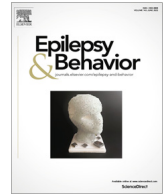




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Epilepsy By the Numbers

COVID-19 vaccination status and related process of care outcomes among U.S. adults with active epilepsy—National Health Interview Survey, United States, 2021

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ARTICLE INFO

Article history:

Received 24 March 2023

Revised 6 April 2023

Accepted 7 April 2023

Available online 14 April 2023

Keywords:

Epilepsy

COVID-19

Vaccination

Population survey

ABSTRACT

Growing research has examined the effects of the COVID-19 pandemic on people with epilepsy. There are no published national estimates of COVID-19 vaccination status among U.S. adults with active epilepsy. The purpose of this study is to use 2021 National Health Interview Survey (NHIS) data to examine select COVID-19-related outcomes by epilepsy status in a nationally representative sample of US adults. The study sample met the criteria for operationalization of epilepsy status (i.e., active epilepsy vs. no epilepsy history) and select questions related to COVID-19 testing, vaccination, delays in care, or experience with virtual care during the COVID-19 pandemic. All analyses accounted for the NHIS complex sample design and response sampling weights. Our study found that in 2021 receipt of one COVID-19 vaccination among U.S. adults with active epilepsy was generally similar to that among adults without a history of epilepsy. By age, adults aged 18–44 years with active epilepsy (27.0%) were significantly less likely to have reported receiving two COVID-19 vaccinations compared with their peers with no epilepsy history (39.1%). Compared to adults with no epilepsy history, adults with active epilepsy reported similar experiences and outcomes regarding COVID-19 testing and obtaining health care during the COVID-19 pandemic. This study provides baseline estimates of select COVID-19 outcomes among US adults with active epilepsy to guide interventions and additional studies.

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1. Introduction

Although active epilepsy itself has not been associated with worse COVID-19 outcomes to date, several studies have suggested those with various neurologic conditions, disabilities, and mental health conditions in which epilepsy may co-occur (e.g., cerebral palsy, dementia, Down Syndrome) may be at higher risk for such outcomes [1–4]. Growing research has examined the effects of COVID-19 infection among people with epilepsy, the safety and tolerability of the COVID-19 vaccines, and the COVID-19 vaccination status among people with epilepsy [5–10]. A review

examining COVID-19 vaccination coverage and willingness to be vaccinated against COVID-19 based on international samples of patients with epilepsy (up to April 30, 2022) reported suboptimal levels of COVID-19 vaccination coverage and intent to vaccinate [11]. There are no published national estimates of COVID-19 vaccination status among U.S. adults with active epilepsy. We examined the following COVID-19-related outcomes by active epilepsy status in a nationally representative sample of US adults who participated in the 2021 National Health Interview Survey who answered questions regarding whether they: (1) ever received a COVID-19 vaccination; (2) received one, two, and more than two COVID-19 vaccinations (overall and by age group); (3) ever tested positive for COVID-19; (4) experienced delays or a barrier to care due to COVID-19; and (5) participated in at least one virtual medical appointment during the pandemic.

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2. Methods

The National Health Interview Survey (NHIS) is a cross-sectional annual survey of the civilian, non-institutionalized U.S. population [12]. Interviews are typically conducted in the household of the participant, and any additional information may be obtained via telephone. In 2021, due to the COVID-19 pandemic, the normal interviewing process was disrupted, resulting in 62.8% of the interviews being conducted at least partially by telephone [12]. We used data from the NHIS interview module. A sample adult, aged ≥ 18 years, is randomly selected from a selected household within a geographic cluster to respond to survey questions. The sample adult responds to survey questions for themselves; if they are unable to respond, a knowledgeable proxy may answer. In 2021, 29,482 sample adults were interviewed, including 582 proxy respondents, with a final response rate of 50.9% [12]. To allow for nonresponse and account for post-stratification, a weighting factor was applied to each participant [12]. Our study sample included adult participants who met the criteria for operationalization of epilepsy status (i.e., active epilepsy vs. no epilepsy history) and select questions related to COVID-19 testing, vaccination, and any delays in care or experience with virtual care during the COVID-19 pandemic [12,13].

Adults were classified as having “active epilepsy” if they reported a history of doctor-diagnosed epilepsy and were taking medication to control it, had had one or more seizures in the past year, or both [13]. Adults classified with inactive epilepsy (i.e., self-reported epilepsy history but not reporting taking anti-seizure medications or any seizures in the past 12 months) were excluded from the study because our focus was on respondents with treated epilepsy or active symptomatology.

Of the multiple COVID-19-related survey questions available on the 2021 NHIS, we chose seven for our analysis. Three questions followed a skip pattern, two of which were included in latter quarters of fielding the survey, as indicated [12]:

- (1) “Have you ever been tested for coronavirus or COVID-19?” (Yes/No/Refused/Don’t know/Not Ascertained)
- (2) (If yes to number 1) “Did the test find that you had coronavirus or COVID-19?” (Yes/No/Did not receive results/Refused/Don’t know/Not Ascertained)
- (3) “Was there any time when you delayed getting medical care because of the coronavirus pandemic?” (Yes/No/Refused/Don’t know/Not Ascertained)
- (4) Was there any time when you needed medical care for something other than coronavirus, but did not get it because of the coronavirus pandemic? (Yes/No/Refused/Don’t know/Not Ascertained)
- (5) (If yes to a survey question asking about any virtual medical appointment in the past 12 months with respect to access to care, in general), Were any of your appointments done by video or phone because of reasons related to the coronavirus pandemic? (Yes/No/Refused/Don’t know/Not Ascertained)
- (6) Have you had a COVID-19 vaccination? (Yes/No/Refused/Don’t know/Not Ascertained/)
- (7) (If yes to number 6) How many COVID-19 vaccinations have you received? (one; two; more than two; Refused/Don’t know/Not Ascertained)

Questions 1–5 were included in the full year of the NHIS. Questions 6 and 7 (i.e., COVID-19 vaccination questions) were fielded only in quarters 2, 3, and 4 of the survey. We followed NCHS guidance regarding the use of appropriate full-year and quarter-specific weights for each question relative to its inclusion on the survey (e.g., use of quarter-specific weights for questions 6 and 7) [12]. All responses that included “refused,” “don’t know,” or “not ascer-

tained” were listed as missing data. About 2% of respondents ($n = 426$) in Quarters 2, 3, and 4 were classified as missing a response to the question of having had a COVID-19 vaccination [12].

Only 9.7% ($n = 1,560$) of the survey sample in quarters 2, 3, and 4 of the survey who answered the question on “having had a COVID-19 vaccination” reported >2 vaccinations by the 4th quarter of the 2021 survey; this includes 8.5% ($n = 1,546$) of those without epilepsy and 8.3% ($n = 14$) of adults classified with active epilepsy (Supplemental file). The latter estimate did not meet reliability standards [15]. Moreover, combining respondents with only two COVID-19 vaccinations with the small number of respondents who reported >2 COVID-19 vaccinations (i.e., “ ≥ 2 vaccinations”) could inadvertently conflate estimates for booster uptake relative to first booster authorization for all individuals ≥ 18 years of age issued on November 19, 2021 [14].

All analyses were performed using SAS-callable SUDAAN, version 11.0.3 (Research Triangle Institute, Research Triangle Park, NC) to account for the NHIS complex sample design and response sampling weights.

We calculated unadjusted prevalence estimates for adults with active epilepsy vs. no epilepsy history overall for each of the dependent variables. Additionally, to examine whether vaccination status (including having received one or two COVID-19 vaccinations) differed by age group, we stratified this analysis by three age groups: 18–44; 45–64, and ≥ 65 years. Non-overlapping 95% confidence intervals of means and univariate Satterthwaite-adjusted chi-square tests of independence were used to compare the differences in weighted percentages within subgroups by epilepsy status. We defined significance for chi-square tests as a P -value of less than 0.05. Estimates met previous NHIS standards of reliability (i.e., relative standard error $<30.0\%$; denominator sample size ≥ 50 persons) unless otherwise noted [15].

3. Results

The final overall analytical sample included 307 adults with active epilepsy and 28,507 with no history of epilepsy. Questions fielded on the survey resulted in different sample sizes by study outcome and epilepsy status as follows. Regarding outcomes for COVID-19 vaccination status (derived from questions fielded in quarters 2, 3, and 4 of the survey) by epilepsy status, the final sample included 241 (population estimate $\sim 2,870,000$) adults with active epilepsy vs. 21,138 (population estimate $\sim 243,926,000$) adults with no history of epilepsy.

In 2021, 67.3% (population estimate $\sim 1,930,000$) of adults with active epilepsy reported ever having had a COVID-19 vaccination, similar to the 71.7 % of the population with no epilepsy history (Table 1). By age group, there were no differences between adults with active epilepsy and those with no history of epilepsy in the percentages who reported having had a COVID-19 vaccination (Fig. 1). Overall, the percentages of adults who received one or two COVID-19 vaccinations did not vary by epilepsy status. However, adults 18–44 years of age with active epilepsy (27.0%) were significantly less likely to have reported receiving two COVID-19 vaccinations compared to their peers with no epilepsy history (39.1%) (Fig. 2).

Regarding outcomes related to experiences with COVID-19 testing and access to medical care or delays in getting medical care due to COVID-19 (derived from questions fielded over the entire year of the survey) similar percentages of adults with active epilepsy (63.0%) vs. no epilepsy history (61.1%) reported ever being tested for COVID-19 (Table 2). There were no significant differences in the percentage testing positive for COVID-19 for those with active epilepsy (20.6%) vs. no epilepsy history (23%). Additionally, there

Table 1

Number and percentage of adults with active epilepsy* and no epilepsy history who reported having a COVID-19 vaccine - National Health Interview Survey, United States, 2021.

Epilepsy Status							
Active				No history			
Characteristic	Sample No. [†]	Population estimate [‡]	% (95% CI)	Sample No. [†]	Population estimate [‡]	% (95% CI)	P-value **
Overall Total	241	2,870,000	-	21,138	243,926,000	-	
COVID-19 vaccination[§]							
Yes	169	1,930,000	67.3 (59.9–73.9)	15,907	174,955,000	71.7 (70.7–72.7)	0.2176
No	72	940,000	32.7 (26.1–40.1)	5,231	68,971,000	28.3 (27.3–29.3)	
Number of COVID-19 vaccinations[¶]							
1 Vaccination	22	270,000	14.0 (8.8–21.7)	1,839	21,733,000	12.4 (11.8–13.2)	0.8900
2 Vaccination	133	1,499,000	77.7 (69.2–84.4)	12,510	138,159,000	79.0 (78.3–79.8)	
>2 Vaccination	14	- [¶]	-	1,546	14,906,000	8.5 (8.0–9.1)	
≥2 Vaccination	147	1,660,000	86.0 (78.3–91.2)	14,056	153,065,000	87.6 (86.9–88.2)	

Abbreviations: CI = confidence interval.

*Doctor-diagnosed active epilepsy was defined as having a diagnosis of epilepsy and either taking medication or have had one or more seizures in the past year, or both.

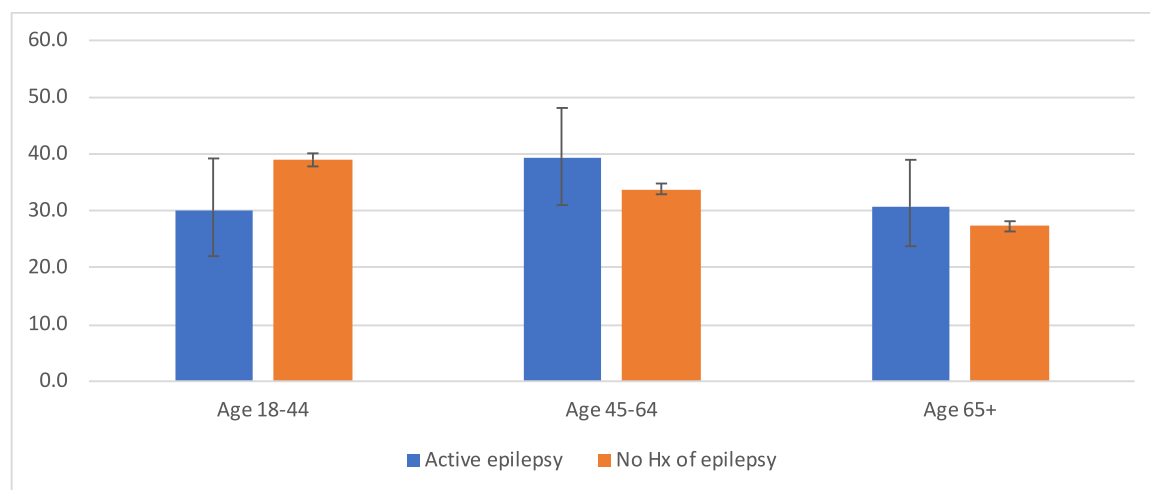
[†]Due to exclusion of vaccination questions in the first quarter of 2021, Table 1 sample size are smaller than the overall analytical sample (i.e., Table 2). Number of respondents is unweighted; population estimate (rounded to 1,000s) and percentage estimates are weighted.[§]COVID-19 vaccination was assessed with the question, "Have you had a COVID-19 vaccination?" Responses included yes; no; refused; don't know; not ascertained. All survey adults were asked this question during quarters 2 through 4 of 2021.[¶]Number of COVID-19 vaccinations was assessed with the question, "How many COVID-19 vaccinations have you received?" Responses included "1 vaccination; 2 vaccinations; More than 2 vaccinations; refused; don't know; not ascertained." All survey adults who responded "yes" to having received a COVID-19 vaccination were asked this follow-up question during quarters 2 through 4 of 2021.[¶]Small sample sizes or estimates with a relative standard error ≥30% are not presented.** P < 0.05, Univariate Satterthwaite-adjusted χ^2 test for comparison of distribution between epilepsy categories.

Fig. 1. Percentage of adults with active epilepsy* or no history of epilepsy who reported having a COVID-19 vaccine[§] by age group—National Health Interview Survey, United States, 2021*. Notes: *Active epilepsy was defined as self-reported doctor-diagnosed epilepsy and either taking medication or have had one or more seizures in the past year, or both. No Hx of epilepsy = No history of self-reported doctor-diagnosis of epilepsy or seizure disorder. [§] COVID-19 vaccination was assessed with the question, "Have you had a COVID-19 vaccination?" Responses included, "yes; no; refused; don't know; not ascertained." Question was available in quarters 2 through 4 of 2021. [†] Error bars represent 95% Confidence Intervals.

were no significant differences by epilepsy status in the percentages who delayed medical care or did not get medical care because of the coronavirus pandemic or had a virtual medical appointment because of reasons related to the coronavirus pandemic (Table 2).

4. Discussion

CDC recommends all people aged ≥6 months of age stay up to date with COVID-19 vaccines [16]. Our study found that in 2021, COVID-19 vaccination uptake for receiving one or two COVID-19 vaccinations among U.S. adults with active epilepsy was generally similar to that among U.S. adults without a history of epilepsy. Findings from the U.S. arm of the COVID-19 and Epilepsy (COVE) global study, an online survey of people with epilepsy and their caregivers regarding their experience with health outcomes, access to care, and uptake with COVID-19 mitigation measures during the

pandemic, indicated that among respondents who completed the survey from March to July 2021, 17.4% reported having received one dose of COVID-19 vaccine and 46.3% had received two doses (i.e., 64% of people with epilepsy received at least 1 dose of COVID-19 vaccine) [17]. Additionally, there is much room to improve vaccination rates of people with epilepsy of all ages (<40% of people with epilepsy were vaccinated at least once against covid in every age stratum in this study). Consistent with findings indicating that COVID-19 vaccination coverage and intent to vaccinate are typically lowest among young adults (e.g., 18–39 years) and our study findings indicating that a significantly smaller percentage of adults 18–44 years of age with epilepsy than those without epilepsy received 2 COVID-19 vaccines, this study suggests that targeted communications for that age stratum may be needed [18]. Common factors associated with an unwillingness to obtain COVID-19 vaccination among people with epilepsy include concerns about aggravating epilepsy outcomes, fear of

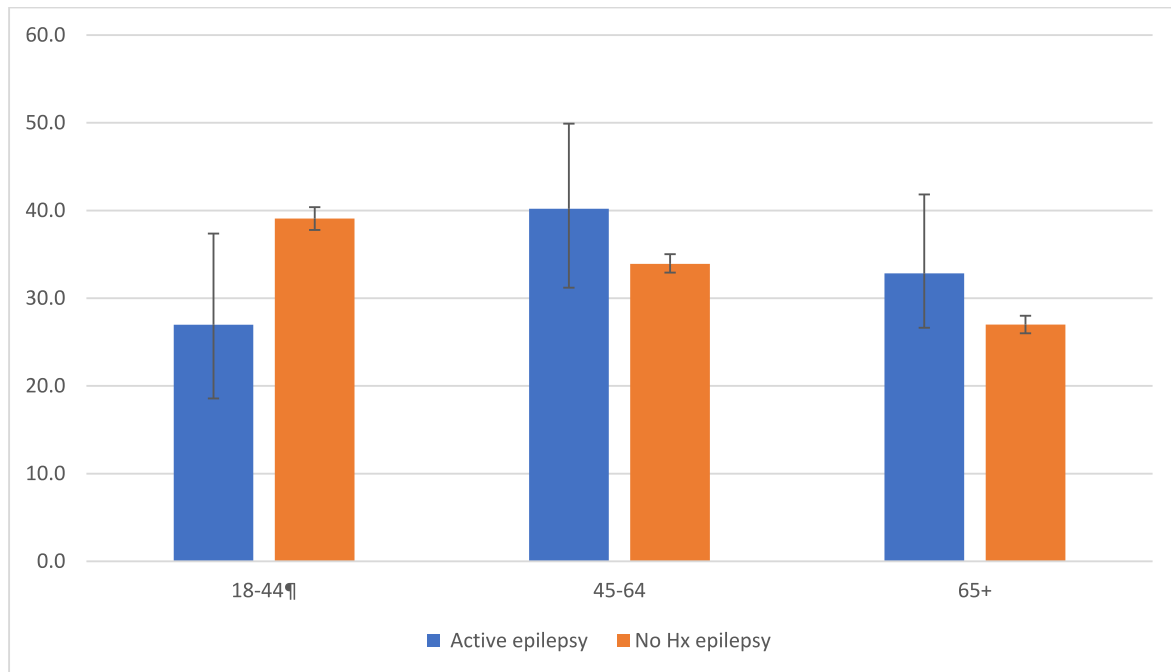


Fig. 2. Percentage of vaccinated adults with active epilepsy* or no history of epilepsy who reported having only two COVID-19 vaccines† by age group—National Health Interview Survey, United States 2021§. Notes: *Active epilepsy was defined as self-reported doctor-diagnosed epilepsy and either taking medication or have had one or more seizures in the past year, or both. No Hx of epilepsy = No history of self-reported doctor-diagnosis of epilepsy or seizure disorder. † All survey adults who responded “yes” to having received a COVID-19 vaccination were asked, “How many COVID-19 vaccinations have you received?” Responses included “1 vaccination; 2 vaccinations; More than 2 vaccinations: refused, don’t know, not ascertained.” Available in quarters 2 through 4 of 2021. § Error bars represent 95% Confidence Intervals. ¶ P < 0.05, Univariate Satterthwaite-adjusted χ^2 test for comparison of distribution between epilepsy categories.

Table 2

COVID-19 testing and experiences with medical care due to COVID-19 among adults with active epilepsy* or no history of epilepsy —National Health Interview Survey, United States 2021.

Epilepsy Status							
Active				No history			
Characteristic [§]	Sample No. [†]	Population estimate [‡]	% (95% CI)	Sample No. [†]	Population estimate [‡]	% (95% CI)	P-value **
Overall Total	307	2,780,000	-	28,507	244,385,000	-	-
Ever been tested for COVID-19							
Yes	191	1,751,000	63.0 (56.5–69.1)	16,969	149,368,000	61.1 (60.3–62.0)	0.5658
No	116	1,029,000	37.0 (30.9–43.6)	11,538	95,017,000	38.8 (38.1–39.7)	
Tested positive for COVID-19							
Yes	35	402,000	23.0 (16.4–31.2)	3,117	30,754,000	20.6 (19.7–21.5)	0.5226
No	154	1,335,000	76.2 (68.0–82.8)	13,762	117,892,000	78.9 (78.0–79.8)	
Missing	2	-¶	-	90	-	-	
Delayed medical care due to COVID-19							
Yes	55	482,000	17.4 (12.8–23.0)	5,689	46,071,000	18.9 (18.2–19.5)	0.5612
No	252	2,298,000	82.7 (77.0–87.2)	22,818	198,314,000	81.2 (80.5–81.8)	
Did not get medical care due to COVID-19							
Yes	47	380,000	13.7 (10.1–18.2)	3,557	28,985,000	11.9 (11.4–12.3)	0.3757
No	260	2,400,000	86.3 (81.8–89.9)	24,950	21,540,000	88.1 (87.7–88.6)	
Virtual medical appointment due to COVID-19							
Yes	153	1,350,000	86.4 (79.1–91.5)	8,895	72,164,000	80.4 (79.3–81.4)	0.0680
No	25	212,000	13.6 (8.6–20.9)	2,105	17,340,000	19.3 (18.3–20.4)	
Missing	-	-	-	37	-	-	

Abbreviations: No Hx. of epilepsy = No history of a doctor-diagnosed seizure disorder or epilepsy; CI = confidence interval.

*Active epilepsy was defined as self-reported doctor-diagnosed epilepsy and either taking medication or have had one or more seizures in the past year, or both.

†Number of respondents are unweighted; population estimate (rounded to 1,000s) and percentage estimates are weighted.

§Survey questions included:

Have you ever been tested for coronavirus or COVID-19?

Did the test find that you had coronavirus or COVID-19? Asked of those who responded yes to being tested.

Was there any time when you DELAYED getting medical care because of the coronavirus pandemic? Asked all adults.

Was there any time when you needed medical care for something other than coronavirus, but DID NOT GET IT because of the coronavirus pandemic? Asked of all adults.

Were any of your appointments done by video or phone because of reasons related to the coronavirus pandemic? Asked of all adults.

¶ Participants missing data; small sample sizes or estimates with a relative standard error $\geq 30\%$ are not presented.

** P < 0.05, Univariate Satterthwaite-adjusted χ^2 test for comparison of distribution between epilepsy categories.

other unknown side effects, and interactions between epilepsy medications and vaccines [11]. Epilepsy health and social service providers can increase awareness of the safety, tolerability, and effectiveness of COVID-19 vaccination among people with epilepsy to improve intent to vaccinate.

Our study provides important baseline data on the percentage of adults with active epilepsy with self-reported COVID-19 infection. Emerging studies demonstrate an increased severity of COVID-19 outcomes among people with epilepsy likely due to increased neuroinflammation (common to both epilepsy and sometimes SARS-CoV-2 infection), compromised respiratory function (e.g., hypoxemia), and complications associated with epilepsy medications and certain COVID-19 treatments (e.g., cardiac arrhythmias or unstable drug levels) [19].

Our study shows that the COVID-19 pandemic resulted in delayed or missed care for at least 1 in 10 adults with active epilepsy, increasing the risk of adverse health and social outcomes for people who may have experienced breakthrough seizures, injuries, or worsening of other outcomes [20]. Like the general population, most adults with active epilepsy participated in at least one virtual medical appointment during the 2021 COVID-19 pandemic period suggesting telehealth was a feasible alternative for many. But, whether one or more virtual medical appointments were related to epilepsy treatment, the quality of the virtual medical appointment and associated impact on epilepsy outcomes is unclear and requires more study [20].

This study has several limitations. First, active epilepsy status may be underestimated because of recall or reporting biases among survey respondents, and the exclusion of adults in institutionalized settings (e.g., nursing homes, active military housing, prisons) not captured in the NHIS sample. Second, responses to COVID-19 vaccination status, COVID-19 testing, testing positive, and delays in or missed medical appointments may be subject to recall or reporting biases. However, these questions underwent cognitive testing prior to their inclusion on the NHIS survey; results generally indicated that respondents understood questions as intended and considered various factors (e.g., symptoms that prompted testing, initial inconclusive COVID-19 test results) when answering them [21]. Third, we were unable to ascertain whether receipt of two COVID-19 vaccinations indicates completion of a primary series as some immunocompromised or other high-risk groups may have required three vaccinations as a primary series. Fourth, reporting testing positive for COVID-19 may be based on different and multiple testing methods with inconsistent results (e.g., false negatives), social desirability bias, memory problems, or other factors; therefore, estimates for positivity may be over- or under-estimated. Fifth, reasons for delays in or missed medical care for respondents with active epilepsy may be attributable to known barriers to medical care (e.g., cost, lack of transportation) that may have been exacerbated by pandemic-related delays [22]. Sixth, the reason for, type of, or quality of virtual medical appointments obtained during the pandemic could not be ascertained and requires more study to understand whether virtual appointments meet the complex needs of patients with epilepsy [20]. Seventh, less than 2% of NHIS respondents had a knowledgeable proxy answer for the Sample Adult because he/she was mentally or physically incapable of answering for himself/herself, precluding reliable examination of COVID-19 vaccination status among adults with active epilepsy and intellectual disability [12]. Finally, these outcomes may differ for adults with inactive epilepsy.

5. Conclusion

This study provides evidence that among US adults with active epilepsy, their experience with obtaining COVID-19 vaccinations,

COVID-19 testing, encountering pandemic-related barriers to health care, or participation in virtual medical care in 2021 during the pandemic, was similar to that of the population without epilepsy. But, consistent with the general population, study findings highlight a potential COVID-19 vaccination gap among adults with active epilepsy, warranting intervention. This study provides baseline estimates of the select process of care outcomes among US adults with active epilepsy. Additional research among adults with active epilepsy with other 2021 NHIS COVID-19 survey questions could provide additional insight into COVID-19's impact on adults with active epilepsy. Researchers can also use NHIS data and reporting guidelines to examine COVID-19 vaccination status among adults with active epilepsy and select comorbidities. Continued monitoring of these outcomes over time is warranted to ensure that people with active epilepsy obtain recommended COVID-19 vaccinations in addition to the medical care they need to prevent adverse health and social outcomes.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.yebeh.2023.109223>.

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