Impact of Prior Season Influenza Vaccination on Influenza Vaccine Effectiveness (VE): A Preliminary Analysis Over Four Seasons from the Serious Outcomes Surveillance (SOS) Network of the Canadian Immunization Research Network (CIRN)


Background

• Influenza is an acute respiratory illness which represents a major burden of disease in Canada; every year 10-25% of Canadians contract influenza, which results in thousands of deaths and hospitalizations [1-4].

• The Public Health Agency of Canada’s (PHAC) National Advisory Committee on Immunization (NACI) recommends most Canadians get vaccinated with seasonal influenza vaccine every year [5].

• Variability in annual influenza vaccine effectiveness (VE) estimates have led to hypotheses about the factors that could influence estimates, including whether receiving repeated influenza vaccinations can inhibit immune responses to influenza vaccinations in future [6-9].

• Impact of prior influenza vaccination on seasonal influenza VE is expected to vary by strain according the antigenic distance between vaccine components and circulating strains [10].

• We investigated this association by examining the impact of prior season influenza vaccination on the subsequent year’s VE for preventing influenza-associated hospitalizations in four recent influenza seasons in Canada.

Methods

SOS Network:

• 2011/2012-15: 15-45 academic and community hospitals across Canada. Active surveillance for influenza infection in adults (≥16 years old) (Starting Nov 15 each season). ClinicalTrials.gov identifier: NCT01517191.

Enrollment:

• Nasopharyngeal (NP) swab obtained from all patients with an admitting diagnosis of respiratory infection or symptom, exacerbation of COPD/asthma, CAP, unexplained sepsis, or cardiac/respiratory diagnosis with fever (≥37.5°C).

• All NP swabs tested for influenza A & B by PCR.

• Influenza typing and B lineage characterization performed at CIRN SOS Central Lab, CCIV, Halifax, NS.

Influenza Cases: Adult patients (≥16 years of age) with positive test for influenza whose admission is attributable to influenza or a complication of influenza.

Test-Negative Controls: Consenting adult patients (≥16 years of age) at same site with:

• diagnosis compatible with influenza (i.e. eligible for NP swab at admission),

• NP swab obtained within 7 days of onset of symptoms, and test negative for influenza,

• Admission date within 14d of DOA of case.

• Cases and controls were enrolled without consent if waiver of consent was granted by local REB.

Data collected:

• Demographics, prior chronic illness (preceding current admission), vaccination status in prior and current year, details of presenting illness. Frailty Index, hospitalization details including management and healthcare utilization at discharge and 30 day post-discharge.

Statistical Analysis

• Cases/controls were divided into 4 categories of vaccination status:

1. Vaccinated in neither season (REFERENT)

2. Vaccinated in current season only

3. Vaccinated in prior season only

4. Vaccinated in both current and prior season

• Odds Ratios (ORs) and corresponding 95% Confidence Intervals (CIs) for influenza outcome were calculated using conditional logistic regression. Final adjusted models were created using backwards stepwise selection at a significance level of p<0.05 with variables that were significantly associated (p<0.1) with influenza outcome in univariate models.

• ORs and corresponding 95% CIs were converted into VE using the following formula:

\[ VE = \frac{1 - OR}{1} \times 100\% \]

Results

2012/2013 Influenza Season

VE for preventing influenza H3N2 associated hospitalizations

Prior Yearly Only: 46.5% (CI: 22.8-67.4)

Both Seasons: 62.1% (CI: 41.8-77.5)

2013/2014 Influenza Season

VE for preventing influenza H1N1 associated hospitalizations

Prior Yearly Only: 41.7% (CI: 12.3-65.8)

Both Seasons: 55.9% (CI: 31.9-73.2)

VE for preventing influenza B associated hospitalizations

Prior Yearly Only: 34.3% (CI: 6.1-56.2)

Both Seasons: 53.0% (CI: 30.9-70.9)

Discussion

• Overall there was some evidence that prior seasonal influenza vaccination could impact subsequent season influenza VE, but this varied considerably between seasons and strains examined. Additionally, wide and overlapping 95% CI’s limit any definitive conclusions beyond trends.

• The largest negative impacts were observed in the 2012/2013 season and the 2014/2015 season, both seasons where influenza A H3N2 was the dominant circulating strain.

• In 2011/2012, in which there was a sufficient level of B viruses circulating, being vaccinated in both seasons tended to result in a high VE in the current season.

• In seasons where the level of H1N1 viruses circulating was sufficient (2011/12, 2013/14), being vaccinated in both seasons resulted in a higher VE in the current season.

Conclusions

Impact of prior season vaccination varied considerably in magnitude and direction by strain and by season. Non-significant findings and the possibility of unmeasured factors should lead to cautious interpretation of these results. Further investigation is needed to examine this phenomenon in randomized trials and laboratory studies.

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