2013 CFID Undergraduate Summer Research Award Proposal

Predictors of Influenza Vaccine Failure and Impact of Influenza Immunization on Severity of Illness and Outcomes among Hospitalized Canadian Adults

Applicant: Riddell, Tara, Dalhousie University

Supervisor: Shelly McNeil MD

Background: The Public Health Agency of Canada/CIHR Influenza Research Network (PCIRN) Serious Outcomes Surveillance Network was established in 2009 to conduct active surveillance for influenza amongst Canadian adults admitted to sentinel hospitals in order to better define influenza burden of disease and to monitor influenza vaccine effectiveness against serious outcomes. The Network has grown from 8 hospitals in 5 Provinces in 2009 to 40 hospitals in 7 Provinces in 2012, encompassing 17,000 hospital beds.

Between 2009/10 and 2012/13, the SOS Network has collected detailed data on approximately 1500 cases of hospitalized, PCR-confirmed seasonal influenza and 400 cases of hospitalized pandemic influenza. Employing a test-negative case-control design, the SOS Network has estimated a seasonal vaccine effectiveness of 34% (90% CI 24-74%) in 2012/13 (based on data available to Jan 10, 2013) to 55% (90% CI 24-74%) in 2010/11, and pandemic vaccine effectiveness of 71% (95% CI 40-86%) for the prevention of hospitalization.

While vaccine effectiveness of 34-55% is clearly not optimal, prevention of one third to one half of influenza-related hospitalizations is nonetheless an important contribution to public health. Despite this, suboptimal vaccine effectiveness is the subject of much negative attention in the media and contributes to inadequate uptake of vaccines among Canadians who are at risk for serious influenza infections, complications, or even death.

By better assessing the clinical characteristics of patients admitted with influenza despite vaccination, it may be possible to identify host factors predictive of failure of conventional influenza vaccines in order to inform policy recommendations for the use of newer, more immunogenic but also more costly vaccines (such as intradermal or adjuvant vaccines). Understanding the benefit of influenza immunization, if any, in attenuating disease severity or improving outcomes in those who acquire influenza despite immunization, is important in quantifying the overall health and economic benefits of immunization. A better understanding of benefits of immunization on outcomes may improve patient and provider uptake of vaccine recommendations.

Study Objectives:

1) To examine risk factors impacting severity of disease and influenza vaccine effectiveness in adults
2) To describe the clinical characteristics of vaccinated adults hospitalized with influenza
3) To assess risk factors for severe disease (ICU admission or death) among vaccinated adults hospitalized with influenza
4) To assess the impact of immunization on severity of disease and outcomes in adults admitted to hospital with lab-confirmed influenza

Methods: Data collected across the SOS Network in 2010/11- 2012/13 will be analyzed. Cases will be defined as adult patients (aged ≥16y) admitted to a participating hospital with community acquired PCR-

-confirmed influenza. Controls will be defined as patients admitted to the same SOS hospital whose presenting illness was consistent with possible influenza (e.g. new acute respiratory disease) but in whom PCR for influenza was negative; PCR must have been collected within seven days of onset of symptoms. Cases and controls will be considered vaccinated if they report receipt of influenza vaccine ≥14 days prior to onset of illness. Where possible, immunization will be verified with the immunization provider.

Objective 1) In order to assess risk factors for severe disease amongst hospitalized adults, PCR-positive cases will be compared to PCR-negative controls matched by age range (≥65y vs <65y) and date of enrollment (± 2 weeks of case). Risk factors for influenza among patients hospitalized with cardio-respiratory disease will be assessed by comparing cases and controls. Risk factors for severe outcomes due to influenza including requirement for admission to ICU, need for mechanical ventilation, death, and functional impairment at one month post-discharge will also be explored. Unless otherwise specified, 95% confidence intervals will be constructed and statistical tests carried out at level ± = 0.05. Continuous variables will be summarized by means and associated t confidence intervals. Categorical variables will be summarized as counts and associated proportions, and binary outcomes will be summarized as proportions and associated confidence intervals. In addition to the univariate analyses, adjustments for covariates will be carried out via logistic regressions.

Objective 2) A descriptive analysis of characteristics of vaccinated patients admitted with lab-confirmed influenza including but not limited to age, gender, functional status/frailty, social determinants of health, and medical comorbidities will be provided.

Objective 3) In order the assess risk factors for severe diseases among vaccinated adults, patients who died or went to ICU will be compared to cases not experiencing these outcomes. Risk factors for severe outcomes due to influenza, including functional impairment at one month post-discharge, will also be explored. Unless otherwise specified, 95% confidence intervals will be constructed and statistical tests carried out at level ± = 0.05. Continuous variables will be summarized by means and associated t confidence intervals. Categorical variables will be summarized as counts and associated proportions, and binary outcomes will be summarized as proportions and associated confidence intervals. In addition to the univariate analyses, adjustments for covariates will be carried out via logistic regressions.

Objective 4) In order to assess the impact of immunization on severity of influenza in those who fail immunization, outcomes will be compared between vaccinated and unvaccinated hospitalized adults with PCR-confirmed influenza. Outcomes to be assessed will include length of stay, ICU admission, mechanical ventilation, in-hospital complications, and functional status at 30 days post discharge (using the validated Frailty Index). In addition to univariate analyses, adjustments for covariates will be carried out via logistic regression.

Ethical considerations: This study has been approved by the Research Ethics Boards of each participating Network hospital and patients of their legally authorized representative have signed written informed consent to participate.