CADTH COVID-19 PANDEMIC

COVID-19 CADTH REFERENCE LIST

Influenza Vaccination and Risk of Subsequent Non-Influenza Respiratory Viruses: Safety

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To produce this report, CADTH used a modified approach to the selection, appraisal, and synthesis of the evidence to meet decision-making needs during the COVID-19 pandemic. Care has been taken to ensure the information is accurate and complete, but it should be noted that international scientific evidence about COVID-19 is changing and growing rapidly.

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

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Questions or requests for information about this report can be directed to **requests@cadth.ca.**

Research Question

What is the safety of influenza vaccination with respect to risk of subsequent non-influenza respiratory viruses?

Key Findings

Three non-randomized studies were identified regarding the safety of influenza vaccination with respect to risk of subsequent non-influenza respiratory viruses.

Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were the influenza vaccine and non-influenza respiratory viruses, as well as a targeted search for virus interference. Search filters were applied to limit retrieval of the main search to safety data. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2015 and May 25, 2020. Internet links were provided, where available.

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Individuals of all ages
Intervention	Influenza vaccine (e.g., inactivated influenza vaccine, live attenuated influenza vaccine)
Comparators	No influenza vaccine; placebo
Outcomes	Incidence of other non-influenza respiratory viruses (e.g., coronavirus, rhinovirus, Middle East respiratory syndrome, severe acute respiratory syndrome)
Study Designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies

Results

Three non-randomized studies[1-3] were identified regarding the safety of influenza vaccination with respect to risk of subsequent non-influenza respiratory viruses. No relevant health technology assessments, systematic reviews or randomized controlled trials were identified.

References of potential interest that did not meet the inclusion criteria are provided in the appendix.

Overall Summary of Findings

Three non-randomized studies[1-3] were identified regarding the safety of influenza vaccination with respect to risk of subsequent non-influenza respiratory viruses. The study by Wolff[1] investigated whether receiving an influenza vaccine increased the risk of contracting other respiratory viruses in Department of Defense personnel, which was referred to as virus interference. There was no statistically significant difference in the odds of contracting non-influenza respiratory viruses between vaccinated and non-vaccinated patients.[1] As such, the author concluded that receiving the influenza vaccine was not associated with virus interference.[1] The second study by Rikin et al.[2] investigated whether receiving an influenza vaccine increased the rate of laboratory confirmed acute respiratory illness in the subsequent post-vaccination time period. The authors found that during the 14-day post-influenza vaccination time period, the hazard of contracting non-influenza respiratory pathogens was higher compared to unvaccinated individuals during the same time period.[2] When stratified by age, the hazard remained higher for children, but not for adults.[2] The authors thus concluded that there was an increased hazard of non-influenza, acute, viral respiratory illness among children in the post-vaccination period compared to unvaccinated children during the same time period.[2] The third study by Feng et al.[3] investigated the potential for virus interference using data from the Influenza Incidence Surveillance Project in the US. After the three-year observational period, the authors found no associations between the detection of non-influenza, respiratory viruses and receiving an influenza vaccination.[3]

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-Analyses

No literature identified.

Randomized Controlled Trials

No literature identified.

Non-Randomized Studies

1. Wolff GG. Influenza vaccination and respiratory virus interference among Department of Defense personnel during the 2017-2018 influenza season. *Vaccine*. 2020 Jan 10;38(2):350-354.
PubMed: PM31607599

2. Rikin S, Jia H, Vargas CY, et al. Assessment of temporally-related acute respiratory illness following influenza vaccination. *Vaccine*. 2018 04 05;36(15):1958-1964.
PubMed: PM29525279

3. Feng S, Fowlkes AL, Steffens A, Finelli L, Cowling BJ. Assessment of Virus Interference in a Test-negative Study of Influenza Vaccine Effectiveness. *Epidemiology*. 2017 07;28(4):514-524.
PubMed: PM28362642

Appendix — Further Information

Systematic Reviews and Meta-Analyses

Alternative Outcome

4. Bitterman R, Eliakim-Raz N, Vinograd I, Zalmanovici Trestioreanu A, Leibovici L, Paul M. Influenza vaccines in immunosuppressed adults with cancer. Cochrane Database Syst Rev. 2018;2(2):CD008983.
Pubmed: PM29388675

5. Demicheli V, Jefferson T, Di Pietrantonj C, et al. Vaccines for preventing influenza in the elderly. Cochrane Database Syst Rev. 2018;2(2):CD004876.
PubMed: PM29388197

6. Li ZY, Chen JY, Zhang YL, Fu WM. Partial protection against 2009 pandemic influenza A (H1N1) of seasonal influenza vaccination and related regional factors: Updated systematic review and meta-analyses. *Hum Vaccin Immunother*. 2015;11(6):1337-1344.
PubMed: PM25692308

Randomized Controlled Trials

Viral Respiratory Illness Not Specified

7. Pepin S, Samson SI, Alvarez FP, Dupuy M, Gresset-Bourgeois V, De Bruijn I. Impact of a quadrivalent inactivated influenza vaccine on influenza-associated complications and health care use in children aged 6 to 35months: Analysis of data from a phase III trial in the Northern and Southern Hemispheres. *Vaccine*. 2019 03 22;37(13):1885-1888.
PubMed: PM30745147

Alternative Outcome

8. Steinhoff MC, Katz J, Englund JA, et al. Year-round influenza immunisation during pregnancy in Nepal: a phase 4, randomised, placebo-controlled trial. *Lancet Infect Dis.* 2017 09;17(9):981-989.
PubMed: PM28522338

Published Outside of Literature Search Timeframe

9. Cowling BJ, Fang VJ, Nishiura H, et al. Increased risk of noninfluenza respiratory virus infections associated with receipt of inactivated influenza vaccine. *Clin Infect Dis*. 2012;54(12):1778-1783.
Pubmed: PM22423139

Non-Randomized Studies

Viral Respiratory Illness Not Specified

10. de Hoog MLA, Venekamp RP, Meijer A, Sanders EAM, Bruijning-Verhagen P. Inactivated influenza vaccine does not reduce all cause respiratory illness in children with pre-existing medical conditions. *Vaccine*. 2020 Apr 09;38(17):3397-3403.
PubMed: PM31859200

11. Baxter R, Eaton A, Hansen J, Aukes L, Caspard H, Ambrose CS. Safety of quadrivalent live attenuated influenza vaccine in subjects aged 2-49years. *Vaccine*. 2017 03 01;35(9):1254-1258.
PubMed: PM28162825

12. Brousseau N, Green HK, Andrews N, et al. Impact of influenza vaccination on respiratory illness rates in children attending private boarding schools in England, 2013-2014: a cohort study. *Epidemiol Infect*. 2015 Dec;143(16):3405-3415.
PubMed: PM25876454

13. Jaiwong C, Ngamphaiboon J. Effects of inactivated influenza vaccine on respiratory illnesses and asthma-related events in children with mild persistent asthma in Asia. *Asian Pac J Allergy Immunol*. 2015 Mar;33(1):3-7.
PubMed: PM25840627

Additional References

14. Skowronski DM, et al. Influenza vaccine does not increase the risk of coronavirus or other non-influenza respiratory viruses: retrospective analysis from Canada, 2010-11 to 2016-17. *Clin Infect Dis.* 2020.
https://pubmed.ncbi.nlm.nih.gov/32442261/

15. Centers for Disease Control and Prevention. Misconceptions about Seasonal Flu and Flu Vaccines. 2019. https://www.cdc.gov/flu/prevent/misconceptions.htm
See: *"Is it true that getting a flu vaccine can make you more susceptible to other respiratory viruses?"*