



Paving The Way for Immunization Innovation

About the Lung Health Foundation

The Lung Health Foundation is the leading health charity dedicated to improving lung health through a uniquely integrated approach that identifies gaps and fills them through investments in groundbreaking research and urgently needed programs and supports; policy and practice change; and promoting awareness about lung health issues affecting all Canadians.

Ontario Lung Association is a registered charity operating as the Lung Health Foundation.



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Letter from the President & CEO

The **Lung Health Foundation** is very excited about enriching our ongoing Breathing Policy Forum series with intimate roundtables that bring together the best minds to tackle pressing lung health issues in Ontario and beyond. Like the larger forum series, our roundtable sessions are aimed at developing creative and actionable solutions that will improve the state of healthcare. It's clear these solutions are needed now more than ever.

Seasonal influenza vaccination is the most effective thing that a Canadian can do to protect themselves from suffering the potentially deadly effects of the flu. But more can be done to cultivate innovations that are necessary to drive vaccine uptake up and drive the incidence of influenza (and its associational healthcare costs) down.

We believe that these challenges are not without practical and cost-effective solutions. This white paper is a result of the ideas and recommendations that came out of this gathering of healthcare providers, thought leaders and public health representatives.

When we create a space for conversation and collaboration, we empower ourselves to play a more profound role in public policy. To address the issue of building a system that champions vaccine innovation within the context of competing healthcare priorities and limited public health spending, collaboration among many stakeholders is key. The Lung Health Foundation is proud of the role it is playing in protecting Canadians against the flu and other preventable diseases.

A stylized, handwritten signature in black ink, appearing to read 'G Habib'.

George Habib
Lung Health Foundation

Setting the Context

Influenza (“the flu”) is a contagious viral infection. Although it can occur at any time throughout the year, the risk generally increases in the fall and peaks in the winter – a time period known as “flu season.”

While most dangerous to some individuals such as the elderly, young children, those with certain medical conditions and pregnant women, influenza can also result in hospitalizations, in otherwise healthy people. In Canada, it is estimated that around 12,200 hospitalizations and 3,500 deaths are a result of the flu each year.ⁱ

Experts agree that the best way to guard against influenza is to get the annual flu shot from a healthcare provider. But research indicates that vaccination rates aren’t increasing significantly. Flu shots may be easier than ever to get – Ontarians, for example, need only visit their local pharmacy for the shot – but many are still not taking advantage of the protection offered by the annual vaccine.

If Canada is to meet its flu vaccination coverage goal for high risk individuals (80%ⁱⁱ) and exceed the World Health Organization’s coverage goal (75%), innovative approaches to the promotion and delivery of influenza vaccines are required.

Challenges and Barriers

The biggest inherent barrier to innovation is the rapidly changing nature of the influenza virus itself. By now it is well known, even among laypeople, that protection offered from the flu vaccine varies from season to season depending on factors like how well the vaccine strains match with the circulating strains. The strains circulating in the population can even change during the time it takes to produce the annual flu vaccine (see Appendix B: How do new influenza vaccines get developed, recommended, and funded?).

Another challenging factor that affects the success of the vaccine is the health and age of the person on the receiving end of the shot. The most vulnerable people – young children, those over 65 years old, and those with underlying medical conditions – may not mount a strong enough immune response to the traditional influenza vaccine to provide good protection. Approaches to improve the response to vaccines in some of these populations do exist, and are publicly funded in some provinces.

The Perfect Influenza Vaccine

A universal flu vaccine doesn't exist – yet. It is likely many years away. The development of a single vaccine that provides safe, long-term immunity against the full spectrum of influenza viruses represents the ultimate innovation – and it will likely be arrived at incrementally with new advances in vaccine technology.

Herd Immunity

Herd immunity occurs when enough individuals are vaccinated that the circulation of a virus through the community decreases overall. This reduces the risk of infection for those who are not immunized, or for whom the vaccine does not work as well.

The potential for achieving herd immunity against influenza has been demonstrated in specific situations. In nursing homes, for example, vaccination of both residents and staff can be associated with reduced risk of influenza outbreaks.ⁱⁱⁱ

However, achieving broader population-level herd immunity requires a reasonably good vaccine match, or very high coverage rates. Neither requirement has been achieved in a substantial number of years.

The Current State of Influenza Immunization in Canada

The questions outlined below provide context for exploring innovative ideas that will support the accessibility and uptake of safe and effective flu vaccines:

Who is getting vaccinated against influenza, and who is most at risk?

During the 2017/18 flu season, only 38.3% of adults 18 to 64 years of age received the seasonal flu vaccine.^{iv}

Among adults 65 years of age and over, who are at increased risk for the complications of influenza due to their age, only 70.7% received their influenza vaccine in 2017/18, below that age group's national coverage goal of 80%."

Among adults 18 to 64 years of age who are at heightened flu risk due to one or more chronic medical conditions, vaccine coverage reached just 39.4% in 2017/18, well below that population's national coverage goal of 80%.^v

Where are Canadians getting vaccinated against influenza?

Among those Canadians vaccinated in the 2017/18 flu season, most received their shot in a pharmacy (34.2%) or doctor's office setting (30.4%).^{vi} Other common sites included temporary vaccine clinics, hospitals, and workplaces.

It's important to note that pharmacists have only been authorized to deliver the flu vaccine in certain provinces, and not in any of the territories.

How can we increase vaccination rates and reduce the burden of influenza?

2017/18 adult flu vaccine coverage estimates showed little growth compared to the coverage estimates of the previous two seasons.^{vii}

Reasons for low coverage include general vaccine hesitancy and lack of understanding of the importance of vaccination for protecting both the individual and the community. In 2017/18, the most commonly reported reasons for avoiding the flu shot were a fear of getting sick from it and simply believing that the vaccine is not necessary, at 38.3% and 22.4% respectively.^{viii}

There is a significant opportunity to increase coverage through public education and promotional efforts. Based on research by the Public Health Agency of Canada, being exposed to three or more sources of flu vaccine messaging was significantly associated with uptake in the 2017/18 flu season.^{ix}

In the policy recommendations that follow, we will suggest strategies to support effective communication with the public about the safety and effectiveness of the flu vaccine.

Farm to Table: Rethinking Egg-Based Vaccines

INNOVATION SPOTLIGHT

Chicken eggs have played a key role in flu vaccine development for more than 70 years. The traditional egg-based production method involves injecting the virus into fertilized eggs, which are incubated to allow the virus to replicate. The virus is then removed, inactivated, and the antigen is refined. Further purification and testing follows.

Egg-based vaccines save lives and reduce the burden of influenza. But what if alternative production innovations could solve some of the method's greatest challenges?

There are three main challenges inherent to egg-based vaccine production. First, the technique requires approximately six months to produce a vaccine, during which time the circulating virus can mutate so much that it is no longer a good match to the vaccine strains. Secondly, it requires a large supply of eggs. And finally, as the virus grows in eggs, it can develop mutations that make it different from, and therefore less effective against, the circulating strain.

Newer alternative vaccine development methods – like a process that swaps chicken eggs for cultured mammalian cells, or makes use of insect cells or tobacco plants to develop vaccines – can produce effective vaccines while greatly reducing manufacturing times.

High Hopes: Ontario Offers Seniors a High-Dose Influenza Vaccine

INNOVATION SPOTLIGHT

No group of Ontarians bears the burden of the flu more seriously than senior citizens. So when the province announced that it would be publicly funding a high-dose influenza vaccine with four times the amount of antigen than the standard vaccine, experts considered it an effective strategy to increase protection against influenza for seniors.

The need to offer a vaccine with more robust protection has long been clear: seniors who become infected are at a much higher risk of the flu's most serious complications. And weaker immune responses to the standard vaccine dose often leave seniors at risk even after they have been immunized.

But even in the case of the high-dose flu vaccine, the journey from research to development to market to provincial funding has been lengthy. Licensed for use in the United States since 2009, the product wasn't licensed in Canada until 2015 and didn't achieve provincial funding until Ontario opted to offer it to its seniors during the 2018/19 flu season.

The high-dose vaccine has been shown to be 24%^x more effective than the standard-dose vaccine at preventing influenza in older adults, but more than five years passed between its debut in the United States and its licensure for use within Canada.

Our Policy Recommendations

Our policy recommendations pave the way for vaccine innovation by highlighting opportunities in three key areas: evaluation, delivery, and awareness.

Opportunity 1

Find the Best Vaccines by Harmonizing the System of Public Funding and Elevating Effectiveness Studies

- As has been demonstrated, there are several challenges with ensuring the effectiveness of influenza vaccines due to the changing nature of the virus, the immune response of certain individuals, and the manufacturing methods used.
- For this reason, we must ensure that Canada's funding environment is allowing for prompt access to innovative new vaccines that have proven to be safe and effective

RECOMMENDATION 1

To facilitate consistent and prompt funding of market authorized vaccines across the country, we recommend that a centralized coordinating committee makes funding decisions for the entire country.

- Provinces and territories face a number of challenges when introducing new vaccines into their publicly funded immunization programs. These include: fiscal constraints, a lengthy centralized procurement process, and a budgeting system that makes it difficult to fund new vaccines.
- Inconsistencies in publicly funding new vaccines across the country can delay the public from accessing vaccines that have demonstrated safety, effectiveness, and cost-effectiveness.
- To minimize the gap between market approval and provincial/territorial funding we recommend that a single, harmonized, coordinating committee with provincial, territorial, and federal representation replaces the existing system where each province and territory decides which influenza vaccines to fund.^{xi}

- The purpose of this committee will be to examine the recommendations made by the National Advisory Committee on Immunization (NACI) to decide which vaccines should be publicly covered.
- This should be tied with federal transfers to the provinces and territories to assist in the implementation of a consistent program across the country. Transfer payments will also serve as an incentive for the provinces/territories to accept the changes to the decision-making structure and the decisions of the coordinating committee.^{xii}

RECOMMENDATION 2

The federal government should encourage innovations in influenza vaccines by publicly funding pilot projects.

- We recommend that pilot programs are publicly funded in select jurisdictions so that real world data on the effectiveness and safety of new vaccines can be gathered.
- Collecting real world data on vaccines post-market authorization will help the coordinating committee ensure that vaccines are working as expected and provide additional data to support preferential use of certain products.
- By gathering data on which vaccines are the most effective in reducing the incidence of influenza and its complications, cost-effective decisions can be made that maximize health benefits.

Opportunity 2: Improve and Standardize Flu Vaccine Delivery

RECOMMENDATION 3

To increase uptake, we recommend standardizing pharmacist's ability to provide vaccinations across Canada.

- Some of the gain in vaccination uptake in Canada over the past three years can be attributed to pharmacists being able to administer vaccinations.
- A study conducted by Isenor et al. (2018) found that in Nova Scotia, after pharmacists were permitted to administer vaccines, influenza vaccine coverage increased from 35.7 to 41.7%.^{xiii}
- Despite this, policies across provinces and territories regarding who is able to deliver vaccinations are inconsistent. We recommend that Nunavut, the Northwest Territories and the Yukon implement policies allowing pharmacists to administer influenza vaccines.

RECOMMENDATION 4

Adopt an incentive-based model for physicians and pharmacists.

- Adopting an incentive-based model will encourage healthcare providers to educate patients regarding the influenza vaccine.
- For example, the Centers for Disease Control and Prevention in the United States developed the Assessment, Feedback, Incentives, and eXchange (AFIX) model with the goal of increasing vaccination uptake in children and adolescents. This model is implemented by individual states.^{xiv}
 - » The AFIX model makes healthcare providers aware of the immunization rates in their practice as well as missed opportunities to vaccinate. In addition, it rewards healthcare providers for improved performance.
- We recommend that the provincial/territorial governments implement a similar system whereby healthcare practitioners are rewarded for vaccinating vulnerable populations including young children, older adults, pregnant women, and those with underlying medical conditions.
- In addition, for provinces where influenza vaccines are publicly funded for all individuals 6 months of age and older, incentives should be given for improvements in overall vaccination rates.

RECOMMENDATION 5

Develop province-wide vaccination registries whereby the type of vaccination individuals receive are documented.

- We recommend that each province develop a vaccination registry that records the type of vaccination individuals have received. This will facilitate the process of evaluating effectiveness among different population groups and seasons.
- The registry should be linked to lab reporting of influenza and accessible to healthcare practitioners reporting adverse events.
- In addition, a registry can be used to monitor coverage, and determine which demographic requires additional efforts to promote uptake of influenza vaccines, and allow for the evaluation of safety.
- Currently:
 - » Each province and territory has its own system for tracking immunization. In most provinces/territories this data is only collected for children. However, the data collected varies by jurisdiction and is not always kept electronically.^{xv}
 - » Provinces such as Ontario, Manitoba, and B.C. utilize the 'Panorama' registry, which varies from province to province. However, there are significant data gaps and challenges with the system.

Opportunity 3:

Build Public Awareness

RECOMMENDATION 6

Frame public immunization campaigns in a manner that projects the effectiveness and safety of vaccinations

- There is a need to address vaccine hesitancy and refusal by raising awareness regarding the importance, benefits, and safety of vaccines. To do this, we recommend that careful attention is given to how vaccine messages are framed.
- How information about vaccine effectiveness is framed can have an impact on how it is interpreted. For example, saying a vaccine is 50-60% effective against influenza may be less impactful than saying that individuals who receive the vaccine are only half as likely to get influenza compared to those who do not.

Appendix A:

Comparing publicly-funded flu vaccines in Ontario (2018/19 season)

Product	What is it?	Who is it funded for? Where can one get it?	Where can one get it?
Quadrivalent Inactivated Vaccines <i>FluLaval®</i> <i>Tetra, Fluzone®</i> <i>Quadrivalent</i>	A vaccine given with a needle via intramuscular injection, usually in the arm. It protects against four influenza strains.	All Ontarians 6 months and older.	<p>Ontarians 5 years of age and older can receive the shot from a trained pharmacist in a pharmacy setting, from a healthcare provider in a clinic setting, and in various other places like long-term care homes, workplaces, hospitals and community health centres.</p> <p>Young children must receive the shot from a physician or nurse.</p> <p>Children 6 months to 8 years of age who have not previously received an influenza vaccine require two doses of the vaccine, given at least four weeks apart.</p>
Quadrivalent - Live Attenuated Influenza Vaccine (Q-LAIV) <i>FluMist®</i> <i>Quadrivalent</i> Note: this will not be available during the 2019/20 flu season	A vaccine given by nose via a prefilled single use sprayer.	All Ontarians between the ages of two and 17.	<p>A physician or nurse practitioner can administer the nasal mist to all ages indicated. Pharmacists can administer the vaccine to children 5 years and older.</p> <p>Children 2 to 8 years of age who have not previously received an influenza vaccine require two doses of the vaccine, given at least four weeks apart.</p>
High-Dose Trivalent Inactivated Vaccine (High-Dose TIV) <i>Fluzone®</i>	A vaccine given with a needle via intramuscular injection, usually in the arm. It contains a higher quantity of the antigens for the three strains, compared to these strains in the QIVs.	All Ontarians aged 65 years and older.	<p>In the 2018/19 flu season, the high-dose vaccine was not available in pharmacies. It was available through primary care providers (e.g. physicians and nurse practitioners), participating retirement homes, long-term care homes and hospitals.</p> <p>This may change in future flu seasons.</p>

Appendix B:

How do new influenza vaccines get developed, recommended, and funded?^{xvi}

World Health Organization (WHO)

Based on global data from more than 100 institutions, the WHO identifies the influenza strain(s) most likely to make people sick in the coming year and makes its recommendations on the composition of the flu vaccine.



Vaccine Manufacturers

Based on viral strain(s) received from the WHO, manufacturers create the vaccine. Clinical trials ensure that the vaccine is safe and effective.



Health Canada

Once a manufacturer has sufficient scientific evidence that their new vaccine is safe and effective, they must apply for market approval. Further testing takes place, which may include evaluation of the manufacturer's production process and facilities. If the benefit of the vaccine is found to outweigh its risks, it is authorized for sale and use in Canada.



Public Health Agency of Canada (PHAC)/ National Advisory Committee on Immunization (NACI)

Scientific recommendations on the vaccine's use are made by NACI, an advisory committee within PHAC that includes experts in the fields of pediatrics, infectious diseases, immunology, medical microbiology, internal medicine and public health.

An example of a scientific recommendation might be the identification of groups at risk of influenza for whom vaccine programs should be targeted – for example, identifying that the high-dose vaccine provides superior protection for seniors compared to standard dose vaccine.



Provincial and Territorial Governments

Each province/territory must decide whether to fund the new vaccine. Ontario, for example, considers scientific evidence, frequency, severity of disease, cost-effectiveness, acceptability (public and stakeholder perspectives), and equity/ethical and legal considerations when deciding whether to fund a new vaccine.

Constant Surveillance

Safety, quality, and efficacy of an influenza vaccine is evaluated at multiple steps throughout the drug's journey from lab to needle.

How the Process Differs for Existing Vaccines

Since the flu vaccine must change every year, manufacturers of existing vaccines must still send updated information on their manufacturing process with the selected strains as well as data from small clinical trials to demonstrate that the vaccine they have produced is able to stimulate the immune system of vaccinated individuals. A group within Health Canada conducts an expedited review of the data and authorizes these modifications.

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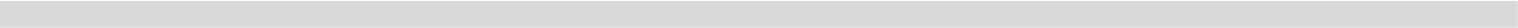
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