Efficiency in Population of Influenza Vaccination of Seasonal 2013-2016 for FLU Prevention of Hospitalized Adults

FLUVAC EV-03.3 – France

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*SP: ITMO de santé public
**I3M: Immunologie, inflammation, infectiologie et microbiologie
Objectives

- **Primary objective**
  
  *Measure the influenza vaccine effectiveness (IVE) by comparing the number of laboratory-confirmed influenza cases in vaccinated and unvaccinated hospitalized patients*

- **Secondary objectives**

  1. Measure VE by age group
  2. Measure VE by influenza type/subtype
  3. Describe and quantify the hospitalized population following influenza and its complications
  4. Understand the factors affecting the EV, the duration of protection, the role of repeated seasonal vaccination
  5. Identify phenotypic or genotypic key developments of the influenza virus that could affect vaccine performance and estimate the EV against specific clades
  6. Identify the differences in efficiency for different types (adjuvant vs non-adjuvant, surface antigens, split virion, trivalent vs quadrivalent) and vaccine marks.
Inclusion and Exclusion criteria

**Inclusion criteria**
- Patients aged ≥18 years
- Signed informed consent by patient or family/support person (or agreement of non-opposition)
- Patients with no protective supervision (curatorship or tutorship) whose sample was obtained as part of their medical care and who comply with the conditions of Article L1121-8 Code de la Santé Publique
- Presence of symptoms of the influenza like illness that began before hospitalization (even if these symptoms are no longer present at the time of inclusion)
- Inpatients admitted for any of the reasons listed in Table 1 (18.0 Annex attached to the protocol)
- Sample performed as soon as possible without exceeding 7 days after ILI onset

**Exclusion criteria**
- Contraindication to influenza vaccine (hypersensitivity to active substance or, excipients)
- **Patient institutionalized** without regular community interaction
- Patient tested positive for any influenza virus in the current season (RT-PCR, multiple RT-PCR and/or culture)
- ILI onset ≥ 48 hours after hospitalization
Map of hospitals participating in the 2015-16 season

5 university hospitals (members of I-REIVAC network) participating to I-REIVAC project:

Paris (Cochin and Bichat hospitals), Lyon, Montpellier, Rennes.

2 university hospitals participating in the GIHSN project: Cochin and Lyon hospitals (red circle).
Definitions

- **ILI case definition:** At least one of the following four systemic symptoms: fever or feverishness, malaise, headache or myalgia.
  
  **AND**

  At least one of the following three respiratory symptoms: cough, sore throat or shortness of breath.

- **Cases:** respiratory sample is positive for any influenza virus (RT-PCR).
- **Controls:** respiratory sample is negative for all influenza viruses.
- **Vaccination status:** onset of ILI symptoms > 14 days after vaccination.

- **Virological analysis were performed at the National Reference Laboratory for Influenza viruses in Lyon.**
Management of Database

- Differences between French and GIHSN database that it was necessary to seek and complete:
  - Autoimmune disease, mechanical ventilation, extracorporeal membrane oxygen, BPCO, Asthma, date of laboratory determination, main and secondary diagnostics at discharge/death, discharged from the hospital in the 30 days, …
  - Codes of admission diagnosis (ICD 9)
  - Codes of discharge diagnosis (ICD 9)
  - Order of data that it was necessary to adapt for GIHSN database
  - These data were sought (call phone, medical register, GP, patients…)

- Coordination of Cochin and Lyon hospitals for GIHSN

- These differences have been integrated in French database for 2016-2017 season
Study design

Screening in emergency room:
All hospitalized patients admitted for any of the reasons ICD 09 listed in protocol and meeting ILI case definition within 7 days before admission.

Selecting patients with inclusion and non-inclusion criteria

Care-related strategy
Nasopharyngeal swab or BAL already performed in the framework care
Study proposed to patient by physician
Non-opposition procedure
Storage of remaining sample

Study-related strategy
Study proposed to patient by physician
Signature of consent
Realization of nasopharyngeal swab sample
Storage of sample

RT-PCR for the influenza viruses (A, B, subtypes (H3N2, H1N1, H1N1v and B Yamagata, B Victoria) and other respiratory viruses
Enrolment by week in 5 hospitals participating on 2015-16 (N = 460)

**Study period:**
- Flu period (InVS): week 4– week 17/2016
- First patient included: January 28, 2016
- Last patient included: April 28, 2016
## Enrolment by hospital participating on 2015-16

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Patients included</th>
</tr>
</thead>
<tbody>
<tr>
<td>Montpellier</td>
<td>136</td>
</tr>
<tr>
<td>Bichat</td>
<td>82</td>
</tr>
<tr>
<td>Rennes</td>
<td>73</td>
</tr>
<tr>
<td>Cochin</td>
<td>85</td>
</tr>
<tr>
<td>Lyon</td>
<td>84</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>460</strong></td>
</tr>
</tbody>
</table>

The 2 hospitals participating to GIHSN project:

Montpellier and Lyon

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## Participating departments in each hospital

<table>
<thead>
<tr>
<th>Hospital ward</th>
<th>Cochin</th>
<th>Lyon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal medicine</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Emergency department</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Intensive care unit</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Respiratory diseases (pneumology)</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Others (Cardiology, …)</td>
<td>x</td>
<td></td>
</tr>
</tbody>
</table>
Introduction

Methodology

Results

Perspectives

Data analysis

460 included in France

- 2 included patients wrongly

458 analyzable in France

169 analyzable for Cochin and Lyon hospitals

53 cases

28 Flu A

25 Flu B

116 controls
Cumulative distribution subtype virus by week of symptom onset in the 2 hospitals participating in GIHSN project
### Repartition of viruses by type and subtype/lineage in the 2 hospitals participating in GIHSN project

<table>
<thead>
<tr>
<th>Virus subtype</th>
<th>Total N=53</th>
<th>Cochin N=36</th>
<th>Lyon N=17</th>
</tr>
</thead>
<tbody>
<tr>
<td>AH1N1</td>
<td>27</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>AH3N2</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>A untyped</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>B Yamagata</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>B Victoria</td>
<td>23</td>
<td>16</td>
<td>7</td>
</tr>
<tr>
<td>B untyped</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
Vaccine coverage of population by department in Cochin and Lyon
### Vaccination coverage among cases and controls by site

<table>
<thead>
<tr>
<th>Study hospital</th>
<th>Cases vaccinated (%)</th>
<th>Controls vaccinated (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total for 2 hospitals N=169</td>
<td>18/53 (34)</td>
<td>55/116 (47)</td>
</tr>
<tr>
<td>Cochin N=85</td>
<td>12/36 (33)</td>
<td>26/49 (53)</td>
</tr>
<tr>
<td>Lyon N=84</td>
<td>6/17 (35)</td>
<td>29/67 (43)</td>
</tr>
</tbody>
</table>

### Repartition of vaccine by brand

<table>
<thead>
<tr>
<th>Study hospital</th>
<th>Vaccinated</th>
<th>Influvac (%)</th>
<th>Vaxigrip (%)</th>
<th>Immugrip (%)</th>
<th>Fluarix (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cochin*</td>
<td>38</td>
<td>9(24)</td>
<td>25 (66)</td>
<td>1(2.6)</td>
<td>1(2.6)</td>
</tr>
<tr>
<td>Lyon**</td>
<td>35</td>
<td>10(29)</td>
<td>20 (57)</td>
<td>1(2.9)</td>
<td>1(2.9)</td>
</tr>
</tbody>
</table>

* Vaccine name is missing for 2 patients
** Vaccine name is missing for 3 patients
Characteristics of population among cases (n=53) and controls (n=116) in Cochin and Lyon
Vaccine coverage of population in Cochin and Lyon

![Bar chart showing vaccine coverage by condition and gender]

- Men
- Women
- Diabetes
- Neoplasm
- Chronic asthma
- Kidney disease
- Cardiovascular diseases
- Rheumatic diseases
- Chronic obstructive pulmonary disease
- Immunotherapies and transplantation
- Antiviral treatments before sampling

**Vaccine coverage (%)**
2015-16 influenza vaccine effectiveness (IVE) against hospitalised influenza (N=454)

<table>
<thead>
<tr>
<th>Fluvac 03.3</th>
<th>Multivariate OR ** Adj.</th>
<th>95%CI</th>
<th>EV (%)</th>
<th>PValue</th>
</tr>
</thead>
<tbody>
<tr>
<td>All: n=454*</td>
<td>0.376</td>
<td>0.183-0.772</td>
<td>62</td>
<td>0.0078</td>
</tr>
<tr>
<td>Influenza A (H1N1)</td>
<td>0.191</td>
<td>0.063-0.578</td>
<td>81</td>
<td>0.0035</td>
</tr>
<tr>
<td>Influenza B (Victoria lineage)</td>
<td>0.877</td>
<td>0.353-2.180</td>
<td>12</td>
<td>0.7762</td>
</tr>
</tbody>
</table>

- **Adjusted IVE was 62% (95%CI 23%-82%):**
  - 81% (95%CI: 42%; 94%) against influenza A(H1N1),
  - 12% (95%CI -118%; 65%) against influenza B (Victoria Lineage).

* The analysis focuses on 454 patients: 1 patient missing vaccination status and 3 patients missing virological diagnosis.
** OR estimates are adjusted on age, sex, chronic diseases, target group, influenza vaccination over the two preceding seasons and number of children in households.
Conclusions

• 2015-16 seasonal influenza vaccine was effective against hospitalized A(H1N1) influenza but not against B (Victoria).

• This lack of protection may result from the mismatch between the vaccine and circulating strains (B Yamagata and B Victoria lineage, respectively).