Unsung Benefits of Influenza Immunization

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Disclosures

• Member, Fluzone HD Advisory Board, Sanofi Pasteur Ltd.
• Speaker’s honoraria for unrestricted presentations from Pfizer and Sanofi-Pasteur in last two years
• Sanofi-Pasteur a sponsor of today’s meeting
• Content of this presentation solely the responsibility of WD Colby
Human Influenza

- Sudden onset fever, chills, cough and myalgia for 3-5 days
- Usually a minor illness in the young and healthy
- Often fatal in the elderly and those with cardiorespiratory disease
- Influenza is *not* vomiting and diarrhoea (but 25% of kids have that with influenza)
Influenza: A Serious Public Health Concern

Annually in Canada, influenza is estimated to cause:

- **180,000** Emergency Room visits
- **12,200** Influenza-related hospital admissions
- **3,500** Influenza-related deaths (highest among vaccine-preventable diseases)

A PHAC survey of CMOHs indicated that better influenza vaccines are a top priority

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4. https://d10k7k7mywg42z.cloudfront.net/assets/53bc4eed6af812ae000106//Influenza_Vaccination_Report_Final.pdf
5. Dr. John Spika, PHAC, Vaccine Industry Committee presentation, April 28 2015.
Figure I. Total number of influenza tests performed and percent of positive tests by report week: Ontario, August 27, 2017 to September 1, 2018

Source: These data have been obtained from the Public Health Agency of Canada’s (PHAC) Centre for Immunization and Respiratory Infectious Diseases (CIRID) respiratory virus detection tables as of September 5, 2018; they are based on data submitted to PHAC from 16 laboratories in Ontario.
Figure 3. Rate of reported laboratory-confirmed influenza per 100,000 population (and counts, in brackets), by public health unit: Ontario, September 1, 2017 to August 31, 2018

Rate per 100,000 population
- 66.7 - 83.0
- 83.1 - 111.0
- 111.1 - 143.1
- 143.2 - 192.0
- 192.1 - 232.2

Source: Ontario Ministry of Health and Long-Term Care (MOHLTC), integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario [2018/10/11]. Population Projections [2017–18], Ontario Ministry of Health and Long-Term Care, IntelliHEALTH ONTARIO, Date extracted: [2017/10/24].
Domino Effect of Influenza
Potential Complications of Influenza

DIRECT EFFECTS:
Respiratory

- Asthma & COPD exacerbations
- Ear/Sinus Infection
- Bronchitis and Pneumonia

INDIRECT EFFECTS:
Multi-Organ Systems

TRIGGER for:
- acute myocardial infarction and cerebrovascular disease

EXACERBATION of:
- hypertension, renal disorders and diabetes

References:
1. "Statement On Seasonal Influenza Vaccine For 2015-2016 - Public Health Agency Of Canada".
Influenza is Associated with Increased Risk of Acute MI

The incidence of acute myocardial infarction (AMI) is 6x higher in the 7 days post-influenza infection.

The incidence ratio (IR) for AMI was higher in 65+

- Age 65+ IR: 7.31 (4.53 – 11.79)
- Age <65 IR: 2.38 (0.59 – 9.66)

And in adults with no previous history of AMI

- No previous AMI IR: 6.93 (4.24–11.33)
- Previous AMI IR: 3.53 (1.12 – 11.14)

Incidence ratio (±95% CI) for acute myocardial infarction (AMI) following influenza infection, relative to control interval. Adapted from Kwong, J. C., et al. (2018). New Engl J Med, 378(4), 345-353.
Influenza is a possible trigger for stroke. Could influenza vaccination help prevent stroke?

- Investigators in the UK analyzed data from strokes suffered by approximately 18,000 adults from September 2001-May 2009
  - 86% were 65 years of age and older
- Self-controlled case series designed to minimize confounding variables
  - Rates of stroke in fixed time periods following influenza vaccination were compared to rate of stroke in a baseline period

Influenza vaccination was associated with a significant reduction in incidence of stroke in the first 59 days post-vaccination.¹

¹ Asghar Z, et al. Vaccine, 2015;33(41), 5458-5463
Influenza Vaccination Lowered the Risk of Major Cause-Specific Mortality

“Influenza vaccine is strongly associated with a lower mortality risk, not only for pneumonia and COPD, but also for other major cause-specific mortalities…”

Effect of Vaccination and Risk Status on Cumulative Mortality

(A) Cumulative all-cause mortality in HIGH-RISK study participants, stratified by influenza vaccination status prior to the study

(B) Cumulative all-cause mortality in LOW-RISK study participants, stratified by influenza vaccination status prior to the study

Canada’s Aging Population

Number of 65+ is projected to **double** in the next 20 years...

5.4 MILLION in 2013¹

11.1 MILLION in 2036¹

Proportion of 65+ already exceeds 14 years & under:

- **16.1%** on July 1, 2016
- **16.5%** on July 1, 2016


Ontario's Aging Population:

The number of individuals ≥65 years of age is projected to increase in the next six years:

- **2.2 million** in 2015
- **3.1 million** in 2025

Influenza in Adults ≥65
A Vulnerable Population

Older Canadians suffer disproportionately from influenza-related morbidity and mortality\textsuperscript{1}:

Adults 65+ represent 16.5\% of Canadians\textsuperscript{2}, but in the 2014-15 influenza season, they accounted for\textsuperscript{1}:

\begin{itemize}
  \item 70\% of hospitalizations
  \item AND
  \item 90\% of deaths
\end{itemize}

Influenza-attributed Mortality is Associated with Pre-existing Chronic Conditions

For persons aged 65 years and over, the risk for influenza-attributed death was:

- 5x greater among those with chronic heart diseases
- 12x greater among those with chronic lung diseases
- 20x greater among those with both chronic heart and lung conditions

It is imperative to prevent influenza in adults 65 years of age and older, especially those with comorbidities.
Influenza Prevention and Rx

- Vaccination
- Infection control
- Rapid multiplex PCR tests for viral antigens in nasal secretions are widely available
- Influenza A and B can be treated and outbreaks in chronic care facilities interrupted by administering oseltamivir (PO), zanamivir (inhaled) or peramivir (IV, adults)
Influenza $R_x$

- Uncomplicated, previously healthy: no treatment
- Uncomplicated but at risk: oseltamivir PO 75mg bid X 5 days
- Complicated$^1$: oseltamivir PO or zanamivir inhalational (IV for ICU)
- Most oseltamivir resistant$^2$ strains are sensitive to zanamivir
- Prophylaxis 75 mg PO OD X 10 days

1. Needing admission, hypoxia, lung infiltrate, CNS involvement etc.
2. Immunocompromised and previously treated with oseltamivir
Influenza Vaccine Effectiveness in Adults ≥65

Vaccination remains the best way to protect against influenza.

Nevertheless, a study spanning multiple influenza seasons found that vaccine effectiveness in adults 65+ is consistently lower, ranging from 62% - 76% for younger adults and 26% - 52% for adults ≥65.¹

Adapted from Monto, 2009.

Improving Influenza Vaccines

- Universal antigenic targets
- Broader antigenic spectrum
- Real time custom vaccine production
- “Live” attenuated vaccine (not available in Canada 2019-2020)
- Adjuvanted vaccine (may ↑ local reactions) **Fluad®**
- Increased antigen load vaccines **Fluzone HD®**
HD Safety: Frequency of Solicited Systemic Reactions, 0-7 Days Post-vaccination (FIM05)¹,²

1.1. FLUZONE® High-Dose Influenza Virus Vaccine Trivalent Types A and B (Split Virion) Product Monograph. Date of Approval: September 2015.
Relative Effectiveness of High-Dose Vaccine

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 et al performed analysis of CMS data from the 2012-2013 influenza season among the ~2.5 million Medicare beneficiaries comparing FLUZONE® High-Dose vaccine to standard-dose influenza vaccines

FLUZONE® High-Dose vaccine gave:

- 22% Better protection against probable influenza illness
- 22% better protection against influenza-related emergency department visits and hospitalizations

US Experience with High-Dose Vaccine

Fluzone High-Dose has been licensed in the US since 2009

70+ million
Approximate number of doses of Fluzone High-Dose distributed in the US since 2009¹

2016-17 influenza season,

60%
of adults 65+ in the US who receive an influenza vaccine vaccinated with Fluzone High-Dose

¹ Sanofi Pasteur Inc. Data on file. Fluzone High-Dose. Doses Distributed
When compared with standard-dose vaccine, high-dose influenza vaccine can reduce risk of respiratory-related hospital admissions from nursing home residents aged 65 years and older.

Published online July 20, 2017 http://dx.doi.org/10.1016/S2213-2600(17)30235-7
In summary, this study presents strong evidence that influenza has a major role in seasonal hospital admissions of older nursing home residents and, taken together with other similar studies of high-dose versus standard-dose vaccines, it seems that high-dose influenza vaccine can reduce this burden substantially better than a standard-dose vaccine.
At the individual level, NACI recommends that high-dose TIV should be offered over standard-dose TIV to persons 65 years of age and older. NACI concludes that, given the burden of disease associated with influenza A(H3N2) and the good evidence of better efficacy compared to standard-dose TIV in this age group, high-dose TIV should be offered over standard-dose TIV to persons 65 years of age and older.

There is insufficient evidence to make comparative recommendations on the use of MF59-adjuvanted TIV and QIV over standard-dose TIV.

*Canada Communicable Disease Report 44-6, June 7, 2018: Vaccine update
When available, IIV3-HD should be used over IIV3-SD, given the burden of influenza A(H3N2) disease and the good evidence of better efficacy compared to IIV3-SD in this age group [≥65].

There is insufficient evidence to make comparative individual-level recommendations on the use of IIV3-Adj or IIV4-SD over IIV3-SD or among IIV3-Adj, IIV3-HD, and IIV4-SD.

Thank-you!

people you protect when you get a Flu Shot

- Someone's cute baby
- Someone's Granny
- Someone's Mom who is an Obama
- Someone's kid
- Someone I love
- Someone's toddler
- Someone's promise
- Someone's babysitter
- Someone's Nurse
- Someone's teacher
- Someone's Nana
- Bella O'Malley