

Supplemental Information

v-safe definitions for injection site reaction, systemic reaction, health impact, and reaction severity

Injection site reactions include itching, injection site pain, redness, and swelling.

Systemic reactions include abdominal pain, myalgia, chills, diarrhea, fatigue, fever, headache, joint pain, nausea, rash, and vomiting.

Health impacts include whether the child was unable to complete normal daily activities, missed school, or received care from a medical professional because of new symptoms or conditions.

Injection site and systemic reactions can be further described by severity as mild (noticeable, but not problematic), moderate (limit normal daily activities), or severe (make daily activities difficult or impossible).

Methods for enhanced surveillance for MIS-C

Enhanced surveillance for MIS-C in persons aged 5 to 11 years who had onset within 90 days of their last COVID-19 vaccine dose is conducted using VAERS, CDC's MIS-C national surveillance system and clinician or health department outreach to CDC, including through Clinical Immunization Safety Assessment Project consultations. Medical records are reviewed and a multidisciplinary team adjudicates cases by use of the CDC MIS-C definition.

US Centers for Disease Control and Prevention case definition for multisystem inflammatory syndrome in children

Must meet all the following clinical and laboratory criteria:

- Age <21 years with subjective or objective (>38.0°C) fever for 24 h or longer
- Clinically severe illness requiring hospitalization
- Multisystem (2 or more) organ system involvement

- **Cardiac:** includes elevated troponin, elevated B-type natriuretic peptide or N-terminal pro hormone BNP, arrhythmia, coronary artery aneurysm, cardiac dysfunction, or shock
- **Renal:** includes acute kidney injury or renal failure
- **Respiratory:** includes pneumonia, acute respiratory distress syndrome, or pleural effusion
- **Hematologic:** includes elevated D-dimer, thrombophilia, or thrombocytopenia
- **Gastrointestinal:** includes elevated bilirubin, elevated liver enzymes, or diarrhea
- **Dermatological:** includes rash or mucocutaneous lesions
- **Neurologic:** includes cerebrovascular accident, aseptic meningitis encephalopathy, or headache
- No alternative plausible diagnosis
- Laboratory evidence of inflammation: elevated C-reactive protein, erythrocyte sedimentation rate, fibrinogen, procalcitonin, D-dimer, ferritin, lactic acid dehydrogenase, interleukin 6, or neutrophils; or reduced lymphocytes or albumin
- Current or recent positive SARS-CoV-2 RT-PCR*, antigen, or serology test; or exposure to a suspected or confirmed COVID-19 case within the 4 weeks before onset of symptoms

* For enhanced surveillance, this criterion could be satisfied by any type of nucleic acid amplification test. The exposure criterion is not currently used in this enhanced surveillance investigation.

MedDRA search terms for myocarditis

Atypical *Mycobacterium* pericarditis
Autoimmune myocarditis
Autoimmune pericarditis
Bacterial pericarditis

Coxsackie myocarditis
Coxsackie pericarditis
Cytomegalovirus myocarditis
Cytomegalovirus pericarditis
Enterovirus myocarditis
Eosinophilic myocarditis
Hypersensitivity myocarditis
Immune-mediated myocarditis
Myocarditis
Myocarditis bacterial
Myocarditis helminthic
Myocarditis infectious
Myocarditis meningococcal
Myocarditis mycotic
Myocarditis postinfection
Myocarditis septic
Pericarditis
Pericarditis adhesive
Pericarditis constrictive
Pericarditis helminthic
Pericarditis infective
Pericarditis mycoplasmal
Pleuropericarditis
Purulent pericarditis
Troponin I increased
Troponin increased
Troponin T increased
Viral myocarditis
Viral pericarditis

Case Definition for Myocarditis

We applied the CDC working definition of acute myocarditis.¹⁶ A probable case of acute myocarditis was defined as the presence of signs and symptoms (1 or more new or worsening of the following: chest pain, pressure, or discomfort, dyspnea, shortness of breath or pain with breathing, palpitations, or syncope; or 2 or more of the following in children ages ≤11 years: irritability, vomiting, poor feeding, tachypnea, or lethargy); and 1 or

more new findings of elevated troponin, electrocardiogram findings consistent with myocarditis, abnormal cardiac function or wall motion on echocardiogram, or cardiac MRI findings consistent with myocarditis. A confirmed case of acute myocarditis was defined as the presence of signs and symptoms (1 or more new or worsening of the following: chest pain, pressure, or discomfort; dyspnea, shortness of breath, and pain with breathing; palpitations, or syncope.

Two or more of the following in children ages ≤11 years: irritability, vomiting, poor feeding, tachypnea, or lethargy); and 1 or more new findings of histopathologic findings consistent with myocarditis; cardiac MRI findings consistent with myocarditis in the presence of a troponin level above the upper limit of normal; and no other identifiable cause for these findings. Both probable and confirmed cases of myocarditis were included for analysis.

SUPPLEMENTAL TABLE 10 Type of Vaccine Administered for Children Ages 5 to 11 Years Registered in v-safe Who Received Another Vaccine at the Time of BNT-162b2 COVID-19 Vaccination^a in the United States From November 3 to February 27, 2022

Vaccine Type ^b	Dose 1 (48 795) N (%)	Dose 2 (39 416) N (%)
Influenza	1552 (3.2)	250 (0.6)
Missing	126 (0.3)	0
Tetanus-containing	74 (0.2)	14 (0.04)
Human papilloma-virus	47 (0.1)	18 (0.05)
Meningococcal	40 (0.1)	8 (0.02)
Measles, mumps, and rubella	17 (0.03)	3 (0.01)
Other	15 (0.03)	1 (0.003)
Poliovirus	15 (0.03)	1 (0.003)
Varicella	11 (0.02)	2 (0.01)
Hepatitis A	6 (0.01)	1 (0.003)
Hepatitis B	5 (0.01)	1 (0.003)
Unknown	4 (0.01)	2 (0.01)
Pneumococcal	2 (0.004)	0

^a Registrants completed at least 1 v-safe health check-in survey on days 0 to 7 after BNT-162b2 COVID-19 vaccination.

^b These categories are not mutually exclusive. The vaccine types were simplified in the v-safe platform for a lay audience. More than 1 vaccine type can be selected.

SUPPLEMENTAL TABLE 11 Type of Vaccine Administered for Children Ages 5 to 11 Years Who Received Another Vaccine at the Time of BNT-162b2 COVID-19 Vaccination – Vaccine Adverse Event Reporting System (VAERS), United States, November 3 to February 27, 2022

Vaccine Name ^a	N
Quadrivalent inactivated seasonal influenza vaccine	126
Cell-culture-derived quadrivalent inactivated seasonal influenza vaccine	11
Tetanus, diphtheria, and acellular pertussis vaccine	10
Meningococcal conjugate vaccine	9
Seasonal influenza vaccine (unknown type)	8
Measles, mumps, rubella, and varicella vaccine	6
Tetanus, diphtheria, acellular pertussis, and inactivated poliovirus vaccine	5
Human papilloma-virus 9-valent vaccine	6
Inactivated poliovirus vaccine	4
Varicella vaccine	4
Diphtheria, tetanus, and acellular pertussis vaccine	2
Quadrivalent live-attenuated seasonal influenza vaccine	2
Hepatitis A vaccine	2
Measles, mumps, and rubella vaccine	2
Adjuvanted quadrivalent inactivated seasonal influenza vaccine	1
Hepatitis B vaccine	1
Japanese encephalitis vaccine	1
Unknown	1

^a These categories are not mutually exclusive. Of the 7578 VAERS reports for children ages 5 to 11 y, 175 indicated another vaccine was administered at the time of BNT-162b2 COVID-19 vaccination; there were 24 reports that indicated 3 or more vaccines were administered.

SUPPLEMENTAL TABLE 12 Top 10 Vaccine Types Administered for Children Ages 5 to 11 Years Who Received Another Vaccine at the Time of Dose 1 BNT-162b2 COVID-19 Vaccination—Vaccine Safety Datalink, United States, October 31, 2021 to February 26, 2022

Vaccine Type ^a	Doses Administered ^b (%)
Influenza	21 591 (5.6)
Human papilloma-virus	1900 (0.5)
Tetanus, diphtheria, and acellular pertussis (Tdap), or Tetanus (Td)	1018 (0.3)
Meningococcal	960 (0.2)
Measles, mumps, and rubella (MMR), or measles, mumps, rubella and varicella (MMRV)	195 (0.1)
Hepatitis A	151 (0.04)
Diphtheria, tetanus, acellular pertussis, and inactivated poliovirus, or diphtheria, tetanus and inactivated poliovirus	144 (0.04)
Hepatitis B	73 (0.02)
Inactivated poliovirus	63 (0.02)
Varicella	50 (0.01)

^a These categories are not mutually exclusive. There were 164 different combinations of vaccines simultaneously received and some individuals, for example, received multiple simultaneous vaccinations. 22 714 persons received simultaneous vaccine(s) with dose 1 and 4443 persons with dose 2.

^b There were 384 905 children ages 5 to 11 y in the Vaccine Safety Datalink who received dose 1 of BNT-162b2 COVID-19 vaccine.