Fields-CQAM Thematic Program on Integrative Modeling of Emerging Infectious Disease Outbreaks

Estimates of COVID-19 and Influenza-Attributable Workplace Absenteeism

SANOFI PASTEUR

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Agenda

- Introduction to Sanofi Pasteur
- Influenza overview
- Impact of influenza on workplace productivity
- Problem: Estimating the impact of COVID-19 and influenza infections on workplace absenteeism

Sanofi Pasteur: Toronto Site

Sanofi Pasteur's Connaught Campus

- Located in Toronto
- 54 acres (22 hectares)
- Comprises **38 active buildings** that serve as office space, R&D labs, vaccine-manufacturing facilities and heritage sites
- Home to approximately **1,500 employees**

Sanofi Pasteur in Canada

- Founded in 1914, Sanofi Pasteur Canada is among the country’s **largest vaccine companies**, with a proud legacy of innovations in Public Health
- Researches, develops, manufactures and distributes vaccines for the Canadian, U.S. and international markets
- Every year, approximately **60 million doses** of vaccine are produced in Toronto and shipped around the world to **more than 60 countries**

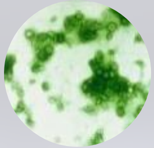
Sanofi's Investments in Canada's Life Sciences Sector

Building 100
- Announced in 2018
- Over $500M CAD investment - most Significant Life Sciences Investment In Canadian History at the time
- Will produce 5cP and diphtheria and tenatus vaccines, license approval for 5cP expected in 2024, diphtheria and tetanus in 2025
- Construction is complete

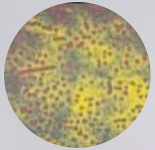
Building 200
- Announced in 2021
- $925M CAD investment in partnership with Government of Canada, Province of Ontario, and City of Toronto
- New, 200,000 sq ft, vaccine manufacturing facility in Toronto to manufacture high-dose influenza vaccine and pandemic influenza vaccine
- Construction beginning summer 2021, operational in 2026

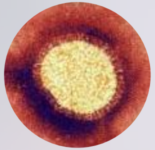
Sanofi Pasteur: Vaccine Portfolio Today

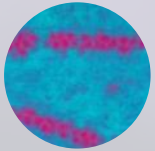
VIRAL DISEASES

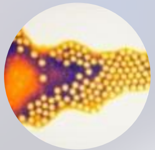

Dengue

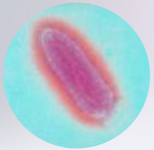

Hepatitis A

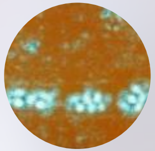

Hepatitis B


Influenza


Japanese encephalitis


Poliomyelitis


Rabies


Yellow fever

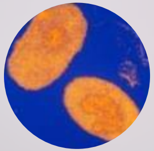
BACTERIAL DISEASES


Cholera

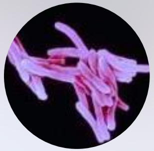

Diptheria

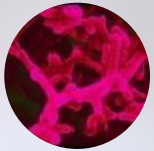

Haemophilus influenzae type b infection


Meningococcal meningitis


Pertussis


Tetanus


Tuberculosis


Typhoid Fever

Sanofi Pasteur: Support for Infectious Disease Modelling

Sanofi Pasteur and NSERC invest in $2.6 million collaboration at York University to combat infectious diseases with Math

January 23, 2018 Faculty of Science, Jianghong Wu, media release, NSERC

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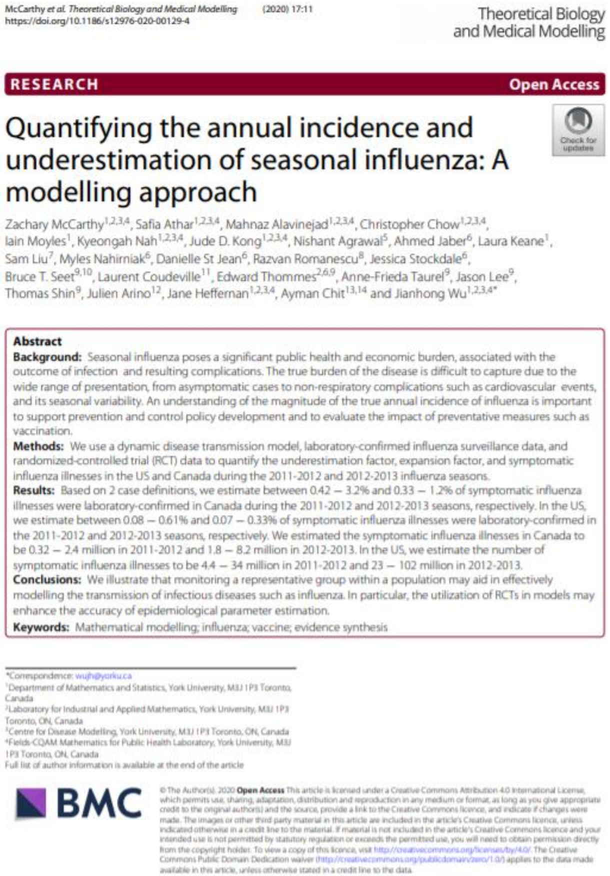
Better analysis of transmission key to targeting flu and childhood diseases

TORONTO, Jan. 23, 2018 – A major new research initiative based in the Faculty of Science at York University will develop mathematical techniques to identify populations most susceptible to infectious diseases and enable manufacturers to produce cost-effective vaccines that can be deployed quickly. The research is also expected to better position Canada to respond rapidly to emerging public health issues such as Zika outbreaks.

The $2.6-million NSERC/Sanofi Industrial Research Chair in Vaccine Mathematics, Modelling and Manufacturing, awarded to York University Distinguished Research Professor Jianhong Wu, was announced at York today. A professor in the Department of Mathematics & Statistics, Faculty of Science, Wu will lead a large team of York professors, post-doctoral fellows and graduate students.

Sanofi at the Industrial Problem-Solving Workshop (May 2019)



McCarthy *et al. Theoretical Biology and Medical Modelling* (2020) 17:11
https://doi.org/10.1186/s12976-020-00129-4

Theoretical Biology and Medical Modelling

RESEARCH Open Access

Quantifying the annual incidence and underestimation of seasonal influenza: A modelling approach

Check for updates

Zachary McCarthy[1,2,3,4], Safia Athar[1,2,3,4], Mahnaz Alavinejad[1,2,3,4], Christopher Chow[1,2,3,4], Iain Moyles[1], Kyeongah Nah[1,2,3,4], Jude D. Kong[1,2,3,4], Nishant Agrawal[5], Ahmed Jaber[6], Laura Keane[1], Sam Liu[7], Myles Nahirniak[6], Danielle St Jean[6], Razvan Romanescu[8], Jessica Stockdale[6], Bruce T. Seet[9,10], Laurent Coudeville[11], Edward Thommes[2,6,9], Anne-Frieda Taurel[9], Jason Lee[9], Thomas Shin[9], Julien Arino[12], Jane Heffernan[1,2,3,4], Ayman Chit[13,14] and Jianhong Wu[1,2,3,4*]

Abstract

Background: Seasonal influenza poses a significant public health and economic burden, associated with the outcome of infection and resulting complications. The true burden of the disease is difficult to capture due to the wide range of presentation, from asymptomatic cases to non-respiratory complications such as cardiovascular events, and its seasonal variability. An understanding of the magnitude of the true annual incidence of influenza is important to support prevention and control policy development and to evaluate the impact of preventative measures such as vaccination.

Methods: We use a dynamic disease transmission model, laboratory-confirmed influenza surveillance data, and randomized-controlled trial (RCT) data to quantify the underestimation factor, expansion factor, and symptomatic influenza illnesses in the US and Canada during the 2011-2012 and 2012-2013 influenza seasons.

Results: Based on 2 case definitions, we estimate between 0.42 – 3.2% and 0.33 – 1.2% of symptomatic influenza illnesses were laboratory-confirmed in Canada during the 2011-2012 and 2012-2013 seasons, respectively. In the US, we estimate between 0.08 – 0.61% and 0.07 – 0.33% of symptomatic influenza illnesses were laboratory-confirmed in the 2011-2012 and 2012-2013 seasons, respectively. We estimated the symptomatic influenza illnesses in Canada to be 0.32 – 2.4 million in 2011-2012 and 1.8 – 8.2 million in 2012-2013. In the US, we estimate the number of symptomatic influenza illnesses to be 4.4 – 34 million in 2011-2012 and 23 – 102 million in 2012-2013.

Conclusions: We illustrate that monitoring a representative group within a population may aid in effectively modelling the transmission of infectious diseases such as influenza. In particular, the utilization of RCTs in models may enhance the accuracy of epidemiological parameter estimation.

Keywords: Mathematical modelling; influenza; vaccine; evidence synthesis

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BMC

Influenza Overview

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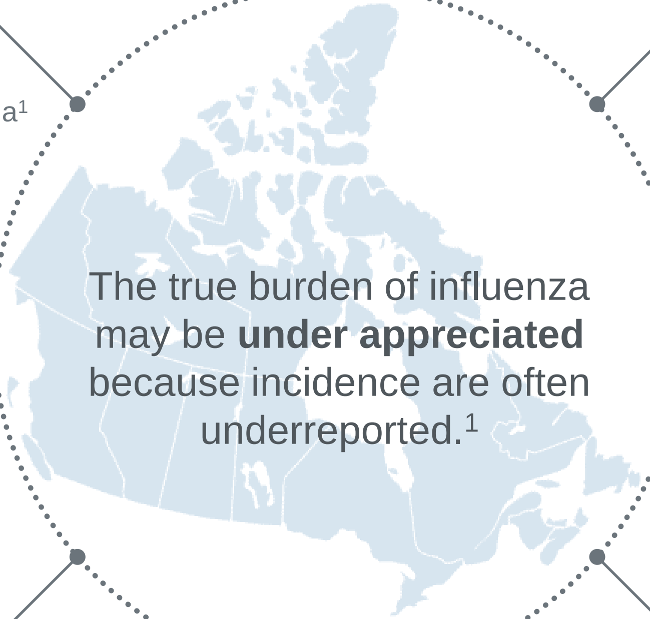
Influenza: Annual Impact on the Canadian Healthcare System

Influenza is estimated to cause
2,500,000
cases of illness annually in Canada[1]

Influenza also results in
3,500
deaths in Canada every year[2]



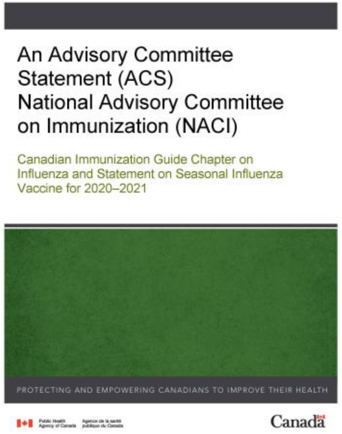
The true burden of influenza may be **under appreciated** because incidence are often underreported.[1]

Influenza also causes
12,200
hospitalizations[2] and
175,000
emergency department visits[2]

Influenza-related deaths are
highest
among vaccine-preventable diseases[3]

References: **1.** Somes MP et al. Vaccine 2018 May;36(23):3199–207. **2.** NACI. (2019). Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2019-2020. **3.** BCCDC. (2013). BC Influenza Prevention Policy: a discussion of the evidence

NACI Canadian Immunization Guide:
Chapter on Influenza and Statement on Seasonal Influenza Vaccine



Influenza vaccines are recommended for all individuals 6 mo and older, with particular focus on people at high risk of influenza-related complications or hospitalizations, including:

- Pregnant women
- **Individuals with chronic illnesses**
  - Cardiac or pulmonary disorders
  - Diabetes and other metabolic diseases
  - Cancer or immune compromising conditions
  - Renal disease
  - Rheumatologic disease
  - Neurologic or neurodevelopment conditions
  - Morbid obesity (BMI ≥40)
- Children (6-59 mo)
- Healthcare Workers
- Essential Community Workers
- Swine/ Poultry Worker
- Elderly (>65 yrs)
- Nursing home/ chronic care facility residents
- Close contacts of high-risk individuals
- Indigenous Peoples

Reference:
1. Advisory Committee Statement: Summary of the NACI Seasonal Influenza Vaccine Statement for 2020–2021. June 7, 2020.

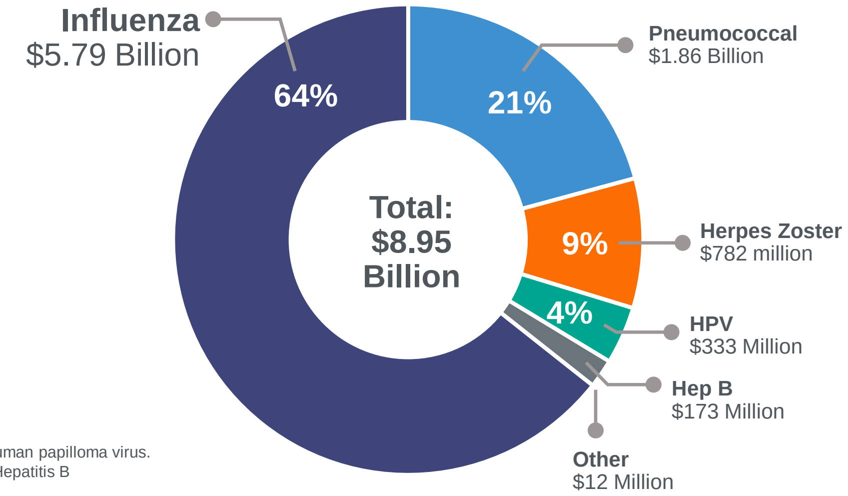
Economic Burden of Influenza

Among vaccine-preventable diseases, influenza has the highest costs, mostly incurred by adults 65+ years of age

Costs of influenza infection includes:

- **Medical costs:**
  Physician visits and Hospitalizations
  (20-30% of total costs)
- **Productivity Costs:**
  Absenteeism in school/ work place
  and loss of productivity
  (70 to 80% of the total costs)
- **Economic losses due to deaths**

Annual economic burden of vaccine-preventable diseases in the US, adults aged ≥19 years, by pathogen, 2015[1]



HPV= human papilloma virus.
Hep B=Hepatitis B

Reference: 1. Ozawa S, et al. Modeling the economic burden of adult vaccine-preventable diseases in the United States. Health Affairs. 2016 Oct 12;35(11):2124-32.

Influenza vaccinations among working age adults

NACI
National Advisory Committee on Immunization

Influenza vaccines are recommended for all individuals 6 months and older, with particular focus on people at high risk of influenza-related complications or hospitalizations[1,2]

Vaccination coverage rates for working age adults (18-64) are low

Vaccine Coverage Rate

Not all provinces provide universal vaccine coverage to working age adults[4]

There is a need to better understand indirect impact of influenza infections on workplace productivity to support policy discussion on increasing vaccine coverage and workplace vaccination programs

1) Zhao, L., et al. (2019). Can Commun Dis Rep, 45(6), 156-158. 2) Public Health Agency of Canada. (2018). 2016/17 Seasonal Influenza Vaccine Coverage in Canada. Accessed on November 6, 2018. 3) https://www.canada.ca/en/public-health/services/publications/healthy-living/2018-2019-influenza-flu-vaccine-coverage-survey-results.html 4) https://www.canada.ca/en/public-health/services/provincial-territorial-immunization-information/routine-vaccination-healthy-previously-immunized-adult.html

Impact of Influenza on Workplace Productivity

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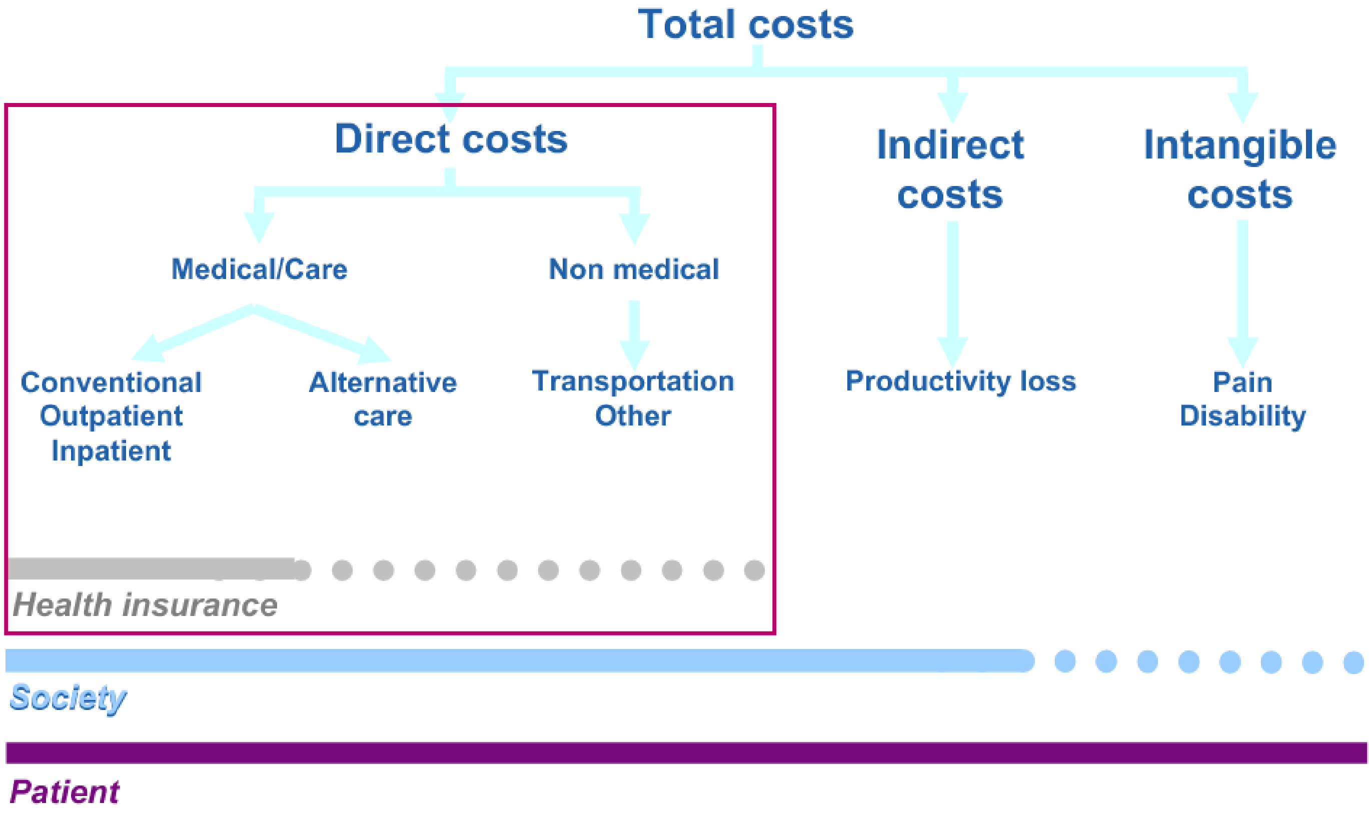
Cost of Influenza Infections



Methods of Ascertaining Indirect Impact of Influenza Infections

Impact of influenza on workplace productivity studied through different approaches

Surveillance/database studies

Examine workdays lost due to influenza from sources such as surveys, database analyses, observational studies, etc.

Health Economic Modelling

Estimate number of influenza cases in a simulated cohort and calculate total workdays lost and productivity losses

Regression Analyses

Statistical methods to estimate excess amount of workplace absenteeism attributable to influenza above the seasonal baseline

Overview of the Literature: Surveillance/Modelling Approaches

Methodology of Recent Publications

Number of working days potentially lost to influenza (International, 2019)[1]

- Estimated the potential **number of working days lost** to flu each year in individuals **aged 50-64 years** in better off countries
- Determined employment rate using data from the World Bank
- Assumed **that 3-5 working days were lost per case of influenza** based on available literature and assumed an **annual flu rate of 10%**
- Estimated total working days lost as follows: ***Working days lost = total infected × employment rate × working days lost per case***

Influenza resulted in **~159 million working days lost** in better off countries in 2018

Productivity loss due to lab-confirmed influenza (US-based, 2017)[2]

- Utilized data **from four annual studies of vaccine effectiveness** in which participants also completed a **questionnaire that assessed workplace productivity loss**
- Used **a linear regression model** to look at **association between influenza and productivity loss** while accounting for **vaccination status and other select covariates**

Influenza resulted in a **mean productivity loss of 69%** in employed adults

Costs to an employer associated with influenza (US-based, 2013)[3]

- Assessed **costs to an employer through indirect productivity losses** associated with influenza
- Conducted a **retrospective longitudinal analysis** of **two US databases** from 2005-2009
  - The MarketScan CCAE database, which includes **medical information** on employees from **over 100 US employers**
  - The MarketScan HPM database, which includes **details on absence** of a smaller proportion of that population

Costs due to **productivity losses associated with influenza per 100,000 employees** enrolled in a health plan increased from **26,479 USD in the 2005-2006 season to 122,811 USD** in the 2008-2009 season

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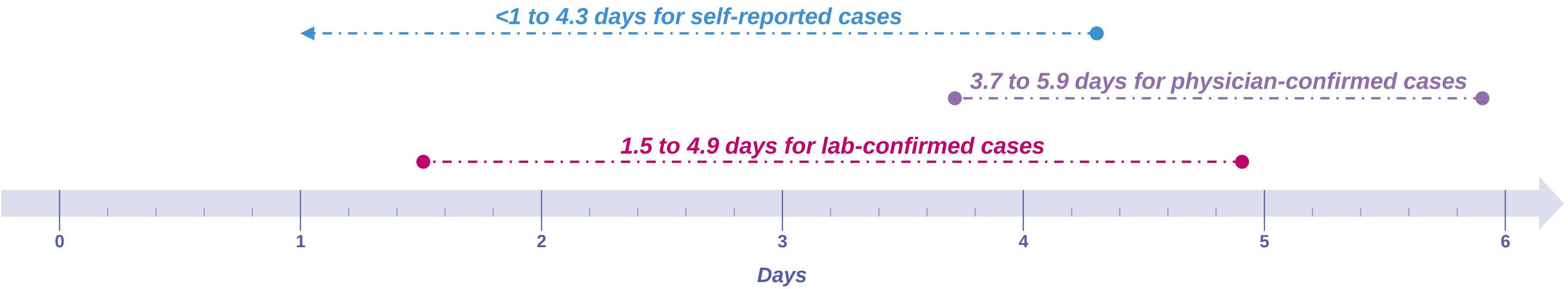
CCAE: Commercial Claims and Encounters Database; HPM: Health and Productivity Management; USD: US Dollars;
1. International Longevity Centre UK. 2019; 2. Van Wormer et al. 2017; 3. Karve et al. 2013; *See slide notes for full references*

Productivity Loss and Absenteeism due to Flu

Overview of the Available Literature

- A review of the literature published in 2008 identified 28 publications with study sites in **North America, Western Europe, Asia and Australia.**[1] The results from this review suggested that the **working days lost per case of influenza** ranged from:



- A **Canadian**, **nationally representative, telephone-based survey** conducted in 2008 included 1,009 households and looked at the **impact of episodes of ILI between January 1st and April 10-13th in 2008**. The survey determined **that ILI resulted in a median loss of 2 days (IQR: 1-5 days) of school or work per household.**[2]

ILI: influenza-like illness;
1. Keech et al. 2008; 2. Ammons et al. 2009; *See slide notes for full references*

Overview of the Literature: **Regression Approach**

Schanzer *et al. BMC Infectious Diseases* 2011, **11**:90
http://www.biomedcentral.com/1471-2334/11/90

BMC
Infectious Diseases

RESEARCH ARTICLE **Open Access**

Statistical estimates of absenteeism attributable to seasonal and pandemic influenza from the Canadian Labour Force Survey

Dena L Schanzer[1*], Hui Zheng[1] and Jason Gilmore[2]

1. Schanzer et al. 2011; *See slide notes for full references*

Schanzer et al (2011)

Methods: Data Sources

- Adapted previously established statistical models used to estimate the morbidity and mortality burden of influenza in order to estimate **workplace absenteeism rates** and the **proportion of potential hours worked that were lost** as a result of influenza

Statistics Canada's Labour Force Survey (LFS)

- Key variables related to absenteeism rates and the proportion of potential hours worked that were lost due to illness or disability, and employee characteristics

Public Health Agency of Canada's (PHAC) FluWatch Program

- Weekly number of laboratory confirmations for influenza A and B from September 1995 to February 2010

Statistical analysis focused on the 11 influenza seasons from the 1999-2000 season to the 2008-2009 season (as they have higher detection rates) and the one pandemic season from May 2009 to April 2010

1. Schanzer et al. 2011; *See slide notes for full references*

Schanzer et al (2011)

Methods: Statistical Analysis

Proportion of potential hours worked that were lost due to own illness or disability modeled as a function of **seasonality** (month), **secular trend**, and the **level of influenza activity** corresponding to the reference week

$$HL/PHW = \sum_{m=1}^{12} \beta_{1,m} Mon_m + \sum_{y=2009/10}^{1996/97} \beta_{2,y} FY_y + \sum_{y=2008/09}^{1996/97} \beta_{3,y} FluAr * FY_y + \beta_4\, fluBpp + \beta_5\, Pandemic2009 + \beta_6\, Hospadmsr + \varepsilon$$

HL = *Hours lost due to own illness or disability*

PHW = *Potential hours worked during the reference week for the category of interest*

$\beta_{1,m}$ = *Accounts for baseline seasonality with monthly indicator variables (*Mon_m*)*

$\beta_{2,y}$ = *Accounts for a general trend with indicator variables for each influenza season or flu year (*FY_y*) starting in Sept*

$\beta_{3,y}$ = *Accounts for lost hours due to influenza A infection, potentially varying by* FY_y

$FluAr$ = *Number of weekly influenza A laboratory confirmations for the reference week, seasonal only*

β_4 = *Accounts for the increase in hours lost due to influenza B infection*

$fluBpp$ = *Percent of tests positive for influenza B*

β_5 = *Accounts for any change in absenteeism behavior once the pandemic was announced, that was note related to the level of influenza activity*

β_6 = *Accounts for hours lost due to the H1N1/2009 pandemic strain*

$Hospadmsr$ = *Number of laboratory confirmed hospital admissions in the reference week*

1. Schanzer et al. 2011; *See slide notes for full references*

Schanzer et al (2011)

Methods: Statistical Analysis

Proportion of potential hours worked that were lost due to own illness or disability modeled as a function of **seasonality** (month), **secular trend**, and the **level of influenza activity** corresponding to the reference week

$$HL/PHW = \sum_{m=1}^{12} \beta_{1,m} M \ldots \quad \ldots 009 + \beta_6\, Hospadmsr + \varepsilon$$

A similar model was fit for the **absenteeism rates**, with the **proportion of employed persons who took time off work** due to their own illness or disability in the reference week **as the dependent variable**

HL = *Hours lost due to c*

PHW = *Potential hours*
reference week

$\beta_{1,m}$ = *Accounts for base*
variables (Mon_m

$\beta_{2,y}$ = *Accounts for a general trend with indicator variables for each influenza season or flu year (*FY_y*) starting in Sept*

$\beta_{3,y}$ = *Accounts for lost hours due to influenza A infection, potentially varying by* FY_y

$FluAr$ = *Number of weekly influenza A laboratory confirmations for the reference week, seasonal only*

ours lost due to influenza B

or influenza B

senteeism behavior once
, that was note related to
the level of influenza activity

β_6 = *Accounts for hours lost due to the H1N1/2009 pandemic strain*

$Hospadmsr$ = *Number of laboratory confirmed hospital admissions in the reference week*

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1. Schanzer et al. 2011; *See slide notes for full references*

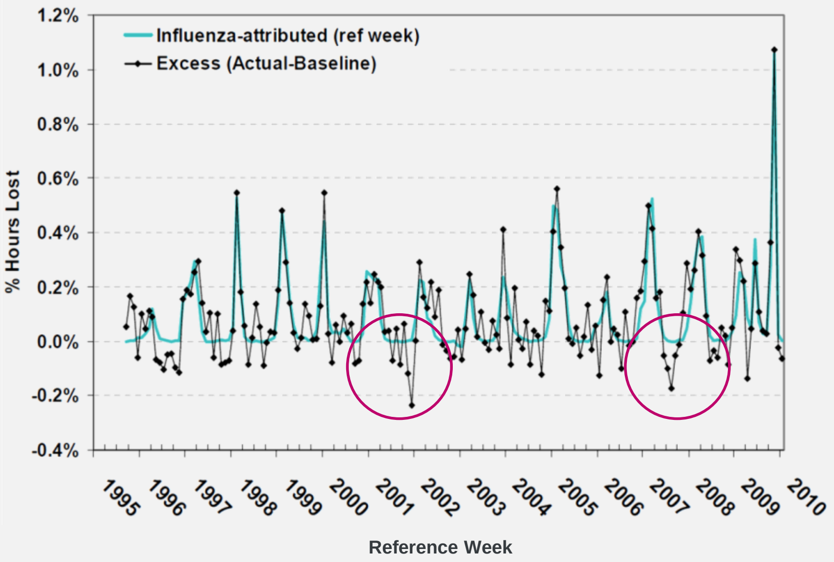
Schanzer et al (2011)

Results: Model Fit

- The **model fit is reasonable**, though the model seems to **miss the occasional dip in hours lost over the summer period**

- This figure compares the **actual hours lost less baseline (excess)** with the **model predicted hours lost less baseline**
- Proxy variables for the level of activity of other respiratory viruses were initially included in the model but were **dropped due to lack of power**
  - Previous models indicate that it is reasonable that **hours lost to other, non-influenza ILI** would be **captured in the seasonal baseline**

Comparison of the attribution of hours lost to influenza: assessing model fit



ILI: influenza-like illness;
1. Schanzer et al. 2011; *See slide notes for full references*

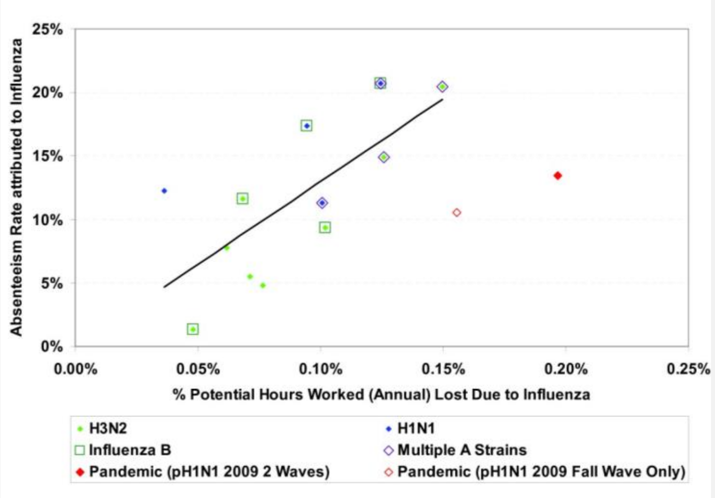
Schanzer et al (2011)

Results: Estimates by Season

- The **proportion of hours lost** due to influenza increases circulation of multiple viral strains

- In 50% of the seasons, absenteeism ranged from **7%-15%,** representing **0.07% to 0.11% of hours worked annually** (IQR)
- Absenteeism rate and hours lost appear well correlated, reflecting consistency of estimates
- Employees who took time off due to a seasonal influenza infection took an **average of 14 hours off per absence**. By comparison, the average absence was **25 hours for the pandemic strain**.

Workplace absenteeism attributed to influenza: seasonal, 1997/98-2008/09, and pandemic 2009



Age Group

1. Schanzer et al. 2011; *See slide notes for full references*

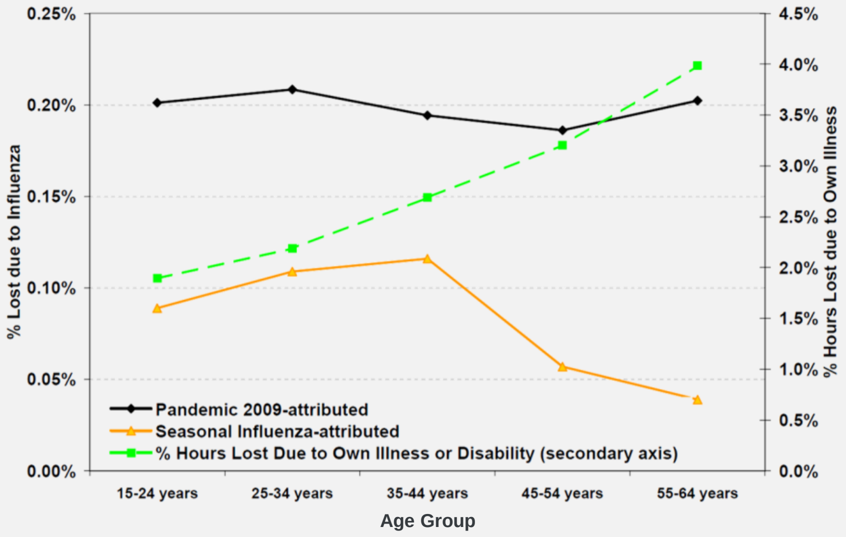
Schanzer et al (2011)

Results: Estimates by Age Group

- The **proportion of hours lost** due to one's own illness or disability (whether or not it is attributable to influenza) **increases significantly with age**

- The proportion attributable to influenza was **similar across age groups for the H1N1/2009 virus**, though the **statistical power to detect age-specific differences was poor**
- The level of influenza B activity was **significantly associated with hours lost in the younger age groups only** *(in previous figure)*, which accounts for higher estimated rates among younger workers for seasonal influenza

Percent of potential hours worked annually that were lost due to influenza illness by age group

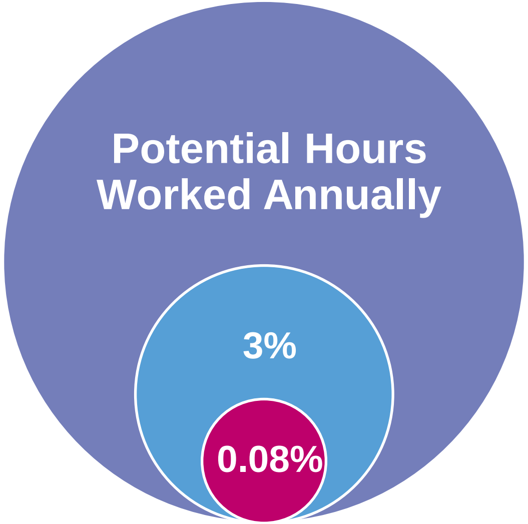


1. Schanzer et al. 2011; *See slide notes for full references*

Schanzer et al (2011)

Results: Proportion of Potential Hours Worked Lost Due to Influenza

- **Approximately 20 days per 100 full time employees are lost during a typical influenza season for a partially vaccinated population and 40 days during the pandemic period.**



Potential Hours Worked that were Lost Due to Own Illness or Disability (~3%) *

Potential Hours Worked that were Lost Due to Own Illness and Attributed to Seasonal Influenza*
(up to 0.2% for pandemic influenza)

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*Not to scale, for visualization purposes only.
1. Schanzer et al. 2011; *See slide notes for full references*

Problem Overview

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Productivity Loss and Absenteeism due to Flu

Why is Productivity Loss due to Influenza Important?

There are few studies that have investigated the **impact of seasonal influenza infection** on **productivity loss or absenteeism**[1,2]

Workplace absenteeism can contribute significantly to the **economic burden of influenza**[3]

Influenza-like illness (ILI) accounted for **39% of all illness-related workdays lost** in unvaccinated employees aged 50-64 years during the influenza season[4,*]

The **lack of Canadian data** on productivity loss attributable to influenza represents a **clear gap in the literature**[2]

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*In a US-based study where employees of the University of Minnesota were invited to participate via email. 497 participants were included of whom 85 (17.1%) experienced an influenza-like illness. Participants were enrolled in October 2006 and followed-up until April 2007.

1. International Longevity Centre UK. 2019; 2. Thommes et al. 2017; 3. Nichol et al. 2001; 4. Nichol et al. 2009; *See slide notes for full references*

Problem Solving Workshop Goals

How to accurately model the indirect burden of COVID-19 and influenza on workplace productivity/absenteeism?

- Very limited research performed in Canada on indirect impact of influenza and COVID-19

- Different approaches in deriving productivity impact estimates
  - Opportunity for novel research into impact of COVID-19, and update estimates for influenza
  - Potential to incorporate previous work on underestimation of influenza

- Results can help support public health decision making on increasing vaccine coverage of working-age adults and implementation of workplace vaccination programs to reduce the societal impact of influenza and COVID-19

THANK YOU

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