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Seasonal influenza vaccine effectiveness against influenza in 2012–2013: A hospital-based case-control study in Lithuania

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ABSTRACT

Background: Due to scarce information on seasonal influenza vaccine effectiveness (SIVE) against severe clinical influenza outcomes in risk populations, we conducted a case-control study to assess its effects against laboratory-confirmed influenza in hospitalized patients during the 2012–2013 influenza season.
Methods: We conducted a test-negative case-control study among ≥18 years old patients with influenza-like illness (ILI) hospitalized in two Lithuanian hospitals. Cases were influenza A(H1N1), A(H3) or influenza B positive by RT-PCR, and controls were influenza negative. Additional demographic and clinical data to assess the role of confounding were collected. SIVE and its confidence intervals (95% CI) were estimated by using multivariate logistic regression as $(1 - \mathrm{OR}) \times 100\%$.
Results: The sample consisted of 185 subjects. Seasonal influenza vaccine uptake was 5%. Among 111 (60%) influenza positive cases, 24.3% were A(H1N1), 10.8% were A(H3) and 24.3% were influenza B cases. Unadjusted SIVE was 79% (95% CI −6% to 96%) and after the adjustment it increased to 86% (95% CI 19% to 97%).
Conclusions: Seasonal influenza vaccination in 2012–2013 was associated with reduced occurrence of laboratory-confirmed influenza, but due to low sample size the estimate of SIVE is imprecise. Given high prevalence of influenza in hospitalized ILI cases and low influenza vaccination coverage, there is a need to increase influenza vaccination rates.

1. Introduction

Influenza virus might cause severe infection and lead to complications, such as pneumonia and/or exacerbations of underlying medical conditions that may even require hospitalization [1–4]. As a prevention measure, seasonal influenza vaccination is recommended to persons with an increased risk of attracting and/or spreading influenza and suffering from its complications [5].

In Lithuania, seasonal influenza vaccination is recommended for everyone, but especially individuals of 65 years old and older, pregnant women, individuals with chronic medical conditions and their family members and/or caregivers, health care workers, and nursing- and social-care-home residents. For the mentioned risk groups the vaccine is provided free of charge [6].

Seasonal influenza vaccine effectiveness against different influenza outcomes appears to be low to moderate [7–11]. There are several reasons that could at least partly explain such effects found in the observational studies. First, the target populations that actually receive influenza vaccine are relatively more frail and due to immune senescence the vaccine might be less effective. Moreover, the vaccine effectiveness might be biased and underestimated when the vaccine does not match circulating viruses or when the timing of influenza peak activity appears before the influenza

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Table 1
Study inclusion criteria.

Inclusion criteria
Hospitalized for at least 24 h
≥18 years old
Willing to participate
Able to communicate
Give informed consent
Lithuanian resident for ≥6 months
A swab taken ≤7 days after the self-reported disease onset
Not tested positive for any influenza virus in the current season before the inclusion
Not institutionalized
No contra-indications for influenza vaccination
Suffering from influenza-like-illness: at least one of the systemic symptoms (fever, myalgia, headache, malaise) and at least one of the respiratory symptoms (cough, sore throat, shortness of breath)

vaccinations have been completed. On the contrary, the healthy user effect or when influenza peak activity was relatively late and/or low might lead to an overestimation of vaccine effectiveness. In addition, different influenza viruses might dominate in different regions or countries, which might also contribute to the diversity of seasonal influenza vaccine effectiveness estimates.

In general, studies assessing seasonal influenza vaccine effectiveness against laboratory-confirmed influenza outcomes are scarce. Even fewer studies have been conducted to assess seasonal influenza vaccine effectiveness to prevent influenza outcomes in frail individuals, such as hospitalized patients [9,12]. Therefore, further studies assessing the effects of seasonal vaccinations against laboratory-confirmed influenza-related outcomes to be able to provide more solid evidence about its effects in the risk populations are necessary. We therefore conducted a case-control study to assess the effectiveness of seasonal influenza vaccine to prevent laboratory-confirmed influenza in hospitalized patients in Lithuania.

2. Methods

2.1. Setting, study population and recruitment procedure

This was a test-negative case-control study conducted in community-dwelling 18 years or older adults who were admitted to one of the infectious disease units of the Infectious Diseases and Tuberculosis Hospital Affiliate of Public Institution Vilnius University Hospital Santariskiu Klinikos, Vilnius (VU hospital) and the Department of Infectious Disease of Lithuanian University of Health Sciences, Kaunas (LUHS hospital). Only the subjects presenting with ILI symptoms (at least one of the systemic symptoms: fever, myalgia, headache or malaise, and at least one of the respiratory symptoms: cough, sore throat, or shortness of breath) were included in the study. The study period was October 21, 2012 to April 16, 2013, which overlapped with influenza season based on the national surveillance data (see Fig. 1, [13]).

Upon admission, ILI patients were screened for a list of inclusion criteria (see Table 1). The eligible patients were then contacted by the trained study physician, who provided information about the study (written and oral) and asked to sign an informed consent. Nasal and/or throat swabs were taken and tested for influenza, and some demographic and clinical information was collected from the patients who agreed to participate and signed an informed consent.

2.2. Study outcome

The study outcome was laboratory-confirmed seasonal influenza confirmed by real time polymerase chain reaction (RT-PCR). Cases were patients who tested positive, and the controls were patients who tested negative for influenza A(H1N1), A(H3) or influenza B viruses that were circulating during the 2012–2013 season [14]. The outcome assessment was blinded for the exposure status.

2.3. Exposure

Study exposure was self-reported seasonal influenza vaccination status that was obtained by questionnaire before the outcome assessment. In accordance with previous observational influenza vaccine studies, we considered a patient as vaccinated when between the self-reported onset of disease and vaccination date there were 14 days or more [9]. We considered a patient unvaccinated when there were less than 14 days between the self-reported onset of disease and vaccination date, or when vaccination status was reported as negative.

In Lithuania, influenza vaccination is centrally purchased by the Ministry of Health and provided free of charge by the general practitioners or state vaccination offices for the risk groups [15]. Private clinics provide influenza vaccinations at person's own cost [15]. Sometimes influenza vaccinations are provided by the employers, who purchase the vaccine from the providers themselves. For the 2012–2013 influenza season, one dose of a formaldehyde-inactivated split-virion trivalent influenza vaccine VAXIGRIP® by Sanofi Pasteur [16] including A/Victoria/361/2011(H3N2), B/Wisconsin/1/2010, and A/California/7/2009 (H1N1)pdm09 influenza virus strains was used [17].

2.4. Covariates

Information on several patient characteristics was collected from the medical records and patient self-reports. Demographic information on age and sex came from the medical records; smoking status, living in urban or rural areas, occupation and education status were collected from self-reports. Clinical characteristics collected from the medical records included antiviral use during current hospitalization, whether during the hospitalization a patient was transferred to the intensive care unit due to disease exacerbation, and length of hospitalization. Self-reported clinical information included occurrence of underlying medical conditions (cardiovascular, lung, renal, rheumatologic, endocrine diseases and diabetes, hematologic and non-hematologic cancer, immunodeficiency and transplantation, dementia, stroke, anemia; see Appendix 1 for disease codes according to International Classification of Diseases, 10th, Clinical Modification), obesity (BMI ≥ 30), number of hospitalizations due to the underlying medical conditions in the preceding year, number of visits to the general practice due to disease or its exacerbation and not repeated prescriptions in the preceding year, and Barthel score to assess daily functioning (the highest score of 100 indicating no limitations to daily functioning).

2.5. Laboratory analysis

When the nasal and/or throat swabs were taken, they were kept in the freezer at low temperatures (−40 °C and −70 °C in Vilnius and Kaunas hospitals respectively). At the end of the study, the samples were mailed to the University Medical Center Groningen laboratory of Clinical Virology in dry ice in less than 24 h, where they were analyzed by a laboratory developed RT-PCR as has been described before [18]. In short, influenza RNA was isolated using the Magna Pure LC Total Nuclei Acid Isolation kit with external lysis protocol (Roche Diagnostics, Indianapolis, USA). Both influenza A and influenza B were detected by generic RT-PCR assay targeting