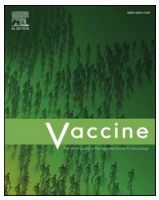
Vaccine 59 (2025) 127254

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine



Short communication

Neurological adverse events following COVID-19 vaccination among Canadians referred to the special immunization clinic network

Tiffany Fitzpatrick [a,b,c], Peter Yamoah [d], David Summerby-Murray [e], Juthaporn Cowan [f,g], Manish Sadarangani [h,i], Alissa Wright [j], Sara Belga [j], Cora Constantinescu [k], Alex Carignan [l], Athena McConnell [m], Karina A. Top [a,b,d,*], on behalf of the Canadian Immunization Research Network Investigators[1]

[a] Department of Community Health and Epidemiology, Dalhousie University, Halifax, NS, Canada
[b] Canadian Center for Vaccinology, IWK Health and Dalhousie University; Halifax, NS, Canada
[c] Public Health Ontario; Toronto, ON, Canada
[d] Department of Pediatrics, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, AB, Canada
[e] Faculty of Medicine, Dalhousie University, Halifax, NS, Canada
[f] Department of Medicine, University of Ottawa, Ottawa, ON, Canada
[g] The Ottawa Hospital Research Institute, Ottawa, ON, Canada
[h] Vaccine Evaluation Center, BC Children's Hospital Research Institute, Vancouver, BC, Canada
[i] Department of Pediatrics, University of British Columbia, Vancouver, BC, Canada
[j] Department of Medicine, University of British Columbia, Vancouver, BC, Canada
[k] Alberta Children's Hospital, University of Calgary, Calgary, AB, Canada
[l] Department of Microbiology and Infectious Diseases, Université de Sherbrooke, Sherbrooke, QC, Canada
[m] Jim Pattison Children's Hospital, University of Saskatchewan, Saskatoon, Saskatchewan, Canada

A B S T R A C T

Neurological adverse events have been reported rarely following COVID-19 vaccination. This study describes the characteristics of adolescents and adults assessed in the Canadian Special Immunization Clinic (SIC) Network for neurological adverse events following immunization (AEFIs) and outcomes of revaccination. Among 60 participants enrolled from January 2021 to February 2023, paresthesia/anesthesia was the most common diagnosis (15/60; 25.0 %), followed by Bell's Palsy (6/60; 10.0 %). Twenty-eight percent (17/60) of participants were hospitalized for their AEFI. Revaccination was recommended to 32/46 (69.6 %) participants due for subsequent doses when assessed in the SIC. Twenty-three participants were revaccinated and 4/23 (17.4 %) had recurrent symptoms of the AEFI; three were milder than the first event and none required hospitalization. Revaccination was generally safe in selected patients after a neurological AEFI. Expert assessment of patients with neurological AEFIs may help to support further vaccination.

* Corresponding author at: Department of Pediatrics, Faculty of Medicine and Dentistry, University of Alberta, 3-588 11405 87 Ave NW, Edmonton, AB T6G 1C9, Canada.

E-mail address: ktop@ualberta.ca (K.A. Top).

[1] Non-author contributors:Special Immunization Clinic (SIC) Network Investigators who contributed to this project are:Shelly McNeil, MD, Scott Halperin, MD, Jeannette Comeau, MD, IWK Health Centre, Halifax, NS;Mary McHenry, MD, Greg Rex, MD, Gina Lacuesta, MD, Halifax Asthma Associates, Halifax, NS;Shelley Deeks, MD, Department of Health & Wellness, Government of Nova Scotia, Halifax, NS;Ian Grant, MD, Division of Neurology, Queen Elizabeth II Health Sciences Centre, Halifax, NS;Sundeep Shivakumar, MD, Department of Medicine, Dalhousie University, Halifax, NS;Remi Gagnon, MD, Isabelle Viel-Theriault, MD, Gaston De Serres, MD, Jean-Philippe Drolet, MD, Centre Hospitalier Universitaire de Québec-Université Laval, Quebec, QC;Marina Salvadori, MD, Montreal Children's Hospital, Montreal, QC;Caroline Quach, MD, Anne Des Roches, MD, Soren Gantt, MD, Centre Hospitalier Universitaire de Ste-Justine, Montreal, QC;Emilia Falcone, MD, Hugo Chapdelaine, MD, Institut De recherche cliniques de Montreal, Montreal, QC; Martin Blaquiere, MD, Centre hospitalier universitaire de Sherbrooke, Sherbrooke QC; Shaun Morris, MD, Julia Upton, MD, Pierre-Philippe Piche-Renaud, MD, The Hospital for Sick Children, Toronto, ON;Anne Pham, Huy, MD, Children's Hospital of Eastern Ontario, Ottawa, ON;C. Arianne Buchan, MD, The Ottawa Hospital, Ottawa, ON;Christine Song, MD, Stephen Betschel, MD, St.Michael's Hospital, Toronto, ON;Zainab Abdurrahman, MD, Jeffrey Pernica, MD, McMaster Children's Hospital, Hamilton, ON;Sarah Wilson, Public Health Ontario, Toronto, ON;Chrystyna Kalicinsky, MD, Lana Rosenfield, MD, Colin Barber, MD, Karver Zaborniak, MD, Tamar Rubin, MD, Elinor Simons, MD, Health Sciences Centre Winnipeg, Winnipeg, MB;Catherine Burton, MD, Sneha Suresh, MD, Ana Bosonea, MD, Wendy Vaudry, MD, Stollery Children's Hospital, Edmonton, AB;Grazia Salvo, MD, Doris Sturtevant, MD, Alberta Health Services, Edmonton, AB;Kyla Hildebrand, MD, Jane Finlay, MD, BC Children's Hospital, Vancouver, BC;Monika Naus, MD, School of Population and Public Health, University of British Columbia, Vancouver, BCAllison Mah, MD, Vancouver General Hospital, Vancouver BC;Scott B. Cameron, MD, Victoria Cook, MD, Allergy Victoria, Victoria, BC;Persia Pourshahnazari, MD, Amin Kanani, MD, Godfrey Lam, MD, Kateryna Vostretsova, MD, Raymond Mak, MD, St. Paul's Hospital, Vancouver, BC

https://doi.org/10.1016/j.vaccine.2025.127254
Received 23 September 2024; Received in revised form 7 April 2025; Accepted 10 May 2025
Available online 20 May 2025

1. Introduction

COVID-19 vaccines are highly effective in preventing severe COVID-19 and are safe, having been monitored rigorously for safety before and after implementation in public health programs. [1,2] Several neurological adverse events following immunization (AEFIs) were identified as "adverse events of special interest" (AESI) for additional monitoring given associations with COVID-19 or with other vaccines, including Bell's/facial palsy, seizure, Guillain–Barré Syndrome (GBS), acute disseminated encephalomyelitis (ADEM), and transverse myelitis. [3] A small increased risk of GBS has been associated with COVID-19 viral vector vaccines ChAdOx1-S (AstraZeneca & Serum Institute of India) and Ad26.COV·S (Janssen). [4–6] In addition, Bell's palsy has been reported following mRNA vaccines while paresthesias have been reported following both mRNA and viral vector vaccines though a causal association with vaccination has not been confirmed. [7–9] Nonetheless, the risk of neurological complications from SARS-CoV-2 infection was substantially higher than the risk associated with vaccination. [4,7]

When a person experiences a neurological event following vaccination, (whether it is confirmed to be caused by the vaccine or is only temporally associated) both the patient and their healthcare provider may have concerns about the safest way to revaccinate with the same vaccine. The Canadian Special Immunization Clinic (SIC) Network has been conducting expert assessment of adults and children who have experienced an AEFI and need further doses of the same vaccine since 2013. [10] The SIC network began accepting referrals for patients with adverse events following COVID-19 vaccination in January 2021, when COVID-19 vaccination was available to priority groups. Both mRNA vaccines and the ChAdOx1-S viral vector vaccine were introduced for the Canadian general population by March 2021. By December 31, 2022, 96.3 million doses had been administered in Canada, comprising of approximately 67 % BNT162b2, 30 % mRNA-1273, and 3 % ChAdOx1-S. [11]

This study sought to describe the clinical characteristics, revaccination recommendations and frequency of AEFI recurrence among adolescents and adults with neurological adverse events following COVID-19 mRNA vaccination and viral vector vaccination assessed in the SIC Network.

2. Methods

Study design and participants: This was a longitudinal study of participants 12 years and older who were referred to one of 15 SIC sites by a healthcare provider from January 1, 2021 to December 31, 2022, and had a final physician diagnosis of neurological AEFI following COVID-19 vaccination after SIC assessment.

Patients underwent standardized assessment by a SIC physician, including review of clinical data and laboratory investigations related to the AEFI, and risk-benefit assessment of revaccination, as described previously. [10] Recommendations for revaccination were made based on network and public health guidance in partnership with the patient, with the patient making the final decision. Participants were followed up approximately 7 and 42 days after revaccination to capture AEFIs.

Data source: Socio-demographic data, medical history, and details of the AEFI were collected from the participant and medical records where available, and immunization records were reviewed. The impact of the AEFI on daily activities and level of medical attention required was reported as low, moderate, high impact, and serious (Supplementary Table 1). [12] Following individual consent, de-identified data were transferred to a central database.

Analysis: Clinical and demographic characteristics, vaccination and AEFI details, revaccination recommendations and AEFI recurrence were extracted from the SIC network database. The final AEFI diagnosis made by the SIC physician was based on *a priori* diagnostic categories listed on the SIC case report form: seizure, GBS, ADEM/myelitis/encephalitis, Bell's/facial palsy, paresthesia/anesthesia, and other neurological events with acute onset. Analysis was stratified by the final physician diagnosis of the AEFI after SIC assessment as this diagnosis guided revaccination recommendations. Summary statistics were used to describe socio-demographics, referral AEFI characteristics, and revaccination recommendations. Revaccination outcomes were summarized for participants recommended for additional COVID-19 vaccination. Brighton Collaboration case definitions (BCCD) were applied retrospectively to cases of GBS, ADEM/myelitis/encephalitis and facial palsy. [13–15] Details of participants experiencing an AEFI following COVID-19 revaccination were presented as a case series. All analyses were performed using SAS v 9.4 (SAS Institute Inc., Cary, NC).

Ethics: Ethics approval was obtained from all participating sites.

3. Results

In total, of 481 eligible referrals to the SIC Network, 60 participants had a final diagnosis of neurological event following COVID-19 vaccination (Supplementary Fig. 1). Thirty-nine (65.0 %) participants were adults aged 31 to 60 years and 44 (73.3 %) were females (Table 1). The AEFI was of high impact for 20/60 (33.3 %) participants (e.g., requiring multiple physician visits, disability lasting 4–14 days), and serious in 18/60 (30.0 %) (e.g., requiring hospitalization or leading to permanent disability).

Paresthesia/Anesthesia was the most common neurological AEFI diagnosed in 15/60 (25.0 %) participants and was reported in association with other symptoms in ten participants diagnosed with other neurological AEFI (Table 1 & Supplementary Table 2). Paresthesia was most frequently associated with BNT162b2 (9/15, 60.0 %) or mRNA-1273 (5/15, 33.3 %). Though most cases were low to moderate impact (10/15, 66.7 %), two participants were hospitalized. Among participants with paresthesia and other symptoms, headache (7/10, 70.0 %), fatigue or weakness (6/10, 60.0 %), and vertigo (3/10, 30.0 %) were reported most frequently.

Bell's palsy was reported by 6/60 (10.0 %) of participants, five of whom had received BNT162b2; three cases met the BCCD. Four participants had a physician diagnosis of GBS, three of whom had received ChAdOx-1.S; none met the BCCD.

Forty-six participants (76.7 %) required additional doses of a COVID-19 vaccine, of which 32/46 (69.6 %) were recommended for further vaccination (see Table 2). Four of 46 participants (8.7 %) were recommended against revaccination: one participant with physician-diagnosed GBS, one with paresthesia/anesthesia, one with functional neurological disorder, and one with vestibular neuritis. A revaccination recommendation was deferred pending further assessment for nine participants and unknown for one.

Twenty-three participants were revaccinated. Most participants (13/23, 56.5 %) received the same mRNA vaccine product associated with their first AEFI, including four participants who developed recurrent symptoms of the AEFI. The AEFIs experienced by the four participants with recurrences were: 1) paresthesia/anesthesia, 2) Bell's palsy, 3) extreme fatigue, headache and difficulty with concentration after dose 1 with recurrence of extreme fatigue, and 4) diplopia six weeks after dose 1 that worsened after dose 2, following initial improvement (but not resolution) between doses 1 and 2 (Table 3). No participant was hospitalized for their recurrence.

4. Discussion

In this national study of individuals 12 years of age and older evaluated for adverse events following COVID-19 vaccination, neurological adverse events represented only 13 % of eligible referrals to the SIC Network. However, the burden of such events was high with 63 % of participants requiring multiple medical visits and/or reporting several days to weeks of disability. Reassuringly, most participants who were revaccinated (83 %) had no recurrence of their AEFI and events that recurred were generally milder than the first event. Similar to prior

Table 1
Characteristics of participants diagnosed with a neurological AEFI following COVID-19 vaccination, stratified by final diagnosis category.

Characteristic	Any neurological AEFI (*N* = 60)	Final Diagnosis of Neurological Event					
		Seizure (*N* = 2)	GBS (*N* = 4)	ADEM/Myelitis/ Encephalitis (*N* = 6)	Bell's Palsy (*N* = 6)	Paresthesia/ Anesthesia (*N* = 15)	Other[1] (*N* = 27)
Sociodemographic characteristics							
Age at screening in years, N (%)							
12–17	4 (6.7)	0	0	0	1 (16.7)	0	3 (11.1)
18–30	8 (13.3)	0	0	3 (50.0)	0	2 (13.3)	3 (11.1)
31–40	13 (21.7)	0	0	2 (33.3)	0	4 (26.7)	7 (25.9)
41–50	12 (20.0)	1 (50.0)	1 (25.0)	1 (16.7)	0	3 (20.0)	6 (22.2)
51–60	14 (23.3)	1 (50.0)	1 (25.0)	0	2 (33.3)	4 (26.7)	6 (22.2)
Older than 60	9 (15.0)	0	2 (50.0)	0	3 (50.0)	2 (13.3)	2 (7.4)
Sex, N (%)							
Female	44 (73.3)	2 (100)	2 (50.0)	5 (83.3)	5 (83.3)	12 (80.0)	18 (66.7)
Male	16 (26.7)	0	2 (50.0)	1 (16.7)	1 (16.7)	3 (20.0)	9 (33.3)
Gender, N (%)							
Woman	38 (63.3)	2 (100)	2 (50.0)	5 (83.3)	3 (50.0)	10 (66.7)	16 (59.3)
Man	15 (25.0)	0	2 (50.0)	1 (16.7)	1 (16.7)	3 (20.0)	8 (29.6)
Other	7 (11.7)	0	0	0	2 (33.3)	2 (13.3)	3 (11.1)
Self-reported race, N (%)							
White	31 (51.7)	1 (50.0)	3 (75.0)	4 (66.7)	4 (66.7)	6 (40.0)	13 (48.1)
Black	2 (3.3)	0	0	0	0	0	2 (7.4)
Asian	2 (3.3)	0	0	1 (16.7)	0	0	1 (3.7)
Not reported	25 (41.7)	1 (50.0)	1 (25.0)	1 (16.7)	2 (33.3)	9 (60.0)	11 (40.7)
Diagnosis of any past medical condition, N (%)							
No	19 (31.7)	0	3 (75.0)	2 (33.3)	3 (50.0)	3 (20.0)	8 (29.6)
Yes	41 (68.3)	2 (100)	1 (25.0)	4 (66.7)	3 (50.0)	12 (80.0)	19 (70.4)
Pre-existing neurological disorder[2] (different from neurological AEFI)	17 (28.3)	2 (100.0)	1 (25.0)	2 (33.3)	1 (16.7)	3 (20.0)	8 (29.6)
History of non-neurological condition	39 (65.0)	2 (100)	1 (25.0)	4 (66.7)	3 (50.0)	12 (80.0)	17 (63.0)
Vaccination and AEFI details							
Brighton Collaboration level of diagnostic certainty[3]	N/A					N/A	N/A
Level 1		2 (100)	0	0	0		
Level 2		0	0	1 (16.7)	0		
Level 3		0	0	5 (83.3)	3 (50.0)		
Level 4		0	4 (100)	0	3 (50.0)		
Dose number, N (%)							
First	49 (81.7)	1 (50.0)	4 (100)	3 (50.0)	6 (100)	13 (86.7)	22 (81.5)
Second	10 (16.7)	1 (50.0)	0	3 (50.0)	0	2 (13.3)	4 (14.8)
Unknown	1 (1.7)	0	0	0	0	0	1 (3.7)
Product Received, N (%)							
ChAdOx1-S	12 (20.0)	0	3 (75.0)	2 (33.3)	1 (16.7)	1 (6.7)	5 (18.5)
mRNA-1273	9 (15.0)	1 (50.0)	0	1 (16.7)	0	5 (33.3)	2 (7.4)
BNT162b2	38 (63.3)	1 (50.0)	1 (25.0)	3 (50.0)	5 (83.3)	9 (60.0)	19 (70.4)
Unknown	1 (1.7)	0	0	0	0	0	1 (3.7)
Onset time, N (%)							
<1 h	11 (8.3)	0	0	0	1 (16.7)	6 (40.0)	4 (14.8)
1–24 h	9 (15.0)	1 (50.0)	1 (25.0)	0	1 (16.7)	2 (13.3)	4 (14.8)
>24 h to <2 days	10 (16.7)	0	0	0	0	3 (20.0)	7 (25.9)
≥2 days	30 (50.0)	1 (50.0)	3 (75.0)	6 (100)	4 (66.7)	4 (26.7)	12 (44.4)
AEFI Impact, N (%)							
Low	5 (8.3)	0	0	0	0	1 (6.7)	4 (14.8)
Moderate	17 (28.3)	2 (100)	0	0	2 (33.3)	9 (60.0)	4 (14.8)
High	20 (33.3)	0	1 (25.0)	1 (16.7)	3 (50.0)	3 (20.0)	12 (44.4)
Serious	18 (30.0)	0	3 (75.0)	5 (83.3)	1 (16.7)	2 (13.3)	7 (25.9)

(*continued on next page*)

Table 1 (*continued*)

Characteristic	Any neurological AEFI (*N* = 60)	Final Diagnosis of Neurological Event					
		Seizure (*N* = 2)	GBS (*N* = 4)	ADEM/Myelitis/ Encephalitis (*N* = 6)	Bell's Palsy (*N* = 6)	Paresthesia/ Anesthesia (*N* = 15)	Other[1] (*N* = 27)
Hospitalized, N (%)	17 (28.3)	0	3 (50.0)	3 (50.0)	1 (16.7)	2 (13.3)	8 (29.6)
Due for subsequent dose(s)[4], N (%)							
No	14 (23.3)	1 (50.0)	0	4 (66.7)	1 (16.7)	4 (26.7)	4 (14.8)
Yes	46 (76.7)	1 (50.0)	4 (100)	2 (33.3)	5 (83.3)	11 (73.3)	23 (85.2)

ADEM, acute disseminated encephalomyelitis; AEFI, adverse event following immunization; N/A, not applicable.

[1] Includes: functional neurological disorder (4), ataxia (2), ataxia with other symptoms (1), acute cerebellitis (1), vestibular neuronitis (2), acute third nerve palsy (1), diplopia (1), extreme fatigue with other symptoms (1), severe headache with other symptoms (1), paresthesia with other symptoms (8), fasciculations/fatiguability (1), unilateral hearing loss (1), vertigo with blurred vision (1), axonal sensorimotor polyneuropathy (1), neuropathic pain (1).

[2] Includes: dystonia, concussion, anxiety, depression, Horner's syndrome, attention deficit hyperactivity disorder, traumatic brain injury, migraine, vertigo, cerebral palsy, multifocal acquired demyelinating sensory motor neuropathy, chronic inflammatory demyelinating polyneuropathy.

[3] Levels of diagnostic certainty were applied as reported in refs 13–15, where Levels 1–3 meet the BCCD and Level 4 is a physician diagnosed case not meeting the BCCD.

[4] Based on recommendations at time of SIC assessment. Some provincial guidelines considered one vaccine dose sufficient for individuals with history of SARS-CoV-2 infection prior to or following the first COVID-19 vaccination.

Table 2
Revaccination recommendations and outcomes among participants due for subsequent COVID-19 vaccination dose(s) stratified by type of neurological AEFI.

Characteristic	Any neurological AEFI (*N* = 46)	Final Diagnosis of Neurological Event					
		Seizure (*N* = 1)	GBS (*N* = 4)	ADEM/Myelitis/ Encephalitis (*N* = 2)	Bell's Palsy (*N* = 5)	Paresthesia/ Anesthesia (*N* = 11)	Other (*N* = 23)
Vaccination recommended, N (%)							
No	4 (8.7)	0	1 (25.0)	0	0	1 (9.1)	2 (8.7)
Yes	32 (69.6)	1 (100)	2 (50.0)	1 (50.0)	5 (100.0)	8 (72.7)	15 (65.2)
Decision deferred pending further assessment	9 (19.6)	0	1 (25.0)	1 (50.0)	0	2 (18.2)	5 (21.7)
Unknown	1 (2.2)	0	0	0	0	0	1 (4.3)
Revaccination intentions among those recommended for vaccination							
Willing to be revaccinated							
No	6 (18.8)	0	0	1 (100)	0	0	5 (33.3)
Yes	14 (43.8)	0	1 (50.0)	0	3 (60.0)	3 (37.5)	7 (46.7)
Decision deferred	11 (34.4)	1 (100)	1 (50.0)	0	2 (40.0)	5 (62.5)	2 (13.3)
Unknown	1 (3.1)	0	0	0	2 (40.0)	0	1 (6.7)
Revaccination outcomes among revaccinated participants							
Total revaccinated	23 (50.0)	1 (100)	1 (25.0)	0	3 (60.0)	5 (45.5)	13 (56.5)
Product received, N (%)							
mRNA-1273	5 (21.7)	1 (100)	0	0	1 (33.3)	2 (40.0)	1 (7.7)
BNT162b2	17 (73.9)	0	1 (100)	0	2 (66.7)	3 (60.0)	11 (84.6)
ChAdOx-1-S	1 (4.3)	0	0	0	0	0	1 (7.7)
AEFI following revaccination, N (%)							
No	15 (65.2)	0	1 (100)	0	2 (66.7)	4 (80.0)	8 (61.5)
Yes	6 (26.1)	1 (100)	0	0	1 (33.3)	1 (20.0)	3 (23.1)[1]
Unknown	2 (8.7)	0	0	0	0	0	2 (15.4)
Revaccination AEFI Characteristics							
Recurrence of referral AEFI, N (%)							
No	2 (33.3 %)	1 (100)	0	0	0	0	1 (33.3)
Yes	4 (66.7 %)	0	0	0	1 (100)	1 (100)	2 (66.7)

ADEM, acute disseminated encephalomyelitis; AEFI, adverse event following immunization.

[1] Includes diplopia (1), hearing loss (1) and extreme fatigue, headache and difficulty with concentration (1).

studies, participants experienced a range of AEFIs including GBS, Bell's/facial palsy, paresthesia/anesthesia, ADEM, functional neurological disorders, and vestibular disturbances. [4–7,9,16–18]

Though referrals for neurological AEFI were uncommon in this study, symptoms such as paresthesia and hypoesthesia were among the most common AEFIs reported to passive surveillance systems in Canada, accounting for 22 % of over 53,000 reports received from 2020 to 2022. [2] It may be that most such events were mild and self-limited, and public health professionals felt comfortable to recommend revaccination without need for SIC referral. SICs with limited capacity may also have triaged referrals to prioritize those with the most severe or serious presentations.

Notably, only 50 % of participants who required additional doses of a COVID-19 vaccine to complete a primary series received subsequent vaccination. In contrast, in a study from Singapore 77 % of individuals who were hospitalized for a neurological event within 6 weeks after their first COVID-19 vaccination, received a second dose. [18] However, those with greater disability following their AEFI were less likely to accept revaccination. In our study, most participants not recommended for revaccination and most who refused revaccination had high and serious impact AEFIs. Our results are similar to prior studies of non-COVID vaccines, which have generally shown lower acceptance of revaccination among those with neurological AEFIs and events that are serious or require medical attention. [19,20] The impact of a serious and/or neurological adverse event on the individual may lead them to weigh the risks of vaccination as being higher than the risk of the

Table 3
Case series of participants experiencing recurrent symptoms of their AEFI following COVID-19 revaccination.

Characteristic	Case 1	Case 2	Case 3	Case 4
Age	31–40	31–40	51–60	18–30
Sex	Female	Female	Female	Female
Gender	Woman	Woman	Woman	Woman
Race	Unknown	White	White	White
Medical History	Mononucleosis (EBV), prior concussion, allergies (food, pollen, animals)	Prior history of myelitis, potential Crohn's, Irritable bowel syndrome, eczema, allergic rhinitis, drug allergies	Psoriatic arthritis, Psoriasis, drug allergy	Cyclic vomiting
Vaccine associated with initial AEFI	BNT162b2	BNT162b2	BNT162b2	BNT162b2
Final AEFI diagnosis	Other neurological event (extreme fatigue, headache and difficulty with concentration)	Paresthesia/Anesthesia (Left hemiface paresthesia)	Bell's/facial palsy	Other neurological reaction (diplopia)
AEFI description	Headache on day 1 -Fatigue, diarrhea, fever, delay of menstrual cycle, palpebral edema from day 5 -Headache persisted with night sweats and weight loss -Difficulties in concentration	Left hemifrontal headache with left hemiface paresthesia	-Dizziness, tongue and throat swelling -Transferred to ED -Developed fatigue, headaches, nausea and chest pain −3 weeks post- vaccination, facial hypoesthesia on left face with pain, evolved to Bell's palsy	6 weeks post- vaccination, developed occasional diplopia to movement such as when driving
Initial AEFI time to onset	24 h	20 min	5 min	42 days
Acute management of AEFI	-Acetaminophen -Ibuprofen -Clonazepam	No treatment given	Unknown	No treatment given
AEFI Impact	High	Low	High	Low
Medical attention required	Consulted a physician	None	Consulted a physician	None
Duration of AEFI	Not reported	Not reported	30 days	Not reported
Product for revaccination	BNT162b2	BNT162b2	BNT162b2	BNT162b2
Vaccine dose for revaccination	2	2	2	2
Final diagnosis after revaccination	Recurrence of referral AEFI	Recurrence of referral AEFI	Recurrence of referral AEFI	Recurrence of referral AEFI
Revaccination AEFI description	Extreme fatigue the first day following vaccination, muscular pain during the first 24 h following vaccination	Numbness in left cheek, less intense than after first dose, no headache reported	One hour after vaccination, developed hypoesthesia on left face. 3 weeks later Bell's palsy recurred, milder than the first with headaches and facial swelling	Persistence of occasional diplopia on movement with same severity as the initial AEFI. Reassessed by optometrist
Time to AEFI onset	24 h	40 min	1 h	0 min
Acute management of AEFI	No treatment given	No treatment given	No treatment given	No treatment given
AEFI Impact	Low	Low	Moderate	Moderate
Severity of recurrent AEFI compared to initial AEFI	Milder	Milder	Milder	Same
Duration of AEFI	2 days	5 days	Unknown	Unknown

AEFI, adverse event following immunization; ED, Emergency Department; N/A, not available.

disease, particularly among younger individuals who may perceive the risk of COVID-19 as low. Further studies of attitudes and perceptions of vaccine safety and confidence in this patient population are needed to improve counselling and risk communication to support vaccination where appropriate.

Overall, AEFI recurrence is uncommon, as demonstrated in prior studies of a range of vaccines. [10,19] In the Singaporean study mentioned above only 2 % of individuals had a recurrence of their neurological symptoms after COVID-19 revaccination. [18] However, few studies have examined recurrence of neurological AEFIs with COVID-19 vaccines. Moreover, too few patients with neurological adverse events of special interest were revaccinated to assess recurrence of specific AEFIs (e.g., GBS, Bell's palsy). Reassuringly, for those who did have a recurrence in our study, the recurrent event was generally reported to be milder than the first event.

This study had limitations. The SIC Network relies on referrals from healthcare providers and only four sites, all in tertiary care centres, recruited adults with neurological AEFIs. This likely led to referral bias toward more severe and complex patients located near tertiary centers. Availability of more adult sites might have contributed to increasing the sample size and improving generalizability of the results. Individuals who chose to be assessed in the SIC network and consented to the study may have been more likely to accept vaccination than the general public. However, some participants may have felt compelled to undergo SIC assessment and/or receive vaccination due to vaccine mandates introduced in most jurisdictions by September 2021 that required proof of primary COVID-19 vaccination or a medical exemption to travel, work in certain sectors, or engage in many leisure activities. [21] These mandates may also have driven the relatively large number of referrals for patients with AEFIs following their first dose compared to the second dose. The case report form was developed before COVID-19 vaccines were implemented which led to heterogeneity in the reporting of the final diagnosis in some cases (e.g., vertigo versus vestibular neuritis), and medical records were not always available to confirm details of the AEFI or extract data needed to apply Brighton Collaboration case definitions. Finally, the sample size was insufficient to assess revaccination outcomes by AEFI type or among adolescents.

Strengths included the study's longitudinal, multi-centre design which enabled follow up of revaccination outcomes and supported generalizability of the results of these rare AEFIs.

5. Conclusion

The results support that clinically significant neurological events after COVID-19 vaccination are an uncommon reason for referral to SICs, and that patients with neurological AEFIs can be safely revaccinated. Expert assessment of patients with neurological AEFIs in SICs may help to support safe revaccination.

CRediT authorship contribution statement

Tiffany Fitzpatrick: Writing – review & editing, Writing – original draft, Visualization, Supervision, Methodology, Formal analysis, Data curation, Conceptualization. **Peter Yamoah:** Writing – review & editing, Visualization, Data curation. **David Summerby-Murray:** Visualization, Methodology, Data curation, Conceptualization. **Juthaporn Cowan:** Writing – review & editing, Supervision, Methodology, Investigation. **Manish Sadarangani:** Writing – review & editing, Methodology, Investigation. **Alissa Wright:** Writing – review & editing, Methodology, Investigation. **Sara Belga:** Writing – review & editing, Methodology, Investigation. **Cora Constantinescu:** Writing – review & editing, Methodology, Investigation. **Alex Carignan:** Writing – review & editing, Methodology, Investigation. **Athena McConnell:** Writing – review & editing, Methodology, Investigation. **Karina A. Top:** Writing – original draft, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization.

Funding statement

This study was funded by the Canadian Institutes of Health Research and Public Health Agency of Canada through the Canadian Immunization Research Network and by the Public Health Agency of Canada through the COVID-19 Immunity Task Force. TF was supported by a Killam Memorial Postdoctoral Fellowship. DSM received support from the Dalhousie University Faculty of Medicine Beth Rafuse Memorial Studentship. MS receives salary support from the BC Children's Hospital Research Institute and Michael Smith Health Research BC. JC receives salary support from Department of Medicine, University of Ottawa.

Declaration of competing interest

MS has been an investigator on projects funded by GlaxoSmithKline, Merck, Moderna, Pfizer and Sanofi-Pasteur. All funds have been paid to his institute, and he has not received any personal payments. SB has received research funding from Moderna and consulting fees from AstraZeneca, Moderna and GlaxoSmithKline unrelated to this study. AM received honoraria for presentations from Pfizer and Sanofi. AC received honoraria for presentations from Pfizer, AstraZeneca, GlaxoSmithKline and Moderna. JC received honoraria from Pfizer, AstraZeneca and was involved in projects funded by GlaxoSmithKline. KAT has received funding to her institution from the Coalition for Epidemic Preparedness Innovations for vaccine safety studies. The remaining authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors acknowledge the expert assistance of Philmona Kebedom (University of Alberta), Adrienne Bellamy, Yun Cai, Raashsni Chandrasekar, Melissa Moore, Lingyun Ye (Canadian Center for Vaccinology) and the SIC network coordinators and nurses.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2025.127254.

Data availability

Data will be made available on request.

References

[1] National Advisory Committee on Immunization. COVID-19 vaccine. Canadian Immunization Guide. Ottawa, ON: Government of Canada; 2025. URL: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-26-covid-19-vaccine.html. Accessed 16 May 2025.
[2] Public Health Agency of Canada. COVID-19 vaccine safety in Canada. Ottawa, ON: Government of Canada; 2024. URL: https://health-infobase.canada.ca/covid-19/vaccine-safety/. Accessed 16 May 2025.
[3] Safety Platform for Emergency Vaccines. COVID-19 AESI list 5th update – October 2022. Decatur, GA: Brighton Collaboration; 2022.
[4] Patone M, Handunnetthi L, Saatci D, Pan J, Katikireddi SV, Razvi S, et al. Neurological complications after first dose of COVID-19 vaccines and SARS-CoV-2 infection. Nat Med 2021;27:2144–53.
[5] Abara WE, Gee J, Marquez P, Woo J, Myers TR, DeSantis A, et al. Reports of Guillain-Barré syndrome after COVID-19 vaccination in the United States. JAMA Netw Open 2023;6:e2253845.
[6] Faksova K, Walsh D, Jiang Y, Griffin J, Phillips A, Gentile A, et al. COVID-19 vaccines and adverse events of special interest: a multinational global vaccine data network (GVDN) cohort study of 99 million vaccinated individuals. Vaccine 2024;42:2200–11.
[7] Frontera JA, Tamborska AA, Doheim MF, Garcia-Azorin D, Gezegen H, Guekht A, et al. Neurological events reported after COVID-19 vaccines: an analysis of VAERS. Ann Neurol 2022;91:756–71.
[8] Garcia-Grimshaw M, Ceballos-Liceaga SE, Michel-Chavez A, Garcia-Alanis M, Cadena-Fernandez A, Galnares-Olalde JA, et al. Transient sensory symptoms among first-dose recipients of the BNT162b2 mRNA COVID-19 vaccine: a case-control study. Vaccine 2021;39:6975–9.
[9] Otero-Losada M, Petrovsky N, Alami A, Crispo JA, Mattison D, Capani F, et al. Disproportionality analysis of adverse neurological and psychiatric reactions with the ChAdOx1 (Oxford-AstraZeneca) and BNT162b2 (Pfizer-BioNTech) COVID-19 vaccines in the United Kingdom. Expert Opin Drug Saf 2023;22:343–9.
[10] Munoz CE, MacDonald B, Pham-Huy A, Vaudry W, Pernica JM, Boucher FD, et al. Revaccination and adverse event recurrence in patients with adverse events following immunization. J Pediatr 2022;250(45–53):e3.
[11] Public Health Agency of Canada. COVID-19 vaccination in Canada. 2024. https://health-infobase.canada.ca/covid-19/vaccination-coverage/. Accessed 16 May 2026.
[12] Law BJ, Lafleche J, Ahmadipour N, Anyoti H. Canadian Adverse Events Following Immunization Surveillance System (CAEFISS): Annual report for vaccines administered in 2012. Can Commun Dis Rep 2014;40:7–23.
[13] Sejvar JJ, Kohl KS, Bilynsky R, Blumberg D, Cvetkovich T, Galama J, et al. Encephalitis, myelitis, and acute disseminated encephalomyelitis (ADEM): case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine 2007;25:5771–92.
[14] Sejvar JJ, Kohl KS, Gidudu J, Amato A, Bakshi N, Baxter R, et al. Guillain-Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine 2011;29:599–612.
[15] Rath B, Gidudu JF, Anyoti H, Bollweg B, Caubel P, Chen YH, et al. Facial nerve palsy including Bell's palsy: case definitions and guidelines for collection, analysis, and presentation of immunisation safety data. Vaccine 2017;35:1972–83.
[16] Samim MM, Dhar D, Arshad F, Anudeep DDS, Patel VG, Neeharika SR, et al. Co-VAN study: COVID-19 vaccine associated neurological diseases- an experience from an apex neurosciences Centre and review of the literature. J Clin Neurosci 2023;108:37–75.
[17] Rafati A, Pasebani Y, Jameie M, Yang Y, Jameie M, Ilkhani S, et al. Association of SARS-CoV-2 vaccination or infection with Bell palsy: a systematic review and Meta-analysis. JAMA Otolaryngol Head Neck Surg 2023;149:493–504.
[18] Koh JS, Hoe RHM, Chen GJ, Goh Y, Tan BYQ, Yong MH, et al. Low incidence of neurological recurrent side-effects following COVID-19 reimmunization. QJM 2023;116:221–6.
[19] Zafack JG, Toth E, Landry M, Drolet JP, Top KA, De Serres G. Rate of recurrence of adverse events following immunization: results of 19 years of surveillance in Quebec, Canada. Pediatr Infect Dis J 2019;38:377–83.
[20] Munoz CE, Pham-Huy A, Pernica JM, Boucher FD, De Serres G, Vaudry W, et al. Factors associated with intention for revaccination among patients with adverse events following immunization. Vaccine 2023;41:6239–47.
[21] Charrier LGJ, Thomas R, Gardois P, Bo M, Zotti CM. An overview of strategies to improve vaccination compliance before and during the COVID-19 pandemic. Int J Environ Res Public Health 2022 Sep;3(19):11044.