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Influenza vaccine effectiveness to prevent influenza-related hospitalizations and serious outcomes in Canadian adults over the 2011/12 through 2013/14 influenza seasons: A pooled analysis from the Canadian Immunization Research Network (CIRN) Serious Outcomes Surveillance (SOS Network)

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Abbreviations: VE, vaccine effectiveness; ICU, intensive care unit; MV, mechanical ventilation; TIV, trivalent influenza vaccine; y, years of age; CIRN, Canadian Immunization Research Network; SOS, Serious Outcomes Surveillance; ILI, influenza-like-illness; ARI, acute respiratory illness; CAP, community-acquired pneumonia; COPD, chronic obstructive pulmonary disease; NP, nasopharyngeal; RT, reverse transcriptase; PCR, polymerase chain reaction; CCfV, Canadian Center for Vaccinology; OR, odds ratio; CI, confidence interval; BMI, Body Mass Index; FI, frailty index; LTCF, long-term care facility; NS, Nova Scotia; ON, Ontario; AB, Alberta; BC, British Columbia; QC, Quebec; MB, Manitoba; NB, New Brunswick; GIHSN, Global Influenza Hospital Surveillance Network.

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ABSTRACT

Background: Ongoing assessment of influenza vaccine effectiveness (VE) is critical to inform public health policy. This study aimed to determine the VE of trivalent influenza vaccine (TIV) for preventing influenza-related hospitalizations and other serious outcomes over three consecutive influenza seasons.
Methods: The Serious Outcomes Surveillance (SOS) Network of the Canadian Immunization Research Network (CIRN) conducted active surveillance for influenza in adults ≥16 years (y) of age during the 2011/2012, 2012/2013 and 2013/2014 seasons in hospitals across Canada. A test-negative design was employed: cases were polymerase chain reaction (PCR)-positive for influenza; controls were PCR-negative for influenza and were matched to cases by date, admission site, and age (≥65 y or <65 y). All cases and controls had demographic and clinical characteristics (including influenza immunization status) obtained from the medical record. VE was estimated as 1-OR (odds ratio) in vaccinated vs. unvaccinated patients × 100%. The primary outcome was VE of TIV for preventing laboratory-confirmed influenza-related hospitalization; secondary outcomes included VE of TIV for preventing influenza-related intensive care unit (ICU) admission/mechanical ventilation, and influenza-related death.
Results: Overall, 3394 cases and 4560 controls were enrolled; 2078 (61.2%) cases and 2939 (64.5%) controls were ≥65 y. Overall matched, adjusted VE was 41.7% (95% Confidence Interval (CI): 34.4–48.3%); corresponding VE in adults ≥65 y was 39.3% (95% CI: 29.4–47.8%) and 48.0% (95% CI: 37.5–56.7%) in adults <65 y, respectively. VE for preventing influenza-related ICU admission/mechanical ventilation in all ages was 54.1% (95% CI: 39.8–65.0%); in adults ≥65 y, VE for preventing influenza-related death was 74.5% (95% CI: 44.0–88.4%).
Conclusions: While effectiveness of TIV to prevent serious outcomes varies year to year, we demonstrate a statistically significant and clinically important TIV VE for preventing hospitalization and other serious outcomes over three seasons. Public health messaging should highlight the overall benefit of influenza vaccines over time while acknowledging year to year variability.
ClinicalTrials.gov Identifier: NCT01517191.

1. Introduction

The seasonal influenza vaccine is a key tool for the prevention of influenza and influenza-related serious outcomes in Canada. Public messaging around the benefits of receiving an influenza vaccination, especially for those individuals at increased risk of influenza virus infection and associated complications, occurs each influenza season [1]. However, recent influenza seasons in Canada (and globally) have been marked by low and variable influenza vaccine effectiveness (VE) as observed by sentinel influenza surveillance networks examining medically-attended influenza in both outpatient and inpatient settings [2–8]. In light of this data, and controversy over the potential negative impact of repeated influenza vaccination [9], this public health message has become diluted.

Influenza is an unpredictable virus characterized as a heterogeneous disease which differentially affects individuals according to their age, health status, as well as their access to care. Not only is influenza infection expected to differ between individuals, but even consecutive influenza seasons may have different virus epidemiology, and varying degrees of antigenic match of the circulating epidemic strain to corresponding vaccine component. Therefore, accurately assessing public health benefit of the influenza vaccine requires accounting for these disparities and investigating all clinically relevant outcomes. In this study, we use influenza surveillance data from The Canadian Immunization Research Network's (CIRN) Serious Outcomes Surveillance (SOS) Network, which conducts active influenza surveillance in hospitals across Canada. The SOS Network has the ability to estimate influenza VE for preventing influenza-related hospitalizations, but also to examine VE against more serious outcomes associated with influenza hospitalizations, such as intensive care unit (ICU) admission, mechanical ventilation (MV), and death. These outcomes may be more clinically relevant for older adults, whose influenza-related complications during hospitalization can lead to other serious health outcomes including functional declines, disabilities or death.

In order to account for this complex disease and the impact of vaccination fluctuating across seasons, here we assess the VE of the trivalent influenza vaccine (TIV) for preventing influenza-related hospitalizations and serious outcomes over three consecutive influenza seasons in Canada. VE estimates are further segregated by age group (≥65 and <65 years of age (y)) and by influenza type/subtype.

2. Methods

2.1. Hospital based surveillance

The CIRN SOS Network was established in 2009 to prospectively monitor seasonal influenza VE for the prevention of laboratory-confirmed influenza hospitalizations in adults ≥16 y [10] (ClinicalTrials.gov Identifier: NCT01517191). In this study, patient data were pooled across three influenza seasons: 2011/2012, 2012/2013, and 2013/2014. During each season the size of the SOS Network fluctuated, but generally represented 9000 to 15,000 acute care hospital beds across 5–7 Canadian provinces: British Columbia, Alberta, Manitoba, Ontario, Quebec, Nova Scotia and New Brunswick.

Starting November 15 of each year, SOS network monitors began enrolling hospitalized patients diagnosed with influenza through routine testing administered as standard of care [11]. Following a week with two or more positive influenza tests in the local hospital site or public health laboratory, active surveillance for influenza began where monitors reviewed all daily admissions of adult patients (≥16 y) to medical wards and medical and

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