to consult – need to look at consulting frequency.
Propensity to consult in year prior to 2011/12 season in patients swabbed by swabbing result

- swab -
- swab +

% of patients

<table>
<thead>
<tr>
<th>Consultations</th>
<th>swab -</th>
<th>swab +</th>
</tr>
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<tbody>
<tr>
<td>none</td>
<td>5%</td>
<td>10%</td>
</tr>
<tr>
<td>quartile 1</td>
<td>15%</td>
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<tr>
<td>quartile 3</td>
<td>35%</td>
<td>35%</td>
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<tr>
<td>quartile 4</td>
<td>40%</td>
<td>40%</td>
</tr>
</tbody>
</table>
2010/11: If true VE is 55% and 50% of ILI swabs are positive then expect to observe 27% VE
Comments

• Using surveillance data and the TNCC design has consistently produced results that are sensible and in line with other studies.

• Pooling UK data from similar schemes has increased power with no evidence of estimates differing by scheme.

• Only adjustment for age and period seems necessary.

• For the cohort analysis more issues with bias from propensity to consult but ILI outcome seems to give sensible results.
Acknowledgements

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- Northern Ireland: Brian Smyth, Catriona Kearns
- i-Move collaborators
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- All participating general practices in the schemes for provision of the data.
References for UK studies