Challenges to measure influenza vaccine effectiveness in Europe

Can we trust our measurements?

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Rationale

Influenza vaccine effectiveness (IVE) needed to:
- decide on recommendations for vaccine use
- target complementary or alternative public health measures
- estimate impact of vaccination on disease burden

At the European level:
- no routine IVE monitoring
- ECDC project on “Monitoring vaccine effectiveness during seasonal and pandemic influenza in EU”
To describe the methods used to measure influenza VE

To identify factors modifying / biasing VE estimates

in order to

identify the best study designs for measuring IVE in EU / EEA countries
Methods

- **Identification of articles on observational studies**
  - Medline
  - Cochrane, Sanofi Pasteur, Health Technology Assessment
  - References of the selected articles

- **Articles were summarised by**
  - Study design
  - Outcome
  - Target population
  - Methods to control for confounding factors
  - Virus

- **Workshop** with 18 partner countries experts and ECDC
Results

- Identified articles 284
- Observational studies 92
  - Cohorts 34
  - Outbreaks 26
  - Case control studies 30
  - Screening 2

- Articles on methods 23
### VE estimates in elderly (> 59 years) with outcome including hospitalisations by study design

<table>
<thead>
<tr>
<th>VE (%)</th>
<th>95% CI</th>
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<tbody>
<tr>
<td>0</td>
<td></td>
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<tr>
<td>10</td>
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<td>20</td>
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<td>90</td>
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<td>100</td>
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#### Chart: VE estimates by study design

- **Cohort**
- **Case control**

The chart visualizes the variation in VE estimates across different studies, indicating the spread and confidence intervals for VE estimates in elderly individuals with hospitalisations as the outcome, grouped by study design (Cohort vs. Case control). The x-axis represents the number of studies, while the y-axis shows the VE (%) along with 95% confidence intervals (95%CI).
VE estimates in elderly in case control studies by outcome

VE (%)
95%CI

ILI  ARI  pneumonia  pneumonia and/or influenza  CVD  deaths  Lab conf. influenza

Studies
Confounding Factors

**Negative**

- Presence of underlying chronic conditions
- Impaired functional status
- Severity of disease

**Positive**

- No smoking
- Previous influenza & pneumococcal vaccination
- Higher socio-economic level
- Higher educational level
- Healthy lifestyle
Magnitude of negative confounding

Difference between crude and adjusted VE estimates in case-control studies by age group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Crude - Adjusted VE (%)</th>
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<tr>
<td>&gt; 64 years</td>
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<tr>
<td>Other age groups</td>
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</table>

Studies
Positive confounding

VE by outcomes among > 64 years, by influenza activity - a cohort study

Source: Jackson LA et al, Evidence of bias in estimates of influenza vaccine effectiveness in seniors, Int.J.Epidemiol. 2006; 35:337-344
Factors related to the virus

- Influenza incidence
- Specimen and laboratory confirmation
  - Time onset / consultation
  - Specimen sampling
  - Laboratory test (culture, RT-PCR, RDT)
- Virus type - Antigenic match
Influenza vaccine efficacy and antigenic distance

Source: Carrat F. Vaccine, 2007;25:6852-62, quoting Gupta and all, Quantifying influenza vaccine efficacy and antigenic distance, Vaccine 2006;24(18):3881–8
Can we trust our measurements?

- VE varies with:
  - target population
  - study design
  - outcome specificity

- VE is biased by positive and negative confounding

- VE depends upon vaccine / circulating strain mismatch
Recommendations

- Develop **pilot studies** using:
  - Same population
  - Same design over time
  - Specific outcome (lab confirmed influenza)

- Control for **confounding** by adjusting for
  - Negative: chronic condition, functional status, severity
  - Positive: smoking, healthy behaviours
Next steps: season 2008-2009

- **6 case control** in elderly
  - Cases: laboratory confirmed influenza
  - Controls:
    - ILI flu negative
    - GP patients
    - Community

- **2 cohorts**: GP databases
  - Lab confirmation in subset
  - Before/during/after season estimates

Data collected on **confounding**

**Early measurement** in season