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Using Influenza and Pneumococcal Vaccines to Lower Antibiotic Resistant Infections: An Antimicrobial Stewardship Strategy

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Faculty/Presenter Disclosure

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Mitigation of bias

1. Disclose conflicts of interest
2. Evidence based presentation
3. Impartial presentation

1 Minute Vaccine Review

The Success of Vaccines in the 20th century

Disease	20th Century Annual Morbidity	2013 Reported Cases	% Decreases
Smallpox	29,005	0	**100%**
Diphtheria	21,053	0	**100%**
Pertussis	200,752	28,639	**86%**
Tetanus	580	26	**96%**
Polio (paralytic)	16,316	1	**>99%**
Measles	530,217	187	**>99%**
Mumps	162,344	584	**>99%**
Rubella	47,745	9	**>99%**
Congenital Rubella Syndrome (CRS)	152	1	**99%**
***Haemophilus influenzae* (B)**	20,000 (est.)	31 §	**>99%**

Appendix E: Impact of Vaccines in the 20th and 21st Centuries. Available at: http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/E/impact.pdf

OBJECTIVES

- **Influenza (Virus):**
  - Understand that the majority of the morbidity and mortality occurs in high risk patients **(65 years +)**

- Review flu vaccination (**SD-Flu**, **HD-Flu**)

- ***Streptococcus pneumoniae*** **(pneumococcus- Bacteria) infection:**
  - Understand that the majority of the morbidity and mortality occurs in high risk patients **(65 years +)**

- Review **PPSV23** and **PCV13** vaccination

Problem # 1
Influenza (Virus)

What Do I Want You to Know ?

1. Influenza is Associated With a Lot of Morbidity and Mortality

2. The Majority of the Morbidity and Mortality Occurs in high risk patients (65 years +)

What Are The Benefits of The Flu Shot

- reduced influenza illness

  - reduced MD/Emerg Visits
  - reduced antibiotic Rx – ↓ antibiotic resistance
  - reduced hospitalization
  - reduced mortality

- reduced spread of virus !!!

Influenza remains a serious public health concern

Annually in Canada, influenza is estimated to cause:

175,000
Emergency room visits[2]

70% (age 65 +)

12,200
Hospital admissions[1]

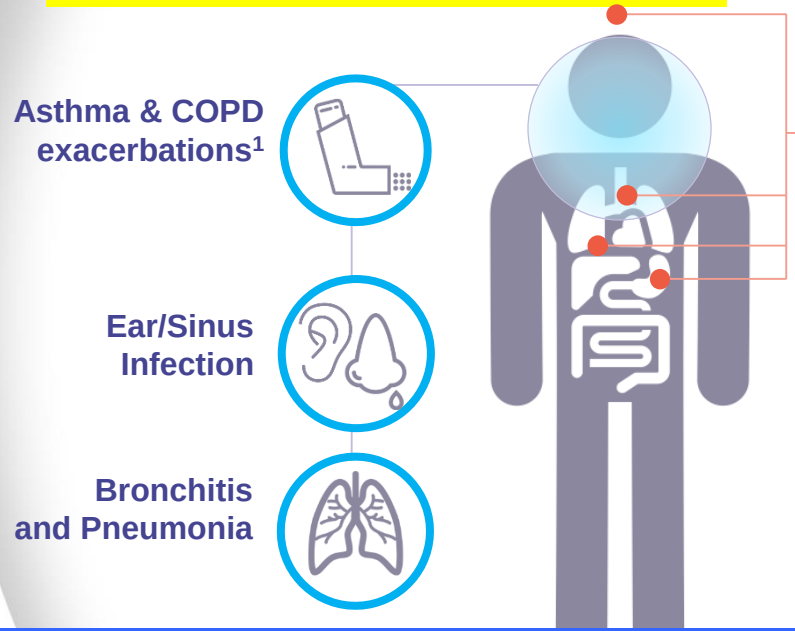
91% (age 65 +)

3,500
Deaths[1]

1. National Advisory Committee on Immunization (NACI). (2019).
2. National Advisory Committee on Immunization (NACI). (2016).
3. BC Centre for Disease Control. (2013).

Potential Complications of Influenza

DIRECT effects: Respiratory



INDIRECT effects: Multi-Organ Systems

TRIGGER for:

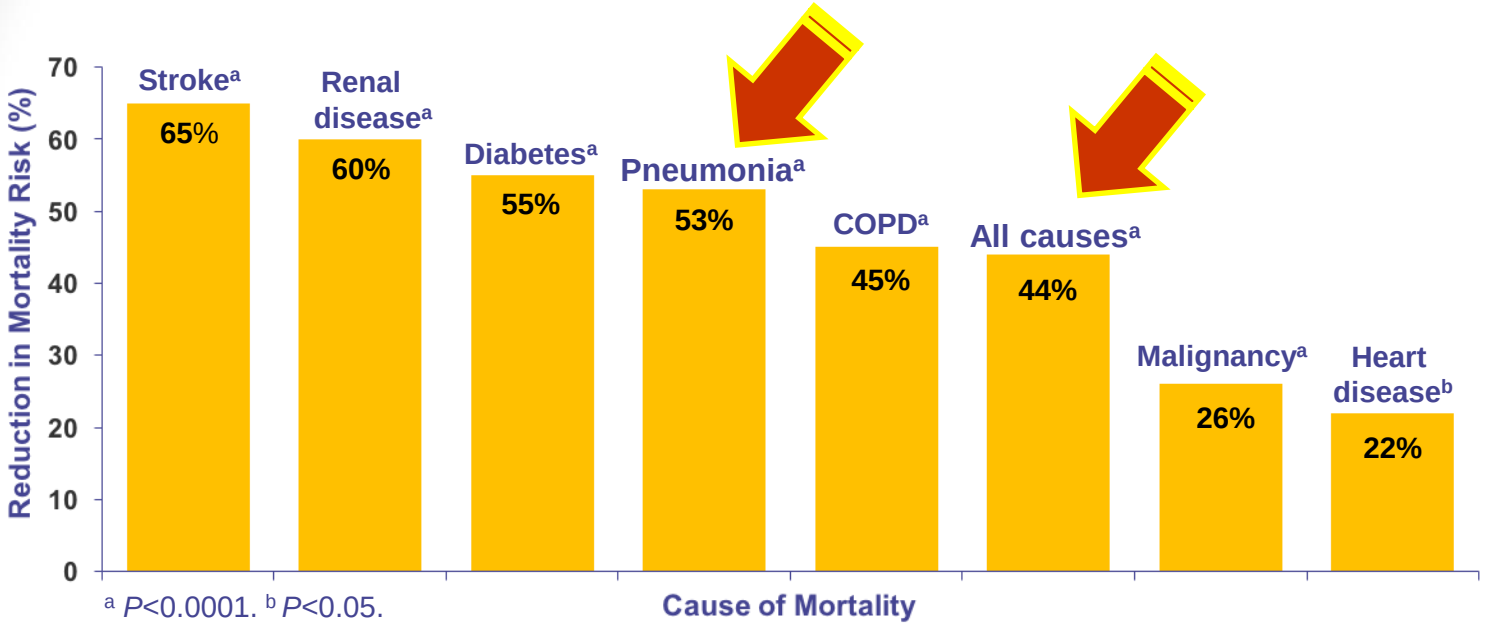
acute myocardial infraction, **ischemic heart disease**, and **cerebrovascular disease**[4-6]

EXACERBATION of:

hypertension, renal disorder[7] and **diabetes**[1]

1. National Advisory Committee on Immunization (NACI). (2019).; Kopsaftis, Z., et al. (2018). *Cochrane Database Syst Rev, 6*, CD002733.; Norhayati, M. N., et al. (2017). *Cochrane Database Syst Rev, 10*, CD010089.; Walter, N. D., et al. (2010). *Clin Infect Dis, 50*(2), 175-183.; Udell, J. A., et al. (2013). *JAMA, 310*(16), 1711-1720. ; Udell, J. A., et al. (2015). *Expert Rev Cardiovasc Ther, 13*(6), 593-596. ; Kwong, J. C., et al. (2018). *N Engl J Med, 378*(4), 345-353. ; Boehme, A. K., et al. (2018). *Ann Clin Transl Neurol, 5*(4), 456-463. ; Chen, C. I., et al. (2016). *Medicine (Baltimore), 95*(5), e2588.; Lau, D., et al. (2014). *Diabetologia, 57*(4), 690-698. ; Campbell, A., et al. (2010). *CMAJ, 182*(4), 349-355.

Influenza Vaccination Lowered the Risk of Major Cause-Specific Mortality (n = 102,698 ≥ 65 yrs)



- **35,637 vaccinated**
- **67,061 unvaccinated**
- **Followed for ~1 year**

- Mortality ↓ in **high-risk** (12.2% to 5.4%)
- Mortality ↓ in **low risk** (3.0% to 1.8%)

Wang et al. Vaccine. 2007;25(7):1196-1203.

What Do I Want You to Do ?

Flu shot for everyone 6 mos + !

- staff ?
- visitors ?

High-Dose FLU is MORE Effective than Standard Dose Influenza Vaccine in Patients 65+ years

Study performed jointly by the **Center for Disease Control and Prevention (CDC)**, **Food and Drug Administration (FDA)**, and the **Centers for Medicare and Medicaid Services (CMS)**

Izurieta **(65+ ye** ...aries

High-Dose FLU reduced mortality by 36.4%

(Shay et al. J Infect Dis. 2017 Mar 2)

Hi

22%

better protection against probable influenza illness

22%

better protection against influenza-related emergency department visits and hospitalizations

Izurieta et al. Lancet Infect Dis 2015;15:293-300

What Do I Want You to Consider/Do ?

Consider and Offer ? High Dose Flu shot in 65+

(NACI says it provides superior protection)

Problem # 2

Streptococcus pneumoniae (pneumococcus-Bacteria) Infection

- #1 Community acquired pneumonia (CAP)
- #1
- #2
- #1 Otitis media

Leading Cause of Bacteremia/sepsis (IPD)

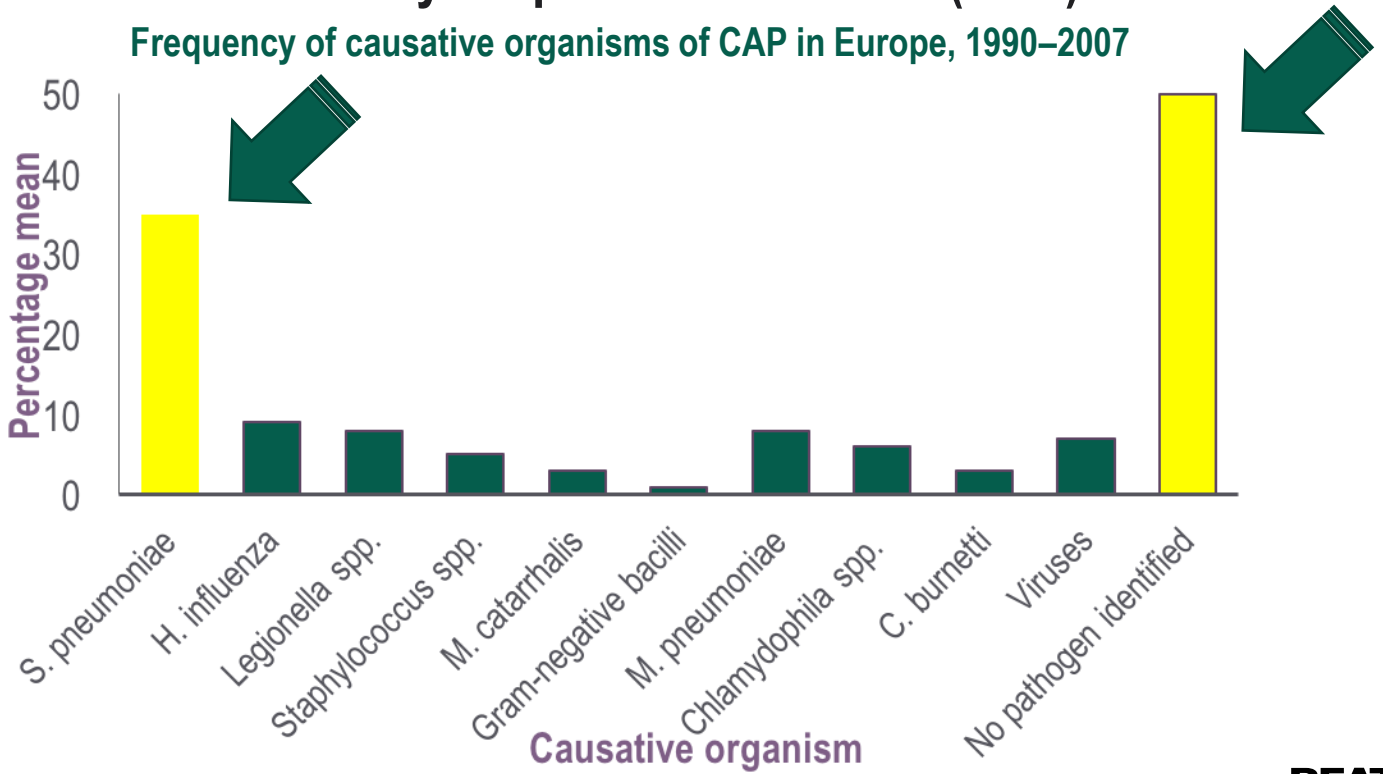
Lynch and Zhanel. Curr Opin Pulm Med. 2010 May;16(3):217-25.

What Do I Want You to Know ?

1. **Pneumococcal Infection is Associated With a Lot of Morbidity and Mortality**

2. **The Majority of the Morbidity and Mortality Occurs in Immunocompromised Patients and in Patients 65 + years of age**

S. pneumoniae is the most frequent pathogen in Community Acquired Pneumonia (CAP)

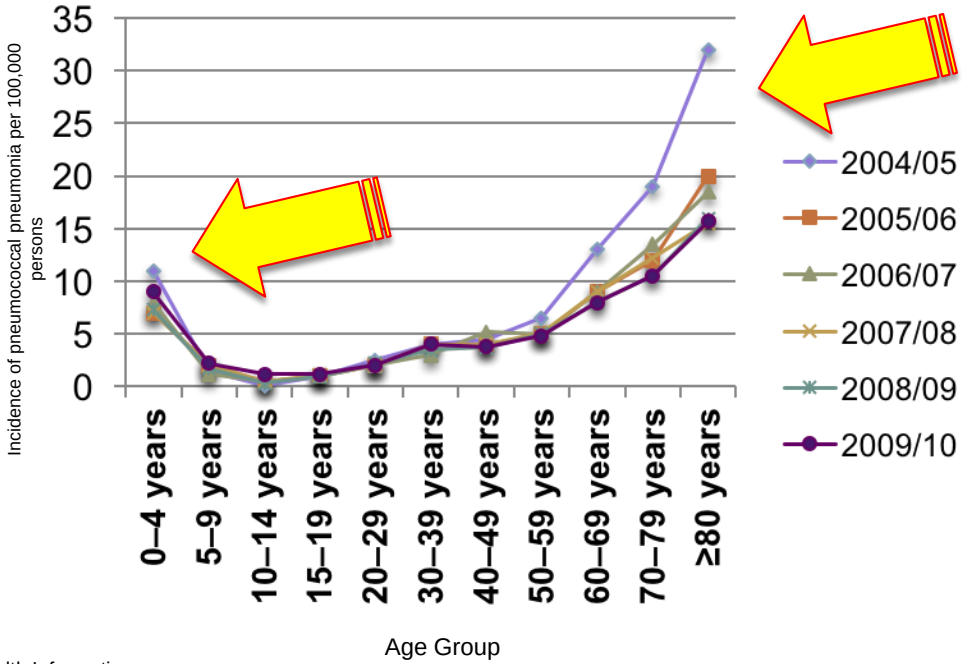


Welte T, et al. Thorax 2012;67:71-79.

BEATING THE ODDS

Hospitalization due to pneumococcal pneumonia increases with age

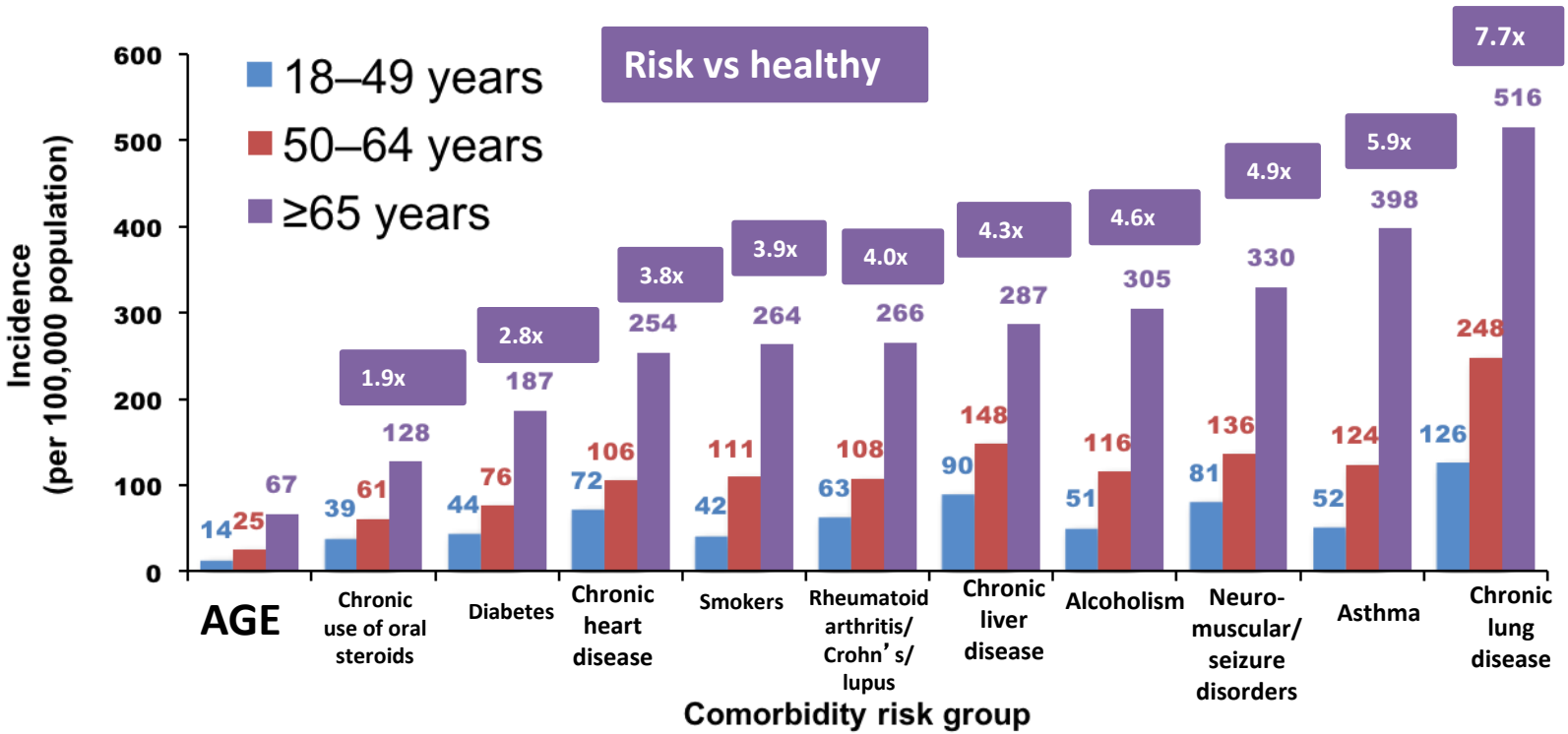
CIHI DAD annual incidence of **hospitalizations in Canada** 2004/05 to 2009/10 due to pneumococcal pneumonia by age and year



CIHI = Canadian Institute for Health Information
DAD = Discharge Abstract Database

McNeil S, Gray S, Zanotti G, et al. Clinical and economic burden of hospitalization due to Streptococcus pneumoniae pneumonia in Canada, 2004 to 2009 [Presented at the 8th Annual International Symposium on Pneumococci and Pneumococcal Diseases (ISPPD), Iguaçu Falls, Brazil, 11–15 March 2012]. 2012.

Age (65 +) and **Comorbidities** increase pneumococcal pneumonia risk in adults



Shea KM, et al. *Open Forum Infect Dis*. 2014;1:ofu024.

What Do I Want You to Do ?

1. Vaccinate with PPSV23 (Pneumovax)

2. Vaccinate with PCV 13 (Prevnar 13)

NACI RECOMMENDATIONS (UPDATED FEBRUARY 2014)

PPSV23 FOR THOSE AT RISK FOR PNEUMOCOCCAL DISEASE

≥ 2 yrs of age with co-morbidities:		Plus: ≥ 18 yrs	≥ 65 yrs
Immuno-competent	Immuno-compromised	With these factors	**All persons**
• Chronic heart disease • Chronic lung disease • Diabetes mellitus • Chronic liver disease • Cerebrospinal fluid leaks • Cochlear implants • Chronic neurologic condition that may impair clearance of oral secretions • Asthma (requiring ongoing medical management) (NEW)	• Functional or anatomic asplenia, sickle cell, hemoglobinopathies • HIV infection • Immune deficiencies • Immune suppression due to disease or **treatment** • Hematopoietic stem cell transplant (recipient) • Solid organ or islet transplant • Malignant neoplasms, including leukemia and lymphoma • Chronic renal disease	• Residents of long term care facilities • Homelessness, alcoholism, smokers, illicit drug use • Asthma (if associated with COPD, emphysema or prolonged systemic corticosteroid)	

Pneumovax 23 (23PPSV)

- **Advantages**
  - Covers 23 serotypes
  - Prevents **I**nvasive **P**neumococcal **D**isease (IPD) - **GOOD**
  - Safe

- **Disadvantages** (**polysaccharide** vaccine, B-cell only)
  - **Poor response in older pts.,** immunocompromised and in children < 2 yrs of age
  - **No** immunologic memory
  - **No** booster effect on revaccination
  - **Lower** response after revaccination, “hyporesponsiveness”
  - **No**, or very limited effect on carriage **(no herd immunity)**
  - **POOR**, prevention of **C**ommunity **A**cquired **P**neumonia (CAP)

Effectiveness of PPSV23 in the General Population of 50 years of Age and Older: (Meta-analysis)

- Vaccine effectiveness for PPSV23 in preventing **IPD** was **50% - 54%...GOOD**

- Vaccine effectiveness for PPSV23 in preventing **CAP** **4% -17%...POOR**

Kraicer-Melamed H, et al. Vaccine, 2016; 34 (13):1540-1550.

NACI RECOMMENDATIONS (UPDATED 2016)

PCV13 for ADULTS:

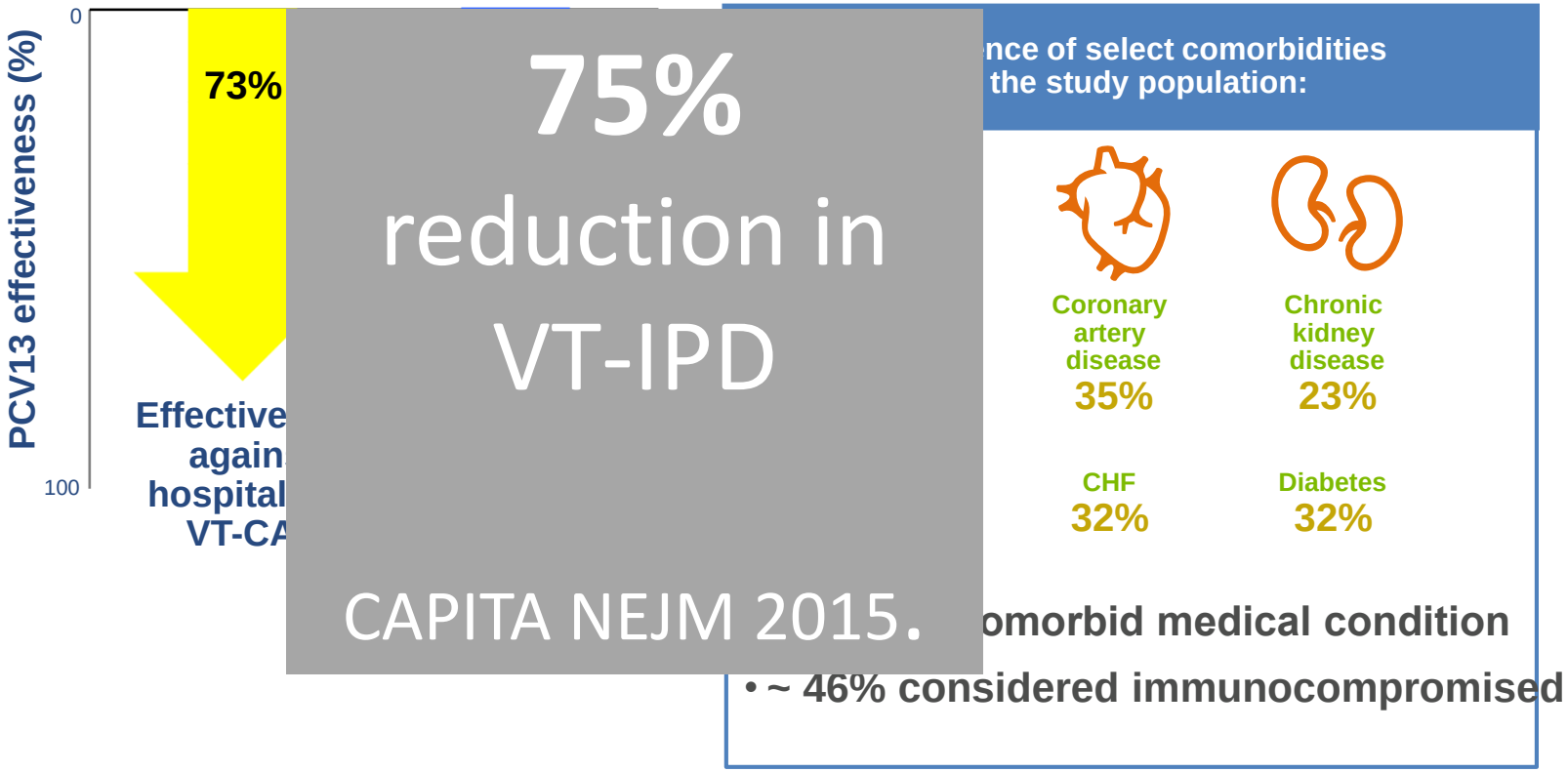
- Immunocompromised (all ages)
- 65 + years of age

Prevnar 13 (PCV13)

- **Advantages** (**conjugate** vaccine, T-cell dependent)
  - Prevents **IPD AND CAP**
  - Safe
  - **Good response in the very old**, immunocompromised and in children < 2 yrs of age
  - Immunologic memory
  - Booster effect on revaccination
  - Eliminates nasopharyngeal carriage (herd immunity)

- **Disadvantages**
  - Only covers 13 serotypes
  - **You don't use it very much in your patients, yet !**

PCV13 Reduces Vaccine Type VT-CAP in 65+ US adults, Including Those with Comorbidities



75%
reduction in
VT-IPD

CAPITA NEJM 2015.

1. McLaughlin JM, et al. *Clin Infect Dis.* 2018;67:1498-1506.

Streptococcus pneumoniae Serotyping and Antimicrobial Susceptibility Assessment for Vaccine Efficacy (SAVE) Study in Canada: 2011 - Present

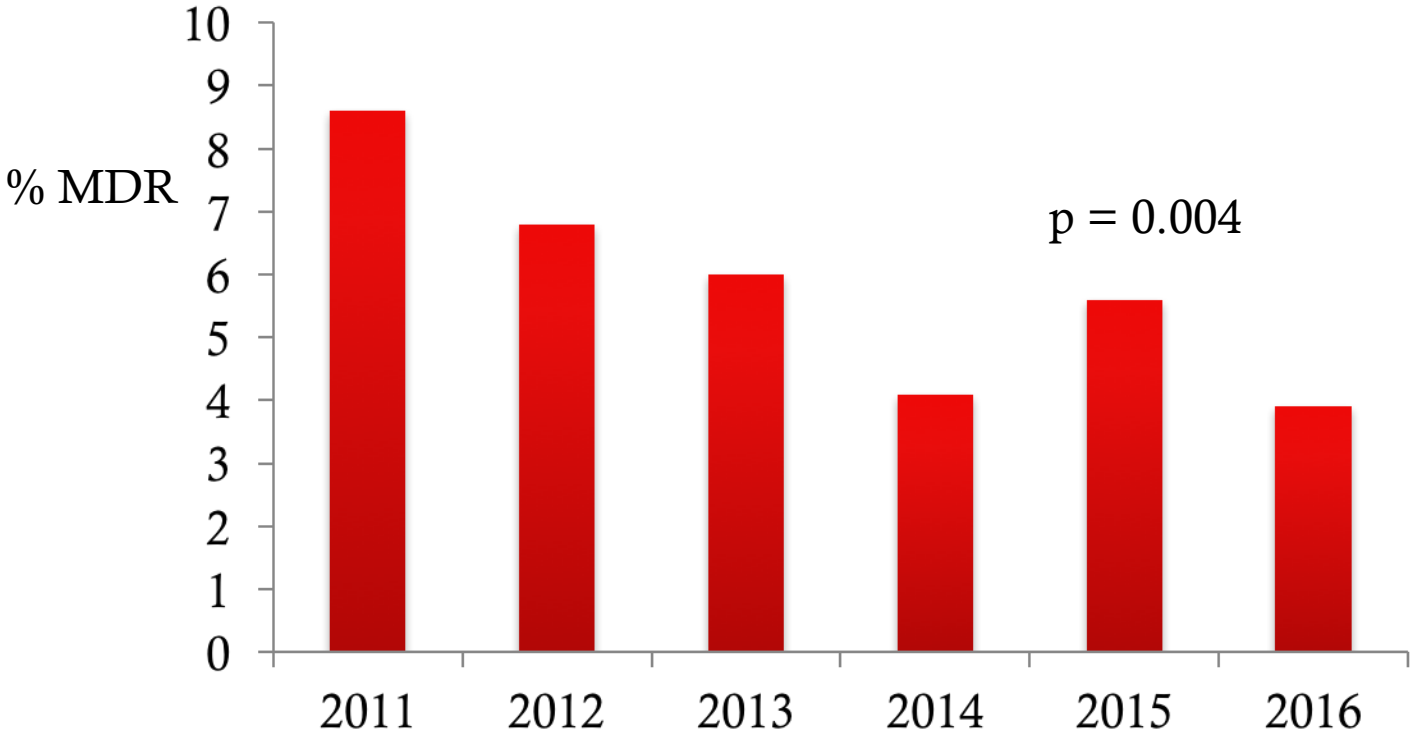
George Zhanel, Heather Adam, Mel Baxter, Alyssa Golden, Kim Nichol, Rachel Hink, Irene Martin, Walter Demczuk, Michael Mulvey, Matt Gilmour, Jack Johnson, Daryl Hoban the Canadian Antimicrobial Resistance Alliance (CARA) and James Karlowsky

A Partnership Between the Canadian Antimicrobial Resistance Alliance (CARA) and the National Microbiology Laboratory (NML) Winnipeg, Canada

Zhanel et al. JAC 2018.; Adam et al. JAC 2018.
Karlowsky et al. JAC 2018.; Golden et al JAC 2018.

CANADIAN ANTIMICROBIAL RESISTANCE ALLIANCE CARA

PCV13 is Reducing MDR *S. pneumoniae* Serotypes in Canada (SAVE 2011-2016)



Karlowsky et al. JAC 2018.; Adam et al ASM Microbe 2018.

CANADIAN ANTIMICROBIAL RESISTANCE ALLIANCE CARA

Who and How To Immunize With PPSV23 and PCV 13

Carole – 55 year old Immunocompromised

- 55 years of age, active and healthy
- Currently on anti-TNF therapy for severe plaque psoriasis
- No previous pneumococcal vaccination
- **Does she need PPSV23 and/or PCV13 ?**

NACI recommendation for pneumococcal vaccination for **high-risk** groups — at-a-glance

Risk Group	PCV13 Recommended	PPSV23 Recommended	PPSV23 Revaccination at 5 yrs
Adults with hematopoietic stem cell transplants (**HSCT**)	✔	✔	✔
Adults with **HIV**	✔	✔	✔
Adults with immunosuppressive conditions including:			
Asplenia (anatomical or functional)	✔	✔	✔
Sickle cell disease or other hemoglobinopathies	✔	✔	✔
Congenital immunodeficiencies*	✔	✔	✔
Immunosuppressive therapy†	✔	✔	✔
Malignant **neoplasms** including leukemia and lymphoma	✔	✔	✔
Solid organ or islet cell **transplant** (candidate or recipient)	✔	✔	✔

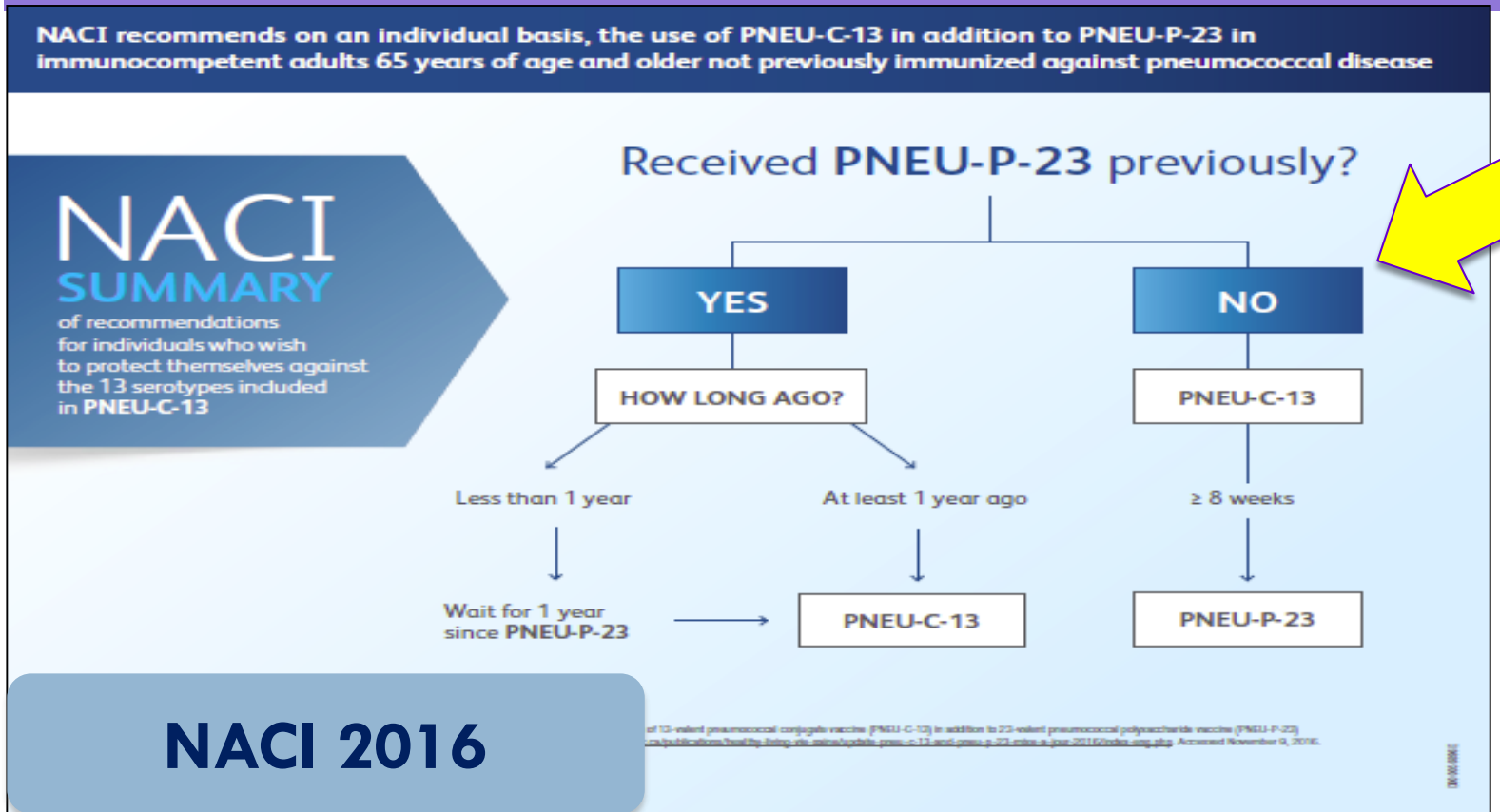
* Involving any part of the immune system, including B-lymphocyte (humoral) immunity, T-lymphocyte (cell) mediated immunity, complement system (properdin, or factor D deficiencies), or phagocytic functions.

† Including use of long- term **corticosteroids, chemotherapy, radiation therapy, post-organ-transplant therapy, and certain disease modifying antirheumatic drugs.**

Florence – Age 65 + (unknown vaccine status)

- 80 years of age
- Increasingly frail
- Used to walk several times a week, now quite sedentary
- Pneumococcal vaccination status unknown
- **Does she need PPSV23 and/or PCV13 ?**

NACI Says Consider BOTH PCV13 and PPSV23 at Age 65 +



Conclusions

- Risk factors for **influenza** and **pneumococcal** disease are similar

- *S. pneumoniae* infections (CAP and IPD) common

- Patients – **65+ yrs**, **immunocompromised**, **cormorbid diseases (< 65 yrs),** greatest risk

- Pneumococcal Vaccines
  - PCV13 (IPD and CAP)
  - PPSV23 (IPD)

Conclusions

- **Who** to Vaccinate:
  - **Influenza** all 6 mos +, **HD for 65+**
  - **PPSV23** (adults with comordid conditions, immunocompromised, ≥ 65yrs)
  - **PCV13** (immunocompromised, ≥ 65yrs, <65 yrs comorbid ?)
- **How** to Vaccinate:
  - PCV13 first, then ≥ 8 weeks PPSV23

Guidelines changing

NACI Recommended for Manitoba

Patient group	Influenza	PPSV23	PCV13
Children < 2 years	yes	no	yes
Adults – 18 + years immunocompromised	yes	yes	yes
Adults 65+ years	Yes HD YES	yes	Yes*
Adults – comorbid illness	yes	yes	Not yet