Safety profiles of COVID-19 vaccines

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Immunization Safety Office

International Workshop on COVID-19 Vaccines

15 December 2022

Topics

- COVID-19 vaccine safety profiles by age groups
  - Adults (18+ years); older children and adolescents (12–17 years); children (5–11 years); young children and infants (6 months – 5 years)
- Selected topics
  - Anaphylaxis
  - Myocarditis (including 90-day follow up data)
  - Thrombosis with thrombocytopenia syndrome (TTS)
  - Pregnancy (including preterm birth and spontaneous abortion)

COVID-19 vaccine safety profiles by age groups

Safety of primary series mRNA COVID-19 vaccination among adults (ages ≥18 years)

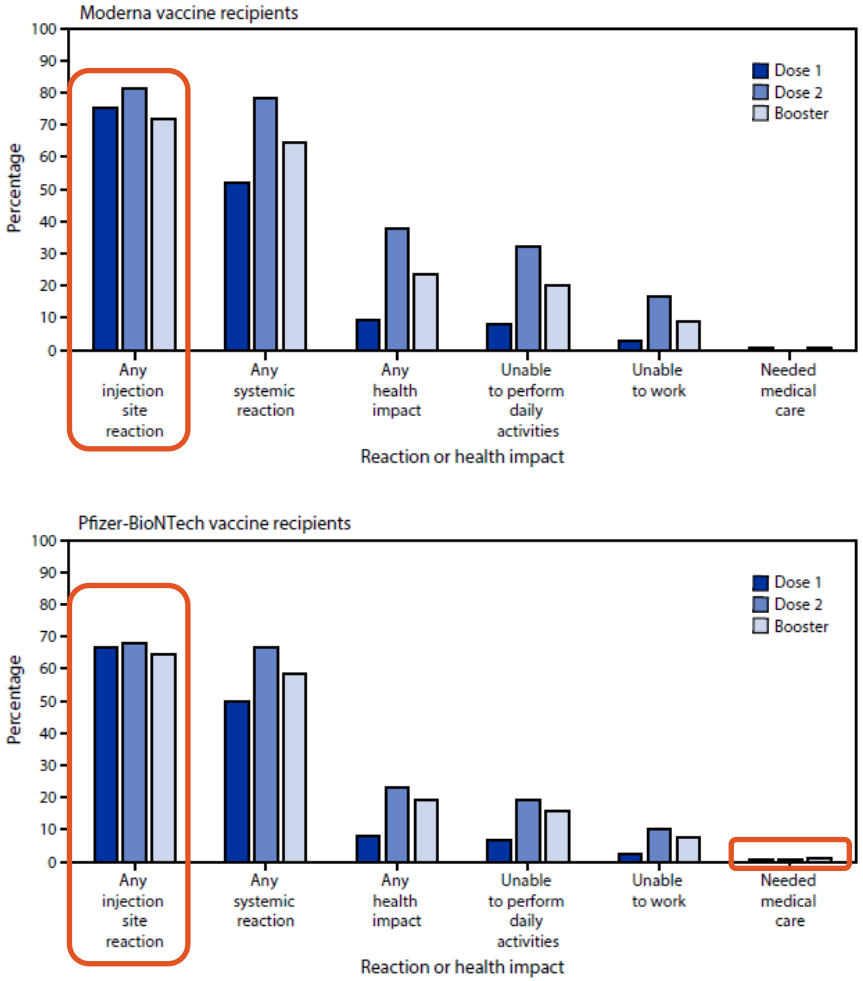
	Both mRNA vaccines		BNT162b2 vaccine		mRNA-1273 vaccine	
	Dose one (n=6775515)	Dose two (n=5674420)	Dose one (n=3455778)	Dose two (n=2920526)	Dose one (n=3319737)	Dose two (n=2753894)
Any injection-site reaction*	4644989 (68·6%)	4068447 (71·7%)	2212051 (64·0%)	1908124 (65·3%)	2432938 (73·3%)	2160323 (78·4%)
Injection-site pain	4488402 (66·2%)	3890848 (68·6%)	2140843 (61·9%)	1835398 (62·8%)	2347559 (70·7%)	2055450 (74·6%)
Swelling	703790 (10·4%)	976946 (17·2%)	246230 (7·1%)	309718 (10·6%)	457560 (13·8%)	667228 (24·2%)
Redness	353788 (5·2%)	640739 (11·3%)	116108 (3·4%)	167127 (5·7%)	237680 (7·2%)	473612 (17·2%)
Itching	376076 (5·6%)	605633 (10·7%)	145596 (4·2%)	191132 (6·5%)	230480 (6·9%)	414501 (15·1%)
Any systemic reaction*	3573429 (52·7%)	4018920 (70·8%)	1771509 (51·3%)	1931643 (66·1%)	1801920 (54·3%)	2087277 (75·8%)
Fatigue	2295205 (33·9%)	3158299 (55·7%)	1127904 (32·6%)	1475646 (50·5%)	1167301 (35·2%)	1682653 (61·1%)
Headache	1831471 (27·0%)	2623721 (46·2%)	893992 (25·9%)	1189444 (40·7%)	937479 (28·2%)	1434277 (52·1%)
Myalgia	1423336 (21·0%)	2478170 (43·7%)	653821 (18·9%)	1085365 (37·2%)	769515 (23·2%)	1392805 (50·6%)
Chills	631546 (9·3%)	1680185 (29·6%)	263617 (7·6%)	642856 (22·0%)	367929 (11·1%)	1037329 (37·7%)
Fever	642092 (9·5%)	1679577 (29·6%)	274650 (7·9%)	656454 (22·5%)	367442 (11·1%)	1023123 (37·2%)
Joint pain	642006 (9·5%)	1440927 (25·4%)	285812 (8·3%)	591877 (20·3%)	356194 (10·7%)	849050 (30·8%)
Nausea	562273 (8·3%)	901103 (15·9%)	267160 (7·7%)	384525 (13·2%)	295113 (8·9%)	516578 (18·8%)
Diarrhoea	383576 (5·7%)	419044 (7·4%)	190542 (5·5%)	198618 (6·8%)	193034 (5·8%)	220426 (8·0%)
Abdominal pain	233511 (3·4%)	359107 (6·3%)	113872 (3·3%)	158251 (5·4%)	119639 (3·6%)	200856 (7·3%)
Rash	85766 (1·3%)	99878 (1·8%)	41565 (1·2%)	42662 (1·5%)	44201 (1·3%)	57216 (2·1%)
Vomiting	55710 (0·8%)	91727 (1·6%)	25336 (0·7%)	36761 (1·3%)	30374 (0·9%)	54966 (2·0%)

www.thelancet.com/infection **Vol 22 June 2022**

- Adverse events after mRNA COVID-19 vaccination similar by Vaccine Adverse Event Reporting System (VAERS) and V-safe health checker; similar regardless of vaccine
- Consistent with observed adverse events during pre-authorization trials

Safety of booster dose monovalent mRNA COVID-19 vaccination among adults (ages ≥18 years)

- Adverse reactions and health impacts no more frequent after booster dose than after dose 2
  - Typically transient (resolving within 3–4 days after vaccination)
- Rarely required medical care (≤3%); mostly outpatient



Safety of primary series BNT162b2 COVID-19 vaccination among ages 12–17 years

Symptom, sign, diagnostic result, or condition	% Reporting
Nonserious reports (n = 8,383)	
Dizziness	21.2
Syncope	14.4
Nausea	10.4
Headache	10.0
Fever	8.3
Loss of consciousness	7.5
Excessive sweating	7.4
Fatigue	7.2
Pallor	7.1
Product administered to patient outside of indicated age range	7.0
Product storage error	6.4
Vomiting	6.4
Difficulty breathing	5.3
Chest pain	4.9
Pain	4.6

Symptom, sign, diagnostic result, or condition	% Reporting
Serious reports, including reports of death† (n = 863)	
Chest pain	56.4
Increased troponin	41.7
Myocarditis	40.3
Increased c-reactive protein	30.6
Negative SARS-CoV-2 test result	29.4
Fever	28.3
Normal echocardiogram	26.9
Abnormal electrocardiogram	25.6
Headache	22.2
Difficulty breathing	21.4
Elevated electrocardiogram ST segment	20.5
Normal chest radiograph	19.7
Intensive care	18.1
Vomiting	17.0
Nausea	16.6

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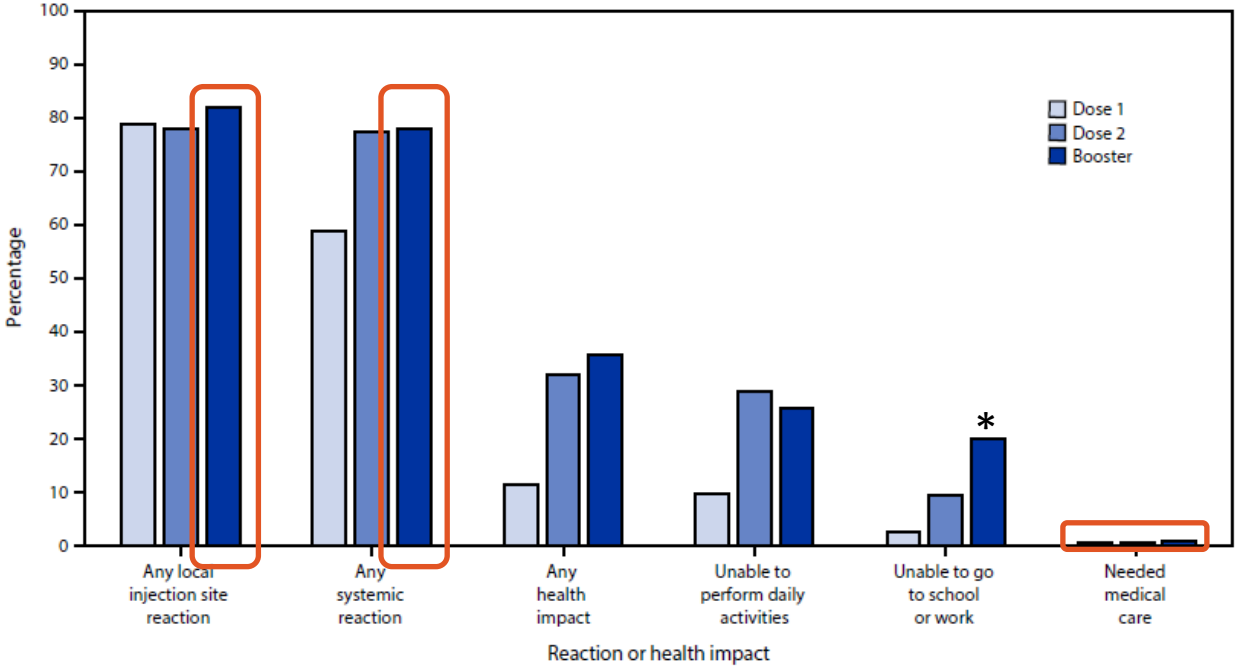
- Most reports to VAERS (91%) were non-serious; consistent with pre-authorization observations
- Most serious reports consistent with myocarditis or potential multisystem inflammatory syndrome
  - Benefit of vaccination outweighs risk, considering risk of negative cardiac outcomes after COVID-19 (Advisory Committee on Immunization Practices meetings 23 Jun 2021; 19 Oct 2022)

Safety of homologous monovalent booster BNT162b2 COVID-19 vaccination among ages 12–17 years

- Local and systemic reactions common
- Very few vaccinated people (≤3%) sought medical care (almost all outpatient)

FIGURE. Adverse reactions and health impacts reported* among persons aged 12–17 years (N = 3,274) who received a homologous Pfizer-BioNTech COVID-19 vaccine booster, by vaccine dose — United States, December 9, 2021–February 20, 2022



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* Many participants received dose 2 during remote learning or summer break

Safety of bivalent booster mRNA COVID-19 vaccination among ages ≥12 years

Adverse events	Vaccine, no. reporting (%)		
	Pfizer-BioNTech	Moderna	Total[§]
Nonserious reports[§§,¶¶]	**2,762 (94.3)**	**2,530 (96.8)**	**5,291 (95.5)**
Headache	343 (12.4)	285 (11.3)	**628 (11.9)**
Fatigue	318 (11.5)	257 (10.2)	**575 (10.9)**
Fever	299 (10.8)	262 (10.4)	**561 (10.6)**
Pain	293 (10.6)	231 (9.1)	**524 (9.9)**
Chills	254 (9.2)	205 (8.1)	**459 (8.7)**
Pain in extremity	209 (7.8)	167 (6.6)	**376 (7.1)**
Nausea	213 (7.7)	144 (5.7)	**357 (6.8)**
Dizziness	212 (7.7)	135 (5.3)	**347 (6.6)**
Injection site pain	138 (5.0)	121 (4.8)	**259 (4.9)**
COVID-19	169 (6.1)	89 (3.5)	**258 (4.9)**

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- Non-serious reports comparable to after monovalent booster mRNA COVID-19 vaccine
- Serious reports comparable to after monovalent booster mRNA COVID-19 vaccine
  - Most frequent reports of death (n=36), stroke (or transient ischemic attack) or pulmonary embolus (n=27), COVID-19 (n=20), arrhythmia (n=13), unspecified chest pain (n=12)

Safety of primary series mRNA COVID-19 vaccination among ages 5–11 years

TABLE 5 Reports of Nonserious and Serious Events to Vaccine Adverse Event Reporting System (VAERS) for Children Ages 5 to 11 y After Receipt of BNT-162b2 COVID-19 Vaccine ($N = 7578$) in the United States From November 3 to February 27, 2022

Reported Events	Number (%) Reporting
Nonserious VAERS reports	7379 (100)
Symptom, sign, diagnostic result, or condition (MedDRA PT[a])	
No adverse event[b]	1651 (22.4)
Product preparation issue	1434 (19.4)
Incorrect dose administered	1361 (18.4)
Pyrexia	541 (7.3)
Vomiting	541 (7.3)
Headache	465 (6.3)
Product storage error	417 (5.7)
Underdose	388 (5.3)
Dizziness	387 (5.2)
Syncope	371 (5.0)
Fatigue	336 (4.6)
Nausea	330 (4.5)
Urticaria	312 (4.2)
Rash	311 (4.2)
Expired product administered	246 (3.3)

PEDIATRICS Volume 150, number 2, August 2022:e2022057313

- Systemic and local adverse reactions slightly more frequent after dose 2; mostly mild-moderate intensity
- Most adverse events (97%) were non-serious; consistent with pre-authorization observations
  - Most frequent were vaccination errors (38%)

Safety of primary series mRNA COVID-19 vaccination among ages 5–11 years (cont'd)

- 21 reports of MIS-C met case definition; 19 had evidence of past SARS-CoV-2 infection
- 15 reports of seizure met case definition; 10 were new-onset seizure
- 17 reports of myocarditis met case definition; 15 patients hospitalized; all had recovered or were recovering

TABLE 5 Reports of Nonserious and Serious Events to Vaccine Adverse Event Reporting System (VAERS) for Children Ages 5 to 11 y After Receipt of BNT-162b2 COVID-19 Vaccine ($N = 7578$) in the United States From November 3 to February 27, 2022

Reported Events	Number (%) Reporting
Serious VAERS reports[c,d,e]	194 (100)[f]
Clinical impression	
Multisystem inflammatory syndrome in children (MIS-C)	26 (13.4)
Seizure[g]	21 (10.8)
Myocarditis[h]	19 (9.8)
Appendicitis	13 (6.7)
Allergic reaction	8 (4.1)
COVID-19	7 (3.6)
Abdominal pain	6 (3.1)
Diabetes mellitus type 1	5 (2.6)
Death	4 (2.1)
Immune thrombocytopenic purpura	4 (2.1)
Asthma	3 (1.5)
Ataxia	3 (1.5)
Kawasaki disease	3 (1.5)
Kawasaki disease, incomplete	3 (1.5)
Migraine	3 (1.5)
Altered mental status	2 (1.0)
Anaphylaxis[i]	2 (1.0)
Chest pain	2 (1.0)
Gastrointestinal infection	2 (1.0)
Nephrotic syndrome	2 (1.0)
Panic attack	2 (1.0)
Pneumonia	2 (1.0)
Reactive arthritis	2 (1.0)
Tachycardia	2 (1.0)

PEDIATRICS Volume 150, number 2, August 2022:e2022057313

Safety of homologous booster dose BNT162b2 COVID-19 vaccination among ages 5–11 years

- Overall reporting of local (69%) and systemic (46%) adverse reactions less frequent than after older age groups (e.g., 12–17 years); mostly mild or moderate intensity
- Most frequent non-serious adverse events were of administration errors
- No reported myocarditis or death

TABLE 1. Most frequently reported adverse reactions reported* to v-safe for children aged 5–11 years who received homologous Pfizer-BioNTech COVID-19 booster vaccination† (N = 3,249), by severity§ and dose — United States, May 17–July 31, 2022

	% Reporting event		
Reported event	Dose 1	Dose 2	Dose 3
Injection site pain	**60.7**	**66.1**	**66.7**
Mild	50.1	50.7	44.9
Moderate	10.2	14.9	20.8
Severe	0.3	0.6	1.0
Fatigue	**22.9**	**29.9**	**28.9**
Mild	15.0	17.5	15.1
Moderate	7.2	11.6	12.0
Severe	0.7	0.8	1.7
Headache	**15.2**	**20.6**	**19.9**
Mild	10.5	13.1	11.4
Moderate	4.4	7.1	7.5
Severe	0.2	0.4	1.0
Myalgia	**7.1**	**10.2**	**13.9**
Mild	4.8	6.0	7.2
Moderate	2.1	4.0	6.3
Severe	0.2	0.2	0.4
Chills	**3.8**	**7.6**	**7.4**
Mild	2.6	4.6	4.1
Moderate	1.1	3.0	2.9
Severe	0.1	0.1	0.4
Fever¶	**1.4**	**3.9**	**5.1**
Mild	0.9	2.2	2.7
Moderate	0.4	1.0	1.4
Severe	0.1	0.6	0.9
Very severe	0.03	0.1	0.1

TABLE 3. Reports of nonserious and serious events to the Vaccine Adverse Event Reporting System for children aged 5–11 years who received a Pfizer-BioNTech COVID-19 booster dose (N = 581) — United States, May 17–July 31, 2022

Reported events	No. (%)
Nonserious VAERS reports	578 (100)
Symptom, sign, diagnostic result, or condition (MedDRA PT*)	
Product preparation issue	145 (25.1)
Incorrect dose administered	128 (22.2)
No adverse event†	105 (18.2)
Product administered to patient of inappropriate age	55 (9.5)
Product preparation error	53 (9.2)
Expired product administered	46 (8.0)
Fever	45 (7.8)
Pain in extremity	38 (6.6)
Fatigue	28 (4.8)
Headache	22 (3.8)
Injection site pain	22 (3.8)
Product storage error	22 (3.8)
Vomiting	22 (3.8)
Chills	18 (3.1)
Dizziness	18 (3.1)
Serious VAERS reports§,¶	**3 (100)**
Clinical impression	
Generalized pain, fatigue, and malaise requiring hospitalization	1 (33.3)
New onset type 1 diabetes	1 (33.3)
Facial swelling	1 (33.3)

Safety of primary series mRNA COVID-19 vaccination among ages 6 months – 5 years (cont'd)

- Most nonserious reports were consistent with preauthorization clinical trials
- Most often vaccination errors
- Most frequent adverse event among serious reports was seizure (7)*
- No reports of death or myocarditis

TABLE 3. Events* reported to the Vaccine Adverse Event Reporting System for children aged 6 months–5 years† after receipt of Pfizer-BioNTech or Moderna COVID-19 vaccine — United States, June 18–August 21, 2022

Adverse events	Vaccine, no. reporting (%)		
	Pfizer-BioNTech	Moderna	Total
Total	**496**	**521**	**1,017**
Vaccination errors	**278 (56.0)**	**177 (34.0)**	**455 (44.7)**
Error without adverse health event	248 (89.2)	162 (91.5)	**410 (90.1)**
Error with adverse health event§	30 (10.8)	15 (8.5)	**45 (9.9)**
Error with nonserious health event¶	30 (10.8)	14 (7.9)	**44 (9.7)**
Error with serious health event	0 (—)	1 (0.6)	**1 (0.2)**
Nonserious reports (excluding vaccination error MedDRA PTs)**	**486 (98.0)**	**512 (98.3)**	**998 (98.1)**
Fever	84 (17.3)	113 (22.1)	**197 (19.7)**
Rash	52 (10.7)	43 (8.4)	**95 (9.5)**
Vomiting	37 (7.6)	42 (8.2)	**79 (7.9)**
Urticaria	23 (4.7)	43 (8.4)	**66 (6.6)**
Fatigue	29 (6.0)	31 (6.1)	**60 (6.0)**
SARS-CoV-2 negative test result	24 (4.9)	33 (6.5)	**57 (5.7)**
Cough	17 (3.5)	34 (6.6)	**51 (5.1)**
Irritability	16 (3.3)	33 (6.5)	**49 (4.9)**
Decreased appetite	17 (3.5)	29 (5.7)	**46 (4.6)**
Diarrhea	19 (3.9)	26 (5.1)	**45 (4.5)**
Erythematous rash	13 (2.7)	28 (5.5)	**41 (4.1)**
COVID-19	19 (3.9)	18 (3.5)	**37 (3.7)**
SARS-CoV-2 positive test result	18 (3.7)	17 (3.3)	**35 (3.5)**

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* Estimated reporting rate <1 per 1 million doses administered

Selected topics

Anaphylaxis after mRNA COVID-19 vaccines

- Consistent with past descriptions of anaphylaxis after other vaccines
  - Mostly among female patients
  - Most symptom onset within 30 minutes of vaccination
- Reporting rate comparable to after other vaccines (McNeil et al (*J Allergy Clin Immunol* (2016))

Table. Characteristics of Reported Cases of Anaphylaxis Following Receipt of Pfizer-BioNTech (9 943 247 Doses) and Moderna (7 581 429 Doses) COVID-19 Vaccines—Vaccine Adverse Events Reporting System (VAERS), US, December 14, 2020-January 18, 2021

Characteristics	No. (%) of cases	
	Pfizer-BioNTech (n = 47)	Moderna (n = 19)
Age, median (range), y	39 (27-63)[a]	41 (24-63)
Female sex	44 (94)	19 (100)
Minutes to symptom onset, median (range)	10 (<1-1140 [19 h])[b]	10 (1-45)
Symptom onset, min		
≤15	34 (76)[b]	16 (84)
≤30	40 (89)[b]	17 (89)
Reported history[c]		
Allergies or allergic reactions	36 (77)	16 (84)
Prior anaphylaxis	16 (34)	5 (26)
Vaccine dose		
First	37	17
Second	4	1
Unknown	6	1
Brighton Collaboration case definition level[d]		
1	21 (45)	10 (52)
2	23 (49)	8 (43)
3	3 (6)	1 (5)
Anaphylaxis reporting rate (cases per million doses administered)	4.7	2.5

Thrombosis with Thrombocytopenia Syndrome (TTS)

- Associated with Ad26.COV2.S (Janssen) vaccine
  - Highest rates among women ages 30s–50s years (10 per million doses administered)
  - Onset ~1–2 weeks after vaccination
  - Thrombocytopenia (<150,000/μL^3)
  - Large vessel thrombi (e.g., cerebral venous sinuses, splanchnic vessels)
  - High concentration of anti-platelet factor 4 antibodies (often OD_{450} ≥2 or 3)
  - Case fatality ~15%

- mRNA COVID-19 vaccination recommended over Ad26.COV2.S (December 2021)

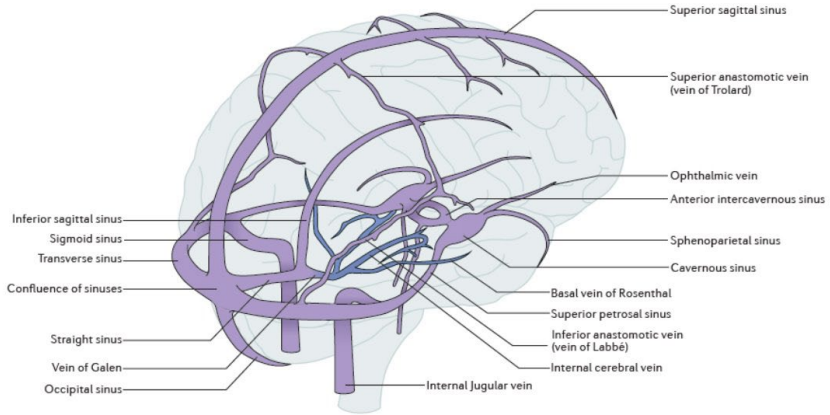


Figure 1 | **Anatomy of the cerebral venous system.** Diagram showing the main components of the cerebral venous system. Blue vessels represent the deep venous system.

Silvis SM et al, *Nature Reviews Neurology* 13, 555-565(2017)

Morbidity and Mortality Weekly Report

Use of the Janssen (Johnson & Johnson) COVID-19 Vaccine: Updated Interim Recommendations from the Advisory Committee on Immunization Practices — United States, December 2021

MMWR / January 21, 2022 / Vol. 71 / No. 3

Myocarditis

	Dose 2 (primary series)		1st booster dose	
Age group	**Male**	**Female**	**Male**	**Female**
5–11 years	2.5	0.7	0.0	0.0
12–15 years	47.1	4.2	12.9	0.7
16–17 years	78.7	7.4	21.6	0.0
18–24 years	39.3	3.9	13.1	0.6
25–29 years	15.3	3.5	4.4	2.2
30–39 years	7.8	1.0	1.9	0.9
40–49 years	3.3	1.6	0.2	0.6
50–64 years	0.7	0.5	0.4	0.1
65+ years	0.3	0.5	0.7	0.2

* As of August 18, 2022. Reports verified to meet case definition by provider interview or medical record review.

Advisory Committee on Immunization Practices (1 Sep 2022)

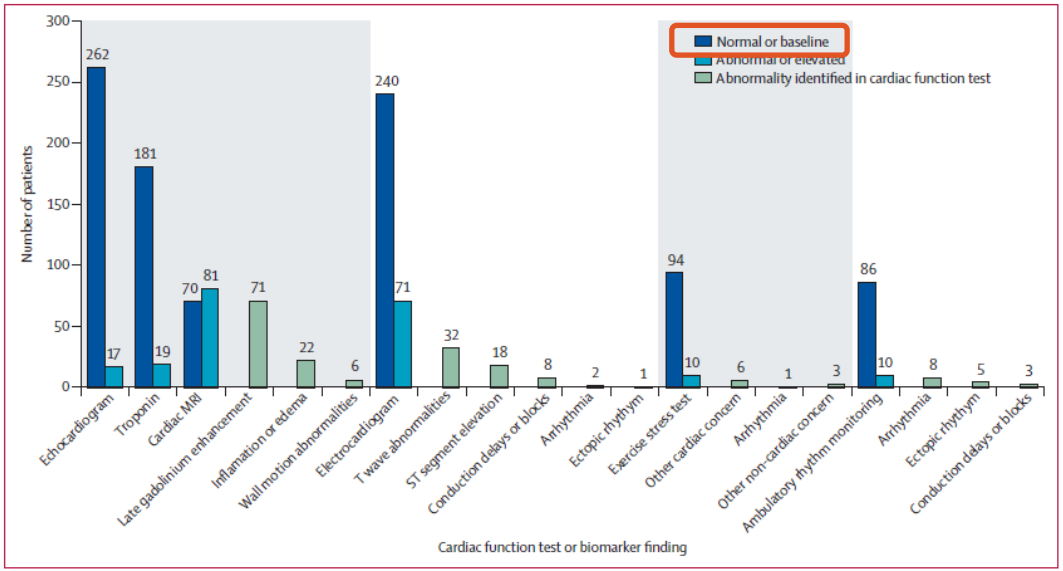
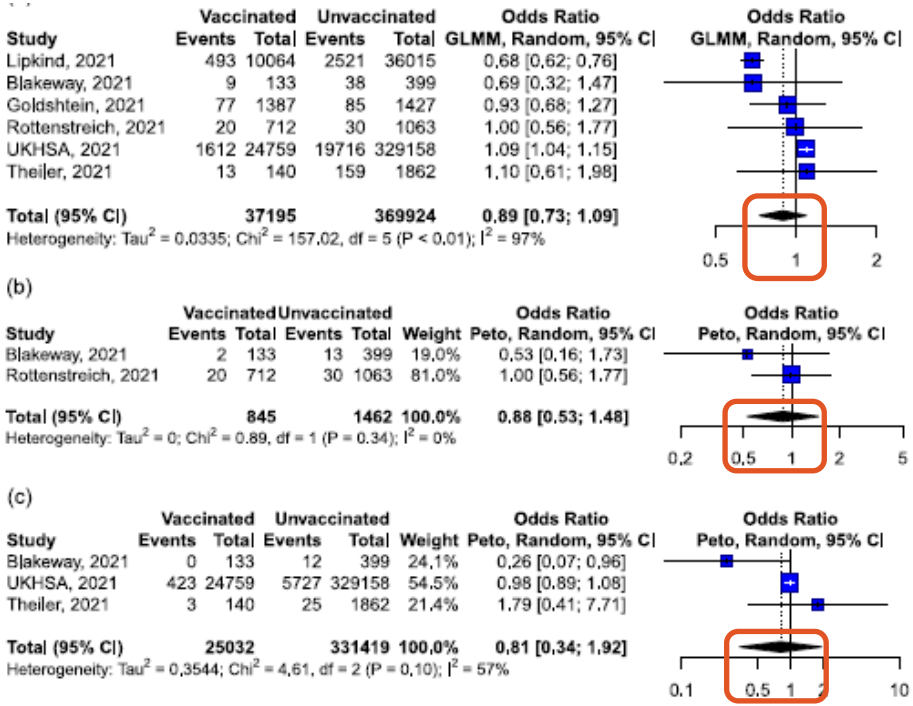


Figure 3: **Follow-up functional status, biomarker testing, and cardiac imaging in patients at least 90 days since onset of myocarditis after mRNA COVID-19 vaccination**

www.thelancet.com/child-adolescent **Published online September 21, 2022**

- Associated with mRNA COVID-19 vaccines
  - Usually within a week after vaccination, most often after dose 2
  - Highest rate among males ages 12–29 years
  - Typically mild, with most patients recovered or recovering 90 days after symptom onset

Safety of mRNA COVID-19 vaccines during pregnancy



Study	Vaccinated Events	Vaccinated Total	Unvaccinated Events	Unvaccinated Total	Odds Ratio GLMM, Random, 95% CI
Lipkind, 2021	493	10064	2521	36015	0.68 [0.62; 0.76]
Blakeway, 2021	9	133	38	399	0.69 [0.32; 1.47]
Goldshtein, 2021	77	1387	85	1427	0.93 [0.68; 1.27]
Rottenstreich, 2021	20	712	30	1063	1.00 [0.56; 1.77]
UKHSA, 2021	1612	24759	19716	329158	1.09 [1.04; 1.15]
Theiler, 2021	13	140	159	1862	1.10 [0.61; 1.98]
Total (95% CI)		**37195**		**369924**	**0.89 [0.73; 1.09]**

Heterogeneity: $Tau^2 = 0.0335$; $Chi^2 = 157.02$, df = 5 (P < 0.01); $I^2 = 97\%$

Odds Ratio GLMM, Random, 95% CI

0.5 1 2

(b)

Study	Vaccinated Events	Vaccinated Total	Unvaccinated Events	Unvaccinated Total	Weight	Odds Ratio Peto, Random, 95% CI
Blakeway, 2021	2	133	13	399	19.0%	0.53 [0.16; 1.73]
Rottenstreich, 2021	20	712	30	1063	81.0%	1.00 [0.56; 1.77]
Total (95% CI)		**845**		**1462**	**100.0%**	**0.88 [0.53; 1.48]**

Heterogeneity: $Tau^2 = 0$; $Chi^2 = 0.89$, df = 1 (P = 0.34); $I^2 = 0\%$

Odds Ratio Peto, Random, 95% CI

0.2 0.5 1 2 5

(c)

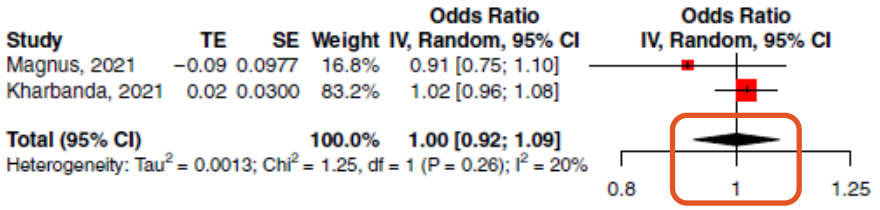
Study	Vaccinated Events	Vaccinated Total	Unvaccinated Events	Unvaccinated Total	Weight	Odds Ratio Peto, Random, 95% CI
Blakeway, 2021	0	133	12	399	24.1%	0.26 [0.07; 0.96]
UKHSA, 2021	423	24759	5727	329158	54.5%	0.98 [0.89; 1.08]
Theiler, 2021	3	140	25	1862	21.4%	1.79 [0.41; 7.71]
Total (95% CI)		**25032**		**331419**	**100.0%**	**0.81 [0.34; 1.92]**

Heterogeneity: $Tau^2 = 0.3544$; $Chi^2 = 4.61$, df = 2 (P = 0.10); $I^2 = 57\%$

Odds Ratio Peto, Random, 95% CI

0.1 0.5 1 10

Fig. 5 Forest plot of studies reporting on preterm birth rate prior to 37 weeks' (a), 34 weeks' (b) and 32 weeks' (c) gestation.



Study	TE	SE	Weight	Odds Ratio IV, Random, 95% CI
Magnus, 2021	−0.09	0.0977	16.8%	0.91 [0.75; 1.10]
Kharbanda, 2021	0.02	0.0300	83.2%	1.02 [0.96; 1.08]
Total (95% CI)			**100.0%**	**1.00 [0.92; 1.09]**

Heterogeneity: $Tau^2 = 0.0013$; $Chi^2 = 1.25$, df = 1 (P = 0.26); $I^2 = 20\%$

Odds Ratio IV, Random, 95% CI

0.8 1 1.25

Fig. 6 Forest plot of studies reporting miscarriage rate and accounting for time-varying confounding.

NATURE COMMUNICATIONS | (2022)13:2414 |

- No increase in odds of preterm birth or spontaneous abortion
- Adverse events consistent with among non-pregnant people (Moro et al, *Obstet & Gynecol* (2022))

Summary

Summary

- Adverse events reported after primary series COVID-19 vaccination generally consistent with observations of preauthorization clinical trials
- Adverse events after booster dose COVID-19 vaccination consistent with primary series vaccination
  - Adverse events after bivalent booster mRNA vaccination consistent with observations after monovalent booster
- Vaccination errors commonly reported among children ages 6 months – 11 years

Summary (cont'd)

- Anaphylaxis after mRNA COVID-19 vaccines comparable to other vaccines
- TTS observed after Ad26.COV2.S vaccine
  - mRNA COVID-19 vaccines preferentially recommended
- Myocarditis most frequent among males ages 12–29 years after dose 2; usually mild and most recover by 90 days after symptom onset
- No increased odds of preterm birth or spontaneous abortion observed among vaccinated pregnant women

Questions?

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Extra slides

Signs and symptoms among serious reports to VAERS after primary series COVID-19 vaccination among adults (ages 18+ years)

	Both mRNA vaccines (n=340 522)*	BNT162b2 vaccine (n=164 669)	mRNA-1273 vaccine (n=175 816)
Signs or symptoms most frequently reported, serious‡			
Total	27 023	14 183	12 839
Dyspnoea	4175 (15·4%)	2210 (15·6%)	1965 (15·3%)
Death§	3802 (14·1%)	1753 (12·4%)	2039 (15·9%)
Pyrexia	2986 (11·0%)	1469 (10·4%)	1517 (11·8%)
Fatigue	2608 (9·7%)	1395 (9·8%)	1213 (9·4%)
Headache	2567 (9·5%)	1360 (9·6%)	1207 (9·4%)
Chest pain	2300 (8·5%)	1310 (9·2%)	990 (7·7%)
Nausea	2228 (8·2%)	1160 (8·2%)	1068 (8·3%)
Pain	2222 (8·2%)	1195 (8·4%)	1027 (8·0%)
Asthenia	2194 (8·1%)	1084 (7·6%)	1110 (8·6%)
Dizziness	2069 (7·7%)	1111 (7·8%)	958 (7·5%)

Safety of primary series COVID-19 vaccination among adults (ages ≥18 years)

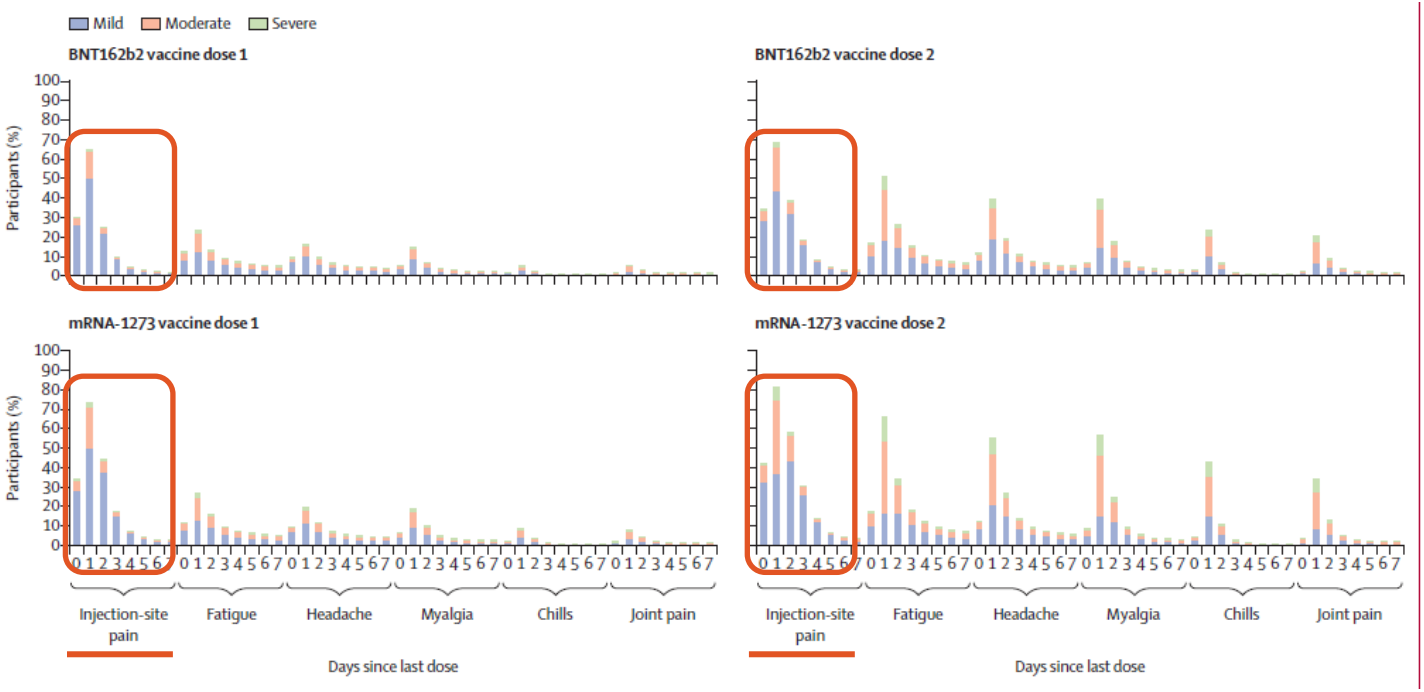
- >81% of reported deaths among people ages ≥60 years
- Causes of death consistent with all-cause morality for the corresponding age group

	Both mRNA vaccines (n=4471*)		BNT162b2 vaccine (n=2086)		mRNA-1273 vaccine (n=2385)	
	n (%)	Reports per million doses administered†	n (%)	Reports per million doses administered†	n (%)	Reports per million doses administered†
Sex						
Female	1906 (42·6%)	12·2	918 (44·0%)	10·6	988 (41·4%)	14·2
Male	2485 (55·6%)	18·5	1116 (53·5%)	15·1	1369 (57·4%)	22·6
Unknown‡	80 (1·8%)	..	52 (2·5%)	..	28 (1·2%)	..
Age, years						
16–17	6 (0·1%)	1·1	6 (0·3%)	1·1	..	..
18–29	51 (1·1%)	1·3	27 (1·3%)	1·1	24 (1·0%)	1·6
30–39	94 (2·1%)	2·4	50 (2·4%)	2·2	44 (1·8%)	2·8
40–49	151 (3·4%)	3·8	74 (3·5%)	3·2	77 (3·2%)	4·6
50–59	328 (7·3%)	6·9	132 (6·3%)	5·0	196 (8·2%)	9·3
60–69	765 (17·1%)	14·4	354 (17·0%)	13·0	411 (17·2%)	16·0
70–79	1117 (25·0%)	28·5	496 (23·8%)	25·9	621 (26·0%)	31·0
80–89	1128 (25·2%)	75·4	529 (25·4%)	72·1	599 (25·1%)	78·6
≥90	637 (14·2%)	207·7	302 (14·5%)	188·1	335 (14·0%)	229·3
Unknown‡	194 (4·3%)	..	116 (5·6%)	..	78 (3·3%)	..

Includes reports made and vaccines administered from Dec 14, 2020, to June 14, 2021. VAERS=Vaccine Adverse Event Reporting System. *Of 4496 deaths, 25 were excluded as they could not be confirmed or were duplicate reports upon review. †Doses of vaccine administered in the study period were used for denominators in each age group; does not include doses administered in Texas because data for Texas were reported to the US Centers for Disease Control and Prevention in aggregate. ‡Reporting rates not shown for unknown categories because of unreliable dose denominators.

Table 3: **Frequency and rates of death reported to VAERS by recipients of mRNA COVID-19 vaccines, by sex and age group**

Safety of primary series COVID-19 vaccination among adults (ages ≥18 years) (cont'd)



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- Adverse reactions transient (often resolve within first 3–4 days after vaccination)
- Slightly more frequent reporting of adverse events
  - After dose 2
  - After mRNA-1273

Safety of heterologous booster dose COVID-19 vaccination among adults (ages ≥18 years)

TABLE 1. Adjusted odds ratios* and 95% CI for reactions and health impacts following homologous or heterologous COVID-19 vaccine booster dose among adults aged ≥18 years, by primary vaccination series and booster vaccine product received (N = 721,562) — United States, September 22, 2021–February 6, 2022

Primary series/Booster vaccine (no.)	No. of booster doses (%)	Reaction† (%)		
		Any injection site reaction	Any systemic reaction	Any health impact
Moderna§ (n = 327,464)				
Moderna	307,998 (94.1)	71.8	64.4	23.6
Pfizer-BioNTech	19,222 (5.9)	70.7	66.7	23.4
aOR (95% CI)	—	0.70 (0.68–0.73)¶	0.85 (0.82–0.88)¶	0.81 (0.78–0.84)¶
Pfizer-BioNTech§ (n = 349,545)				
Pfizer-BioNTech	332,588 (95.1)	64.3	58.4	19.1
Moderna	16,725 (4.8)	87.7	82.9	39.5
aOR (95% CI)	—	2.41 (2.30–2.53)¶	2.24 (2.14–2.33)¶	2.06 (1.99–2.13)¶
Janssen (n = 44,553)**				
Janssen	7,656 (17.2)	52.3	56.2	16.6
Moderna	23,310 (52.3)	65.9	58.2	19.0
OR (95% CI)	—	1.76 (1.67–1.86)¶	1.08 (1.03–1.14)¶	1.18 (1.10–1.26)¶
Pfizer-BioNTech	13,587 (30.5)	62.0	56.6	16.8
OR (95% CI)	—	1.49 (1.41–1.57)¶	1.01 (0.96–1.07)	1.01 (0.94–1.09)

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- Adverse reactions and/or health impacts generally less frequent after homologous mRNA COVID-19 booster vaccine than dose 2

Safety of primary series BNT162b2 COVID-19 vaccination among ages 12–17 years (cont'd)

	% of v-safe enrollees reporting reaction or health impact*			
	Age 16–17 yrs, dose (no.)		Age 12–15 yrs, dose (no.)	
Event	Dose 1 (66,350)	Dose 2 (41,040)	Dose 1 (62,709)	Dose 2 (38,817)
Any injection site reaction	62.7	64.4	63.9	62.4
Any systemic reaction	55.7	69.9	48.9	63.4
Any health impact	11.0	28.6	10.6	25.4

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- Adverse reactions and health impacts generally more frequent after dose 2
  - Slightly more frequent among ages 16–17 years

Safety of homologous booster BNT162b2 COVID-19 vaccination among ages 12–17 years (cont'd)

Reported event	No. (%) reporting
Nonserious VAERS reports	
Symptom, sign, diagnostic result, or condition (MedDRA PT*)	**837 (100.0)**
Product storage error	123 (14.7)
Dizziness	100 (11.9)
Syncope	87 (12.0)
Fever	75 (9.0)
No adverse event†	70 (8.4)
Headache	69 (8.2)
Inappropriate schedule of product administration	56 (6.7)
Fatigue	55 (6.6)
Nausea	52 (6.2)
Pain	52 (6.2)
Expired product administered	40 (4.8)
Pain in extremity	40 (4.8)
Chest pain	39 (4.7)
Underdose	39 (4.7)
Vomiting	39 (4.7)

Reported event	No. (%) reporting
Serious VAERS reports§,¶	
Clinical impression	**77 (100.0)**
Myocarditis	47 (61.0)
Insufficient data to make a clinical impression	10 (13.0)
Appendicitis	3 (3.9)
Acute embolic stroke	2 (2.6)
Anaphylaxis or allergic reaction	2 (2.6)
Tachycardia	2 (2.6)
Acute pancreatitis	1 (1.3)
Exacerbation of existing genetic disorder	1 (1.3)
Guillain-Barré syndrome	1 (1.3)
Immune thrombocytopenia	1 (1.3)
Injection site pain	1 (1.3)
Pericardial effusion	1 (1.3)
Rhabdomyolysis	1 (1.3)
Severe headache	1 (1.3)
Side effect of prescription medication	1 (1.3)
Spontaneous tension pneumothorax	1 (1.3)
Transverse myelitis	1 (1.3)

MMWR / March 4, 2022 / Vol. 71 / No. 9

- Most reports to VAERS (92%) non-serious; consistent with after primary series
- Most serious reports of myocarditis
  - 32 met case definition; all 27 hospitalized patients recovered or were recovering

Safety of primary series mRNA COVID-19 vaccination among ages 5–11 years

TABLE 2 Reactions Reported for Children Ages 5 to 11 y (N = 48 795) Who Completed at Least 1 v-safe Health Check-in Survey on Days 0 to 7 After Receiving Pfizer BioNTech COVID-19 Vaccine in the United States From November 3 to February 27, 2022

	% of v-safe Enrollees Reporting Reaction or Health Impact															
	Dose 1 (48 795)									Dose 2 (39 416)								
Event	Days 0–7[a]	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Days 0–7[a]	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Any injection site reaction	54.9	43.2	58.1	27.0	10.9	5.3	3.2	2.0	1.5	56.8	43.4	62.7	33.4	13.8	5.9	3.2	2.1	1.7
Any systemic reaction	35.3	14.2	26.2	17.2	11.5	8.9	7.5	6.6	6.5	41.0	11.5	40.4	21.9	11.8	7.9	6.2	5.2	5.3
Any health impact	11.4	2.0	6.1	4.5	3.5	2.9	2.7	2.5	2.3	15.4	1.8	13.9	6.1	2.9	2.1	1.9	1.8	1.9

- Adverse reactions or health impacts generally transient, resolving in a week or earlier

Safety of primary series mRNA COVID-19 vaccination among ages 5–11 years

TABLE 3 Most Frequently Reported Solicited Reactions Reported for Children Ages 5 to 11 y Who Completed at Least 1 v-safe Health Check-in Survey on days 0 to 7 After Receiving BNT-162b2 COVID-19 ($N = 48795$) in the United States From November 3 to February 27, 2022

	% of v-Safe Enrollees Reporting Reaction[a]							
	Dose 1 (48795)				Dose 2 (39416)			
	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Injection site pain	42.0	10.2	0.5	52.7	40.9	13.4	0.7	55.0
Fatigue	12.1	7.3	1.0	20.4	13.7	10.5	1.5	25.7
Headache	8.9	4.8	0.7	14.4	11.2	7.5	1.0	19.7
Myalgia	4.4	2.9	0.4	7.7	5.6	4.5	0.4	10.6
Chills	2.4	1.5	0.2	4.2	3.8	2.8	0.4	6.9
Fever[b]	1.5	0.9	0.8	3.2	2.5	1.6	0.9	5.1

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- Adverse reactions slightly more frequent after dose 2
  - Mostly mild to moderate in intensity
  - Frequency lower than among older age groups (e.g., ages 12–17 years)

Safety of primary series mRNA COVID-19 vaccination among ages 6 months – 5 years

TABLE 1. Adverse reactions and health impacts reported for children aged 6 months–5 years* (N = 23,266) who received Pfizer-BioNTech or Moderna COVID-19 vaccine — United States, June 18–August 21, 2022

	Vaccine, age group, % reporting reaction or health impacts after vaccination†							
	Pfizer-BioNTech (N = 8,541)				Moderna (N = 14,725)			
	6 mos–2 yrs (n = 4,749)		3–4 yrs (n = 3,792)		6 mos–2 yrs (n = 8,338)		3–5 yrs (n = 6,387)	
Event	Dose 1 (4,749)	Dose 2 (2,467)	Dose 1 (3,792)	Dose 2 (2,060)	Dose 1 (8,338)	Dose 2 (4,288)	Dose 1 (6,387)	Dose 2 (3,549)
Any injection site reaction	19.0	18.3	28.4	26.5	19.2	26.7	32.4	47.1
Any systemic reaction	55.8	47.1	32.2	29.2	55.7	58.2	34.5	49.9
Any health impact	10.3	7.5	9.3	7.4	9.8	11.6	10.8	15.9

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- Systemic reactions more frequent among ages 6 months – 2 years
  - Consistent with preauthorization clinical trials
  - Common after childhood vaccination in general

Adverse events not specific to pregnancy after COVID-19 vaccination

Table 3. Most Common MedDRA (Medical Dictionary for Regulatory Activities) Codes After Primary Series and Booster Doses of Coronavirus Disease 2019 (COVID-19) Vaccination in Pregnant People Among Non–Pregnancy-Specific Reports (n=156), Vaccine Adverse Event Reporting System, September 22, 2021–March 24, 2022*

Adverse Event	Primary Series COVID-19 Vaccination Reports in Pregnant People (N=1,995)†	Booster Doses in Pregnant People		
		All Vaccine Brands (n=207)	Pfizer–BioNTech Vaccine (n=106)	Moderna Vaccine (n=101)
Headache	392 (19.7)	42 (20.3)	26 (24.5)	16 (15.8)
Fatigue	377 (18.9)	32 (15.5)	20 (18.9)	12 (11.9)
Pyrexia	321 (16.1)	33 (15.9)	18 (17.0)	15 (14.9)
Pain	317 (15.9)	25 (12.1)	15 (14.2)	10 (9.9)
Chills	311 (15.6)	26 (12.6)	16 (15.1)	10 (9.9)
Nausea	277 (13.9)	24 (11.6)	14 (13.2)	10 (9.9)
Pain in extremity	262 (13.1)	19 (9.2)	13 (12.3)	6 (5.9)
Dizziness	224 (11.2)	17 (8.2)	11 (10.4)	6 (5.9)
Injection site pain	173 (8.7)	17 (8.2)	9 (8.5)	8 (7.9)
Vomiting	164 (8.2)	16 (7.7)	6 (5.7)	10 (9.9)

COVID-19, coronavirus disease 2019.
Data are n (%).
* Adverse events are not mutually exclusive; percentages of adverse events do not constitute reporting rates.
† Reports after primary series of COVID-19 vaccination (Pfizer–BioNTech and Moderna combined) in pregnant people who reported to the Vaccine Adverse Event Reporting System, September 22, 2021–March 9, 2022.[22]