Potential Impact of Routine Use of 13-valent Pneumococcal Conjugate Vaccine on Hospitalizations for Pneumonia Among Older Adults in Canada

J. Vojicic[1], S. Dion[1], R.E. Isturiz[2], C. Laferriere[3], M. Major[1], R.M. Nepal[1], J.A. Suaya[4], J.M. McLaughlin[2]

[1] Pfizer Canada, Kirkland, QC
[2] Pfizer Vaccines, Collegeville, PA, USA
[3] University of Toronto, Toronto, ON
[4] Pfizer Vaccines, New York, NY, USA

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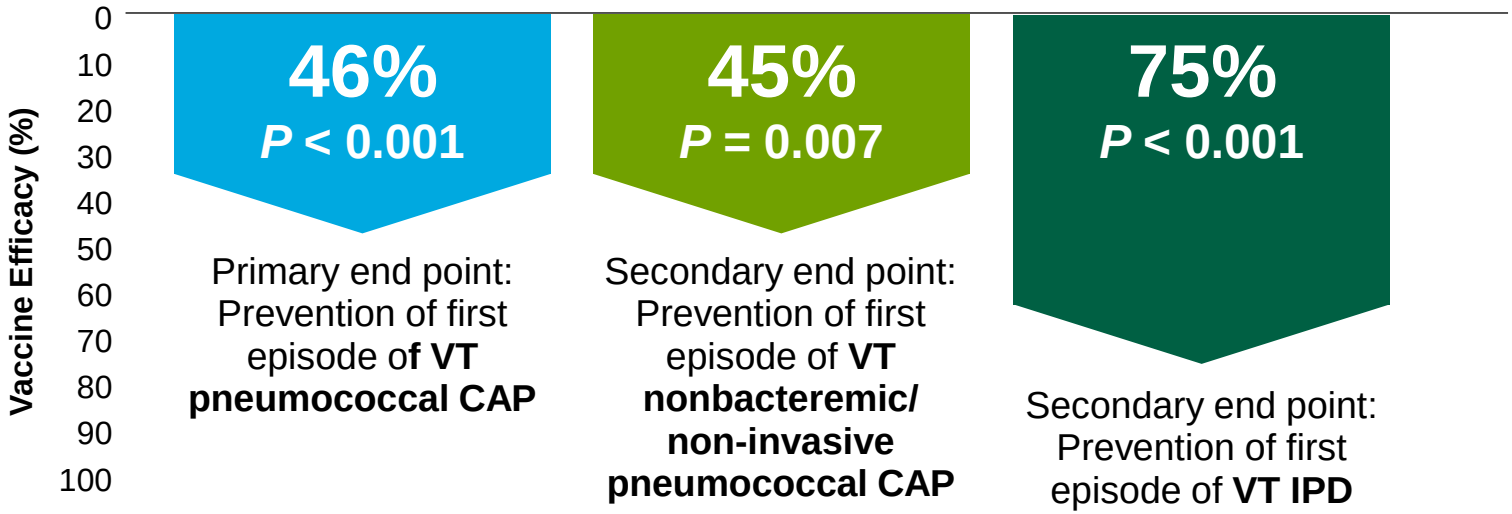
Background

- Prevention of non-bacteremic pneumococcal CAP in older adults = unmet medical need.
- In July of 2015, PCV13 was licensed in Canada for the prevention of vaccine-type (VT) pneumonia in adults, based on demonstrated efficacy in individuals ≥65 years of age:[1,2]



CAP=community-acquired pneumonia; PCV13=13-valent pneumococcal conjugate vaccine; IPD=invasive pneumococcal disease

1. Prevnar 13 Product Monograph, Pfizer Canada Inc. July 27th, 2015; 2.Bonten MJ et al. *N Engl J Med.* 2015 Mar 19;372(12):1114-25

Current Recommendations/Funding for PCV13 Use in Adults

Individuals ≥ 18 Years of Age with Immunocompromising Conditions[1]

(Population-based NACI recommendation; funding is province/ territory-dependent)

Individuals ≥65 Years of Age[2]

(Individual-level NACI recommendation; no provincial/territorial funding)

- No population-based recommendation[3]
  - Perceived low preventable disease burden, and
  - Expectation of its ongoing decrease through herd effect

PCV13=13-valent pneumococcal conjugate vaccine

1. An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI). *Statement on the Use of Conjugate Pneumococcal Vaccine – 13 valent in Adults (Pneu-C-13), 2013;* **2**. An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI*). Update on the use of 13-valent pneumococcal conjugate vaccine (PNEU-C-13) in addition to 23-valent pneumococcal polysaccharide vaccine (PNEU-P-23) in immunocompetent adults 65 years of age and older – Interim Recommendation*, 2016; **3**. An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI). *Update on the use of pneumococcal vaccines in adults 65 years of age and older – A Public Health Perspective*, 2018

Objective

To evaluate the potential impact of a routine PCV13 immunization program for Canadian adults aged ≥65 years on hospitalizations for CAP, using available Canada-specific data

PCV13=13-valent pneumococcal conjugate vaccine; CAP=community-acquired pneumonia

Methods

- We constructed a deterministic model based on Canada-specific burden of disease estimates, published estimates of PCV13 efficacy/effectiveness, and duration of vaccine protection to estimate
  - The cumulative number of hospitalizations,
  - Corresponding hospital days and
  - Number of deaths
- That could be potentially preventable over a 5-year period through PCV13 immunization of adults ≥65 years

PCV13=13-valent pneumococcal conjugate vaccine

Methods

- Hospitalizations potentially averted were estimated as the product of:
  - The incidence of hospitalized (all-cause) CAP*,
  - The proportion of hospitalized CAP that is PCV13-type*,
  - PCV13 efficacy/effectiveness against hospitalized VT-CAP,
  - The size of the Canadian population aged ≥65 years**
  - The duration of protection for PCV13 over a 5-year time horizon
- Hospital days potentially averted = hospitalizations potentially averted **x** median hospital length of stay
- Deaths potentially averted = hospitalizations potentially averted **x** 30-day mortality rate

CAP=community-acquired pneumonia; PCV13=13-valent pneumococcal conjugate vaccine; VT=vaccine-type

* Assumed to remain constant over the 5-year period
** Assumed 5-year annual all-cause mortality

Model Assumptions

Parameter	Value	Source
Annual All-cause Hospitalized CAP Incidence	**1,692/100,000**	Canadian Institute of Health Information Discharge Abstract Database (CIHI-DAD), 2015 (data on file)
% of All-cause CAP Caused by PCV13 Serotypes	**5% (assumption)**	LeBlanc, et al. *Vaccine*. 2017;35(29):3647-3654
	3%, 7%	
PCV13 VE Against Hospitalized VT-CAP	**45.6% (95.2% CI 21.8%-62.5%);**	Bonten, et al. *NEJM* 2015; 372(12):1114-25;
	72.8% (95% CI 12.8%-91.5%)	McLaughlin, et al. *Clin Infect Dis*. 2018 Oct 30;67(10):1498-1506
Population Size	**6,195,500**	Statistics Canada, 2017
Duration of PCV13 Effectiveness	**5 years (no waning)**	Patterson, et al. *Trials Vaccinol*. 2016;5:92-96
Median Length of Hospital Stay (Pneumococcal CAP)	**8.6 days**	LeBlanc, et al. *Vaccine*. 2017;35(29):3647-3654
30-day Mortality (Pneumococcal CAP)	**13.6%**	LeBlanc, et al. *Vaccine*. 2017;35(29):3647-3654

CAP=community-acquired pneumonia; VE=vaccine efficacy/effectiveness

Data Sources: Incidence of All-cause CAP

- Canadian Institute of Health Information Discharge Abstract Database (CIHI-DAD)
  - Hospitalized CAP cases across Canada (except BC, QC-data not available), adults ≥65 years
- ICD-10-CM Codes: J12-J18
  (J12.0–2, J12.8, J12.9; **J13**; J14; J15.0-9; J16.0, J16.8; J17.0–3, J17.8; J18.0–2, J18.8, J18.9)
- Pneumonia coded as:
  - Primary, or most responsible diagnosis (MRDx),
  - "Proxy MRDx" (secondary Dx assessed to be chiefly responsible for patient's hospitalization)

CAP=community-acquired pneumonia
ICD-10-CM= International Classification of Diseases, Tenth Revision, Canadian Modification

Data Sources: Proportion of CAP that is PCV13-type

Canadian Immunization Research Network – Serious Outcome Surveillance (CIRN – SOS) Network

- Surveillance of all-cause CAP in adults admitted to sentinel hospitals across 5 provinces
  - Clinical and radiologic confirmation of pneumonia
  - Culture and urinary assays (including PCV13-specific urine assay) to determine % of CAP that is PCV13-type

PCV13-type CAP

% CAP that is PCV13-type , 2011-2015:[1,2]

	2011	2012	2013	2014	2015
All Ages	17.7%	17.1%	12.8%	6.2%	8.5%
65+	15.5%	11.7%	10.8%		

?

CAP=community-acquired pneumonia

1. LeBlanc JJ et al *Vaccine.* 2017 Jun 22;35(29):3647-3654; 2. LeBlanc JJ et al. Is streptococcus pneumoniae serotype 3 masking PCV13-mediated herd immunity in adults hospitalized with community acquired pneumonia? Presented at ISPPD-11, Melbourne, Australia, April 15-19, 2018

Evolution of the Herd Effect (IPD, Adults ≥65): Post-PCV7 vs Post-PCV13

AB "Near eradication"[1]

2002 — 8 Years → 2010

BC 91% reduction[2]

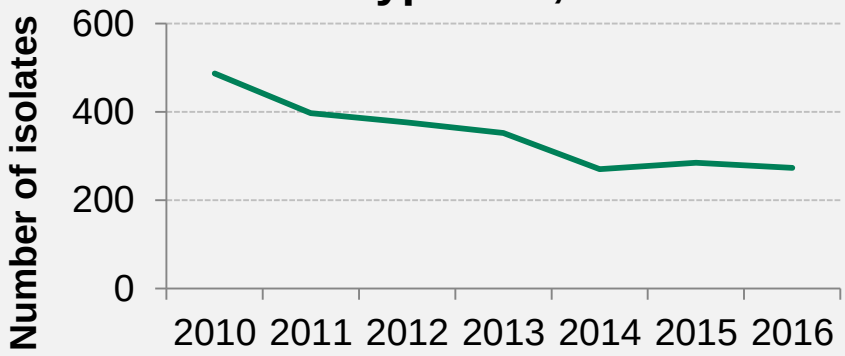
2002 — 8 Years → 2010

ON 89% reduction[3]

2001 — 10 Years → 2011

Predicted 90% reduction for 6 additional STs in PCV13[4]

2010 — 9.5 Years → 2019



PCV13 STs 50% to 25%

6 Years

6 addit. STs in PCV13 31% to 19%

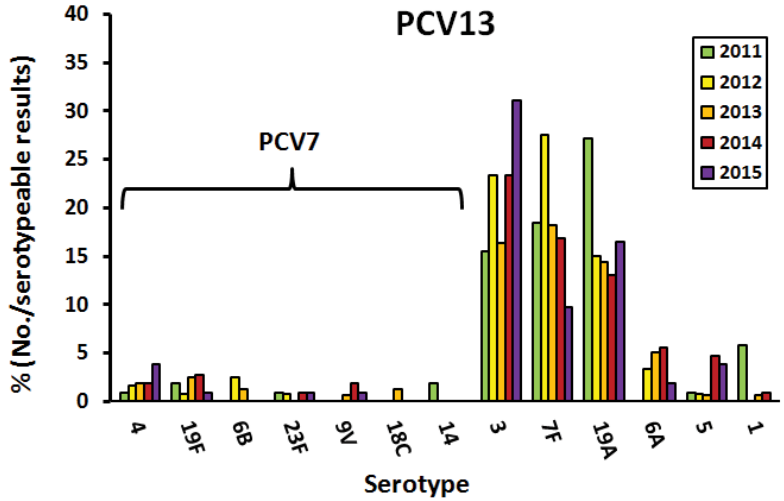
TIBDN: "From 2013-17, the distribution of vaccine group STs has not changed." "… the incidence of adult IPD appears to have stabilized, with PCV13 ST strains contributing 37% of IPD."[6]

IPD-invasive pneumococcal disease; PCV7=7-valent pneumococcal conjugate vaccine; PCV13=13-valent pneumococcal conjugate vaccine; STs=serotypes; TIBDN=Toronto Invasive Bacterial Diseases Network

1. Leal J et al. *Pediatr Infect Dis J.* 2012;31(9); **2.** Sahni V et al. *Can J Public Health*. 2012;103(1):29-33; **3**.Rudnick W et al. *Vaccine.* 2013;31(49):5863-71.; **4**. Shiri T et al. *Lancet Global Health.* 2017;5(1):e51-9; **5**. Public Health Agency of Canada. Nation al Laboratory Surveillance of Invasive Streptococcal Disease in Canada – Annual Summary Reports 2014 and 2016.; **6.** Nayani S et al. Impact of Routine Pediatric PCV13 on the Incidence and Severity of Invasive Pneumococcal Disease in Adults in Ontario, Canada. Presented at ID Week, San Francisco, USA, October 3-7, 2018.

Evolution of the Herd Effect Post-PCV13 (PCV13-CAP, Adults ≥65)

S. Pneumoniae Serotype Distribution in CAP



Reported % of PCV13-type CAP (2011-2015):[1,2]

	2011	2012	2013	2014	2015
All Ages	17.7%	17.1%	12.8%	6.2%	8.5%
65+	15.5%	11.7%	10.8%		

5%
(3%-7%)

PCV13=13-valent pneumococcal conjugate vaccine; CAP=community-acquired pneumonia

1. LeBlanc JJ et al *Vaccine.* 2017 Jun 22;35(29):3647-3654; 2. LeBlanc JJ et al. Is streptococcus pneumoniae serotype 3 masking PCV13-mediated herd immunity in adults hospitalized with community acquired pneumonia? Presented at ISPPD-11, Melbourne, Australia, April 15-19, 2018

Data Sources: PCV13 Effectiveness Against Vaccine-type Community-acquired Pneumonia

Louisville Pneumonia Surveillance Study[1,2]

Prospectively enrolled adults (≥18 years) living in Louisville, KY who were hospitalized with CAP in one of the 9 adult acute-care hospitals serving the Louisville area

October 7 2013

Sept. 2014: ACIP PCV13 Recommendation in ≥65y[3]

September 30 2016

CAP IR: 2,093/100,000

Setting:

- 3+1 pediatric PCV13 program
- Median age – 76
- 88% w/risk conditions

Test-Negative Design (TND)
Nested Case Control Among ≥65 Years

April 1 2015

Time frame for Analysis

Detailed pneumococcal vaccination status obtained from health insurers for all patients

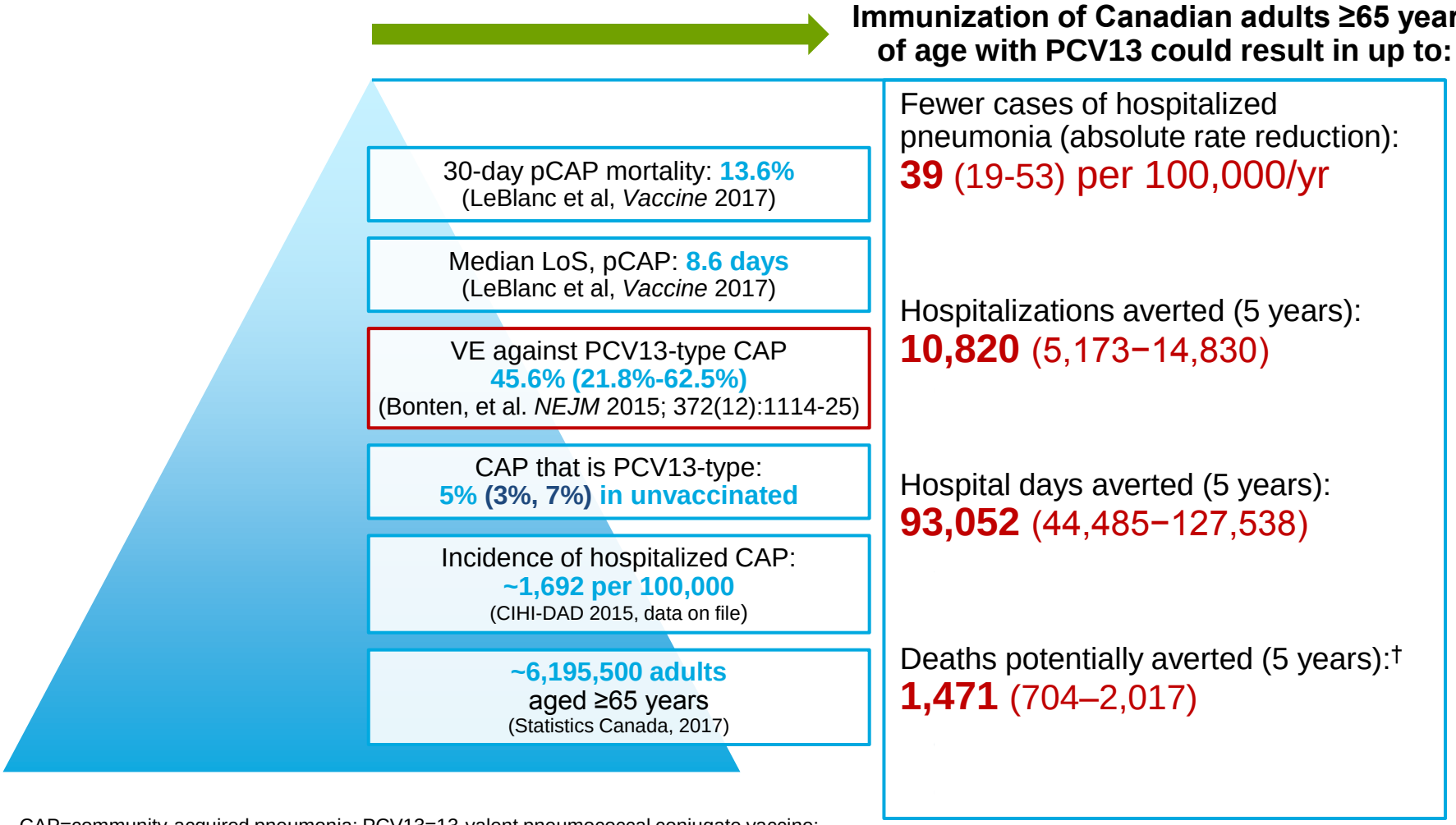
April 30 2016

VE Against VT-CAP – 72.8%
(95%CI: 12.8−91.5)

PCV13=13-valent pneumococcal conjugate vaccine; VE=vaccine effectiveness; CAP=community acquired pneumonia; IR=incidence rate; VT=vaccine-type

1. Ramirez et al. *Clin Infect Dis*, 2017;65(11):1806–1812.; 2. Alexander R, et al. *Univ Louisville J Respir Infect.* 2017;1(4):35-39; 3. Tomczyk S, et al. *MMWR Morb Mortal Wkly Rep* 2014; 63:822–5

Results: Burden of CAP Potentially Preventable by Routine Use of PCV13 in Canadian Adults Aged ≥65 Years

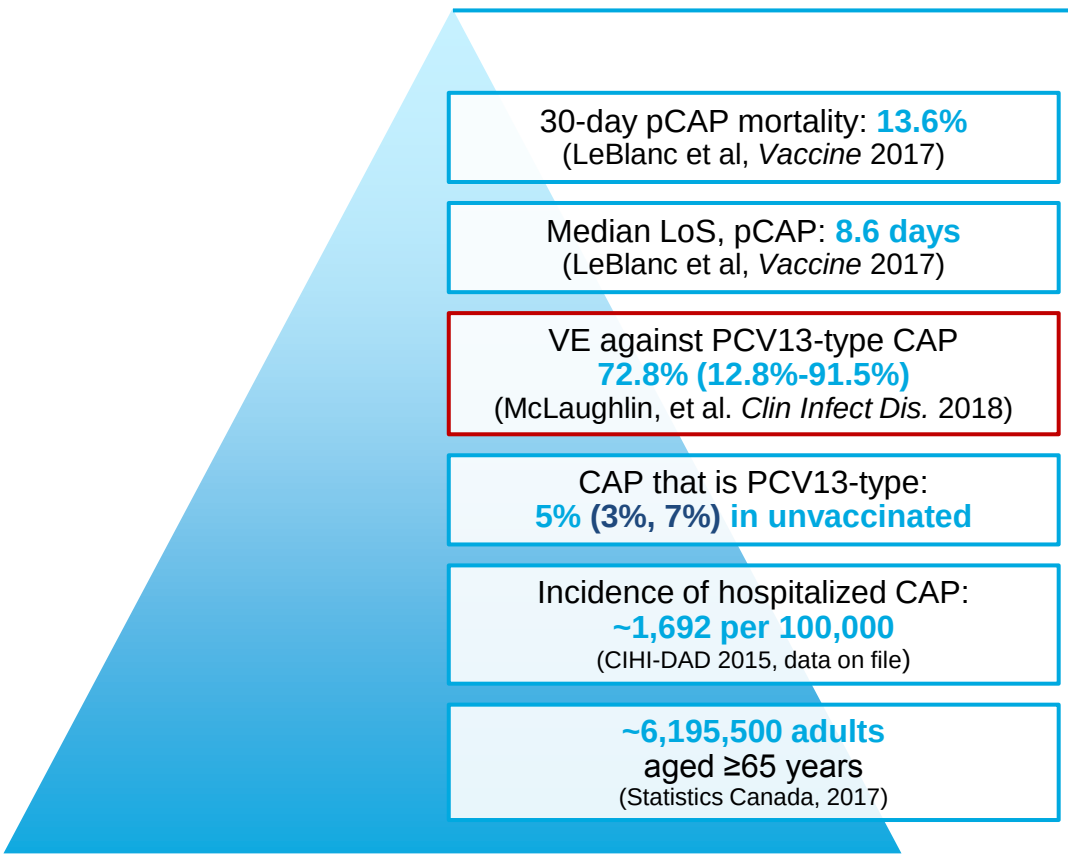


CAP=community-acquired pneumonia; PCV13=13-valent pneumococcal conjugate vaccine; pCAP=pneumococcal CAP; VE=vaccine effectiveness; LoS=length of stay

*Assumes 5% all-cause mortality each year and 100% vaccine uptake

†A significant effect on all-cause mortality was not demonstrated in Community Acquired Pneumonia Immunization Trial in Adults (CAPiTA)

Results: Burden of CAP Potentially Preventable by Routine Use of PCV13 in Canadian Adults Aged ≥65 Years



Immunization of Canadian adults ≥65 years of age with PCV13 could result in up to:

Fewer cases of hospitalized pneumonia (absolute rate reduction):
62 (11-77) per 100,000/yr

Hospitalizations averted (5 years) :
17,274 (3,037−21,711)

Hospital days averted (5 years):
148,557 (26,120−186,716)

Deaths potentially averted (5 years):†
2,349 (413-2,953)

CAP=community-acquired pneumonia; PCV13=13-valent pneumococcal conjugate vaccine; pCAP=pneumococcal CAP; VE=vaccine effectiveness; LoS=length of stay

*Assumes 5% all-cause mortality each year and 100% vaccine uptake

†A significant effect on all-cause mortality was not demonstrated in Community Acquired Pneumonia Immunization Trial in Adults (CAPiTA)

Study Limitations

- All-cause CAP incidence was obtained from a retrospective administrative database study, and it may be an underestimate of the true disease burden
  - Codes for influenza with pneumonia not included
- The proportion of VT-CAP is an assumption, based on extrapolation of available data from a Canadian sentinel surveillance study, and recent IPD surveillance results informing about herd effect
- The analysis assumes 100% vaccine uptake
- Duration of vaccine protection was assumed to be limited to 5 years

CAP=community-acquired pneumonia; VT= vaccine-type; IPD=invasive pneumococcal disease

Conclusions

- While PCV13-type disease in Canadian older adults appears low (3-7% of all-cause CAP in our analysis), given the large burden of all-cause CAP, this represents a meaningful remaining disease burden

- Despite herd effects from the pediatric immunization programs, routine immunization of individuals ≥65 years of age with PCV13 could result in considerable additional reduction in pneumonia hospitalizations

PCV13=13-valent pneumococcal conjugate vaccine; CAP=community-acquired pneumonia

Thank You

Back-up

Administrative Database Studies: Importance of Understanding Coding Practices

- In individuals with chronic comorbidities and pneumonia, the comorbid condition may need to be sequenced first:[1]

Canadian Coding Standards

Example:

A 68-year-old man with severe COPD contracts the common cold. He is being treated by his family physician for exacerbation of COPD. His condition worsens, and he is brought into the emergency department. Chest X-ray reveals pneumonia. He is subsequently admitted for treatment of COPD exacerbation and pneumonia.

Code	DAD	NACRS	Code Title
J44.0	(M)	MP	Chronic obstructive pulmonary disease with acute lower respiratory infection
J18.9	(1)	OP	Pneumonia, unspecified

- Focusing solely on pneumonia coded as primary diagnosis will underestimate disease burden[2]

1. Canadian Institute for Health Information. *Canadian Coding Standards for Version 2018 ICD-10-CA and CCI.* Ottawa, ON: CIHI; 2018.;
2. Breton MC et al. The hidden clinical and economic burden of pneumonia. Poster # 96 Canadian Immunization Conference, Ottawa, Canada, Dec 4-6, 2018

PT07

Identifying Patients Hospitalized with Community-Acquired Pneumonia with the International Classification of Diseases coding: Including Secondary Diagnoses is Mandatory

C Grenier[1], A Carignan[1,2], C Abou Chakra[2], G Lapointe[1], A Marcil-Héguy[1], L VALIQUETTE[1,2]

[1]Centre de recherche du CHUS, CIUSSS de l'Estrie-CHUS, Sherbrooke, QC; [2]Department of Microbiology and Infectious Diseases, Université de Sherbrooke, Sherbrooke, QC

- **Aim:** to assess the benefit of adding secondary Dx to identify patients hospitalized with CAP
- **Methods:** screening of adults ≥65 years admitted in 2015 with a **principal OR secondary Dx of pneumonia**
  - ICD-9/10-CM codes, AND
  - New infiltrate on chest X-ray/thoracic CT scan
- **Results:** among 243 included cases, 117 had CAP coded as secondary Dx
  - *S pneumoniae* was the most common pathogen in both
  - Secondary Dx patients – 82% COPD, higher ICU admission

Grenier C et al. Identifying Patients Hospitalized with Community Acquired Pneumonia with the International Classification of Diseases coding: Including Secondary Diagnoses is Mandatory. Presented at AMMI Canada 2018, May 2-5th, Vancouver, Canada

Results

Cases of Hospitalized VT-CAP, Hospital Days and Deaths Potentially Preventable Per Year

Year After Vaccination	Cases of Hospitalized PCV13-type CAP Averted (95 %CI)	Hospital Days Averted (95% CI)	Deaths Averted
Year 1	2391 (1143-3278)	20,567 (9,832-28,189)	325 (155-446)
Year 2	2272 (1086-3114)	19,538 (9341-26,780)	309 (148-424)
Year 3	2158 (1032-2958)	18,562 (8874-25,441)	293 (140-402)
Year 4	2050 (980-2810)	17,633 (8,430-24,169)	279 (133-382)
Year 5	1948 (931-2670)	16,752 (8,009-22,960)	265 (127-363)
Total	**10,820 (5,173-14,830)**	**93,052 (44,485-127,538)**	**1,471 (704-2,017)**

VT=vaccine-type; CAP=community-acquired pneumonia; PCV13=13-valent pneumococcal conjugate vaccine