Flu Vaccines for Older Adults: Decoding the Latest Recommendations

November 2024

This initiative was made possible through the financial support of Sanofi and the opinions expressed are those of its authors and do not necessarily reflect the views and opinions of Sanofi.

Table of Contents

Executive Summary

Influenza poses a significant health threat to Canadians, particularly adults aged 65 and older, who face higher rates of severe illness, hospitalization, and mortality. While influenza is vaccine-preventable, recent changes to the National Advisory Committee on Immunization (NACI) recommendations for adults 65+ have implications for provincial vaccination programs and clinical practices. This white paper, developed through an evidence review and expert consultation, addresses the challenges posed by these new recommendations and outlines opportunities and strategies to protect older adults through vaccination.

Key Messages

Burden of Influenza: Adults 65+ are disproportionately affected by influenza, accounting for higher rates of complications and deaths.

Vaccine Options: Several enhanced influenza vaccines are available for older adults, but comparative effectiveness data are limited.

NACI Guideline Changes: Recent updates recommend any enhanced vaccine (high dose, adjuvanted, or recombinant) for adults 65 and older, without preferential recommendation.

Implementation Challenges: Healthcare providers face difficulties in interpreting and applying the new guidelines into clinical practice and accessing an adequate supply of enhanced influenza vaccines.

Key Recommendations

Improve Vaccine Accessibility: Ensure access to enhanced vaccines across all Canadian provinces for all older adults.

Develop Individual-Level Recommendations: Provide individual level recommendations to support healthcare providers with creating stronger, personalized vaccine recommendations for people at highest risk of influenza.

Prioritize Evidence-Informed Decision Making: Prioritize scientific evidence favoring improved health outcomes over cost considerations in vaccine recommendations.

Enhance Provider Education: Provide clear, concise scientific updates on new influenza vaccine recommendations to support informed clinical decisions and optimize appropriate vaccine delivery.

Equip Providers with Comprehensive Patient Communication Tools: Equip healthcare providers with resources to effectively discuss vaccine options.

Maintain Transparency and Trust: Ensure consistent public messaging about vaccine recommendations while being transparent about the ongoing review of evidence and any changes to guidelines.

Fund High Quality Comparative Trials: Fund randomized controlled trials comparing enhanced influenza vaccines to identify optimal vaccines for older Canadians.

Background & Context

What is Influenza and how does it impact adults ages 65 and older?

Influenza, commonly known as the flu, is a highly contagious respiratory illness caused by influenza viruses. It can lead to mild to severe illness, but hospitalizations and deaths due to influenza are highest in older Canadians.

For adults 65 and over, influenza can have serious consequences for several reasons:

Influenza is estimated to cause about 12,200 hospitalizations [6] and 3,500 deaths [7] annually in Canada, with the majority of these deaths occurring in older Canadians [8].

- **Immune systems weaken with age:** As people age, their immune system tends to weaken, making it harder to fight off infections like the flu [1].
- **Immune responses to standard dose influenza vaccines are lower:** Standard dose influenza vaccines have lower effectiveness and insufficiently protect older adults, which is why specially-designed vaccines for older adults are crucial to provide the best protection.
- **A higher risk of complications exists:** Older adults are more susceptible to experiencing complications from influenza, such as pneumonia, bronchitis, sinus infections, cardiovascular events and worsening of chronic health conditions (e.g., asthma, diabetes, heart disease). They also have more comorbidities that can increase their risk of infection.
- **A significant loss of functional independence can occur:** When older adults get the flu, they are at significant risk of not recovering back to their baseline and requiring assistance with performing activities of daily living. 1 in 3 lose function and 50% of those will not recover their function at 6 months and beyond [2].
- **Hospitalization rates increase with age:** This age group has >6X higher hospitalization rates due to severe flu symptoms and complications compared to adults ages 45-64 years old [3].
- **Older adults experience the highest mortality rates**: Older adults have the highest rates of influenza-related deaths at 108.8 per 100 000 vs 4.0 per 100 000 in 50-64 year olds [4]. In H3N2 dominant seasons, >80% of influenza-associated deaths occurred in adults 65+ [5].

What influenza vaccines are available for older Canadians and what evidence currently exists to support the use of enhanced influenza vaccines?

In Canada, there are several influenza vaccines authorized and available for use in adults 65 years of age and older:

- High-dose inactivated influenza vaccine
- Adjuvanted inactivated influenza vaccine
- Recombinant influenza vaccine
- Standard dose inactivated influenza vaccines

In the 2024 Supplemental Guidance on Influenza Vaccination in Adults 65 years of Age and Older, NACI conducted an updated evidence and economic review to determine whether any age-appropriate influenza vaccine(s) should be preferentially used in adults 65+ [5].

In the statement, NACI summarized findings from independent reviews conducted by the Advisory Committee on Immunization Practices (ACIP) and the Drug Safety and Effectiveness Network's Methods and Applications Group for Indirect Comparisons (DSEN MAGIC). Consistent with their previous review in 2018, NACI found that:

1

HIGH DOSE
Strongest supporting evidence with systematic reviews and randomized controlled trials (RCTs) showing superior efficacy [5, 9-13].

2

ADJUVANTED
Second most evidence-supported influenza vaccine [5, 14].

3

RECOMBINANT
Third most supported influenza vaccine [5, 15].

4

STANDARD DOSE
All 3 enhanced vaccines are more effective than standard dose vaccines. [5]

Due to limited high quality or randomized studies directly comparing high dose, adjuvanted, and recombinant vaccines, no definitive conclusion was reached regarding superiority of one vaccine over the other, although the high dose vaccine had the most substantial body of evidence.

Vaccines designed to enhance protection in older adults, commonly referred to as "enhanced vaccines", include high-dose, adjuvanted and recombinant vaccines. All have been shown to offer superior protection compared to standard-dose vaccines for older adults.

What does NACI Recommend?

The National Advisory Committee on Immunization (NACI) is Canada's authoritative body for vaccine recommendations and their approach to vaccine guidance has evolved over time.

Evolution of NACI's Framework

- **Prior to 2019:** NACI focused primarily on disease burden, vaccine efficacy and effectiveness, immunogenicity, and safety.
- **Post-2019:** NACI expanded its scope to include ethics, acceptability, feasibility, economics and equity.

2024/2025 NACI Guidelines for Influenza Vaccination Older Canadians

NACI has updated its guidelines for influenza vaccination in adults 65 years and older [5]. Key changes include:

- **Enhanced Vaccines Preferred:** NACI now recommends the use of any of the following enhanced influenza vaccines for older adults:
  - High-dose vaccine
  - Adjuvanted vaccine
  - Recombinant vaccine

- **No Specific Preference Among Enhanced Options:** NACI does not express a preference for any enhanced vaccine over the others.

- **Standard Dose as Backup:** If none of the enhanced vaccines are available, any age-appropriate standard dose influenza vaccine should be used.

- **Removal of Individual vs. Programmatic Recommendation:** NACI has combined its previously separate individual and programmatic recommendations into a single guideline.

- **Emphasis on Vaccination:** NACI's overall key message is that receiving any approved influenza vaccine is better than no vaccination.

Key Changes from Previous Guidelines Impacting Recommendations

Previous guidelines gave a preferential recommendation for the high-dose vaccine at the individual level. The distinction between individual and programmatic recommendations has been removed.

The Challenges

The new NACI recommendations pose several challenges:

- **Interpretation Complexity**: The shift from separate individual and programmatic recommendations to a combined guideline may create confusion for patients and healthcare providers who previously relied on individual level recommendations.

- **Lack of Preferential Recommendation:** Unlike previous guidelines that favored high-dose vaccines, the new recommendations do not express a preference among available enhanced vaccines, potentially complicating decision-making for healthcare providers, patients, and provincial governments.

- **Evidence Gaps:** While all enhanced vaccines (high dose, adjuvanted, recombinant) are recommended, the depth of supporting evidence for each vaccine varies. Although high dose vaccines have the most substantial body of evidence, limited studies directly comparing high dose vs adjuvanted vs recombinant vaccines makes it challenging to definitively determine the most effective option.

- **Patient Education**: Healthcare providers may face difficulties in explaining the changes to patients, especially those who were previously recommended to and/or received high-dose vaccines. The potential mixed messaging may cause confusion and decrease vaccine confidence and uptake.

- **Resource Allocation:** With multiple enhanced vaccine options now recommended equally, healthcare systems and providers may struggle with decisions about which vaccines to stock and offer.

- **Individualized Care**: The removal of individual-level recommendations and lack of specificity amongst enhanced vaccines may make it more challenging for healthcare providers to tailor their vaccine recommendations to address specific patient needs and preferences.

Ensuring **equitable access** to enhanced vaccines remains a significant challenge across provinces.

- **Implementation of New Guidelines:** Healthcare systems and providers will need to adapt their practises and potentially update their protocols to align with the new recommendations.
- **Vaccine Availability:** There is usually a suboptimal supply of enhanced vaccines across provinces to meet the demand. When enhanced vaccines are in limited supply, it can be challenging to ensure equitable access to the optimal vaccines across different healthcare settings and geographic regions.
- **Cost Considerations:** With multiple enhanced vaccines now recommended, there may be challenges in balancing cost-effectiveness with the desire to offer a vaccine with the most clinical benefit.

> ***"The problem is inadequate enhanced vaccine purchase and distribution by provinces which creates the moral dilemma between offering a standard-dose vaccine or the patient potentially being unvaccinated." -*** **Dr. Sherilyn, Houle**

- **Ethical Challenge:** NACI now recommends the use of enhanced vaccines (high-dose, adjuvanted, or recombinant) over standard dose vaccines for older adults. However, if enhanced vaccines are not available, healthcare providers have to decide whether to offer standard-dose influenza vaccines (which are less effective in older adults) or wait until an enhanced vaccine is available. In this scenario, patients should discuss their individual needs, risks and priorities with their healthcare provider to determine the optimal flu vaccine strategy.

These challenges highlight the need for clear communication strategies, educational resources, and practical guidance for healthcare providers to effectively implement the new NACI recommendations for influenza vaccination in older adults.

Recommendations

Through an evidence review and a roundtable discussion with subject matter experts, including infectious diseases physicians, geriatricians, family doctors, pharmacists, and nurse practitioners, we have developed key recommendations to raise awareness about changes to the NACI recommendations with the overall goal to optimize influenza protection in adults 65+.

Improve Vaccine Availability: NACI performs rigorous scientific and economic literature reviews to guide their recommendations, which may apply to individual patients or inform public health program policy decisions. This unique context results in inter-provincial variation in vaccine availability, schedules, and funded vaccine products [16].

Access and availability to enhanced vaccines varies across provinces, with many provinces consistently having limited supply throughout influenza seasons, posing a significant challenge for older adults in receiving these more effective vaccines. Advocacy for consistent, adequate supplies of enhanced influenza vaccines to meet community demand, across all provinces throughout influenza season, is vital to ensuring influenza protection in older adults. Standard dose vaccines should only be utilized in older adults when no other enhanced options are available.

"For geriatricians, these changes in influenza vaccine recommendations are particularly significant. We need to ensure our approach aligns with the specific needs of our older patients." **- Dr. Samir Sinha**

Develop Individual-Level Recommendations: In previous NACI recommendations, high dose flu vaccine was the preferred vaccine for adults 65+. As every individual is unique, creating stronger, personalized vaccine recommendations allows providers to customize individual recommendations to ensure their patient receives optimal flu protection. Additionally, depending on an individual's unique circumstances, comorbidities, frailty status, and preferences, a patient may want to choose which influenza vaccine to receive. even if there is a cost associated with it Informed decision-making should be prioritized.

In the 2024/2025 NACI statement [5], it is recommended that if enhanced vaccines are in limited supply, priority should be given to people at highest risk of severe influenza outcomes, including those aged 75 and over, those with comorbidities, frail older adults, and residents of nursing homes and other chronic care settings. This recommendation aligns with the Comité sur l'immunisation du Québec (CIQ) [17], who recommend that the high dose vaccine be favored over other enhanced and standard dose vaccines in people aged 75 and over with chronic illnesses. The high dose vaccine could be offered to all people aged 75 and over, despite the much higher costs.

Prioritize Evidence-Based Decisions: High dose and adjuvanted vaccines were found to be cost-effective options compared to standard dose when considering healthcare and societal perspectives (18-20), cost-effectiveness (21), and cost-benefit analyses [22, 23].

Evidence-based vaccine selection should prioritize clinical efficacy and safety over cost considerations.

While cost-effectiveness is important for budget considerations, vaccine selection for optimal clinical protection should primarily be based on safety, efficacy and effectiveness data. Regardless of cost, adults 65+ should have access to higher efficacy vaccines with the strongest supporting data on individual and programmatic levels. .

Enhance Provider Education: Develop clear, concise communications about changes to vaccine recommendations and strategies for successful adoption into clinical practise. Distribute these through professional associations and governing bodies to ensure healthcare providers are informed and can implement changes into their practices accordingly.

Maintain Transparency and Trust: NACI, scientists, and healthcare providers will continue to review the best available evidence for influenza vaccines for older adults as new data becomes available. It is important to communicate consistent public messaging that does not undermine existing recommendations in order to maintain vaccine confidence and trust in public health programs. Ensure consistent public messaging about vaccine recommendations. Be transparent about the ongoing review of evidence and any changes to guidelines to maintain public trust in the vaccination program.

"In family practice, we're on the front lines of vaccine discussions. It's crucial that we have clear, practical guidance on implementing these new recommendations." - Dr. Alan Kaplan

Equip Providers with Patient Communication Tools: When guidelines change without clear and effective communication, it can lead to confusion, vaccine hesitancy or even vaccine refusal among patients. Older adults have strong familiarity and preferences for high-dose vaccines due to previous recommendations and awareness campaigns. Confusion, frustration, and declines in vaccine confidence can arise in the absence of clear messaging and/or unavailability of preferred vaccines.

Healthcare providers are the most trusted source for vaccine information. They need resources and tools in order to provide patients with clear information about different vaccine options.
Resources conveying key messages will help healthcare providers effectively communicate with patients about:

***"Our role as healthcare providers is not just to administer vaccines but to foster trust and understanding in our patients about their health choices."* - Dr. Vivien Brown**

- Benefits of different vaccine options
- What vaccines are available and managing expectations around different vaccines
- Importance of vaccination, regardless of specific product
- Empowering patients to make informed decisions based on individual preferences and health needs

"As someone involved in vaccine trials, I'm excited to see how these new recommendations will shape future research directions in influenza vaccination." - Dr. Mark Loeb

Fund High Quality Comparative Trials: Currently available studies support the value of each enhanced vaccine; however, the absence of directly comparative studies between enhanced vaccines makes it difficult to provide definitive recommendations on which vaccine is most beneficial.

Governments and manufacturers should invest in high-quality head-to-head randomized controlled trials comparing enhanced influenza vaccines. This will strengthen the overall evidence and provide better clarity on the safest, most effective vaccine option for older adults, thereby allowing more precise vaccination recommendations to be developed.

Conclusions

Older adults are disproportionately affected by influenza and other respiratory illnesses, making it essential to prioritize preventative strategies including vaccinations. The recommendations outlined in this paper aim to enhance vaccination efforts and ensure that all older adults receive the most effective vaccines. By implementing these strategies in a timely manner, we can work together to reduce the impact and burden of influenza across Canada. This approach not only supports the overall health of our aging population but also strengthens our healthcare system as a whole. We believe that with concerted efforts from healthcare providers, policymakers, and community organizations, we can create a supportive environment that encourages optimal vaccination and promotes better health outcomes for older Canadians. Together, we can make a meaningful difference in the fight against influenza.

By implementing these strategies in a **timely manner**, we can reduce the impact of influenza across Canada and **improve health outcomes for older Canadians**.

Contributors

Chair: Dr. Angel Chu, MD, FRCPC, Infectious Diseases Specialist, Clinical Assistant Professor Cumming School of Medicine

Participants:

- Dr. Vivien Brown, MDCM, CCFP, FCFP, MSCP, Assistant Professor, Department of Family & Community Medicine University of Toronto; Board Member, Immunize Canada
- Dr. Zain Chagla, MD, FRCPC, DTMH. Associate Professor, McMaster University.
- Chelsea D'Silva, MHSc, Director of Research & Impact, 19 To Zero
- Dr. Mohamed El-Hussein, NP, PhD , Professor, School of Nursing and Midwifery; Faculty of Health, Community & Education, Mount Royal University. Acute Care Nurse Practitioner Medical Cardiology, Coronary Care Unit - Rockyview General Hospital
- Dr. Tamas Fulop MD, PhD, FCAHS, Full Professor, Geriatrician, Department of Medicine, University of Sherbrooke,
- Dr. Wayne Ghesquiere, MD FRCPC, Infectious Diseases/Tropical Diseases and Internal Medicine Consultant Clinical Assistant Professor of Medicine, University of British Columbia
- Dr. Jeff Habert MD, CCFP, FCFP, Assistant Professor, University of Toronto, Dept. of Family and Community Medicine
- Dr. Sherilyn Houle, BSP, PhD. Associate Professor, University of Waterloo School of Pharmacy
- Dr. Alan Kaplan, MD, CCFP, FCFP, Chair, Family Physician Airways Group of Canada, Family Physician, Aurora, Ontario
- Dr. Mark Loeb, MD, MSc, FRCPC, Professor, Departments of Pathology and Molecular Medicine, and Health Research Methods, Evidence and Impact (formerly Clinical Epidemiology and Biostatistics) McMaster University
- Dr. Salah Mahmud, MD, PhD, FRCPC, Professor of Community Health Sciences and Pharmacy, University of Manitoba; Director, University of Manitoba Vaccine and Drug Evaluation Centre
- Kari Remington, Project Lead, 19 To Zero
- Dr. Samir Sinha, MD, DPhil, FRCPC, FCAHS, AGSF. Geriatrician and Clinician Scientist, Sinai Health and University Health Network. Toronto; Professor of Medicine, University of Toronto
- Theresa Tang, BSc, Co-Founder & CEO, 19 To Zero
- Dr. Karl Weiss, MD, MSc, FRCPC, Chief, Division of Infectious Diseases and Microbiology Hôpital général juif-Jewish General Hospital; Professor of Medicine, McGill University and Université de Montréal Department of Medicine
- Dr. George Zhanel, MD, FCAHS, Professor and Associate Head, Medical Microbiology and Infectious Diseases, University of Manitoba

About 19 to Zero

19 To Zero is a non-profit coalition formed during the pandemic, focused on promoting safer public health behaviors. It comprises academics, public health experts, and community agencies dedicated to improving public perceptions of health issues.

Our Approach:

- **Data-Driven:** Utilizing evidence from various sources to understand public health challenges.
- **Tailored Solutions:** Recognizing that different populations require unique approaches.
- **Community Engagement:** Building relationships with communities to collaboratively solve health issues.
- **Collaborative Efforts:** Working with experts across sectors to address health gaps effectively.

Contact Us

Theresa Tang
Co-Founder & CEO
Theresa.Tang@19tozero.ca

Chelsea D'Silva
Director, Research & Impact
Chelsea.dsilva@19tozero.ca

Kari Remington
Project Lead
Kari.Remington@19tozero.ca

References

1. Nichols MK, Andrew MK, Hatchette TF, Ambrose A, Boivin G, Bowie W, Chit A, Dos Santos G, ElSherif M, Green K, Haguinet F. Influenza vaccine effectiveness to prevent influenza-related hospitalizations and serious outcomes in Canadian adults over the 2011/12 through 2013/14 influenza seasons: a pooled analysis from the Canadian Immunization Research Network (CIRN) Serious Outcomes Surveillance (SOS Network). Vaccine. 2018 Apr 12;36(16):2166-75.
2. Szanton SL, Leff B, Wolff JL, Roberts L, Gitlin LN. Home-based care program reduces disability and promotes aging in place. Health Affairs. 2016 Sep 1;35(9):1558-63.
3. Schanzer DL, Saboui M, Lee L, Nwosu A, Bancej C. Burden of influenza, respiratory syncytial virus, and other respiratory viruses and the completeness of respiratory viral identification among respiratory inpatients, Canada, 2003-2014. 2018 Jan;12(1):113-21
4. Schanzer DL, Tam TW, Langley JM, Winchester BT. Influenza-attributable deaths, Canada 1990–1999. Epidemiology & Infection. 2007 Oct;135(7):1109-16.
5. National Advisory Committee on Immunization (NACI). An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI) Supplemental guidance on influenza vaccination in adults 65 years of age and older. July 2024. ISBN: 978-0-660-71464-6
6. Schanzer DL, McGeer A, Morris K. Statistical estimates of respiratory admissions attributable to seasonal and pandemic influenza for Canada. Influenza and other respiratory viruses. 2013 Sep;7(5):799-808.
7. Schanzer DL, Sevenhuysen C, Winchester B, Mersereau T. Estimating influenza deaths in Canada, 1992–2009. PloS one. 2013 Nov 27;8(11):e80481.
8. Mitchell R, Taylor G, McGeer A, Frenette C, Suh KN, Wong A, Katz K, Wilkinson K, Amihod B, Gravel D, Canadian Nosocomial Infection Surveillance Program. Understanding the burden of influenza infection among adults in Canadian hospitals: a comparison of the 2009-2010 pandemic season with the pre pandemic and post pandemic seasons. American journal of infection control. 2013 Nov 1;41(11):1032-7.
9. DiazGranados CA, Dunning AJ, Kimmel M, Kirby D, Treanor J, Collins A, Pollak R, Christoff J, Earl J, Landolfi V, Martin E. Efficacy of high-dose versus standard-dose influenza vaccine in older adults. New England Journal of Medicine. 2014 Aug 14;371(7):635-45.
10. DiazGranados CA, Dunning AJ, Jordanov E, Landolfi V, Denis M, Talbot HK. High-dose trivalent influenza vaccine compared to standard dose vaccine in elderly adults: safety, immunogenicity and relative efficacy during the 2009–2010 season. Vaccine. 2013 Jan 30;31(6):861-6.
11. Lee JK, Lam GK, Yin JK, Loiacono MM, Samson SI. High-dose influenza vaccine in older adults by age and seasonal characteristics: Systematic review and meta-analysis update. Vaccine: X. 2023 Aug 1;14:100327.

12. Loeb N, Andrew MK, Loeb M, Kuchel GA, Haynes L, McElhaney JE, Verschoor CP. Frailty is associated with increased hemagglutination-inhibition titers in a 4-year randomized trial comparing standard-and high-dose influenza vaccination. InOpen Forum Infectious Diseases 2020 May (Vol. 7, No. 5, p. ofaa148). US: Oxford University Press.
13. Skaarup KG, Lassen MC, Modin D, Johansen ND, Loiacono MM, Harris RC, Lee JK, Dufournet M, Vardeny O, Peikert A, Claggett B. The Relative Vaccine Effectiveness of High-Dose vs Standard-Dose Influenza Vaccines in Preventing Hospitalization and Mortality: A Meta-Analysis of Evidence From Randomized Trials. Journal of Infection. 2024 May 23:106187.
14. Beran J, Reynales H, Poder A, Charles YY, Pitisuttithum P, Yuan LL, Vermeulen W, Verhoeven C, Leav B, Zhang B, Sawlwin D. Prevention of influenza during mismatched seasons in older adults with an MF59-adjuvanted quadrivalent influenza vaccine: a randomised, controlled, multicentre, phase 3 efficacy study. The Lancet Infectious Diseases. 2021 Jul 1;21(7):1027-37.
15. Dunkle LM, Izikson R, Patriarca P, Goldenthal KL, Muse D, Callahan J, Cox MM. Efficacy of recombinant influenza vaccine in adults 50 years of age or older. New England Journal of Medicine. 2017 Jun 22;376(25):2427-36.
16. Andrew MK, McNeil SA. Influenza vaccination and the evolution of evidence-based recommendations for older adults: A Canadian perspective. Vaccine. 2021 Mar 15;39:A36-41.
17. Gilca R, Doggui R, Brousseau N, de Wals P. Utilisation des vaccins à haute dose ou adjuvantés dans le Programme d'immunisation contre l'influenza: Avis et Recommandations. Comité sur l'immunisation du Québec. Juin 2023. ISBN : 978-2-550-95357-9 (PDF)
18. Becker DL, Chit A, DiazGranados CA, Maschio M, Yau E, Drummond M. High-dose inactivated influenza vaccine is associated with cost savings and better outcomes compared to standard-dose inactivated influenza vaccine in Canadian seniors. Human Vaccines & Immunotherapeutics. 2016 Dec 1;12(12):3036-42.
19. Chit A, Becker DL, DiazGranados CA, Maschio M, Yau E, Drummond M. Cost-effectiveness of high-dose versus standard-dose inactivated influenza vaccine in adults aged 65 years and older: an economic evaluation of data from a randomised controlled trial. The Lancet Infectious Diseases. 2015 Dec 1;15(12):1459-66.
20. Chit A, Roiz J, Aballea S. An assessment of the expected cost-effectiveness of quadrivalent influenza vaccines in Ontario, Canada using a static model. PLoS One. 2015 Jul 29;10(7):e0133606.
21. Piercy, J., Ryan, J., & Megas, F. Economic evaluation of MF59 adjuvanted vaccine against influenza in the high-risk elderly population in France. Journal of Medical Economics. 2004 Jan 6;7(1–4): 1–18. https://doi.org/10.3111/200407001018
22. Shireman TI, Ogarek J, Gozalo P, Zhang T, Mor V, Davidson HE, Han L, Taljaard M, Gravenstein S. Cost benefit of high-dose vs standard-dose influenza vaccine in a long-term care population during an A/H1N1-predominant influenza season. Journal of the American Medical Directors Association. 2019 Jul 1;20(7):874-8.
23. van Aalst R, Russo EM, Neupane N, Mahmud SM, Mor V, Wilschut J, Chit A, Postma M, Young-Xu Y. Economic assessment of a high-dose versus a standard-dose influenza vaccine in the US Veteran population: Estimating the impact on hospitalization cost for cardio-respiratory disease. Vaccine. 2019 Jul 26;37(32):4499-503.