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COVID-19 Vaccine Safety in Adolescents Aged 12–17 Years — United States, December 14, 2020–July 16, 2021

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Resumen

¿Qué es lo que ya se sabe sobre este tema?

En los ensayos de preautorización de la vacuna contra la COVID-19 de Pfizer-BioNTech, los adolescentes de 12 a 17 años informaron reacciones leves y moderadas locales y sistémicas. La miocarditis se ha observado después de la vacunación con vacunas de ARNm en el seguimiento posterior a la autorización.

¿Qué añade este informe?

Las reacciones locales y sistémicas después de la vacunación con la vacuna de Pfizer-BioNTech fueron comúnmente reportadas por adolescentes de 12 a 17 años a los sistemas de monitoreo de seguridad de la vacuna de los Estados Unidos, especialmente después de la dosis 2. Una pequeña proporción de estas reacciones son consistentes con miocarditis.

¿Cuáles son las implicaciones para la práctica de la salud pública?

Las reacciones locales y sistémicas leves son comunes entre los adolescentes que siguen la vacuna de Pfizer-BioNTech, y los eventos adversos graves son raros. El Comité Asesor sobre Prácticas de Inmunización llevó a cabo una evaluación de riesgo-beneficio y continúa recomendando la vacuna contra el COVID-19 de Pfizer-BioNTech para todas las personas de ≥12 años.

Al 30 de julio de 2021, entre las tres vacunas contra el COVID-19 autorizadas para su uso en Estados Unidos, solo la vacuna contra el COVID-19 de Pfizer-BioNTech BNT162b2 mRNA está autorizada para adolescentes de 12 a 17 años. La Administración de Alimentos y Medicamentos (FDA, por sus, emitió una Autorización de Uso de Emergencia (EUA, por sus, por sus, por sus ≥ 16 años de edad, el 11 de diciembre de 2020 (*1*); la UCE se amplió para incluir a adolescentes de 12 a 15 años el 10 de mayo de 2021 (*2*), sobre la base de los resultados de un ensayo clínico de Fase 3 (*3*). A partir de junio de 2021, comenzaron a notificarse casos de miocarditis y miopericarditis (en adelante, miocarditis) tras la recepción de la vacuna de Pfizer-BioNTech, principalmente entre varones jóvenes tras la recepción de la segunda dosis (*4,5*). El 23 de junio de 2021, el Comité Asesor sobre Prácticas de Inmunización (ACIP, por sus) de los CDC revisó los datos disponibles y concluyó que los beneficios de la vacunación contra la COVID-19 para las personas individuales y la población superan los riesgos de miocarditis y recomendó el uso continuado de la vacuna en personas de ≥12 años de edad (*6*). Para caracterizar aún más la

(VAERS) y los eventos adversos y las evaluaciones de impacto en la salud reportados en v-safe (un sistema de vigilancia de seguridad basado en teléfonos inteligentes) para adolescentes estadounidenses de 12 a 17 años de edad entre el 14 de diciembre de 2020 y el 16 de julio de 2021. Al 16 de julio de 2021, aproximadamente 8,9 millones de adolescentes estadounidenses de entre 12 y 17 años habían recibido la vacuna de Pfizer-BioNTech.* EL VAERS recibió 9.246 informes después de la vacunación de Pfizer-BioNTech en este grupo de edad; El 90,7% de ellos fueron por eventos adversos no graves y el 9,3% por eventos adversos graves, incluida la miocarditis (4,3%). Aproximadamente 129,000 adolescentes estadounidenses de 12 a 17 años de edad se inscribieron en v-safe después de la vacunación de Pfizer-BioNTech; reportaron reacciones locales (63,4%) y sistémicas (48,9%) con una frecuencia similar a la reportada en ensayos clínicos de preautorización. Las reacciones sistémicas fueron más frecuentes después de la dosis 2. Los CDC y la FDA continúan monitoreando la seguridad de las vacunas y proporcionando datos a ACIP para guiar las recomendaciones de vacunas covid-19.

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VAERS es un sistema pasivo de vigilancia de la seguridad de las vacunas comanaged por los CDC y la FDA que monitorea los eventos adversos después de la vacunación (*7*). VAERS acepta informes de cualquier persona, incluidos proveedores de atención médica, fabricantes de vacunas y miembros del público. Bajo los requisitos de la EUA de la vacuna COVID-19, los proveedores de atención médica deben informar ciertos eventos adversos después de la vacunación al VAERS, incluida la muerte.† Los miembros del personal del VAERS asignan términos preferidos a los signos, síntomas y hallazgos de diagnóstico en los informes del VAERS al Diccionario Médico para Actividades Regulatorias (MedDRA, por sus mis). Los informes del VAERS se clasifican como graves si se informa de cualquiera de los siguientes: hospitalización o prolongación de la hospitalización, enfermedad potencialmente mortal, discapacidad permanente, anomalía congénita o defecto congénito, o muerte. Los informes de eventos adversos graves reciben seguimiento para obtener información adicional, incluidos los registros médicos; para los informes de defunción, se obtienen certificados de defunción e informes de autopsia, si están disponibles. Los médicos de los CDC revisaron la información disponible para cada difunto para formarse una impresión sobre la causa de la muerte.[§¶]

CDC established v-safe, a voluntary smartphone-based active safety surveillance system, to monitor adverse events after COVID-19 vaccination. Adolescents who receive a COVID-19 vaccine are eligible to enroll in v-safe, through self-enrollment or as a dependent of a parent or guardian, and receive scheduled text reminders about online health surveys.** Health surveys sent in the first week after vaccination include questions about local injection site and systemic reactions and health impacts.[††] If a report indicated medical attention was sought, VAERS staff members contacted the reporter and encouraged completion of a VAERS report, if indicated.

VAERS and v-safe data were assessed by sex, age group, and race/ethnicity for U.S. adolescents aged 12–17 years who received Pfizer-BioNTech vaccine during December 14, 2020–July 16, 2021. VAERS reports for adolescents aged 12–15 years were excluded if vaccination occurred before EUA age expansion on May 10, 2021. FDA used empirical Bayesian data mining to monitor for disproportional reporting of adverse events by vaccine among VAERS reports for persons aged 12–17 years (*8*). SAS software (version 9.4; SAS Institute) was used to conduct all analyses. These surveillance activities were reviewed by CDC and conducted consistent with applicable federal law and CDC policy.[§§¶¶]

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Review of VAERS Data

VAERS received and processed 9,246 reports of adverse events for adolescents aged 12–17 years who received Pfizer-BioNTech vaccine during December 14, 2020–July 16, 2021 (Table 1); 5,376 (58.1%) were in adolescents aged 12–15 years and 3,870 (41.9%) in persons aged 16–17 years.*** No adverse events were reported disproportionately to VAERS in association with Pfizer-BioNTech vaccination. Common conditions among all reports included dizziness (1,862; 20.1%), syncope (1,228; 13.3%), and headache (1,027; 11.1%). Among the 1,228 reports of syncope, 901 met a standard case definition[†††]; 548 (60.8%) of these events occurred in females, and median age was 15 years. Among those who met the syncope case definition, 147 (16.3%) reported a history of anxiety around needles, and 145 (16.1%) were transported to an emergency department for further evaluation.

Overall, 8,383 (90.7%) VAERS reports were for nonserious events, and 863 (9.3%) for serious events, including death; 609 (70.6%) reports of serious events were among males, and median age was 15 years. The most commonly reported conditions and diagnostic findings among reports of serious events were chest pain (56.4%), increased troponin levels (41.7%), myocarditis (40.3%), increased c-reactive protein (30.6%), and negative SARS-CoV-2 test results (29.4%) (Table 2); these findings are consistent with a diagnosis of myocarditis. Myocarditis was listed among 4.3% (397) of all VAERS reports.

CDC reviewed 14 reports of death after vaccination. Among the decedents, four were aged 12–15 years and 10 were aged 16–17 years. All death reports were reviewed by CDC physicians; impressions regarding cause of death were pulmonary embolism (two), suicide (two), intracranial hemorrhage (two), heart failure (one), hemophagocytic lymphohistiocytosis and disseminated

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Review of v-safe Data

During December 14, 2020–July 16, 2021, v-safe enrolled 66,350 adolescents aged 16–17 years who received Pfizer-BioNTech vaccine (Table 3). After Pfizer-BioNTech vaccine was authorized for adolescents aged 12–15 years (beginning May 10, 2021), v-safe enrolled 62,709 adolescents in this age group. During the week after receipt of dose 1, local (63.9%) and systemic (48.9%) reactions were commonly reported by adolescents aged 12–15 years; systemic reactions were more common after dose 2 (63.4%) than dose 1 (48.9%). Reporting trends were similar for adolescents aged 16–17 years: systemic reactions were reported among 55.7% after dose 1 and 69.9% after dose 2. For each dose and age group, reactions were reported most frequently the day after vaccination. The most frequently reported reactions for both age groups after either dose were injection site pain, fatigue, headache, and myalgia.

During the week after receipt of dose 2, approximately one third of adolescents in both age groups reported fever. Nearly one quarter of adolescents in both age groups reported they were unable to perform normal daily activities the day after dose 2. Fewer than 1% of adolescents aged 12–17 years required medical care in the week after receipt of either dose; 56 adolescents (0.04%) were hospitalized.

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Discussion

The findings summarized in this report are consistent with the safety data observed in preauthorization trials for Pfizer-BioNTech after vaccination among persons aged 12–25 years, with the exception of myocarditis, a serious adverse event detected in postauthorization safety monitoring (*3*). Trial participants who received vaccine (1,131 aged 12–15 years; 537 aged 16–25 years) reported local and systemic reactions that were mostly mild (i.e., did not interfere with activity) or moderate (some interference with activity); no serious adverse events related to vaccination were reported (*3*). Similarly, local and systemic reactions were commonly reported by U.S. adolescents aged 12–17 years who enrolled in v-safe; a minority (<25%) reported they were unable to perform normal daily activities the day after receipt of dose 2. A small number of v-safe participants reported they were hospitalized after vaccination; however, v-safe does not record reason for hospitalization, and it cannot be determined whether hospitalization was related to vaccination.

Among 8.9 million adolescents vaccinated during the study period, VAERS reports were received for approximately one per 1,000 vaccinees, and 90% of these reports were for nonserious conditions. Syncope was among the events most commonly reported to VAERS in this age group and is common among adolescents after any vaccination (*9*). Other conditions associated with vasovagal response to vaccination were also frequently reported. Among the serious reports, myocarditis and other conditions that might be associated with myocarditis were among the most common terms reported; however, these terms did not account for a large proportion of VAERS reports overall. No reports of death to VAERS were determined to be the result of myocarditis. Impressions regarding cause of death did not indicate a pattern suggestive of a causal relationship with vaccination; however, cause of death for some decedents is pending receipt of additional information. ACIP conducted a risk-benefit assessment based in part on the data presented in this report and continues to recommend the Pfizer-BioNTech COVID-19 vaccine for all persons aged ≥12 years (*6*). An updated EUA now includes information on myocarditis after mRNA COVID-19 vaccines.[§§§]

The findings in this report are subject to at least five limitations. First, VAERS is a passive surveillance system and is subject to underreporting and reporting biases (*7*); however, under EUA, health care providers are required to report all serious events following vaccination. Second, medical review of reported deaths following vaccination is dependent on availability of medical records, death certificates, and autopsy reports, which might be unavailable or not available in a timely manner. Third, lack of a statistical safety signal in planned monitoring does not preclude a safety concern. For example, although a statistically significant data mining alert has not been observed for myocarditis following Pfizer-BioNTech vaccination, myocarditis has been identified as an adverse event following mRNA COVID-19 vaccines in multiple surveillance systems (*10*). Fourth, this study was not designed to identify all cases of myocarditis; only reports that listed the MedDRA term "myocarditis" were included. Finally, v-safe is a voluntary self-enrollment program that requires children aged <15 years be enrolled by a parent or guardian and relies on vaccine administrators to promote the program. Therefore, v-safe data might not be generalizable to the overall vaccinated adolescent population.

The initial safety findings of Pfizer-BioNTech vaccine administered to U.S. adolescents aged 12–17 years are similar to those described in the clinical trials, with the exception of myocarditis, a rare serious adverse event associated with receipt of mRNA-based COVID-19 vaccines; follow-up of reported myocarditis cases is ongoing (*6*). CDC and FDA will continue to monitor for adverse events, including myocarditis, after mRNA COVID-19 vaccination and share available data with ACIP to guide risk-benefit assessments for all COVID-19 vaccines.

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All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

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* https://covid.cdc.gov/covid-data-tracker/#datatracker-home

† https://vaers.hhs.gov/faq.html

§ Each VAERS report might be assigned more than one MedDRA preferred term. A MedDRA-coded event does not indicate a medically confirmed diagnosis. https://www.meddra.org/how-to-use/basics/hierarchy

¶ Based on the Code of Federal Regulations Title 21. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr

** Adolescents aged <15 years must be enrolled by a parent or guardian and may not self-enroll. Health check-ins are sent via text messages that link to web-based surveys on days 0–7 after vaccination; then weekly through 6 weeks after vaccination; and then 3, 6, and 12 months after vaccination.

†† Participants in v-safe self-identify the severity of their symptoms, defined as mild (noticeable, but not problematic), moderate (limit normal daily activities), or severe (make daily activities difficult or impossible). Health impacts include whether the vaccine recipient was unable to perform normal daily activities, missed school or work, or received care (i.e., telehealth, clinic or emergency department visit, or hospitalization) from a medical professional because of new symptoms or conditions.

§§ FDA used the Multi-Item Gamma Poisson Shrinker algorithm to calculate the Empirical Bayes Geometric Mean and its associated 90% confidence interval (EB05, EB95). An EB05 ≥2 (more than twice expected) was considered the threshold for defining a vaccine-event pair reported disproportionately.

¶¶ 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

*** Processed VAERS reports are those that have been coded using MedDRA, have been deduplicated, and have undergone standard quality assurance and quality control review.

††† CDC reviewed VAERS reports of syncope for additional information. Syncopal events that occurred off-site or ≥1 hour after vaccine administration were excluded from analysis.

§§§ An updated letter of authorization for the Pfizer-BioNTech COVID-19 vaccine is available at https://www.fda.gov/media/150386/download .

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TABLE 1. Adverse event reports for adolescents aged 12–17 years who received the Pfizer-BioNTech COVID-19 vaccine, by demographic characteristics and reported symptoms (N = 9,246) — Vaccine Adverse Event Reporting System, United States, December 14, 2020–July 16, 2021

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Characteristic	Total, % (N = 9,246)	Severity, %* Nonserious (n = 8,383)	Serious, excluding death (n = 849)	Death (n = 14)
Sex				
Female	52.9	55.3	29.1	35.7
Male	45.8	43.2	70.7	64.3
Unknown	1.4	1.5	0.2	0
Age group, yrs				
12–15	58.1	58.7	53.4	28.6
16–17	41.9	41.3	46.6	71.4
Ethnicity				
Hispanic or Latino	10.4	9.6	18.4	7.1
Non-Hispanic or Latino	44.1	43.4	51.2	50.0
Unknown ethnicity	45.5	47.1	30.4	42.9
Race				
American Indian or Alaska Native	0.8	0.8	0.5	0

Characteristic	Total, % (N = 9,246)	Severity, %* Nonserious (n = 8,383)	Serious, excluding death (n = 849)	Death (n = 14)
Black	3.2	3.0	5.3	7.1
Native Hawaiian or Pacific Islander	0.3	0.2	0.7	0
White	45.1	44.2	53.8	71.4
Multiracial	2.1	2.2	2.0	0
Other	13.1	13.9	5.4	0
Unknown race	30.2	30.8	25.0	14.3

Abbreviation: VAERS = Vaccine Adverse Event Reporting System.
* VAERS reports are classified as serious if any of the following are reported: hospitalization or prolongation of hospitalization, life-threatening illness, permanent disability, congenital anomaly or birth defect, or death.

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TABLE 2. Most frequent symptoms, signs, diagnostic results, and conditions* reported to the Vaccine Adverse Event Reporting System for adolescents aged 12–17 years after receipt of the Pfizer-BioNTech COVID-19 vaccine (N = 9,246) — United States, December 14, 2020–July 16, 2021

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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

Symptom, sign, diagnostic result, or condition	% Reporting
Vomiting	6.4
Difficulty breathing	5.3
Chest pain	4.9
Pain	4.6
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

Abbreviations: MedDRA = Medical Dictionary for Regulatory Activities; VAERS = Vaccine Adverse Event Reporting System.
* Signs and symptoms in VAERS reports are assigned MedDRA preferred terms by VAERS staff members. Each VAERS report might be assigned more than one MedDRA preferred term, which can include normal diagnostic findings. A MedDRA-coded event does not indicate a medically confirmed diagnosis. https://www.meddra.org/how-to-use/basics/hierarchy
[†] VAERS reports are classified as serious if any of the following are reported: hospitalization, prolongation of hospitalization, life-threatening illness, permanent disability, congenital anomaly or birth defect, or death.

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TABLE 3. Reactions reported by adolescents aged 12–17 years (N = 129,059) who completed at least one v-safe health check-in survey on days 0–7 after receiving Pfizer BioNTech COVID-19 vaccine — United States, December 14, 2020–July 16, 2021

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Event	% of v-safe enrollees reporting reaction or health impact* Age 16–17 yrs, dose (no.)		% of v-safe enrollees reporting reaction or health impact* Age 12–15 yrs, dose (no.)	
	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
Itching	5.7	6.3	5.8	5.5
Pain	60.2	62.0	61.2	59.9
Redness	3.4	4.9	4.1	5.3
Swelling	7.7	9.9	7.5	8.9
Any systemic reaction	55.7	69.9	48.9	63.4
Abdominal pain	4.7	8.5	4.1	7.0
Myalgia	25.4	40.7	21.4	31.4
Chills	8.3	26.2	6.8	21.1
Diarrhea	4.2	4.9	3.1	3.3
Fatigue	34.1	52.3	27.4	44.6
Fever	9.9	31.0	9.3	29.9
Headache	29.8	50.6	25.2	43.7
Joint pain	7.9	18.2	6.3	12.4
Nausea	10.2	19.8	7.5	14.8
Rash	1.2	1.1	1.2	1.2
Vomiting	1.1	2.3	1.0	2.6
Any health impact	11.0	28.6	10.6	25.4
Unable to perform normal daily activities	9.0	24.7	9.3	23.1
Unable to work or attend school	3.7	11.6	2.4	6.1
Needed medical care	0.5	0.6	0.5	0.8
Telehealth	0.1	0.2	0.1	0.2
Clinic	0.2	0.2	0.2	0.3
Emergency department visit	0.1	0.2	0.1	0.2
Hospitalization	0.02	0.03	0.02	0.04

* Percentage of enrollees who reported a reaction or health impact at least once during days 0–7 post-vaccination.

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