The Risk of Febrile Seizures Following Influenza and 13-Valent Pneumococcal Conjugate Vaccines

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1489. Pneumococcal Vaccination Provides Substantial Value for Money for Canadians

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Background. Introduction of pneumococcal conjugate vaccines (PCVs) 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.

Objective. To evaluate the economic impact of PCVs to Canadian society following nationwide RIS implementation.

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 Canadians. A steady state scenario using pre-PCV incidence rates was projected to Dec 2015 to estimate the number of cases without PCVs. Averted cases were obtained by subtracting the cases reported from the estimated case count without PCVs. Disease specific costs were assigned to averted cases and vaccine spend was subtracted from the total to obtain net savings to Canadian society.

Results. Successful implementation of PCVs on the provinces’ RIS saved 2,365 lives and resulted in net savings of CAD $203 million between Jan 2005 and Dec 2015. These savings stem from averted direct and indirect medical costs associated with IPD, PNE and AOM cases.

Table 1 – BOD and related costs avoided by PCV use, 2005–2015

<table>
<thead>
<tr>
<th>Disease</th>
<th>With PCVs</th>
<th>Without PCVs</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteremia</td>
<td>27,041</td>
<td>36,808</td>
<td>-9,767</td>
</tr>
<tr>
<td>Meningitis</td>
<td>14,461</td>
<td>19,685</td>
<td>-5,224</td>
</tr>
<tr>
<td>Hospitalized PNE</td>
<td>366,927</td>
<td>386,413</td>
<td>-19,486</td>
</tr>
<tr>
<td>Nort-hospitalized PNE</td>
<td>545,230</td>
<td>589,251</td>
<td>-44,021</td>
</tr>
<tr>
<td>AOM</td>
<td>3,629,952</td>
<td>4,374,467</td>
<td>-744,514</td>
</tr>
<tr>
<td>Costs ($ million)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease related</td>
<td>$7,123</td>
<td>$8,078</td>
<td>-955</td>
</tr>
<tr>
<td>Vaccine cost</td>
<td>$753</td>
<td>$0</td>
<td>$753</td>
</tr>
<tr>
<td>Total</td>
<td>$7,876</td>
<td>$8,078</td>
<td>-$203</td>
</tr>
<tr>
<td>Other (no cost considered)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>36,917</td>
<td>39,282</td>
<td>-2,365</td>
</tr>
</tbody>
</table>

Conclusion. Introduction of PCVs resulted in reduced pneumococcal burden of disease and net economic benefits to Canadian society.

Disclosures. 1Employee; 2Pfizer Inc.; 3Employee; 4Salary; 5M. C. Breton, Pfizer; Employee; Salary; 6Wasserman, Pfizer; Employee; 7Salary; 8Member, FIFA; 9Employee, Consultant; Consultant, Consulting fee; 10McDade, Pfizer; Consultant, Consulting fee; 11Farkouh, Pfizer; Employee, Salary

1491. The Risk of Febrile Seizures Following Influenza and 13-Valent Pneumococcal Conjugate Vaccines

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Background. Evidence on the risk of febrile seizures (FS) after vaccination with inactivated influenza vaccine (IIV) and 13-valent pneumococcal conjugate vaccine (PCV13) is mixed. Among children 6–23 months, we examined the risk of FS following IIV and PCV13 during the 2013–14 and 2014–15 influenza seasons, for which vaccine virus strains were the same.
Methods. We used claims data from 4 large national insurers in the FDA-sponsored Sentinel Initiative, which was developed to monitor the safety of FDA-regulated medical products. With a self-controlled risk interval design, the risk of FS in 0–1 days following IV and following PCV13 was compared with a comparison interval (14–20 days), adjusting for confounding by age, calendar time, and concomitant vaccination with the other vaccine. In exploratory analyses, we assessed whether the effect of IV is modified by concomitant administration of PCV13.

Results. During the study period, 355,486 children received IV and 581,687 received PCV13. We observed an incidence rate ratio (IRR) of 1.12 (95% CI 0.80, 1.56) for the risk of FS following IV after adjustment for age, calendar time and concomitant PCV13. PCV13 was associated with an increased risk of FS (IRR adjusted for age, calendar time and concomitant IV, 1.80, 95% CI 1.29, 2.52). The attributable risk for PCV13 ranged from 0.3 to 5.16 per 100,000 doses.

The age and calendar-time adjusted IRR comparing exposed time to unexposed time was greater for concomitant IV and PCV13 (IRR 2.80, 95% CI 1.63, 4.83), as compared with that for PCV13 without concomitant IV (IRR 1.54, 95% CI 1.04, 2.28). However, the formal test assessing for interaction between IV and PCV13 was not statistically significant.

Conclusion. We found an elevated risk of FS after PCV13 vaccine but not after IV, when adjusting for concomitant administration of the other vaccine. We found some evidence to suggest that concomitant administration of IV with PCV13 might interact to increase the independent effects of PCV13, but the study was not powered to assess this interaction. The risk of seizures associated with PCV13 is low compared with a child's lifetime risk of FS. Findings should be interpreted in the context of the importance of preventing influenza and pneumococcal infections in young children.

Disclosures. L. Li, sanofi pasteur: The author is currently employed by Sanofi Pasteur, Genzyme, which shares the same parent company as sanofi pasteur, the manufacturer of the Flu vaccine. However, the work was done while this author was still employed by Harvard Pilgrim Health Care Institute., No financial benefit received

1492. Invasive Pneumococcal Disease Before and During an Era of Use of Three Different Pneumococcal Conjugate Vaccines in Quebec
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Background. In Quebec, 7-valent (PCV7), 10-valent (PCV10) and 13-valent (PCV13) pneumococcal conjugate vaccines were successively used for children immunization according to a 2 + 1 doses schedule.

Objective. To assess the impact of this program on the epidemiology of invasive pneumococcal disease (IPD).


Results. In children <5 years, IPD rate decreased from 69/100,000 in 2003 to 12/100,000 in 2016 (83% reduction). Following PCV7 introduction in 2004, there was a rapid decline in incidence of homologous serotypes. 7F cases and 19A decreased following PCV10 introduction in 2009 and PCV13 in 2011, whereas decreased in serotypes 3, 5 and 6B was minimal. Non-vaccine types IPD increased and represented 79% of cases in 2016. All dispensed prescriptions for oral antibiotics at the HMO were recorded and the use of broad-spectrum antibiotics was strongly associated with increased IPD incidence (IRR 1.08 per 10,000 doses).

Conclusion. Compared with previous cultures, we found a 50% increase in IPD detection using combined lytA and piaB multiplex RTPCR. Similarly, the proportion of children colonized with vaccine serotypes increased from 2% to 7%. This work is funded by an investigator initiated grant to BUMC from Pfizer.

Disclosures. K. M. Shea, PhD, MPH, Consulting fee and Grant recipient; S. I. Pelton, Pfizer: Board Member and Grant Investigator, Consulting fee and Grant recipient; S. I. Pelton, Pfizer: Board Member and Grant Investigator, Consulting fee, Research grant and Speaker honorarium; Merck vaccines: Board Member, Consulting fee and Speaker honorarium; GSK: Board Member, Consulting fee and Speaker honorarium; Novartis: Board Member, Consulting fee and Speaker honorarium

1494. Antibiotic Prescription Rates in Children <24 Months Old Following PCV7/PCV13 Sequential Implementation
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Background. PCV7/PCV13 (PCV) implementation markedly impacted on acute respiratory infection rates in young children, and is thus expected to reduce antibiotic use. We conducted a community-wide study to determine the extent of antibiotic prescription rates (APRs) following PCV implementation.

Methods. The study was conducted from July 2005 through June 2016 among all Jewish children <24m, insured by the Clalit Health Maintenance Organization (HMO) in southern Israel (74% of all the region's Jewish children; n = 8,483, 2005; n = 13,604, 2016). All dispensed prescriptions for oral antibiotics at the HMO were recorded and yearly APRs were calculated by antibiotic category. PCV7 and PCV13 were implemented in July 2009 and November 2010 respectively and rapidly reached 90% coverage for 3 doses. Epidemiological years were from July through June.

Results. Overall, high APRs were seen throughout the study. A total of 226,035 antibiotic prescriptions were dispensed. Overall annual APR means (per 1,000 s: SD) were 2068.9 ± 15.2 and 1841.1 ± 39.1 in 2005–2009 and 2013–2016, respectively (11% reduction; 95% CI 10–12%) (Figure 1). Amoxicillin, the most commonly prescribed antibiotic drug (60.8% of all prescriptions) was reduced by 14% (95% CI 13–15%) (Figure 2). Similar reductions were seen for oral cephalosporins and amoxicillin/clavulanate. However antibiotic use declined continuously throughout the study. Calculation of linear trends before and after PCV implementation demonstrated a significant change in trends for amoxicillin, oral cephalosporin and total APRs, strongly suggesting a causative role of PCVs. PCV implementation resulted in an overall reduction of 45,320 prescriptions for a cohort of 100,000 children during their first 2 years of life (95% CI 41,512 to 49,007).

Conclusion. A clear and significant change in all APR trends associated with PCV implementation was observed in children <24 months old with a baseline high APR. This resulted in a marked decline in antibiotic use. Continuous surveillance is needed to determine further trends, including those for specific antibiotic categories.