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Post-licensure Safety Surveillance of 20-Valent Pneumococcal Conjugate Vaccine (PCV20) Among US Adults in the Vaccine Adverse Event Reporting System (VAERS)

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Abstract

Background—On June 8, 2021, a new 20-valent pneumococcal conjugate vaccine (PCV20, PREVNAR 20[®], Pfizer, Inc.) was licensed for use in adults aged ≥ 18 years by the US Food and Drug Administration (FDA).

Objective—To describe reports to the Vaccine Adverse Event Reporting System (VAERS) after administration of the 20-valent pneumococcal conjugate vaccine in adults.

Methods—We searched the VAERS for reports of adverse events involving persons aged ≥ 19 years who received PCV20 during October 20, 2021, through December 31, 2023. Our evaluation included automated analysis of reports, clinical review of serious reports and pre-specified events

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Author contributions PLM and MMO originated the study, supervised its implementation, conducted the analysis, and led the writing of the manuscript summarizing the findings. PM, CE, PB, KW, NN, and MT assisted in one or more aspects, including study design, review of VAERS reports and medical records, technical advice, administrative support, and writing of the report. All authors read and approved the final version.

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Declarations

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s40264-024-01498-2>.

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Disclaimer The findings and conclusions in this manuscript are those of the author and do not necessarily represent the official position of the CDC or FDA.

Ethics approval This activity was reviewed by the CDC and was considered to be consistent with applicable federal law and CDC policy. Informed consent was not obtained for this secondary use of existing information; see 45 CFR part 46.102(l)(2), 21 CFR part 56, 42 USC §241(d), 5 USC §552a, and 44 USC §3501 et seq.

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of special interest, empirical Bayesian data mining to assess for disproportionate reporting, and estimation of reporting rates for reports of Guillain-Barré syndrome (GBS).

Results—The VAERS received 1976 reports after PCV20 administration in persons aged ≥ 19 years (6% of reports involved serious events). The most common adverse events among persons aged 19–64 years ($n = 798$) were injection-site reactions (231, 29%), pain (134, 17%), erythema (118, 15%), and fever (117, 15%). For persons aged ≥ 65 years ($n = 1178$), the most common adverse events were injection-site reactions (417, 35%), pain (180, 15%), pain in extremity (162, 14%), and erythema (158, 13%). A data mining alert (EB05 = 3.812) for the MedDRA Preferred Term “Guillain-Barre syndrome” was observed for serious reports. Clinical review verified 11 of 20 GBS reports; 7/11 vaccine recipients were aged ≥ 65 years. Among the 11 verified cases, the median time from vaccination to symptom onset was 14 days. Five persons received another vaccine on the same visit. The reporting rate of GBS after PCV20 receipt was 0.5 cases per million doses distributed. No other safety concern was identified.

Conclusions—During the period of this post-licensure review of PCV20, we found most reports were non-serious and comprised mostly local and systemic (e.g., fever) reactions consistent with prelicensure studies. In serious reports, we also identified a data mining alert for GBS after receipt of PCV20, which Centers for Disease Control and Prevention and the FDA are investigating further. No other new or unexpected safety concern was identified.

1 Introduction

On June 8, 2021, the Food and Drug Administration (FDA) approved the 20-valent pneumococcal conjugate vaccine (PCV20, PREVNAR 20[®], Pfizer, Inc.) for adults aged ≥ 18 years to prevent pneumonia and invasive disease caused by pneumococcal serotypes contained in the vaccine [1]. On October 20, 2021, the Advisory Committee on Immunization Practices (ACIP) recommended the use of PCV20 for PCV-naïve adults who are either aged ≥ 65 years or aged 19–64 years with certain risk conditions [2]. Phase 3 clinical trials in 6470 subjects exposed to either PCV20 or control vaccines revealed the tolerability and safety profile of PCV20 was similar to PCV13 [3–5]. Among adults aged 18–49 years of age, the reported rates of serious adverse events (SAEs) were low and were similar between the PCV20 and PCV13 groups. Serious adverse events were unrelated to the vaccine and consistent with medical diagnoses that occurred in the age group of the study population [5]. Among adults aged 60–64 years of age, SAEs were not considered to be related to the vaccine [4]. This study seeks to assess adverse event (AE) reports after PCV20 in adults aged ≥ 19 years in the Vaccine Adverse Event Reporting System (VAERS), a national passive surveillance system used to monitor the post-licensure safety of US-licensed vaccines.

2 Methods

2.1 Data Source

The VAERS is a national spontaneous surveillance system managed by the Centers for Disease Control and Prevention (CDC) and the FDA, which serves primarily for safety signal detection and hypothesis generation and is used to monitor the post-licensure safety of US-licensed vaccines [6]. The VAERS accepts reports from various sources, including

healthcare professionals, vaccine manufacturers, and the general public. The data in VAERS encompass information such as demographic details of the vaccinated individuals, vaccine types administered, and details of the AE reports [6]. Adverse events and their associated signs and symptoms, along with physician diagnoses, if available, are coded using the Medical Dictionary for Regulatory Activities (MedDRA). The MedDRA is a medically validated and internationally standardized terminology [7]. Each VAERS report may contain one or more MedDRA Preferred Terms (PTs), which are specific descriptors for symptoms, signs, diseases, treatments, procedures, and medical, social, or family history characteristics [8]. Preferred terms are not necessarily medically confirmed diagnoses. The VAERS may also receive reports of vaccination errors (e.g., extra dose administered) not describing an AE. In accordance with the Code of Federal Regulations, a VAERS report is classified as serious if one or more of the following are reported: death, life-threatening illness, hospitalization (including prolonged existing hospitalization), permanent disability, or a birth defect [9]. It is important to note that a report submitted to VAERS does not imply causation but rather indicates that an AE occurred following vaccination.

We analyzed the safety of PCV20 in adults aged ≥ 19 years vaccinated from October 20, 2021, through December 31, 2023, using four methods: (1) automated analysis of VAERS data; (2) clinical review of serious reports and reports of adverse events of special interest (AESIs) such as anaphylaxis, seizures, and Guillain-Barré syndrome (GBS); (3) empirical Bayesian data mining to assess for disproportionate reporting compared to AEs after other vaccines in the VAERS database; and (4) crude reporting rates for selected AESIs (i.e., GBS) using doses of PCV20 distributed in the USA during 2022 and 2023.

2.2 Automated Analysis

We searched the VAERS database for US reports following PCV20 for persons vaccinated from October 20, 2021, through December 31, 2023. We analyzed reports by age groups (19–64 years, ≥ 65 years), sex, seriousness, time from vaccination to onset of symptoms (onset interval), and the most commonly reported MedDRA PTs.

2.3 Clinical Review

The Centers for Disease Control and Prevention (CDC) physicians reviewed reports of PCV20 that were AESIs and/or were classified as serious. Based upon the primary diagnosis (i.e., the event that appeared to trigger the reporter to report to the VAERS), the reviewer categorized reports by main condition using system organ classes (SOCs) [8]. For death reports, the primary cause of death was obtained from reviewing the autopsy report, death certificate, and/or available medical records; in the absence of these documents, a preliminary impression of cause of death was made based on the initial report. We searched for and reviewed reports and any associated available medical records for the following AESIs: anaphylaxis, GBS, and seizures. We used the Brighton Collaboration case definitions for anaphylaxis, GBS, and seizures [10–12]. Reports of patients diagnosed with GBS by the attending physician but not meeting the Brighton criteria were also considered cases of GBS. We used MedDRA PTs to search and identify reports of AESIs as previously described [13].

2.4 Data Mining

We used empirical Bayesian (EB) data mining [14] to identify AEs reported more frequently after PCV20 than after other vaccines in the VAERS database during the period of this review. We used a threshold of $EB05 > 2.0$, where EB05 represents the lower bound of the 90% confidence interval (CI) surrounding the EB geometric mean [15]. An $EB05 > 2.0$ indicates that a particular vaccine-event pair occurs at least twice as often as expected than by chance alone. An elevated EB05 value does not imply a causal relationship but can be used as a threshold for further assessment of an event [15].

2.5 Crude Reporting Rates

Crude reporting rates for GBS were estimated by dividing the number of verified reports by the number of doses of PCV20 distributed by the manufacturer during 2022 and 2023. Crude reporting rates were not estimated if less than 3 AESI reports could be verified.

3 Results

3.1 Descriptive Analysis

During the study period, the VAERS received a total of 1976 PCV20 reports in adults aged ≥ 19 years (19–64 and ≥ 65 years). Of the total reports, 798 (40%) were in persons aged 19–64 years, of which 49 (6%) were serious, including two death reports; 1178 (60%) reports were in persons aged ≥ 65 years, which included 70 (6%) serious reports that included nine death reports. For both age groups, most reports occurred after PCV20 was administered alone: 438 (55%) for persons aged 19–64 years and 711 (60%) for those aged ≥ 65 years. The median age was 54 years (interquartile range [IQR] 45, 60) for the 19–64 age group and 69 years (IQR 66, 75) for ≥ 65 years. In most (1428 [72%]) of the reports, the patient was female (Table 1). The most commonly reported MedDRA PTs for non-serious reports in persons aged 19–64 years were injection-site reactions (227, 30%), pain (124, 17%), and erythema (117, 16%) (Table 2). The most common MedDRA PTs for serious reports in persons aged 19–64 years were fever (14, 29%), dyspnea (12, 25%), and condition aggravated (10, 20%) (Table 2). For persons aged ≥ 65 years, the most frequently reported MedDRA PTs for non-serious reports were injection-site reactions (412, 37%), pain (166, 15%), and erythema (157, 14%). The most common MedDRA PTs for serious reports in persons aged ≥ 65 years were pain (14, 20%), asthenia (13, 19%), gait disturbance (11, 16%), and GBS (11, 16%) (Table 3). The top 10 MedDRA PTs after PCV20 administered alone were similar to those after PCV20 given in combination with other vaccines during the same visit (data not shown).

3.2 Clinical Review

3.2.1 Non-Death Serious Reports—There were a total of 108 (5.5%) reports of serious non-death AEs: 47 (5.9%) in adults aged 19–64 years, and 61 (5.2%) in adults aged ≥ 65 years. Table S1 (Online Resource) shows data for non-death serious reports in adults aged ≥ 19 years.

In individuals aged 19–64 years, the most common AEs by SOC categories were nervous system disorders (11, 23%), general disorders and administration site conditions (10, 21%),

respiratory, thoracic, and mediastinal disorders (6, 13%), and vascular disorders (4, 9%). In adults aged ≥ 65 years, the most common diagnoses by SOC categories were nervous system disorders (20, 33%); followed by respiratory, thoracic, and mediastinal disorders; vascular disorders; and general disorders and administration site conditions (8, 13%) each (Table 4).

3.2.2 Reports of Death—We identified 11 death reports after PCV20 administration. Eight had a documented cause of death or medical condition information, two in persons aged 19–64 years and six in persons aged ≥ 65 years (Table 5). Three reports in adults aged ≥ 65 years did not specify age or circumstances of death.

3.2.3 Adverse Events of Special Interest

3.2.3.1 Anaphylaxis: We identified two reports of possible anaphylaxis, but there was insufficient information to determine if they met the Brighton Collaboration case definition [10] for anaphylaxis.

3.2.3.2 Guillain-Barré Syndrome: We identified 20 reports of GBS after PCV20, 11 of which met the Brighton Collaboration case definition [11]. Among the 11 verified reports, the median onset interval of symptoms was 14 days (range 0–23 days). Median age was 66 years (range 46–79); seven cases were in females, and four were in males. All 11 cases met the Brighton case definition [11] for GBS (two Level 1, six Level 2, and three Level 3). One patient had a norovirus infection 1–2 days before onset of neurological symptoms. Five of the 11 received other vaccines at the same visit: two individuals were vaccinated with recombinant zoster vaccine (GSK), one with adjuvanted quadrivalent influenza vaccine (Seqirus, Inc.), one with bivalent mRNA COVID-19 (Pfizer-BioNTech), Fluzone high dose quadrivalent influenza (Sanofi), and GSK RSV vaccines, and one with Tdap (GSK).

3.2.3.3 Seizures: Ten reports of seizure were reported to VAERS following PCV20: seven in males and three in females. Four were in adults aged 19–64 years and six in adults aged ≥ 65 years. Pneumococcal conjugate vaccine 20 was the only vaccine administered in four adults. One report met Brighton Level 3 criteria for seizures [12] in a male aged 42 years who experienced a seizure after an undefined period of time following PCV20 vaccination.

3.3 Data Mining

Data mining is used to identify AEs reported after PCV20 that were disproportionately reported (i.e., the AE is present in a higher proportion of the VAERS reports for PCV20 than other vaccines in the VAERS database) [14, 15]. Among VAERS reports, overall, data mining findings between the age groups of 19–64 years and ≥ 65 years were similar. Preferred terms disproportionately reported after PCV20 in both age categories involved injection-site reactions (e.g., bruising, erythema, induration, pain, pruritus, swelling, warmth at the injection site) as well as local and systemic events commonly observed after vaccination (e.g., erythema, induration, swelling). Cellulitis was disproportionately reported in both age categories. Three PTs (injection-site cellulitis, rash, and rash erythematous) were disproportionately reported for the ≥ 65 years age group that were not disproportionately reported for the 19–64 years group. More PTs were disproportionately reported for females ($n = 32$) compared to males ($n = 17$); PTs for both groups tended to reflect

injection/vaccination-site reactions and events observed after vaccination (e.g., erythema, induration, swelling). Some PTs were disproportionately reported for females that were not disproportionately reported for males; such PTs included allergy to vaccines, cellulitis, and hypersensitivity. Overall, data mining findings by age categories and sex did not reveal unexpected AEs.

Among serious reports, the MedDRA PT “Guillain-Barre syndrome” was disproportionately reported as it exceeded the EB05 threshold in reports made after PCV20 (EB05 = 3.812); characteristics of these reports have been described above. Other PTs in serious reports with disproportionate reporting included pain, gait disturbance, and gait inability. Gait disturbance and gait inability clinically overlap with GBS; along with GBS, pain and gait disturbance appear among the most commonly reported MedDRA PTs among serious reports in persons aged ≥ 65 years (Table 3).

3.4 Reporting Rates

During the period of this review, the VAERS received 11 verified reports of GBS. The number of PCV20 doses distributed in the USA during 2022 and 2023 was 20,579,720. Using this value, we calculated a reporting rate of 0.5 cases per 1 million doses of PCV20 distributed. This is equivalent to 0.9 cases per 100,000 person-years.

4 Discussion

This study is the first post-licensure safety review of the 20-valent pneumococcal conjugate vaccine (PCV20) in adults aged ≥ 19 years in the USA. During 2022 and 2023, which covers most of the period of this review, 20,579,720 doses of PCV20 were distributed in the USA. As of December 31, 2023, the VAERS has received 1976 reports after PCV20 in persons aged ≥ 19 years. Most reports (94%) were non-serious and comprised self-limiting local and systemic reactions such as injection-site pain, erythema, fever, and fatigue, consistent with findings from pre-licensure studies [2–5]. These safety findings are also similar to those in a review in the VAERS of the safety of 13-valent pneumococcal conjugate vaccine (PCV13) in adults aged ≥ 19 years [16].

As part of post-licensure safety monitoring of PCV20, we used four levels of analysis, which included automated analysis of reports, empirical Bayesian data mining, clinical review of reports, and reporting rate calculations for verified cases of GBS.

Through empirical Bayesian data mining, we found disproportional reporting for GBS when the analysis was limited to serious reports. The reporting rate for GBS was 0.5 cases per million doses distributed or 0.9 cases per 100,000 person-years, which is comparable to background rates for GBS in this age group [17]. However, this crude reporting rate should be interpreted with caution, as it is not known how many of the doses distributed were administered to the population at higher risk of GBS.

GBS is an acute, immune-mediated paralytic disorder of the peripheral nervous system [18]. The risk of GBS increases with age and is higher in males [19]. The background incidence

of GBS among males aged ≥ 65 years in the UK was approximately 4.6 cases per 100,000 inhabitants during a 42-day period [20].

Guillain-Barré syndrome cases after administration of pneumococcal vaccines have been described in the literature, but no causal association has been established between any pneumococcal vaccine and GBS [16, 21]. A review of the safety of PCV13 in adults aged ≥ 19 years in the VAERS found 11 reports of GBS out of 2976 total reports received, but no data mining signal for GBS or any other medical condition was observed [16]. A study of PCV13 safety in the Vaccine Safety Datalink (VSD) did not find an increased rate of GBS or several other outcomes following PCV13 administration in adults aged ≥ 65 years [22]. In the VSD, another study of the association of GBS with several vaccines, including the 23-valent pneumococcal polysaccharide vaccine, found no increased risk [23]. Our finding of disproportionate reporting of GBS after PCV20 is a preliminary finding that both CDC and the FDA are monitoring closely. Data mining values do not, by themselves, demonstrate causal associations; rather, they may serve as a signal for further investigation [14, 15]. Preliminary findings from the Centers for Medicare & Medicaid Services have not identified any safety signal or concern for GBS after PCV20 in the CMS population, but safety monitoring is ongoing [24]. No other unexpected safety concerns after PCV20 administration were found.

Important strengths of the VAERS include its broad national scope and timeliness [6]. It is useful for rapidly detecting rare AEs that, if new or unexpected, can be studied in other more robust and active vaccine safety surveillance systems (e.g., the CDC VSD) or special epidemiological studies [25]. Importantly, as a passive surveillance system, the VAERS has several inherent limitations that call for careful interpretation of the findings. Some of these limitations include biased reporting (over- or under-reporting) and inconsistency in the quality and completeness of reports [6]. In addition, the VAERS data generally cannot be used to assess whether a specific vaccine caused an AE.

5 Conclusion

Our assessment of the safety data of PCV20 found that the vast majority of AEs were self-limited, non-serious, and consistent with events observed during prelicensure clinical trials [2–5]. We observed disproportionate reporting for GBS, which we will continue to monitor in the VAERS. Otherwise, no new or unexpected safety issues were identified. The CDC and the FDA continue to monitor the safety of PCV20.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Availability of data and materials

Data from the VAERS system is available to everyone through the VAERS Wonder database available at: <https://wonder.cdc.gov/vaers.html>. Anyone with internet access may use this site and conduct basic analysis to confirm some of the findings described in the manuscript. However there are data in this manuscript which come from review of medical records of the patients who experienced an adverse event. The data cannot be shared openly to protect patient privacy.

References

1. Food and Drug Administration. Prevnar 20. <https://www.fda.gov/vaccines-blood-biologics/vaccines/prevnar-20>
2. Kobayashi M, Farrar JL, Gierke R, et al. Use of 15-valent pneumococcal conjugate vaccine and 20-valent pneumococcal conjugate vaccine among U.S. adults: updated recommendations of the Advisory Committee on Immunization Practices—United States, 2022. *MMWR Morb Mortal Wkly Rep* 2022;71:109–17. 10.15585/mmwr.mm7104a1. [PubMed: 35085226]
3. Essink B, Sabharwal C, Cannon K, Frenck R, Lal H, Xu X, Sundaraiyer V, Peng Y, Moyer L, Pride MW, Scully IL, Jansen KU, Gruber WC, Scott DA, Watson W. Pivotal phase 3 randomized clinical trial of the safety, tolerability, and immunogenicity of 20-valent pneumococcal conjugate vaccine in adults aged ≥18 years. *Clin Infect Dis* 2022;75(3):390–8. 10.1093/cid/ciab990. [PubMed: 34940806]
4. Hurley D, Griffin C, Young M, Scott DA, Pride MW, Scully IL, Ginis J, Severs J, Jansen KU, Gruber WC, Watson W. Safety, tolerability, and immunogenicity of a 20-valent pneumococcal conjugate vaccine (PCV20) in adults 60 to 64 years of age. *Clin Infect Dis* 2021;73(7):e1489–97. 10.1093/cid/ciaa1045. [PubMed: 32716500]
5. Klein NP, Peyrani P, Yacisin K, Caldwell N, Xu X, Scully IL, Scott DA, Jansen KU, Gruber WC, Watson W. A phase 3, randomized, double-blind study to evaluate the immunogenicity and safety of 3 lots of 20-valent pneumococcal conjugate vaccine in pneumococcal vaccine-naïve adults 18 through 49 years of age. *Vaccine*. 2021;39(38):5428–35. 10.1016/j.vaccine.2021.07.004. (Epub 2021 Jul 24). [PubMed: 34315611]
6. Shimabukuro TT, Nguyen M, Martin D, DeStefano F. Safety monitoring in the vaccine adverse event reporting system (VAERS). *Vaccine*. 2015;33(36):4398–405. 10.1016/j.vaccine.2015.07.035. [PubMed: 26209838]
7. Medical dictionary for regulatory activities. <https://www.meddra.org/>
8. International conference on harmonization of technical requirements for registration of pharmaceuticals. <http://www.ich.org/products/meddra.html>
9. Code of Federal Regulations. 21 CFR §600.80. <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=600.80>
10. Gold MS, Amarasinghe A, Greenhawt M, Kelso JM, Kochhar S, Yu-Hor Thong B, Top KA, Turner PJ, Worm M, Law B. Anaphylaxis: revision of the Brighton collaboration case definition. *Vaccine*. 2023;41(15):2605–14. 10.1016/j.vaccine.2022.11.027. (Epub 2022 Nov 24). [PubMed: 36435707]
11. Sejvar JJ, Kohl KS, Gidudu J, et al. Brighton Collaboration GBS Working Group. Guillain-Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. *Vaccine*. 2011;29(3):599–612. 10.1016/j.vaccine.2010.06.003. [PubMed: 20600491]
12. Bonhoeffer J, Menkes J, Gold MS, de Souza-Brito G, Fisher MC, Halsey N, Vermeer P, Brighton Collaboration Seizure Working Group. Generalized convulsive seizure as an adverse event following immunization: case definition and guidelines for data collection, analysis,

- and presentation. *Vaccine*. 2004;22(5–6):557–62. 10.1016/j.vaccine.2003.09.008. [PubMed: 14741144]
13. Moro PL, Leung J, Marquez P, Kim Y, Wei S, Su JR, Marin M. Safety surveillance of varicella vaccines in the vaccine adverse event reporting system, United States, 2006–2020. *J Infect Dis* 2022;226(Suppl 4):S431–40. 10.1093/infdis/jiac306. [PubMed: 36265846]
 14. DuMouchel W Bayesian data mining in large frequency tables, with an application to the FDA spontaneous reporting system. *Am Stat* 1999;53:177–90.
 15. Szarfman A, Machado SG, O'Neill RT. Use of screening algorithms and computer systems to efficiently signal higher-than-expected combinations of drugs and events in the US FDA's spontaneous reports database. *Drug Saf* 2002;25:381–92. [PubMed: 12071774]
 16. Haber P, Arana J, Pilishvili T, Lewis P, Moro PL, Cano M. Post-licensure surveillance of 13-valent pneumococcal conjugate vaccine (PCV13) in adults aged ≥ 19 years old in the United States, vaccine adverse event reporting system (VAERS), June 1, 2012–December 31, 2015. *Vaccine*. 2016;34(50):6330–4. 10.1016/j.vaccine.2016.10.052. (Epub 2016 Nov 9). [PubMed: 27836437]
 17. Gubernot D, Jazwa A, Niu M, Baumblatt J, Gee J, Moro P, Duffy J, Harrington T, McNeil MM, Broder K, Su J, Kamidani S, Olson CK, Panagiotakopoulos L, Shimabukuro T, Forshee R, Anderson S, Bennett S. U.S. population-based background incidence rates of medical conditions for use in safety assessment of COVID-19 vaccines. *Vaccine*. 2021;39(28):3666–77. 10.1016/j.vaccine.2021.05.016. (Epub 2021 May 14). [PubMed: 34088506]
 18. Hauser SL, Amato AA. Guillain-Barré syndrome and other immune-mediated neuropathies. Chronic inflammatory demyelinating polyneuropathy. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Larry Jameson J, Loscalzo J, editors. *Harrison's principles of internal medicine*. New York: The McGraw-Hill Companies, Inc.; 2012. p. 3473–9.
 19. Sejvar JJ, et al. Population incidence of Guillain-Barré syndrome: a systematic review and meta-analysis. *Neuroepidemiology*. 2011;36(2):123–33. [PubMed: 21422765]
 20. Black S, Eskola J, Siegrist CA, Halsey N, MacDonald N, Law B, Miller E, Andrews N, Stowe J, Salmon D, Vannice K, Izurieta HS, Akhtar A, Gold M, Oselka G, Zuber P, Pfeifer D, Vellozzi C. Importance of background rates of disease in assessment of vaccine safety during mass immunisation with pandemic H1N1 influenza vaccines. *Lancet*. 2009;374(9707):2115–22. 10.1016/S0140-6736(09)61877-8. (Epub 2009 Oct 31. Erratum in: *Lancet*. 2010 Jan 30;375(9712):376). [PubMed: 19880172]
 21. Shimabukuro T Safety of 13-valent pneumococcal conjugate vaccine (PCV13) in adults aged ≥ 65 years old. In: Advisory Committee on immunization practices (ACIP) meeting. June 21, 2018. <https://stacks.cdc.gov/view/cdc/60494>.
 22. Tartof SY, Nelson J, Jackson LA, Daley MF, Weintraub E, Klein NP, Belongia E, Liles EG, Jacobsen SJ. Pneumococcal conjugate vaccine safety in elderly adults. *Open Forum Infect Dis* 2018;5(6):ofy100. 10.1093/ofid/ofy100. [PubMed: 29977960]
 23. Baxter R, Bakshi N, Fireman B, Lewis E, Ray P, Vellozzi C, Klein NP. Lack of association of Guillain-Barré syndrome with vaccinations. *Clin Infect Dis* 2013;57(2):197–204. 10.1093/cid/cit222. (Epub 2013 Apr 11). [PubMed: 23580737]
 24. FDA CBER: Safety assessment of 20-valent pneumococcal conjugate vaccine (PCV20). ACIP February 2024. www.cdc.gov/vaccines/acip/meetings/downloads/slides-2024-02-28-29/05-Pneumococcal-Forshee-508.pdf.
 25. McNeil MM, Gee J, Weintraub ES, Belongia EA, Lee GM, Glanz JM, Nordin JD, Klein NP, Baxter R, Naleway AL, Jackson LA, Omer SB, Jacobsen SJ, DeStefano F. The vaccine safety datalink: successes and challenges monitoring vaccine safety. *Vaccine*. 2014;32(42):5390–8. 10.1016/j.vaccine.2014.07.073. [PubMed: 25108215]

Key Points

VAERS received 1,976 reports after PCV20 in adults during October 2021-December 2023. Most common adverse events were injection site (e.g. injection site erythema) and systemic reactions (e.g. fever)

Disproportionate reporting for Guillain-Barré Syndrome (GBS) identified in VAERS after PCV20 vaccine (11 verified GBS cases in adults)

Potential safety signals detected in VAERS need to be evaluated in more robust population-based active systems such as the Vaccine Safety Datalink (VSD) or Center for Medicaid Services (CMS)

Separate studies currently in progress in the VSD (CDC) and CMS (FDA) to assess PCV20 vaccine safety; CDC and FDA will continue to closely monitor the safety of PCV20

Characteristics of reports after 20-valent pneumococcal conjugate vaccine in the Vaccine Adverse Event Reporting System, October 2021–December 2023

Table 1

Characteristics	19–64 years N (%)	≥ 65 years N (%)	All N (%)
Total reports	798	1178	1976
Female	582 (72.9)	846 (71.8)	1428 (72.3)
Male	212 (26.6)	330 (28.0)	542 (27.4)
Unknown sex	4 (0.5)	2 (0.2)	6 (0.3)
Serious reports ^a	49 (6.1)	70 (5.9)	119 (6)
Deaths ^a	2 (0.3)	9 (0.8)	11 (0.6)
Median age [IQR] in years	54 [45, 60]	69 [66, 75]	65 [56, 70]
Median onset interval [IQR], in days	1 [0, 2]	1 [0, 2]	1 [0, 1]
Received PCV20 alone	438 (54.9)	711 (60.4)	1149 (58.1)
Race/ethnicity			
Non-Hispanic White	280 (35.1)	487 (41.3)	767 (38.8)
Hispanic Latino ^b	89 (11.5)	89 (7.6)	178 (9.0)
Non-Hispanic Black	49 (6.1)	37 (3.1)	86 (4.4)
Non-Hispanic Asian	26 (3.3)	41 (3.5)	67 (3.4)
Non-Hispanic multiple	9 (1.1)	5 (0.4)	14 (0.7)
Non-Hispanic AI/AN	3 (0.4)	4 (0.3)	7 (0.4)
Non-Hispanic other	12 (1.5)	6 (0.5)	18 (0.9)
Race not reported	330 (41.4)	507 (43.0)	837 (42.4)

^a A report is considered serious based on the Code of Federal Regulations (21 CFR) definition if one or more of the following are reported: death, life-threatening illness, hospitalization or prolongation of existing hospitalization, congenital anomaly, permanent disability, or medical intervention to prevent the afore-mentioned outcomes

^b Hispanic includes people of known Hispanic ethnicity and unreported race

AI/AN American Indian/Alaska Native, NHOP/Native Hawaiian/Other Pacific Islander

Table 2

Most commonly reported MedDRA Preferred Terms (PTs) among non-serious ($n = 749$), serious ($n = 49$), and all ($n = 798$) reports of 20-valent pneumococcal conjugate vaccine in adults aged 19–64 years in the Vaccine Adverse Event Reporting System, October 2021–December 2023

MedDRA PT ^a	Non-serious, <i>n</i> (%)	MedDRA PT	Serious, <i>n</i> (%)	MedDRA PT	All reports, <i>n</i> (%)
Injection-site reaction group ^b	227 (30)	Fever	14 (29)	Injection-site reaction group ^b	231 (29)
Pain	124 (17)	Dyspnea	12 (25)	Pain	134 (17)
Erythema	117 (16)	Condition aggravated	10 (20)	Erythema	118 (15)
Fever	103 (14)	Cough	10 (20)	Fever	117 (15)
Pain in extremity	90 (12)	Pain	10 (20)	Pain in extremity	98 (12)
Peripheral swelling	77 (10)	Nausea	9 (18)	Peripheral swelling	79 (10)
Headache	59 (8)	Pain in extremity	8 (16)	Headache	66 (8)
Skin warm	59 (8)	Dizziness	7 (14)	Fatigue	63 (8)
Fatigue	56 (7)	Fatigue	7 (14)	Nausea	61 (8)
Arthralgia	52 (7)	Headache	7 (14)	Skin warm	59 (7)

^aMedDRA Preferred terms (PTs) are not medically confirmed diagnoses. More than one PT may be assigned to a single report (i.e., not mutually exclusive)

^bGroup of injection-site PTs, which may include any of the following: injection-site erythema, injection-site swelling, injection-site warmth, injection-site pain, injection-site induration, injection-site pruritus, injection-site rash, injection-site reaction, local reaction, injection-site urticaria, injection-site vesicles, injection-site cellulitis, injection-site oedema, injection-site mass, erythema, rash, rash erythematous, rash generalized, blister, rash vesicular, rash papular, rash macular, rash maculo-papular, rash pruritic

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Table 3

Most commonly reported MedDRA Preferred Terms (PTs) among non-serious ($n = 1108$), serious ($n = 70$), and all ($n = 1178$) reports of 20-valent pneumococcal conjugate vaccine in adults aged ≥ 65 years in the Vaccine Adverse Event Reporting System, October 2021–December 2023

MedDRA PT ^a	Non-serious, n (%)	MedDRA PT	Serious, n (%)	MedDRA PT	All reports, n (%)
Injection-site reaction group ^b	412 (37)	Pain	14 (20)	Injection-site reaction group ^b	417 (35)
Pain	166 (15)	Asthenia	13 (19)	Pain	180 (15)
Erythema	157 (14)	Gait disturbance	11 (16)	Pain in extremity	162 (14)
Pain in extremity	156 (14)	Guillain Barré Syndrome	11 (16)	Erythema	158 (13)
Fever	127 (12)	Dyspnea	8 (11)	Fever	135 (12)
Peripheral swelling	101 (9)	Fatigue	8 (11)	Peripheral swelling	103 (9)
Rash	98 (9)	Fever	8 (11)	Rash	99 (8)
Fatigue	88 (8)	Chest pain	7 (10)	Fatigue	96 (8)
Headache	84 (8)	Death	7 (10)	Headache	88 (7)
Pruritus	78 (7)	Dysphagia	7 (10)	Pruritus	78 (7)

^aMore than one MedDRA Preferred Term (PT) may be assigned to a single report (i.e., not mutually exclusive), PTs are not medically confirmed diagnoses

^bGroup of injection-site PTs, which may include any of the following: injection-site erythema, injection-site swelling, injection-site warmth, injection-site pain, injection-site induration, injection-site pruritus, injection-site rash, injection-site reaction, local reaction, injection-site urticaria, injection-site vesicles, injection-site cellulitis, injection-site oedema, injection-site mass, erythema, rash, rash erythematous, rash generalized, blister, rash vesicular, rash papular, rash macular, rash maculo-papular, rash pruritic

Table 4

Main conditions (System Organ Class) for non-fatal serious reports after administration of 20-valent pneumococcal conjugate vaccine among persons aged 19–64 years and ≥ 65 years in the Vaccine Adverse Event Reporting System, October 2021–December 2023

Diagnostic category	Aged 19–64 years (n = 47) (%)	Aged ≥ 65 years (n = 61) (%)
Nervous system disorders	11 (23)	20 (33)
General disorders and administration site conditions	10 (21)	8 (13)
Respiratory, thoracic and mediastinal disorders	6 (13)	8 (13)
Vascular disorders	4 (9)	8 (13)
Immune system disorders	3 (6)	0
Infections and infestations	3 (6)	5 (8)
Musculoskeletal and connective tissue disorders	2 (4)	4 (7)
Cardiac disorders	2 (4)	5 (8)
Other	6 ^a (13)	3 ^b (5)

^aIncludes one report each of eye disorders, skin and subcutaneous tissue disorders, hepatobiliary disorders, gastrointestinal disorders, renal and urinary disorders, psychiatric disorders

^bIncludes one report of each: a fractured wrist, cystitis, and diarrhea

Table 5

Documented cause of death or medical condition (*n* = 11) after administration of 20-valent pneumococcal conjugate vaccine in the Vaccine Adverse Event Reporting System, October 2021–December 2023

Age group	<i>N</i>
Age group 19–64 years	
Acute brain herniation and edema secondary to acute left temporal hemorrhage	1
Hepatic encephalopathy secondary to liver cirrhosis	1
Age group ≥ 65 years	
Cardiac arrest due to hypertension	1
Malignant neoplasm and acute gastric ulcer	1
Intracranial hemorrhage	1
Cardiovascular disease	1
Cause unknown but suffered ischemic stroke around time of death	1
Cause of death unknown but experienced gastrointestinal hemorrhage, decreased appetite, diarrhea around time of death	1
Reports in adults, no diagnosis listed in report	3
Total	11

By autopsy report, death certificate, and/or other medical records