Influenza vaccine effectiveness in Romania 2011/2012: results of a case-control study

Daniela Pitigoi [1,2], Emilia Lupulescu[1], Viorel Alexandrescu[1], Alina Elena Ivanciuc[1], George Necula[1], Maria Elena Mihai[1], Camelia Savulescu[2]

1. NIRDMI Cantacuzino, Bucharest, Romania; 2. University of Medicine and Pharmacy Carol Davila Bucharest, Romania

Background

National Institute of Research and Development for Microbiology and Immunology Cantacuzino participates to the ECDC funded I-MOVE project (Influenza Monitoring Vaccine Effectiveness in Europe) from its first season (2008-2009) with a case-control study based on the national influenza sentinel surveillance network and carried out following an adapted generic protocol provided by ECDC.

Objectives

We aimed to estimate 2011/12 seasonal influenza vaccine effectiveness (IVE) against medically-attended influenza-like illness (ILI) laboratory-confirmed for influenza.
As secondary objective we estimated IVE in the target group for vaccination.

Methods

We conducted a test-negative case-control study embedded in the influenza sentinel surveillance system, between week 48/2011 and week 16/2012. Cases were ILI laboratory confirmed for influenza A(H3N2). Controls were ILI cases testing negative for any influenza. Data collected included demographic and laboratory information, vaccination status and data on different confounding factors, identified in the literature. IVE was calculated as 1 minus the odds ratio for vaccination. A 95% confidence interval (CI) was calculated around the point estimate.

Results

The 2011-2012 influenza season in Romania was mild, with lower ILI /ARI consultation rates and fewer virological influenza detections compared with previous years.

One hundred sentinel GPs (31.9%) from 16 districts (38.1%) participated in the study and 71 recruited at least one case.

A total of 238 ILI patients were enrolled and 207 (87%) were analysed: 107 cases (three vaccinated) and 100 controls (eight vaccinated) (fig 1).

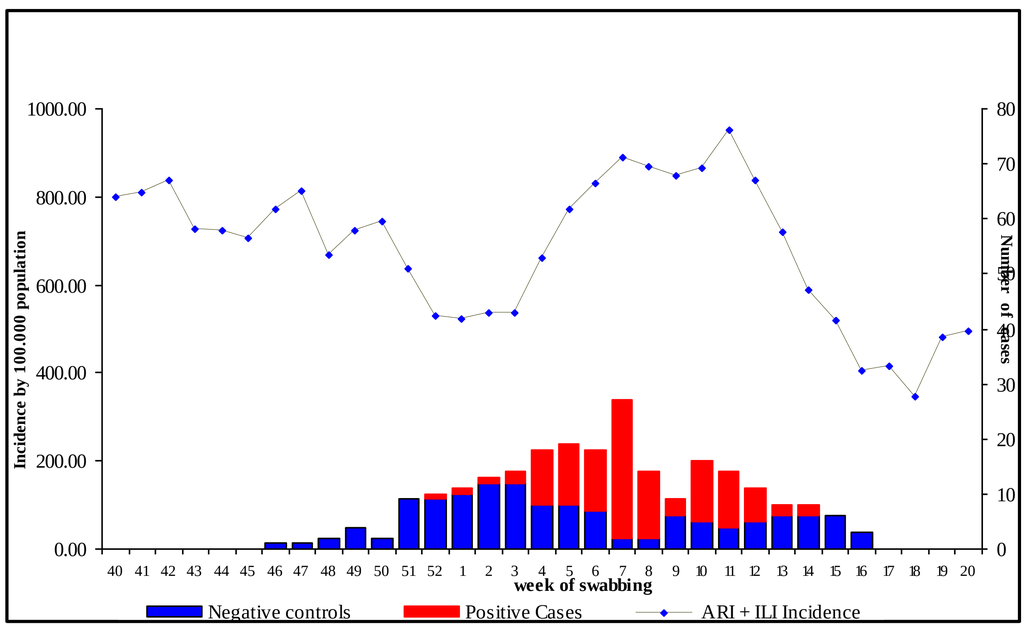

Fig. 1 ARI and ILI evolution vs I-MOVE cases (N=107) and controls (N=100) by week of swabbing in Romania, season 2011-2012

Compared to controls a higher proportion of cases were male, living in urban area and a lower proportion had chronic conditions (p<0.05) (table 1).

Table 1: Characteristics of medically attended Influenza like illnesses laboratory confirmed cases, (n=107) and test-negative controls (n=100), Romania, season 2011-2012

Characteristic	Cases n (%)	Controls n (%)	p value
Sudden onset	107 (100)	100 (100)	-
Fever	104 (97.2)	89 (89.0)	0.019
Headache	93 (86.9)	71 (71.0)	0.005
Malaise	85 (79.4)	54 (54.0)	0.000
Myalgia	86 (80.4)	57 (57.0)	0.000
Cough	100 (93.5)	89 (89.0)	0.255
Sore throat	89 (83.2)	66 (66.0)	0.004
Shortness of breath	15 (14.0)	15 (15.0)	0.841
Mean age (± Standard Deviation)	25.5 ±20.6	30.8±26.8	0.115
Sex: male	60 (56.1)	31 (31.0)	**0.000**
Residence: urban	89 (83.2)	61 (61.0)	**0.000**
At least one hospitalization in the previous year	4 (3.7)	7 (7.0	0.296
More than one GP visit in the previous year	21 (19.6)	26 (26.0)	0.274
Any chronic condition	25 (23.4)	36 (36.0)	**0.046**
Poor functional status	0	0	
Smoking	6 (5.6)	1 (1.0)	**0.067**
Eligible for vaccination	33 (30.8)	45 (45.0)	0.036
Seasonal vaccination 2011/12	3 (2.8)	8 (8.0)	0.103
Pandemic vaccination A(H1N1)pdm2009 in the season 2009/10	6 (5.7)	10 (10.0)	0.244
Any seasonal influenza vaccination in the previous two seasons	8 (7.6)	14 (14.0)	0.154

Results

The overall adjusted IVE for age, sex, residence, chronic conditions, previous seasonal vaccination and month of swabbing was 42% (95% CI: -295, 92) and for patients eligible for vaccination (N= 78) was 40% (95% CI: -534, 94) (fig 2).

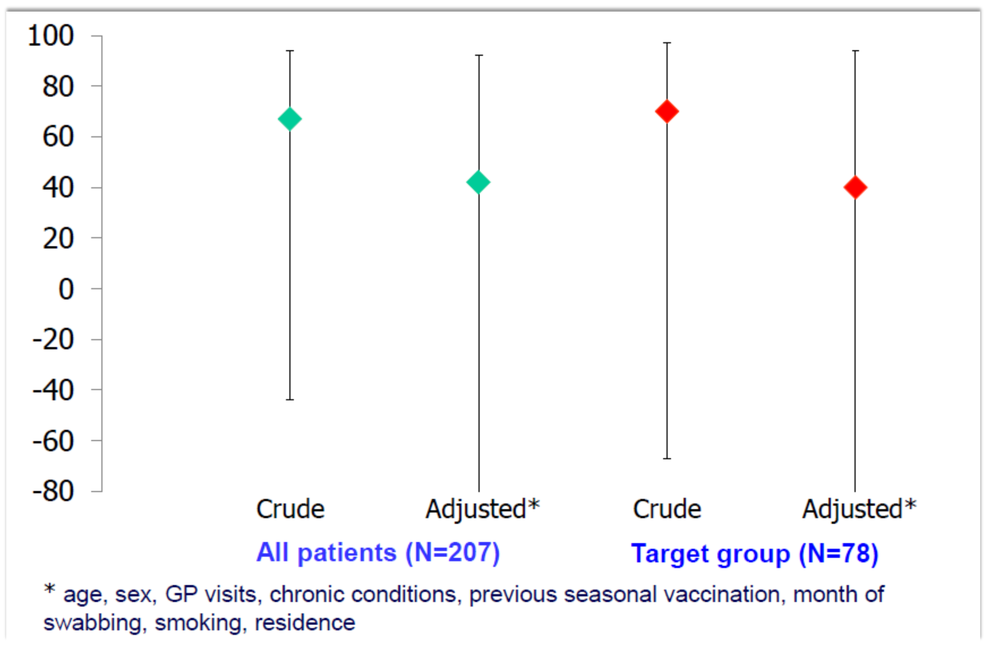

Fig 2. Influenza vaccine effectiveness, 2011-2012

All season was largely dominated by influenza A/H3N2, antigenically similar to vaccine strain and sensitive to NAI, and only a few influenza type B detections (table 2).

Table 2. Antigenic characterisation and antiviral resistance results of samples received in the national influenza surveillance system between week 40/2011 and week 20/2012

		Results
No. of samples tested		755
RT – PCR positive samples		221 (97.7% A/H3 and 5 type B)
Antigenic characterisation		50 - A/H3N2 – A/Perth/16/09 like 1 - influenza type B - B/Bangladesh/3333/07 like
Antiviral resistance testing	Phenotypic (chemiluminescence)	49 isolates were tested- all were sensitive to oseltamivir and zanamivir
	Genotypic (sequencing)	5 phenotypically sensitive isolates (4 A/H3N2 and one influenza type B) were also tested genotypically for antiviral resistance – the results confirmed the absence of antiviral resistance substitutions

From the genetic characterization (HA gene) of circulating viruses in 2011-2012 influenza season, we established that 20 A/H3N2 strains fell into Victoria/208 genetic clade. All HA gene sequences had the following substitutions: K62E, K144N (potential glycosilation site) and T212A – shared with Perth/16 genetic clade. Phylogenetic analysis of HA genes revealed that 14 strains belong to genetic group 6 – prototype strain A/Iowa/19/2010, having the following characteristic substitutions: D53N, Y94H, S199A, I230V and E280A; 5 strains fell in genetic group 3C - A/Hong Kong/3969/2011 with substitutions: T48I, A198S, V223I and N312S. A single strain fell in genetic group 3A – A/Stockholm/18/2011 (N145S, V223I and D487N).

All four A/H3N2 NA gene sequences had two common substitutions - S367N and K369T. The single influenza B (NA gene) fell in clade 3 - B/Bangladesh/3333/2007 (B/Yamagata genetic line).

Conclusions

The participation in the I-MOVE multicentre case-control study allowed developing the vaccine effectiveness study in Romania.

The results suggest a moderate protection of the 2011/12 seasonal influenza vaccine against ILI medically-attended taking into account the small sample size and the low vaccination coverage (3%).

Repeating the study in the further seasons will give us the opportunity to investigate other aspects of influenza epidemiology and vaccination in Romania.

Acknowledgements

We are grateful to all participating sentinel GPs in the study and the following local level epidemiologists: Elena Duca (PHD Iasi), Suzan Ibram (PHD Constanta), Dan Decebal (PHD Prahova), Carmen Sima and Ecaterina Szekely (PHD Maramures), Camelia Truica (PHD Calarasi), Ella Marialaki (PHD Mures), Mariana Ioan (PHD Galati), as well to the national level epidemiologists Adriana Pistol and Rodica Popescu (National Institute of Public Health - NCSCCD, Bucharest, Romania).

We also thank to Esther Kissling, Marta Valenciano, Alain Moren (EpiConcept, France) and Bruno Ciancio (ECDC, Stockholm) for their support in the project.