Poster Abstract Program
Programme des résumés d'affiches

Safety of H1N1 pandemic vaccines during the 2009 outbreak in Manitoba, Canada

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Introduction/Background: The 2009 pandemic was caused by influenza virus A/H1N1 and led to a mass vaccination campaign in Manitoba, Canada. Data on safety of the H1N1 vaccines used during the campaign is scarce. Hence, we aimed to assess this.

Methods: We conducted a matched cohort study of vaccinated and unvaccinated subjects using Manitoba Health's vaccine registry with hospital and physician claims databases. We calculated the age-standardized incidence rates and ratios (ASRs and ARRs) of certain adverse events of special interest (AESIs; anaphylaxis, Bell's palsy, demyelination disorders, encephalitis, myelitis and encephalomyelitis [EME], Guillain-Barré syndrome, neuritis, vasculitis and narcolepsy) following influenza vaccination between September 15, 2009 and March 15, 2010.

Results and Analysis: The H1N1 vaccine was not significantly associated with an increased risk of AESIs except for convulsions and EME. The ASR per 100,000 person-years in convulsions was 103.1 (95% confidence interval 90.5-115.7) for the vaccinated versus 75.0 (61.2-88.9), for the unvaccinated. A larger ARR was observed following TIV (trivalent influenza vaccine) alone, 1.9 (1.3-2.9), than H1N1 vaccine alone, 1.3 (1.0-1.7). Of the 10 hospitalizations for EME, 9 were among individuals who received H1N1 vaccine alone and none in the unvaccinated. There was an increase in convulsions, standardized incidence ratio (SIR multiplied by 100), 120 (106-134), and EME, 238 (114-437), in vaccinated individuals compared to the general population. The increase was higher following TIV alone, 129 (101-162) than H1N1 alone, 118 (101-135) in convulsions.

Conclusions and implications for vaccinology: Vaccination with pandemic H1N1 vaccine is not associated with an increased risk of AESIs, except for convulsions. A follow-up study showed that the increase of EME hospitalizations was not related to H1N1 vaccine use during the pandemic.

Investigating the effect of seasonal influenza vaccination on the development of anesthesia/paresthesia, headaches, and seizures, Canadian Immunization Research Network (CIRN), 2012-2016.

Ahmed M, Valiquette L, Vanderkooi O, Coleman B, De Serres G, Top K, Isenor J, Kellner J, McCarthy A, Singer J, Naus M, Bettinger J

Introduction/Background: Anesthesia/paresthesia (numbness, tingling, pins and needles, decreased sensation, or burning sensations anywhere in the body) was reported after the 2009 pandemic influenza vaccine from several countries, including Canada. Headaches, as an adverse event following immunization (AEFI), were also reported in the United States as the most common AEFI following seasonal influenza vaccination (SIV) between 1990 and 2014. Our aim is to determine risk of developing select neurologic events in the presence and absence of SIV.

Methods: Data were analyzed from CIRN's Canadian National Vaccine Safety Network that annually analyses safety data before core weeks of the SIV campaign. Events were self-reported and prevented daily acitivity, led to absenteeism, or medical attention. Controls were previous year vaccinees. Total sample size for investigating anesthesia/paresthesia was 107,565 from 2012-2016, and 97,420 for investigating headaches and seizures from 2013-2016. Multivariable logistic regression was used to determine the association between SIV and developing anesthesia/paresthesia or headaches adjusted for gender, age group, reporting center, and year. Fisher's exact test was used to measure risk of developing seizures.

Results and Analysis: 104 (0.10%) participants reported anesthesia/paresthesia; 63 (0.09%) versus 41 (0.11%) in vaccinees and controls, respectively. Headaches were reported by 1,361 (1.40%) participants; 907 (1.48%) versus 454 (1.26%) in vaccinees and controls, respectively. Adjusted OR of SIV on reporting anesthesia/paresthesia was 0.89 (95% CI= 0.60, 1.32), and headaches was 1.21 (95% CI=1.08, 1.36). Three participants were identified with seizures; difference in proportions between groups was not statistically significant (p= 0.301).

Conclusions and implications for vaccinology: Results are reassuring on safety of SIV. The significant association between SIV and headaches are comparable to results from clinical trials. No associations were found for anesthesia/paresthesia and seizures. Anesthesia/paresthesia was a rare AEFI (≥0.01 and <0.1%), headaches were common (≥1% and <10%), and seizures were a very rare AEFI (<0.01%). Ongoing monitoring is crucial to maintain confidence in SIV safety.

Does consecutive influenza vaccination reduce protection against influenza: A systematic review and meta-analysis

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Introduction/Background: Vaccination against influenza on an annual basis is widely recommended, yet recent studies suggest consecutive vaccination may reduce vaccine effectiveness (VE). We aimed to assess whether when examining the entirety of existing data consecutive influenza vaccination reduces VE compared to current season influenza vaccination.

Methods: MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL) from inception to April 26, 2017, along with citations of included studies, were searched. Randomized, controlled trials (RCTs) and observational studies of children, adults and/or the elderly that reported laboratory-confirmed influenza infection over 2 or more consecutive influenza seasons were eligible. Data related to study characteristics, participant demographics, cases of influenza infection by vaccination group and risk of bias assessment was extracted in duplicate.

Results and Analysis: Five RCTs involving 11,987 participants did not show a significant reduction in VE when participants vaccinated in two consecutive seasons (VE 71%, 95% CI 62 – 78%) were compared to those vaccinated in the current season (VE 58%, 95% CI 48 – 66%) (odds ratio [OR] 0.88, 95% CI 0.62 – 1.26, p=0.49, I2=39%). Twenty-eight observational studies involving 28,627 participants also did not show a reduction (VE for two consecutive seasons 41%, 95% CI 30 – 51% compared to VE for current season 47%, 95% CI 39 – 54%; OR 1.14, 95% CI 0.98 – 1.32, p=0.09, I2=63%). Results from subgroup analyses by influenza type/subtype, vaccine type, age, vaccine match and co-morbidity support these findings; however, dose-response results were inconsistent.

Conclusions and implications for vaccinology: Available evidence does not support a reduction in VE with consecutive seasonal influenza vaccination, supporting current vaccination strategies. Our certainty in this evidence is very low: the findings are imprecise and do not rule out the possibility of reduced effectiveness.

B cell responses to 13-valent pneumococcal conjugate vaccine in adult patients with severe chronic kidney disease

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Introduction/Background: In Canada, 23-valent pneumococcal polysaccharide vaccine (PPV23) is recommended for adults with chronic kidney disease (CKD). Some data suggest that previous PPV23 immunization may affect responses to subsequent immunization with 13-valent pneumococcal conjugate vaccine (PCV13) due to depletion of the peripheral memory B cell pool. Our objective is to compare numbers of circulating memory B cells and antibody secreting cells (ASC) in adults with severe CKD without previous pneumococcal vaccination (group-1) and previously immunized with PPV23 (group-2).

Methods: Fifty-nine adults with severe CKD received one dose of PCV13 (group-1, n=23, group-2, n=36). Blood was collected pre- and 7 days post-immunization. Proportions of B cells (CD19+) and subpopulations: naïve (IgM+CD27-), IgM memory (IgM+CD27+), class switched (IgM-CD27-), class switched memory (IgM-CD27+), B-1a (CD5+) and B-1b (CD5-) were determined by flow cytometry analysis. Absolute cell numbers were calculated using lymphocyte counts. ASC specific for serotypes 6B and 14, and total IgG were determined using ELISPOT.

Results and Analysis: Pre-immunization, group-1 had a significantly greater proportion of IgM-CD27+ cells (28.8+/-4.5%) compared to group-2 (19.4+/-3.2%), p=0.04, group-1 also had significantly greater absolute numbers of IgM-CD27+ (3.6+/-0.7x10^7/L) compared to group-2 (1.7+/-0.3x10^7/L), p=0.01. Although post-immunization proportions of all subpopulations were not significantly different between the groups, group-1 had a greater absolute number of IgM-CD27- than group-2, i.e. 2.9+/-0.8x10^7/L vs. 1.3+/-0.1x10^7/L, p=0.02 and IgM-CD27+ cells, i.e. 4.0+/-0.1x10^7/L vs. 1.7+/-0.2x10^7/L, p=0.03, correspondingly. No significant differences in numbers of antigen specific or total IgG ASC were detected.

Conclusions and implications for vaccinology: Based on preliminary analysis, it appears that previous immunization with PPV23 has a negative effect on class switched B cells and class switched memory B-cell subpopulations in CKD adults immunized with PCV13. The data suggest that CKD patients previously immunized with PPV23 may need additional doses of PCV13. Results of the study will aid in optimization of pneumococcal immunization schedules for adults with severe CKD.

Immunogenicity and safety of the 13-valent pneumococcal conjugate vaccine compared to 23- valent pneumococcal polysaccharide in immunocompetent adults: A systematic review and meta-analysis

Vadlamudi N, Parhar K, Malana L, Kang A, Marra F

Introduction/Background: Despite the use of 23 valent –pneumococcal polysaccharide vaccine (PPV23) in adults from 1980s, there is substantial morbidity and mortality in elderly due to pneumococcal infections. Since 2010, the 13-valent pneumococcal conjugate vaccine (PCV13) is in use for infant immunization programs, but is not routinely used in adults. Recent literature suggests PCV13 may be used in adult vaccination programs as well, but few PCV13 trials have reported the immunogenicity and safety response in adults.

Methods: Design: Systematic review and meta-analysis

Setting: Randomized controlled trials evaluating immunogenicity of a single dose of PCV13 and PPV23 in adults by the opsonophagocytic assay (OPA) geometric mean titer (GMT) response at 1-month post-vaccination were considered for inclusion. GMT ratio and safety events reported up-to 14 days were pooled using random effects models.

Results and Analysis: Five randomized trials were included with 4561 subjects, ranging 50 to 95.5 years, consisting of 51% females. The pooled immunogenicity OPA GMTs ratio (GMTR) in the PCV13 arm was statistically significantly higher for 10/13 serotypes (1, 4, 5, 6A, 6B, 9V, 18C, 19A, 19F and 23F) compared to PPV23 ($p<0.0001$). The pooled GMTR for combined 13 serotypes GMTR was 2.05 (95% CI: 1.77, 2.37;$p<0.0001$). Overall, pooled risk ratios (RR) for any local (RR 1.09, 95%CI: 0.96, 1.23) and systemic reactions (RR 0.96; 95%CI 0.91, 1.02) did not differ between PCV13 and PPV23. Pneumococcal naïve subjects experienced significantly higher local reactions in PCV13 arm compared to PPV23 (RR 1.15; 95%CI: 1.05,1.26, p=0.003).

Conclusions and implications for vaccinology: A single dose of PCV13 elicits a better immune response among adults compared to PPV23, while having a similar safety profile to PPV23.

Knowledge, attitudes, beliefs and behaviours (KABB) of the general public about the role of pharmacists as immunizers

Di Castri A, Halperin D, Isenor J, Halperin S, for the Canadian Immunization Research Network (CIRN)

Introduction/Background: Vaccine coverage falls consistently below desired levels in Canada despite National Advisory Committee on Immunization recommendations. One solution to improve coverage is to offer vaccines in more convenient locations, such as in pharmacies by pharmacists. We explore the KABB of the general public in Nova Scotia (NS) and New Brunswick (NB) about the changing role of pharmacists as immunizers.

Methods: An online survey was developed and assessed for content validity and test-retest reliability. Adult members of the public in four communities in NB and NS were surveyed. Participants were invited to complete

the survey through local advertisements in print and online, posters, via social media, and through email lists at local universities.

Results and Analysis: Of the 985 respondents, 742 lived in NS (75.3%) and 243 in NB (24.7%). Immunization status varied across vaccines with slightly over half of respondents (51.8%) reporting receipt of a seasonal influenza vaccine last year, 38.0% reporting receipt of the meningococcal C or ACWY vaccine and 77.7% reporting receipt of the tetanus, diphtheria, acellular pertussis vaccine. Most respondents (50.9%) reported receipt of all vaccines recommended for adults, while 31.5% did not know. 38.98% of respondents had received a vaccination by a pharmacist in a pharmacy. Respondents reported that it was convenient for them to receive their vaccines from their pharmacist (67.9%) and were comfortable doing so (75.0%). 76.9% of respondents indicated that they get their vaccine-related information from their family physician, 31.6% from their nurse, 35.3% from their pharmacist, and 49.2% from the internet. Respondents were more convinced about the severity of infectious diseases than they were about their risk of developing them. Most respondents were willing to receive vaccines if they were provided free of charge.

Conclusions and implications for vaccinology: This study suggests that pharmacists are well positioned to improve vaccine coverage, and communicate recommendations and other vaccine-related information to recipients.

Content development and validity testing of a framework for the assessment of health-related risks, including vaccination needs, among travellers by pharmacists in Ontario

Fernandes H, Houle S

Introduction/Program need and objectives: In December 2016, the scope of pharmacist-administered immunizations expanded in Ontario to include 13 vaccine-preventable diseases – many of which are travel-related. Among the plethora of resources available in travel medicine, a lack of direction on ascertaining a patient's vaccination needs continues to remain. Current resources focus on the country's requirements, as opposed to the patient's individual risk. This research aims to create and test an evidence-based framework that pharmacists can apply to to guide their assessment of patients who are planning travel.

Program methods and activities: A three-stage process will be employed: development, judgment-quantification, and reconstruction. The framework's domains will follow the Ontario College of Pharmacists Practice Assessment Criteria. These domains have been identified as having the greatest potential impact on patient and public safety from the National Association of Pharmacy Regulatory Authorities' Standards of Practice. The domains include patient assessment, decision making, documentation, and communication and education. Item generation and framework creation will utilize the Delphi method among a panel of experts, including those that have obtained the Certificate in Travel Health from the International Society of Travel Medicine. Content validity-related estimates, including content validity ratio and content validity index, will be employed to quantify the framework's content validiation. Based on these expert opinions and measurements, the framework will be finalized and tested in practice for feasibility assessment.

Program results or outcomes (including evaluation): The framework is currently under development, with a completed framework and content validity results expected for presentation by the time of the conference.

Implications for practice or policy: This practice tool will be the first to be created and tested specifically for application to travel medicine assessment and immunizations. While the tool will be feasibility-tested among pharmacists initially, further evaluation will examine its feasibility in practice among family physicians and nurses who are also interested in introducing pre-travel assessments into their practice.

Development and testing of a framework for the assessment of health-related risks, including vaccination needs, among travellers by pharmacists in Ontario

Fernandes H, Houle S

Introduction/Program need and objectives: In December 2016, the scope of pharmacist-administered immunizations expanded in Ontario to include 13 vaccine-preventable diseases – many of which are travel-related. Pharmacists can positively impact immunization rates, but remain hesitant due to lack of confidence regarding travel-related care and lack of direction on its integration into existing practice. My project aims to support the uptake of pharmacists as immunizers in travel medicine by creating an evidence-based framework that pharmacists can apply to guide their assessment of patients who are planning travel.

Program methods and activities: The project is divided into 2 stages: framework creation and assessment. The creation of the framework follows the clinical recommendations outlined in the CDC Yellow Book 2018, tailored for pharmacists. Content validity will utilize the Delphi method among a panel of experts, including those that have obtained the Certificate in Travel Health from the International Society of Travel Medicine. Feasibility of the framework will be tested across pharmacies at different levels of adoption of travel medicine care. Pretest and posttest interviews will then be used to assess its impact on pharmacists' practice.

Program results or outcomes (including evaluation): Preliminary results indicate that additional training is the primary facilitator for implementation of travel medicine services. The processes for completing a pre-travel assessment, and several areas of travel medicine-related education were identified as priority learning areas. Framework development will take these identified barriers, facilitators, and knowledge needs into consideration. It is expected that the framework will also be developed and assessed for content validity by the time of the conference.

Implications for practice or policy: This practice tool will be the first to be created specifically for application to travel medicine and pharmacist-provided immunizations. With the aim of increasing pharmacists' confidence regarding pre-travel assessment and travel-related diseases/vaccinations, it will address the primary barrier recognized as preventing pharmacists from taking a larger role in providing immunization care.

Developing product monograph language that supports evidence-informed use of vaccines in pregnancy

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Introduction/Background: Cautionary language in vaccine product monograph (PM) statements about use in pregnancy may raise safety concerns despite clinical evidence of safety. For example, inactivated influenza vaccination (IIV) is recommended in pregnancy, but the FluLaval® PM states: "use only following the advice of a healthcare professional….consider[ing] the benefits and risks to the mother and foetus." This project aimed to develop non-ambiguous evidence-informed statements about use in pregnancy for vaccine PMs.

Methods: We conducted a multi-stage consensus-methods project with key stakeholders from across Canada, including: healthcare providers, regulators, industry representatives, and experts from public health, communications, law, ethics, vaccine evaluation, and social sciences. Our approach was mixed methods, but primarily qualitative. First, we collectively revised statements in a nominal group technique meeting. Second, we evaluated the revised statements in a Delphi survey. Third, stakeholders revised PM statements during a consensus workshop. We analyzed stakeholders' responses and revised the statements at each stage for both consensus and innovative PM language ideas.

Results and Analysis: Workshop time constraints limited PM revisions to IIV and Tdap vaccines only. The revised statements align with the identified goals of meeting participants (N=28) that PMs be evidence-informed, consistently structured, succinct, gender-neutral, and readable. The revised IIV safety statement is: "No vaccine related serious adverse pregnancy, fetal, or neonatal outcomes have been observed…". We are testing these statements in a survey of Canadian healthcare providers.

Conclusions and implications for vaccinology: Revising PM statements is challenging because of regulatory and other legal requirements. The revised PM statements are expected to improve consistency between the use in pregnancy sections of the IIV and Tdap PMs and public health recommendations. Further work could assess how the public interpret the revised statements and develop statements for other vaccine products.

The Effect of Timing of Tetanus-diphtheria-acellular pertussis Vaccine Administration in Pregnancy on The Avidity of Pertussis Antibodies

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Introduction/Background: Tetanus-diphtheria-acellular pertussis (Tdap) vaccination in pregnancy is currently recommended in Canada and other countries. The optimal timing of pertussis immunization in pregnancy is not well established, leading to different recommendations. We aimed to determine the effect of timing of vaccination with Tdap in pregnancy on the umbilical cord avidity (the binding strength of an antibody for an antigen) of immunoglobulin G (IgG) to pertussis toxin (PT).

Methods: Ammonium thiocyanate (NH4SCN) was used as a bond-breaking agent to measure the avidity of anti-PT IgG using a range of concentrations between 0.25M (to measure low-avidity antibodies) and 3M (to measure very high-avidity antibodies). Anti-PT IgG levels achieved at each NH4SCN concentration were calculated. Anti-PT IgG levels in cord blood of newborns of women vaccinated in early (28-32 weeks gestation [WG]) vs. late (33-36 WG) 3rd trimester, and between newborns of women vaccinated 5-12 vs. 1-4 weeks prior to delivery were compared using t-tests.

Results and Analysis: Newborns of women vaccinated with Tdap in early 3rd trimester (n=43) had higher levels of medium and high-avidity anti-PT IgG antibodies compared with newborns of women vaccinated in late 3rd trimester (n=47), 2.4 international units (IU)/ml vs. 1.9 IU/ml (p=0.0073) and 2.3 IU/ml vs. 1.7 IU/ml (p=0.0354), (p=0.0073 and p=0.0354, adjusted for gestational age at birth), respectively. Newborns of women vaccinated with Tdap 5-12 weeks prior to delivery had higher levels of high and very high avidity anti-PT IgG antibodies compared with newborns of women vaccinated within 4 weeks prior to delivery, 2.3 IU/mL vs. 1.2 IU/mL, 2.5 IU/mL vs. 1.5 IU/mL, (all p<0.03), respectively.

Conclusions and implications for vaccinology: Vaccination against pertussis during early 3rd trimester results in higher levels of high-avidity antibodies in newborns compared with vaccination in late 3rd trimester. High-avidity antibodies may confer greater protection to the neonate, supporting recommendations for vaccination at 28-32 over 33-36 WG.

Prevention of human papillomavirus (HPV)-associated anal cancer among men living with HIV: examining knowledge, attitudes and beliefs regarding HPV-associated disease and prevention

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Introduction/Background: Men living with HIV have high burden of HPV-associated disease. In particular among HIV-positive men who have sex with men (MSM), the incidence of anal cancer, a vaccine preventable disease, is 100-fold higher than the general male population. We examined factors influencing uptake of HPV-associated disease prevention in this population.

Methods: A questionnaire, developed using Theory of Planned Behaviour, examining knowledge, attitudes and beliefs regarding HPV, its associated diseases and their prevention was administered in 2016-17 to 1688 HIV-positive men in the Ontario HIV Treatment Network Cohort Study which follows people attending specialty HIV care clinics.

Results and Analysis: The median age was 53 (interquartile range: 45-59); 67% of men identified as White, 11% as African, Caribbean or Black, and 7% as Indigenous. Most men identified as MSM (72% gay; 8% bisexual). Almost half of the men (48%) were unfamiliar with HPV; young men (<30 years) and gay men were more familiar. Knowledge gaps remained: 25% of men familiar with HPV didn't know HPV caused anogenital warts or

anal cancer; 30% thought HPV could be cured by medication; and 21% didn't know HIV increased their risk for HPV-associated cancers. Moreover, 71% men felt they had no or low chance of acquiring HPV and associated diseases. Yet, the majority of men (85%) were comfortable discussing their anal health with their doctor and 90% would be willing to undergo anal cancer screening.

Conclusions and implications for vaccinology: Low HPV literacy and perceived risk, factors that may influence participation in HPV-associated cancer prevention, were observed among men in this study. Although young gay men, who may be eligible for targeted HPV vaccine programs, were more familiar with HPV, knowledge gaps remained. Messaging regarding HPV, HPV-associated disease risk and HPV prevention should be targeted to HIV-positive men who are at particularly high-risk for HPV vaccine preventable cancers.

Rates of cervical intraepithelial neoplasia in women in British Columbia: A data linkage evaluation of the school-based HPV immunization program

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Introduction/Background: HPV vaccines were highly efficacious in the prevention of cervical cancer precursors in large-scale trials. However, monitoring of population-based data is critical to understand real-world vaccine impact. Our analysis evaluated the impact of the school-based quadrivalent HPV immunization program on cervical dysplasia in British Columbia.

Methods: Data linkage was performed using records from the provincial Cervical Cancer Screening Program and immunization registries. In screened women born in 1994 through 2005, the relative incidence rates (RR) of precancerous outcomes based on cytology and histopathology (CIN2, CIN3 and CIN2+) using adjusted Poisson regression were compared between HPV vaccine recipients and unvaccinated women. A complete series was considered 2 doses for those born in 2003 or later, and 3 doses for those born in 1994 – 2002 per the provincial schedule.

Results and Analysis: There was a higher rate of CIN2+ in women who received a complete HPV series (all recommended doses based on schedule) starting at 15 years or older (n=1,312), compared to women with a complete series beginning at 9-14 years of age (n=12,910), RR 2.50 (95%CI 1.25-4.68). Women who received any HPV vaccine dose between the ages of 9 and 14 years (n=14,199) had a RR 0.51 (95%CI 0.35-0.75) for CIN2+ compared to unvaccinated women (n=12,762). There was no significant difference in the RR of CIN2+ in women with incomplete series (i.e. not in accordance with recommended schedule at time of vaccination) compared to unvaccinated women.

Conclusions and implications for vaccinology: Women who received HPV vaccine at 9-14 years of age had half the rate of high-grade cervical lesions compared to unvaccinated women. Pre-adolescent immunization should be encouraged, as per the provincial schedule. Continued program monitoring will be important for measuring long-term population impact.

Human papillomavirus (HPV) vaccine uptake in gay, bisexual, and other men who have sex with men (gbMSM) in Montreal, Toronto, and Vancouver: A CIRN-funded study

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Introduction/Background: gbMSM are at increased risk for HPV-associated cancers. Vaccination protects against the HPV types responsible for most anal and oral cancers. In 2015/2016, British Columbia, Ontario, and Quebec implemented HPV vaccine programs for gbMSM aged ≤26. We explored potential barriers and facilitators to vaccine uptake.

Methods: Engage is an ongoing sexual health biobehavioural study of gbMSM aged 16+ in Montreal, Toronto and Vancouver. Men are recruited using respondent driven sampling (RDS). We used the Fisher's exact test to compare preliminary data on RDS unadjusted proportions by age group (≤26 vs. >26) for responses to HPV-related questions on vaccine receipt and willingness, healthcare use, and sexual orientation disclosure.

Results and Analysis: As of 28/02/2018, 1,358 men enrolled (21.6% were ≤26; 66.6% were from Montreal). In Montreal, Toronto, and Vancouver, 67.3%, 82.4% and 83.5% were aware of the HPV vaccine, respectively. Compared to men aged ≤26, in most cases, more men >26 had a regular provider (71.5% vs. 55.5% p<0.0001; 89.6% vs. 69.6% p=0.002; 77.5% vs. 56.7% p=0.002), were willing to get vaccinated (79.4% vs. 61.2% p<0.0001; 89.9% vs. 81.0% p=0.459; 85.7% vs. 58.6% p=0.003), and disclosed their sexual orientation to their provider (87.8% vs. 75.0% p=0.002; 85.0% vs. 87.5% p=1.000; 81.7% vs. 50.0% p<0.0001) for the three cities, respectively. More men aged ≤26 compared to men >26 had 1+ dose of the vaccine (39.3% vs. 5.2% p<0.0001; 39.1% vs. 27.4% p=0.060; 55.4% vs. 24.8% p<0.0001) in the three cities, respectively.

Conclusions and implications for vaccinology: Based on RDS unadjusted findings, provincial programs may have an impact on vaccine uptake among younger gbMSM. Nevertheless, most older gbMSM remain unvaccinated. Among gbMSM ≤26, not having a regular provider, and in Montreal and Vancouver, not disclosing their sexual orientation and willingness to get vaccinated may be barriers to vaccine uptake. There is opportunity to increase uptake through promotion and access to vaccination services.

Experiences and attitudes towards HPV and HPV vaccination among GB2M in Ontario, Canada: Results from the #iCruise Study

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Introduction/Background: Gay, bisexual, two-spirit and other men who have sex with men (GB2M) are at higher risk for human papillomavirus (HPV)-related diseases, particularly anal cancer. In September 2016, Ontario introduced a program to provide free HPV vaccine to young GB2M aged ≤26 years.

Methods: #iCruise is an Ontario-wide study of GB2M seeking sexual health information online. GB2M were recruited through websites and mobile location-based dating applications ("socio-sexual apps") such as Grindr from July 2017-January 2018. Items included awareness of HPV and willingness to get vaccinated using Likert scales in different scenarios, such as varying levels of cost or disclosure of same-sex activity. We compared younger men (≤26) to older men (>26) using Pearson's chi-square tests to assess their experience and attitudes.

Results and Analysis: 975 participants aged 14-89 years, with 34.7% aged ≤26, completed the baseline questionnaire. Most had heard of HPV (94.0%) and the HPV vaccine (79.2%). A higher proportion of younger versus older men reported discussing the vaccine with a health professional (41.5% vs 30.2%,p=0.005) and received 1+ doses (25.5% vs 14.3%,p<0.001). However, within the younger group, fewer men aged 14-21 reported receiving 1+ doses compared to men aged 22-26 (20.4% vs 27.6%, p=0.001), with 23.5% of the 14-21 group responding "don't know/don't remember" versus 8.4% in the 22-26 group. All GB2M were less likely to get vaccinated if they had to pay out-of-pocket costs or disclose same-sex activity to obtain free vaccine; this was significantly more so among younger GB2M.

Conclusions and implications for vaccinology: GB2M were willingness to get vaccinated, particularly if it were free. Younger GB2M were more likely to have received the vaccine, reflecting its availability. That 75% of younger GB2M had not been vaccinated, suggests a need for increased vaccine awareness and ensuring accessibility in non-stigmatizing and welcoming healthcare environments.

Persistence of antibodies after a single dose of quadrivalent HPV vaccine and the effect of a dose of nonavalent vaccine given several years later

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Introduction/Background: This study assessed the persistence of antibodies after a single dose of quadrivalent vaccine (4vHPV) and the effect of a dose of nonavalent vaccine (9vHPV) given 3-8 years later on antibody titers. Such data might be of interest in the decision-making process concerning the completion of the 2-dose course in non-compliant vaccinees in jurisdictions which switched from 4vHPV to 9vHPV.

Methods: Girls living in the Québec City area who received a single dose of 4vHPV were eligible to participate. Blood specimens were collected just before and one month post-9vHPV administration. The specimens were tested by ELISA for antibodies to 9 HPV types included in the 9vHPV.

Results and Analysis: 31 girls aged 13-18 years (mean 15.5 years) participated in the study. Pre-9vHPV administration all participants were seropositive to the 4 HPV types included in the 4vHPV and 58%-87% were seropositive to the additional five HPV types included in the 9vHPV. GMTs were 8.1AU/ml, 9.7 AU/ml, 22.4IU/ml and 8.0IU/ml for HPV6, HPV11, HPV16 and HPV18, respectively. The GMTs were lower for the other five HPV types (2.4-4.2AU/ml). One month post-9vHPV administration all 31 participants were seropositive to 9 HPV types with a 25.3-73.3-fold increase of GMTs.

Conclusions and implications for vaccinology: High seropositivity rates to 9HPV types observed several years after a single dose of 4vHPV and 100% seropositivity after a dose of 9vHPV suggest that this schedule might be used in non-compliant vaccinees. Moreover, these results, coupled with previous reports on protection ensured by a single dose of HPV vaccine against infections, precancers and genital warts, question the additional value of the second dose.

Cross-reactive priming effect of bivalent and quadrivalent vaccine for HPV 31/33/45/52/58: Bridging analysis from two clinical trials

Sauvageau C, Panicker G, R. Unger E, Ouakki M, De Serres G, **Gilca V**

Introduction/Background: The bivalent (2vHPV) and quadrivalent (4vHPV) HPV vaccines induce cross-reactive antibodies and cross-protection to some HPV types not included in these vaccines. No data is available regarding the immune response to HPV31/33/45/52/58 when a dose of nonavalent vaccine (9vHPV) is administered to subjects who previously received a dose of 2vHPV or 4vHPV compared to naïve (unvaccinated) subjects.

Methods: We analysed results from two clinical trials conducted by the same team in the same region. Subjects were 9-10-year-old at the time of first visit. In one study a dose of 9vHPV was administered 6 months post a single dose of 2vHPV (n=90) and to naïve subjects (n=179). In another study 9vHPV was administered to subjects 36-96 months (mean 65 months) post a single dose of 4vHPV (n=31). Blood samples were collected 1 month post-9vHPV. In both studies anti-HPV IgG were assessed using multiplex ELISA (M9ELISA).

Results and Analysis: All subjects were seropositive to the 9vHPV types with exception of one naïve subject who seroconverted for all types except HPV45. In (I) naïve subjects, (II) subjects previously vaccinated with 2vHPV or (III) 4VHPV the GMTs were as follows: HPV31:23/126/194AU/ml; HPV33:34/58/109AU/ml; HPV45:29/170/106AU/ml; HPV52:28/53/73AU/ml and HPV58:72/79/120AU/ml. GMTs to all HPV types were higher (all $p<0.05$) in subjects who previously received either a dose of 2vHPV or a dose of 4vHPV; except for HPV58 in the 2vHPV group. No difference in GMTs was observed between the 2vHPV and 4vHPV groups.

Conclusions and implications for vaccinology: The enhanced antibody response to HPV31/33/45/52/58 after 9vHPV among subjects who had received a dose of 2vHPV or 4vHPV suggests cross-reactive priming has occurred. This priming effect may persist for up to 8 years.

No prevalent HPV 16/18 infections after two-doses of HPV vaccine in girls; An interim analysis from the Quadrivalent HPV Vaccine Evaluation Study

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Introduction/Background: HPV vaccines were originally licensed in a three-dose schedule. However, for adolescents <15 years, two doses of vaccine are now recommended based on immuno-bridging studies. Limited data are available on effectiveness of <3 dose schedules. We report an interim analysis of HPV prevalence after two-doses of quadrivalent vaccine.

Methods: QUadrivalent HPV vaccine Evaluation STudy (QUEST) is a Canadian cohort of girls 9-14 years at enrollment. Based on their provincial program, girls received either two or three doses of vaccine. Comprehensive follow-up includes self-collected vaginal specimens, blood samples and online health surveys. First available swab of two-dose participants (available up to 2017-08-20) was used to obtain an interim HPV prevalence estimate. Samples were screened for high-risk (hr) HPV using the Roche Cobas HPV Test, and if positive, genotyped by Roche Linear Array HPV Genotyping Test.

Results and Analysis: 1133 swabs were available for analysis. Median time since first dose: 4.4 years (range 3.3-9.3), median interval between the two doses was 198 days (range 62-364), median age of participants at time of swab collection was 15.7 years (range 14.3-22.5) and 14.2% of participants reported to have ever had sexual intercourse. Among those sexually active, 9.32% (95%CI 5.31-14.90%) had HrHPV, however, no HPV16/18 infections were identified (0.00% 95%CI 0.00-2.43%).

Conclusions and implications for vaccinology: In this analysis to estimate HPV prevalence among sexually active recipients of a two-dose quadrivalent HPV vaccination schedule, no HPV16/18 infections were identified, suggesting protection for at least 4 years. Long-term follow-up in the full cohort is ongoing. This study, as one of the first observational studies powered for this purpose globally, indicates effective protection after two-doses of HPV vaccine against vaccine types HPV16/18. This adds to the growing body of evidence supporting reduced dosing HPV vaccination schedules.

Effectiveness of one-dose of quadrivalent HPV vaccine against HSIL and CIN; A data-linkage study

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Background: Although originally approved for three-doses, HPV vaccines were later approved for a two-dose schedule for 9-14 year olds. Post-hoc analyses have indicated the potential for efficacy of only one-dose of vaccine. We aimed to estimate effectiveness of one-dose of quadrivalent HPV vaccine against high-grade squamous intraepithelial lesion (HSIL) and cervical intraepithelial neoplasia grade 2 or higher (CIN2+) in screened young women.

Methods: Data-linkage was performed between the population Cervical Cancer Screening Program (CCSP) and immunization registries in British Columbia, Canada. Occurrence of HSIL and CIN2+ were compared in a screening cohort of women born between 1994-2005 who were unvaccinated or vaccinated between 9-14 years of age with one-dose or were completely vaccinated (2-doses 150 days apart or 3-doses with at least 28 days between dose one and two, and 94 days between dose two and three). Relative incidence rates (RR, (95%CI)) were calculated using adjusted Poisson regression.

Results and Analysis: We observed significant protection among completely vaccinated (n=12,910, mean age at vaccination 13.8 years) compared to unvaccinated women (n=12,762) for HSIL and CIN2+. Adjusted RR for HSIL was 0.62 (0.49-0.80), and for CIN2+ 0.50 (0.34-0.74). No significant protection against HSIL and CIN2+ was observed after one dose (n=348, mean age at vaccination 13.5 years), respective adjusted RR 0.98 (0.35-2.14) and 1.42 (0.35-3.85).

Conclusions and implications for vaccinology: While no evidence of protection of one-dose against HSIL and CIN2+ was observed in this observational study, the sample size was small, and women who have received one-dose may have been previously exposed or had other underlying exposure risks that differed from unvaccinated women. Further analyses with larger numbers are required to fully assess the impact of single dose vaccination.

Evaluation of immunization in the neonatal intensive care unit at British Columbia Women's Hospital

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Introduction/Background: Term and preterm infants in the neonatal intensive care unit (NICU) should be immunized at the same chronological age and on the same schedule as healthy term infants, but are often under-immunized. Reasons for under-immunization in this population have not been well-defined. The aim of this study was to assess the immunization rates of hospitalized term and preterm infants in the NICU and examine reasons for under-immunization.

Methods: Pharmacy and NICU databases were utilized to determine the immunization rates of eligible babies admitted to the NICU between 2011 and 2015. A retrospective review of unimmunized infants was undertaken to identify potential barriers to timely immunization. Clinical information, including reasons for the lack of immunization were evaluated by detailed review of the hospital medical records.

Results and Analysis: Of the 3,261 babies admitted to the NICU during the study period, 534 (16%) were still hospitalized at ≥8 weeks of age, when first immunizations are due. Of these, 144 (27%) received no immunizations in hospital. Sixty two of these cases were reviewed in detail. Mean gestational age at birth was 30.6 weeks. Twenty nine (47%) medical records did not document that immunizations were due. In 21 (34%) of the 62 cases, there was no clear reason for lack of immunization. In 27 cases (44%), infants were deemed too unwell, including concerns of compromised immunity (including sepsis), severe respiratory problems or palliative care. Of those who were deemed too unwell, 11 (44%) died during the hospitalization. In 8 cases (13%), parents refused vaccinations. Vaccines were deferred to the discharging hospital in 7 (11%) cases. 29/62 (47%) medical records did not even document that immunizations were due.

Conclusions and implications for vaccinology: Significant comorbidity appeared to be the major reason behind vaccination delays, with 27% of vaccine-eligible infants unimmunized. Significant improvements are required to ensure these babies receive vaccines upon recovery from their illness, and to ensure absence of immunization is clearly documented upon hospital discharge.

Molecular epidemiology of Neisseria meningitidis in children and adults with invasive meningococcal disease in Canada between 2002 and 2017 and correlation with outcomes

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Introduction/Background: Invasive meningococcal disease (IMD) has a case-fatality rate of 5-10%, and 20-30% of survivors suffer long term complications. Previous studies have suggested more severe disease is caused by clonal complex 11 isolates. The aim of this study was to correlate bacterial characteristics with outcomes after IMD.

Methods: Active, population-based surveillance for IMD was conducted by IMPACT, covering ~50% of the population and ~90% of pediatric tertiary care beds in Canada. IMD cases included children and adults with positive sterile site culture/PCR for Neisseria meningitidis. Clinical details were collected from hospital records. Bacterial typing was performed at the National Microbiology Laboratory. Associations between bacterial factors and outcomes were analyzed by chi-squared tests and one-way analysis of variance.

Results and Analysis: A total of 1,125 cases of IMD had data on capsular group, 604 had MLST data and 305 factor H binding protein (FHbp) designation. The most common group was B (n=650) and the most common clonal complexes were ST-269 (n=156), ST-41/44 (n=129), and ST-11 (n=94). The highest complication rate occurred in ST-11 cases – (48% vs. 26% other clonal complexes). ICU admission was more likely ($p \leq 0.002$) in individuals infected with capsular group C (64% vs. 54% other groups), ST-11 (69% vs. 54% other clonal complexes) or FHbp family B/variant 1 (60% vs. 42% other family/variants) isolates. Overall hospital length of stay (LOS) amongst survivors was longest in those infected with group C (median 10 days) and ST-11 (median 11 days) organisms.

Conclusions and implications for vaccinology: Infection with capsular group C, clonal complex ST-11 isolates was associated with more severe disease, highlighting the value of MenC vaccine programs on reducing IMD disease burden.

Evaluation of transferrin receptor protein B (TbpB)-based vaccine formulations against N. gonorrhoeae.

Islam E, Fegan J, Ahn S, Ng D, Moraes T, Schryvers A, Gray-Owen S

Introduction/Background: Developing a vaccine against N. gonorrhoeae (Ngo), the bacterium that causes gonorrhea, has become an urgent priority due to the emergence of multidrug-resistant superbug strains. The gonococcal transferrin receptor has long been considered an attractive vaccine target due to its ubiquitous presence in all sequenced strains, surface exposure and essential role in iron acquisition during infections. Herein, we evaluated the potential for utilizing transferrin receptor protein B (TbpB), the lipoprotein component of this receptor complex, as a vaccine antigen by examining the protective efficacy and coverage of various TbpB-based formulations.

Methods: Mouse models were utilized to determine the protective efficacy of various TbpB-based compositions during genital tract infections. Phylogenetic analysis of publicly available Ngo genomes was performed to gain an understanding of TbpB diversity. Serum and mucosal anti-TbpB antibody titres were quantified using ELISA (enzyme-linked immunosorbent assay) against a panel of representative Ngo strains to evaluate vaccine coverage.

Results and Analysis: TbpB formulated with Alum or an oil-in-water based adjuvant conferred significant protection against the homologous challenge strain in a model of lower genital tract colonization, compared to naïve mice. Diversity analysis of TbpB sequences revealed two major phylogenetic clusters, which can be suitably represented by a panel of 15 distinct TbpB variants comprising TbpBs from 12 clinically relevant strains and 3 commonly used laboratory strains. Studies are currently underway using this panel to determine adjuvant effects on the cross-reactive and cross-protective response and to identify the minimal number of TbpB antigens that will be required for full vaccine coverage.

Conclusions and implications for vaccinology: Our systematic approach to evaluate vaccine efficacy in mouse models, target diversity and potential vaccine coverage indicate that targeting TbpB of the essential transferrin receptor complex will be an effective vaccination strategy.

Meningococcal Antigen Typing System (MATS) analysis of Canadian Invasive Serogroup B *Neisseria meningitidis* isolates, 2010-2014

Law D, De Paola R, Stella M, Giulian M, Zhou J, Serino L, Tsang R

Introduction/Background: The introduction of 4CMenB (Bexsero, GSK) vaccine to confer protection against invasive serogroup B *Neisseria meningitidis* (MenB) is considered a significant recent new vaccine development. MATS assay was used to predict coverage of 4CMenB on Canadian isolates from 2010 to 2014.

Methods: MATS is a sandwich Enzyme-Linked ImmunoSorbent Assay (ELISA) designed to measure the immunological cross-reactivity and quantity of the three 4CMenB antigens (fHbp, NHBA and NadA) in any MenB isolate. In addition, for each isolate, the *porA* VR2 sub-type was determined. Isolates were compared to a reference MenB strain specific for each antigen to generate relative potency (RP) values to determine whether the strains were covered.

Results and Analysis: From 2010 to 2014, a total of 550 invasive *N. meningitidis* case isolates were provided by the Provincial Public Health Laboratories to the National Microbiology laboratory, of which 349, 41, 125, 27 and 8 were MenB, MenC, MenY, MenW and other serogroups, respectively. 250 representative MenB isolates were tested by the MATS assay. MATS predicted an overall coverage of 74% (184/250) (95% Coverage Interval: 54%-85%) and varied by year from 64% in 2010 and 2012 to 82% in 2013 and 84% in 2014. 73% and 81% of the isolates from infant and young people (15 to 24 years old) were predicted to be covered, respectively. In

addition, coverage by single antigen and combined antigens were as follow: fHbp (22%), fHbp + NHBA (25.2%) and PorA + fHbp + NHBA (12.4%). Also, isolates from the most representative clonal complexes in Canada (cc-269 and cc-41/44) were predicted with coverage of 89% and 73% respectively.

Conclusion and implications for vaccinology: MATS predicted a 74% overall coverage by 4CMenB on Canadian MenB strains collected from 2010 to 2014 which matched favourably with similar earlier findings using isolates from 2006 to 2009.

Revealing processes that confer immunity to nasal infection by Neisseria meningitidis

Currie E, Gray-Owen S

Introduction/Background: Neisseria meningitidis is an obligate colonizer of the human nasopharynx where it may persist asymptomatically or, under rare circumstances, progress to cause lethal sepsis and meningitis. The most effective way to prevent meningococcal disease is through an immunization program that prevents both invasive and nasal infections, thereby conferring herd immunity to the immunized population. Unfortunately, the immunological processes that prevent nasal colonization are poorly defined, and are thus difficult to target during vaccine design. Using an infection induced mouse model of immunity against nasal infection by N. meningitidis, we sought to identify immunological factors required to prevent colonization.

Methods: N. meningitidis does not naturally colonize the mouse nasopharynx. Herein we make use of mice that express transgenic human CEACAM1 (hCEACAM1) which facilitates prolonged nasal colonization. Immunity to meningococcal colonization can be induced via repeated nasal infection. Using a combination of immunodeficient mice and antibody mediated depletion of immune cells, we assessed the relative contribution of immune cell populations in mediating mucosal immunity to N. meningitidis.

Results and Analysis: Immunocompetent infection experienced mice clear N. meningitidis infection within 24 hours post infection. Infection experienced B cell knockout mice display comperable bacterial burdens to naïve mice, revealing a lack of protection in the absence of B cells. Depletion of neutrophils prior to challenge resulted in a high bacterial burden in infection-experienced mice, revealing a loss of immunity and therefore implying an essential role for neutrophils in maintaining mucosal immunity at the time of meningococcal challenge.

Conclusions and implications for vaccinology: These data reveal an essential role for both B cells and neutrophils in maintaining immunity to nasal colonization by N. meningitidis. These findings can facilitate vaccine design by targetting these immune cells through appropriate antigen adjuvant combinations.

The use of novel hybrid antigens of the bacterial transferrin receptor for protection against Neisseria meningitidis and Neisseria gonorrhoeae

Fegan J, Islam E, Calmettes C, Yu R, Ahn S, Moraes T, Gray-Owen S, Schryvers A

Introduction/Background: Neisseria meningitidis (Nme), the causative agent of meningococcal disease, and Neisseria gonorrhoeae (Ngo), the causative agent of gonorrhea, are closely related bacterial pathogens that share a conserved iron uptake system which has been identified as an attractive vaccine target. This receptor is composed of an integral membrane channel (transferrin binding protein A; TbpA) and a surface-anchored lipoprotein (transferrin binding protein B; TbpB). While both antigens elicit bactericidal antibodies, vaccine development has predominantly focused on TbpB as a soluble, stable antigen that can be produced in large quantities. However, TbpB is highly variable, thus achieving broad cross-protection has been considered challenging. In comparison, TbpA is highly conserved but production is technically challenging and not considered practicable for large-scale development.

Methods: To exploit the high sequence conservation of TbpA we developed a chimera approach allowing the display of surface-exposed TbpA epitopes in a structurally-relevant context on a soluble TbpB scaffold. These hybrid antigens were used to immunize mice and the antiserum was tested for immunogenicity and bactericidal

activity. Separately, immunized mice were challenged with acute sepsis (Nme) or lower genital tract infection (Ngo).

Results and Analysis: The hybrid antigens elicit antibody against both TbpA and TbpB by ELISA. Antiserum is bactericidal against Nme in vitro, including against a TbpB deletion strain, indicating that the chimeric antigens elicited functional anti-TbpA antibodies. Mice immunized with TbpA or the hybrid scaffold were protected against lethal challenge. In the gonococcal infection model, female mice immunized with Nme TbpA or the hybrid hosting an Nme TbpA loop rapidly cleared the gonococci compared control mice, demonstrating cross-species protection.

Conclusions and implications for vaccinology: Our rationally-designed hybrid antigens target both components of an essential iron acquisition pathway. We have shown that a single protein can elicit protection against Nme invasive disease and Ngo colonization, providing us with the potential to confer broad-spectrum protection against these two devastating pathogens.

Childhood vaccine safety: Background rates of three conditions of interest

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Introduction/Background: Knowledge of expected incidence (i.e. background rate) of adverse events following immunization (AEFIs) is important to vaccine safety surveillance. We selected three rarely-reported AEFIs representing the spectrum of causality from proven (immune thrombocytopenia [ITP]); to possible (Kawasaki disease [KD]); to unsubstantiated (multiple sclerosis [MS]); to demonstrate that their background rates can be estimated using readily available health administrative data.

Methods: We extracted data on hospitalizations (CIHI Discharge Abstract Database) for ITP, KD, and MS among Ontario children age 1-17 years for the period 2005 to 2014 from Ontario's IntelliHEALTH knowledge repository. For ITP, we also extracted emergency department visits from the CIHI National Ambulatory Care Reporting System. We only counted first visits and for ITP only the hospitalization was included if the same child also had an ED visit. We calculated rates by year, age and sex using population estimates from 2005-2014, focusing on age groups that align with the Ontario immunization schedule for the vaccines of interest based on the AEFIs studied.

Results and Analysis: Annual age-specific incidence of ITP in children age 1-7 years ranged from 8.9 to 12.2 per 100,000 and incidence peaked at 1-2 years of age (17.6 per 100,000). Among 1-5 year olds, incidence of ITP was greater in boys than girls, with the male to female ratio decreasing until 6 years of age. The annual incidence of KD in children < 5 years ranged from 19.1 to 32.1 per 100,000. Highest rates of KD were observed in children age 1-2 years. Boys had higher rates of KD than girls, especially in the youngest ages. The average annualized incidence of adolescent (11-17 years) MS overall was 0.8 per 100,000.

Conclusions and implications for vaccinology: Despite limitations, including lack of clinical validation, we determined background rates of AEFIs through administrative data. This approach could assist with vaccine safety surveillance and be used by public health.

Determining the policies and practices of childhood immunization reminders and recalls in Alberta

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Introduction/Background: Immunization reminders (of upcoming appointments) and recalls (for overdue vaccines) are known to enhance immunization rates. Yet, there is no provincial policy on their use in Alberta. The purpose of this study was to explore any existing reminder/recall policies in each of the 5 Alberta Health Services (AHS) zones. Future work will focus on how reminder/recall systems are operationalized in practice in public health centres (PHCs) across the province.

Methods: An environmental scan of reminder/recall policies was conducted in Alberta using structured telephone/in-person interviews of AHS zone public health leaders. Where a policy existed, we assessed policy characteristics and perceived strengths/weaknesses.

Results and Analysis: Of the 4 zones that participated, 2 have reminder policies and 4 have recall policies. All zones use telephone reminders 1-2 days before appointments, half using manual calls and half with automated delivery. One zone with an automated system also sends text message reminders, and manages reminders centrally rather than at the PHC level. For recalls for overdue vaccines, all zones conduct telephone recalls, and 3 zones follow-up via letters/postcards. Differences in automated versus manual recall delivery also exist between zones. Challenges reported by participants included that current manual reminder/recall systems are time-intensive, language barriers are not addressed, telephone calls are no longer the best mode of communication, and not all zones have resources for text messaging. Participants believed that automated systems would have the benefit of lessening staff workload and improving text message functionality, but highlighted the need to maintain the flexibility to tailor reminder/recall systems to the unique needs of their communities.

Conclusions and implications for vaccinology: There was variability among the zones regarding the presence of reminder/recall policies, and the specific guidelines for how PHCs should conduct reminders/recalls. Building on this policy assessment, the next step will be to focus on assessing reminder/recall operational practices in PHCs across Alberta.

Immunization by history in the school-based setting

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Introduction/Program need and objectives: The National Advisory Committee on Immunization has defined optimal immunization practice in Canada through the National Guidelines for Immunization Practice. These guidelines specify that immunization services should be readily available; that vaccine providers facilitate timely receipt of vaccine; use all clinical opportunities to screen for needed vaccines; and to administer all doses for which the client is eligible at each visit. In British Columbia (B.C.) most health authorities have used a standard immunization consent which is limited to only the vaccines that were part of the school based program. The use of the Panorama-generated Personalized Consent (PPC) reports within the Public Health Information System would assist Public Health Nurses (PHNs) in B.C. to demonstrate best practice through immunization by history at school immunization clinics.

Program methods and activities: During the 2015/16, 2016/17 school years, two health authorities in B.C. piloted the use of PPC. The piloting of the PPC was done gradually by increasing the number of schools involved over 3 years. The expanded use of the PPC in these health authorities presented an opportunity to solicit user feedback. This was done using an online survey tool called Checkbox®.

Program results or outcomes (including evaluation): The survey respondents provided valuable feedback on what was working well and how the PPC could be improved. As a result of the evaluation, essential revisions were made to the PPC which were seen to provide more clarity for users to complete the PPC, and improve accuracy and efficiency.

Implications for practice or policy: This evaluation has helped to inform the revisions to the PPC to improve the process of immunization by history at school immunization clinics in two health authorities in B.C. Personalized immunization consent generated through an electronic immunization registry will improve quality by assisting public health immunizers to apply optimal immunization practice in school based immunization programs.

The CARD system for improving the vaccination experience at school: Results of a small-scale implementation project

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Introduction/Background: Vaccinations at school can be stressful for students. We implemented a multi-faceted knowledge translation intervention - The CARD System (CARD: C-Comfort, A-Ask, R-Relax, D-Distract) - to improve the vaccination experience at school and evaluated impact on program delivery outcomes.

Methods: Mixed methods study involving a controlled clinical trial and focus group interviews. CARD was implemented in 5 schools; 5 other schools acted as controls. In CARD schools, school liaison public health nurses secured preferred spaces for clinic days (i.e., library and private room) and permission for students to use external distraction devices. Nurses educated students about coping strategies in an in-class lesson and students selected their preferred coping strategies for upcoming vaccinations. On the day of vaccination, injecting nurses accommodated student requests. Outcomes included; school vaccination rate, student symptoms, and perceptions of CARD by all stakeholder groups - students, nurses, school staff and parents.

Results and Analysis: Altogether, 247 students were vaccinated in round 1 clinics and 223 in round 2. Seventy-eight students, nurses, school staff and parents participated in focus group interviews. The vaccination rate did not differ between groups in CARD vs. non-CARD schools for round 1 (76% vs. 77%) or round 2 (68% vs 70%). Fewer students ($p<0.05$) in CARD schools reported high levels of fear and dizziness during vaccination. There was no impact on student pain. All participants felt that CARD promoted a student-centred approach to vaccination and were in favour of using CARD for school vaccinations. Nurses reported acceptability, appropriateness, feasibility and satisfaction with CARD.

Conclusions and implications for vaccinology: This small-scale implementation study demonstrated that CARD is a promising new approach for improving the delivery of vaccinations at school. Additional work is recommended to evaluate its impact in other public health units and school vaccination contexts. This includes evaluating vaccination uptake. Improving the vacccination experience for students has the potential to benefit vaccination uptake because measures are being taken to address students' primary concern about vaccination - the needle.

Protecting York Region's private school students from vaccine preventable diseases

Chao M

Introduction/Program need and objectives: York Region Public Health (YRPH) is responsible for ensuring students have up-to-date immunization information on file with public health for diseases identified within Ontario's *Immunization of School Pupils Act* (ISPA). Under the ISPA, students with incomplete information can be suspended for up to 20 school days. Historically, YRPH focused on ensuring the immunziation information of students aged 7 and 17 attending publicly funded school boards were in compliance with the ISPA. In the 2017/18 school year, YRPH assessed private school students aged 7-17 against the ISPA for the first time.

Program methods and activities: A tailored approach was required based on the governance structure of private schools in York Region. Unlike publicly funded schools, private schools are independently governed. YRPH established 70 independent relationships with private schools. An inclusive and collaborative approach was implemented focusing on students, parents/guardians, school administrators and health care providers, including: contacting individual administrators to provide them with information on the ISPA; sending up to three letters to students/parents/guardians reminding them of the importance of immunization and risk of potential suspension; providing a dedicated phone line for parents/guardians; supporting health care providers with information about the ISPA; and offering additional evening and suspension day immunization clinics.

Program results or outcomes (including evaluation): Overall, 9,029 private school students were assessed against the ISPA. Of these, 4,167 (46%) students were identified as having outdated information. Only 111 (2.7%) students were suspended and all were back in school within a few days. Our inclusive and collaborative approach resulted in 100% of private school students having up-to-date immunization information on file with public health for ISPA designated diseases.

Implications for practice or policy: Private schools' decentralized governance structure can present additional challenges, requiring intensive individualized working relationships. By implementing a robust, collaborative and inclusive approach, private school students can be equally supported to ensure protection against designated vaccine preventable diseases under the ISPA.

Staying clear of pain and fear: A survey of policies and practices in Ontario public health school immunization clinics

Bucci LM, Taddio A, MacDonald NE, Segall R

Introduction/Background: Youth pain and fear of needle injections account for 1 of 5 vaccine refusals (Taddio et al., 2012). Despite the existence of evidence-based clinical practice guidelines (CPG), there is little evidence to suggest that youth are benefitting from pain and fear interventions (Taddio, et al., 2015). This study identifies pain and fear policies and practices by Ontario public health units.

Methods: We developed and pre-tested a telephone-administered survey of 53 questions in binary, multiple choice, and open ended formats with the Canadian Nurses Coalition on Immunization (CNCI). One respondent was invited from each public health unit in Ontario (n=36). Eligible respondents included public health nurses, vaccine preventable disease managers, supervisors, or directors of immunization clinics familiar with policies and practices. The approximate duration was 1 hour.

Results and Analysis: The study is ongoing. Since September 2017, 10 public health units were invited; 9 participated. We found that a majority of units have formal policies and practice procedures on pain and fear management; and the most reported interventions used are object distraction and peer presence. Survey participants noted challenges to implementing interventions, including: 1) unit budget; 2) school logistics (i.e., a private room is only available if the school can accommodate); 3) school policies (i.e., not all schools permit electronic distractions); and 4) poor communication and/or relationships between the unit and the schools. At the same time, none of the units surveyed reported monitoring for pain and fear practice outcomes. These findings were consistent for units serving rural, urban, or mixed communities.

Conclusions and implications for vaccinology: This study demonstrates the existence of policies and procedures for pain and fear mitigation in Ontario public health units. However, evidence-based interventions are under-utilized. By identifying challenges to implementation, we are taking the first step in making changes to improve the immunization experience for youth. This, in turn, has the potential to improve vaccination acceptance and improve long-term health outcomes.

A multi-site examination of factors related to vaccine uptake in youth with autism spectrum disorder

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Introduction/Background: Youth with autism spectrum disorder (ASD) may be under-vaccinated for many reasons, including persisting parental beliefs in a relationship between vaccines and ASD, difficulty tolerating medical procedures, and factors contributing to vaccine hesitancy in the general population. Studies to date have not thoroughly examined vaccination rates or factors that contribute to omitted or missed vaccinations in this group.

Methods: We are carrying out a multi-site study (in Nova Scotia and Alberta; NS and AB) to examine factors related to vaccine uptake in youth with ASD. To accomplish this, we have conducted focus groups and interviews with parents of youth with ASD in NS and AB. Parents were selected to represent varied vaccination-related decisions and experiences. Through a second part of the study, not described here, we are employing database linkage methods to look at the comparative rates of vaccine uptake in youth with ASD and their peers without ASD.

Results and Analysis: Data collection (4 focus groups; 34 interviews) was completed in June 2018. A constant-comparative and concept development analysis has been conducted for NS data and is underway for AB data.

Thus far, our findings suggest that many parents of youth with ASD support childhood vaccination. Although some have concerns about a vaccine-ASD link, misgivings about vaccination in this group are similar to those observed in the general population. Parents of youth with ASD described a number of barriers to vaccination, including anxiety, sensory sensitivities, previous negative medical experiences, inexperienced/unfamiliar healthcare providers, and difficulties tailoring school-based vaccination experiences.

Conclusions and implications for vaccinology: Individuals with ASD face considerable barriers in accessing health care services. By identifying factors that influence vaccine uptake for youth with ASD, this study will inform the development of tailored interventions to respond to the unique needs of this group. This will have important public health implications, both for a vulnerable group and for society.

Vaccine coverage among children with epilepsy in Ontario, Canada

Donelle J, Top K, Righolt C, Pabla G, Brna P, Deeks S, Smith B, Mahmud S, Hawken S

Introduction/Background: Children with epilepsy are at increased risk of complications from vaccine-preventable infections. Previous studies of vaccine coverage in this vulnerable population suggest that they may be under-immunized compared to other children, despite immunization guidelines encouraging adherence to standard schedules. The objective of this study was to estimate the risk of incomplete immunization in children with epilepsy in Ontario, Canada.

Methods: We conducted a retrospective cohort study including all live births in Ontario, creating two cohorts: infants (born 2005-2013) and preschoolers (born 2005-2008). We extracted demographic information, epilepsy status, and routine childhood immunization visits from administrative healthcare databases housed at the Institute for Clinical Evaluative Sciences. Incomplete immunization status was defined as <5 immunization visits by 2 years of age or no visits between 17 and 24 months (infant cohort), and <6 immunization visits by age 7 or no visits between 4th and 7th birthdays (preschooler cohort). Multivariable logistic regression models, adjusted for gender, income quintile, regional health authority, and mental health comorbidity, were used to estimate the association between epilepsy and immunization completeness.

Results and Analysis: The infant cohort included 1,234,263 eligible infants, 15,905 (1.3%) of whom were diagnosed with epilepsy by 18 months. The preschooler cohort included 536,789 children with 12,521 (2.3%) being diagnosed with epilepsy before the age of 4. Complete immunization coverage was the same in children with and without epilepsy for each cohort: 65% (infant) and 54% (preschooler). There were no significant differences in immunization completeness in children with and without epilepsy for infants (adjusted odds ratio 0.98; 95% confidence interval 0.95-1.01) or preschoolers (1.03; 0.99-1.06).

Conclusions and implications for vaccinology: Our findings suggest children with epilepsy have similar immunization coverage to children without epilepsy in Ontario. With overall immunization coverage in Canada being below the World Health Organization's target, methods to address vaccine hesitancy and improve coverage are still needed.

Vaccine coverage among children with epilepsy in Manitoba, Canada: A Canadian Immunization Research Network Study

Righolt C, **Top K**, Pabla G, Donelle J, Brna P, Deeks S, Smith B, Hawken S, Mahmud S

Introduction/Background: Children with epilepsy are at increased risk of complications from vaccine-preventable infections. Previous studies of vaccine coverage in similar populations suggested that they may be under-vaccinated despite guidelines encouraging adherence to routine immunization schedules. The objective of this study was to estimate the risk of incomplete vaccination in children with epilepsy in Manitoba, Canada.

Methods: We conducted a retrospective cohort study including all live births in Manitoba, creating two cohorts: infants (born 2005-2013) and preschoolers (born 2005-2008). We extracted demographic information, epilepsy status, and routine childhood vaccinations from administrative health databases maintained by Manitoba

Health. Incomplete vaccination status was defined as <5 vaccination visits by age 2 years or no visit between 17 and 24 months (infant cohort), and <6 vaccination visits by age 7 or no visit between the fourth and seventh birthdays (preschooler cohort). Multivariable logistic regression models, adjusted for gender, income quintile, regional health authority, and mental comorbidity, were used to estimate the association between epilepsy and vaccine completeness.

Results and Analysis: The infant cohort included 134,166 eligible infants, 653 (0.5%) of whom were diagnosed with epilepsy by age 18 months. 68% of infants with epilepsy were up-to-date with their vaccinations at age 2 compared to 73% of those without epilepsy. The preschooler cohort included 53,569 children with 483 (0.9%) diagnosed with epilepsy by age 4. 74% of preschoolers with epilepsy were up-to-date with their vaccinations at age 7 compared to 76% of those without epilepsy. Vaccine completeness was slightly lower among infants with epilepsy (odds ratio 0.8; 95% confidence interval 0.7-0.9), no difference was observed among preschoolers (0.9; 0.7-1.1).

Conclusions and implications for vaccinology: Our findings suggest children with epilepsy in Manitoba have a lower vaccine coverage at age two than children without epilepsy. This difference does not persist, as coverage is similar at age seven.

Varicella antibody levels in children less than 1 year: Assessment of waning immunity

Hughes S, Science M, Savage R, Severini A, McLachlan E, Richardson S, Crowcroft N, Deeks S, Halperin S, Hatchette T, Gubbay J, Mazzulli T, **Bolotin S**

Introduction/Background: Infants <12 months are at risk for severe disease and complications from varicella. Although infants receive transplacental antibodies from their mothers during pregnancy, not all mothers are immune to varicella. Protection in infants of immune mothers wanes due to antibody decay, leaving them susceptible before their first varicella vaccination, which in Ontario is administered at 15 months. The objective of this study was to investigate immunity to varicella in infants <12 months in Ontario.

Methods: Infants <12 months who were born at ≥37 weeks gestational age and had sera collected at The Hospital for Sick Children (Toronto, Canada) between 1/1/2014 and 12/31/2016 were included. Infants with suspected or confirmed immune deficiency, an underlying condition associated with antibody loss, received intravenous immunoglobulin, intramuscular immune globulin or blood transfusions, or had a history of varicella were excluded. Eight age bands were used to group the proportion of samples considered immune, using a previously determined varicella gpELISA neutralization threshold of 150mIU/mL.

Results and Analysis: Sera from 196 infants were tested; 56% (110/196) were male, and 35% (69/196) had underlying medical conditions. The most common underlying conditions were central nervous system (e.g. - seizure disorder), or gastrointestinal disorders. In the first month of life, 92% (23/25) of infants had antibodies above the protective threshold. By three months, protection decreased to 21% (5/24), by six to eight months none of the infants had levels above the threshold. Four percent (1/24) of infants age nine to eleven months were immune.

Conclusions and implications for vaccinology: We found that varicella maternal antibody protection in infants wanes rapidly, resulting in most infants being susceptible by three months of age. This susceptibility gap has implications for isolation of hospitalized infants exposed to varicella, public health management of daycare exposures, and the need for herd protection of infants through high vaccine coverage in older children and healthcare workers.

Measles antibody levels in children less than 1 year: Assessment of waning immunity

Bolotin S, Savage R, Severini A, McLachlan E, Richardson S, Crowcroft N, Deeks S, Halperin S, Hatchette T, Gubbay J, Mazzulli T, Science M

Introduction/Background: Infants are at risk for severe complications from measles. In the Americas, where measles elimination was recently certified and maternal immunity is mainly from vaccination rather than natural infection, infant immunity may wane below the protective threshold sooner than anticipated. The objective of this study was to investigate humoral immunity to measles in infants <12 months of age in Ontario.

Methods: We randomly selected sera collected at The Hospital for Sick Children (Toronto, Canada) between January 1, 2014 and December 31, 2016 from infants <12 months who were born at ≥37 weeks gestational age. We excluded infants with suspected or confirmed immune deficiency, an underlying condition associated with antibody loss, if they had received intravenous immunoglobulin, intramuscular immune globulin or blood transfusions, or had a history of measles or measles vaccination. Up to twenty-five sera from eight predetermined age bands were selected and tested for measles neutralizing antibody using the gold-standard plaque reduction neutralization test. The proportion of samples considered immune at each age-band was calculated, using a previously determined threshold neutralization titre of 192mIU/mL.

Results and Analysis: We included 196 infants in the study; 56% (110/196) were male, and 35% (69/196) had underlying medical conditions, most commonly central nervous system disorders (e.g. - seizure disorder), or gastrointestinal disorders. In the first month of life, 80% (20/25) of infants had antibodies above the protective threshold. By three months, this decreased to 8% (2/24) and by six months none of the infants had titres above the protective threshold.

Conclusions and implications for vaccinology: In an elimination setting, measles maternal antibody protection in infants wanes earlier than previously observed in non-elimination settings, with most infants becoming susceptible by three months of age. Our findings have important policy implications relating to the timing of the first dose of measles-containing vaccine and infant post-exposure prophylaxis recommendations.

Measles importations in Canada, 1998 to 2017

Saboui M, Humber L, Huang G, Hiebert J, **Reyes-Domingo F**

Introduction/Problem definition that demonstrates the need for a policy change: Endemic transmission of measles has been eliminated in Canada since 1998. However, Canada's elimination status remains a challenge due to importations of measles from other countries, where the disease is still endemic. This study describes measles importations to Canada from 1998 to 2017.

Research Methods: Case data, including immunization information were obtained from the Canadian Measles and Rubella Surveillance System (CMRSS). Isolates were sent to the National Microbiology Laboratory for confirmation of genotype and further studies including strain identification. Incidence rates (IRs) were calculated per 100,000 population.

Results and Analysis: Since the inception of the enhanced surveillance system (CMRSS) in 1998, a total of 200 importations have been reported. The Philippines, Pakistan, France and India accounted for the majority of importations. The median age of imported cases was 14 years. Average IRs were highest among infants less than one year of age (5.8), followed by children 1 to 9 years of age (0.62). Immunization information was available for 76% of cases. Measles imported cases tended to be unimmunized (128/152). Cases imported to Canada who were fully immunized represented a small proportion of cases (7/152). Among the 200 imported cases 64 cases were associated with domestic outbreaks and among these cases, 37 were index cases of outbreaks in Canada. Genotype B3 accounted for the largest proportion of importations (39%), followed by D8 (23%) and D4 (21%).

Recommendations and implications for practice: Despite importations of measles cases from abroad, Canada continues to successfully maintain its elimination status, likely due to high rates of immunization coverage and timely case and contact follow-up. The importance of maintaining high vaccine coverage is key to preventing importation of measles among Canadians travelling abroad to prevent further transmission once the virus has been imported to Canada.

Epidemiology of a measles outbreak in Toronto, Canada - March to May 2017

Kadri O, Finkelstein M, Hu J, Arthur A, Dubey V

Introduction/Background: While endemic transmission of measles has been interrupted in Canada, imported cases continue to be reported. Despite high measles immunization coverage rates, a measles outbreak occurred in Toronto in spring 2017 linked to travel. Two of the three cases were exposed to the index case, a Nova Scotia resident who travelled to Halifax via Toronto's Pearson Airport on March 10 2017 while contagious. One additional confirmed case was also investigated concurrently. An extensive public health investigation was initiated, including an outbreak declaration, media messages, and activation of Toronto Public Health's (TPH) Incident Management System (IMS). The aim of this study is to summarize the key epidemiologic and public health response indicators related to the outbreak investigation.

Methods: Data for confirmed and suspect cases reported to TPH, as well as a subset of high-risk contacts, were captured in the integrated Public Health Information System (iPHIS). Panorama was used to determine immune status, where possible for exposed students. Descriptive analyses were conducted of measles cases and associated contacts using Microsoft Excel 2013 and SAS version 9.3. Variables included demographics, source of infection, vaccination status and periods of communicability.

Results and Analysis: Three confirmed cases of measles among adult Toronto residents were identified, all with the D8 genotype. In total, 1,163 contacts were investigated, and five post-exposure prophylaxis immunization clinics were held. A total of 573 students, staff, and other contacts associated with a Toronto elementary school were assessed and 186 were initially excluded under Ontario's Immunization of School Pupils Act.

Conclusions and implications for vaccinology: As a global transportation hub, importation of measles cases to Toronto from other parts of the world is a real and significant risk. It is critical to continue robust routine surveillance programs to detect these cases, initiate rapid case and contact follow-up, and maintain programmatic efforts to keep vaccination rates high in all Toronto neighbourhoods.

Vaccine safety surveillance and trends in adverse events following immunization (AEFI) reporting in Toronto, 2010 to 2017

Kadri O, Dowsett K, Beckermann K, Dubey V, Stuart R

Introduction/Background: In Toronto, surveillance and timely reporting of AEFI is a key component for a functional vaccine safety monitoring system. This reporting allows for monitoring of vaccines administered to the population. Although vaccines are designed to be both safe and effective, AEFI do occur and need to be reported in order to identify issues and take appropriate corrective action. The aim of this study is to document trends and summarize the reports of AEFI for administered vaccines in Toronto from 2010 to 2017.

Methods: Confirmed AEFI reported following vaccines administered from 2010 to 2017 were extracted from the Ontario integrated Public Health Information Database (iPHIS). Current and 7-year historical AEFI data were analyzed with Microsoft Excel 2013 and SAS version 9.3. AEFI reporting rates were calculated per 100,000 population and vaccine-specific reporting rate per 100,000 doses distributed.

Results and Analysis: 513 confirmed AEFI were reported from 2010 to 2017, with an overall reporting rate of 2.3 per 100,000 population. 72 (14.0%) of the reported AEFI were considered medically important events; 25% of these events were reported following influenza vaccinations. The most commonly reported medically important events were: anaphylaxis (28%), and other severe/unusual events (21%). The vaccines for which AEFI were most commonly reported over the last 8 years were influenza (22%) and adacel (Tdap) (10%). The annual reporting rate between 2010 and 2017 ranged from 1.8 to 2.9 per 100,000 population. In 2017, the annual AEFI reporting rate (2.7/100,000 population) in Toronto was 23% higher than the previous 7-year mean reporting rate (2.2/100,000 population).

Conclusions and implications for vaccinology: AEFI reporting, examination of reports and investigation of serious cases are essential to ensure the quality and safety of immunization services. Overall, we found a low

AEFI reporting rate, with fluctuations from year to year. The most commonly reported AEFI were mild and serious adverse events were very rare.

Preventability of invasive pneumococcal disease in children under 5 years of age, BC 2014 - 2017

Treloar C, Naus M

Introduction/Background: The purpose of this analysis was to characterize trends in preventability of invasive pneumococcal disease (IPD) cases in British Columbia among both healthy and medically high risk children <5 years of age, based on reported risk factors. Infants and children at high risk for IPD are recommended for additional doses of pneumococcal conjugate and polysaccharide vaccine, based on age at development of risk factors.

Methods: In June 2018, IPD case reports for children <5 years of age from 2014 to 2017 were extracted from the provincial pediatric IPD database. The database contains data on IPD risk factors, immunization history prior to onset, and serotyping results. Risk factor data were used to categorize cases as children as high risk for IPD or healthy. Cases' immunization status was assessed using documented records of pneumococcal vaccine(s) and date(s) of receipt to classify cases by preventability.

Results and Analysis: From 2014 to 2017 there were 79 cases of IPD among children <5 years of age. The majority of cases (n=57) were not preventable by the current program. Ten cases were preventable; among these, six cases were due to IPD serotypes covered only in the 23-valent pneumococcal polysaccharide vaccine (PPV23) among children eligible for, but with no documented receipt of, PPV23.

Conclusions and implications for vaccinology: Pneumococcal polysaccharide vaccine is indicated for medically high-risk individuals 2 years of age and older; for children immunized according to the routine immunization schedule, the first routine opportunity for immunization catch-up after becoming age eligible for PPV23 occurs at Kindergarten entry. Opportunities to improve PPV23 uptake by children with at-risk health conditions are recommended at multiple levels of the health care system.

Decline in adverse event following immunization (AEFI) reporting in British Columbia (BC), 2005 to 2017

Treloar C, Naus M

Introduction/Background: In May 2004, BC introduced voluntary electronic reporting of AEFI through the public health information system. To reduce the reporting burden during the H1N1 pandemic influenza immunization campaign, two local event types were made non-reportable in September 2009. The national report form was implemented in BC in 2013, which led to further changes to reportable events. A descriptive analysis was undertaken to explore AEFI reporting trends and understand the impact of these changes.

Methods: AEFI reports from January 2005 to December 2017 were extracted from the Public Health Data Warehouse. Reports following H1N1 vaccine alone were excluded. Reports were summarized by the type of event(s), vaccine(s), recipient demographics, and seriousness. Historic reports with event types that were changed were identified. To explore the impact of these changes, AEFI trends with and without these reports were compared.

Results and Analysis: The annual average number of AEFI reports in BC dropped nearly 75% between 2005-2008 and 2015-2017 (1,855 vs. 472 reports). When reports with solely event types that were changed in 2009 and 2013 were excluded, the average number of reports from 2005-2008 decreased to 985 annually. Approximately 350 AEFI reports per year were reported solely with events that became non-reportable in 2009, with the remainder of the difference accounted for by event types impacted by the implementation of the national reporting form. The number of reports categorized as a serious AEFI remained relatively stable throughout (range: 107 to 171 annually).

Conclusions and implications for vaccinology: The impacts of changes to reportable events need to be understood in order to meaningfully interpret AEFI trends in BC. After accounting for these artifactual changes, the declining trend in AEFI reports remained, but was more moderate. Changes to the BC immunization schedule may contribute to the remaining decline.

Revisiting the epidemiology of pertussis in Canada

Thommes E, Wu J, Tomovici M, Lee J, Chit A

Introduction/Background: Inferring and interpreting the dynamics of pertussis in Canada from surveillance data has been the subject of much research, leading to a variety of conclusions about the role played by the introduction of successive new vaccine technologies. A major challenge here is that the level of detail of Canadian pertussis reporting has significantly changed over time. Yet, accurately characterizing the burden of pertussis is of critical importance because it informs public health decision-making. Here, we aim to curate a picture of pertussis disease in Canada using over 90 years of publically reported data.

Methods: Using published yearly reports, we assemble and present Canadian pertussis data for the period from 1924 to 2015, encompassing the pre-vaccine era, introduction of vaccine, changes to vaccine technology and finally the introduction of booster doses. A significant fraction of cases, especially prior to 1988, do not include age information. We impute missing ages by assuming that their age distribution follows that of the age-specific cases.

Results and Analysis: We obtain an adjusted age-stratified, longitudinal view of the burden of pertussis in Canada, in which, below age 20, the incidence from 1972 to 1988 is significantly higher than existing estimates. This has two key implications: i) The surge in the average yearly incidence of pertussis that began in 1988 was less strong than currently inferred, and ii) contrary to current understanding, the average yearly incidence of pertussis from 2000 (when the incidence dropped again) to 2015 has been lower, not higher, than it was from 1972 to 1988.

Conclusions and implications for vaccinology: Changes in the epidemiology of pertussis over time have been used to draw conclusions about the effectiveness of whole-cell, adsorbed whole-cell, and acellular pertussis vaccine in Canada. This work suggests that the current understanding of the relative performance of these different vaccine technologies may need to be reassessed.

Asymptomatic infection and transmission of pertussis in households: A systematic review

Craig R, Kunkel E, **Crowcroft N**, Fitzpatrick M, de Melker H, Althouse B, Merkel T, Scarpino S, Koelle K, Bolotin S

Introduction/Background: The global resurgence of pertussis is a complex phenomenon, which remains poorly understood. Recent evidence suggests asymptomatic infection may have an important role in transmission dynamics and ongoing pertussis circulation, however the burden of asymptomatic infection has not been studied in detail. We completed a systematic review to describe the burden of asymptomatic infection amongst household contacts of pertussis cases, and examine for evidence of asymptomatic transmission.

Methods: We searched MEDLINE, Embase, CINAHL, BIOSIS Previews, Scopus, and CENTRAL for eligible studies published before November 22, 2016. To be included, each study needed to: 1) document household exposure to a laboratory-confirmed pertussis case, 2) collect and test specimens from household contacts regardless of symptom presentation, and 3) report the number or proportion of laboratory-confirmed cases and contacts with typical, mild/atypical or asymptomatic infection. We used the Meta Quality Appraisal Tool (MetaQAT) to assess the quality of included studies.

Results and Analysis: Our search retrieved 14,408 titles and abstracts. Of these, 26 studies were included. Across studies, asymptomatic infection was detected in 4.8% (95%CI: 2.6, 7.1%) to 55.6% (95%CI 32.6, 78.5%) of household contacts tested, and mild/atypical infection was detected in 3.0% (95%CI: 0.3, 6.2%) to 46.2% (95%CI: 27.0, 65.3%) of contacts tested. We identified seven studies presenting evidence consistent with asymptomatic

pertussis transmission, although the direction of transmission in these studies was not always clear due to limitations in study design.

Conclusions and implications for vaccinology: Our results demonstrate a high prevalence of subclinical infection in household contacts of index cases, which often remains undiagnosed and uncounted, but may play a substantial role in the ongoing transmission of disease. Further, our review reveals the need for research that directly explores the roles that immunization and asymptomatic infection play in pertussis transmission. Filling these gaps in our understanding is essential to support the development of better tools for controlling pertussis.

Developing agent-based modeling platform to test interventions to control pertussis: A Canadian Immunization Research Network study.

Hempel K, McDonald W, Osgood N, Fisman D, Doroshenko A

Introduction/Background: Pertussis (whooping cough) is a vaccine preventable contagious respiratory disease that has seen a recent resurgence in vaccinated populations. The National Advisory Committee on Immunization (NACI) in Canada recently recommended maternal pertussis immunization to protect infants, who represent the most vulnerable group. There is a need to develop tools to evaluate the effectiveness of this and other interventions on pertussis control. Agent-based models provide opportunities to test such strategies on realistically simulated populations.

Methods: We constructed a flexible agent-based model using AnyLogic software for simulating pertussis in Alberta. The population agents were explicitly modeled as individuals associated with households and schools (for children), with realistic birth rates and age distributions. We placed agents in a stylized distance-based network. Population characteristics were calibrated with data from published literature, vital statistics reports, department of education school tables, and the 2016 Census. Pertussis biology and immunization schedules were depicted using model structures found in published literature and using a *de novo approach*.

Results and Analysis: Our model currently has the capability to realistically simulate complex interacting dynamics including household and school contacts, waning of natural and vaccine-acquired immunity, changing age-structure and vaccine attitudes translating into variable vaccine coverage. Furthermore, our model is the first agent-based model to depict the mechanism whereby protection derived from maternal immunization can translate into various levels of protection in infants. This feature of the model enables simulation and exploration of synergistic effects of maternal-infant immunization and potential blunting of immune response in infants.

Conclusions and implications for vaccinology: Our agent-based model is a valuable platform to assist public health authorities in evaluating the effect of maternal immunization and other public health interventions on pertussis control. This modeling approach offers strong value proposition for combining intrinsic characteristics of agents with network dynamics.

The evolving nature of Bordetella pertussis in Ontario, 2009-2017

Tsang R, Shuel M, Cronin K, Deng S, Whyte K, Marchand-Austin A, Ma J, Bolotin S, Crowcroft N, Schwartz K, Van Domselaar G, Graham M, Jamieson F

Introduction/Background: Pertussis is currently controlled by acellular pertussis vaccine in Canada. Despite vaccination, resurgence of pertussis is reported in a number of countries. This study examined the characteristics of Bordetella pertussis in Ontario in order to understand changes in the bacterium.

Methods: B. pertussis was cultured from all PCR-positive specimens at the Public Health Ontario Laboratory in Toronto between January 1, 2009 and December 31, 2017. All available cultures were characterized for expression of pertactin and serotype by immunoassay. Strains were genotyped by analysis of their vaccine antigen (fimbriae 3, pertussis toxin, filamentous hemagglutinin, pertactin) genes.

Results and Analysis: Of the 413 cultures, 399 or 96.6%; 11 or 2.7%; 1 or 0.2% expressed serotype 3, 2, and 2,3 antigens respectively while two were non-typeable due to lack of serotype antigens. Pertactin-deficient strains first emerged in Ontario in 2011 and their prevalence increased since from 16.7% (two isolates) to 70.8% (34 isolates) in 2016 and decreased to 46.2% (30 isolates) in 2017. Two sequence types (STs) predominated throughout the study and their prevalence fluctuated with time. While the rate of ST-1 decreased from 80.3% in 2009 to 20.0% in 2014 and increased again to 58.5% in 2017; ST-2 increased from 18.4% in 2009 to 80.0% in 2014 and decreased to 26.2% in 2017. More ST-2 (46.6%) than ST-1 (16.8%) strains were pertactin-deficient. Two newer ST-21 and ST-22 emerged in 2015-2017 and they were uniformly pertactin-negative.

Conclusions and implications for vaccinology: This study documented the emergence and increase in its prevalence of pertactin-deficient B. pertussis in Ontario. Two predominant genotypes also exhibited a potential cyclic pattern in their prevalence. These changes may be due to vaccine pressure and natural immunity in the population. Further studies will be required to understand how changes in the bacteria may affect disease rates and vaccine effectiveness.

Invasive meningococcal disease in Canada, 2012 to 2016

Roy M, Saboui M, Tsang R

Introduction/Background: Since the implementation of routine vaccination, the incidence of Invasive meningococcal disease (IMD) due to serogroup C in Canada has significantly declined. Vaccines targeting IMD serogroup B are not currently included in routine vaccination programs in Canada. This study describes the epidemiology of IMD and serogroup B in Canada from 2012 to 2016.

Methods: Case data were obtained from the National Enhanced IMD Surveillance System. The National Microbiology Laboratory confirmed serogroup and completed phenotype and clonal complex identification. Epidemiologic and laboratory data were linked retrospectively by probabilistic matching. Descriptive analyses of incidence by age, serogroup and phenotype were conducted. Incidence rates (IRs) were calculated per 100,000 population.

Results and Analysis: During the study period case reports of IMD decreased yearly, with a total of 583 cases reported from 2012 to 2016, corresponding to an annual average of 117 cases and an average annual IR of 0.33. Average IRs were highest among infants <1 (3.28), 1 to 4 (1.01), and 15 to 19 (0.79) year olds. Among the 63 cases reported in infants <1, 48% occurred before six months of age. Fifty-eight deaths were reported. Infants <1 year of age and adults aged 60 years and older accounted for the largest proportion of deaths (17% and 31% respectively). Serogroup B accounted for the majority of cases (61%) with serogroup information, followed by Y (21%), W (7%) and C (6%).

Conclusions and implications for vaccinology: IMD is a rare but severe infection in Canada that mostly affects the very young and young adults. Serogroup B continues to account for the greatest proportion of disease. In light of the study findings and the National Advisory Committee on Immunization recommendation to vaccinate against this serogroup only those at increased risk of IMD or in outbreak situations, it is important to continue to monitor the trends of IMD.

Clinical and economic impact of adolescent meningococcal serogroup B vaccination with a new vaccine in the Canadian population

Breton M, Huang L, Snedecor S, **Fanton-Aita F**

Introduction/Background: Invasive meningococcal disease (IMD) is uncommon but life threatening. The largest cause of IMD in Canada is now serogroup B meningococci. Between 2006-2011, incidence caused by serogroup B (MnB) was highest with 0.33 cases/100,000. Although infants have the highest incidence, adolescents and young adults are at highest risk of carrying and transmitting the bacteria. We assessed the clinical and economic

impact of adolescent vaccination against MnB disease considering alternate ages of administration and vaccine uptake.

Methods: A dynamic difference equation model was developed to simulate the transmission of MnB carriage among the entire Canadian population over 30 years. The age-group based IMD incidence, bacterial carriage, probabilities of disease outcomes, costs, and impact on quality of life were obtained from Canadian surveillance data and published literature. The vaccine was assumed to provide 85% protection against IMD and 26.6% against carriage acquisition. The model estimated vaccination impact following implementation of one of 3 routine MnB vaccination strategies: (1) age 14 with 75% uptake, along with existing vaccination school-based programs; (2) age 17 with 75% uptake, assuming school vaccination and; (3) age 17 with 30% uptake, assuming vaccination outside of school. Costs were calculated from the Canadian societal perspective.

Results and Analysis: With no vaccination, an estimated 3974 serogroup B cases would be expected over 30 years. Vaccination with strategies 1-3 estimated to avert 688, 1033, and 575 cases, respectively. These outcomes were associated with incremental costs per quality-adjusted life year of $976 000, $685 000, and $490 000.

Conclusions and implications for vaccinology: Our model indicated that if the vaccine reduces risk of carriage, vaccination of older adolescents even at lower uptake could be a clinically beneficial strategy to prevent life-threatening IMD. Due to the low disease incidence, MnB vaccination is unlikely to be cost-effective. When evaluating new MnB vaccination programs, decisions must rely on all criteria from the Erickson Framework.

Epidemiology of invasive Haemophilus influenzae (Hi), invasive pneumococcal disease (IPD), and invasive meningococcal disease (IMD) in northern Canada, 2001 – 2015

Huang G, Tsang R, Martin I, Demczuk W

Epidemiology of invasive *Haemophilus influenzae* (*Hi*), invasive pneumococcal disease (IPD), and invasive meningococcal disease (IMD) in northern Canada, 2001 – 2015

Introduction/Background: Although the incidence rates of invasive bacterial diseases have decreased since routine vaccination programs have been introduced, rates are still much higher in northern Canada. The objective is to describe the epidemiology of *Hi*, IPD, and IMD in northern Canada from 2001-2015.

Methods: Data for northern Canada were obtained from the International Circumpolar Surveillance network. Data for the rest of Canada were from the Canadian Notifiable Disease Surveillance System and the enhanced Invasive Meningococcal Disease Surveillance System. Population estimates were from Statistics Canada. Descriptive analyses of serotype/serogroup and incidence by year and age groups were conducted.

Results/Analysis: A total of 735 cases were reported: 513 cases (70.0%) of IPD, 200 cases (27.2%) of Hi, and 22 cases (3.0%) of IMD. The annualized incidence of IPD, *Hi*, and IMD per 100,000 were 23.1, 8.9, and 1.0, respectively. Incidence rates during this period for IPD and IMD were 2.8 (95% CI: 2.6-3.1) and 1.7 (95% CI: 1.2-2.7) times higher than the rest of Canada. For Hib, the incidence rate was 1.1/100,000 (n=25), 14.5 times (95% CI: 9.7-21.7) higher than the rest of Canada. Forty-four percent (n=228) of IPD cases had serotypes covered by the PCV13 vaccine and 32.6% (n=167) by PPV23 exclusively. Sixty-one percent (n=122) of *Hi* cases were serotype a, for which no vaccine is available. Eighteen percent (n=4) of IMD cases had serogroups covered by the MenC vaccine and 27.3% (n=6) by the quadrivalent vaccine exclusively. Annualized incidence rates per 100,000 were highest in the <2 year olds: 132.6 for IPD, 160.4 for Hi, and 18.9 for IMD.

Conclusions and implications for vaccinology: Sixty percent of cases had vaccine preventable serotypes. Further analyses on vaccination history and underlying conditions may inform public health action within this population. The high proportion of *Haemophilus influenzae* type a cases supports the development of a targeted vaccine.

Continuing surveillance of Haemophilus influenzae in Northwestern Ontario and the emergence of serotype a as a significant cause of invasive disease

Cerqueira A, Tsang R, Jamieson F, Ulanova M

Introduction/Background: Prior to the introduction of a pediatric conjugate vaccine in the early 1990s, Haemophilus influenzae serotype b (Hib) was a major cause of infant mortality globally. Inclusion of the Hib vaccine into pediatric immunization programs eliminated Hib disease almost entirely; however, an increased incidence of H. influenzae serotype a disease is now reported in several countries with a disproportionate burden of disease in Canadian First Nation, Inuit, and Alaskan Indigenous populations. Previous studies by our group found an increased incidence of invasive disease caused by H. influenzae serotype a (Hia), f (Hif), and non-typeable H. influenzae in Northwestern Ontario (50 cases between January 2002 to July 2011).

Methods: Here we reviewed the clinical presentations and pathogen characteristics of 21 cases of invasive H. influenzae disease hospitalized in Thunder Bay, Ontario, over a 5.5-year period (August 2011 – March 2017).

Results and Analysis: Among them there were two cases of Hib, seven cases of Hia, and twelve cases of non-typeable H. influenzae. Six cases presented as pneumonia, 5 resulted in respiratory failure, 3 resulted in septicemia and septic shock. Four out of five cases of respiratory failure resulted in fatality, with Hia infection associated in 1 case and NTHi implicated in the other 3. Moreover, 2 non-fatal adult cases of Hia presented as epiglottitis, which was not previously reported in the literature, and 1 fatal adult case of NTHi presented as necrotising fasciitis. Four pediatric cases under 3 years emerged as febrile illnesses, with two cases (1 Hia and 1 Hib) requiring urgent transfer to a tertiary care centre for further treatment. The solitary pediatric NTHi case presented as non-fatal respiratory distress.

Conclusions and implications for vaccinology: Our results stress the importance of continued surveillance of H. influenzae in the post Hib-vaccine era, and further support the significance of developing a Hia vaccine to prevent severe invasive disease.

Canadian pandemic influenza preparedness: How Canada is preparing for an influenza pandemic

Smith S, Henry B, Paddle L

Introduction/Problem definition that demonstrates the need for a policy change: Preparing to respond effectively to an influenza pandemic requires a comprehensive approach and collaboration among all levels of government. Key components of Canada's plan include: establishing and maintaining a long-term contract for a domestic supply of pandemic vaccine; procuring antivirals for national stockpiles; developing planning guidance for federal, provincial, territorial (FPT) health sectors outlining how we work together to prepare for and respond to an influenza pandemic. The purpose of this presentation is to highlight the components of the Canadian Pandemic Influenza Preparedness: Planning Guidance for the Health Sector (CPIP) and to demonstrate the importance of each component in an effective pandemic response.

Research Methods: In 2012, the FPT Deputy Ministers of Health directed that the CPIP be renewed based on the 2009 influenza pandemic experience, advancements in science and new approaches to emergency management planning. Since then, experts have led the renewal of the CPIP considering domestic and international H1N1 lessons learned reviews, relevant scientific and emergency management literature, international pandemic plans and key stakeholder input.

Results and Analysis: The CPIP now incorporates a risk management approach to pandemic planning. The 2009 pandemic taught us that a flexible and proportionate pandemic response is essential. Key components are: pandemic influenza vaccine; antiviral use and stockpiling; surveillance; laboratory; health care services; public health measures ; communications and research. The CPIP illustrates the importance of a coordinated and consistent approach to preparedness and response and using an approach consistent with the Canadian context, such as tailored approaches for those living in remote and isolated communities.

Recommendations and implications for practice: The CPIP is not an operational response plan. Rather, it provides planning guidance for the FPT health sector to use and adapt for their own pandemic plans. It highlights the crucial role of each response component and recommendations for each level of government.

Pandemic influenza severity assessment: Modelling Canadian influenza epidemic activity and severity thresholds using the moving epidemic method.

Sevenhuysen C, Shi Y, Sinilaite A, Lee L, Bancej C

Introduction/Background: Comparable seasonal influenza surveillance is essential for pandemic preparedness. Countries participating in the WHO Pandemic Influenza Severity Assessment (PISA) project use thresholds based on historical data to compare influenza activity across three parameters: virus *transmission*, *seriousness* of disease, and societal or healthcare *impact.* In Canada, three national surveillance indicators were selected for the PISA assessment based on their comparability over recent seasons. In this analysis, we explore the value of additional indicators in broadening the assessment of seasonal influenza severity.

Methods: For the parameter of *transmission*, two FluWatch indicators are used: the percentage of laboratory specimens positive for influenza, and the percentage of sentinel primary care visits for influenza-like illness. For the *seriousness* parameter, the number of sentinel paediatric hospitalizations with influenza is used. Two additional FluWatch indicators are considered: number of influenza outbreaks in long-term care facilities and hospitals (for *transmission*), and influenza-associated hospitalization rate per 100,000 population (for *seriousness*). The Moving Epidemic Method was applied to these five national surveillance indicators.

Results and Analysis: During the 2017/18 influenza season, the three indicators compared for the *transmission* assessment crossed the seasonal threshold within a week of each other. The outbreaks indicator crossed the high threshold at the peak of the season while the other two indicators stayed within the moderate level. Both indicators for *seriousness* crossed the seasonal threshold at a similar time, but the assessment levels using hospitalization rate were more variable over the course of the season.

Conclusions and implications for vaccinology: PISA assessments permit in-season assessments of transmission and severity of an influenza season relative to historical norms in near real time. The 2017-18 PISA assessment for Canada revealed a moderate influenza season compared to previous years. The assessments using influenza outbreaks and hospitalization rate may reflect the different impact on adult and paediatric populations. The PISA assessment for Canada may be improved by age-stratification or changing data into proportions.

Adverse events following immunization (AEFI) with influenza vaccines during the 2017/18 influenza season

Coulby C

Introduction/Background: Every year during seasonal influenza vaccination campaigns, the Public Health Agency of Canada (PHAC) and the Federal/Provincial/Territorial Vaccine Vigilance Working Group (VVWG) of the Canadian Immunization Committee conduct weekly enhanced monitoring of adverse events following influenza immunization. The objective of this seasonal adverse events surveillance system is to detect new or unusual patterns in the frequency or severity of adverse event reports following influenza immunization in order to identify possible vaccine safety issues that require further investigation. AEFI reports received at the federal/provincial/territorial level are voluntarily reported to PHAC for entry in to the Canadian Adverse Events Following Immunization Surveillance System (CAEFISS).

Methods: A descriptive analysis of AEFI reports following influenza vaccines administered between September 1, 2017 and February 15, 2018 and received by CAEFISS by March 1, 2018 was conducted. Data elements included in this analysis were demographics, AEFI category, seriousness, and vaccine trade name and lot number.

Results and Analysis: 675 AEFI reports were submitted to CAEFISS for the reporting period out of over 11 million influenza vaccine doses distributed. 31 reports (5%) were classified as serious adverse events (SAE). Hospitalization was the most frequent reason for classifying AEFI as serious (74%). The median age for all influenza AEFI reports was 36 years old (range: 6 months to 98 years). 64% of influenza AEFI reports were in

females. The most frequently reported AEFI category was vaccination site reaction (27%), followed by allergic reaction (18%).

Conclusions and implications for immunization programs: The number of AEFI reports received to date is below or within the average of previous seasons. Based on the continued low proportion of serious AEFI, the benefits of influenza vaccination continue to outweigh the risk.

FluWatchers: Evaluation of a crowd-sourced influenza-like illness surveillance application for influenza seasons, 2015-16 to 2017-18

Lee L, Bancej C, Mukhi S, Shi Y

Introduction/Program need and objectives: Participatory surveillance is an emerging field in syndromic surveillance that relies on "crowd-sourced" data. Traditional syndromic surveillance, including sentinel practitioner influenza-like illness (ILI) surveillance, has limitations including reporting delays, low participation, biases, and excludes individuals who do not seek medical care. To address these limitations, the Public Health Agency of Canada developed FluWatchers, Canada's first online crowd-sourced application for national population-based ILI surveillance.

Program methods and activities: FluWatchers tracks ILI across Canada by collecting weekly symptom-based reports via an online questionnaire from volunteer Canadians. Participants are asked whether they had a cough and/or fever in the past week. Data on influenza immunization status, absenteeism and health care utilization are also collected. The FluWatchers application was developed by and managed on the Canadian Network for Public Health Intelligence platform.

Program results or outcomes (including evaluation): FluWatchers was first launched as a pilot in the 2015-16 influenza season. Weekly participants have increased from a median of 398 in 2015-16, 749 in 2016-17 to 1,424 in 2017-18. Retention rates between the 2015-16 and 2016-17 and the 2016-17 and 2017-18 season were 79% and 80%, respectively. FluWatchers ILI and Sentinel ILI rates had a correlation of 0.56, 0.70, and 0.85 during the 2015-16, 2016-17, and 2017-18 seasons, respectively. In 2017-18, FluWatchers was formally incorporated into the FluWatch surveillance program, supplying data for several core indicators in the weekly FluWatch report.

Implications for practice or policy: FluWatchers is an example of an innovative surveillance program that is scalable, economical and acceptable to participants. In the past three seasons, FluWatchers has grown in participation. There have been no added program costs and there has been high retention among participants. FluWatchers shows great potential to inform public health policies by providing timely quantitative information needed for surveillance and health and economic modelling of vaccine program and policy options.

Development of the indicator framework for FluWatch, Canada's National Influenza Surveillance Program

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Introduction/Program need and objectives: During 2016-2017 the Public Health Agency of Canada set out to modernize FluWatch, Canada's national seasonal influenza surveillance program, established in 1996. One of three modernization goals was to align FluWatch surveillance indicators with a clearly defined vision for national influenza surveillance. Influenza surveillance experts from across Canada (n = 15), selected a core set of indicators for national influenza surveillance using a formal consensus process.

Program methods and activities: A literature search of indicators represented in global, national, and sub-national influenza surveillance reports and guidance documents identified candidate indicators for four current and one proposed FluWatch surveillance system components: virologic; syndromic; activity levels and outbreaks; severe outcomes and vaccine monitoring (proposed). Expert input was sought to expand the literature derived list. A survey was then administered to obtain expert assessment on the comprehensive set of indicators against 5 a priori determined criteria (comparable; relevant; evidence-based; sustainable;

understandable). Indicators for each FluWatch system component were ranked from highest to lowest overall score and presented to the expert group for discussion and final selection.

Program results or outcomes (including evaluation): The literature search yielded 34 unique indicators for further consideration via the survey. In total 17 indicators were deemed core to achieving FluWatch objectives. All but 3 of the selected core indictors received a weighted score of >70% against the 5 selection criteria; those ranking below (influenza associated mortality and hospitalized case fatality rates and influenza vaccine coverage) signalled indicators of public health importance where surveillance capacity has eroded or is yet to be sufficiently developed within FluWatch.

Implications for practice or policy: This core set of 17 indicators will serve to focus and inform investments to strengthen existing and develop new data sources to fulfill FluWatch's purpose to detect epidemics and other events of public health concern to contribute to the evidence base necessary for planning, development and implementation of programs and healthy public policies for the control of influenza.

Using routinely collected laboratory and health administrative data to assess influenza vaccine effectiveness: Introducing the Flu and Other Respiratory Viruses Research (FOREVER) Cohort

Chung H, Buchan S, Campitelli M, Schwartz K, Crowcroft N, Jackson M, Gubbay J, Karnauchow T, Katz K, McGeer A, McNally D, Richardson D, Richardson S, Rosella L, Simor A, Smieja M, Zahariadis G, Kwong J

Introduction/Background: Frequent changes in circulating influenza viruses and vaccine components necessitate annual estimates of vaccine effectiveness (VE). Traditionally, VE studies enroll patients who fulfill case definitions for respiratory infections and are tested for influenza. Linking data on laboratory specimens collected during clinical practice with administrative data permits highly powered studies to be conducted at low cost. We evaluated the validity of using such data for estimating VE.

Methods: We created the Flu and Other Respiratory Viruses Research (FOREVER) Cohort by linking laboratory results from 2009-2014 from 11 public health and 8 hospital laboratories across Ontario to databases housed at the Institute for Clinical Evaluative Sciences, including databases with billing claims for physician- and pharmacist-administered influenza vaccines. We evaluated the presence of information and selection biases and estimated VE in older adults (>65) using the test-negative design under conditions that emulated the inclusion criteria in traditional VE studies.

Results and Analysis: The FOREVER Cohort included results from 283,711 respiratory specimens. The overall linkage proportion to health administrative databases was 97.5%. Influenza positivity for older adults with unknown lag between illness onset and specimen collection was similar to those for whom illness onset date was documented to be ≤7 days before specimen collection, suggesting minimal outcome misclassification associated with information bias. The likelihood of influenza testing was similar between vaccinated and unvaccinated individuals, suggesting an absence of selection bias that could arise without a case definition for influenza testing. Lastly, VE estimates were similar under various conditions, were higher when accounting for misclassification of vaccination status, and were comparable to published estimates.

Conclusions and implications for vaccinology: The FOREVER Cohort can be used to estimate VE with negligible bias. Compared to traditional VE studies, routinely collected specimens create a larger, more generalizable sample. Linkage to health administrative databases can identify those with comorbidities and permit evaluation of VE in high-risk groups.

Influenza vaccine effectiveness in cancer patients: A population-based study using health administrative and laboratory testing data from Ontario, Canada

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Introduction/Background: Immunosuppression caused by cancer or its treatment may decrease influenza vaccine effectiveness (VE), but annual vaccination is still recommended. In this study, we estimated VE against laboratory-confirmed influenza among adult cancer patients.

Methods: We used the test-negative design to estimate VE in cancer patients and survivors aged ≥18 years who were tested for influenza during the 2010-11 to 2015-16 influenza seasons in Ontario, Canada. We identified patients using the Ontario Cancer Registry and linked their records to results from public health and hospital laboratories across Ontario and health administrative databases housed at the Institute for Clinical Evaluative Sciences, which includes databases with billing claims for physician- and pharmacist-delivered influenza vaccines. We used multivariable logistic regression to estimate the association between influenza vaccine receipt and laboratory-confirmed influenza.

Results and Analysis: We included 24,668 adult cancer patients, with 16% testing positive for influenza, 44% vaccinated, 79% having a solid tumour malignancy most recently, and 23% undergoing active chemotherapy. The overall VE against laboratory-confirmed influenza was 21% (95%CI, 15%-27%). Patients with solid tumour malignancies experienced higher VE than those with hematologic malignancies (25%; 95%CI, 19%-31% versus –2%; 95%CI, –20% to 14%, p-value for interaction=0.01). Those receiving active chemotherapy had a trend towards lower VE than those who were not (9%; 95% CI, –7% to 23% versus 23%; 95% CI, 17%-29%, p-value for interaction=0.12). VE was 16% (95%CI, 9%-23%) for patients >65 years and 30% (95%CI, 19%-39%) for patients ≤65 years, increasing to 28% (95%CI, 19%-36%) and 41% (95%CI, 30%-51%), respectively, when accounting for exposure misclassification.

Conclusions and implications for vaccinology: Although our results support general recommendations for cancer patients and survivors, patients with hematologic malignancies and those undergoing active chemotherapy may experience diminished VE. Strategies to increase influenza vaccine coverage among cancer patients and survivors, and alternative approaches to protect them from influenza such as immunization of their contacts, are warranted.

How to achieve consensus in complex decision-making processes? The case of the Quebec Influenza Immunization Program revision

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Introduction/Background: In 2015-2017 the Quebec immunization Committee (CIQ) revised the provincial Influenza Immunization Program (QIIP). Due to multiple criteria to consider, it was not possible to reach consensual decisions regarding the groups to be included in the QIIP. An approach based on Delphi technique was used.

Methods: The Delphi technique is widely used and well suited method for consensus-building that uses a series of questionnaires to collect data from a panel of stakeholders. A 3-iterations Delphi process was conducted using a standardized questionnaire based on the criteria of Erickson-De Wals Analytical Framework. For each of the 14 examined groups, CIQ members had to weight 15 criterias and to reach a decision using a 4-point Likert scale. After each round, answers were dichtomized to represent exclusion (strongly disagree + disagree) or inclusion (agree + strongly agree) in the QIIP. Results of each round were presented in details to the CIQ members and groups for which consensus was obtained were removed from the next round of consultation. The first two rounds were performed on-line and the third in person, during a CIQ meeting.

Results and Analysis: The first round resulted in unanimous consensus for 9 groups, in a majority for 2 groups and in conflicting results for 3 groups. The second round included only the 3 groups with conflicting responses. This round resulted in a majority for 2 groups and conflicting result for 1 group, although responses were less polarized compared to the first round. The last round focused on the same 3 groups, and resulted in unanimity for one group, and consensus for remaining two groups.

Conclusions and implications for vaccinology: Our use of the Delphi technique has allowed achieved consensus in a complex decision-making process. This technique is a transparent, consistent and simple approach regarding the decision-making for the optimisation of existing and implementation of new immunization programs.

Estimating the hospital burden of influenza in Canada, 2006-2016

Nwosu A, Shi Y, Schanzer D, McMullen C, Bancej C

Introduction/ Background: Annual epidemics of influenza result in substantial morbidity and mortality, especially amongst young children and adults above the age of 65 years. Influenza surveillance systems aim to provide near real-time detection of influenza activity, patterns and trends but do not capture absolute burden. In Canada, indirect statistical models are used to estimate the annual number of influenza-attributed hospitalizations. The aim of this study is to update estimates of the influenza- attributed hospitalization burden in Canada from 2006 to 2016 and to review validation evidence and methodological limitations of the model-based estimates.

Methods: Inpatient records for all provinces and territories in Canada except Québec were extracted from the Canadian Institute for Health Information (CIHI) discharge abstract database (DAD) by ICD-10 codes. A Poisson regression model of respiratory hospitalizations, excluding the pandemic season, was used to estimate the number of influenza-associated hospitalizations in Canada from September 2006 to August 2016. Sensitivity analyses assessed the stability of disease burden estimates under various model parameterizations.

Results and Analysis: Over the study period, there was an average of 179 000, 3300 and 1440 respiratory, pneumonia and influenza (P&I), and influenza hospitalizations per year. P&I and influenza were identified in 2% and 0.8% of all reported respiratory hospitalizations. The highest cumulative influenza hospitalization rate was reported in infants less than 2 years of age: 36 hospitalizations per 100,000 infants per year. Previous 2003-2014 estimates of influenza-attributed hospitalizations (33 hospitalization per 100 000 population per year) will be updated.

Conclusions and implications for vaccinology: Surveillance-based and administrative database hospitalization counts for influenza continue to underestimate the burden of influenza. In Canada, updated model-based estimates are needed to provide a more accurate picture of the burden of influenza. Annual estimates of the hospital burden of influenza are important to evaluate public health programs, inform vaccination guidance, allocate resources and understand the severity of this disease in the population.

Adverse events following immunization with a live zoster vaccine in Ontario, 2012-2017

Lim G, Harris T, **Murti M,** Meyer W, Hillier K, Deeks S

Introduction/Background: Zostavax® is a live zoster vaccine (LZV) approved in Canada since August 2008. In Ontario, a publicly funded program for adults 65-70 years was implemented in September 2016. We assessed adverse events following immunization (AEFIs) reported in Ontario following administration of LZV between 2012 and 2017 to inform program monitoring and evaluation.

Methods: AEFIs from January 1, 2012 to December 31, 2017 were extracted from the integrated Public Health Information System on May 11, 2018. Annual AEFI reporting rate was calculated by doses distributed (public and private combined). AEFIs were described by median age before and after the program and by sex. AEFIs were categorized by provincial surveillance definitions. We described serious AEFIs (World Health Organization definition) and medically important events (provincial definition).

Results and Analysis: During the study period, 280 LZV AEFIs were reported, representing 6.9% (280/4068) of total AEFI reports (all vaccines). The annual LZV reporting rate ranged between 15.6-27.6 reports per 100,000 doses distributed. AEFIs were predominantly reported among women (80.7%, 226/280). The median age before and after public program introduction increased from 60.8 to 65.4 years, respectively. The most frequently reported events (percentage of all LZV events; per 100,000 doses distributed) were: pain/redness/swelling

(59.3%; 12.8), cellulitis (24.6%; 5.3), rash (18.6%; 4.0) and allergic skin reactions (11.1%; 2.4). There was one serious AEFI reported during the study period (0.8 per 1,000,000 doses). This was a death in an elderly adult on immune-compromising medications. Four medically important events were reported: Guillain-Barré Syndrome, anaphylaxis, acute disseminated encephalomyelitis, and lab-confirmed zoster meningitis (genotyping not done).

Conclusions and implications for vaccinology: Median age of LZV AEFIs has increased with public program introduction. Overall findings are consistent with the LZV safety profile. Ongoing LZV safety surveillance is indicated in the context of the publicly funded program in Ontario.

Healthcare worker absenteeism rates after vaccinate-or-mask policy implementation in British Columbia, 2012-2017

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Introduction/Background: In 2012, British Columbia (BC) implemented a province-wide influenza prevention policy requiring healthcare workers (HCW) to either vaccinate or mask in patient care areas during influenza season. One policy goal was to reduce influenza-related HCW absenteeism. We describe differences in HCW absenteeism by vaccination reporting status since policy implementation.

Methods: Employee payroll data from seven health authorities in BC were extracted from December 1, 2012 to March 31, 2017. Data included birth year, gender and daily all-cause sick time, productive time and other leave time. Employee annual vaccination status (reported before December 1, reported December 1-March 31, not reported), were linked from the Workplace Health Indicator Tracking and Evaluation database. Sick rates were calculated as proportion of sick time to sick time plus productive time. Annual influenza season was defined as December 1 to March 31, when the policy is in effect. We compared influenza season sick rates in years with any vaccination to years with no vaccination reported among HCWs employed over the study period.

Results and Analysis: There were 107,258 employees; mean birth year was 1970.7 (range: 1932-1998) and 84% were females. Proportion reporting vaccination before December 1 ranged from 64.7% in 2012 to 70.4% in 2014. Sick rates by vaccination status in influenza season vs non-influenza season were: 5.16% vs 4.24% (reported before December 1), 6.05% vs 5.46% (reported after December 1) and 6.26% vs 5.98% (not reported), $p<0.01$. Among 6953 employees with more than one vaccination status, mean influenza season sick rate was 4.61% (vaccinated years) vs 4.71% (not reported years), $p=0.6$.

Conclusions and implications for vaccinology: HCWs not reporting vaccination have significantly higher sick rates in both influenza and non-influenza seasons compared to those vaccinated before December 1. Within individual HCWs, influenza season sick rates were not significantly different in years when they reported vaccination compared to years when they did not report.

Could a third dose of mumps containing vaccine be considered for healthcare workers (HCWs) in Alberta during mumps outbreaks?

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Introduction/Program need and objectives: Alberta Health Services (AHS) is a province wide health care organization in western Canada with over 100,000 HCWs. While it is unknown if a third dose of mumps containing vaccine will be helpful in limiting spread of mumps in a healthcare context, recent publications focused on community settings, have suggested that providing a third dose to at risk individuals may help to control outbreaks; especially if several years have elapsed since a second vaccine dose.

Program methods and activities: The AHS workplace health and safety program implemented a standardized baseline communicable disease assessment (CDA) as a condition of employment in 2017 to record immunization

histories, and to provide immunizations when applicable. HCW immunization records are stored in an internal database (MySafetyNet) that can be searched in order to review HCW immunization status.

Program results or outcomes (including evaluation): A search of the CDA/MySafetyNet database yielded record of 162,163 mumps immunizations (MMR or MMRV). Of those, 61,524 were recorded as having been administered between June 2008 and June 2018. Results for those HCWs born before 1970 and those born after 1970 were compared.

Implications for practice or policy: If a third dose of vaccine is proposed for outbreak control, then those workers who have had more than 10 years since their last vaccine could be targeted by using the MySafetyNet database. This intervention would be relevant to roughly half of the HCW population in AHS with variations observed between specialties, and based on birth year. This study helps to estimate workflow, volume, and cost.

Changes in the burden of laboratory-confirmed influenza in hospitalized adults: Toronto Ontario, 2010/11 to 2016/17: Association with testing for influenza

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Introduction/Background: As indications for testing for influenza broaden, influenza is increasingly being diagnosed in association with hospitalization in adults. We report data on the burden of illness associated with laboratory confirmed influenza requiring hospitalization (LCI-H) in Toronto, Canada from 2010/11 to 2016/17.

Methods: TIBDN (Toronto Invasive Bacterial Diseases Network) performs population-based surveillance for LCI-H in adults (≥15years) in Toronto and Peel Region, Canada. All positive tests for influenza are reported by participating laboratories and data collected by chart review and patient and physician interview. Death within 30 days of hospitalization was considered associated with influenza. Population data were obtained from Statistics Canada and the number of influenza tests completed from CIHI.

Results and Analysis: Over the 7 seasons, 9014 LCI-H episodes were reported. The median age of patients was 77 years (IQR: 62-86), 4787 (53%) were female, 4091 (45%) were vaccinated against influenza, and 7744 (86%) had underlying chronic disease. In Ontario, the rate of influenza testing increased from 1357 to 2921 per 100,000 population between 2010/11 and 2016/17 (Ptrend <0.0001). The age-standardized rates of LCI-H increased from 22.8 to 39.2 per 100,000 for the same period (Ptrend <0.001). Age-standardized mortality rate (ASMR) increased from 2.7 to 3.5 per 100,000 (Ptrend <0.001). For 15-64 year-olds, mortality rates were similar for A(H3N2) and A(H1N1)09pdm, both higher than B. For those over 65 years, mortality rates were significantly higher for A(H3N2) than for other types/sub-types.

Conclusions and implications for vaccinology: Influenza is a significant cause of LCI-H and mortality. Testing for influenza and rates of LCI-H have both increased substantially, as has the recognition of influenza as a cause of death in hospitalized patients. Furuther data are needed to determine what fraction of the burden of serious morbidity and morality from influenza is contributed by LCI-H.

Which healthcare workers work with acute respiratory illness? Evidence from Canadian acute care hospitals during four winters from 2010/2011 to 2013/2014

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Introduction/Background: Healthcare workers (HCWs) working with acute respiratory illness (ARI) may contribute to the transmission of ARI in the hospital settings.

Methods: From 2010/2011 to 2013/2014, HCWs at 8 acute care hospitals were enrolled into active surveillance for ARI during winter seasons. Daily online diaries were collected for reported ARI episodes. Information regarding symptoms, work attendance, and medical consultations were collected.

Results and Analysis: Over 2744 person-seasons contributed by 2096 HCW participants, 6589 illness diaries were eligible for the analysis. Working while ill was reported in 5304 (80.5%) diaries averaging 1.9 days of working while ill due to ARI per person-season.

Reasons for working with symptoms were: symptoms were mild and they were feeling well enough to work (67%), feeling miserable but had work that needed to be done (10%), feeling miserable but felt required to work (7%), felt well when they left home for work but worsened later (7%), and could not afford to stay home (3 %).

Multivariate modelling showed that working while ill was less likely to occur for: nurses vs other HCWs, respiratory with constitutional and/or gastrointestinal symptoms vs respiratory symptoms alone, moderate or severe vs mild symptoms, those seeking medical consultation vs those not, and those working on ward/departments with a work safety culture score of ≥61 vs those with scores of <20. Meanwhile, it was more likely to occur on the illness onset date or 6 days post illness onset rather than days 1-5, for physicians than other HCWs and if the person worked in emergency department, intensive care unit, adult medical ward, or paediatric inpatient unit than other hospital wards/units.

Conclusions and implications for vaccinology: Although most people who worked while symptomatic had mild symptoms, the magnitude of risk of transmission to patients and colleagues is unknown. Further research into the risk of transmission based on the severity of symptoms is recommended.

Hemagglutinin-inhibition (HI) assay titres: Levels associated with protection against laboratory-confirmed influenza

Coleman B, Hatchette T, Katz K, Powis J, McNeil S, Langley J, Loeb M, Drews S, Simor A, Muller M, McGeer A

Introduction/Background: Hemagglutinin-inhibition (HAI) titres of ≥1:40 are considered protective against influenza illness for 50% of individuals. These levels are instrumental in the licensing of influenza vaccines.

Methods: Canadian adults 18-69 years old who participated in the Influenza Cohort Study, conducted in the 2010/11-2013/14 influenza seasons, were eligible if they provided a 21 day post-vaccination blood sample and participated for ≥90 days. We compared HAI titres for participants with and without laboratory-confirmed influenza (PCR positive nasal swab and/or 4-fold or greater increase in HAI titres between post-vaccine and end-of-season blood samples). HAI titres were specific to the strain of influenza used in the season's vaccine.

Results and Analysis: The cohort included 1421 adults, median age 46 years (range 22-69), median participation 203 days (range 90-271), 85% female, 89% worked in an acute care hospital, and 80% vaccinated against influenza in the current season. Pre-season titres were significantly higher for participants vaccinated in the current season and those younger than 50 years. The percentage of participants with laboratory-confirmed influenza was significantly higher for those with pre-season HAI titres <1:40 compared to those with titres of ≥1:40 for A/California/07/2009 (10.4 vs 2.5%, respectively; p<0.001), A/Perth/16/2009 (2.9 vs 0.3%; p=0.01), B/Wisconsin/01/2010 (16.1 vs 3.7%; p<0.001), and B/Massachusetts/2/2012 (13.9 vs 3.6%) but not for A/Victoria/361/2011 (8.7 vs 5.8%; p=0.32), A/Texas/50/2012 (2.0 vs 0; p=0.06), or B/Brisbane/60/2009 (2.8 vs 2.0; p=0.52). HAI titres of ≥1:1280 were 100% protective for all strains with the exception of one 34 year old female with a post-vaccination titre of ≥1:1280 who had PCR-confirmed influenza. The rate of protection was 99% for all strains at post-vaccination titres of ≥1:160.

Conclusions and implications for vaccinology: Higher titres correlate with higher rates of protection in healthy working-age adults. Vaccines that induce HAI titres consistently reaching ≥1:160 may be more effective in preventing influenza in working-age adults than current vaccines. This may be a target that licensing bodies consider for annual influenza vaccines.

Quantification of the total neuraminidase content in influenza vaccines (2015 to 2018)

Withers S, Gao Z, **Skowronski D**, Robinson K, Serres G

Introduction/Background: Antibody response to influenza virus is predominantly directed toward two glycoproteins, hemagglutinin (HA) and neuraminidase (NA), present on the viral surface in a ratio of about 4:1. Whereas current influenza vaccines contain standardized amounts of HA (minimum 15 µg per antigen per 0.5mL), the NA content is not regulated or specified. Here we demonstrate a simple fluorimetric reagent that may be used to accurately quantify NA content in influenza vaccine.

Methods: A variety of commercially-available trivalent and quadrivalent influenza vaccines available during the 2015-16 to 2017-18 seasons in Canada were assessed, including: live and inactivated; split and subunit; standard dose and high dose; and non-adjuvanted and adjuvanted products. Our recently described (Gao et al. Angew Chemie 2017;56:6112-6116) NA titration reagent was added to vaccine samples in the cell of a fluorimeter and the released fluorescence monitored by spectometry. Using a simple calibration curve the concentration of fluorophore released was quantified, providing a measure of NA concentration reported in micrograms/mL for each product.

Results and Analysis: In total, 21 influenza vaccines were assessed for the 2015-16 (8 vaccines), 2016-17 (8 vaccines) and 2017-18 (5 vaccines) seasons. Total NA content ranged widely from 0.6 µg/mL up to 9.7 µg/mL. The high-dose vaccine had the greatest NA content each season (n=3) that it was assessed, ranging 5.9-9.7 µg/mL, which was approximately 2-2.5-fold higher than the same manufacturer's standard dose vaccine for the same seasons that both products were assessed (n=2). A clear difference was not evident between split and subunit products although NA content was lowest for the adjuvanted subunit and live vaccines compared to all other products each season they were assessed (n=3 and n=1, respectively).

Conclusions and implications for vaccinology: Since anti-NA responses may contribute to vaccine protection, quantifying the variability in NA content between available vaccine products and seasons may be relevant to understanding variability in vaccine performance.

Repeated exposure to an adjuvanted quadrivalent subunit influenza virus vaccine (aQIV): A randomized, observer blind, multicenter study

Boikos C, Daly W, Ramsey K, Forsten A, Leav B, Oberye J, Zhang B, Pacciarini F, Vesikari T

Introduction/Background: The safety, immunogenicity and efficacy associated with administration of of aQIV in children between 6 months through 5 years of age was investigated in study V118_05. Although enhanced immunogenicity in children has been demonstrated for MF59-adjuvanted influenza vaccines after first administration, the impact on immunogenicity and safety with repeated vaccination has not been evaluated extensively.

Methods: A total of 607 subjects who participated in parent study V118_05, now aged 12 months through 6 years, were enrolled the subsequent year and received a single dose of study vaccine. Enrolled subjects received the same type of influenza vaccine administered in the parent study (aQIV or non-adjuvanted comparator). Blood samples were taken for immunogenicity assessment prior to the second year vaccination, and 21 and 180 days after vaccination.

Results and Analysis: At baseline, approximately 12 months after vaccination in the parent study V118_05, subjects in the aQIV group had significantly greater geometric mean titer (GMT) values against all 4 homologous strains compared with subjects in the non-adjuvanted vaccine group. After year two vaccination, CBER criteria for seroconversion and hemagglutination inhibition (HI) titer ≥1:40 were met for the aQIV group for all 4 homologous strains tested at Day 22. At both Day 22 and Day 181, subjects who received aQIV had significantly greater GMT values for HI against all 4 homologous strains compared with those who received non-adjuvanted vaccine. Increased immune response of aQIV versus non-adjuvanted vaccine was also observed for the selected heterologous strains tested at baseline, Day 22 and Day 181. In terms of safety, transient and generally mild to moderate reactogenicity was more commonly observed in the aQIV group versus the nonadjuvanted group, but overall safety profiles were similar and comparable to the parent study.

Conclusions and implications for vaccinology: This first-year revaccination study in young children confirms enhanced immunogenicity and similar safety profile after repeat aQIV vaccination compared to repeat non-adjuvanted influenza vaccination.

An enhanced vaccination program with the adjuvanted seasonal influenza vaccine is highly cost-effective at the programmatic level in Manitoba, Alberta and Nova Scotia

Nguyen V, **Boikos C**, Mansi J

Introduction/Background: Enhanced influenza vaccines (adjuvanted, inactive, trivalent influenza vaccine [aTIV]; high-dose inactive, trivalent influenza vaccine [HD-TIV]) provide improved protection for immunosenescent older adults compared to standard influenza vaccines. The current analysis evaluates the public health impact of enhanced influenza vaccines for Canadian provinces such as Manitoba (MN), Alberta (AB) and Nova Scotia (NS).

Methods: An adaptation of a published, Canadian, dynamic influenza transmission model (Fisman & Tuite) was used to assess the impact of enhanced flu vaccines. Seven age groups were modeled, including a high-risk group in long-term care (LTC). Each province's reference scenario was their respective influenza vaccination program for the 2017-18 season. For example, quadrivalent, inactive influenza vaccine (QIV) for all ages and HD-in-LTC for MN and NS and QIV-for-all-ages in AB. Three alternative programs were evaluated for individuals 6-24 months, 2-64 years of age and 65+ years of age. Conservative vaccine efficacy & effectiveness estimates and public health costs were extracted from published literature.

Results and Analysis: For all provinces, the inclusion of aTIV in a 65+ program was cost-saving (number of cases, hospitalizations and medical consultations) relative to each provinces' current influenza program. For the three example provinces, in MN and NS, the aTIV-in-LTC program was dominant: the aTIV-LTC program would result in savings of approximately $1 million in NS and $1.18 million in MN. In AB, compared to a QIV-for-all program, the addition of an aTIV 65+ program in LTC is the most cost effective scenario, followed by aTIV in all 65+, compared to other enhanced vaccine programs for older adults in the province.

Conclusions and implications for vaccinology: For the provinces of MN, AB and NS, at the programmatic level, the greatest PH impact is obtained by an enhanced vaccination program inclusive of aTIV. These results are consistent for the other Canadian provinces.

Retrospective evaluation of mismatch from egg-based isolation of influenza strains compared to cell-based isolation and the possible implications for vaccine effectiveness

Boikos C, Rajaram (Raja) S, van Boxmeer J, Leav B, Suphaphiphat P, Iheanacho I, Kistler K

Introduction/Background: Lower influenza vaccine effectiveness (VE) against circulating H3N2 strains compared to other influenza viruses, is partly explained by antigenic mismatch between circulating strains and the vaccine strain (Belongia 2016). This mismatch has recently been linked to a new glycosylation site introduced in the egg-adaptation step (Zost 2017) and HA L194P substitution (Wu 2017) for H3N2. Vaccine manufactured using seed virus wholly grown in mammalian (e.g. Madin-Darby Canine Kidney – MDCK) cells, as with the NH17-18 version of Flucelvax®, avoids these mutations. This study aimed to compile existing data on antigenic similarity to measure the degree of match with circulating wild-type isolates of egg- and MDCK-propagated versions of the vaccine H3N2 virus over multiple seasons.

Methods: Using publicly available reports from the Worldwide Influenza Centre, London(crick), we compiled data on antigenic similarity, defined as H3N2 circulating wild-type virus isolates showing no more than a four-fold reduction in titer to antisera raised against wholly MDCK- or egg-propagated versions of the vaccine H3N2 viruses. Titers were compared using hemagglutination inhibition (HI) assays and/or plaque reduction neutralization assays (PRNA).

Results and Analysis: Data from Northern Hemisphere influenza seasons of 2011–12 to 2017–18, show a substantially higher proportion of tested circulating influenza H3N2 viruses matched the MDCK-propagated

reference viruses than did corresponding egg-propagated reference vaccine viruses. In half of the seasons evaluated, there was little to no antigenic similarity between circulating viruses and the egg-based vaccine viral seed.

Conclusions and implications for vaccinology: These data suggest higher levels of mismatch have occurred consistently with egg-propagated H3N2 reference viruses compared to MDCK-propagated reference viruses when measured against circulating wild-type isolates and may further explain the potential for lower VE observed against H3N2 historically. Further, these data point to the importance of continuing to utilize cell-derived seeds in creating seasonal influenza vaccines for this strain.

Effectiveness of the cell culture-based and egg-based, seasonal influenza vaccines during the 2017-2018 Northern Hemisphere influenza season

Boikos C, Sylvester G, Sampalis J, **Mansi J**

Introduction/Background: The overall interim vaccine effectiveness (VE) estimate for 2017-2018 in the U.S. at 40% highlights an ongoing reduced effectiveness against the dominant A/H3N2 circulating strain due to viral mutations related to vaccine production in eggs. Evaluating the effectiveness of seasonal influenza vaccines is important towards undertading how novel production platforms, such as a cell-culture based vaccine (QIVc), may help address these ongoing challenges.

Methods: Data from electronic medical records obtained between August 1 2017 and March 31 2018 from patients presenting to primary care in the U.S. are being evaluated as a retrospective cohort study. Preliminary descriptive statistics of the database were estimated with summary statistics and corresponding 95% confidence intervals (CIs). Relative effectiveness will be estimated using regression models adjusted for confounders chosen based on biological plausibility and subject matter experts. Robustness of results will be evaluated by conducting sensitivity analyses to check for residual confounding, measurement error and selection bias.

Results and Analysis: Within this large primary care data set, the following exposures were observed for QIVc, standard quadrivalent egg-based (QIV), and standard trivalent egg-based (TIV) respectively: 92,192 with a median age of 59 years 95% CI (59.00-60.00), 1,255,983 with a median age of 41 years 95% CI (41.00-42.00), and 30,448 with a median age of 58 years 95% CI (58.00-59.00). Enhanced egg-based vaccines were also documented, such as the adjuvanted TIV (aTIV) with 29,527 exposures and a median age of 74.00 years 95% CI (74.00-75.00). VE estimate will be presented adjusted for age, sex, race/ethnicity, geographic region, and health status.

Conclusions and implications for vaccinology: The 2017-18 influenza season in the U.S. was predominated by drifted H3N2 influenza viruses arising from viral mutations related to vaccine production in eggs. Estimating the relative vaccine effectiveness of seasonal influenza vaccines is seminal in understanding the clinical and public health impact of different vaccine options.

Laboratory-confirmed influenza hospitalizations among pregnant women: Clinical outcomes and effectiveness of maternal vaccination from the PREVENT international study

Fell D, Thompson M, Dawood F, Azziz-Baumgartner E, Ball S, Barda N, Booth S, Chung H, Drews S, Effler P, Feldman B, Fink R, Garg S, Jackson M, Katz M, Klein N, Kwong J, Levy A, Regan A, Riesel D, Russell M, Simmonds K, Svenson L, Wyant B, Naleway A

Introduction/Background: Limited data exist on clinical outcomes and influenza vaccine effectiveness (VE) among pregnant women during seasonal influenza epidemics. We aimed to describe clinical characteristics among pregnant women hospitalized with laboratory-confirmed influenza infection and estimate VE against influenza resulting in hospitalization.

Methods: Seven sites from four countries participating in the PREVENT study contributed data, including Australia (Western Australia), Canada (Ontario, Alberta), Israel, and the United States (California, Oregon,

Washington). Using a common data protocol, each site identified pregnant women hospitalized with acute respiratory infection or febrile illness (ARFI) who had specimens tested for influenza by reverse-transcription polymerase chain reaction (RT-PCR) during the 2010-2016 influenza seasons. Clinical characteristics were identified using a standard list of diagnosis codes. Using a test-negative design, we estimated VE against laboratory-confirmed influenza hospitalization adjusted for study site, seasonal factors, and presence of high-risk medical conditions. The clinical characteristics of women who tested positive for influenza infection were described.

Results and Analysis: Among 18,048 ARFI-coded hospitalizations during the six influenza seasons, 1,064 (6%) included RT-PCR testing for influenza viruses, and of these, 58% (614/1064) tested positive for influenza virus. Approximately one-third of pregnant women who tested positive for influenza infection had low socioeconomic status (35%), 20% had high-risk medical conditions, and 67% were admitted in the third trimester of pregnancy. The median length of influenza-positive hospitalizations was 2 days, 10% were associated with pneumonia and 2% with sepsis, 5% required intensive care, 1% resulted in respiratory failure, and no maternal deaths were recorded. Thirteen percent of influenza-positive cases and 22% of influenza-negative controls were vaccinated, producing an adjusted VE of 40% (95% CI: 12-59%) against influenza hospitalization.

Conclusions and implications for vaccinology: The majority of influenza-positive hospitalizations were among pregnant women without underlying chronic medical conditions and those who were unvaccinated against influenza. During 2010–2016, influenza vaccination during pregnancy provided moderate protection against laboratory-confirmed influenza hospitalization.

Safety of inactivated influenza vaccination in first trimester of pregnancy in an Australian population-based cohort study

Regan A, Pereira G, Effler P

Introduction/Background: The World Health Organization lists pregnant women as the highest priority group for seasonal influenza vaccination; however, influenza vaccine uptake consistently remains suboptimal, with an estimated 40% of Australian pregnant women receiving an influenza vaccine annually. Poor uptake has partly been attributed to safety concerns, particularly during early pregnancy.

Methods: We conducted a population-based cohort study of 10,371 women who received seasonal influenza vaccine in the first trimester of pregnancy and 84,123 unvaccinated women in Western Australia. Birth information from the state's perinatal data collection and register of developmental anomalies was probabilistically linked with vaccination information from the state antenatal vaccination register. We estimated the relative risk of spontaneous preterm birth, small-for-gestational age, birth defects, and stillbirth for vaccinated and unvaccinated women using log-binomial regression models. Models were adjusted for maternal age, parity, socioeconomic status, pre-existing health conditions, and Indigenous status. Stratified analyses factored for whether the woman delivered during periods of peak influenza virus circulation.

Results and Analysis: Overall, we observed no differences in the risk of adverse birth outcomes among vaccinated and unvaccinated women. However, among women who delivered during the of peak influenza season, the risk of spontaneous preterm birth and stillbirth was lower in vaccinated compared to unvaccinated women (RR: 0.55 [95% CI 0.43-0.68] and RR: 0.37 [95% CI: 0.15-0.90]). The risk of small-for-gestational age birth was similar in vaccinated and unvaccinated women (RR: 1.12 [95% CI 0.85-1.49].

Conclusions and implications for vaccinology: These findings suggest vaccination during early pregnancy was safe and was not associated with any increase in the risk of adverse outcomes at birth. These results should reassure pregnant women and their providers around the safety of influenza vaccination in the first trimester of pregnancy.

Health outcomes of children born to mothers who received pandemic H1N1 influenza vaccination during pregnancy

Fell D, Walsh L, Donelle J, Dodds L, Hawken S, Kwong J, Top K, MacDonald N, Benchimol E, Chakraborty P, Guttmann A, Ortiz J, Sprague A, Walker M, Wen S, Wilson K

Introduction/Background: Concern about safety is a commonly-cited reason for low influenza vaccine uptake during pregnancy. The lack of information on long-term health outcomes in children exposed to influenza vaccination in utero remains a potential barrier to achieving higher uptake in pregnant women.

Methods: We conducted a retrospective cohort study of all live births from November 2009 to October 2010 in Ontario, using the province-wide birth registry containing information on pandemic H1N1 (pH1N1) influenza vaccination during pregnancy. These data were linked with provincial health administrative data to ascertain child health outcomes in the first 5 years of life: infectious diseases, atopic diseases, neoplasms, sensory disorders (vision or hearing loss), rates of urgent or in-patient health services utilization, and a composite indicator for pediatric complex chronic conditions. Cox proportional hazards, negative binomial, and log binomial models were used to estimate adjusted hazard ratios (aHR), incidence rate ratios (aIRR), and risk ratios (aRR), respectively. We used inverse probability of treatment weights based on propensity scores to adjust for confounding.

Results and Analysis: Among 104,249 live births, 31,295 (30%) were exposed to pH1N1 influenza vaccination in utero. There were no significant associations with upper or lower respiratory infections, otitis media, any infectious diseases, neoplasms, sensory disorders, urgent and in-patient health services utilization, or pediatric complex chronic conditions. Although we observed a slight increased association between prenatal pH1N1 vaccine exposure and asthma (aHR: 1.06; 95% CI: 1.02-1.10), and inverse association with gastrointestinal infections (aIRR: 0.94; 95% CI: 0.91-0.98), these results were attenuated toward the null and no longer statistically significant following additional adjustment for having regular access to a healthcare provider.

Conclusions and implications for vaccinology: This study provides new evidence on longer-term pediatric health outcomes following pandemic influenza vaccination during pregnancy, which was not significantly associated with negative 5-year health outcomes in children. These results should be reassuring to pregnant women receiving influenza immunization.

Can we predict who will get a flu shot in pregnancy? Determinants of pregnant Canadians' intentions regarding influenza immunization

Greyson D, Sadarangani M, Dubé E, Cook J, Bettinger J

Introduction/Background: Pregnancy increases the risk of influenza-related morbidity and mortality. Influenza vaccination has been recommended for pregnant women in Canada since 2007, but uptake remains well below the recommended target of 80%. While some barriers and facilitators to influenza vaccination in pregnancy have been identified, we do not yet know how to predict which pregnant individuals are more or less likely to be vaccinated, and therefore where promotion efforts are best targeted.

Methods: Bilingual online surveys based on the Theory of Planned Behaviour were conducted with a panel of 600 pregnant Canadian women in October 2017. The questionnaire assessed potential determinants of vaccination (attitudes/beliefs, social norms, perceived behavioural control), respondents' influenza vaccination intentions, and self-reported demographics. Analysis included descriptive statistics, testing for correlation among model constructs, and multivariable linear regression analysis to assess factors associated with intention to be vaccinated.

Results and Analysis: Among survey respondents: 238 (40%) were in their first trimester, 235 (39%) in the second, and 127 (21%) in the third trimester of pregnancy. Intentions regarding influenza vaccination were fairly evenly distributed from very likely to very unlikely, with slightly more (38%) not intending to be vaccinated than intending to (29%) or being unsure (32%). Belief that getting vaccinated would be helpful, social norms supporting influenza vaccination, and feeling that it would be easy to obtain vaccination all predicted intention to be immunized (significant at $p < 0.01$). Demographic factors were not significantly associated with intentions,

even those previously identified to be facilitators of vaccination in pregnancy (e.g., chronic health conditions, minor children at home).

Conclusions and implications for vaccinology: Beliefs, community social norms, and perception of easy access to vaccination all predict intentions to get a flu shot. These factors may transcend demographic predictors.

Communauté de pratique en organisation des services de vaccination

Clément P, **Guay M,** Landry M

Introduction/Besoin et objectifs du programme : Un modèle éprouvé d'organisation des services de vaccination (OSV) aux enfants québécois de 0-5 ans a été produit en 2015 par une recherche-action faisant émerger le besoin d'échanger et de partager en matière d'OSV. C'est ainsi qu'une communauté de pratique (CP) en OSV a été mise sur pied en 2017 dont les objectifs sont : 1) Échanger sur les bonnes pratiques en matière d'OSV au Québec; 2) partager les apprentissages mutuels et les outils produits de part et d'autre; 3) partager les connaissances scientifiques portant sur l'OSV.

Méthode, activités et évaluation du programme : Les responsables des programmes de vaccination des directions de santé publique du Québec ont été invités à participer à la CP. Une étude de besoins par un sondage en ligne a été réalisée auprès des participants de la CP afin de déterminer le mode de fonctionnement souhaité et le déroulement préféré aux rencontres.

Résultats ou effets du programme : Les 25 participants à la CP proviennent de 12 des 18 régions du Québec. Les rencontres par webinaire de 2 heures aux 3 mois permettent l'interaction et la prise de parole. Deux personnes animent les rencontres où un thème choisi préalablement est couvert. Les thèmes abordés jusqu'ici ont été : hésitation à la vaccination et utilisation de l'entretien motivationnel en vaccination, technologies de l'information pour la confirmation de rendez-vous de vaccination, collaboration inter directions et plans d'action pour améliorer l'OSV. Les discussions sont alimentées par les témoignages sur leurs pratiques des participants à la CP et par des capsules théoriques faisant état des données probantes. Des nouvelles demandes de participation à la CP arrivent régulièrement.

Répercussions pour les pratiques ou les politiques : La CP constitue un mode de travail collaboratif efficace et répond à un réel besoin tel qu'en témoigne sa popularité grandissante. Le défi consiste maintenant à assurer une continuité entre les rencontres de la CP pour en augmenter sa portée.

Evolution of recommendations and uptake of maternal immunization in Canada

Vargas J, Hector A, Kandeil W, Mukherjee P

Introduction/Background: Maternal immunization (MI) is a recognized strategy to help provide protection to pregnant women (PW), foetus and new-borns against several infectious diseases. In the last decade, new MI recommendations have been issued worldwide. This systematic literature review summarizes MI recommendations and vaccine uptake during pregnancy in Canada.

Methods: PubMed, EMBASE and grey literature sources were searched in 2018 using two search strings on articles issued by any medical association, governmental body or independent-medical institution on MI recommendations or uptake.

Results and Analysis: 263 published vaccine recommendations were screened, 45 provided MI recommendations and were included. Currently, only influenza and tetanus-diphtheria-acellular pertussis (Tdap) vaccines are recommended in PW, both inactivated vaccines. Influenza recommendations were introduced in the 2007-2008 season by the National Advisory Committee on Immunization (NACI) and the Society of Obstetricians and Gynaecologists of Canada (SOGC). In 2018, NACI recommends Tdap vaccination in every pregnancy between 27th-32nd week gestation, but as early as 13th week. SOGC recommends vaccination between 21st-32nd week gestation. The use of live-vaccines is generally contraindicated in PW and the use of other

inactivated vaccines is recommended in circumstances where benefits outweigh risks. 244 publications on MI uptake were screened; 10 were included, from which only uptake data for the seasonal (n=2) and pandemic (n=8; H1N1) influenza vaccines were retrieved. For seasonal influenza, uptake ranged from 2.6% of PW before national recommendations were issued to 16% 3 to 5 years after. For pandemic influenza (2009-2010), uptake ranged from 34.2% to 80%, with larger studies having uptake between 42.6%-49.4%.

Conclusions and implications for vaccinology: Despite long-standing recommendations, there is a limited body of evidence on the uptake of influenza vaccines in PW. As Tdap MI programs are adopted in Canada, data on burden of disease and vaccine uptake would be critical to evaluate the impact of MI strategy and guide public health decisions.

The effect of information—motivation—behavioral skills model-based continuing medical education on pediatric influenza immunization uptake: A randomized, controlled trial

Fisher W, Gilca V, Murti M, Orth A, Roumeliotis P, Rampakakis E, Brown V, Yaremko J, Van Buynder P, Boikos C, Mansi J

Introduction/Background: Seasonal vaccination against influenza is the most important public health strategy to prevent influenza morbidity and mortality in children 6- 23 months of age. However, influenza immunisation uptake in this population remains sub-optimal. While parents look to health care professionals (HCPs) for guidance, HCPs may be neither aware of the burden of influenza disease in infants nor familiar with ways to address parental influenza vaccine hesitancy. The objective was to describe the impact of an Information—Motivation—Behavioral Skills model (IMB)-based, accredited, online Continuing Medical Education (CME) program on seasonal influenza vaccination in children 6-23 months of age in Ontario, Canada during the 2016/17 influenza season.

Methods: A multi-center, randomized, controlled trial was conducted whereby HCPs were randomized to either an accredited IMB-based CME or to routine practice (no CME). The CME addressed influenza burden in young children and identified parental barriers (hesitancy) to influenza vaccination, , designed to inform, motivate, and upskill HCPs. All vaccine options were reviewed, including the adjuvanted, trivalent, inactive, influenza vaccine (aTIV). Immunisation rates were compared between groups using Pearson's chi-squared and a logistic regression model adjusting for socioeconomic status at the clinic-level.

Results and Analysis: A total of 68 HCPs were recruited: 33 randomized to the CME group and 35 to routine practice. HCP interactions with parents were evaluated during 628 visits: 292 visits by HCPs in the CME group and 336 by HCPs in the routine practice group. Parents seen by HCPs in the CME group were ~ 30% more likely to agree to immunize their child with seasonal influenza vaccination compared to parents seen by HCPs in the control group (p=0.007). The adjusted odds of influenza immunization were 1.5 times higher in the CME group compared to the control group. Children in the CME group were ~ 20% more likely to receive aTIV compared to children in the control group (p<0.001).

Conclusions and implications for vaccinology: HCP education with a tailored health behavior uptake model based CME addressing the burden of influenza disease in young children and influenza vaccine hesitancy was associated with a significant increase in influenza immunization.

Mandatory immunization education sessions for parents seeking a philosophical or religious exemption: A survey of parents attitudes and beliefs

Dubey V, Kadri O, Beckermann K, Cameron J

Introduction/Program need and objectives: In September 2017, the province of Ontario implemented a mandatory in person education session for parents seeking a philosophical or religious exemption for their child under the Immunization of School Pupils Act. The session consists of watching a Ministry developed, 30-minute video. For the 2017-18 school year, in Toronto, 593 certificates were handed out to parents who completed the

education sessions in either large, small or one-on-one sessions. While the policy intent is to ensure parents make an informed choice, at the local level, we are interested to understand attitudes and beliefs towards immunization of these parents and to evaluate the education session.

Program methods and activities: A survey was constructed and piloted in late 2017. From January to June 2018, parents completing immunization education sessions were asked to fill out a revised optional survey to assess their attitudes and beliefs towards immunization and evaluate the session. Information collected were input and analyzed using CheckMarket.

Program results or outcomes (including evaluation): There were 110 completed surveys out of 360 participants in the first half of 2018 with a response rate of 31%. Opposition to immunization declined 8% from 76% before to 68% after the education session, while 80% still intended to seek an exemption for their child. The most important reasons to get an exemption were because of concerns about the ingredients in vaccines (60%), concerns about the side effects (58%), to prevent their child from being suspended (38%) and because of their religious beliefs (32%). Additionally, 75% of respondents felt the education session was provided in a respectful manner.

Implications for practice or policy: Since in-person education is mandatory for parents seeking a philosophical or religious exemption, conducting a survey of parents provided insightful information on why these parents have chosen not to vaccinate their child for school. Ongoing monitoring of these session is important to determine impact and to address underlying attitudes and beliefs.

Mandatory infant and childhood immunization: Rationales, issues and knowledge gaps

Harmon S, MacDonald N

Introduction/Problem definition that demonstrates the need for a policy change: Globally, infant and childhood vaccine uptake rates are not high enough to control vaccine preventable diseases, with outbreaks occurring even in high-income countries. This has lead a number of high- and middle-income countries to enact, strengthen or contemplate mandatory infant and/or childhood immunization to try to address the gap. Mandatory immunization may reduce or eliminate individual choice about whether or not to accept immunization, but it is also often controversial. Further, mandatory approaches vary widely in terms of vaccines included, age groups covered, penalties or incentives given, degree of enforcement and by whom, and whether or not there is a compensation program for serious AEFI. In short, there is no standard approach, which gives rise to manifold practical challenges when considering moving in that direction.

Research Methods: Desktop legal and ethical research. Scoping.

Results and Analysis: This concise overview exposes some of the many knowledge-gaps that exist for policymakers considering a move to a mandatory or partially mandatory immunization program.

Recommendations and implications for practice: If policymakers wish to make evidence-informed decisions, they need to consider a range of factors, some general, and others intimately related to their particular socio-cultural context. We offer some policy considerations as well as a template of elements that may be considered in an instrument mandating infant and/or child immunization and summarizes the limited outcome data.

Physician dismissal of vaccine refusers: A legal and ethical analysis

Harmon S, MacDonald N, Faour D

Introduction/Problem definition that demonstrates the need for a policy change: While vaccines represent one of the most effective health of the 20th century, most vaccine-suppressed infectious diseases are merely contained within a defined geographical area for as long as preventative measures can overcome effective transmission. A difficulty faced by public health authorities is that, once outbreaks become rare, parents of minor children who are meant to commence their scheduled vaccines may question whether vaccination is

necessary. This hesitancy can be compounded, or transformed into vaccine refusal, by social circles and vaccine-negative social media campaigns. As a result, some parents refuse some or all vaccines for their children. Indeed, vaccine hesitancy and/or refusal has increased in the last decade. Some physicians have responded by dismissing refusers and their families from their practice. While dismissal data is not readily available for most jurisdictions, dismissal of patients is a serious and growing concern.

Research Methods: Desktop legal and ethical research and analysis.

Results and Analysis: This paper offers an analysis of the legal and ethical implications of physician dismissal of patients who are hesitant or who refuse to vaccinate their children, focusing on Canada. It concludes that, while physician dismissal can be supported both legally and in terms of professional duties, the complex healthcare context in Canada, together with broader physician responsibilities suggests that it is, in fact, unethical to do so.

Recommendations and implications for practice: The paper closes with some suggestions for managing vaccine refusal in the clinical setting.

Increasing timely immunization uptake in infants

Tuchscherer R, Shahab S, Stang M, Khan S, VanHaarlem L, Schilling T

Introduction/Program need and objectives: Timely initiation and completion of childhood immunisation programs reduces morbidity and mortality from vacine preventable diseases in infancy.

Program methods and activities: Immunization data from Panorama is received monthly. Coverage rates calculated by various strata (e.g. age, antigen, sex, jurisdiction and dose). The denominator is number of children registered in Panorama with the following criteria:

- Of specified age (e.g., 3 months) by specified time (e.g. by December 31, 2017)
- Has Saskatchewan provincial health coverage
- Flagged as being under a health region jurisdiction for public health services

The numerator is number of children from denominator who received recommended number of doses of respective antigen by specified age

Program results or outcomes (including evaluation): A number of analyses on immunization coverage can be performed using the Panorama Immunizations Module. Some of the analyses performed by the Population Health Branch include:

- Quarterly childhood immunization rates for pertussis, measles and meningococcal serogroup C by the age of two years
- Annual immunization coverage for vaccine preventable diseases (VPDs)
- Counts of immunization refusal (e.g., for pertussis by the age of 91 days)
- Progress in reaching a goal of 90% of infants immunized with 1 dose of pertussis by the age of 91 days

Implications for practice or policy:

- To set goals and targets based on historical coverage rates to improve the level of herd or community immunity.
- To measure progress in meeting a defined goal
- To identify gaps for focused intervention.
    - For example, pneumococcal vaccine is recommended for healthy children at two and four months with a booster dose at 12 months. Provincially only 59.2% of 13-month-old toddlers are fully immunized. Regions could use this information to consider why this might be happening and develop strategies to improve the uptake of the 12-month booster dose on time.

Serotype-specific trends in invasive pneumococcal disease: Patterns of serotype replacement

Mungall B, Izurieta P, Nieto J, Soumahoro L

Introduction/Background: Pneumococcal conjugate vaccine introduction has resulted in a dramatic reduction in most vaccine serotypes (VTs) as a cause of invasive pneumococcal disease (IPD). However, these decreases have been offset to varying degrees in different countries by an increase in replacement serotypes, primarily non-vaccine serotypes (NVTs). We assessed the trends of serotype replacement IPD in <5-year-olds in countries following the introduction of PCVs.

Methods: IPD datasets for children <5 years old before and after PHiD-CV/PCV13 introduction were identified by literature search and from publicly available surveillance reports in January 2018. Datasets were limited to countries with robust epidemiologic surveillance (n=6). Case numbers before and after PHiD-CV/PCV13 introduction were converted to % change relative to the PHiD-CV/PCV13 introduction year for each country. The average % change over all 6 countries was calculated per year pre/post-introduction.

Results and Analysis: Our analysis revealed:

- Sufficient data was available to analyse replacement disease trends for 16 NVTs and 1 VT displayed a lack of vaccine effectiveness.
- Ten serotypes (3, 10A, 11A, 15A, 22F, 23A, 23B, 33F, 35F and 38) revealed trends for increasing disease prior to PHiD-CV/PCV13 introduction and 1 serotype decreased in the PCV7 period (15C).
- After PHiD-CV/PCV13 introduction, 4 of these serotypes (3, 15C, 35F and 38) stabilized, 2 serotypes (10A, 22F) trended downwards, while the remaining 5 serotypes (11A, 15A, 23A, 23B, 33F) continued to trend upwards.
- For the remaining serotypes, a modest reduction in serotype 6C, no change in serotype 8, and trends for increases in disease due to serotypes 9N, 12F and 35B was observed following PHiD-CV/PCV13 introduction.

Conclusions and implications for vaccinology: Substantial variability in serotype replacement is seen in different countries. Ongoing surveillance will be necessary to monitor the future impact of these serotypes.

A systematic literature review and network meta-analysis feasibility study to assess the comparative efficacy and comparative effectiveness of pneumococcal conjugate vaccines

McGirr A, **Iqbal S**, Izurieta P, Talarico C, Luijken J, Redig J, Newson R

Introduction/Background: Network meta-analyses (NMAs) allow for indirect comparison of multiple interventions, even when direct head-to-head studies do not exist. This feasibility study (GSK study identifier: HO-17-18418) evaluated whether NMA methodology can be used to evaluate comparative vaccine efficacy/effectiveness (VE) of pneumococcal conjugate vaccines (PCVs) in preventing invasive pneumococcal disease (IPD) in children ≤5 years old.

Methods: A systematic search was performed in June 2017 using predefined strings and selection criteria in Ovid and Cochrane databases. Key outcomes extracted included VE against IPD of all serotypes and vaccine type IPD. A NMA feasibility assessment using standard approaches evaluated the possibility to synthesize study results to estimate the comparative VE of PCVs. Differences within and between direct treatment comparisons were considered and study quality was assessed using Cochrane Risk of Bias tool for randomized controlled trials (RCT) and Newcastle-Ottawa scale for observational

Results and Analysis: 5,292 unique publications were screened, of which 26, published between 2000-2016, were included in the NMA feasibility assessment (4 publications from 2 RCTs, 7 indirect cohort analyses, and 15 case-control studies). Preliminary NMA feasibility assessment highlighted a disconnected evidence network when only RCTs were considered and heterogeneity across study designs and reporting of data (e.g., age group analysed, dose and schedule of vaccines, level of vaccine exposure, and patient characteristics such as age, gender, immunocompromised status, and comorbidities).

Conclusions and implications for vaccinology: Preliminary feasibility assessment suggests NMA methodology is not able to be used to indirectly compare VE of PCVs due to an inability to create a network structure with available studies and to the heterogeneity between studies evaluating PCVs.

Predicting invasive pneumococcal disease incidence: A forecasting approach

Wasserman M, Wilson M, Earnshaw S, McDade C, Pugh S, Moffatt M, Sings H, Hilton B, Farkouh R

Introduction: Infant pneumococcal conjugate vaccines (PCVs) have reduced invasive pneumococcal disease (IPD) due to vaccine-specific serotypes. Predicting future pneumococcal epidemiology is challenging given the complex nature of serotype dynamics and vaccine impact. We developed an intuitive approach to modeling IPD through observed PCV impact in various settings.

Research Methods: Historical age-group and serotype-specific IPD incidence was obtained from three PCV10 settings (Finland, Netherlands, and Colombia) and four PCV13 settings (United Kingdom, United States, Quebec, and Ontario). Equations were fitted to longitudinal changes in incidence for each age group, serotype, and setting over time periods when a serotype was covered or not covered by infant vaccination. We forecasted population impact of PCV13 and PCV10 and report results among infants (ages <2 years) and elderly (65+ years) over 5-years post-vaccine introduction in each setting.

Results and Analysis: Based on forecasted impact over 5 years post-vaccine introduction, PCV13 was estimated to have greater average overall IPD incidence reduction than PCV10 in infants and the elderly, primarily due to reductions in serotypes 3 and 19A (Table). Both vaccines largely eliminated disease from common PCV10 serotypes. Increases in non-vaccine-type disease greatly varied by setting.

Conclusions: Forecasting IPD incidence using real-world impact is an intuitive process that illustrates benefits of PCV13 and PCV10 by identifying age- and serotype-specific trends that inherently capture direct and indirect effects of vaccination.

Table: Results Forecasted as Percentage Change in IPD Incidence Over 5 Years

Average (Min, Max)	Serotype 3	Serotype 19A	Common (PCV10)	Non-PCV13 Type	Overall
Ages <2 Years					
PCV10 Settings	+43.1% (+22.7%, 68.1%)	+36.9% (-3.5%, +58.6%)	-82.7% (-71.1%, -93.0%)	+12.8% (+7.0%, +22.8%)	-42.9% (-10.7%, -68.2%)
PCV13 Settings	-54.5% (-38.1%, -75.4%)	-96.4% (-87.2%, -100%)	-97.7% (-95.1%, -100%)	+20.0% (-3.0%, +39.5%)	-67.6% (-38.4%, -84.9%)
Ages 65+ Years					
PCV10 Settings	+30.2% (+1.5%, +52.1%)	+57.0% (+29.1%, +72.8%)	-47.2% (-29.6%, -57.7%)	+51.1% (+30.9%, +90.2%)	+1.0% (-20.7%, +15.0%)
PCV13 Settings	-26.0% (-8.6%, -41.3%)	-66.8% (-35.1%, -100%)	-74.9% (-60.0%, -97.1%)	+17.9% (6.4%, 31.1%)	-30.9% (-18.1%, -44.2%)

Twenty-six years of invasive pneumococcal disease in Canadian children, 1991-2017, the Canadian Immunization Monitoring Program, Active

Bettinger J, Sadarangani M, Morris S, Kellner J, Le Saux N, Embree J, Vanderkooi O, Martin I, Demczuk W, Tyrrell G, Vaudry W, Halperin S, Canadian Immunization Monitoring Program, Active

Introduction/Background: Before implementation of the first Canadian pneumococcal conjugate vaccine (PCV) program in 2002, invasive pneumococcal disease (IPD) accounted for most severe, invasive bacterial infections in children. PCV programs were implemented with the expectation that the IPD disease burden would decrease. This study examines 26 years of surveillance data to describe the epidemiology of Canadian IPD.

Methods: The Canadian Immunization Monitoring Program, Active (IMPACT) captures all lab-confirmed IPD cases presenting at 12 tertiary care pediatric hospitals across Canada. Nurses complete a standardized report form. Isolates are serotyped at a central reference laboratory. Incidence rates are reported per 100,000. A p-value <0.05 was considered significant.

Results and Analysis: The pre-vaccine era (~1991-2004) averaged 279 IMPACT cases annually with an incidence of 55 (95% CI 51-58) cases per 100,000 children 0-16 years of age. The PCV7/10 era (~2005-2010) averaged 141 cases annually with an incidence of 40 (37-43) cases. The PCV13 era (2011-2017) averaged 159 cases with an incidence of 26 (24-29) cases. Incidence in children younger than 1 and 5 years of age decreased significantly from 270 to 71 and 147 to 57, respectively. The incidence of PCV7 strains decreased significantly over time, while PCV13 strains increased significantly during the PCV7/10 era then decreased significantly during the PCV13 era. The incidence of non-vaccine strains increased significantly during the PCV7 era. Penicillin nonsusceptibility was 12% in the pre-vaccine era, 20% in the PCV7 era and 19% in the PCV13 era. Third generation cephalosporin resistance increased significantly from 1% in the pre-vaccine era to 4% in subsequent eras.

Conclusions and implications for vaccinology: While the incidence of IPD decreased significantly among children admitted to the IMPACT centers with the implementation of PCVs, penicillin and third generation resistance increased. Replacement with non-vaccine strains occurred with PCV7 but has not increased with use of PCV13.

Decline in incidence of hospitalization due to pneumococcal and all-cause pneumonia in Canadian children, 2004 to 2015

Loeb M, Qizilbash N, Nepal R, Major M, **Dion S**, Vojicic J, Laferriere C

Introduction/Background: Pneumonia is a common, potentially severe illness. The impact of pneumococcal conjugate vaccine (PCV) immunization programs has been monitored using surveillance of invasive pneumococcal disease (IPD), but information is needed on the effect of these programs on pneumococcal pneumonia (PP) and all-cause pneumonia (ACP). This retrospective study was undertaken to determine pediatric PP and ACP hospitalization rates in Canada (excluding Quebec, and BC after 2010) from 2004 to 2015.

Methods: Case data were obtained from the Canadian Institute for Health Information Discharge Abstract Database (CIHI DAD). PP and ACP were defined using ICD-10-CA codes. Data are included from all Canadian provinces except Quebec, and excluding BC after 2010 due to unavailability of data. Incidence rates were calculated using population data obtained from Statistics Canada.

Results and Analysis: The incidence of hospitalized PP in children <5 years declined from 10.6 per 100,000 per year in 2004/05 to 7.1 in 2005/06, but then increased to 9.15 in 2010/11, coinciding with the emergence of non-vaccine serotypes and H1N1 influenza. After the introduction of higher valence PCVs in 2010 and 2011 the rate then declined to its lowest rate of 2.88 in 2013/14. Similarly, the incidence of ACP declined from 693 (per 100,000 per year) in 2004/05 to 535 in 2007/08, then increased to 921 in 2010/11. This was followed by a decline to its lowest rate of 452 in 2013/14. Changes in the incidence of ACP were on average 25.7 times greater than changes in incidence of PP.

Conclusions and implications for vaccinology: The temporal trends in the incidence of hospitalized ACP in children < 5 years paralleled that of PP from 2004/05 to 2014/15, suggesting that the changes in ACP have the same etiology as PP. Although more investigations are needed to understand this relationship, the impact of PCV on the disease burden may be greater than estimated by PP alone.

Shared medical surveillance program: A collaborative resource of the IWK Health Centre and Dalhousie University

Green K, MacPherson I, Whynot B, Shephard C, MacDougall M, Leadon K, Brophy K, Aquina J, Gallant P, Thompson R

Introduction/Program need and objectives: Federal government Bill C11- Human Pathogens and Toxins Act requires all laboratories with biohazard certification to have a defined medical surveillance program in place to ensure the protection of the public, laboratory staff and their environment when handling human and terrestrial animal pathogens, prions, and biological toxins. IWK Occupational Health Safety and Wellness Department, IWK Research Services, and Dalhousie University Safety Office came together to find cost effective ways to address the shortfalls we faced in addressing the new regulations, to create federally acceptable guidelines that would meet the requirements of the new act and enable us to implement appropriate changes and controls into our existing framework wherever possible.

Program methods and activities: IWK research laboratories are a mixture of IWK and Dalhousie personnel (staff, learners and volunteers). The level of medical surveillance within the IWK Occupational Health Screening program was not sufficient, nor vetted for risk assessment based on biological pathogens being used within the laboratories and was not inclusive.

This shared program was developed to build on the existing expertise, provide specialized consulting, ensure both institutions are exercising due diligence in the care of all personnel while meeting federal guidelines and minimizing additional financial burden. The IWK screening and follow up requirements are based on risk assessment protocols developed by a Dalhousie consultant.

Program results or outcomes (including evaluation): The first group of personnel were processed in May of 2017, over 50% of all Laboratory personnel. Initial Hepatitis B vaccination series, 97 vaccines for non-immunity to childhood diseases (MMR, Varicella) and 58 Tdap were administered. In addition, 42 booster doses of Hepatitis B vaccine and 153 Tuberculosis tests were performed. The first of its kind, this is a unique collaborative partnership.

Implications for practice or policy: Continuation of this program ensures both institutions are now fully compliant with all federal requirements; thus protecting the health and safety of the public.

Prevention of respiratory syncytial virus (RSV) in Nunavik infants: Qualitative evaluation of the immunoprophylaxis program with palivizumab

Lorcy A, **Dubé E**, De Serres G, Rochette M, Gilca R

Introduction/Background: RSV is a major cause of hospital admissions for lower respiratory tract infections in children. Inuit children who reside in circumpolar regions have higher hospital admission rates for respiratory illness compared to southern regions. An immunoprophylaxis program with palivizumab has been in place in Nunavik (Northern Quebec) since 2005 for children at higher risk of serious respiratory illness due to RSV. In 2016, the recommendations were enlarged to include all healthy Nunavik children born at term and <3 months of age. In addition to an evaluation of the epidemiological impact of this new recommendation, a qualitative study was conducted to explore acceptability and feasibility issues.

Methods: Semi-structured interviews with Nunavik healthcare workers were conducted after the first season of implementation.

Results and Analysis: 7 nurses, 4 midwives, 4 pharmacists, 2 physicians, 2 laboratory professionals, 1 family educator, and 1 coordinator working in 4 Nunavik villages were interviewed. The main feasibility issue identified was the lack of financial, material or human resources to implement the new recommendation. This has resulted in shifting resources dedicated to other activities that were perceived as more important than RSV prevention by some informants (e.g., control of STDs or tuberculosis). Lack of information and evidence-based data to support the new recommendation was underscored by some nurses and midwives. The fact that Inuit were not involved in the decision-making process was also identified as an issue by many healthcare workers. Finally, concerns regarding the informed consent by Inuit parents were raised. Some healthcare workers have mentioned that Inuit parents may have felt under pressure to accept the palivizumab administration.

Conclusions and implications for vaccinology: Significant feasibility, acceptability and ethical issues were raised. For a new prevention program to be successful, it is of critical importance to involve Inuit communities and Inuit leaders in the decision-making and implementation processes and to provide resources tailored to local needs.

Limited impact of pneumococcal vaccines on invasive pneumococcal disease in Nunavik (Quebec)

Le Meur J, **De Wals P**, Lefebvre B, Proulx J

Introduction/Context: In 2002, a mass immunization campaign using the 23-valent pneumococcal polysaccharide vaccine (PPV23) was carried out in Nunavik to control an outbreak caused by a virulent clone of serotype 1 Streptococcus pneumoniae. At the same time, the 7-valent pneumococcal conjugate vaccine (PCV7) was introduced for routine immunization of infants, replaced by the 10-valent vaccine (PCV10) in 2009, and the 13-valent vaccine (PCV13) in 2011. The objective was to describe the epidemiology of invasive pneumococcal disease (IPD) in relation to pneumococcal vaccine use.

Methods: Retrospective analysis of IPD cases identified by the Quebec Public Health Laboratory during the period 1997-2017.

Results and analysis: 139 IPD cases were identified during the study period. In adults, serotype 1 incidence decreased following the 2002 PPV23 mass campaign but breakthrough cases occurred. Following PCV use, the incidence of vaccine-type IPD decreased markedly in children and also in adults but serotypes not covered by conjugate vaccines increased. The overall IPD rate was 43/100,000 person-years in the 1997-1999 pre-vaccine era and 58/100,000 person-years in 2010-2017.

Conclusions and implications for vaccinology: The 2002 PPV23 mass immunization campaign may have contributed to control the serotype 1 outbreaks in Nunavik but its effect was short-lived as IPDs caused by serotypes included in this vaccine continued to occur after 2005. PCV use in children induced important modifications in the epidemiology of IPD but most of benefits were eroded by serotype replacement.

Effectiveness of pneumococcal conjugate vaccines (PCVs) to prevent serotype 3 invasive pneumococcal disease (IPD) in Quebec, Canada

Deceuninck G, Lefebvre B, De Serres G, De Wals P

Background: In Quebec, a PCV program was implemented in December 2004 and the recommended schedule is 2+1 doses for low-risk infants. PCV-7 was first used, replaced by PCV-10 in June 2009, and by PCV-13 in January 2011. From the beginning, vaccine uptake has been high and stable: > 90% of children are receiving the recommended number of doses. The objective is to assess the effectiveness of PCV13 to prevent serotype (ST) 3 IPDs.

Methods: IPD cases in children 2–59 months and reported during the years 2010–2016 were eligible and controls randomly identified in the provincial health insurance registry. Parents were interviewed by telephone and immunization records reviewed. Vaccine effectiveness (VE) was computed using unconditional logistic regression models, adjusting for underlying condition, year, season and age.

Results: Out of 514 IPD cases reported, full participation was obtained for 371cases (63%), of these 18 were of serotype 3, and for 1357 controls. VE are shown in the Table.

Conclusion: Although PCV13 VE estimates are statistically non-significant, results suggest some protection after immunisation which is waning rapidly.

Vaccine effectiveness of ≥ 1 dose of PCV13 against 3-serotype IPD (2010-2016)		
	Vaccine effectiveness	95%IC
Any age	-10%	[-441%;78%]

Age< 24months	90%	[-33%;99%]
Age≥24 months	-77%	[-2096%;86%]
In the first 365 days after the last dose	79%	[-148%;98%]
More than 365 days after the last dose	-199%	[-2004%;57%]

No hyporesponsiveness to serotype 3 with repeated doses of 13-valent pneumococcal conjugate vaccine (PCV) – an analysis of 9 pediatric clinical trials

Sings H, Jiang Q, Zhang P, Center K, Gurtman A, Vojicic J, Isturiz R, Scott D

Introduction/Background: Post-licensure studies in children have reported varying degrees of PCV13 effectiveness against invasive pneumococcal disease (IPD) caused by *Streptococcus pneumoniae* serotype 3 in vaccinated individuals and some have reported limited herd effect for serotype 3 in the 2-6 years following PCV13 introduction. We examined the immune response to serotype 3 across nine pediatric studies to determine if the observed effect of PCV13 on serotype 3 IPD epidemiology was due to hyporesponsiveness, a concern raised by lower lgG geometric mean concentrations seen after the booster dose in some studies.

Methods: We calculated the geometric mean fold rise (GMFR) of opsonophagocytosis assay (OPA) titers from after the primary series to post-booster dose in the 9 pediatric clinical studies for which paired OPA data were available. The studies were conducted in the United States, Europe or Asia and assessed PCV13 or control in a 2+1 or 3+1 regimen (see Figure).

Results and Analysis: The GMFR from one-month post-primary series to one month post-booster dose and 95% CI are shown in the figure. A booster response to serotype 3 was observed in 9 out of 11 analyzed groups from the 9 included pediatric studies. In these studies, serotype 3 GMFRs were within the range seen for some other PCV13 serotypes.

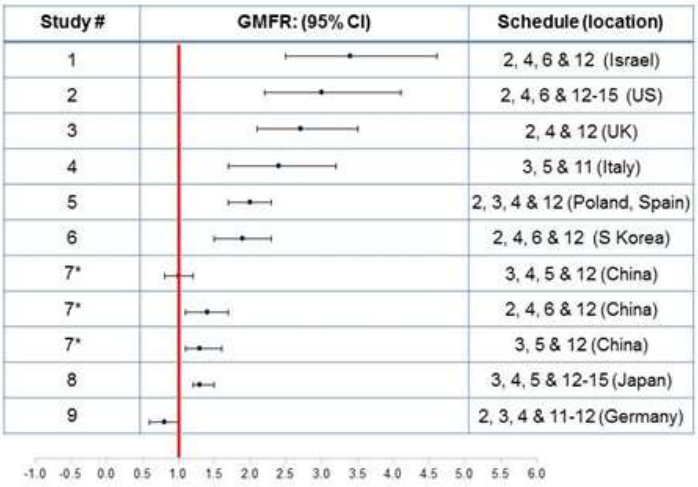

Figure. Geometric Mean Fold Rises from one-month post-infant series to one month post-booster dose and 95% CI. *In study 7, infants were randomized to receive PCV13 in one of 3 dosing regimens

Conclusions and implications for vaccinology: These data show no evidence of hyporesponsiveness to *S pneumoniae* serotype 3 following administration of multiple doses of PCV13.

Persistance of vaccine serotypes causing invasive pneumococcal disease after introduction of the 13-valent vaccine in Calgary, Canada

Kellner J, Ricketson L, Vanderkooi O, MacDonald J

Introduction/Background: After the introduction of PCV7 in 2002, IPD caused by PCV7 serotypes (STs) was nearly eliminated at all ages. We now report on invasive pneumococcal disease (IPD) trends in the PCV13 era.

Methods: The Calgary Area Streptococcus pneumoniae Epidemiology Research (CASPER) has conducted surveillance on IPD in Calgary since 1998. Here we report on the incidence and ST trends pre-PCV13 (2008-09) and post-PCV13 (2010-16).

Results and Analysis: The overall IPD incidence was 8.7 cases/100,000/year pre-PCV13. By 2016 there was no significant change with an incidence of 9.5 cases/100,000/year (Risk difference of 0.08 (95%CI -3.1 to 14.6) per 100,000). All PCV13 ST declined in children but PCV13 STs persisted to cause 24% of childhood IPD in 2016. In adults, a ST4 outbreak, predominantly in homeless persons, persisted from 2014 to 2016 (causing 15% of IPD in 2016). ST3 and ST19A remained common (9% and 7% of IPD cases in 2016, respectively).

Conclusions and implications for vaccinology: More than 6 years after PCV13 introduction in Calgary, vaccine ST IPD is uncommon in children. However, ST3, ST7F and ST19A remain common in adults and an outbreak of ST4 predominantly in homeless persons, indicates that the indirect (herd) effect of 3-dose PCV13 given to children is not consistent to prevent all vaccine serotype IPD in adults adults.

Frequency of physician claims for otitis media in children aged < 2 years in relation with conjugate pneumococcal vaccines use in Quebec

Zhou Z, Deceuninck G, Gilca R, Boucher F, De Wals P

Introduction/Background: In Quebec, routine pneumococcal conjugate vaccination (PCV) for children started in December 2004 and three different products were used sequentially. The objective of the study was to investigate the frequency of physician claims for otitis media (OM) in children aged < 2 years in relation with PCV use

Methods: Physician claims for OM in a random sample of children born in 2000-2012 and observed up to their 2nd year anniversary were obtained from the provincial health insurance board. Poisson regression models were constructed using first OM episode after the age of 3 months as the dependent variable and adjusting for main vaccines used in each cohort, season of birth, age, ambient air temperature, indicators of respiratory virus circulation, and a proxy of overall health services use.

Results and Analysis: A total 1,050,940 OM episodes, including 349,139 first episodes, were recorded among 700,658 children. There was a downward trend in OM frequency starting before PCV introduction. Age at first OM episode was slightly higher in children exposed to PCV10 than in other birth cohorts. In univariate analysis, cumulative OM rate was 58.0% among children not exposed to PCV versus 47.9%, 47.2% and 45.1% among those exposed, respectively, to PCV7-only, PCV10-only and PCV13-only schedules ($p<0.0001$). In multivariate analyses, age, ambient air temperature and overall health service use, were independent predictors of 1st OM episode after the age of 3 months but there was no statistically significant differences between cohorts exposed to schedules containing PCV10 and/or PCV13.

Conclusions and implications for vaccinology: Interpretation of results of this ecological study should be made cautiously because changes in practice related to OM diagnosis and treatment occurred during the study period. Both univariate and multivariate analyses showed no substantial differences between children exposed to schedules containing PCV10 or PCV13.

Impact of the 13-valent pneumococcal conjugate vaccine (PCV13) on invasive pneumococcal disease in Alaskan children and adults

Bruce M, Zulz T, Bulkow L, Singleton R, Rudolph K, Hurlburt D, Bruden D, Hennessy T

Background: Alaska Native (AN) children have experienced high rates of invasive pneumococcal disease (IPD). In April 2010, PCV13 was introduced statewide in Alaska. We evaluated the impact of PCV13 on IPD in children and adults prior to, and 7 years after introduction.

Methods: Pneumococcal sterile site isolates, reported through state-wide surveillance, were serotyped using standard methods. We defined a pre-PCV13 time period 2005-2008 and post-PCV13 time period 2011-2017.

Results: Among Alaska children <5 years, PCV13 serotypes comprised 65% of IPD in the pre-PCV13 period and 18% in the post-PCV13 period. Among all Alaska children <5 years, IPD rates decreased from 60.5 (pre) to 21.8 (post) per 100,000/yr (P<.001); PCV13 serotype IPD decreased from 37.4 to 4.0 (P<.001). Among AN children <5 years, IPD rates decreased from 144.9 to 51.7 (P<.001); PCV13 serotype IPD decreased from 84.0 to 9.4 (P<.001). Rates of non-PCV13 serotype IPD did not change significantly. Among persons 5-17 and ≥ 50 years, the post-vaccine IPD rate was similar to the baseline period, but declined in persons 18-49 years (37%, P<0.001); this decline was similar in AN and non-AN persons (42%, P<0.001, 35%, P<0.001, respectively). Among adults ≥ 50 years, rates of PCV13 serotype IPD decreased from 14.0 to 7.0 (P<.001); this decline was similar in AN and non-AN persons (50%, P=0.005, 50%, P<0.001. Among adults ≥ 50 years, non-PCV13 serotype IPD increased 55% from 16.6 to 25.8 (P<0.001); an increase was also noted in non-AN persons (82%, P<0.001) but not in AN persons.

Conclusions: During the 93 months after PCV13 introduction, overall IPD and PCV13-serotype IPD rates decreased 64% and 89%, respectively, in Alaska children <5 years of age when compared with 2005-2008. We observed evidence of indirect effect among adults with a 50% reduction in PCV13 serotype IPD among adults > 50 years of age.

Shifting epidemiology of pneumococcal vaccine serotypes among various age groups in Canada from 2010 to 2017

Griffith A, Demczuk W, Martin I, Lefebvre B, McGeer A, Tyrrell G, Zhanel G, Mulvey M, The Canadian Public Health Laboratory Network

Introduction/Background: Pediatric vaccine programs using the 7-valent pneumococcal conjugate vaccine (PCV7) implemented in 2001 was replaced with an expanded PCV13 vaccine across Canada during 2010 to 2011. This study examines changes of in serotypes in age groups over 2010–2017 in Canada.

Methods: A total of 20,058 invasive Streptococcus pneumoniae isolates collected from 2010–2017 were serotyped by Quellung reaction using commercial antisera. Data for 2017 is preliminary and includes only isolates serotyped by the NML. The data were aggregated into <2 year, 2-4 year, 5–14, 15–49 year, 50–64 year and ≥65 year age groups.

Results and Analysis: From 2010–2017 PCV serotypes declined in all age groups with the greatest reductions seen in children <5 years of age. In children <2 years PCV7 serotypes remained low over the study period from 4.4% to 0%. The additional six PCV13 serotypes declined dramatically from 59.3%–10.9% whereas non-PCV serotypes increased from 36.3%–89.1%. A similar trend was seen among the 2–4 year olds with PCV serotypes declining from 73.1%–25.0%, despite an increase of PCV7 serotypes from a low of 0% in 2015 to 8.3% in 2017. In the 15–49 and 50–64 age groups, PCV7 serotypes increased from 6.5% and 3.9% in 2013 to 19.9% and 16.0% in 2017, respectively; primarily due to a regional outbreak of serotype 4. PCV13 serotypes decreased from 46.0%–22.2% in 15–49 year olds, from 43.8%–18.3% in 50–64 year olds; and from 40.6%–6.4% in people ≥65 years old.

Conclusions and implications for vaccinology: Continued surveillance of serotypes is imperative to evaluate vaccine effectiveness and identify emergent replacement serotypes to inform future vaccine development. In this study, the proportion of PCV associated IPD serotypes identified has declined concurrently with an increase on non-PCV serotypes in all age groups.

Potential clinical and economic impact of switching from the 13-valent to 10-valent pneumococcal conjugate vaccine in Quebec

Breton M, Vojicic J, Wilson M, McDade C, Farkouh R, Wasserman M

Background: The 13-valent pneumococcal conjugate vaccine (PCV13) is part of the routine infant immunization schedules in Canada. Recently, Quebec has changed the recommendation to the 10-valent pneumococcal

conjugate vaccine (PCV10). The purpose of this study is to evaluate the health and economic implications of potential disease re-emergence following a switch to a lower-valent vaccine in Quebec.

Research Methods: A decision-analytic model using historical pneumococcal disease surveillance data to estimate disease trends and to forecast serotype re-emergence and/or reduction was applied. Serotype-specific incidence was modeled to compare maintaining PCV13 use versus switching to PCV10. For each vaccination program, health outcomes (cases of invasive pneumococcal disease, pneumonia, and otitis media (OM)), associated health-care costs, and changes in antimicrobial prescriptions and resistance were estimated. Costs (2018 Canadian dollars), utility weights, and risk of disease-specific sequelae were derived from available published sources. Incremental cost-effectiveness ratios were calculated across a number of scenarios.

Results and Analysis: Assuming a 1 year lag before serotype replacement, maintaining PCV13 would avert an additional 180,000 cases of pneumococcal disease and 130 associated deaths compared to switching to PCV10 over 5 years. This would correspond to a net reduction of approximately 167,000 antibiotic prescriptions, or 1 prescription for every 2.5 infants vaccinated with PCV13. While vaccine costs were higher, PCV13 would be cost-saving due to fewer cases of disease in the PCV13 population. PCV13 remained cost-saving and under a number of sensitivity analyses.

Recommendations and implications for practice: The results demonstrate that continued use of PCV13 in Quebec would provide greater public health and economic benefit compared to switching to PCV10. It is important that policy makers consider the potential implications of disease re-emergence when considering modifications to vaccination strategies.

Pneumococcal vaccination provides substantial value for money for Canadians

Breton M, Peloquin F, Wasserman M, Wilson M, McDade C, Farkouh R

Introduction: Introduction of pneumococcal conjugate vaccines (PCV) to the Canadian childhood routine immunization schedules (RIS) resulted in significant benefits. The 7-valent PCV was added to all provinces' RIS between 2002 and 2006. The 10-valent PCV was used in Ontario and Quebec for 12 to 18 months in 2009 and 2010. The 13-valent PCV was marketed in 2010 and rapidly adopted by all provinces by 2011. Direct vaccine protection reduced incidence of invasive pneumococcal disease (IPD), pneumonia (PNE) and acute otitis media (AOM) in vaccinated children. Indirect vaccine protection also reduced the burden of disease in other age groups. The objective of this study is to evaluate the economic impact of PCVs following nationwide RIS implementation.

Research Methods: Canadian databases and literature were reviewed to obtain pre- and post-PCV incidence of IPD, PNE and AOM, as well as direct and indirect medical costs (reported in 2017 $ CAD). Case counting index date was set to Jan 2005, at which point PCV RIS were implemented for over 90% of children. A steady state scenario using pre-PCV incidence rates was projected to Dec 2015 to estimate the number of cases expected in the absence of PCVs. Averted cases were obtained by subtracting the cases reported from the estimated case count without PCVs. Disease costs were assigned to averted cases and vaccine spend was subtracted from the total to obtain net savings.

Results and Analysis: Successive implementation of PCVs on the provinces' RIS saved 9,767 lives and resulted in net savings of CAD $1.76 billion between Jan 2005 and Dec 2015. These savings stem from averted direct and indirect medical costs associated with IPD, PNE and AOM cases.

Recommendations and implications for practice: Introduction of PCVs resulted in reduced pneumococcal burden of disease and net economic benefits to Canadian society and sustained PCV funding will continue to accrue these benefits.

The hidden clinical and economic burden of pneumonia

Breton M, Vojicic J, Fanton-Aita F, Dobrescu A

Introduction: Pneumonia (PNE) hospitalization burden is often assessed based on administrative hospital records and on PNE coded as the "most responsible diagnosis" (MRDx). Coding practices and other factors however may require that PNE is coded as "other than most responsible diagnosis" (ODx). This study assesses the health care utilization and discharge dispositions of PNE cases by MRDx and ODx in adults ≥65 years in Canada.

Research Methods: Data was obtained from the Canadian Institute for Health Information (CIHI) Discharge Abstract Database (DAD) and the Canadian Management Information System Database. Individuals aged ≥65 hospitalized between January 2014 and March 2015 with no hospitalization for PNE in the previous year were included. PNE cases (coded as MRDx or ODx) and non-PNE cases were analyzed for: average length of hospital stay including alternate level of care (LOS+) and associated costs, in-hospital mortality, discharge pathways (home care and residential care) and readmission rates.

Results and Analysis: Over the study period, there were 50,324 PNE and 522,050 non-PNE hospitalizations. Of all PNE hospitalizations, 64% were coded as ODx. Compared to MRDx, ODx-coded cases had higher mortality (19.21% vs 9.85%), LOS+ (20.49 vs 10.44 days) and associated average cost per hospitalization ($18,700 vs $8,615). ODx-coded cases accounted for >75% of deaths, hospital days and hospitalization costs following initial PNE admission. When compared to non-PNE, PNE cases overall had higher mortality (15.8% vs 5.4%), discharge to residential care (17.08% vs 11.9%), readmission for PNE within a year (4.9% vs 1.4%), and LOS+ (16.83 vs 10.59 days).

Recommendations and implications for practice: Exclusion of PNE cases coded as ODx could lead to several-fold lower estimates of clinical and economic burden of pneumonia in Canadian elderly; factors that influence coding should be well understood when analyzing administrative data. PNE cases in this population have worse discharge dispositions compared to non-PNE cases, which further underlines the importance of prevention.

The public health impact of herpes zoster immunization in Canada

Van Oorschot D, McGirr A, Widenmaier R, Varghese L, Curran D

Introduction/Background: Herpes zoster (HZ), also known as shingles, results from the reactivation of latent Varicella Zoster virus. In Canada, approximately 1 in 3 people will develop HZ over their lifetime, with this risk increasing to almost 50% by age 85. HZ leads to significant morbidity in older adults, including development of a number of significant complications, including post-herpetic neuralgia (PHN). The aim of this study is to predict the public health impact of using Zoster Vaccine Live (ZVL) and the adjuvanted Recombinant Zoster Vaccine (RZV) in adults ≥50 years of age (YOA), stratified by age cohort.

Methods: The ZOster ecoNomic Analyses (ZONA) model predicts the public health impact of RZV and ZVL immunization over the cohort lifetime. Demographic data was obtained from Statistics Canada, vaccine efficacy estimates from clinical trials, and HZ and PHN epidemiologic and healthcare utilization parameters from publicly available literature. Additional assumptions included 80% coverage rate and 75% second dose compliance for RZV. Age cohorts were selected based on those outlined by the National Advisory Committee on Immunization.

Results and Analysis: In Canadian adults ≥50YOA, the ZONA model predicts that immunization with RZV would prevent an additional 741,116 cases of HZ compared to ZVL (by age cohort, 50-64YOA: 483,142; 65-79YOA: 196,146; 80+YOA: 61,827). This would translate into 177,031 additional PHN cases prevented compared to ZVL over the lifetime of the cohort (by age cohort, 50-64YOA: 117,371; 65-79YOA: 43,326; 80+YOA: 16,335). The model predicts an additional 7,411 hospitalizations and 1,845,378 additional general practitioner visits could be avoided by using RZV compared to ZVL.

Conclusions and implications for vaccinology: The ZONA model predicts a greater reduction in HZ and PHN morbidity and healthcare utilization associated with RZV compared to ZVL immunization in all cohorts studied. This analysis can help healthcare practitioners, policy makers, and public health officials make informed decisions about HZ vaccines.

Vaccines for herpes zoster: A Canadian cost-effectiveness analysis

McGirr A, **Van Oorschot D**, Widenmaier R, Stokes M, Ganz M, Varghese L, Curran D

Introduction/Background: Herpes zoster (HZ) is a painful and costly reactivation of latent varicella zoster virus in older adults. There are two vaccines licensed to prevent HZ in Canadian adults ≥50 years of age (YOA): the Recombinant Zoster Vaccine (RZV) and the Zoster Vaccine Live (ZVL). In this study, we assess the potential impact and cost-effectiveness of RZV and ZVL in Canadian adults ≥50 YOA.

Methods: The ZOster ecoNomic Analysis (ZONA) model was used to estimate the impact and cost-effectiveness in terms of the number of cases of HZ and postherpetic neuralgia (PHN) avoided, the number needed to vaccinate, and the incremental cost-effectiveness ratio (ICER). Population demography, Canadian specific epidemiology, and Canadian healthcare utilization data were used to parameterize the model. Analyses were conducted from the healthcare payer's perspective and followed the Canadian Agency for Drugs and Technologies in Health guidelines with a 1.5% discount rate for both costs and effectiveness. Additional assumptions included list price of the vaccines, 80% vaccine coverage rate, and 75% second dose compliance for RZV. Deterministic and probabilistic sensitivity analyses were conducted to explore the robustness of the results.

Results and Analysis: For the approximately 12 million Canadians ≥50 YOA, the model predicts that RZV would prevent 741,116 additional cases of HZ, 177,031 additional cases of PHN, and 234 additional deaths compared to ZVL. Compared to no vaccination, the ICER for RZV was estimated at $30,402 per quality-adjusted life-year (QALY) gained. For ZVL, compared to no vaccination, the ICER was estimated at $89,737 per QALY. Model results were most sensitive to the discount rate, annual waning of vaccine efficacy, and annual incidence of HZ.

Conclusions and implications for vaccinology: At a commonly used willingness-to-pay threshold of $50,000 per QALY, RZV is a cost-effective option, robust to a variety of sensitivity analyses, for immunizing Canadian adults ≥50 YOA.

The impact of reactogenicity after administration of the recombinant zoster vaccine upon the physical functioning and quality of life of older adults

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Introduction/Background: Herpes zoster (HZ) and its related complications are associated with a significant burden of illness in older adults, which negatively impacts patients' physical functioning and quality-of-life (QoL). The recombinant zoster vaccine (RZV) shows high efficacy for the prevention of HZ in older adults and is associated with local and systemic reactions. Therefore, this study assessed the impact of RZV reactogenicity upon the physical functioning and QoL of participants.

Methods: 401 adults aged ≥50 years received a dose of RZV at 0 and 2 months in this open-label, single-arm, multicenter study (NCT02979639). Changes in mean SF-36 Physical Functioning score were assessed between pre-dose-1 vaccination and post-dose-1 vaccination for 7 days (primary endpoint). Decreased scores are associated with decreased physical functioning. QoL, reactogenicity and safety were also assessed. The current analysis was performed post-dose-1 vaccination of the 2-dose RZV schedule.

Results and Analysis: No clinically meaningful reductions in overall mean SF-36 Physical Functioning scores from pre- to post-RZV dose-1 were observed (mean +1.9 points) and no overall quality-adjusted-life-year loss was recorded post-dose-1. However, grade 3 reactogenicity occurred in 9.5% of participants, and was associated with a transient, clinically-important decrease in SF-36 Physical Functioning score (impacting activities such as walking, carrying groceries, climbing stairs) on Days 1-2 post-first-vaccination. The solicited local symptoms were pain (77.5%), redness (23.0%) and swelling (13.3%); the most frequent solicited systemic reactions were fatigue (33.5%), headache (28.3%) and myalgia (26.8%).

Conclusions and implications for vaccinology: Overall, the physical functioning and QoL of older adults were not significantly affected by the first RZV dose. Grade 3 reactogenicity was associated with a small transient decrease in physical functioning 1-2 days post-dose-1 that resolved by Day 3 post-vaccination.

A systematic review on the risk of herpes zoster and complications in immunocompromised adults

Buchan S, Kraicer-Melamed H, Wilson S, Deeks S

Introduction/Background: Reactivation of varicella zoster virus results in herpes zoster (HZ) and can lead to a variety of complications. There are certain groups at high risk of HZ, including those who are immunocompromised due to an underlying condition or use of immunosuppressive agent. However, there are limited data regarding the relative risk of developing HZ or subsequent complications in this population relative to immunocompetent populations. In Canada, there are two vaccines authorized to protect against HZ, however one is contraindicated in immunocompromised populations. The objective of this study is to summarize the risk of HZ and related complications in immunocompromised adults to assist with decision-making.

Methods: We performed a preliminary systematic search of the literature in Medline, with additional databases to be included in our ongoing review (results available by December). We included studies related to the risk or burden of HZ and its complications in immunocompromised populations.

Results and Analysis: At this first stage, we retrieved 692 articles that were screened by title and abstract for inclusion. We screened 75 articles at the full-text level; of these, 19 articles met our inclusion criteria and were included in the preliminary review. Fourteen of the included articles estimated the risk of HZ in those immunocompromised relative to those who were immunocompetent, although definitions of being immunocompromised varied. Of these, 12 studies reported an increased risk of HZ in their comparison. Five studies reported on complications of HZ and four demonstrated an increased risk of complications.

Conclusions and implications for vaccinology: Preliminary results indicate an increased risk of HZ in immunocopromised populations. With the recent addition of a recombinant adjunvanted subunit zoster vaccine, opportunities to reduce the burden of disease and complications in this high-risk group can be explored. Future work will expand the search and databases to identify additional studies and will explore risk in different sub-populations of immunocompromised status.

The comparative efficacy, safety, and reactogenicity, of herpes zoster vaccines: A network meta-analysis

McGirr A, Widenmaier R, Curran D, Espie E, Mrkvan T, Oostvogels L, Simone B, McElhaney J, Haeussler K, Thano A, Newson R

Introduction/Background: We estimated the relative efficacy, safety, and reactogenicity of vaccines for prevention of herpes zoster (HZ) using network meta-analysis (NMA) based on evidence from randomized controlled trials.

Methods: A systematic literature review evaluated two different HZ vaccines: adjuvanted recombinant zoster vaccine (RZV) and zoster vaccine live (ZVL), with different formulations assessed. Detailed feasibility assessment indicated that a NMA was feasible for efficacy (against HZ and postherpetic neuralgia (PHN)), safety (serious adverse events), and reactogenicity (injection-site reactions, systemic reaction) outcomes. Primary analyses included frequentist NMAs with fixed effects for efficacy outcomes, due to limited data availability, and both fixed and random effects for safety and reactogenicity outcomes. As age is a known effect modifier of vaccine efficacy (VE), VE analyses were stratified by age.

Results and Analysis: RZV demonstrated significantly higher HZ efficacy than ZVL in adults ≥60 years of age (YOA) (VE[RZV]=0.92 (95% confidence interval (95%CI): 0.88, 0.94), VE[ZVL]=0.51 (95%CI: 0.44, 0.57)) and adults ≥70 YOA (VE[RZV]=0.91 (95%CI: 0.87, 0.94), VE[ZVL]=0.37 (95%CI: 0.25, 0.48)). Similarly, RZV demonstrated significantly higher PHN efficacy than ZVL in adults ≥60 YOA (VE[RZV]=0.89 (95%CI: 0.70, 0.96), VE[ZVL]=0.66 (95%CI: 0.48, 0.78)) and adults ≥70 YOA (VE[RZV]=0.89 (95%CI: 0.69, 0.96), VE[ZVL]=0.67 (95%CI: 0.44, 0.80)).

The 95%CIs of the differences of VE[RZV] and VE[ZVL] estimates did not contain 0, indicating that these were statistically significant. RZV was associated with significantly more injection-site and systemic reactions compared to most formulations of ZVL and placebo, however definitions and data collection procedures differed. There were no statistically significant differences found between RZV and any formulation of ZVL or placebo for serious adverse events.

Conclusions and implications for vaccinology: RZV is significantly more effective in reducing HZ and PHN incidence in adults ≥60 YOA when compared to ZVL. As anticipated with an adjuvanted vaccine, RZV results in more reactogenicity following immunization, but no safety differences were found between RZV and ZVL.

Looking beyond the number of serotypes: A Canadian cost-effectiveness modelling approach comparing PCV13 and PHiD-CV

Olbrecht J, Simone B, Izurieta P, **McGirr A**

Introduction/Background: The 13-valent pneumococcal conjugate vaccine (PCV) (PCV13/Prevnar 13/Pfizer) and the 10-valent PCV (PHiD-CV/Synflorix/GSK) prevent invasive pneumococcal disease (IPD), pneumonia, and acute otitis media (AOM). Cost-effectiveness models comparing both vary widely, using different vaccine efficacy (VE) estimates from literature against serotypes (ST) 3, 19A, and non-typeable Haemophilus influenzae (NTHi), as well as herd effect (HE). This study evaluates the impact of these input parameters on the public health impact and the cost-effectiveness of PCVs.

Methods: A published Markov cohort model comparing PCV13 and PHiD-CV was adapted to operate with ranges of VE against ST3, ST19A, NTHi, and HE instead of arbitrary point estimates for these values. Ranges included confidence intervals of the relevant values from available literature. Where possible, the model was populated with Canadian epidemiology and resource utilization data. Reduction in number of cases, healthcare utilization, deaths, and the incremental cost-effectiveness ratios (ICERs) were compared for PCV13 and PHiD-CV for the 2016 Canadian birth cohort over a lifetime horizon.

Results and Analysis: Varying VE against ST3, ST19A, and HE in the model projected no differences in number of deaths and one more IPD case using PHiD-CV versus PCV13 (507 and 506 respectively). Varying NTHi VE affected the model outcomes for AOM. PHiD-CV however prevented on average 8,597 more AOM cases than PCV13 (associated with 1,134 hospitalizations and 14,742 physician visits). Additionally, the cost-effectiveness of PHiD-CV remained dominant over PCV13 with both single end point observations and using the ranges.

Conclusions and implications for vaccinology: This study shows that variations in model inputs for debated parameters such as VE against ST3, ST19A, as well as herd effect, do not seem to impact the final outputs significantly. Focusing on overall VE against all pneumococcal infections, regardless of serotype, may be a more meaningful approach when evaluating PCVs.

PCV13 serotype trends over time in pneumococcal community acquired pneumonia: Which method(s) work best?

LeBlanc J, ElSherif M, Ye L, MacKinnon-Cameron D, Ambrose A, Hatchette T, Martin I, Andrew M, Boivin G, Bowie W, Green K, Johnstone J, Loeb M, McCarthy A, McGeer A, Semret M, Trottier S, Valiquette L, Webster D, McNeil S, on behalf of the Serious Outcomes Surveillance (SOS) Network of the Canadian Immunization Research Network (CIRN)

Introduction/Background: The 13-valent pneumococcal conjugate vaccine (PCV13) has recently been shown effective at preventing vaccine-type pneumococcal community acquired pneumonia (CAP_{Spn}) in healthy adults. With the anticipated herd immunity from routine infant immunization with PCV13 used since 2010, the benefits of adult immunization in Canada were unclear and surveillance for CAP_{Spn} with serotype distributions was needed. This study aimed to compare PCV13 serotype trends in CAP_{Spn} from 2010 to 2015 using various laboratory methods.

Methods: Active surveillance for CAP was performed from 2010 to 2015 in adult hospitals across five Canadian provinces. Bacteremic CAP_{Spn} cases were identified using blood culture, and non-bacteremic CAP_{Spn} cases by sputum culture or using a PCV13-specific urine antigen detection (UAD_{PCV13}). Serotype was assigned using Quellung reaction, PCR, or UAD_{PCV13}. CAP_{Spn} cases were categorized by laboratory test(s), age, or disease (bacteremic or non-bacteremic CAP_{Spn}).

Results and Analysis: A diagnostic test for *S. pneumonia*e was performed on 6687 CAP cases, and 1198 CAP_{Spn} cases were identified. *S. pneumoniae* positivity in CAP decreased from 22.1% in 2011 to 10.2% in 2014, and increased again in 2015 to 14.3%. PCV13 serotypes followed a similar trend, where the decline in PCV13 serotypes attributed to serotypes 7F and 19A was noted, and the proportion of serotype 3 increased over time. Similar trends were seen regardless of whether data was categorized by laboratory test(s), age, or disease.

Conclusions and implications for vaccinology: Our data suggest that all methods showed similar trends in PCV13 serotype distribution over 2010 to 2015, but laboratory test combinations increased the diagnostic yield. CAP_{Spn} remained a significant cause of morbidity and mortality in hospitalized adult but herd immunity through childhood immunization with PCV13 was evident for some serotypes like 7F and 19A. Serotype 3 seems to be persisting despite herd immunity, and ongoing surveillance is required.

Multi-target plasmid controls for conventional and real-time PCR-based serotyping of *Streptococcus pneumoniae*

Schembri J, Gillis H, Lang A, Warhuus M, Martin I, Demczuk W, ElSherif M, McNeil S, **Leblanc J**

Introduction/Background: Serotyping of *Streptococcus pneumoniae* is an integral part of disease surveillance, with over 92 serotypes characterized to date using traditional serotyping. To identify the most predominant disease causing serotypes, molecular serotyping methods are now increasingly being used, like conventional and real-time multiplex PCR (cmPCR and rmPCR, respectively). Given that cmPCR consists of eight reactions spanning 41 targets, and rmPCR consists of seven triplex reactions, standardizing positive controls for these assays is challenging. As such, a 43-target plasmid for cmPCR (pSpn-CM1) and a 23 target plasmid for rmPCR (pSpn-RM1) were designed and validated.

Methods: Plasmid pSpn-RM1 was designed and synthesized as chimeric DNA sequences to include all PCR target primer binding sites sequences for cmPCR. Plasmid pSpn-RM1 consisted of all primer and probe sequences required for rmPCR. Additional targets (*lytA* and *cpsA*) were included in both plasmids for quantification, following their propagation and purification from *Escherichia coli*.

Results and Analysis: When tested using the cmPCR reactions, all targets could be reproducibly be detected using pSpn-CM1 as template, with good amplicon visibility at a concentration of $1.4 (\pm 0.3) \times 10^5$ copies/ml was used. For the rmPCR reactions, all targets were reproducibly amplified with a concentration of $1.1 (\pm 0.2) \times 10^4$ copies/ml of pSpn-RM1, and the PCR efficiency for each target was equivalent to DNA extracted from representative *S. pneumoniae* serotypes.

Conclusions and implications for vaccinology: These quantifiable multi-target plasmids simplify the preparation of controls for PCR-based serotyping of *S. pneumoniae*, and methods herein could be extended to other highly multiplexed PCR assays.

Streptococcus pneumoniae serotyping: assessing the performance of a PCR- and sequencing-based testing algorithm

Gillis H, Lang A, ElSherif M, Demczuk W, Martin I, McNeil S, **Leblanc J**

Introduction/Background: *Streptococcus pneumoniae* is a bacterium that causes significant morbidity and mortality worldwide. Its capsule polysaccharides have been used successfully as vaccine targets, and to characterize *S. pneumoniae* into 92 different serotypes. Phenotypic (Quellung reaction) or genotopic (PCR or sequencing) methods can be used for serotype assignment, but the performance may vary between methods.

This study compared the performance of Quellung reaction, to an algorithm using PCR- and sequence-based serotyping technologies for vaccine-preventable or closely related serotypes.

Methods: A panel of geographically diverse isolates of *S. pneumoniae* spanning 92 different serotypes was provided by various references laboratories worldwide. Each isolate was subjected to conventional multiplex PCR methods, using previously established methods. Sanger sequencing was performed using genetic signatures defined in the PneumoCaT database. When discrepant, Quellung reaction were repeated, and next generation sequencing and comparative genomics was used to evaluate the sequence composition of the *cps* loci.

Results and Analysis: As expected, PCR was unable to assign serotype in some cases, and some serotype results were insufficiently discriminatory. Following sequencing, 86.3% (404/468) of isolates were concordant with the Quellung serotyping. Discrepant analyses are underway.

Conclusions and implications for vaccinology: An algorithm based on PCR and sequencing, or next-generation sequencing alone, shows much promise for serotyping of *S. pneumoniae*. However, discrepant results were noted, suggesting either our current understanding of genetic signatures conferring serotype-specificity might not be complete, or the Quellung reaction results were incorrect. Accurate methods for serotyping are essential to monitor the impact of pneumococcal vaccines, and understand the epidemiology of *S. pneumoniae* diseases.

Whole genome phylogenetic analysis of *Streptococcus pneumoniae* causing an outbreak of serotype 4 (st4) invasive pneumococcal disease (ipd) outbreak in Alberta, Canada

Vanderkooi O, Ricketson L, Tyrell G, Demczuk W, Martin I, Kellner J

Introduction/Background: Since 2014, there has been a sharp increase in ST4 IPD cases in adults in the province of Alberta, particularly in homeless persons. In the city of Calgary, ST4 has caused 14% of all IPD in adults from 2014-16.

Methods: All ST4 IPD isolates from Calgary and Edmonton from 2010-16 were analyzed by whole genome sequencing (WGS).

Results and Analysis: Isolates from 140 cases that occurred primarily in males (76%), with a median age of 48 and, when recorded, 55% were homeless. Two major multi-locus sequence types (MLST) were found consisting of MLST-205 (n = 19) and MLST-244 (n = 115). WGS using core single nucleotide variant (SNV) phylogenetic cluster analysis identified the two clades (n=15) of MLST-205 isolates from Calgary, which grouped distantly from clades of ST-244 isolates (n=115). The MLST-244 strains clustered phylogenetically into 8 clades (n=53) with regional and temporal clustering evident. Two clades had a large proportion of isolates from homeless people and other homeless isolates were distributed among the miscellaneous isolates not grouped into clades. Temporal clustering was observed in clades C and K with strains collected from 2010–2013, whereas clades D, E, F, G, H and J were more recently collected during 2014–2016.

Conclusions and implications for vaccinology: The increase of ST4 IPD isolates in Alberta can be attributed predominantly to a cluster of MLST-205 isolates in Calgary and a larger increase of MLST-244 isolates in Calgary and Edmonton. WGS defined sub-clades of the MLST-244 isolates associated with homelessness, and with temporal and regional clustering. The indirect (herd) effect through vaccination of children did not prevent this outbreak of vaccine-serotype IPD in adults.

The incidence and economic burden of clostridium difficile in Ontario, Canada

Pereira J, McGeer A, Tomovici A, Selmani A, Chit A

Introduction/Background: In Ontario, Clostridium difficile is among the top 10 infectious disease causes of morbidity and mortality. Although historically considered a hospital-acquired infection, recent data indicate epidemiological shifts in location of acquisition and symptom onset. Given that such changes are likely to have

consequences on healthcare system costs, we used health administrative data to establish the incidence and economic burden of CD Infection (CDI) in Ontario, Canada, stratifying cases by acquisition and onset.

Methods: We performed a retrospective analysis using individual-level data from linked Ontario health databases from 2005 to 2014, identifying CDI requiring hospitalization in adults ≥ 18 years per 100,000 person-years (PYs) for six categories of acquisition and onset: ACH-acquired/ACH-onset, ACH- or LTCF-acquired/ACH-onset, LTCF-acquired/LTCF-onset, LTCF- or ACH-acquired/LTCF-onset, community-acquired/community-onset, and ACH-acquired/community-onset. We estimated costs of ACH-acquired, LTCF-acquired and community-acquired CDI using a population-based matched cohort study for 180 and 365 days post-admission.

Results and Analysis: Between 2005 and 2014, 33,909 individuals in Ontario were hospitalized with CDI, of which 17,272 (50.9%) were ACH-acquired/ACH-onset. The ACH-acquired/community-onset group contributed the second highest CDI incidence rate until 2009, when it was replaced with the community-acquired/community-onset group. Community-acquired/community-onset cases have shown a fairly consistent upwards trend, rising by 36.3% since 2005, with 9.56 cases per 100,000 PYs (95% CI: 8.98-10.15) in 2014. Most costs associated with CDI were incurred within the first 180 days post-admission, mainly comprising inpatient hospitalization. Those who acquired ACH in-hospital had the highest total costs and the largest CDI-attributable cost (median: $38,953 for the CDI cohort vs. $13,542 for the control group) although large differences in cost between disease cohort and matched controls were also seen with community-acquired CDI (median: $20,258 vs $1,144).

Conclusions and implications for vaccinology: Recent increases in community-acquired CDI cases have cost implications, both warranting the need for additional prevention efforts in outpatient settings, and demonstrating the potential impact of emerging vaccines.

A comparative evaluation of the burden of disease caused by influenza A and influenza B during the 2011-2014 influenza seasons in Canada: An analysis from the Canadian Immunization Research Network (CIRN) Serious Outcomes Surveillance (SOS) Network

McParland C, **Nichols M**, Andrew M, Hatchette T, Elsherif M, Ye L, McNeil S, on behalf of the Canadian Immunization Research Network (CIRN) Serious Outcomes Surveillance (SOS) Network Investigators

Introduction/Background: When assessing burden of influenza disease, influenza B has typically been associated with infection in children and young adults, and is considered less prevalent and/or severe in older adults. We sought to assess the burden of influenza type A vs. B disease in Canadian adults hospitalized with laboratory-confirmed influenza.

Methods: The Canadian Immunization Research Network (CIRN) Serious Outcomes Surveillance (SOS) Network conducted active surveillance for influenza in hospitalized adults (≥16 years) across Canada during the 2011-2014 influenza seasons. Eligible patients were admitted to hospitals with any acute respiratory illness/symptom and had a nasopharyngeal swab tested for influenza using reverse transcriptase polymerase chain reaction (PCR). Demographic/clinical information and in-hospital outcomes were collected. Frailty Index scores were recorded at baseline and 30-days after discharge in patients ≥65 years. Clinical characteristics and outcomes between influenza A and B cases were assessed; discrete outcomes were compared using Chi-squared (χ^2); continuous outcomes were compared using student's t-tests.

Results and Analysis: Overall, 3484 influenza A cases and 1375 influenza B cases were enrolled from 2011-2014. Influenza B cases were significantly older than influenza A cases (mean age 71.2y vs 65.8y, respectively; $p<0.01$), were more frail prior to the onset of illness (mean Frailty Index 0.22 vs 0.21, respectively; $p<0.01$), and were more likely to be admitted from long-term care (12.1% vs 5.5%, respectively; $p<0.01$). There was no significant difference between influenza B and influenza A with respect to length of hospitalization (10.27 days vs 11.1 days, respectively, $p=0.07$) or mortality rate (9.45% vs 9.01%, respectively; $p=0.63$).

Conclusions and implications for vaccinology: While Influenza A is generally felt to be the more significant virus in terms of morbidity and mortality in adults, influenza A and B were associated with similar duration of

hospitalization and mortality rates. Influenza B also predominantly affected the frail elderly, highlighting the importance of optimizing influenza B vaccine protection in this population.

2016/2017 influenza burden of disease and end-of-season influenza vaccine effectiveness (VE) estimates for preventing influenza-related hospitalization among Canadian adults: An analysis from the Canadian Immunization Research Network (CIRN) Serious Outcomes Surveillance (SOS) Network

Nichols M, Andrew M, Hatchette T, Ambrose A, Boivin G, ElSherif M, Green K, Johnstone J, Katz K, LeBlanc J, Loeb M, Mackinnon-Cameron D, McCarthy A, McElhaney J, McGeer A, Poirier A, Powis J, Richardson D, Semret M, Smyth D, Trottier S, Valiquette L, Webster D, Ye L, McNeil S, on behalf of the CIRN SOS Network Investigators and the Toronto Invasive Bacterial Diseases Network (TIBDN) Investigators

Introduction/Background: To inform public health decision making around influenza prevention and treatment, the Canadian Immunization Research Network (CIRN) Serious Outcomes Surveillance (SOS) Network conducts active surveillance each influenza season to characterize influenza burden of disease and provide influenza VE estimates for preventing influenza-related hospitalization in Canadian adults (≥16y).

Methods: Active surveillance for influenza was conducted at 13 hospitals in four provinces beginning on November 15th, 2016 and ending April 30th, 2017. Patients admitted with any acute respiratory diagnosis or symptom were eligible for enrolment; eligible patients had a nasopharyngeal swab tested for influenza using polymerase chain reaction (PCR). Patients who tested positive for influenza were considered cases; patients who tested negative for influenza were eligible to become matched controls. Detailed demographic/clinical information was obtained from the medical record. Influenza VE was estimated as 1- odds ratio (OR) of influenza in vaccinated vs. unvaccinated patients x 100% using conditional logistic regression, with corresponding 95% confidence intervals (CIs).

Results and Analysis: A total of 1431 influenza cases were enrolled; the majority were influenza A (n=1299) and 100% of patients with known influenza A subtype were A/H3N2. Among all influenza cases, 144 (10.1%) patients were admitted to the intensive care unit (ICU) and 91 (6.4%) patients died within 30 days of discharge. Overall adjusted influenza VE for prevention of influenza-related hospitalization in all ages was 23.3% (95% CI: 2.9-39.4%), with lower VE observed in patients ≥65y (VE: 19.4%; 95% CI: -7.8-39.8%) than in patients <65y (VE: 47.9%; 95% CI: 9.9-69.9%).

Conclusions and implications for vaccinology: Overall, influenza VE was low but effective (VE: 23%) for preventing influenza-related hospitalization in adults during the 2016/2017 season. Given the low influenza VE observed, continued assessment of influenza VE is crucial to inform immunization policy in Canada, and to emphasize the importance of the development and utilization of improved influenza vaccines.

Influenza vaccine effectiveness in older adults and the impact of repeated vaccination, 2010-2011 to 2015-2016 influenza seasons in Ontario, Canada

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Introduction/Background: Although annual influenza vaccination is recommended for older adults, the effect of repeated vaccination in this population is unclear. We investigated VE against laboratory-confirmed influenza healthcare encounters and the impact of repeated vaccination on current season VE.

Methods: We conducted a test-negative study in community-dwelling adults aged >65 years in Ontario, Canada for the 2010-2011 to 2015-2016 seasons by linking respiratory virus test results to health administrative data. Influenza vaccination status was determined using physician and pharmacist billing claims. We estimated VE for the 2010-11 to 2015-16 seasons combined and for various subgroups using multivariable logistic regression. We also conducted a number of sensitivity analyses, including correcting for misclassification of vaccination status.

The impact of repeated vaccination was assessed based on two approaches: 1) using a common reference group that had not been vaccinated in any of the seasons studied; and 2) stratifying by previous vaccination history.

Results and Analysis: We included 54,110 patients, with 10,595 (20%) testing positive for influenza and 28,644 (53%) vaccinated. The overall adjusted VE against any influenza subtype for the 6 seasons combined was 22% (95% CI, 18%-25%) with variation by influenza subtype and season, and increased to 40% (95% CI, 36%-43%) after correcting for misclassification of vaccination status. Compared to a common reference group that was not vaccinated in any season, in most situations VE seemed to be higher for patients vaccinated in the current season than for those vaccinated only in previous seasons. When stratifying by previous vaccination history, VE against all subtypes appeared to decrease with increasing numbers of previous vaccines received.

Conclusions and implications for vaccinology: Although VE appeared to decrease in relation to the number of previous vaccines received, VE was consistently higher among patients vaccinated in the current season and remained significant against all subtypes except A(H1N1) even with as many as 5 previous vaccines received.

High-dose influenza vaccine program evaluation in Manitoba

Hossack I, Wei J, Navitka K, Baydack R, Hilderman T, Kurbis C

Introduction/Program need and objectives: Influenza A (H3N2) causes severe illness and complications, particularly among seniors. The National Advisory Committee on Immunization's 2017/18 influenza statement reported that the high-dose influenza vaccine should provide superior protection compared to the standard-dose vaccine. For the 2017/18 season, Manitoba Health, Seniors and Active Living (MHSAL) introduced the high-dose influenza vaccine to long-term care facility (LTCF) residents aged 65 years and older, with the objectives of:

1. reducing the morbidity and mortality associated with influenza in this vulnerable population
2. maintaining or increasing vaccine acceptance

Program methods and activities: MHSAL lead the program evaluation with participation from the regional health authorities and long-term facility staff, to:

1. assess high-dose influenza vaccine acceptability among LTCF staff and residents
2. examine the morbidty and mortality in LTCFs among residents aged 65 years and older
3. gain feedback on the overall launch of offering a senior-specific influenza vaccine in LTCFs

An open-ended survey was administered to 125 LTCFs in Manitoba on March 9, 2018. Additionally, MHSAL extracted and analyzed data from five provincial databases/registeries from May 4 to June 14, 2018, including:

1. the Communicable Disease Control Surveillance System
2. the provincial Personal Care Home Registry
3. the provincial Outbreak Tracking database
4. the Immunization Registry module of Panorama
5. the Adverse Events Following Immunization module of Panorama.

Program results or outcomes (including evaluation): When analyzing the 2017/18 season compared to the 2014/15 season (which saw the same strain, disease peak and severity), the results demonstrate that among LTCF residents aged 65 years and older, there were:

1. fewer outbreaks of influenza A
2. fewer confirmed cases of influenza
3. a statistically significant decrease in influenza attack rate
4. fewer all-cause deaths
5. constant vaccine uptake
6. no vaccine safety signals

Implications for practice or policy: Publicly-fund the high-dose influenze vaccine for residents of LTCFs aged 65 and older in Manitoba while continuing to evaluate the safety and effectiveness of offering a senior-specific influeunza vaccine to residents of LTCFs.

Examining the knowledge, attitudes and experiences of Canadian seniors towards influenza (the EXACT survey)

Andrew M, Gilca V, Waite N, Pereira J

Introduction/Background: Although the majority of individuals with influenza will recover within 10 days, older adults are at high risk for related complications, leading to worsening frailty and function. We surveyed older Canadians to determine how influenza knowledge influences vaccination decision-making, and explore the impact of influenza.

Methods: We disseminated an online survey through a national polling panel, including questions about the respondents' vaccination status and knowledge about influenza. Respondents were asked whether during the 2016/17 influenza season, they were diagnosed with influenza, or experienced an undiagnosed influenza-like illness (ILI) consisting of sore throat, fever, runny nose and cough. Using validated measures, they reported frailty and functional status prior to the influenza season, during illness (if applicable), and following the season. Regression analyses were used to examine predictors of poor functional outcomes.

Results and Analysis: Between March and April 2017, completed surveys were collected from 5,014 people 65 years and older, with representation from all Canadian provinces: mean age was 71.3 ± 5.17 years (range = 65-96), 50% were male, 42.6% had one or more chronic conditions, and 9.6% considered themselves vulnerable or frail. 67.9% reported receiving last season's influenza vaccine. Those who rarely/never receive the influenza vaccine were significantly less likely to correctly answer questions about influenza's impact than those who receive the vaccine more consistently. Of the 1035 (21.5%) who reported experiencing influenza or ILI last season, one-fifth had health and function declines during this time, 40% indicated a recovery longer than two weeks and 3.1% "never fully recovered". Older age, memory loss, and having influenza/ILI were among the independent predictors of persistent declines in health and function.

Conclusions and implications for vaccinology: Given that frailty and function are important considerations for older adults' well-being and independence, healthcare decision-makers must understand the potential for significant temporary and long-term impacts of influenza to make informed vaccine-related policies and recommendations.

Determinants of uptake and adherence to seasonal influenza vaccination among the elderly North Americans: A systematic review and meta-analysis

Okoli G, Gieni R, Neilson C, Chit A, Thommes E, Abou-Setta A, Mahmud S

Introduction/Background: Understanding determinants of uptake/adherence to seasonal influenza vaccination (SIV) and their complex interactions are essential for designing effective interventions and optimization of vaccination programs, and public health decision-making.

Methods: We undertook a systematic review following the Cochrane Handbook for Systematic Reviews of Interventions guidelines. We searched MEDLINE, Embase, CINAHL, Scopus, and relevant websites for population-based clinical trials or observational studies conducted from 2000-2017 in the USA/Canada, and published in English. We considered only populations comprising average-risk, community-based elderly (≥65 years old) individuals. Outcome of interest was determinant of uptake and/or adherence to SIV. Two reviewers independently screened the citations against the eligibility criteria using a two-stage sifting approach. One reviewer extracted data from the included studies and a second reviewer checked the extracted data for errors. Two reviewers independently assessed study quality using the National Institute of Health quality assessment tool for observational cohort and cross-sectional studies. We synthesized study results using inverse variance, or narratively where there was marked heterogeneity between the included studies.

Results and Analysis: Five moderate to high quality, cross-sectional studies (over 13 million participants) met our eligibility criteria. These studies, all conducted in the USA, focused on only SIV uptake. Being older (Odds

ratio (OR) 1.01, 95%CI 1.00 to 1.03), white (OR 1.37, 95%CI 1.09 to 1.75), married, and having a college or higher education, higher annual income (OR 1.06, 95%CI 1.04 to 1.09), a comorbidity and/or disability, healthcare coverage (OR 1.59, 95%CI 1.15 to 2.17) and a regular doctor were found to be determinants of uptake. We found no studies on adherence to SIV that met our inclusion criteria.

Conclusions and implications for vaccinology: Limited evidence indicates some socio-economic and health-related determinants of uptake of SIV in elderly Americans. Further evidence is needed to provide a more conclusive evidence base.

Protocol registration number: PROSPERO – CRD42018086803

An overview of the Canadian Armed Forces Immunization Program

Lamontagne M, Barnes K, **Tepper M**

Introduction/Program need and objectives: Canadian Forces Health Services (CFHS) provides health care, including immunizations, to Canadian Armed Forces (CAF) personnel across Canada and overseas whenever required, independently of the Provincial/Territorial (P/T) Health Care Plans. Historically and currently, the immunization program (IP) has been considered a key component in enhancing the success of CAF operations at home and abroad.

Program methods and activities: Generally, the CFHS IP follows the Canadian Immunization Guide (CIG). All CAF members are recommended to be up-to-date for routine adult vaccines, including vaccines that are not publicly funded in P/T IP for healthy adults (hepatitis A; hepatitis B; acellular pertussis; human papilloma virus; and varicella). Updating of vaccination status is started during recruit training, completed during the next posting, reviewed before all deployments and during periodic health assessments. Certain travel-specific vaccines are recommended when indicated. On occasion, vaccines not currently licensed in Canada may be recommended for a specific deployment. An important part of the IP is an Immunization Competency Training Program (ICTP) which includes an academic and a clinical skills portion before "certification" as a Primary Immunizer (PI) is granted.

Program results or outcomes (including evaluation): Immunizations are recorded in an electronic database accessible by CFHS clinics throughout Canada. Adverse Events Following Immunization are reported centrally and then to PHAC. The CFHS designates and oversees 20 Yellow Fever Vaccination Clinics. Outside of influenza, very few vaccine-preventable diseases are reported in the CAF.

Implications for practice or policy: The CAF has a robust IP which largely exceeds that provided by publicly funded civilian programs. The use of deployment-specific vaccines is based on risk assessment; the CFHS tends to have a lower threshold for vaccine use than in the civilian sector. All vaccines are voluntary and are at no cost to the CAF member.

Impact of the addition of new vaccines in the early childhood schedule on vaccine coverage by 24 months of age from 2006-2016, Quebec, Canada

Kiely M, Boulianne N, Talbot D, Ouakki M, Guay M, Landry M, Zafack J, Sauvageau C, DeSerres G

Introduction/Background: Between 2004 and 2016 in the province of Quebec (Canada), 4 new antigens were added in the early childhood vaccine schedule from birth to 18 months, increasing the number of injections or doses needed from 7 to 12. These additions may have decreased the proportion of children who had received all recommended vaccines.

The objectives of this study were to assess the impact of the introduction of new vaccines to the childhood schedule on the 24-month vaccine coverage from 2006 to 2016 and identify factors associated with incomplete vaccination status by 24 months of age.

Methods: We used the data from six cross-sectional vaccine coverage surveys conducted every two years which included a total of 3515 children aged 2 years old and randomly selected from the Quebec public health insurance database. Factors associated with an incomplete vaccine status by 24 months were identified with multivariable logistic regression.

Results and Analysis: Despite the addition of 4 new vaccine antigens since 2004, the vaccine coverage remained high from 2006 (82.4%) through 2016 (88.3%) for vaccines present in the schedule since 2006. In 2016, vaccine coverage was 78.2% for all vaccines included in the schedule. The vaccine coverage of new vaccines increases rapidly within 2 years of their introduction. For both new and older vaccines, incomplete vaccine status by 24 months of age is associated with a delay of 30 days or more in receiving the vaccines scheduled at 2 and 12 months of age.

Conclusions and implications for vaccinology: Increasing to 12 the number of doses in the recommended schedule has slightly reduced the vaccine coverage by 24 months of age and the vaccine coverage of vaccines already in the schedule remained stable over the years. Future additions to the vaccine schedule may not be similarly accepted by the population and this will required continuing the monitoring of vaccine coverage.

Impact of vaccine delays at the 2, 4, 6 and 12 month visits on incomplete vaccine status by 24 months of age in Quebec, Canada

Kiely M, Boulianne N, Talbot D, Ouakki M, Guay M, Landry M, Sauvageau C

Introduction/Background: Timeliness in the administration of recommended vaccines is often evaluated using vaccine delays and provides more information regarding the susceptibility of children to vaccine-preventable diseases compared with vaccine coverage. The importance of on-time administration of vaccines scheduled at the first visit is well documented, but data are scarce about the impact of vaccine delays at other visits on vaccine coverage by 24 months of age.

Using vaccine delays for the first three doses of DTaP-containing vaccines and for the first dose of measles-containing vaccines as markers of timeliness at the 2, 4, 6 and 12 month visits, we estimated the proportion of incomplete vaccine status by 24 months of age attributable to a vaccine delay at each of these visits.

Methods: We used the data from six cross-sectional postal surveys realised in the Province of Quebec from 2006 to 2016 which included 7196 children randomly selected from the universal health insurance database. A vaccine dose was considered delayed if received 30 days or more after the recommended age. The impact of new vaccine delay at each visit on incomplete vaccination status by 24 months of age was estimated with the attributable risk in the population.

Results and Analysis: The proportion of children with vaccine delay was 5.4% at 2 months, 13.3% at 4 months, 23.1% at 6 months and 23.6% at 12 months. Overall, 73% of all 2-year-old children with an incomplete status by 24 months were associated to a vaccine delay of which 16% were associated to a vaccine delay that first occurred at 2 months, 11% at 4 months, 14% at 6 months and 32% at 12 months.

Conclusions and implications for vaccinology: While great emphasis has been put on vaccine delay at the first vaccination visit, we observed that the prevalence of vaccine delay was greater with later visits and that most children with an incomplete vaccine status by 24 months had a vaccine delay occurring during these later visits. Interventions to improve timeliness should address vaccine delays at each visit and not focus on the first visit.

Vaccine manufactures' potential liability in negligence for overstating product risks

Faour D, Hadskis M

Introduction/Background: In Canada, pharmaceutical manufacturers owe a duty under negligence law to provide "full and current information" about risks inherent in their products. This duty is intended to correct the knowledge imbalance between manufacturers and pharmaceutical consumers by forewarning these consumers

of potential dangers so that they can make informed choices. Cases dealing with this duty have involved circumstances where consumers were harmed by undisclosed risks.

However, a unique problem has recently been identified in studies finding that monograph warnings published by some vaccine manufacturers do not reflect fresher evidence indicating that their products may pose less risk, and that this risk overstatement can distort consumers' and healthcare professionals' beliefs about vaccine safety. This situation raises the issue of whether such monographs could expose vaccine manufacturers to liability if consumers, who may have benefited from a vaccine, ultimately do not receive it because of risk overstatement.

Methods: Jurisprudence from Canada and other common law countries was reviewed to determine whether pharmaceutical manufactures' disclosure duties under negligence law encompass an ongoing obligation to communicate up-to-date evidence supporting a lower risk profile.

Results and Analysis: No cases directly address whether pharmaceutical manufacturers can be held liable for not ensuring that their monograph warnings portray new evidence indicating a lower risk profile. However, it is reasonably possible that the leading Canadian jurisprudence on negligent warning may be broadly interpreted by a future court in a manner which supports the existence of a duty to disclosure this type of information.

Conclusions and implications for vaccinology: A legal duty to not overstate vaccine risks would be consistent with the goal of protecting patients' right to be properly positioned to make informed vaccine choices. The threat of potential liability for breaching this duty may enhance the achievement of this goal by encouraging manufacturers to adequately communicate evidence of downgraded risk profiles on an ongoing basis.

Exploring the effect of risk and benefit information on the intention to vaccinate: A survey-based study

Mostafapour M, **Meyer S**, Scholer A

Introduction/Background: In the era where people are bombarded with misinformation about vaccination, it is critical to investigate the degree to which and how various types of information affects perceptions of vaccines and intention to vaccinate. However, there is little work that quantitatively investigates the degree to which various information affect's people perception of the vaccines. This work investigates the degree to which information regarding risks and benefits affect individuals' vaccination decisions.

Methods: 400 survey respondents were recruited through Amazon Mechanical Turk. At the onset, respondents received general information about a fictitious disease and related vaccine (designed to be similar to Miseales and the MMR vaccine). Respondents wer e then assigned to four different controled scenarios where they were offered information regarding the high or low risk of the vaccine, or the high or low benefit of the vaccine. Respondents perceieved risks and benefits of the vaccine and their intention to vaccine were measured before and after receiving the new information to idetnify the degree to which the new piece of information affected their evaluation of the vaccine.

Results and Analysis: This work is one of the first studies that quantitatively identifies the degree to which risks and benefits information affect vaccination decisions. We found that information conveying the low risk or high benefit of the vaccine carried similar outcomes in the degree to which they increase intention to vaccinate. Providing people with information implying the low benefit of a vaccine was found to significantly decrease intention to vaccinate. Exposure to information implying that a vaccine may be high risk has detrimental effects on the intention to vaccinate.

Conclusions and implications for vaccinology: In order to increase the uptake of vaccines, it is crucial to clearly communicate the benefits and the safety of the vaccines to the audience and to regulate the dissemination of misinformation about the risks of the vaccines.

Vaccine hesitancy around the globe: Analysis of three years of WHO/UNICEF Joint Reporting Form data 2015-2017

Lane S, MacDonald N, Marti M, Dumolard L

Introduction/Background: In order to gather a global picture of vaccine hesitancy and whether/how it is changing, an analysis was undertaken to review three years of data available as of june 2017 from the WHO/UNICEF Joint Reporting Form (JRF) to determine the reported rate of vaccine hesitancy across the globe, the cited reasons for hesitancy, if these varied by country income level and/or by WHO region and whether these reasons were based upon an aassessment.

Methods: The reported reasons from three years of WHO/UNICEF Joint Report Form (JRF) data were classified using the Strategic Advisory Group of Experts on Immunizations matrix of hesitancy determinants.

Results and Analysis: Hesitancy was reported by >90% of countries. The list of cited reasons covered 22 of 23 WHO determinants matrix categories. The reasons varied by country income level, by WHO region and over time and within a country. However, the rigour of the cited reasons could be improved as only just over 1/3 countries reported that their reasons were assessment based, the rest were opinion based. With respect to any assessment done in the previous five years, upper middle income countries were the least likely to have done an assessment.

Conclusions and implications for vaccinology: These analyses provided some of the evidence for the 2017 Assessment Report of the Global Vaccine Action Plan recommendation that each country develop a strategy to increase acceptance and demand for vaccination, which should include ongoing community engagement and trust-building, active hesitancy prevention, regular assessment of vaccine concerns, and crisis response planning. The results of this project will contribute to the understanding of vaccine hesitancy throughout the world and to the development of strategies to reduce vaccine hesitancy.

Implementation of an immunization assessment tool (IAT) for adults in Prince Edward Island (PEI): A public health nursing (PHN) perspective

Halperin D, DiCastri A, Bentley E, Rowswell C, Phillips K, Morrison H, Halperin S

Introduction/Background: In 2015, the PEI Department of Health and Wellness began an initiative to improve suboptimal adult immunization rates that included the implementation of the IAT. We assessed knowledge, attitudes, beliefs, and behaviors of PHNs towards adult immunization, readiness to address vaccine hesitancy, and experiences with administering the IAT.

Methods: A paper-based survey was developed, assessed for content validity and test-retest reliability, and administered to PHNs prior to IAT implementation. Attitudes and beliefs were assessed using a 5-point Likert scale. Focus groups explored experiences in administering the IAT. Data were examined using thematic analysis.

Results/Analysis: Of the 39 respondents, 92.3% had ≥11 years in practice. In total, 97.4% agreed that vaccine preventable diseases pose a risk for adults and that vaccines are effective and safe. Only 12.8% did not have enough scientific knowledge to recommend vaccines to adults. With respect to adult immunization guidelines, 12.8% were unaware of the Canadian guidelines, 30.8% agreed, or neither agreed nor disagreed (33.3%), that the Canadian guidelines are confusing; 51.3% agreed that it was difficult to keep up with current guidelines, and 48.7% disagreed that the guidelines were promoted adequately. Most (76.9%) respondents indicated that vaccine hesitancy was a problem for the public, citing concerns about vaccine necessity and the role of the pharmaceutical industry. PHNs indicated a need for information on national adult immunization targets, techniques for addressing vaccine hesitancy, provincial adult immunization schedule, and strategies for increasing vaccine coverage. Facilitators and barriers to implementing the IAT identified in focus groups included identification of under immunized clients, awareness of the importance of adult vaccination, workload issues, ability to immunize "on-the-spot", and self-administered usability of the tool.

Conclusion/Implications for Vaccinology: Tools such as the IAT can help address knowledge gaps in adult immunization and assist in improving coverage rates. Contextual challenges of incorporating this tool into practice must be considered.

Knowledge, attitudes, beliefs and behaviours regarding adult immunization in Prince Edward Island (PEI)

DiCastri A, **Halperin D**, Bentley E, Rowswell C, Phillips K, Morrison H, Halperin S

Introduction/Background: Despite an increasing number of vaccines recommended for adults, vaccine coverage is suboptimal. The PEI Department of Health and Wellness developed an Immunization Assessment Tool (IAT) for adults to identify gaps in an individuals' vaccination status. We undertook a survey of PEI adults to assess their knowledge, attitudes, beliefs, and behaviors related to their immunization status and their willingness to update their vaccinations.

Methods: A paper-based survey was developed, assessed for content validity and test-retest reliability, and administered to adults attending public health administered influenza clinics during the 2017-2018 influenza season. Attitudes and beliefs were assessed using a 5-point Likert scale.

Results and Analysis: In total, 990 surveys were available for analysis (65% females). Respondents were well-distributed between 25-75 years of age; ages 18-24 years and >75 years were underrepresented. Of the respondents, 61% were aware that PEI had recommendations for adult immunization, 47% reported that a healthcare provider had informed them about recommended vaccines, and 33% reported they were aware which vaccines were recommended. The most common source for vaccine information was family physicians (46%), although most (63%) received their immunizations through public health. Knowledge was low about specific vaccine recommendations and which health conditions increase the risk of vaccine-preventable diseases. Vaccine coverage was low; only tetanus-diphtheria vaccine exceeded 50%. Most respondents expressed pro-vaccination attitudes; over 90% agreed that vaccination was important to them and that getting vaccinated helps to protect people they care for; 87% trusted scientific evidence about vaccination, and 89% thought that vaccine benefits outweighed the risks. In contrast, 18% of respondents were uncertain about whether or not to get vaccinated.

Conclusions and implications for vaccinology: Knowledge about adult vaccine recommendations was low, and was associated with low vaccine coverage. Respondents had favorable attitudes and beliefs about vaccination, although a sizeable minority remain vaccine hesitant. Strategies such as the IAT may enhance adult vaccination rates.

Viral hepatitis B immunization among newcomers to Ontario, Canada

Yasseen A, Kwong J, MacDonald L, Feld J, Crowcroft N

Introduction/Background: Hepatitis B virus is among the most burdensome infectious diseases in Ontario, Canada and disproportionately represented among immigrants. There is a paucity of information on HBV immunity among immigrant groups and we present estimates from a cohort created by linking Public Health Ontario laboratory data to health administrative records.

Methods: We used linked laboratory and imigration data for individuals undergoing confirmatory HBV testing at Public Health Ontario (PHO) laboratories in Ontario, Canada (1997-2014). Immigration status and country of origin was collected by Immigration, Refugee, and Citizenship Canada (IRCC) and categorized into the five major world regions, as well as HBV endemic (>3% HBV prevalence) countires. Immunization status was determined using HBsAg, HBsAb, and HBcAb serology results and categorized into natural, vaccine, and ambigous immunity.

Results and Analysis: A total of 1,141,119 individuals were included in the cohort, and groupd into four categories: 575,927 (50.5%) Not immune, 239,528 (21.0%) with vaccine induced immunity, 100,302 (8.8%) with Infection induced immunity, and 225,362 (19.8%) that were Immune but unknown. Of these there were 199,791 (17.5%) immigrants: 50,290 (25.2%) from Africa and the middle east, 89,669 (44.9%) from Asia and Pacific, 23,536 (11.8%) from Europe and the UK, 32,645 (16.3%) from South and Central Americas, and 3,651 (1.8%) from the US; and 81,309 (40.7%) were from HBV endemic countries. Overall 17.0% and 22.5% of immigrants had vaccine and infection induced immunity, respecitvly. This is compared to 21.8% and 5.9% vaccine and infection

induced immunity observed among long term residents, respecivly. Those emigrating from HBV endemic countries had the lowest proportion of vaccine induced immunity and the highest proportion of infection induced immunity (13.8% and 39.4%, respectivly).

Conclusions and implications for vaccinology: We present much needed information on HBV immunity among immigrant groups in Ontario. This is useful knowledge for the development and implementation of immunization programs.

Immunization: A fundamental first service for newly arrived refugees

Beckermann K, Liddy A, **Mathur A**

Introduction/Program need and objectives: Refugees arriving in Toronto are dealing with multiple settlement issues simultaneously (e.g. housing, employment, and language). Immunization is an essential early public health measure to provide basic protection against vaccine preventable diseases. Many refugees are partially immunized but lack documentation. Providing vaccines required for school in Ontario supports transition to school and prevents potential outbreaks.

Program methods and activities: Beginning with the Syrian migration in 2015/16, Toronto Public Health (TPH) developed a response approach to meet the growing need among newcomers. TPH partnered with settlement agencies to provide vaccines at interim lodging hotels. We established processes for logistics, including frequency, pre-screening and documentation. Each site was visited prior to clinic day to confirm space requirements, establish language needs and obtain client details to ensure safe clinic operations. The approach was implemented and adapted to provide ongoing support and programming when newcomer clinics are required.

Program results or outcomes (including evaluation): In winter 2016 TPH provided 4,324 vaccines to 1,856 Syrian clients at 14 clinics at 5 sites.

Toronto continued to operate interim housing sites as refugees arrived from many countries and overwhelmed the shelter system. Using the tested processes to provide short-term immunization services in temporary housing locations to newcomers, in 2017, TPH provided 1,838 vaccines to refugees from multiple countries at 11 clinics at 3 sites. Clinics have been adapted to meet the need, e.g. flu only in fall, school vaccines for children year round, and outbreak response as needed.

Implications for practice or policy: Re fugees are vulnerable when arriving in a new country and meeting their immunization needs is an important first step for their wellbeing. Building on our initial processes we developed an approach to address this on-going need, while continuing to deliver services to the Toronto population. Flexible, scalable models will make it easier for everybody to meet this need while delivering core programming.

HPV knowledge, attitudes and beliefs: newcomer perspectives on the HPV vaccine

Wilson L, Rubens-Augustson T, Paradis M, Murphy M, Day P, Rahman S, Evans B, Hui C, Pottie K, Jardine C, Crowcroft N, Wilson K

Introduction/Background: Human Papillomavirus (HPV) is the most common sexually transmitted infection in Canada. Despite the effectiveness and availability of a vaccine against HPV, uptake of HPV vaccination is generally quite low in Canada. One group for whom it is particularly difficult to ascertain HPV vaccination uptake is newcomers to Canada. Previous research suggests that newcomers face numerous barriers to HPV vaccination, including inadequate information. We sought to explore newcomers' knowledge, attitudes, and beliefs about HPV vaccination.

Methods: Informed by a systematic review focusing on newcomer-identified barriers to vaccination uptake, we are conducting surveys and semi-structured interviews with newcomer parents and youth aged 16-27. Participants are being recruited from local community health centres and vaccine clinics in Ottawa, Canada.

Eligible participants are English-, French-, or Arabic-speaking, capable of providing informed consent, and were born outside of Canada.

Results and Analysis: To date, 18 participants have been recruited and have completed the survey (14 adults, 4 youth). Preliminary results suggest that most participants (72%) have never heard of HPV or the HPV vaccine. Most parents indicated that they had or believed they would have their children vaccinated against HPV (58%), even though many had never heard of the vaccine. Among participants who had not decided whether to have their child vaccinated (n=6), two-thirds (67%) indicated that they would do so if a doctor recommended it.

Conclusions and implications for vaccinology: There is a need for greater access to appropriate, accessible HPV-related information for newcomers. Healthcare providers should ensure that they actively recommend HPV vaccination to eligible individuals, given the widespread reporting from undecided individuals that a provider recommendation would make them more likely to have their children vaccinated. The results of this study will be used to inform the development of a digital HPV education tool for newcomers within the CANImmunize platform. Study ongoing.

Exploration of HPV vaccine coverage, series commencement and completion among grade 9 girls in Vancouver Coastal Health (VCH), British Columbia

Hu Y, Chu T, Forsting S, Dawar M

Introduction/Program need and objectives: HPV vaccine acceptance remains the lowest of all immunization programs. VCH intends to increase HPV uptake by identifying areas with low coverage and programmatic factors impacting series completion.

Program methods and activities: HPV vaccine is offered to female students in grades 6 and 9. Series completion is also offered to grade 7 and 10 students with active consent from prior grade. Thus VCH students have two formal opportunities to initiate series and up to five to complete series. Information on school registration and HPV immunization history was extracted from the Primary Access Regional Information System for girls who enrolled in grade 9 during 2016/17 academic year. Rates of zero dose, partial immunization, full protection and series commencement and completion time were analyzed using Stata 14. In order to assess the impact of grade 10 series completion, HPV vaccine coverage for this cohort will be analyzed in the summer of 2018.

Program results or outcomes (including evaluation): Among 4810 grade 9 students, 76% were fully immunized, 10% were partially immunized and 14% were unimmunized. Of those fully immunized, 87% completed series before grade 9, 8% started and completed series in grade 9 and the rest 5% started series prior to but completed in grade 9. Of the partially immunized, 89% started series in grade 9. Among unimmunized students, 42% had dissented to HPV vaccine and 18% indicated a deferral, with a total of 274 students who had no active dissent or deferral in the records. Reaching these students who are potentially 'open' to considering HPV vaccine and those partially immunized will help VCH meet the national HPV vaccination target.

Implications for practice or policy: The analysis provides actionable information to support the development of a VCH HPV immunization strategy and has wider implications for other jurisdictions.

Last call for HPV vaccine in Toronto: Sending a reminder letter to Grade 12 females to improve HPV vaccination rates

Beckermann K, Huang S, Kadri O, Mathur A, Dubey V

Introduction/Program need and objectives: Despite being publicly funded, Human Papillomavirus (HPV) vaccine coverage rates are low compared to other funded vaccines. In Ontario, HPV vaccine is funded in grade 7 until August 31st in the year a student finishes high school. This provides ample time to access the vaccine, particularly if a parent or student changes their mind about vaccination. A reminder-recall letter was sent to

grade 12 females who were not up-to-date with HPV vaccination to provide one final opportunity to receive publicly funded vaccine.

Program methods and activities: Toronto Public Health (TPH) completed a direct mail in December 2017, to grade 12 girls in the 2017-18 school year who had not completed their HPV vaccine series, inviting them to attend a community clinic. HPV vaccine doses given by TPH at community clinics from January to May 2018 were compared to the same period in 2017. HPV coverage for grade 12 females in December was compared to June.

Program results or outcomes (including evaluation): As of December 2017, 4,806 of grade 12 females (N=13,057) were not up-to-date with their HPV vaccinations. In 2017, TPH offered 29 clinics from January to May 2017, where 2,445 doses of HPV vaccine were given compared to 43 clinics in 2018 where 3,947 doses were given for the same period. Average doses of HPV vaccine provided per clinic in 2017 was 84 compared to 92 in 2018. Coverage increased from 66.7% in December to 69.4% in June 2018. Further increase in coverage is likely as grade 12 females who started the series complete it by August 2018.

Implications for practice or policy: A reminder letter sent to unvaccinated grade 12 females to encourage HPV vaccination was a simple and effective strategy to increase coverage and attendance at public health clinics. Incorporating this practice ongoing may be effective to improve HPV vaccination rates.

Addressing vaccine hesitancy: Identifying gaps in knowledge and skills among frontline vaccine preventable diseases (VPD) program staff

Kaashoek J, Barati S, **Beckermann K**, Dubey V, Shen S

Introduction/Program need and objectives: Toronto Public Health (TPH) is incorporating strategies to address vaccine hesitancy in all vaccine programs and services provided by the health unit. To equip front line VPD clerical and nursing staff to have the tools to properly respond to vaccine hesitency, we used a two-step process: a) Identifying desired staff competencies (knowledge, skill, and attitude) and b) finding gaps between staff identified knowledge and skills and expected competencies.

Program methods and activities: To develop staff competencies we completed a literature review and undertook a validation process with management. To compare expected competencies with current practice, focus groups were held with three groups of VPD program staff: support assistants, registered practical nurses working in clinics, and registered practical nurses providing telephone support to the public and health–care providers. Standardized questions were asked at each focus group session, with respondents' answers taped, transcribed, analyzed, and themed.

Program results or outcomes (including evaluation): A framework of staff competencies was developed. Knowledge competencies include knowing how cultural beliefs may contribute to vaccine hesistancy, skill competencies include being able to assess the level and type of information a client wants and to adapt to this, and attitudinal ones include understanding personal assumptions and how to suspend judgement before acting. Preliminary focus group results identified the need to improve knowledge and skills pertaining to working with vaccine hesitant clients, including ways to confidently and appropriately address client concerns in a short interaction and how to close a conversation respectfully.

Implications for practice or policy: An action plan to develop and implement staff competencies for staff working in local public health to address vaccine hesitancy is an important step to increase vaccine confidence.

Immunization resources: Are they meeting the practical needs of immunization program managers?

Sondagar C

Introduction/Background: A significant body of multifaceted research and resources are being developed to better understand the underlying causes of, and interventions for achieving optimal vaccine acceptance and uptake (VAU). To assess the number of resources that are available to support and inform immunization

program/promotional managers (IPM) towards improving VAU, the Canadian Public Health Association conducted an environmental scan for resources relevant to the Canadian context. Findings from the scan identified a number of information and resource gaps, bringing attention to areas where further research and development is needed. Results of the environmental scan will additionally be used to guide the development of the 'Canadian Vaccination Evidence Resource and Exchange Centre' (CANVax), a national bilingual online immunization resource centre that aims to offer access to the latest evidence-based products, resources and tools to support VAU in Canada.

Methods: An environmental scan of grey literature using the search engine Google and a search of known Canadian and international websites were conducted to identify resources relevant to the Canadian context. The search strategy combined relevant immunization topics and key word searches focused on VAU. Search results were collected and summarized for review based on set inclusion and exclusion criteria.

Results and Analysis: A total of 793 resources were identified with 553 resources meeting inclusion criteria. Review of resources highlighted a number of gaps and areas where further resource development is needed. Major areas included strategies and tools to support and operationalize evidence to action, evaluations for VAU interventions and campaign and engagement strategies, especially for working with specific populations.

Conclusions and implications for vaccinology: Despite the wealth of resources that are available, not all are relevant or meet the practical needs of IPM. Findings from the environmental scan bring attention to information and resource gaps where further focus and development are needed to support IPM in facing the growing challenges to improving VAU.

A dynamic web-based visualization of herd immunity

Hakim H, Parent E, Roberge J, Dubé E, Paquette J, Sander B, Tremblay-Breault M, Reinharz D, Witteman H

Introduction/Background: 'Herd immunity' or 'community immunity' refers to the reduced risk of infection among susceptible individuals in a population through the presence and proximity of immune individuals. Recent studies suggest that improving understanding of community immunity may increase laypeople's intentions to be vaccinated.

Methods: Our multidisciplinary team developed a dynamic visualization (a short web-based animation) about community immunity based on epidemiological evidence. We used pertussis, measles and influenza as test cases such that the visualization may be adjusted for different vaccine-preventable diseases. The visualization shows how different parameters (e.g., vaccine coverage, intra-community contact) influence community immunity. We tested iterative versions of our visualization in a human-computer interaction laboratory and in an informal setting (a cafeteria) with a total of 19 participants, a standard sample size for this type of digital media study.

Results and Analysis: Participants responded positively to most aspects of the visualization; for example, the use of colour to signal vulnerability, infection and vaccination. Participants understood a yellow background indicating vulnerable people and a thick blue band representing herd immunity. Participants understood how community immunity safeguards vulnerable people when sufficient people around them are vaccinated, and how lower vaccine coverage puts communities and the people within them at risk. However, some aspects of the visualization require improvement in future versions; for example, the visualization does not yet help participants to understand the role of vaccine effectiveness in community immunity.

Conclusions and implications for vaccinology: Better understanding of community immunity and its impact on others may help in improving vaccine acceptance and uptake. Our visualization helped people understand the concept of community immunity. We are currently refining the visualization to test a third version. The final version will be evaluated for its effects on risk perception, knowledge, and vaccination intentions in a randomized controlled trial.

Evaluation of an online immunization communication course

Chilton K, Cranch J, Taylor C, Professional Education Working Group, Subgroup of the BC Immunization Committee

Introduction/Program need and objectives: Midwives in British Columbia (BC) were involved at any point of maternal and/or newborn care in 22.4% of all deliveries in 2015/2016. As midwives are the first point of contact for many new families, they have the opportunity to have timely immunization conversations and as a result, the online Immunization Communication Course started with Midwives being the target audience. The course was jointly developed by the BC Centre for Disease Control, a representative from the Midwives Association of BC, and a cohort of University of British Columbia nursing students. The course was opened in 2014 to all interested healthcare providers. This course highlights the importance of effective immunization communication and helps to improve knowledge, ability and confidence of healthcare providers in having effective immunization conversations with clients and families.

Program methods and activities: An online survey was developed through FluidSurveys© to determine whether the course met the needs of users. The survey, posted from December 2014 to December 2015, also sought feedback as to how the course could be improved.

Program results or outcomes (including evaluation): During the survey period, the course was completed by 141 participants, 58 of which responded to the survey, resulting in a response rate of 41.1%. All of the respondents agreed the content addressed the course learning objectives and 84.4% of respondents stated that they felt more confident in their ability to engage clients in immunization conversations. Feedback from the survey also helped to inform updates to the course content.

Implications for practice or policy: As vaccine hesitancy continues to be a global concern, having healthcare providers (whether they immunize or not) feel comfortable to engage in immunization conversations, while providing clear and consistent recommendations is vital. Partnership and collaboration with a specific healthcare group in BC was beneficial in the development of this course to ensure the approaches would be relevant to their work with clients and families.

Integrating vaccine coverage data and marketing analytics to create local profiles of individuals who may be less likely to be vaccinated

Reidt T, Craig C

Introduction/Program need and objectives: York Region Public Health serves over 1.2 million residents from nine demographically diverse municipalities that are both rural and urban. Our objective was to leverage available data sources to develop a better understanding of the specific demographic characteristics of York Region residents from areas with lower vaccine uptake to inform future targeted immunization health promotion campaigns.

Program methods and activities: We used student-level immunization record data from the provincial immunization database to assign individual immunization status based on an administered dose count for Human Papilloma Virus (HPV) and Meningococcal disease among 12 year olds and Measles Mumps and Rubella (MMR) among 7 year olds. We then used immunization status to estimate immunization coverage rates for small geographic areas in York Region. Marketing data from a third party provider provided insight into the values, priorities, habits and communication preferences of each small neighborhood area in York Region, categorized into archetypes or "profiles." We integrated this third party geographic information with our immunization coverage results to identify pre-defined profiles for individuals living in areas with low vaccine coverage. Using these profiles, we developed York Region-specific characteristics of residents who may be less likely to vaccinate their children.

Program results or outcomes (including evaluation): Pairing surveillance data with marketing analytics may help us create more impactful targeted communication campaigns that may inspire changes in attitudes towards vaccination and may contribute to increased vaccination rates in these communities.

Implications for practice or policy: The next steps include: combining information from the marketing analytics product with a literature review to create messaging, tactics or strategies that resonate with the identified York Region-specific profiles; collaborating with members of these communities to evaluate messages/tactics/strategies; and leveraging marketing tactics and demographic data alongside census data to guide dissemination of a targeted communications campaign.

These methods may apply to other public health areas developing targeted approaches that resonate with intended audiences.

A scoping review: Understanding the Canadian dialogue on vaccine-injury compensation

Hapuhennedige S, Nisbet C, Gardner C, Lee C

Introduction/Background: Serious adverse events following immunization (AEFIs) are rare experiences that can lead to long-term disability. These dramatic events have influenced discussions regarding compensation, where 19 jurisdictions worldwide have now implemented a vaccine-injury compensation (VIC) program, including Quebec. The unavailability of VIC in other provinces/territories has raised concern. The main objective of this research was to explore the Canadian dialogue on VIC and understand why it remains intangible in other provinces/territories.

Methods: This study involved a search of three databases (Medline, CINAHL, JSTOR). Using purposive sampling, nationally-recognized subject-matter experts (SMEs) were interviewed (N = 11) to learn more about immunization priorities in Canada. Grey literature from three sources were included: Custom Search for Canadian Government Documents, Canadian Newsstream (ProQuest), and social media.

Results and Analysis: There has been minimal academic discussion on the topic of VIC in Canada. SMEs contextualized this finding by revealing current immunization priorities (e.g. vaccine hesitancy), therein suggesting the lack of a policy window at present. However, review of the grey literature revealed numerous news articles, blog posts and reports that have discussed VIC in more recent years; this dialogue indicates enduring interest in VIC.

Conclusions and implications for vaccinology: This study provides a synthesis of the Canadian dialogue on VIC since the 1980s. Methodological triangulation enhanced the analysis of this dialogue and provided insight on the various factors that have promoted or compromised the VIC agenda. These collated findings help to answer the question of why provinces/territories, other than Quebec, continue to lack a VIC program and reveals areas of investigation that may rekindle the dialogue.

Growing interest in this subject-matter has implications for safety and regulatory aspects of vaccination. Given the public health importance of vaccines, this dialogue also obligates ethical and economic considerations for vaccine policy and programming.

From knowledge to practice: Developing infographics to implement guidelines to reduce the pain of immunization

Huang S, Chan J, Segal S, Beckermann K, Dubey V

Introduction/Program need and objectives: Canadian guidelines to reduce the pain of immunization were updated in 2015. For the guideline to have impact, knowledge translation is needed to move research information into a quick, accessible format for practitioners and families. The objective is to create an infographic that is visually appealing, inclusive and optimizes health literacy. Implementing these guidelines may improve vaccination experiences in children and youth. This is one strategy to enhance vaccine confidence.

Program methods and activities: Guidelines were reviewed and age-based recommendations to reduce the pain of immunization were summarized for 3 groups– infants, children and teens. We considered clear language, images and information flow to present the information in digestible and bite size recommendations. An

iterative process involving experts in communication, health promotion and subject matter led to the final products.

Program results or outcomes (including evaluation): Each infographic was sequenced into before, during and after vaccination recommendations. Recommendations in each category were limited to 2 to 4 per section recognizing that too much information often leaves the parent confused. With the help of an illustrator and graphic designer, images and text were developed and placed to ensure the final product simply stated the message. Final infographics will be displayed.

Implications for practice or policy: Use of graphic designs to translate research knowledge into accessible formats for students, parents and families may improve vaccination experiences in children and empower youth. Also, summarizing complex evidence-based guidelines into useable tools can influence health care provider practice.

Using a quality improvement approach to addressing medication incidents at vaccine clinics

Welsh L, Beckermann K

Introduction/Program need and objectives: From June to December 2016, Toronto Public Health (TPH) encountered 25 medication incidents (MIs) at vaccine clinics. To reduce MIs we used a Quality Improvement (QI) approach with a focus on frontline staff engagement.

Program methods and activities: Recognizing that frontline staff understand the reality of clinics, we conducted a staff only Root Cause Analysis (RCA) to explore underlying factors contributing to MIs. Two focus groups were conducted with a total of 16 staff. One focus group was with TPH staff and the other with contracted agency staff. Two Quality Improvement Specialists used fishbone diagrams and 5-Why's to identify potential root causes of two major categories of MIs, i.e. consent related and vaccine spacing related. The fishbone diagrams were analyzed using qualitative coding and impact vs control analysis to identify the top priority areas to address. Analysis was validated with group participants.

Program results or outcomes (including evaluation): The priority areas identified in the analyses were the need to revise the consent form layout, include pre-clinic consent screening in business processes and address key learning needs. Additional overarching areas to address were reducing time pressure at clinic and changing training methodologies to combine procedural and electronic database training.

After dedicated efforts by staff and management on the identified areas, 7 MIs were reported from June to December 2017, a reduction of 72%.

Implications for practice or policy: A QI approach presents a practical and effective way to reduce MIs while improving program safety. Additionally, engaging frontline staff in a structured process can identify underlying root causes, generate staff commitment and transform staff into owners of solutions.

Social media strategies to increase vaccine uptake and reach urban hipsters: Responding to a mumps outbreak in Toronto

Maclachlan J, Dubey V, McEachern J, Bromley L, Ozaldin O

Introduction/Program need and objectives: In 2017, Toronto Public Health (TPH) experienced the largest mumps outbreak in over 20 years. Most of the cases were adults aged 18-35, and only 25% of cases were adequately vaccinated. Many cases had links to west downtown Toronto bars. The ability to inform this age group about the outbreak and vaccine recommendations presented a challenge and required novel outreach strategies not usually incorporated by outbreak response teams.

Objective: To create an innovative outbreak response communications campaign to reach young adults in Toronto and other stakeholders within the target age group.

Program methods and activities: A low-budget, communications campaign was developed in house to target 18-35 year old adults living or working in downtown Toronto. The main messages included getting vaccinated, preventing mumps by not sharing drinks or food and to watch for signs and symptoms.

Program results or outcomes (including evaluation): During the first wave of the outbreak, initial messages focused on young adult "hipsters" through targeted social media content including Twitter messages and promoted Facebook posts. These messages focused on ways to prevent mumps infection and to be aware of the symptoms. Messages targeting parents of young children who are also in this age group were also created. As the outbreak continued, posters and messages were designed to target bar patrons and in the west downtown Toronto area, as well as staff at gyms and community centres. Posters were also created for doctor's offices across the city. Social media statistics through the outbreak were positive and performed well above the industry standards for social media engagement rates.

Implications for practice or policy: Communicating with young urban adults who are not associated with a post-secondary institution can be challenging during an outbreak of a vaccine preventable disease. Using innovative and ongoing communication and social media strategies to target different groups of young adults can be low-cost and a necessary addition to traditional outbreak control strategies.

A missing link? The use of public health data linkage to improve data completeness in mumps case investigations

Seo C, Harris T, **Wilson S**

Introduction/Background: The timely assessment of cases' immunization status is critical in understanding the drivers of vaccine-preventable disease outbreaks (i.e. under-immunization, waning of vaccine-derived immunity). Our objective was to explore whether immunization data completeness in Ontario's reportable disease information system (iPHIS) can be improved by linking to Ontario's Digital Health Immunization Repository (DHIR), two distinct systems often accessed by different individuals. We selected mumps to carry-out this objective.

Methods: We extracted confirmed and probable mumps cases with onset dates in 2017 from iPHIS on June 8, 2018. Immunization records were extracted from the DHIR on June 19, 2018 and were linked to iPHIS cases via matching on health card number (HCN) or using probabilistic linkage based on name, date or birth, and gender. Linkage was performed on cases who had unknown immunization status using iPHIS data alone; immunization status was assessed both pre- and post-linkage.

Results and Analysis: In 2017, 259 cases of mumps were reported in Ontario. Using iPHIS data alone, immunization status was known for 174 cases (67.2%) and unknown for 85 cases (32.8%). Of those with unknown status, 23 cases (27.1%) were successfully linked: 18 matched on HCN and 5 matched on name, date of birth and sex. All 23 linked cases had at least one immunization record in the DHIR. Data linkage increased the percent of cases with known immunization status by 8.9% to 76.1%. Immunization status of the cases using the linked data, with changes achieved through the linkage, was: 28.6% with one dose (+3.9%), 31.3% with ≥2 doses (+3.9%), 16.2% unimmunized (+1.2%), and 23.9% with unknown immunization status (-8.9%).

Conclusions and implications for vaccinology: A provincial immunization repository can be an important source of immunization status of cases. Processes to efficiently link different public health information systems should be further explored to better leverage available data.

Weaving the web: Enhancing online vaccine safety surveillance information in Ontario

Harris T, Meyer W, Murti M, Deeks S

Introduction/Program need and objectives: Confidence in vaccine safety is essential to the success of immunization programs. With the proliferation of vaccine misinformation available online, public health organizations play an important role in providing credible, evidence-based, transparent information about

vaccine safety. We aim to describe Public Health Ontario (PHO) initiatives to increase the availability and reach of relevant and timely information about vaccine safety in Ontario.

Program methods and activities: Starting in 2012, PHO utilized various assessment methods and activities to inform the creation and expansion of our online vaccine safety information including: an environmental scan of other jurisdictions' websites , evaluation of our existing resources, consultation with end-users, as well as monitoring our website trends and usage through Google Analytics. Public health stakeholders were engaged iteratively for feedback on online content changes to ensure the content meet their needs.

Program results or outcomes (including evaluation): One of the first, most substantial, initiatives implemented by PHO was the online publication of the Annual Report on Vaccine Safety in Ontario, providing transparent and accessible communication of provincial surveillance of adverse events following immunization (AEFIs). We then developed a new vaccine safety webpage housing a variety of resources including reporting tools and live-stream and video-recorded webinars. We used blog posts and social media (i.e., Twitter) to promote new vaccine safety knowledge products and events. Leveraging results from an evaluation of the annual vaccine safety report, we launched an open-access online interactive data visualization tool of provincial AEFI surveillance information.

In 2017, PHO's website was evaluated and approved as a Vaccine Safety Net Member by the World Health Organization, thereby joining a global network of websites that provide reliable information on vaccine safety.

Implications for practice or policy: Our initiative demonstrates a continuous quality improvement approach to expanding the online availability of evidence-informed vaccine safety resources tailored to our stakeholders enabling effective communication about vaccine safety in Ontario.

Improving vaccine coverage amongst adults: Knowledge, attitudes, beliefs and behaviours (KABB) of healthcare providers regarding the role of pharmacists as immunizers.

Di Castria A, Halperin D, Isenor J, **Halperin S**, for the Canadian Immunization Research Network (CIRN)

Introduction/Background: Despite recommendations by the National Advisory Committee on Immunization (NACI), vaccine coverage among adults remains suboptimal. The scope of practice of pharmacists has been expanded to include vaccination, with the hope it will increase vaccine coverage, particularly in adults. We explored the KABB of healthcare providers about the changing role of pharmacists.

Methods: An online survey was developed and assessed for content validity and test-retest reliability. Pharmacists and vaccine providing nurses in the participating communities were invited to participate through publications distributed by professional associations and through posters on bulletin boards in local hospitals. Physicians were recruited through the regional hospital medical staff offices and provincial medical societies. Attitudes and beliefs were assessed using a 5-point Likert scale.

Results and Analysis: The 245 respondents comprised pharmacists (49%), family physicians (19%), nurses (15%) and other HCP (17%); 64% were from NS. 98% agreed that vaccines were safe and effective. 84% supported the expansion of pharmacist scope of practice to include vaccination of adults, 76% to include children 5-18 years, and 32% to children <5 years. 67% agreed that pharmacists have sufficient training to vaccinate and 50% would refer an individual to a pharmacist for vaccination; 78% believed that vaccines should be provided by physicians, pharmacists, and public health. Over 96% trusted scientific evidence about vaccinations and recommendations by public health and NACI. 80% reported being up to date for recommended adult vaccines; 91% reported having received the annual influenza vaccine. 93% thought NACI-recommended vaccines should be publicly funded. Practice logistical issues (55%), record keeping (31%), compensation (22%), and inreasing number of vaccines (13%) were cited as barriers to providing vaccinations.

Conclusions and implications for vaccinology: There is strong support for an increasing role of pharmacists in provision of vaccination services, particularly for adult vaccines. While logistical issues need to be addressed, pharmacists may contribute to improved vaccine coverage amongst adults.

Barcode standards for vaccine products in Canada

Bell C, Automated Identification of Vaccine Products Task Group

Introduction/Program need and objectives: Standardized vaccine product identification based on GS1 global standards on all levels of vaccine product packaging enables efficient and complete electronic health record (EHR) collection at the point of service; reduces immunization errors through improved completeness and accuracy of records; expedites the follow up of adverse events after immunization; and supports real-time inventory management. In Canada, the practice of scanning barcoded vaccine products had been piloted in select settings but has not been widely or routinely adopted.

Program methods and activities: Barcode standards for vaccine products in Canada were developed in 2009 by the Automated Identification of Vaccine Products (AIVP) Advisory Task Group and updated in 2014-15. The AIVP Advisory Task Group reports to the Canadian Immunization Registries and Coverage Network, which in turn reports to the Canadian Immunization Committee, a part of the Public Health Network structure.

Program results or outcomes (including evaluation): Barcodes on all levels of packaging should include the Global Trade Item Number (GTIN), lot number, and expiry date. Primary level packaging should include a 2D barcode, whereas secondary level packages can either have a 2D or 1D barcode. Case level packages are only expected to have 1D barcodes. Variables related to barcode data are contained in both the Vaccine Identification Database Search (VIDS) application and the Canadian Vaccine Catalogue (CVC).

Implications for practice or policy: The barcode standards for vaccine products in Canada are being implemented on a voluntary basis by vaccine manufacturers. Implementing bar code standards entails both a commitment from the vaccine manufacturers to manage production lines, as well as a commitment by end users (health care settings) to ensure camera-ready scanners are in place and software is ready to take full advantage of the bar code and vaccine information mapping systems.

The influence of gender on adult vaccine uptake: Results from the 2016 adult Immunization Coverage Survey

Bell C, Gendron M

Introduction/Background: While the majority of routine vaccination occurs during childhood, a number of vaccines are also recommended in adulthood. The Public Health Agency of Canada monitors vaccination coverage for recommended adult vaccines through surveys, including the adult National Immunization Coverage Survey (aNICS) administered every two years. We sought to measure if there were differences in vaccine coverage between male and females in the Canadian population.

Methods: The 2016 aNICS survey was conducted by random digit dialling between September and October 2016. The sample was weighted to be nationally representative based on data from the 2011 Canadian Census. Reported vaccine uptake relied on memory recall. Respondent demographics were assessed at the time of interview. We used Pearson's χ^2 test to analyze gender differences in coverage for seasonal influenza, tetanus, and pertussis vaccines among four age categories (18-44, 45-64, 65-74, and 75+ years), whereas pneumococcal vaccine coverage was assessed only in the latter two groups.

Results and Analysis: Overall, 3,024 respondents completed the interview, of which 52% were female. For seasonal influenza, females had higher reported coverage in the 18-44 year age group [34% vs. 25% ($p<0.001$)] and 45-64 year age group [43% vs. 34% ($p=0.003$)] only. Coverage for pertussis was higher in females in those aged 18-44 years [14% vs. 6% ($p<0.001$)] and 45-64 years [13% vs. 6% ($p<0.001$)] only. Pneumococcal coverage was higher in females aged 65-74 years [46% vs. 28% ($p=0.002$)], but no differences were observed in those aged ≥75 years. No significant coverage differences were observed for tetanus.

Conclusions and implications for vaccinology: Our results demonstrate higher vaccination coverage among females across all vaccines included in the analysis (except for tetanus). More study is required to determine the factors associated with the observed differences.

How does relative vaccine efficacy translate into absolute vaccine efficacy to inform incremental population benefit and public health recommendations?

De Serres G, Skowronski D

Introduction/Background: Clinical studies to demonstrate enhanced protection of a new over a current vaccine product often lack a placebo control group because precluded in the context of universal or indicated target group recommendations. In the absence of a placebo arm, such studies can only provide relative vaccine efficacy (VE) estimates. However, an understanding of the absolute improvement in VE conferred by the new over the current product is required in order to quantify and understand its actual incremental population benefit.

Methods: Attack rates (AR) were modelled and compared for three groups of participants, including those: (1) vaccinated with the "new" product; (2) vaccinated with the comparator vaccine; and (3) unvaccinated (placebo recipients). Absolute VE was derived relative to placebo as (ARunvaccinated-ARvaccinated)/(ARunvaccinated). Relative VE between vaccinated groups was derived as (ARcomparator-ARnew)/(ARcomparator). The absolute difference in VE (ΔVE) was assessed under varying conditions of AR, baseline VE of the comparator product, and relative VE of the new product.

Results and Analysis: Findings show that unless the comparator vaccine has no efficacy, the absolute ΔVE will always be less than the reported relative VE. Furthermore, the higher the baseline VE of the comparator product, the smaller will be the absolute ΔVE compared to the relative VE increase. For example, given baseline comparator VE=10%, then a relative VE=25% translates into a ΔVE=23% and the new product is still anticipated to have VE of just 33% overall (i.e. 10%+23%). Conversely, with baseline comparator VE=70%, the same relative VE=25% translates into a lower ΔVE=8% and new product VE=78%. Relative VE and absolute ΔVE are independent of the AR; however, the absolute number of cases prevented is dependent upon AR.

Conclusions and implications for vaccinology: Relative VE estimates may amplifies the impression of a new product incremental benefit, particularly where the comparator product already provides substantial protection. The absolute increment in VE should also be taken into account before making public health (or preferential use) recommendations on the basis of relative VE findings.

Planning for post-regulatory guidance on therapeutic vaccines for infectious diseases in Canada

Tunis M

Introduction/Problem definition that demonstrates the need for a policy change: Immunotherapies, including therapeutic vaccines, are one of the fastest-growing categories of products in the Health Canada regulatory approval pipeline. The post-regulatory guidance pathways have not been clearly defined for these anticipated products.

Research Methods: The Public Health Agency of Canada has reviewed the vaccine pipeline for infectious disease therapeutic vaccines, and discussed potential scenarios with Health Canada and the Canadian Agency for Drugs and Technologies in Health (CADTH).

Results and Analysis: While there is no standard definition for "therapeutic vaccines", they generally have two distinct characteristics:

- employ vaccine technology
- treat clinical disease

Therapeutic vaccines are being developed to treat a wide range of conditions including cancers, allergies, and infectious diseases that may prevent the risk of re-infection or community spread. The post-regulatory guidance pathways have not been clearly defined for these anticipated products. The National Advisory Committee on Immunization (NACI) traditionally issues guidance on the use of preventive vaccines for infectious diseases in Canada, whereas the Canadian Agency for Drugs and Technologies in Health (CADTH) traditionally issues

guidance on the use of drugs and health technologies for therapeutic applications. In this presentation, the Public Health Agency of Canada will identify emerging areas of research for infectious disease therapeutic vaccines and will outline the results of early discussions with CADTH on the appropriate pathways for post-regulatory guidance on these anticipated products.

Recommendations and implications for practice: Federal agencies are working collaboratively to ensure that infectious disease therapeutic vaccines will be reveiwed by the appropriate committee once authorised by Health Canada. This will ensure timely access to these new products by Canadians.

Canada's new national vaccination coverage goals and disease reduction targets

Pulickal J, Squires S, Cantin L

Introduction/Problem definition that demonstrates the need for a policy change: Canada's Budget 2016 announcement and Minister of Health's Mandate Letter supported updating Canada's national vaccination coverage goals (VCG) and vaccine preventable disease (VPD) reduction targets (RT). Updating the goals ensured that Canada's targets align with recent evidence, improved the ability to set and report on domestic vaccination priorities, and allow Canada to monitor progress towards increasing vaccination coverage and reducing rates of VPD.

Research Methods: Initiated in 2016, the following steps were taken: a critical review of past VCG and VPD-RT; an environmental scan of international processes and outputs; and the development of proposed VCG and VPD-RT by multi-disciplinary expert group. Drafted goals and targets were based on scientific evidence, practicalities of Canadian vaccination programs and VPD surveillance systems; and consultations with provinces and territories (PT). Final endorsement of the proposed goals and targets was sought and received through the pan-Canadian Public Health Network.

Results and Analysis: The new VCG and VPD-RT are achievable over time. They are evidence-based and consistent with the World Health Organization elimination targets and VCG. VCG are established: for all childhood vaccines by two and seven years of age; adolescent vaccines; seasonal influenza vaccine in targeted groups; hepatitis B vaccine for healthcare professionals; and for pneumococcal vaccine in those >65 years of age. VPD-RT are grouped into three categories with corresponding RT. The categories are: diseases under elimination; endemic diseases with low level incidence; and endemic disease with moderate level incidence.

Recommendations and implications for practice: Given the broad endorsement received of VCG and VPD-RT, it is hoped that public health decision makers will consider them when setting their vaccination priorities and establishing VPD prevention programs. Progress towards achieving these goals and targets will be reported as national data becomes available.

Incorporation of health economic evaluations into immunization decision-making in Canada: Barriers, facilitators and next steps

Hopman H**, Langley J**, Crowcroft N, Cesuroglu T

Introduction/Problem definition that demonstrates the need for a policy change: Despite the recommendation by the WHO that economic evaluations should be incorporated into national immunization decision-making, a standardized process for conducting and using economic evaluations for vaccine decision-making is lacking in Canada. Furthermore, there has been little research into how to incorporate economic evaluations into immunization decision-making and what barriers and facilitators exist in Canadian context. This study aims to investigate barriers and facilitators identified federal, provincial and territorial (FPT) and immunization research stakeholders, to using economic evaluations in decision-making for public health immunization programs in Canada.

Research Methods: Stakeholders were identified through the FPT Canadian Immunization Committee (CIC) and the Canadian Immunization Research Network (CIRN). Eleven semi-structured interviews were conducted during

April-May 2017. A cross-sectional web-based survey was send to 31 CIC members and 214 members of CIRN on April, 26. Twelve CIC and 51 CIRN-members completed the survey (response rate 38.7 and 23.8% respectively). Barriers and facilitators were categorized according to accessibility and acceptability using the conceptual approach of Williams and Bryan (2007).

Results and Analysis: The respondents(survey and interview) support economic evaluations being used more, becoming a routine part of the immunization decision-making process. Seventy percent of the survey respondents identified limited resources (human and financial) as accessibility barrier to using economic evaluations. Also lack of understanding of economic evaluations by decision makers was a barrier(39%). Perceiving effectiveness of the vaccine and burden of disease as more important than cost-effectiveness was mentioned as main acceptability barrier by survey respondents and interviewees. Concerns about methodology of economic evaluations was also identified by the survey respondents as a barrier. Potential facilitators were for economic evaluations to either be done national level or through a distributed local system.

Recommendations and implications for practice: Barriers to incorporating economic evaluation in vaccine decision-making may be overcome through increased capacity at the national level, or through, collaborating and sharing economic evaluations between FPT.

Economic evaluation of an expanded high-risk hepatitis A immunization program in Ontario, Canada

Ramsay L, Anyiwe K, Li M, Macdonald L, Coyte P, **Sander B**

Introduction/Background: Currently, Ontario provides a publicly-funded hepatitis A virus (HAV) vaccine for some populations at high risk of HAV infection (e.g., persons who inject drugs and those with chronic liver disease) but not for travellers to endemic countries, which contributes to the burden of HAV in Ontario. The objective of this study was to determine the cost-effectiveness of publicly funding HAV immunization for people travelling to HAV-endemic regions from the healthcare payer perspective.

Methods: We conducted a cost-utility analysis comparing an expanded high-risk publicly-funded hepatitis A vaccine program that includes travellers to endemic regions to the current program (vaccine available for private purchase by travellers). We used a Markov state transition model to simulate HAV risk and health outcomes over a lifetime time horizon. Outcomes include quality-adjusted life years (QALYs), costs, and an incremental cost-effectiveness ratio (ICER). A base-case analysis was performed, using a mean start age of 30 years. Parameter uncertainty was explored through deterministic and probabilistic sensitivity analyses. Future costs and health outcomes were discounted at 1.5%.

Results and Analysis: The expanded HAV immunization program provided a mean expected health gain of 0.037 QALYs (0.053 undiscounted) for an incremental cost of $124,310.00 ($126,89.00 undiscounted) per 1,000 people relative to the status quo comparator. The ICER of the expanded HAV immunization program is $3,391,504 per QALY gained ($2,403,144 undiscounted). Two-way sensitivity analysis – on the probability of HAV infection when traveling to an endemic region and the vaccine program cost – demonstrated few combinations of these variables in which the expanded program would be considered cost effective. Probabilistic sensitivity analysis found that at a $50,000/QALY gained cost-effectiveness threshold 100% of simulations would not be considered cost-effective.

Conclusions and implications for vaccinology: The expanded vaccine program significantly exceeds commonly accepted cost-effectiveness thresholds. Further research should focus on a more comprehensive understanding of specific risk behaviours during travel to endemic regions.

Cost-effectiveness of a hypothetical vaccination program for West Nile virus in Ontario, Canada

Nam A, Yeung M, Shing E, Loeb M, Naimark D, Nelder M, Zhu H, **Sander B**

Introduction/Problem definition that demonstrates the need for a policy change: The incidence of West Nile virus (WNv) infections has been increasing with infections associated with non-neuroinvasive and neuroinvasive

disease. Case fatality for neuroinvasive disease is high at approximately 10%. Human vaccines are under development and phase II trial results are promising. The purpose of this study was to assess the potential cost-effectiveness of a hypothetical universal vaccination program for West Nile virus from the healthcare payer perspective in Ontario, Canada.

Research Methods: We developed a mathematical model to estimate infections, neuroinvasive and non-neuroinvasive cases, deaths, quality- adjusted life years (QALYs), and costs (in Canadian dollars) associated with West Nile virus (WNv) exposure over the lifetime of an Ontario adult population. The model was used to project the cost-effectiveness of a hypothetical vaccine program. Utilities of short-term sequelae were obtained from a Canadian WNv cohort. Costs of healthcare encounters were derived from health administrative data. Remaining model parameters were obtained from the published literature. QALYs and costs were discounted at 1.5%. We assessed parameter uncertainty in deterministic sensitivity analyses.

Results and Analysis: We estimated that WNv exposure is associated with 1,064 infections, resulting in 188 non-neuroinvasive cases and 17 neuroinvasive cases, and 6 deaths per 100,000 persons over the lifetime of the cohort. In the reference case, a universal WNv vaccination program (with assumed effectiveness of 80%) projected 833 fewer infections, 150 fewer non-neuroinvasive cases, 11 fewer neuroinvasive cases, and 4 fewer deaths. At a vaccine price of $100, the vaccination program was dominant compared to no vaccination with lifetime cost savings of $54 million and 173 additional QALYs. The results were robust to vaccine price where effectiveness was greater than 60%.

Recommendations and implications for practice: A universal West Nile virus vaccination program is likely to be cost-effective at a wide price range and a vaccine effectiveness of at least 60%.

Addressing the immunization research-to-policy gap in Canada: Collaborative development of an integration pathway to assist strategic planning

Espinoza Moya M, Crowcroft N, Quach-Thanh C, Halperin S, Desai S, Langley J, Lerch R, Bolotin S, Bjornson G, Sale J, De Wals P, Upshur R, Tran D

Introduction/Problem definition that demonstrates the need for a policy change: Maximizing the impact of immunization programs requires timely and effective translation of monitoring, evaluation and research findings into policy and practice. Despite an increasing number of studies conducted in this field, results of those assessments are not systematically used to inform decision-making, or vice-versa. Accordingly, we investigated the perspectives of immunization program stakeholders on specific actions needed to enhance research-to-policy integration, and collaboratively developed a pathway to assist strategic planning.

Research Methods: Concept Mapping was used to elicit, organize, and produce a visual representation of stakeholders' perspectives on the topic. Fifty-six stakeholders involved in program planning, implementation, evaluation/research, policy-making, and industry representatives participated in two face-to-face workshops in May, 2017. Items generated through brainstorming were synthesized, sorted and rated by participants during the 1st workshop. Assisted by R-CMap software, Multidimensional Scaling and Hierarchical Cluster Analysis were subsequently used to generate Conceptual Point, Cluster, and Go-Zone Maps. During the 2nd workshop, participants interpreted these outputs and reached consensus on the names and final number of clusters of similar concepts and specific dimensions/regions in the map. A draft pathway was developed by complementing this information with findings from the literature on research-policy collaborations in other fields, and iteratively refined through a consultation process.

Results and Analysis: Participants identified 38 different actions, related to six areas: "Funding and Infrastructure"; "Capacity Building"; "Planning and Evaluation"; "Collaboration and Exchange"; "National Advisory Committee on Immunization process"; and "Values, Trust and Accountability". Overall, "Ongoing strategic planning process to identify priorities for research/program evaluation" was deemed the most important and feasible action, yet considerable variation was observed across stakeholders categories. The final

pathway outlines inputs and processes required to enhance integration, as well as the expected outcomes and contextual factors that could influence it.

Recommendations and implications for practice: Our research-to-policy pathway provides a shared vision on how to shape and direct future integration efforts in this field.

Critical assessment of economic evaluations on protein-based meningococcal vaccines in developed countries

Espinoza Moya M, De Wals P, Beutels P

Introduction/Problem definition that demonstrates the need for a policy change: Invasive meningococcal disease (IMD) is a rare and severe condition with a high probability of complications, mortality and long-term sequelae. At present, most IMD cases in Canada are caused by serogroup B strains. This systematic review examines main factors influencing results of economic evaluations on protein-based meningococcal vaccines, the conditions under which acceptable incremental cost-effectiveness ratios (ICER) are generated, and their applicability to the Canadian context.

Research Methods: A comprehensive search in four journal-indexing databases and grey literature was conducted in November 2017, using a combination of terms related to the vaccine, the disease, and economic evaluations. Two independent reviewers screened titles and abstracts followed by the full text. Articles were included for qualitative synthesis if they described a full economic evaluation of a licensed protein-based meningococcal vaccine for use in the general population in a developed country. A detailed analysis of model characteristics, parameters used, vaccine/disease related assumptions, results and conclusions was performed.

Results and Analysis: The systematic review yielded 14 ex-ante evaluations on 4CMenB, conducted for eight developed countries between 2013 and 2017. Preliminary findings are limited to these 14 studies and show considerable differences in the model's set-up and main assumptions and parameters used across assessments. Overall, ICERs were most sensitive to disease incidence, vaccine price, duration of protection, herd effect and discount rate applied. Conceptual methodological differences, in addition to major differences in disease epidemiology, health services delivery structure and costs, and other contextual factors, add to limiting the potential transferability of most study results to Canada.

Recommendations and implications for practice: We are aware of the preparation of an economic evaluation of Trumemba that will have to be included in the review and could provide additional information for judging the societal value of these vaccines.

The development of rVSV-ZEBOV 'Canada's vaccine for Ebola': A programmatic approach to clinical trials at the Canadian Immunization Research Network

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Introduction/Program need and objectives: The Canadian Immunization Research Network (CIRN), formed in 2009, addresses knowledge gaps in immunization programs and policy. CIRN's Clinical Trials Network (CTN) was built to rapidly evaluate vaccines. During the 2014-16 Ebola outbreak in West Africa, CIRN's CTN collaborated with stakeholders to mobilize three projects supporting the development of the rVSV-ZEBOV vaccine. These were (1) a first-in humans (Phase 1) trial in 40 adults in Halifax (NCT02374385); (2) a Phase II/III study of 40 laboratory workers and first responders in Winnipeg, in collaboration with the NIH (PREPARE; NCT02788227), and (3) a Phase II trial in 200 HIV-infected persons in Canada, Senegal and Burkina Faso (ACHIV-Ebola; NCT03031912).

Program methods and activities: CIRN partnered with the Public Health Agency of Canada (PHAC), the Canadian Institutes of Health Research (CIHR), International Development Research Centre (IDRC), NewLink and Merck to establish novel research funding frameworks. Collaborators were identified through CIRN sites, IDRC, and the research community. CIRN led the project management, data and laboratory activities, regulatory submissions, study protocols, contracts and budgets, and study monitoring in collaboration with partners. CIRN formed

steering committees, facilitated investigator meetings, and held site initiation visits in Halifax, Ottawa, Montreal, Dakar, and Winnipeg. Ongoing, regular communication with all stakeholders occurs through web meetings, teleconferences and electronic means.

Program results or outcomes (including evaluation): The Phase I study found the vaccine safe, with minimal adverse events (doi: 10.1503/cmaj.170074). Enrolment in PREPARE is ongoing, with preliminary results expected in late 2018. The ACHIV-Ebola study, which enrolls five successive cohorts over 2.5 years, has enrolled in Ottawa and Montreal, with enrolments in Senegal and Burkina Faso planned in Q3 of 2018. Implications for practice or policy: Multi-stakeholder, multi-site, multi-country vaccine research is needed for some vaccines. CIRN has experienced and gained substantial learning through the coordination of the rVSV-ZEBOV Ebola vaccine trials. Although challenging, the unique alliances are highly rewarding and build capacity for ongoing evaluation of vaccines.

Global environmental scan of legislation governing National Immunization Technical Advisory Groups (NITAG), mandatory vaccine programs, and compensation for serious adverse events following immunization (AEFI) in high-, middle-, and low-income countries

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Introduction/Background: Some 83 countries have WHO-recognized NITAGs, which provide governments with independent, evidence-based recommendations respecting immunization. Although WHO recommends a legislative basis for NITAGs, to date there has been no systematic formal cataloging of specifics of different legislative regimes used. In light of this shortcoming, the 2017 WHO Global Vaccine Action Plan Assessment Report recommended undertaking a global audit to document ways in which legislation can strengthen or undermine NITAGs and, more broadly, national immunization programs, including legislation for mandatory immunization and compensation for serious AEFIs.

Methods: A survey covering the nature of any laws or regulations governing a) NITAG formation, powers and operation, b) mandatory immunization programs, and c) compensation programs for serious AEFIs was distributed in June 2018 to health officials representing 38 Global NITAG Network countries. A copy of any relevant legislation was also collected. Questions included impact of these regimes on immunization uptake and acceptance. NITAG legal instruments were analyzed and categorized according to the power, authority, and independence they bestow. Instruments regarding mandatory immunization programs and AEFI compensation schemes were analyzed and categorized. Survey comments were analyzed for common themes and principles.

Results and Analysis: Very preliminary analysis of laws in Serbia, Australia, and Kenya, call into question the assumption that mandatory vaccination legislation significantly and ethically increases vaccine uptake in the long-term. The full analysis will provide a more complete picture of the limitations and successes of legislative shaping of vaccine policy.

Conclusions and implications for vaccinology: In addition to gaining a greater understanding of current legislative support for immunization programs, the survey provides legislative options to countries aiming to create or reform a NITAG, and establish a AEFI compensation program, and/or mandatory vaccine program.

Environmental scan of public health recommendations for off-label use of vaccines amongst Global NITAG (National Immunization Technical Advisory Groups) Network (GNN) countries

Top K, Esteghamati A, Graham J, Henaff L, MacDonald N

Introduction/Background: New vaccines are reviewed by National Regulatory Authorities who approve the indications for use in the product monograph. Occasionally, National Immunization Technical Advisory Groups (NITAGs) make "off-label" recommendations for vaccine use in different age groups, populations, dosing, schedules, etc. from those listed in the product monograph.

We aimed to determine the rationale, policies and procedures of NITAG off-label recommendations and Ministry of Health responses.

Methods: We conducted an environmental scan of Global NITAG Network (GNN) members, immunization program managers and regulators in 38 high-, middle- and low-income countries. Participants completed an online survey regarding NITAG policies, procedures, and legislation governing development of off label recommendations. Opinio survey software was used.

Results and Analysis: To date, responses were received from 30 respondents in 24/38 countries surveyed (63%); 77% were NITAG members or immunization program managers. 57% of respondents reported no definition for off-label vaccine use in their country. One-third reported no off-label vaccine use in their countries. Where decisions about off-label vaccine use were made, 45% (9/20) of respondents indicated that the NITAG was responsible for such decisions with 4/9 (44%) stating that the NITAG received requests from the Ministry of Health or another body to make off label recommendations. The main reasons for making off-label vaccine recommendations were for guidance in specific populations, and to respond to disease outbreaks and vaccine shortages. NITAGs claimed evidence for off label decisions came from observational studies, randomized control trials, disease and adverse event surveillance data, and manufacturer data. 80% of respondents reported there were no standard operating procedures (SOPs) for developing off-label recommendations and 50% indicated there were no policies to support implementation of off-label recommendations.

Conclusions and implications for vaccinology: SOPs on best practice for developing and implementing recommendations for off-label vaccine use is a gap globally that needs to be addressed.

Generation of poliovirus-negative serum using immunoadsorption

Elsherif M, LeBlanc J, Barrett L, McNeil S, Ward B, Hatchette T

Introduction/Background: According to the World Health Organization (WHO), failure to eradicate poliovirus in remaining strongholds due to poor vaccination uptake could result in 200,000 new cases annually worldwide, within 10 years. Assays measuring serum antibody responses to vaccines are vital to monitor population immunity or susceptibility to disease. However, validation of these assays may be difficult as they require non-immune or "negative" sera, which are difficult to obtain in highly vaccinated populations. This study describes a method to generate non-immune sera for poliovirus through immunoadsorbtion.

Methods: Using a poliovirus microneutralization assay, low to medium titer sera from both inactivated or oral poliovirus vaccine-primed individuals were identified. To remove poliovirus antibodies, protein A magnetic beads were coupled with poliovirus type 1 mouse monoclonal antibodies, followed by capturing cultured poliovirus virus particles from a high titer suspension. Sera were incubated with the antibody and virus coupled beads, and subjected to up to 6 rounds of immunoadsorption. After each step, an aliquot of the serum sample was taken for quantification using microneutralization assay established by the Centers for Disease Control and Prevention (CDC).

Results and Analysis: Overall, each immunoadsorption step reduced the neutralization titer by approximately 15 to 25%, until the lower limit of detection of the microneutralization assay was reached. While additional reproducibility data is underway, this study demonstrated that immunoadsorption is a simple, effective method for removing specific antibodies from serum.

Conclusions and implications for vaccinology: The ability to remove specific antibodies from sera is invaluable in generating negative controls for serologic assays used to assess population-based protection against vaccine-preventable diseases.