First estimates of influenza vaccine effectiveness among severe influenza cases, France, 2011/12

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Following a suspected virus-vaccine mismatch, the screening method was used to estimate in almost real time the influenza vaccine effectiveness (VE) against severe cases in high-risk individuals. Data on vaccination status were provided by the influenza severe surveillance system and data on vaccination coverage by the National Social Security Scheme. The analysis showed a decline of the vaccine effectiveness in 2011/12 (VE: 30% (95% CI: 22–39)) compared to 2010/11 (VE: 53% (95% CI: 40–67)).

Introduction

In France, the 2011/12 influenza epidemic started in week 5 of 2012 (30 January–5 February 2012), peaked in week 8 of 2012 (20–26 February 2012), and was dominated by the influenza A(H3N2) virus. In week 6 of 2012, the National Reference Laboratory for influenza reported a possible mismatch between the A(H3N2) vaccine strain and the circulating strains [1]. We used the available surveillance data in France in order to assess in real time the influenza trivalent vaccine effectiveness (VE) against severe cases in high-risk individuals targeted for vaccination (see below).

Methods

In France, a nationwide exhaustive hospital-based surveillance of severe influenza cases has been implemented since the 2009 pandemic [2]. Clinicians are requested to report to the French Institute for Public Health Surveillance (Institut de Veille Sanitaire – InVS) all probable and confirmed influenza cases admitted to intensive care unit (ICU) through a standardised notification form. Confirmed cases are patients positive for influenza by RT-PCR performed on a nasal swab. Age is recorded as a quantitative variable and vaccine status and risk factors targeted by the vaccination as dichotomous variables. Information on the type of underlying medical conditions and on the vaccination date is not collected.

The French influenza vaccination strategy targets individuals aged 65 years old or older and persons below 65 years of age with specific chronic underlying conditions (such as chronic respiratory diseases, diabetes), pregnant women and obese persons [3]. Each autumn, the National Health Insurance Scheme for Employees (Caisse nationale de l'assurance maladie des travailleurs salariés – CNAMTS), the main social security scheme, covering about 85% of the French population, sends an individual vaccination voucher to the population targeted by the influenza vaccination strategy. The voucher allows the recipients to get the vaccine from the pharmacist and its administration by the general practitioner (GP) free of charge. The pharmacist issuing the vaccine returns the voucher to the CNAMTS in order to get refunded. In 2011, pregnant women and obese persons did not receive a voucher if they had no chronic co-morbidities. During the vaccination campaign, the vaccine uptake, based on the voucher return rates, is monitored by CNAMTS which provides InVS with provisional weekly estimates for the population targeted by the vaccination (obese persons and pregnant women excluded), stratified into three age groups: under 65 years, between 65 and 69 years and 70 years old or older.

We estimated the VE against laboratory-confirmed influenza ICU cases through the screening method [4]. The proportion of vaccinated cases (PCV) was provided by the ICU influenza surveillance. A case was defined as an influenza laboratory-confirmed patient with a known vaccination status. The proportions of the population vaccinated (PPV) in the three categories (under 65 years, between 65 and 69 years and 70 years old or older) were provided by the voucher return rates. The data were adjusted on age and sex as a previous analysis based on the same source of data has shown that vaccine coverage was lower among women [5]. VE was calculated using the formula shown and based on a log-linear model, as proposed by Farrington [6].

$$VE = \frac{PPV - PCV}{PPV\,(1-PCV)}$$

The 95% confidence intervals (CI) were estimated through the delta method. Pregnant women and obese persons were excluded from the analysis.

We compared the VE in the 2011/12 season with the estimate for the 2010−11 season obtained through the same method and source of data.

Results

On 31 January 2012, which represents the end date of the vaccination campaign, the provisional influenza vaccination uptakes were 40% in the population under 65 years targeted by the vaccination, 41% in the 65−69 age group and 60% in the age group of individuals aged 70 years old or older, in plateau since mid-December 2011. These results are in line with the 2010/11 CNAMTS final consolidated data.

As of 18 April 2012, 308 severe influenza cases had been notified by the ICU clinicians. Of these, 294 were laboratory-confirmed and are described in the table.

The virus subtype was known for 119 in 288 influenza A cases and A(H3N2) virus accounted for 90% (n=107) of them.

Among the 234 severe influenza cases confirmed in high-risk individuals, the vaccination status was available for 176 cases: 67 under 65 years old, 20 aged between 65-69 years and 89 aged 70 years or more. The proportions of vaccinated cases were 30%, 30% and 43%, respectively. This corresponds to a trivalent VE of 30% (95% CI: 22−39).

In 2010/11, the VE for high-risk individuals was estimated from 239 confirmed severe cases with a known vaccine status and it was 53% (95% CI: 40−67).

Conclusions

Our study shows a significant decrease of the trivalent influenza VE against severe influenza cases in high-risk patients in 2011/12, as compared to the previous season. These data are consistent with the A(H3N2) antigenic variations from the vaccine strain observed by the National Reference Laboratory for influenza. They explain, at least partially, the particularly high number of acute respiratory infections clusters notified in nursing homes in France this season (884 [7] as compared to 153 last year [8]). They also support the World Health Organization's (WHO) recommendation of changing the A(H3N2) strain to be included in the vaccine for the next season [9]. However, the VE point estimate is

lower than the recent estimates yielded by studies performed in general practice sentinel networks (adjusted VE against any type: 55% (95% CI: 3−79) in Spain and adjusted VE against A(H3N2): 43% (95% CI: −0.4 to 67.7) in the European project, Influenza - Monitoring Vaccine Effectiveness (I-MOVE) [10,11]. Although VE is expected to be higher for the prevention of the most severe influenza outcomes, this result may illustrate the fact that the high-risk individuals presenting with severe influenza requiring ICU may be, on average, more immunocompromised and may not respond well to the vaccine as those in general practices for instance. Consolidated data with a narrower interval are expected from the European project, I-MOVE with a comparison between the vaccine efficacy in GP sentinel networks this season and the previous season [12].

The study has however several limitations. Firstly, vaccination dates of the patients were not available. As the vast majority of cases occurred after January 2012 and the vaccine uptake has reached a plateau since December 2011, we assumed that patients were vaccinated more than two weeks before the onset of the disease. Secondly, even though the vaccination coverage was calculated in the population of high-risk individuals, as was the proportion of vaccinated cases, it was not possible to investigate the type and severity of the underlying conditions. We could only stratify the analysis according to sex and age. We assumed that if confounding did occur, it should have affected similarly the results during the two seasons. Thirdly, the vaccine status was missing for 25% (n=58/234) of the high-risk patients. We think that missing data are more likely to occur among unvaccinated patients leading to an underestimation of the VE. In 2010−11, information on vaccination status was unavailable for 34% of the cases. Therefore, the substantial decrease of VE between the two seasons is likely to be real and potentially underestimated. Fourthly, the vaccine coverage data we used are provisional. However, the experience accumulated over the years has shown very little variations between provisional estimates available in March and the definitive figures. It is important to note that coverage data from the other Social Security Schemes (covering about 15% of the population) are usually very close to data from CNAMTS (personal communication, CNAMTS, January 2012).

The study found a decline of the VE in the context of a mismatch of the vaccine strains with circulating viruses

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TABLE

Severe laboratory-confirmed cases of influenza, France, 2011/12 (n=294)

Description	Results	Number of cases for whom the information is available
Male to female sex ratio	1.2:1	292
Mean age (years)	59 (95% CI: 56−61)	290
Number of patients with risk factors	234	290
Number of vaccinated patients	65	222

and showed the usefulness of the screening method for almost real-time monitoring of VE during the influenza season.

Acknowledgements

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