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Revaccination of individuals with cardiac adverse events following COVID-19 vaccination: A Canadian Immunization Research Network study

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ABSTRACT

Introduction: Myocarditis and pericarditis are well-described rare adverse events following immunization (AEFI) associated with COVID-19 mRNA vaccines. Safety data on revaccination among people with previous cardiac AEFIs are lacking. This study assessed outcomes of COVID-19 revaccination among participants assessed for cardiac AEFIs.

Abbreviations: **AEFI**, Adverse Event Following Immunization; **BCCD**, Brighton Collaboration Case Definition; **cMRI**, Cardiac Magnetic Resonance Imaging; **SIC**, Special Immunization Clinic; **NACI**, National Advisory Committee on Immunization; **ECG**, Electrocardiogram; **WHO**, World Health Organization; **LOC**, Level of diagnostic certainty; **IQR**, Interquartile range.

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Methods: The Special Immunization Clinic Network database, containing data from consented participants across twelve sites, was analyzed. Cases were classified using the Brighton Collaboration Case Definitions (BCCDs) for mutually exclusive diagnoses of myocarditis, myopericarditis or pericarditis. Subjects with cardiac symptoms not meeting the BCCD and with no alternative diagnosis were categorized as chest pain/other cardiac diagnosis. Revaccination recommendations were based on physician judgment, informed by national guidelines. Participants were followed up to 42 days after revaccination to capture AEFI recurrence.
Results: Between January 1, 2021 and February 23, 2023, 114 participants were enrolled, including 46 with myocarditis (40.4 %), 26 (22.8 %) with myopericarditis, 11 (9.6 %) with pericarditis, and 31 (27.1 %) with chest pain/other cardiac diagnosis. Twenty-seven of 71 participants (38.0 %) who required further COVID-19 vaccine doses were recommended for revaccination. Sixteen participants were revaccinated: two with myocarditis, two with myopericarditis, two with pericarditis and 10 with chest pain/other cardiac diagnosis. Four adults had recurrent symptoms of the AEFI: 2/10 with previous chest pain/other cardiac diagnosis, one participant with previous pericarditis and multiple comorbid conditions, and one participant with previous myopericarditis who required hospitalization.
Conclusions: COVID-19 mRNA revaccination may be considered for individuals with chest pain not meeting criteria for myocarditis but caution is warranted in adults with prior confirmed myopericarditis post-COVID-19 mRNA vaccination.

1. Introduction

Vaccination has played an essential role in mitigating the health burden of SARS-CoV-2 infection [1]. While COVID-19 vaccines were assessed for safety during clinical trials, rigorous post-marketing surveillance of adverse events following immunization (AEFIs) has been of utmost importance to maintain trust in the vaccination campaign [2]. Cases of myocarditis and pericarditis were first reported following BNT162b2 in Israel in March 2021 [3], with surveillance systems in other countries subsequently confirming the signal and association between COVID-19 mRNA vaccination and myopericarditis and pericarditis, most often in younger men 16 to 30 years of age [4–11]. The Vaccine Safety Datalink in the United States reported that myocarditis/pericarditis occurred 0 to 7 days after COVID-19 mRNA vaccination in approximately 1 in 200,000 vaccinees aged 5 to 39 years after the first dose, 1 in 30,000 after second dose, and 1 in 50,000 doses after the first booster [12]. Reassuringly, observational studies have shown that patients with pericarditis, myocarditis or myopericarditis following COVID-19 vaccination typically improve within 3 months with conservative treatment and rest [4–11,13]. However, some patients have changes on cardiac magnetic resonance imaging (cMRI) that have persisted on follow-up imaging [14–16].

Immunization guidelines have generally recommended against further mRNA vaccination for patients with a history of myocarditis or pericarditis following COVID-19 mRNA vaccination [17,18]. However, for patients with cardiac AEFIs after the first primary dose or those at increased risk of complications from SARS-CoV-2 infection, data are lacking on the risk of recurrence of cardiac AEFIs following subsequent vaccination that could inform risk-benefit assessment. The current study aims to fill this knowledge gap by describing revaccination practices and outcomes among a cohort of individuals who experienced cardiac AEFIs and were referred to the Canadian Special Immunization Clinic (SIC) Network.

The SIC Network was established in 2013 to improve immunization practices for individuals with prior AEFIs or medical conditions that are precautions to immunization [19]. In Canada, the first COVID-19 mRNA vaccines were authorized by Health Canada on December 9, 2020, for individuals aged 16 years and older (BNT162b2) [20]. The first mRNA vaccines were subsequently approved for children aged 12 to 15 years on May 5, 2021, for children 5 to 11 years old on November 19, 2021, and for children 6 months to 4 years on July 14, 2022 [21,22]. The SIC Network was leveraged to assess patients who experienced adverse events following COVID-19 vaccines, and to provide guidance around revaccination. This analysis thus aims to describe revaccination practices among patients who experienced cardiac adverse events following COVID-19 vaccines, and to estimate the risk of AEFI recurrence following revaccination.

2. Materials and methods

2.1. Study population

This was a prospective observational study in individuals who were referred to the SIC Network and enrolled from January 1, 2021 to February 23, 2023. Patients who were assessed for an adverse event following COVID-19 vaccination with symptoms that were suggestive of a cardiac event (e.g., chest pain, dyspnea, palpitations) were eligible for inclusion. Twelve SIC sites in five Canadian provinces accepted referrals for cardiac AEFIs during the study period, including seven pediatric centers, three adult centers and two pediatric/adult centers. SIC assessment occurred as part of routine clinical care, with usual care provided for the diagnosed cardiac condition. Clinical care was informed by local and national guidelines, including a clinical care guideline developed by a group of infectious diseases physicians, cardiologists, rheumatologists and emergency physicians at The Hospital for Sick Children and circulated to the SIC network, the Canadian Cardiovascular Society guideline for post-vaccine myocarditis, and the National Advisory Committee on Immunization (NACI) guidance on myocarditis after COVID-19 vaccination with regards to decision for revaccination [23–25].

2.2. Clinical procedures

Investigations and management at the time of participants' initial presentation with their AEFI were led by the primary treating physician (e.g., emergency physician, primary care physician and/or cardiologist), who made recommendations for follow-up care, including additional investigations such as repeat troponins or inflammatory markers, electrocardiogram (ECG), echocardiogram, or cMRI as indicated for clinical care, and consideration of referral to a SIC. In the SIC, participants underwent standardized clinical assessment of the AEFI including a detailed review of the event, clinical history, and medical record review.

As determined by the SIC physician at the time of assessment, based on their clinical judgment, some participants were recommended to undergo additional investigations for causes of myocarditis/pericarditis other than vaccination. Following clinical assessment and results of investigations, the SIC physician assessed causality of the AEFI and association with vaccination based on the World Health Organization (WHO) algorithm [26]. Recommendation for revaccination was made by the SIC physician based on a risk-benefit assessment and informed by local and national guidelines and in collaboration with cardiology, as needed. Participants recommended for revaccination were followed up to capture details of the immunization and occurrence of adverse events at 7 days and 30–42 days post-revaccination to assess for symptoms of an AEFI. AEFI recurrence was defined as occurrence of signs and symptoms

suggestive of a cardiac adverse event following a subsequent dose of COVID-19 vaccine.

2.3. Data collection and sources

Participant data including age, sex, race/ethnicity, past medical history, details of the AEFI, results of investigations (including all cardiac-related investigations), AEFI diagnosis by the physician (myocarditis, myopericarditis, pericarditis, other cardiac AEFI), AEFI impact, causality assessment, revaccination recommendations, and outcomes were captured in a standard data collection form. The form included the required information to apply the Brighton Collaboration Case Definitions (BCCDs) for myocarditis and pericarditis [27]. The impact of the AEFI on daily activities and need for medical attention was defined as per the Public Health Agency of Canada: low impact (i.e., impacted patient's daily activities for up to 1 day, event managed by vaccine clinical staff or without medical care), moderate impact (e.g., 1–3 days disability, unscheduled physician visit), high impact (4–14 days disability, multiple unscheduled physician visits or up to 24 h in-hospital observation), or serious (e.g. requiring hospitalization, life-threatening) (Supplementary Table 1) [28]. De-identified data were entered into the SIC network's centralized electronic database.

2.4. Application of the Brighton Collaboration Case Definitions (BCCD)

Cases were classified retrospectively by one author (PPPR) and adjudicated by four other authors (AJ, SKM, JC, KAT) according to the BCCDs for myocarditis and pericarditis (2021 version), based on the initial physician diagnosis (Supplementary Tables 2 and 3) [27]. Cases with physician-diagnosed myocarditis were adjudicated under the BCCD myocarditis definition, cases with physician-diagnosed pericarditis were adjudicated under the BCCD pericarditis definition, and cases with physician-diagnosed with myopericarditis were adjudicated under both the BCCD pericarditis and myocarditis definitions. Cases meeting level of diagnostic certainty (LOC) 1, 2 or 3 for the applicable case definition (s) were considered to meet the BCCD. Cases of physician-diagnosed myopericarditis were analyzed as myopericarditis if they met both case definitions, as myocarditis if they met the myocarditis but not pericarditis case definition, and as pericarditis if they only met that case definition. Participants with physician diagnosis of cardiac AEFI who did not meet the BCCD criteria (for example, chest pain with a normal or incomplete cardiac workup) and without an alternate diagnosis were categorized as having "chest pain/other cardiac diagnosis" following COVID-19 vaccination.

2.5. Statistical analyses

Descriptive statistics were reported for the overall cohort characteristics, including demographic characteristics, AEFI diagnosis (myocarditis, myopericarditis, pericarditis, or chest pain/other cardiac diagnosis), interval from vaccination to onset, AEFI impact, healthcare utilization (e.g., emergency visit, hospitalization), vaccine product received, number of doses received, dosing interval (if applicable), treatment received, recommendations for revaccination, receipt of further COVID-19 vaccine doses, and outcomes of revaccination. Results of cardiac-related investigations were classified as either meeting or not meeting BCCD criteria for myocarditis and pericarditis, including ECG, echocardiogram and cMRI, if performed (Supplementary Tables 2 and 3). Troponins were considered elevated when the value was 1.5 times above the locally established threshold for upper limit of normal to account for differences between assays used in different centers. Dichotomous and categorical variables were described using frequencies and percentages. Continuous variables were described using median and interquartile range (IQR). Descriptive statistics were also performed by subgroups of interest (by AEFI diagnosis, revaccination recommendation and recurrence of AEFI). All analyses were performed using SAS OnDemand.

3. Results

3.1. Study cohort characteristics

The analysis included a total of 114 participants, including 55 children aged 12–17 years (48.3 %), three children aged 5–11 years (2.6 %), and 56 adults aged ≥18 years (49.1 %) (Table 1). There was no participant younger than five years. Most participants were male (n = 87, 76.3 %) and 42 (36.8 %) participants had a comorbid condition, including 13 (11.4 %) with an underlying cardiovascular comorbidity (congenital heart disease, arrhythmia, hypertension or previous history of pericarditis). Most participants presented with their AEFI in June and July 2021 (n = 64, 56.1 %) (Fig. 1).

Forty-six participants had myocarditis (40.4 %), 11 pericarditis (9.6 %), 26 myopericarditis (22.8 %) and 31 (27.2 %) participants had a diagnosis of chest pain/other cardiac diagnosis. Most participants had received BNT162b2 (n = 82, 71.9 %) prior to their initial AEFI, 29 (25.4 %) received mRNA-1273, and one participant with chest pain/other cardiac diagnosis had received ChAdOx1 vaccination. Most cases occurred after the second dose (n = 62, 54.4 %). The median onset of symptoms after vaccination was 2 days (IQR 1–5 days). Median duration of symptoms for the overall cohort was 7 days (IQR 3–28 days). Most participants with myocarditis (n = 28, 60.9 %) and myopericarditis (n = 15, 57.7 %) were hospitalized, while only three (27.3 %) participants with pericarditis and three (9.7 %) with chest pain/other cardiac diagnosis were hospitalized. Thirteen (22.4 %) children required hospital admission, as opposed to 36 (64.3 %) adults (Table 2). Two participants with myocarditis and one with pericarditis required intensive care unit (ICU) admission.

3.2. Recommendation for revaccination and outcomes

At time of SIC assessment, 71 (62.3 %) participants were determined to require further COVID-19 vaccine doses to complete the primary series or as a booster (Table 3). After risk/benefit assessment, revaccination was recommended to 27 subjects (38.0 %), with six having a diagnosis of myocarditis, four pericarditis, three myopericarditis and 14 chest pain/other cardiac diagnosis. Half of subjects recommended for revaccination had an underlying comorbid condition (n = 14, 51.9 %) and five (18.5 %) had an underlying cardiovascular comorbidity.

Sixteen participants were revaccinated: two with myocarditis, two with myopericarditis, two with pericarditis, and 10 with chest pain/other cardiac diagnosis. Most cases were revaccinated with BNT162b2 (13/16, 81.3 %), one was revaccinated with mRNA-1273, and one case was revaccinated with protein subunit vaccine (Nuvaxovid). Most cases received the same product that they had received for their initial vaccination (11/16, 68.8 %).

Four revaccinated patients (25.0 %) experienced recurrent symptoms of the cardiac AEFI following revaccination, three of whom had underlying medical conditions (Table 4). All recurrences occurred in adults. The first participant was a healthy male 18–30 years old who had an initial AEFI diagnosis of myopericarditis after dose 2 mRNA-1273 that required hospitalization and subsequently had a recurrence after the third dose (with BNT162b2) that also required hospitalization. The third dose was given 18 months after the second dose. The second participant was a male 31–64 years old with an underlying immunocompromising condition. He experienced non-specific chest pain/other cardiac diagnosis following dose 1 BNT162b2 and reported recurrence of non-specific chest pain starting 14 days after dose 2 BNT162b2. The third participant was a female 31–64 years old who was diagnosed with chest pain/other cardiac diagnosis attributed to an emerging underlying condition and was considered inconsistent with causal association to immunization. She experienced recurrence of dyspnea after revaccination that had indeterminate causal association with vaccination and did

Table 1
Characteristics of the study participants by final diagnosis.

Participant characteristics	BCCD confirmed diagnosis[a]			Chest pain / other cardiac diagnosis	Total
	Myocarditis	Pericarditis	Myopericarditis		
Total	**46**	**11**	**26**	**31**	**114**
Participants' characteristics					
Age group					
5–11 years	1 (2.2)	0	1 (3.9)	1 (3.2)	3 (2.6)
12–17 years	23 (50.0)	1 (9.1)	12 (46.2)	19 (61.3)	55 (48.3)
18–30 years	12 (26.1)	3 (27.3)	9 (34.6)	5 (16.1)	29 (25.4)
31–64 years	9 (19.6)	5 (45.5)	4 (15.4)	4 (12.9)	22 (19.3)
≥65 years	1 (2.2)	2 (18.2)	0	2 (6.5)	5 (4.4)
Age in years (Median, IQR)	17 (15–23)	38 (29–52)	19 (15–27)	16 (13–27)	17 (15–29)
Sex (n,%)					
Male	40 (87.0)	8 (72.7)	19 (76.9)	19 (61.3)	87 (76.3)
Female	6 (13.0)	3 (27.3)	6 (23.1)	11 (35.5)	26 (22.8)
Other/Unknown	0	0	0	1 (3.2)	1 (0.9)
Self-reported race (n,%)					
White	23 (50.0)	4 (36.4)	8 (30.8)	12 (38.7)	47 (41.2)
Black	1 (2.2)	1 (9.1)	0	0	2 (1.8)
Asian[b]	4 (8.7)	1 (9.1)	1 (3.9)	4 (12.9)	10 (8.8)
Middle eastern	4 (8.7)	0	3 (11.5)	1 (3.2)	8 (7.0)
Not reported	14 (30.4)	5 (45.5)	14 (53.9)	14 (45.2)	47 (41.2)
Any underlying comorbid condition (n,%)[c]	17 (37.0)	6 (54.6)	8 (30.7)	11 (35.5)	42 (36.8)
Cardiovascular comorbidity[d]	4 (8.7)	2 (18.2)	3 (11.5)	4 (12.9)	13 (11.4)
Chronic respiratory disease[e]	12 (26.1)	4 (36.4)	3 (11.5)	2 (6.5)	21 (18.4)
Diabetes or other metabolic disorder[f]	3 (6.5)	2 (18.2)	1 (3.9)	2 (6.5)	8 (7.0)
Chronic kidney disease[g]	1 (2.2)	0	0	1 (3.2)	2 (1.8)
Chronic liver disease[h]	0	1 (9.1)	0	1 (3.2)	2 (1.8)
Other gastrointestinal diseases[i]	3 (6.5)	1 (9.1)	0	2 (6.5)	6 (5.3)
Neurological disorder[j]	3 (6.5)	1 (9.1)	0	2 (6.5)	6 (5.3)
Autoimmune disorder[k]	3 (6.5)	0	3 (11.5)	2 (6.5)	8 (7.0)
Immunosuppressive condition[l]	0	2 (18.2)	0	0	2 (1.8)
Any history of SARS-CoV-2 infection prior to AEFI (n,%)	6 (13.0)	2 (18.2)	4 (15.4)	4 (12.9)	16 (14.0)
Vaccine and AEFI characteristics					
Vaccine product received (n,%)					
BNT162b2	30 (65.2)	9 (81.8)	14 (53.8)	29 (93.6)	82 (71.9)
mRNA-1273	15 (32.6)	2 (18.2)	11 (42.3)	1 (3.2)	29 (25.4)
ChAdOx1	0	0	0	1 (3.2)	1 (0.9)
Not specified	1 (2.2)	0	1 (3.8)	0	2 (1.8)
Vaccine dose associated with initial AEFI (n,%)					
1	14 (31.1)	6 (54.6)	5 (19.2)	21 (67.7)	48 (42.1)
2	29 (64.4)	5 (45.4)	19 (73.1)	10 (32.3)	62 (54.4)
3	2 (4.4)	0	2 (7.7)	0	4 (3.5)
Interval from vaccination to onset of symptoms in days (median, IQR)	2 (1–4)	6 (2–18)	1 (0–3)	2 (1−10)	2 (1–5)
Duration of symptoms in days (median, IQR)	7 (3−21)	5 (1–28)	13.5 (3−30)	7 (2−30)	7 (3–28)
Initial physician diagnosis					
Myocarditis	46 (100.0)	0	0	11 (35.5)	57 (50.0)
Pericarditis	0	10 (90.9)	0	6 (19.4)	16 (14.0)
Myopericarditis	0	0	26 (100.0)	1 (3.2)	27 (23.7)
Other cardiac AEFI	0	1 (9.1)	0	13 (41.9)	14 (12.3)
Impact of the AEFI (n,%)[m]					
Low	0	0	0	1 (3.2)	1 (0.9)
Moderate	14 (30.4)	6 (54.6)	10 (38.5)	22 (70.9)	52 (45.6)
High	8 (17.4)	2 (18.2)	4 (15.4)	6 (19.4)	20 (17.5)
Serious	24 (52.2)	3 (27.3)	12 (46.2)	2 (6.5)	41 (36.0)
Causality assessment[n]					
Consistent causal association	36 (78.3)	6 (54.5)	24 (92.3)	18 (58.1)	84 (73.7)
Inconsistent	1 (2.2)	0	0	4 (12.9)	5 (4.4)
Indeterminate	9 (19.6)	5 (45.5)	2 (7.7)	9 (29.0)	25 (21.9)
Required hospitalization (n,%)	28 (60.9)	3 (27.3)	15 (57.7)	3 (9.7)	49 (43.0)
Duration of hospitalization in days (median, IQR)	3 (2–4)	4 (1–4)	4 (3–4)	5 (2–5)	3 (2–4)
Required ICU admission (n,%)	2 (4.4)	1 (9.1)	0	0	3 (2.6)
Treatment received					
NSAIDS	8 (17.4)	5 (45.5)	7 (26.9)	4 (12.9)	24 (21.1)
Steroids	0	2 (18.2)	1 (3.2)	0	3 (2.6)
Colchicine	6 (13.0)	3 (27.3)	5 (19.2)	1 (3.2)	15 (13.2)
Other treatment[o]	3 (6.5)	2 (18.2)	1 (3.2)	3 (9.7)	9 (7.9)
Investigation results					
ECG result (n,%)					
Normal	19 (41.2)	0	8 (30.8)	16 (51.6)	43 (37.7)
Abnormal[p]	25 (53.4)	10 (90.9)	16 (61.5)	8 (25.8)	59 (51.8)
Not performed	2 (4.4)	1 (9.1)	2 (7.7)	7 (22.6)	12 (10.5)
Echocardiogram result (n,%)					

(*continued on next page*)

Table 1 (*continued*)

Participant characteristics	BCCD confirmed diagnosis[a]			Chest pain / other cardiac diagnosis	Total
	Myocarditis	Pericarditis	Myopericarditis		
Normal	32 (69.6)	4 (36.4)	19 (73.1)	20 (64.5)	16 (14.0)
Abnormal[q]	7 (15.2)	3 (27.2)	5 (19.2)	1 (3.2)	75 (65.8)
Not performed	7 (15.2)	4 (36.4)	2 (7.7)	10 (32.3)	23 (20.2)
Cardiac MRI (n,%)					
Normal	4 (8.8)	1 (9.1)	0	3 (9.7)	8 (7.0)
Abnormal[r]	4 (8.8)	2 (18.2)	5 (19.2)	0	11 (78.6)
Not performed	38 (82.6)	8 (72.7)	21 (80.8)	28 (90.3)	95 (83.4)
Laboratory result (n,%)					
Elevated troponins[s]	37 (80.4)	0	22 (84.6)	3 (9.7)	62 (54.4)
Missing value for troponins or troponins not performed	6 (13.0)	10 (90.9)	2 (7.7)	28 (90.3)	46 (40.4)
Elevated CRP	22 (47.8)	8 (72.7)	12 (46.2)	3 (9.7)	45 (39.5)
Elevated ESR	2 (4.4)	4 (36.4)	4 (15.4)	1 (3.2)	11 (9.7)
Elevated D-Dimers	4 (8.7)	3 (27.3)	1 (3.9)	3 (9.7)	11 (9.7)
Troponin value in ng/L (median, IQR)	589.5 (144–1885)	17 (17–17)	344 (155.5–1216.5)	97.5 (43–152)	413 (134–1321)

Abbreviations: AEFI: adverse event following immunization; BCCD: Brighton Collaboration Case Definition; CRP: C-reactive protein; ECG: electrocardiogram; ESR: erythrocyte sedimentation rate; ICU: intensive care unit; IQR: interquartile range; MRI: magnetic resonance imaging

[a] Cases meeting the Brighton Collaboration Case Definition (BCCD) level of diagnostic certainty 1–3 as per pericarditis and myocarditis criteria[27].

[b] Including east Asian, south Asian, southeast Asian, Indian.

[c] One subject may have multiple underlying comorbid conditions.

[d] Including any underlying cardiac conditions, such as congenital heart disease, arrhythmia, hypertension, history of previous pericarditis.

[e] Including asthma, sleep apnea, chronic obstructive pulmonary disease, cystic fibrosis, bronchiectasis.

[f] Including type 2 diabetes, diabetes insipidus, dyslipidemia, obesity.

[g] Including chronic kidney disease, Alport syndrome, kidney stones.

[h] Including cirrhosis, liver transplant.

[i] Including epilepsy, dyspraxia, Tourette syndrome, migraines.

[j] Including eosinophilic esophagitis, inflammatory bowel disease, celiac disease, irritable bowel syndrome, colon polyps.

[k] Including rheumatoid arthritis, inflammatory bowel disease, psoriasis, pericarditis, alopecia universalis, polyarthritis, celiac disease, auto-immune hypothyroidism.

[l] Including cancer and chemotherapy.

[m] Classification as per Public Health Agency of Canada AEFI impact category definitions[28].

[n] As per the World Health Organization (WHO) algorithm for AEFI classification as reported by the SIC site investigator[26].

[o] Including aspirin, anti-hypertensive medications, IVIg.

[p] Including ST elevation, arrhythmia, bundle branch block.

[q] Including decreased cardiac function, wall motion abnormality, pericardial effusion.

[r] Including pericardial thickening, pericardial enhancement, left ventricular dysfunction.

[s] Defined as a 1.5× elevation above locally-established threshold for upper limit of normal.

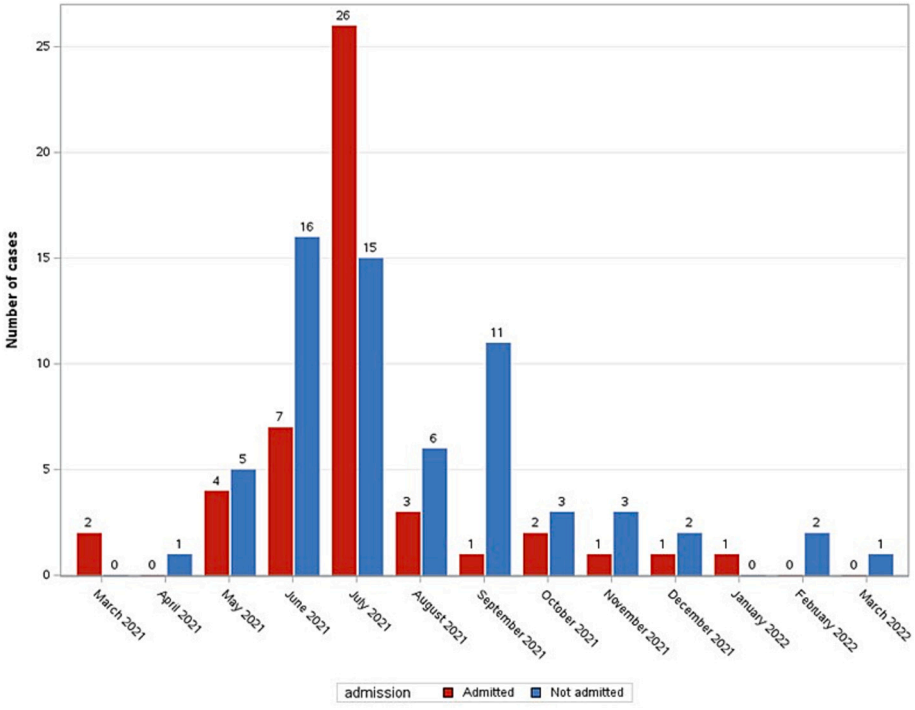

Fig. 1. Trend of cardiac adverse event following immunization (AEFI) cases over time by admission status. The x-axis represents month of diagnosis of the cardiac AEFI.

Table 2
Participants' characteristics, revaccination recommendations, practices and recurrences by age group.

Participant characteristics	Age group		Total
	Children (≤18yo)	**Adults (>18yo)**	
Participants' characteristics			
Total	**58**	**56**	**114**
Sex (n,%)			
Male	47 (81.0)	40 (71.4)	87 (76.3)
Female	11 (26.8)	15 (26.8)	26 (22.8)
Other/Unknown	0	1 (1.8)	1 (0.9)
Self-reported race (n,%)			
White	19 (32.8)	28 (50.0)	47 (41.2)
Black	1 (1.7)	1 (1.8)	2 (1.8)
Asian[a]	8 (13.8)	2 (3.6)	10 (8.8)
Middle eastern	1 (1.7)	7 (12.5)	8 (7.0)
Not reported	29 (50.0)	18 (32.1)	47 (41.2)
Any underlying comorbid condition (n,%)[b]	16 (27.6)	26 (46.4)	42 (36.8)
Cardiovascular comorbidity[c]	4 (6.9)	9 (16.1)	13 (11.4)
Chronic respiratory disease[d]	6 (10.3)	15 (26.8)	21 (18.4)
Diabetes or other metabolic disorder[e]	1 (1.7)	7 (12.5)	8 (7.0)
Chronic kidney disease[f]	0	2 (3.6)	2 (1.8)
Chronic liver disease[g]	0	2 (3.6)	2 (1.8)
Other gastrointestinal diseases[h]	3 (5.2)	3 (5.4)	6 (5.3)
Neurological disorder[i]	3 (5.2)	3 (5.4)	6 (5.3)
Autoimmune disorder[j]	2 (3.4)	6 (10.7)	8 (7.0)
Immunosuppressive condition[k]	0	2 (3.6)	2 (1.8)
Any history of SARS-CoV-2 infection prior to AEFI (n,%)	10 (17.2)	6 (10.7)	16 (14.0)
Vaccine product received (n,%)			
BNT162b2	55 (94.8)	27 (48.2)	82 (71.9)
mRNA-1273	2 (3.4)	27 (48.2)	29 (25.4)
ChAdOx1	0	1 (1.8)	1 (0.9)
Not specified	1 (1.7)	1 (1.8)	2 (1.8)
Vaccine dose associated with initial AEFI (n,%)			
1	23 (40.4)	23 (41.1)	48 (42.1)
2	30 (52.6)	33 (58.9)	62 (54.4)
3	4 (7.0)	0	4 (3.5)
Initial physician diagnosis			
Myocarditis	34 (58.6)	23 (41.1)	57 (50.0)
Pericarditis	2 (3.5)	14 (25.0)	16 (14.0)
Myopericarditis	14 (24.1)	13 (23.2)	27 (23.7)
Other cardiac AEFI	8 (13.8)	6 (10.7)	14 (12.3)
Final diagnosis[l]			
Myocarditis	24 (41.4)	22 (39.3)	46 (40.4)
Pericarditis	1 (1.7)	10 (17.9)	11 (9.7)
Myopericarditis	13 (22.4)	13 (23.2)	26 (22.8)
Other cardiac AEFI	20 (34.5)	11 (19.6)	31 (27.2)
Impact of the AEFI (n,%)[m]			
Low	1 (1.7)	0	1 (0.9)
Moderate	37 (63.8)	15 (26.8)	52 (45.6)
High	11 (19.0)	9 (16.1)	20 (17.5)
Serious	9 (15.5)	32 (57.1)	41 (36.0)
Required hospitalization (n,%)	13 (22.4)	36 (64.3)	49 (43.0)
Duration of hospitalization in days (median, IQR)	2 (1–3)	4 (2–5)	3 (2–4)
Required ICU admission (n,%)	1 (1.7)	2 (3.6)	3 (2.6)
Requires further doses of COVID-19 vaccine (n,%)			
Yes	36 (62.1)	35 (62.5)	71 (62.3)
No	22 (37.9)	21 (37.5)	43 (37.7)
Revaccination recommendations among participants requiring further COVID-19 vaccine doses			
Total requiring further doses	**36**	**35**	**71**
Revaccination recommendation			
Recommended	10 (27.8)	17 (48.6)	27 (38.0)
Not recommended	12 (33.3)	13 (37.1)	25 (35.2)
Recommendation deferred	14 (38.9)	5 (14.3)	19 (26.8)
Revaccination practices among participants recommended for revaccination			
Total recommended for revaccination	**10**	**17**	**27**
Revaccinated			
Yes	6 (60.0)	10 (58.8)	16 (59.3)
No	4 (40.0)	7 (41.2)	11 (40.7)
Outcomes among revaccinated participants			
Total	**6**	**10**	**16**
Recurrence of cardiac AEFI			
Yes	0	4 (40.0)	4 (25.0)
No	6 (100.0)	6 (60.0)	12 (75.0)

Abbreviations: AEFI: adverse event following immunization; ICU: intensive care unit; IQR: interquartile range.

[a] Including east Asian, south Asian, southeast Asian, Indian.

[b] One subject may have multiple underlying comorbid conditions.

[c] Including any underlying cardiac conditions, such as congenital heart disease, arrhythmia, hypertension, history of previous pericarditis.

[d] Including asthma, sleep apnea, chronic obstructive pulmonary disease, cystic fibrosis, bronchiectasis.

[e] Including type 2 diabetes, diabetes insipidus, dyslipidemia, obesity.

[f] Including chronic kidney disease, Alport syndrome, kidney stones.

[g] Including cirrhosis, liver transplant.

[h] Including epilepsy, dyspraxia, Tourette syndrome, migraines.

[i] Including eosinophilic esophagitis, inflammatory bowel disease, celiac disease, irritable bowel syndrome, colon polyps.

[j] Including rheumatoid arthritis, inflammatory bowel disease, psoriasis, pericarditis, alopecia universalis, polyarthritis, celiac disease, auto-immune hypothyroidism.

[k] Including cancer and chemotherapy.

[l] Cases meeting the Brighton Collaboration Case Definition (BCCD) level of diagnostic certainty 1–3 as per pericarditis and myocarditis criteria[27]

[m] Classification as per Public Health Agency of Canada AEFI impact category definitions[28].

not require any medical care. The fourth participant was a male ≥65 years old who had history of metastatic cancer and experienced recurrence of pericarditis of milder severity than the initial AEFI, which did not require hospitalization.

4. Discussion

Although multiple reports have described the clinical course of post-COVID-19 vaccination myocarditis and pericarditis, data remain limited on best practices around revaccination. The need for additional data on

Table 3
Revaccination recommendations, practices and recurrences by final diagnosis.

Participant characteristics	BCCD confirmed diagnosis			Chest pain/other cardiac diagnosis	Total
	Myocarditis	Pericarditis	Myopericarditis		
Total	**46**	**11**	**26**	**31**	**114**
Requires further doses of COVID-19 vaccine (n,%)					
Yes	28 (60.9)	9 (81.8)	11 (42.3)	23 (74.2)	71 (62.3)
No	18 (39.1)	2 (18.2)	15 (57.7)	8 (25.8)	43 (37.2)
Revaccination recommendations among participants requiring further COVID-19 vaccine doses					
Total requiring further doses	**28**	**9**	**11**	**23**	**71**
Revaccination recommendation					
Recommended	6 (21.4)	4 (44.4)	3 (27.3)	14 (60.9)	27 (38.0)
Not recommended	15 (53.6)	3 (33.3)	6 (54.6)	1 (4.4)	25 (35.2)
Recommendation deferred	7 (25.0)	2 (22.2)	2 (18.2)	8 (34.8)	19 (26.8)
Revaccination practices and characteristics among participants recommended for revaccination					
Total recommended for revaccination	**6**	**4**	**3**	**14**	**27**
Age group					
5–11 years	0	0	0	1 (7.1)	1 (3.7)
12–17 years	2 (33.3)	0	1 (33.3)	6 (42.9)	9 (33.3)
18–30 years	0	0	1 (33.3)	3 (21.4)	4 (14.8)
31–65 years	4 (66.7)	3 (75.0)	1 (33.3)	3 (21.4)	11 (40.7)
≥65 years	0	1 (25.0)	0	1 (7.1)	2 (7.4)
Any underlying comorbidity (n,%)	3 (50.0)	4 (100.0)	1 (33.3)	6 (42.9)	14 (51.9)
Cardiovascular comorbidity (n,%)	1 (16.7)	1 (25.0)	1 (33.3)	2 (14.3)	5 (18.5)
Vaccine dose at the time of initial AEFI (n,%)					
1	5 (83.3)	3 (75.0)	1 (33.3)	14 (100.0)	23 (85.2)
2	1 (16.7)	1 (25.0)	2 (66.7)	0	4 (15.4)
3	0	0	0	0	0
Causality (n, %)					
Consistent with causal association to immunization	4 (66.7)	2 (50.0)	3 (100.0)	3 (21.4)	12 (44.4)
Inconsistent with causal association to immunization	1 (16.7)	0	0	4 (28.6)	5 (18.5)
Indeterminate	1 (16.7)	2 (50.0)	0	7 (50.0)	10 (37.0)
Impact of the AEFI (n, %)					
Low	0	0	0	1 (7.1)	1 (3.7)
Moderate	2 (33.3)	2 (50.0)	1 (33.3)	10 (71.4)	15 (55.6)
High	0	1 (25.0)	1 (33.3)	2 (14.3)	4 (14.8)
Serious	4 (66.7)	1 (25.0)	1 (33.3)	1 (7.1)	7 (25.9)
Product recommended for revaccination					
BNT162b2	4 (66.6)	3 (75.0)	3 (100.0)	10 (71.4)	20 (74.1)
mRNA-1273	0	0	0	2 (14.3)	2 (7.4)
Nuvaxovid	1 (16.7)	1 (25.0)	0	2 (14.3)	4 (14.8)
Not specified	1 (16.7)	0	0	0	1 (3.7)
Revaccinated					
Yes	2 (33.3)	2 (50.0)	2 (66.7)	10 (71.4)	16 (59.3)
No	4 (66.7)	2 (50.0)	1 (33.3)	4 (28.6)	11 (40.7)
Revaccination practices among participants who were revaccinated					
Total revaccinated	**2**	**2**	**2**	**10**	**16**
Dose received for revaccination					
Second dose	2 (100.0)	2 (100.0)	1 (50.0)	10 (100.0)	15 (93.8)
Third dose	0	0	1 (50.0)	0	1 (6.3)
Product received for revaccination					
BNT162bn2	1 (50.0)	2 (100.0)	2 (100.0)	8 (80.0)	13 (81.3)
mRNA-1273	0	0	0	1 (10.0)	1 (6.3)
Nuvaxovid	1 (50.0)	0	0	0	1 (6.3)
Not specified	0	0	0	1 (10.0)	1 (6.3)
Vaccine product received relative to initial vaccination					
Same product	1 (50.0)	2 (100.0)	0	8 (80.0)	11 (68.8)
Different product	1 (50.0)	0	2 (100.0)	1 (10.0)	4 (25.0)
Not specified	0	0	0	1 (10.0)	1 (6.2)
Vaccine platform received relative to initial vaccination					
Same platform	1 (50.0)	2 (100.0)	2 (100.0)	9 (90.0)	14 (87.5)
Different platform	1 (50.0)	0	0	1 (10.0)	2 (12.5)
Outcomes among revaccinated participants					
Total	**2**	**2**	**2**	**10**	**16**
Recurrence of cardiac AEFI					
Yes	0	1 (50.0)	1 (50.0)	2 (20.0)	4 (25.0)
No	2 (100.0)	1 (50.0)	1 (50.0)	8 (80.0)	12 (75.0)

Abbreviations: AEFI: adverse event following immunization; BCCD: Brighton Collaboration Case Definition.

revaccination practices in individuals who have experienced cardiac AEFIs has become increasingly important with the availability of updated COVID-19 vaccines that are targeting the most recently circulating SARS-CoV-2 lineages [17]. In this cohort of 114 individuals who experienced cardiac adverse events following COVID-19 vaccination and were assessed in the SIC network, 16 participants were revaccinated, most of whom had underlying medical conditions and/or a diagnosis of chest pain/other cardiac diagnosis. Though only two of 10

Table 4
Characteristics of revaccinated subjects who experienced AEFI recurrence.

Participant characteristics	#1	#2	#3	#4
Age group	18–30	31–64	31–64	≥65
Sex	Male	Male	Female	Male
Underlying medical condition	Anxiety	Status post-liver transplantation, autoimmune disease	Hypertension, anxiety	Metastatic cancer
History of COVID-19 prior to the AEFI	Yes	No	No	No
Initial AEFI				
Vaccine product received	mRNA-1273	BNT162b2	BNT162b2	BNT162b2
Vaccine dose at the time of initial AEFI	2	1	1	1
Physician diagnosis	Myopericarditis	Other cardiac event	Other cardiac event	Pericarditis
Final diagnosis	Myopericarditis	Chest pain following COVID-19 vaccination/other cardiac diagnosis	Chest pain following COVID-19 vaccination/other cardiac diagnosis	Pericarditis
AEFI description	Participant presented at the ED with retrosternal chest pain, worsening when taking a deep breath. Participant denied shortness of breath or nausea. Treated with colchicine and ibuprofen.	Chest tightness and burning sensation with increasing chest pain, causing the participant to present to the ED. He was kept overnight and started colchicine/NSAIDs. Discharged with cardiology follow-up. Chest pain intermittent in the following month.	Presented with tachycardia and dyspnea 2–3 weeks after vaccination. At the ED, cardiac investigations were negative. Two subsequent visits at the ED due to apnea alarms. CT scan and D-dimers normal. No chest pain, or pleuritic chest pain. Treated with high dose NSAIDs which improved the pain.	Chest pain, orthostatic hypotension with syncope. Known pericardial effusion and ECG suggesting of pericarditis.
Onset time	5 days	17 days	14 days	30 days
Symptoms duration	N/A	30 days	60 days	N/A
Investigations	Abnormal ECG, normal troponins, no echocardiogram result reported.	Abnormal ECG, elevated CRP. No echocardiogram result reported.	Normal ECG and echocardiogram.	Abnormal ECG (ST segment elevation) and echocardiogram (pericardial effusion)
Level of healthcare required	Hospitalization	Consulted at the ED	Multiple physician visits	Hospitalization
Impact	High	High	High	High
Management	NSAIDs	N/A	N/A	Received trial of prednisone and colchicine.
Revaccination AEFI				
Vaccine product received	BNT162b2	BNT162b2	BNT162b2	BNT162b2
Vaccine dose at the time of revaccination	3	2	2	2
Dosing interval	18 months between second and third dose	4 months between first and second dose	3 months days between first and second dose	N/A
AEFI description	N/A	Participant reported recurrence of intermittent chest pain 14 days after his second dose. Presented to the ED, ECG performed and referred to cardiology. Mildly elevated CRP, echocardiogram normal, ECG showing no changes.	Slight shortness of breath noticeable on slight exertion, starting about 3 weeks after dose 2. Chest was clear, no pain with SOB. No specified diagnosis.	Recurrence of pericarditis requiring increase in prednisone dose.
Onset time	3 days	14 days	21 days	10 days
Causality	Consistent	Consistent	Indeterminate	Consistent
Level of healthcare required	Hospitalized	Consulted a physician	None	N/A
Management	N/A	NSAIDs, colchicine.	N/A	Increase in steroid dose
Participant-reported AEFI severity relative to first event	Same severity	Milder severity	Same severity	Milder severity

N/A: not available.
abbreviations: CRP: C reactive protein; CT: computed tomography; ECG: Electrocardiogram; ED: Emergency Department; NSAIDs: nonsteroidal anti-inflammatory drugs; SOB: shortness of breath.

participants with chest pain/other cardiac diagnosis had recurrent symptoms with neither requiring medical attention, one participant with history of myopericarditis had a recurrence after booster mRNA vaccination more than 1 year after the prior dose and required hospitalization. The results suggest that revaccination may be considered in individuals who experienced chest pain/other cardiac diagnosis, but caution is indicated for those with clinically confirmed myocarditis, myopericarditis and pericarditis, even with extended intervals after the last vaccine dose, especially in adults.

Some studies describe the risk of recurrence of myocarditis/pericarditis after COVID-19 vaccination in individuals who have previously experienced myocarditis from other causes [29]. Montgomery et al. described a cohort of 172 patients who previously experienced smallpox vaccine-associated myocarditis, myopericarditis or pericarditis and were vaccinated with a COVID-19 vaccine. Among this cohort, four (2.3 %) experienced recurrence of cardiac events that were mild and resolved

quickly [30].

In Canada, NACI has recommended that further doses of mRNA COVID-19 vaccines be deferred in individuals who experienced myocarditis and/or pericarditis within 6 weeks following a previous dose of an mRNA COVID-19 vaccine, though the lack of data is acknowledged [17]. The guidelines stipulate that some individuals may choose to receive another dose of vaccine after discussing the risks and benefits with their healthcare provider [17]. Aligned with this recommendation, at the time of SIC evaluation, many factors may have influenced the risk-benefit assessment of revaccination, such as age, underlying comorbid conditions predisposing to severe COVID-19, and whether the participant had completed the primary vaccination series. The patients in this study were assessed for revaccination in 2021 to 2023, and since then the benefits of revaccination have evolved due to mutation and recombination in the SARS-CoV-2 genome, which has led to the spread of variants with high potential for immune escape even with updated mRNA vaccines (e.g., JN.1, KP.2, KP.3, LP.8.1) [31]. In addition, the risk of severe COVID-19 in healthy individuals has decreased due to immunity from prior SARS-CoV-2 infection(s) and vaccination. Consequently, many countries now recommend COVID-19 vaccination only for high-risk groups [17,32].

In our cohort, most participants recommended for revaccination had experienced a cardiac AEFI after dose 1 and had an underlying medical condition, putting them at increased risk of severe disease with SARS-CoV-2 infection. No individual with an underlying medical condition had a serious AEFI following revaccination, though our sample size was small. Moreover, no participant with chest pain/other cardiac diagnosis developed confirmed myocarditis or pericarditis upon revaccination. Lastly, all episodes of recurrences occurred in adult participants. Together the findings support a role for individual risk-benefit assessment of revaccination in select individuals at increased risk of severe COVID-19, and the involvement of cardiology and/or specialist immunization clinic assessment if COVID-19 vaccination is being considered for individuals with prior myocarditis and pericarditis post-vaccination.

For individuals who have previously experienced post-vaccination myocarditis or pericarditis, NACI supports the preferential use of the BNT162b2 product for revaccination given the slightly higher risk of myocarditis/pericarditis reported with mRNA-1273 [17,33]. When it originally became available and approved by Health Canada in February 2022, the COVID-19 protein subunit vaccine Nuvaxovid was thought to be a possible alternative to mRNA platforms for revaccination of individuals who experienced cardiac AEFI [34]. However, data from observational studies subsequently suggested a potential association of myocarditis/pericarditis with Nuvaxovid vaccine [35]. In our study, BNT162b2 was the vaccine administered most frequently, with only one subject revaccinated with Nuvaxovid. Access to Nuvaxovid in Canada has been limited, with mRNA vaccines being the only products available in 2024–2025 and 2025–2026. Further studies of the safety of protein subunit COVID-19 vaccines in individuals who experienced cardiac AEFIs to mRNA vaccines are needed to confirm safety in this population. However, such research is difficult when these products are not readily available. Moreover, though hesitancy was not directly assessed in this study, we did observe that 40 % of participants recommended for revaccination did not have a record of being revaccinated, higher than reported in our previous research, for both COVID-19 and non-COVID-19 vaccines [19,36]. It is possible that individuals with mRNA vaccine-associated cardiac AEFI may be more willing to receive a different vaccine product in the future.

This study had several limitations. Although this was a national prospective study of individuals who experienced cardiac events following COVID-19 vaccination, most participants were not recommended for revaccination and/or did not receive further vaccination, and thus, data and experience around revaccination remain limited. Our study may be prone to referral bias given that we could only include participants who were initially referred to a SIC which may represent a specific subset of patients who experienced cardiac AEFIs, such as those experiencing cardiac events following their first dose of COVID-19 vaccine. SICs are located in tertiary care centers in major cities and individuals living outside those centers may have been less likely to be referred for assessment. Practices around the investigation and management of myocarditis and pericarditis following COVID-19 vaccination differed between centers and between age groups (e.g. threshold for hospital admission, access to cMRI), which could have also influenced the diagnosis and decisions around revaccination. We aimed to account for this limitation by classifying cases using the BCCD for myocarditis, pericarditis and myopericarditis. The study was conducted during the first two years of the COVID-19 vaccine roll-out before recommendations for routine annual COVID-19 vaccination and before the availability of updated COVID-19 vaccines, and therefore few participants were assessed for safety of additional vaccination (i.e., third and subsequent doses). Additionally, we did not collect long-term data on vaccinated or revaccinated subjects. Lack of evidence-based guidance could have contributed to differences in revaccination recommendations between centers. Lastly, although our study provides important insights on revaccination practices in individuals who have experienced cardiac events following COVID-19 vaccination, only one subject was vaccinated with a third dose and all received mRNA vaccines. Additional data that reports on revaccination with booster doses and non-mRNA products, especially with the use of updated vaccines targeting novel variants, are required to inform revaccination guidance. Data reporting on the risk of cardiac symptoms following infection with novel SARS-CoV-2 variants would also be informative with regards to the risk/benefit decision around revaccination.

Notable strengths of the study include the national sample with standardized data collection and follow up to ensure high data quality, as well as application of standard case definitions with cases adjudicated by multiple authors.

5. Conclusion

In this prospective national cohort, a minority of participants with cardiac adverse events following COVID-19 vaccination were recommended for revaccination, most of whom developed their AEFI after the first vaccine dose and/or had risk factors for severe COVID-19. Reassuringly, most participants with chest pain/other cardiac diagnosis were safely revaccinated. However, recurrences did occur in adults with BCCD-confirmed myopericarditis and pericarditis after revaccination. Individualized counselling on risks and benefits to inform decision-making, and cautious monitoring are recommended for individuals with a history of confirmed myocarditis or pericarditis following COVID-19 vaccination who are being considered for revaccination. In individuals without risk factors for severe COVID-19 who experienced myocarditis or pericarditis following a previous COVID-19 vaccination, the potential risk of AEFI recurrence may outweigh the benefits of revaccination. This study also underscores the need for further research on the safety of revaccination, particularly with non-mRNA COVID-19 vaccines, in patients at increased risk of severe outcomes from SARS-CoV-2 infection who may benefit from further vaccine doses.

CRediT authorship contribution statement

Pierre-Philippe Piché-Renaud: Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **C. Arianne Buchan:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Catherine Burton:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Hugo Chapdelaine:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Aamir Jeewa:** Writing – review & editing, Validation, Investigation. **Shaun K. Morris:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Jeffrey M. Pernica:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Anne Pham-Huy:** Writing – review &

editing, Methodology, Investigation, Conceptualization. **Manish Sadarangani:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Marina I. Salvadori:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Sneha Suresh:** Writing – review & editing, Methodology, Conceptualization. **Tahir S. Kafil:** Writing – review & editing, Validation, Methodology. **Juthaporn Cowan:** Writing – review & editing, Validation, Methodology, Investigation, Conceptualization. **Karina A. Top:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization.

Ethics statement

Research Ethics Board approval was obtained at each of the participating sites. Participants provided informed consent prior to enrollment.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Karina A Top reports financial support was provided by Canadian Institutes of Health Research. Karina A Top reports financial support was provided by Public Health Agency of Canada. Manish Sadarangani reports financial support was provided by BC Children's Hospital Research Institute. Manish Sadarangani reports financial support was provided by Michael Smith Health Research BC. Juthaporn Cowan reports financial support was provided by University of Ottawa. Catherine Burton, Manish Sadarangani report a relationship with Moderna Inc. that includes: funding grants. Aamir Jeewa, Jeffrey M Pernica, Manish Sadarangani report a relationship with Merck & Co Inc. that includes: funding grants. Aamir Jeewa reports a relationship with Bristol-Myers Squibb Company that includes: funding grants. Aamir Jeewa reports a relationship with Berlin Heart Gmbh that includes: funding grants. Shaun K Morris reports a relationship with GlaxoSmithKline LLC that includes: consulting or advisory and speaking and lecture fees. Shaun K Morris reports a relationship with Sanofi Pasteur Inc. that includes: consulting or advisory and speaking and lecture fees. Shaun K Morris, Juthaporn Cowan report a relationship with Pfizer Inc. that includes: consulting or advisory and speaking and lecture fees. Jeffrey M Pernica reports a relationship with MedImmune LLC that includes: funding grants. Manish Sadarangani, Juthaporn Cowan report a relationship with GlaxoSmithKline LLC that includes: funding grants. Manish Sadarangani reports a relationship with Pfizer Inc. that includes: funding grants. Manish Sadarangani reports a relationship with Sanofi Pasteur Inc. that includes: funding grants. Juthaporn Cowan reports a relationship with AstraZeneca Canada Inc. that includes: funding grants. Sneha Suresh reports a relationship with CSL Behring LLC that includes: consulting or advisory. Karina A Top reports a relationship with the Coalition for Epidemic Preparedness Innovations that includes: funding grants. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2025.128016.

Data availability

Study data may be made available from the authors upon request.

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