



Information for Health Care Providers on Delayed Injection Site Reactions following administration of mRNA COVID-19 vaccines

Presenters: Elissa Abrams and Nooshin Ahmadipour
Q and A: Joseline Zafack, Gina Lacuesta
March 11, 2021



Conflicts of interest

- Elissa Abrams– no conflicts of interest to declare
- Nooshin Ahmadipour– no conflicts of interest to declare
- Joseline Zafack– no conflicts of interest to declare
- Gina Lacuesta– no conflicts of interest to declare

Objectives

- To provide an overview of delayed injection site reactions following administration of mRNA COVID-19 vaccines based on data from the Canadian Adverse Events Following Immunization Surveillance System (CAEFISS) and data from the Moderna clinical trial
- To describe the features and management of delayed injection site reactions following administration of mRNA COVID-19 vaccines
- To provide guidance on distinguishing these delayed injection reactions from other local reactions such as cellulitis

Outline

- Delayed injection site reactions
- Data from the Canadian adverse Event Following Immunization Surveillance System (CAEFISS)
- Data from the Moderna COVID-19 vaccine clinical trial
- Distinguish a delayed injection site reaction from a cellulitis
- Management of a delayed injection site reaction

Injection site reactions (local reactions)

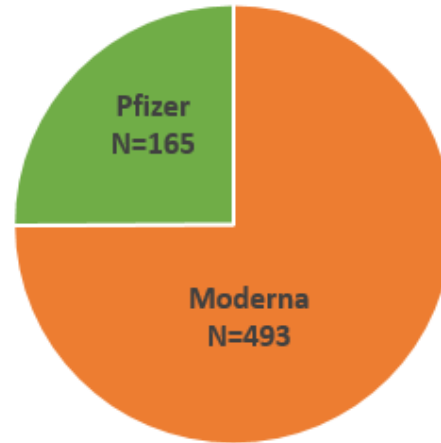
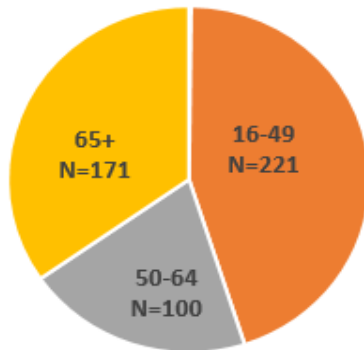
- Injection site reactions or local reactions (swelling, redness, mild tenderness) after vaccination are common
 - Usually occur within a few hours; resolve quickly
 - Usually mild or moderate
 - Part of the normal immune response of the body
- Delayed local reactions have been described in the past
 - Occur within hours to days but can be delayed weeks
 - Can be immunologically or non-immunologically mediated (nonspecific inflammation, T cell mediated)
 - Self-limited, do not contraindicate administration of future vaccine doses
- Delayed local reactions following Moderna COVID-19 vaccination
 - Expected adverse event, usually mild or moderate and self-limited
 - T-cell mediated hypersensitivity
 - Does not contraindicate administration of future vaccine doses
 - Does not increase risk of anaphylaxis

Blumenthal KG, et al. Delayed large local reactions to mRNA-1273 vaccine against SARS-CoV-2. NEJM 2021
Kelso JM, et al. Adverse reactions to vaccines practice parameter. J Allergy Clin Immunol 2012;130: 25-43
McNeil MM,. Vaccine-associated hypersensitivity. J Allergy Clin Immunol 2018;141: 463-72

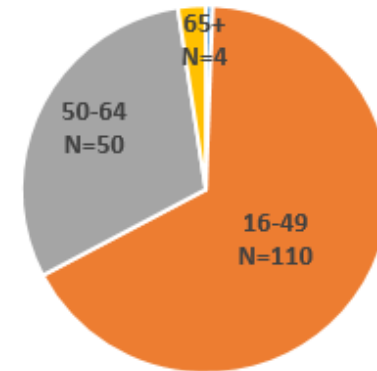
Data from the Canadian adverse Event Following Immunization Surveillance System (CAEFISS)

AEFI reports with at least one local reaction (CAEFISS, February 23)

Reports by age group
(Moderna)



Reports by age group
(Pfizer/BioNTech)



V site reporting rate for Pfizer: 12/100,000 doses distributed

V site reporting rate for Moderna: 95/100,000 doses distributed

Data from the Canadian adverse Event Following Immunization Surveillance System (CAEFISS)

AEFI reports with at least one local reaction by delay of onset (CAEFISS, Feb 24, 2021)

Time of onset after vaccination	Moderna	Pfizer-BioNtech
0-3 days	139 (25%)	127(69%)
>3 to <8 days	150 (27%)	15 (8%)
8+ days	214 (38%)	17 (9%)
Missing	53 (10%)	26 (14%)
Total	556 (100%)	185 (100%)

At the time of report, outcome of Moderna injection site reactions was comparable between the various delays of onset.

Data from the Canadian adverse Event Following Immunization Surveillance System (CAEFISS)

Injection site reactions following **Moderna** COVID-19 vaccines (CAEFISS, February 23, 2021)

Reaction at the vacc. site	N total	0-3 d Row %	>3 to <8 d Row %	8+ d Row %	Missing onset Row %
Erythema	262	20.23	30.92	41.22	7.63
Pain	258	43.02	28.29	20.93	7.75
Swelling	204	21.57	34.31	38.73	5.39
Warmth	165	22.42	35.15	36.97	5.45
Pruritus	111	11.71	45.05	34.23	9.01
Cellulitis	104	24.04	31.73	40.38	3.85
Inflammation	83	18.07	21.69	53.01	7.23
Induration	68	22.06	33.82	32.35	11.76
Rash	53	9.43	47.17	37.74	5.66
Extensive swelling	14	78.57	14.29	0	7.14
Oedema	12	16.67	33.33	33.33	16.67
Urticaria	12	50	41.67	8.33	0
Total (all)*	1,534	24.32	31.36	37.16	7.17

*Includes frequencies 1-2 that were removed from the two tables

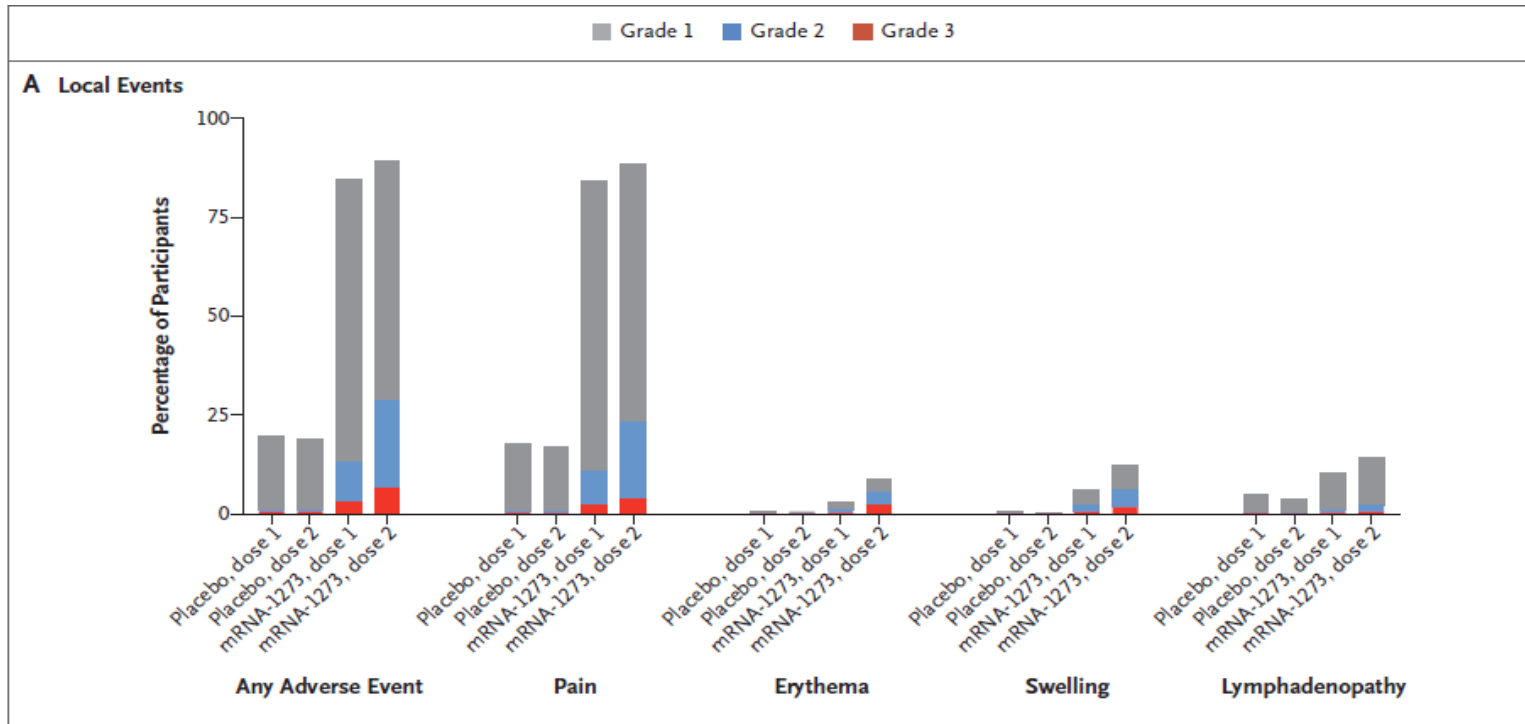
Data from the Canadian adverse Event Following Immunization Surveillance System (CAEFISS)

Injection site reactions following **Pfizer-BioNtech** COVID-19 vaccines (CAEFISS, February 23, 2021)

Reaction at the vacc. site	Total	0-3 d Row %	>3 to <8 d Row %	8+ d Row %	Missing onset %
Pain	140	76.43	4.29	6.43	12.86
Erythema	53	64.15	9.43	18.87	7.55
Swelling	49	67.35	10.2	12.24	10.2
Warmth	32	81.25	6.25	9.38	3.13
Pruritus	22	54.55	18.18	22.73	4.55
Induration	14	71.43	21.43	0	7.14
Extensive swelling	12	91.67	0	8.33	0
Cellulitis	12	75	8.33	8.33	8.33
Paraesthesia	9	66.67	11.11	11.11	11.11
Rash	9	66.67	0	33.33	0
Inflammation	6	83.33	0	0	16.67
Nodule	3	100	0	0	0
Total (all)*	407	71.25	8.6	10.57	9.58

*Includes frequencies 1-2 that were removed from the two tables

Data from the Moderna COVID-19 vaccine trial



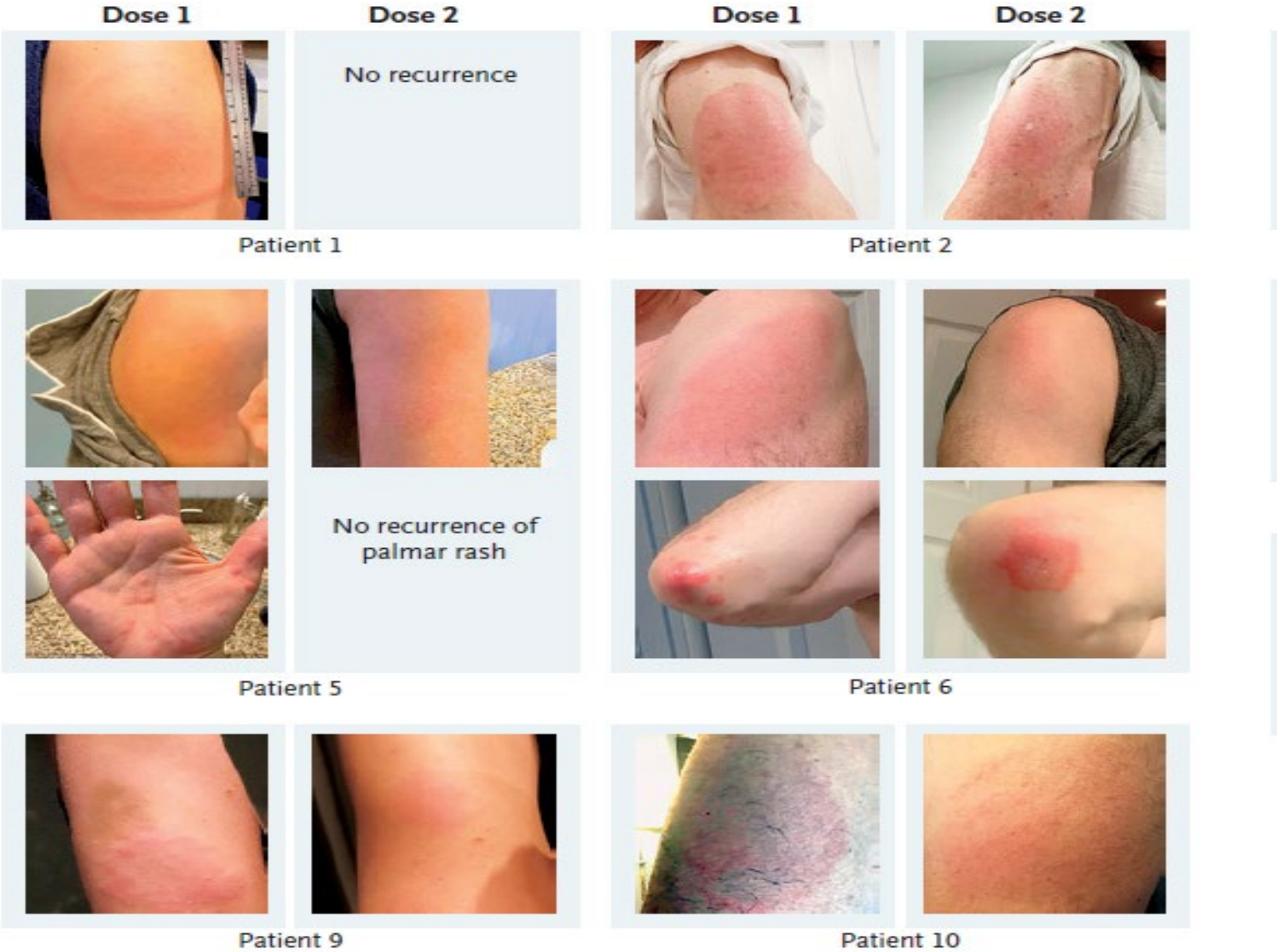
- Local reactions occurred in up to 80% of trial participants overall
 - Majority of mild to moderate local reactions
 - Pain mainly, erythema, swelling, lymphadenopathy at the site of injection
 - Not harmful, not a contraindication for future vaccination

Delayed local reactions following COVID-19 vaccines

- Reaction seen to COVID-19 mRNA vaccines around the injection site
 - Induration
 - Swelling
 - Erythema
 - Pain/tenderness
 - Median onset on day 8 (range 4 to 11)
 - Resolve within 6 days (range 2 to 11)
 - Systemic AE in some patients
- Thus far appear to be more common with Moderna COVID-19 vaccine
- Observed in the Moderna clinical trial
 - Dose 1: 0.8% of vaccine recipients
 - Dose 2: 0.2% of vaccine recipients
- 50% recurrence after dose 2 (similarly or less severe than the 1st reaction)

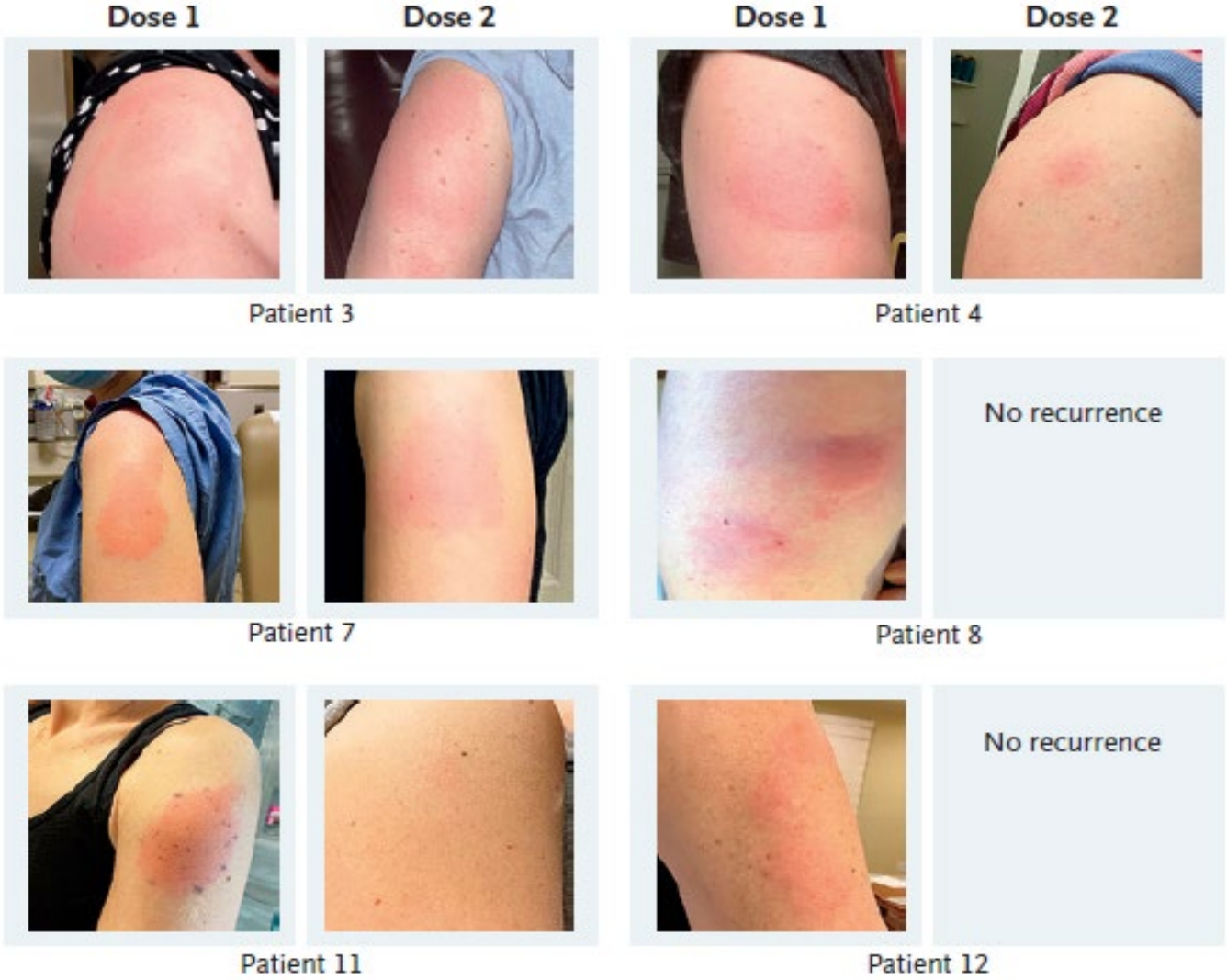


Delayed Cutaneous Reactions to Moderna COVID-19 Vaccine (1)



Blumenthal KG, Freeman EE, Saff RR et al. Delayed large local reactions to mRNA-1273 vaccine against SARS-CoV-2. NEJM 2021 [epub ahead of print]

Delayed Cutaneous Reactions to Moderna COVID-19 Vaccine (2)



Blumenthal KG, et al. Delayed large local reactions to mRNA-1273 vaccine against SARS-CoV-2. NEJM 2021

Distinguish a delayed injection site reaction from cellulitis

- On clinical presentation delayed local reaction may resemble cellulitis
 - Risk of unnecessary antibiotic treatment
- The main difference between the two is presence or absence of systemic symptoms
 - Cellulitis: fevers, chills, malaise
 - Local reaction: in general no systemic symptoms
 - Cellulitis: Faster onset, day 3-5
 - Cellulitis: Less demarcation or clear edges
- If no systemic symptoms monitor for progression of fever, systemic symptoms, or worsening local discomfort over time



Photo c/o Dermnetz.org

Management of delayed injection site reactions

- Reassurance
- Ice packs or cold compresses
- Analgesics
- Antihistamines (for the pruritus and burning)
- Avoid systemic steroids (as it may blunt response to vaccine)
Topical steroids if symptomatic relief needed.
- Monitor the evolution of signs and symptoms

Key messages

- Delayed local reactions are an injection site reaction occurring days after vaccination
 - Inform vaccinated patients that these reactions can occur
 - Reassure all patients (especially those who have experienced it) that the reaction is benign
- Delayed local reactions may look similar to cellulitis but resolve without the use of antibiotics and in general have no systemic symptoms
- Delayed local reactions are usually not serious and will self-resolve
- Delayed local reactions do not preclude future vaccination and do not increase the risk for anaphylaxis with future vaccination
- There is a decreased frequency of these delayed local reactions following the 2nd dose of vaccine.

Canadian Immunization Guide

- Refer to Part 2 - [Vaccine Safety](#) in the Canadian Immunization Guide (CIG) for definitions of AEFIs and additional general information.

The screenshot shows the top of the Canadian Immunization Guide website. At the top left is the Government of Canada logo. To the right is a search bar with the text 'Search Canada.ca' and a magnifying glass icon. Below the logo is a 'MENU' dropdown. A breadcrumb trail reads: 'Canada.ca > Health > Healthy living > Vaccines and immunization > Canadian Immunization Guide'. The main heading is 'Canadian Immunization Guide: Part 2 - Vaccine Safety'. Below this is a 'Table of contents' section with five links: 'Vaccine safety and pharmacovigilance', 'Contraindications, precautions and concerns', 'Anaphylaxis and other Acute Reactions following Vaccination', 'Anaphylactic hypersensitivity to egg and egg-related antigens', and 'Adverse Events Following Immunization (AEFI)'. On the right side, there are two boxes. The top one is titled 'Organization:' and contains 'Public Health Agency of Canada' and 'Updated: see Table of Updates'. The bottom one is titled 'Related Topics' and contains a list of links: 'Canadian Immunization Guide', 'Introduction', 'Part 1 - Key Immunization Information', 'Part 3 - Vaccination of Specific Populations', 'Part 4 - Active Vaccines', and 'Part 5 - Passive Immunizing Agents'.

Government of Canada / Gouvernement du Canada

Search Canada.ca

MENU

Canada.ca > Health > Healthy living > Vaccines and immunization > Canadian Immunization Guide

Canadian Immunization Guide: Part 2 - Vaccine Safety

Table of contents

- [Vaccine safety and pharmacovigilance](#)
- [Contraindications, precautions and concerns](#)
- [Anaphylaxis and other Acute Reactions following Vaccination](#)
- [Anaphylactic hypersensitivity to egg and egg-related antigens](#)
- [Adverse Events Following Immunization \(AEFI\)](#)

Organization:
Public Health Agency of Canada
Updated: see [Table of Updates](#)

Related Topics

- [Canadian Immunization Guide](#)
- [Introduction](#)
- [Part 1 - Key Immunization Information](#)
- [Part 3 - Vaccination of Specific Populations](#)
- [Part 4 - Active Vaccines](#)
- [Part 5 - Passive Immunizing Agents](#)

Subscribe for NACI publications and updates to the CIG

The screenshot shows a web browser window with the URL health.canada.ca/en/health-canada/services/healthy-living/immunization-and-vaccines/canadian-immunization-guide/subscribe.html. The page is in French, as indicated by the 'Français' language selector in the top right. The header includes the Government of Canada logo and a search bar. A breadcrumb trail reads: Home > Health Canada > Healthy living > Immunization and vaccines > Canadian Immunization Guide. The main heading is 'Canadian Immunization Guide updates and National Advisory Committee on Immunization - publications mailing list'. Below this, a section titled 'On this page' contains two links: 'Subscribe' and 'Cancelling your subscription'. The 'Subscribe' section includes a paragraph: 'To receive information regarding updates to the Canadian Immunization Guide and new National Advisory Committee on Immunization (NACI) recommendations, statements and literature reviews, please enter your e-mail address below and click on the "Subscribe" button.' There are two form fields: one for 'Your E-mail address (required)' and another for 'Preferred update(s) (required)'. The second form field has two radio button options: 'Canadian Immunization Guide' and 'NACI Recommendations, Statements and Updates'. The Windows taskbar at the bottom shows the time as 12:49 PM on 2021-02-02.

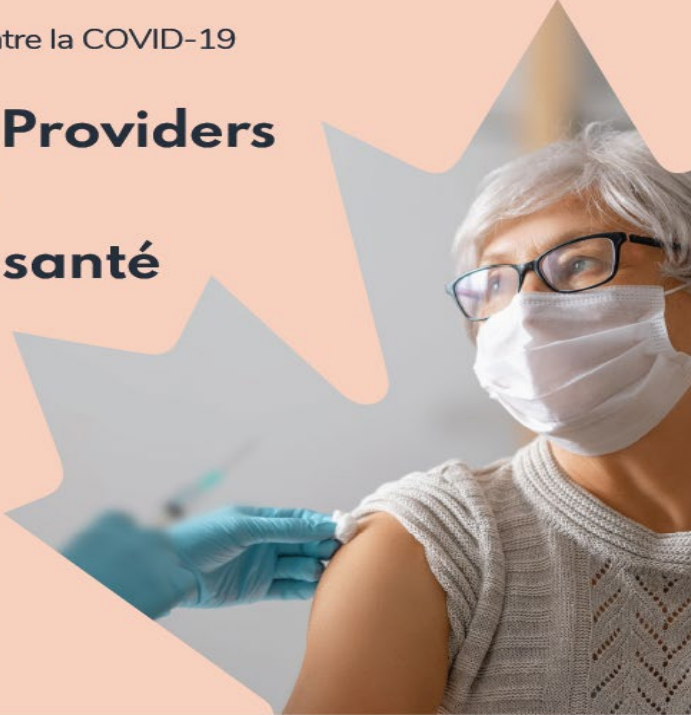
Resources for healthcare providers


COVID-19 Vaccination Information Resources
Ressources documentaires sur la vaccination contre la COVID-19


Tool Kit for Health Care Providers Trousse à outils pour les fournisseurs de soins de santé

English > Français >

Accessible versions of Government of Canada resources in this tool kit can be found at Canada.ca/coronavirus.
Vous trouverez les versions accessibles des ressources du gouvernement du Canada dans la présente trousse à outils sur le site Canada.ca/le-coronavirus.



 Public Health Agency of Canada  Agence de la santé publique du Canada



- COVID-19 vaccination tool kit for health care providers can be found at Canada.ca/coronavirus

Additional resources

- How to report an AEFI: <https://www.canada.ca/en/public-health/services/immunization/reporting-adverse-events-following-immunization.html>
- AEFI report form: [Reporting Adverse Events Following Immunization \(AEFI\) in Canada](#)
- Submission of AEFI reports: [User guide to completion and submission of the AEFI reports](#)

Acknowledgements

- PHAC Vaccine Safety Section
- NACI Vaccine Safety Working Group
- National Collaborating Centre for Infectious Diseases (NCCID)

THANK YOU

QUESTIONS?