









RESEARCH ARTICLE

COVID-19 vaccine in patients with Dravet syndrome: Observations and real-world experiences

Veronica Hood¹  | Anne T. Berg²  | Kelly G. Knupp³  | Sookyong Koh⁴ | Linda Laux⁵ | Mary Anne Meskis¹ | Quratulain Zulfiqar-Ali⁶  | M. Scott Perry⁷  | Ingrid E. Scheffer⁸  | Joseph Sullivan⁹ | Elaine Wirrell¹⁰  | Danielle M. Andrade^{1,11,12} 

¹Dravet Syndrome Foundation, Cherry Hill, New Jersey, USA

²Department of Neurology, Northwestern Feinberg School of Medicine, Chicago, Illinois, USA

³Department of Pediatrics and Neurology, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA

⁴Department of Pediatric Neurology at University of Nebraska Medical Center, Omaha, Nebraska, USA

⁵Epilepsy Center, Department of Pediatrics, Ann & Robert H. Lurie Children's Hospital, Chicago, Illinois, USA

⁶Adult Epilepsy Genetics Program, Krembil Brain Institute, Toronto Western Hospital, Toronto, Ontario, Canada

⁷Jane and John Justin Neurosciences Center, Cook Children's Medical Center, Fort Worth, Texas, USA

⁸Epilepsy Research Centre, University of Melbourne, Austin Health; Royal Children's Hospital, Florey Institute; Murdoch Children's Research Institute, Melbourne, Victoria, Australia

⁹Departments of Neurology and Pediatrics, University of California, San Francisco, San Francisco, California, USA

¹⁰Child and Adolescent Neurology, Mayo Clinic, Rochester, Minnesota, USA

¹¹Division of Neurology, Krembil Brain Institute, Toronto Western Hospital, University of Toronto, Toronto, Ontario, Canada

¹²Adult Genetic Epilepsy Program, University of Toronto, Toronto, Ontario, Canada

Correspondence

Danielle M. Andrade, University of Toronto, Toronto Western Hospital, 5W-445, 399 Bathurst Street, M5T 2S8 Toronto, ON, Canada.
Email: Danielle.andrade@uhn.ca

Abstract

Objective: Vaccination against the SARS-CoV-2 virus is a primary tool to combat the COVID-19 pandemic. However, vaccination is a common seizure trigger in individuals with Dravet syndrome (DS). Information surrounding COVID-19 vaccine side effects in patients with DS would aid caregivers and providers in decisions for and management of COVID-19 vaccination.

Methods: A survey was emailed to the Dravet Syndrome Foundation's Family Network and posted to the Dravet Parent & Caregiver Support Group on Facebook between May and August 2021. Deidentified information obtained included demographics and vaccination status for individuals with DS. Vaccine type, side effects, preventative measures, and changes in seizure activity following COVID-19 vaccination were recorded. For unvaccinated individuals, caregivers were asked about intent to vaccinate and reasons for their decision.

Results: Of 278 survey responses, 120 represented vaccinated individuals with DS (median age = 19.5 years), with 50% reporting no side effects from COVID-19

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial](https://creativecommons.org/licenses/by-nc/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2022 The Authors. *Epilepsia* published by Wiley Periodicals LLC on behalf of International League Against Epilepsy

vaccination. Increased seizures following COVID-19 vaccination were reported in 16 individuals, but none had status epilepticus. Of the 158 individuals who had not received a COVID-19 vaccination, 37 were older than 12 years (i.e., eligible at time of study), and only six of these caregivers indicated intent to seek vaccination. The remaining 121 responses were caregivers to children younger than 12 years, 60 of whom indicated they would not seek COVID-19 vaccination when their child with DS became eligible. Reasons for vaccine hesitancy were fear of increased seizure activity and concerns about vaccine safety.

Significance: These results indicate COVID-19 vaccination is well tolerated by individuals with DS. One main reason for vaccine hesitancy was fear of increased seizure activity, which occurred in only 13% of vaccinated individuals, and none had status epilepticus. This study provides critical and reassuring insights for caregivers and health care providers making decisions about the safety of COVID-19 vaccinations for individuals with DS.

KEYWORDS

COVID-19, Dravet, survey, vaccine

1 | INTRODUCTION

According to the World Health Organization, the global coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has claimed >5 million lives.¹ Vaccination against the SARS-CoV-2 virus, or “COVID-19 vaccination,” has become a primary tool in combatting this pandemic, and so far, >7 billion vaccine doses have been administered across the globe.¹ At the time of this study, two vaccine options, Moderna² and Johnson & Johnson/Janssen,³ had received emergency use authorization for ages 18 years and older. An additional vaccine (Pfizer-BioNTech⁴) had emergency use authorization for ages 12 years and older by the US Food and Drug Administration (FDA) and Health Canada.⁵ Additionally the Oxford/AstraZeneca vaccine was being utilized internationally for individuals older than 18 years.¹ Although in the general population, approved COVID-19 vaccines have been well tolerated, little has been reported for individuals with disabilities. In the United States, data indicate that adults with disabilities have lower rates of vaccination overall.⁶ Unfortunately, individuals with disabilities are often at higher risk of infection or severe illness from COVID-19 due to their underlying medical conditions, living situations, or difficulty following COVID-19 precautions.^{7,8} Furthermore, a recent study of COVID-19 hospitalizations in children and adolescents found that neurologic symptoms related to COVID-19 infection were more common in patients with known underlying neurological disorders.⁸

Additional knowledge regarding responses to COVID-19 vaccination within patient populations with underlying neurological disease could provide critical information to help caregivers make rational, informed decisions regarding vaccine uptake.

Dravet syndrome (DS) is a severe developmental and epileptic encephalopathy affecting approximately 1:15 700 individuals.⁹ DS is caused by mutations in *SCN1A* in >90% of cases and is characterized by often prolonged, intractable seizures that typically begin in the first 18 months of life. Intellectual disability, motor impairments, and other functional limitations develop over time.^{10,11} Early childhood vaccinations coincide with initial seizure onset in one third of patients with DS,¹² where seizures occur in temporal proximity (up to 72 h after) to vaccination.¹¹⁻¹⁸ In the past, some vaccines (particularly pertussis) were thought to cause encephalopathy in typically developing patients. Those patients presented with seizures and subsequent developmental delays following childhood vaccinations. However, a retrospective study investigating alleged incidents of vaccine encephalopathy found the majority of these cases had DS with causal *de novo* variants identified in *SCN1A*.¹⁴

Seizures in DS are commonly triggered by hyperthermia, including fever.^{10,11,19} However, in patients with DS who have experienced vaccine-triggered seizures, a fever is not always present, implicating other immune-related pathways in seizure causation.^{11,12,14} Regardless of the specific mechanism, decisions around vaccination are particularly complex for caregivers of individuals with DS.

The expert consensus remains in support of vaccination in individuals with DS; however, prophylactic measures including the use of antipyretics and bridge antiseizure medications (ASMs) are often recommended.^{20,21}

The COVID-19 pandemic has created significant levels of burden and psychosocial stressors on families living with DS,²² which are now amplified by the decision-making process regarding COVID-19 vaccination for individuals with DS who may have a prior history of seizures proximal to vaccination.^{10–19} A recent study reported positive outcomes for 15 individuals with DS in the UK surrounding COVID-19 vaccination with only 20% reporting an increase in seizure activity.²³ However, the sample size was small and primarily composed of individuals who had received only the first vaccine dose.²³ More information regarding the side effects and impact on seizure activity of COVID-19 vaccination in individuals with DS is critical for families and care providers. The aim of this study was to collect information on the experiences of patients with DS surrounding COVID-19 vaccination, including preventative measures and side effects, to better inform the decision-making process for caregivers and health care providers. Additionally, the study sought to better understand the decisions and hesitations of caregivers for individuals with DS who have not yet received COVID-19 vaccination.

2 | MATERIALS AND METHODS

The Dravet Syndrome Foundation (DSF) worked with a panel of clinicians serving on the DSF Medical Advisory Board to develop a survey to capture the experiences of individuals with DS receiving a COVID-19 vaccine. The survey also included questions to capture information on caregivers deciding against COVID-19 vaccination for the individual with DS. Although children younger than 12 years would not have been eligible for vaccination at the time of this survey, we included them so that we could learn about attitudes toward COVID-19 vaccination. Survey questions were multiple choice, with some opportunities to provide open-ended responses. Demographic information and responses to vaccination were only collected in relation to the individual with DS and not the caregivers responding to the survey. The DSF distributed the online survey to the registered emails of primary caregivers in the DSF Family Network (2316 emails) and to members of the private Dravet Parent & Caregiver Support Group on Facebook (3056 members) between May 17, 2021 and August 2, 2021. Invitations to participate went out via email once monthly in June and July 2021. Invitations to participate were posted in the caregiver groups three times throughout the study period.

Key Points

- Vaccination is a common seizure trigger for individuals with DS, making decisions about COVID-19 vaccination more complex for caregivers and providers. Little is known about the side effects and seizure outcomes for individuals with DS after COVID-19 vaccination.
- Of 120 individuals with DS older than 12 years who had received at least one dose of a COVID-19 vaccine, caregivers for only 16 individuals with DS reported any increase in seizure activity following COVID-19 vaccination. Furthermore, 50% of caregivers reported no side effects were detected for the individual with DS following vaccination. The most common side effects reported were lethargy and soreness at the injection site.
- Vaccine hesitancy remains high among caregivers for individuals with DS. At the time of the survey, 50% of caregivers to the <12 years age group were not planning to vaccinate when the individual with DS became eligible. An additional 31 (20%) caregivers to individuals with DS older than 12 years and within the eligibility criteria at the time of the study indicated they would not seek vaccination.
- A primary reason for vaccine hesitancy among caregivers to individuals with DS was indicated as fear of increased seizures, which was addressed by this study. Overall, only 13% of patients experienced increased seizures following COVID-19 vaccination, and there were no reports of status epilepticus.

Consent for use of deidentified data was collected prior to the survey. Incomplete surveys were not included in the analysis. Data were analyzed using SPSS Statistics version 28.0 (IBM, 2021). Associations were assessed using a chi-squared test ($\alpha = .05$). The study received research ethics board approval from the University Health Network (reference #21-5522).

3 | RESULTS

The survey received 278 completed responses from caregivers of individuals with DS. Demographic information is listed in [Table 1](#). Responses indicated that 216 (78%) of the individuals with DS were located in the United States, and 268 (96%) of the individuals with DS lived at home

TABLE 1 Demographic and background information

| Characteristic | Vaccinated, n = 120 | Unvaccinated, n = 158 | Total, N = 278 |
|--|------------------------|--------------------------|-------------------|
| Age | | | |
| <12 years | 1 (.8%) | 121 (76.6%) | 122 (43.9%) |
| Range | 11 | <1–11 | |
| Median | 11 | 6 | |
| 12–19 years | 59 (49.2%) | 27 (17.1%) | 86 (30.9%) |
| Range | 12–19 | 12–19 | |
| Median | 15.1 | 15 | |
| ≥20 years | 60 (50%) | 10 (6.3%) | 70 (25.1%) |
| Range | 20–42 | 20–31 | |
| Median | 25 | 21 | |
| Sex | | | |
| Female | 67 (55.8%) | 100 (63.3%) | 167 (60%) |
| Male | 53 (44.2%) | 58 (36.7%) | 111 (40%) |
| Country/region of residence | | | |
| United States | 91 (75.8%) | 125 (79.1%) | 216 (77.7%) |
| Canada | 8 (6.7%) | 11 (7%) | 19 (6.8%) |
| Australia | 4 (3.3%) | 3 (1.9%) | 7 (2.5%) |
| Europe | 15 (12.5%) | 13 (8.2%) | 28 (10.1%) |
| Asia | 2 (1.7%) | 5 (3.2%) | 7 (2.5%) |
| South America | | 1 (.6%) | 1 (.4%) |
| Gene mutation | | | |
| SCN1A+ | 113 (94%) | 150 (94.9%) | 263 (94.6%) |
| Variant in another gene | 2 (1.7%) | 3 (1.9%) | 5 (1.8%) |
| No variant identified | 5 (4.2%) | 3 (1.9%) | 8 (2.9%) |
| No genetic testing | | 2 (1.3%) | 2 (.7%) |
| Living arrangement | | | |
| Lives with family | 110 (91.7%) | 158 (100%) | 268 (96.4%) |
| Group home/supported living | 10 (8.3%) | | 10 (3.6%) |
| Seizures with prior vaccination | | | |
| Yes | 29 (24.2%) | 76 (48.1%) | 105 (37.8%) |
| No | 91 (75.8%) | 82 (51.9%) | 173 (62.2%) |

Note.: Values are given as n (%) unless otherwise indicated.

with family. Consistent with variant rates reported in recent studies, 263 (95%) of the individuals with DS were reported to have pathogenic variants in *SCN1A*.¹¹

3.1 | Vaccination rate

At the time of the survey, vaccination was only available for individuals aged 12 years and older. Survey responses from 156 caregivers represented individuals with DS aged 12 and older; of these, 119 (76%) reported having received at least one dose of COVID-19 vaccination. One additional survey response indicated an individual with DS received

a vaccination at age 11 years, for a total representation of 120 vaccinated individuals (median age = 19.5 years, 55.8% female).

Of the 120 individuals who had received at least one dose of a COVID-19 vaccine, 99 (83%) received the Pfizer-BioNTech vaccine, 16 (13%) received Moderna, three (2%) received Oxford/AstraZeneca, and two (2%) received Johnson & Johnson/Janssen (Figure 1A). Completed vaccine schedules, as recommended by the FDA emergent use authorization,⁵ were reported for 96 (80%) individuals. The remaining 24 (20%) individuals with DS had received the first dose of a two-dose vaccination schedule at the time of the survey. All 24 caregiver responses indicated

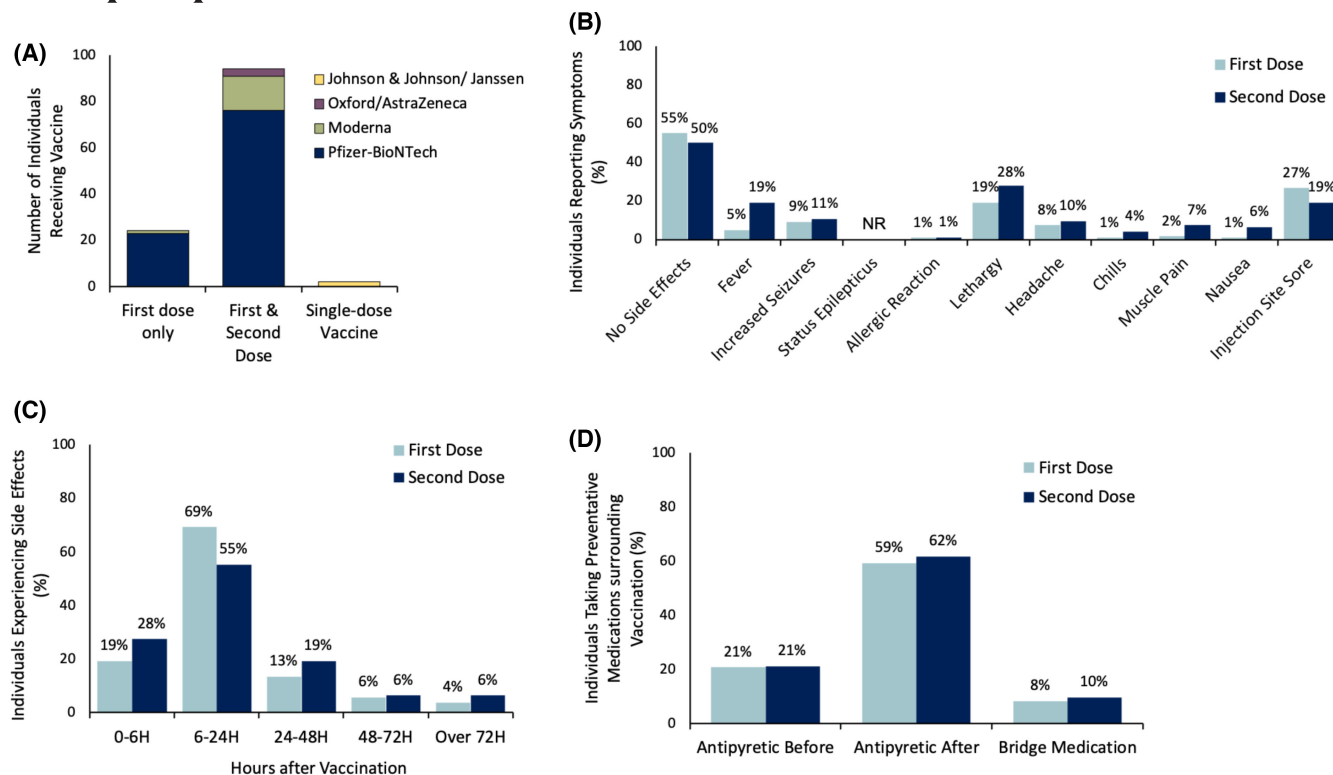


FIGURE 1 COVID-19 vaccination and side effects in individuals with Dravet syndrome (DS). (A) Number of individuals ($n = 120$) receiving each brand of vaccine and number of doses received. (B) Percentage of individuals with DS experiencing side effects, or lack thereof, following vaccination ($n = 120$). (C) Timing of presence of side effects following each dose of COVID-19 vaccination (first dose, $n = 52$; second dose, $n = 47$). (D) Percentage of individuals using antipyretic agents before and after vaccination, and bridge antiseizure medication. NR, none reported

intent for the individual with DS to receive the second vaccine dose when eligible.

3.2 | Symptoms and side effects following COVID-19 vaccination

No side effects were reported for 66 (55%) individuals with DS following a first COVID-19 dose (D1) and 47 (50%) following a second dose (D2; Figure 1B). The most commonly reported side effects were lethargy for 23 (19%, D1) and 26 (28%, D2) individuals, and soreness at the injection site for 32 (27%, D1) and 18 (19%, D2) individuals (Figure 1A). Fewer than 10% reported headache, muscle pain, nausea, or chills after a COVID-19 vaccine dose. There was one report of an allergic reaction following both doses of the Pfizer vaccine, for which the caregiver provided details in the open-ended response that mentioned redness and swelling in the face and neck, and one other report of allergic reaction following Moderna vaccine D2, for which additional details were not provided. Fever was reported for six (5%) after D1, and for 18 (19%) after D2. Several caregivers noted that they had difficulty assessing symptoms in individuals

with DS due to the individual's limited ability to clearly communicate how they were feeling and any subjective side effects such as headache. There was a significant association between the presence of any side effects following D1 and the subsequent presence of side effects following D2 ($\chi^2 = .513$, $df = 1$, $p < .001$).

After D1, 11 (9%) individuals with DS had increased seizure activity. Of these 11 individuals, eight had also received D2 at the time of the survey, with five of these eight again reporting increased seizures after D2. An additional five individuals who had not reported increased seizures following D1 did report an increase following D2, totaling 10 patients (11%). There was no significant association between reported prior incidence of increased seizures following a non-COVID-19 vaccination and increased seizures following a COVID-19 vaccine dose. Taken together, of 216 vaccination events (sum of D1 and D2), increase in seizures was reported 21 times (9.7%).

Fever was indicated by some caregivers as a direct seizure trigger; one caregiver noted that "once the fever was controlled (by acetaminophen) the seizures stopped." Of particular note, no individual had status epilepticus (SE) following COVID-19 vaccination (Figure 1B). Side effects

across all categories, other than injection site soreness, were reported slightly more frequently following D2 of COVID-19 vaccination than D1. When side effects occurred, they were most likely to appear between 6 and 24 h following COVID-19 vaccination for either dose (Figure 1C).

3.3 | Preventative measures surrounding COVID-19 vaccination

Given the associations between vaccines, fever, and increased seizures in many patients with DS, it is not uncommon for physicians to recommend additional preventative measures such as antipyretic agents and bridge ASMs surrounding vaccination.^{20,21} Antipyretics were given to 25 (21%) individuals during the 4 h before D1 and to 20 (21%) individuals before D2. Following the COVID-19 vaccine, antipyretics were given to 71 (59%) individuals after D1 and to 74 (79%) individuals after D2. Patients received an average of 3.2 doses of antipyretics, most commonly in the first 24 h following vaccination. Bridge ASMs were used for 10 (8%) individuals after D1 and for nine (10%) individuals after D2, with patients receiving an average of 3.6 doses of ASMs beginning 12 h prior to and up to 72 h after D1 and D2. Bridge ASMs included clonazepam (D1, $n = 5$; D2, $n = 4$), clobazam (D1, $n = 3$), lorazepam (D1, $n = 1$; D2, $n = 3$), clorazepate (D1, $n = 1$; D2, $n = 1$), and diazepam (D2, $n = 1$).

Overall, the use of antipyretics or bridge ASMs was not linked to increased seizure activity. Increased seizure activity was instead more likely to be reported in individuals using antipyretics following D1 (10/71, 14.1%, $p = .03$) than those who did not use antipyretics (1/49, 2.0%), although not with D2. Additionally, increased seizure activity was also more likely to be reported in those who indicated use of a bridge ASM with D1 (3/10, 30%, $p = .02$) or with D2 (3/9, 30%, $p = .02$) versus reports of increased seizures in those who did not use bridge ASMs (D1: 8/110, 7.3%; D2, 7/85, 8.2%).

3.4 | COVID-19 vaccine hesitancy among caregivers of individuals with DS

Caregivers reported that 158 individuals with DS had not yet received a COVID-19 vaccination. Of these, 121 children were too young at the time of the survey to receive a COVID-19 vaccine (<12 years of age), but 61 (50%) caregivers indicated their intention to have their child vaccinated as soon as he or she became eligible. Of caregivers for 27 unvaccinated individuals in the 12–19-year age range, only four still intended to seek COVID-19 vaccination for

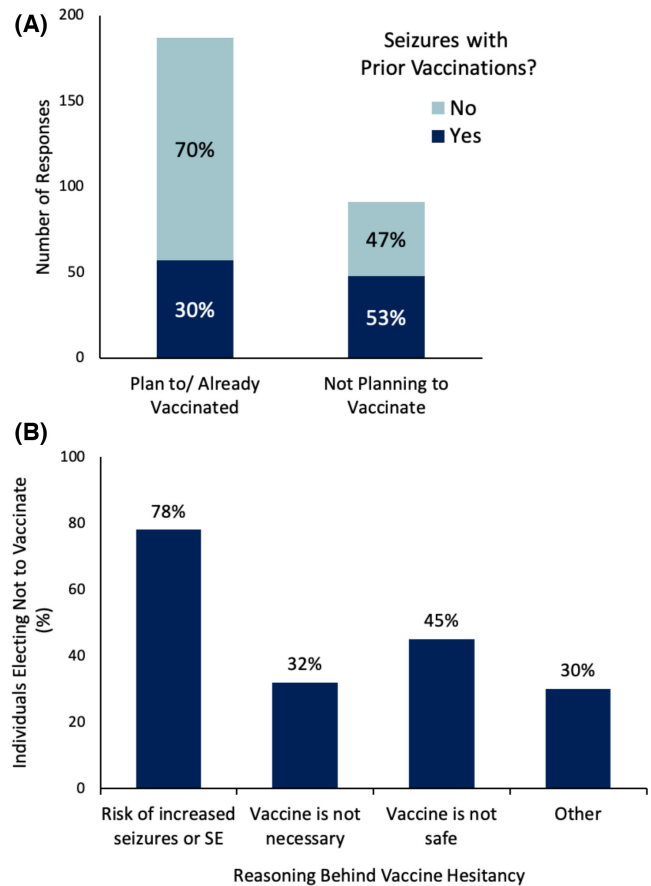


FIGURE 2 COVID-19 vaccination hesitancy in caregivers of individuals with Dravet syndrome. (A) Responders indicating caregivers' intentions for COVID-19 vaccination and reported prior incidence of seizures with non-COVID-19 vaccinations ($n = 278$). (B) Reasons cited for electing not to proceed with vaccination ($n = 91$ individuals). SE, status epilepticus

the individual with DS. There were 10 responses from caregivers of adults with DS older than 20 years who had not received a vaccination, of whom only two indicated intent to still seek vaccination for the adult with DS.

Prior association of seizures proximal to non-COVID-19 vaccinations correlated with the decision not to seek COVID-19 vaccination. Specifically, 48 (53%) of those intending not to vaccinate had prior exacerbations of seizures with non-COVID-19 vaccinations (Figure 2A; $p < .001$), versus 57 (30%) individuals who did not have an increase in seizures with prior vaccinations and had received or whose caregiver indicated intent to have them receive a COVID-19 vaccine. In a follow-up question to those electing not to seek COVID-19 vaccination, the concern about increased seizures or SE was indicated as a reason not to vaccinate by 71 (78%) caregivers (Figure 2B). Additionally, 29 (32%) caregivers indicated they did not feel the vaccine was necessary, and 41 (45%) were concerned about the safety of the vaccine in general. Twenty-seven of the 91 caregivers to unvaccinated individuals

with DS also provided open-ended responses regarding vaccine hesitancy and cited the newness of the vaccine as well as the lack of full FDA approval of any of the vaccines at the time of the survey. Six responses indicated concerns regarding the lack of data about long-term side effects of vaccination and information specific to the responses of people with DS to COVID-19 vaccination. Additionally, five caregiver responses contained information they were concerned about that was not based on scientifically factual information surrounding the COVID-19 vaccines.

4 | DISCUSSION

COVID-19 vaccines are by far the best defense available against the serious illness associated with COVID-19 infection. Individuals with DS may be at higher risk of exposure to the SARS-CoV-2 virus due to difficulty or inability to maintain COVID-19 safety precautions such as wearing a face covering and social distancing. They also have an increased risk of seizures and SE triggered by infectious illnesses, vaccines, and fever. Many families have implemented measures, such as social isolation, to counterbalance these concerns, although this also creates additional psychosocial burden for individuals with DS and their families.²² As such, vaccination is of paramount importance for individuals with DS to remain protected from complications of COVID-19 and to ease the burden of extensive preventative measures. However, in DS, vaccination (to several diseases) also carries the risk of increased seizures and SE, complicating the decision-making process for caregivers and health care providers. This study provides important insights into the experiences of individuals with DS following COVID-19 vaccination, overall reporting positive outcomes, with only 13% of individuals who received a COVID-19 vaccination reporting increased seizure activity and none having SE.

In DS, fever is often surmised to be the precipitating factor for seizures following vaccination,^{10,11,19} although several studies have found that fever is not always present in individuals experiencing vaccine-proximate seizures.^{11,12,14} Although fever was reported more often following COVID-19 vaccine D2 than D1, increased seizures following vaccination was similar between the two doses (9% and 11%, respectively). Open-ended responses indicated that the seizures were often associated with fever in these cases.

Several caregivers indicated the use of bridge ASMs (8% and 10% for D1 and D2, respectively) and/or antipyretic medications (59% and 79%) for the individual with DS surrounding COVID-19 vaccination. Use of bridge ASMs and antipyretics did not immediately appear to be preventative for seizure increases surrounding COVID-19 vaccination.

Rather, use of either antipyretics or ASMs was actually associated with a report of increased seizures following D1, but not D2, of a COVID-19 vaccine. These associations could be representative of reactive use of antipyretics and bridge ASMs rather than their proactive use, making the causal relationship difficult to interpret. Several caregivers noted the usefulness of antipyretic medications to reduce fever and, subsequently, seizure activity following COVID-19 vaccination. It is also possible that individuals with poorer baseline seizure control or more sensitivity to seizure triggers may have been more likely to utilize preemptive preventative measures such as a bridge ASM, perhaps explaining this association.

Vaccine hesitancy remains high for caregivers of individuals with DS. Over one third of the total survey responders indicated they did not plan for the individual with DS they care for to receive a COVID-19 vaccine when they became eligible, and among caregivers of children younger than 12 years, only 50% indicated the intent to seek vaccination once the child was eligible. One of the primary reasons for vaccine hesitancy was caregiver concerns over increased seizure activity or SE following vaccination. In the open-ended responses, several caregivers indicated a desire for additional information about the effects of COVID-19 vaccination in the DS population specifically. Importantly, the results from this survey directly address this concern with information on 120 individuals, 94 of whom had received two doses of the vaccine, showing that increased seizure activity occurred in only 16 individuals (13%), without any instances of SE.

COVID-19 infection is usually responsible for severe symptoms in older patients; however, children and adolescents may also have life-threatening neurological involvement. A recent US study looked at 1695 patients aged <22 years who were hospitalized for COVID-19 infection. Twenty-two percent of patients developed neurological symptoms, with the majority being mild and transient. Of those 22% who developed neurological manifestations, 12% had a COVID-19-related life-threatening neurological disorder (aseptic meningitis, encephalitis, acute disseminated encephalomyelitis, acute ischemic or hemorrhagic stroke, Guillain-Barré syndrome and variants, or severe encephalopathy with or without COVID-19-related neuroimaging abnormalities [virus-associated necrotizing disseminated acute leukoencephalopathy and/or cytotoxic splenic lesions]), 25% died, and 40% survived with new neurologic sequelae.⁸ Although that study did not address patients with DS specifically, it found that patients with underlying neurological diseases, including epilepsy, have a higher chance of developing COVID-related neurological complications when infected by COVID-19. There have been reports of Guillain-Barré syndrome following vaccination against COVID-19 (and other viruses); however,

there is no evidence currently that COVID-19 vaccines represent a higher risk of neurological complication than COVID-19 infection.^{24,25} The infection appears to lead to more severe neurological complication, especially in those patients with pre-existing neurological problems, such as patients with DS. Although the evidence is limited, one previous report indicated that 50% of individuals with DS who developed symptoms consistent with COVID-19 infection had worsening in seizures.²² Reports have also suggested possible associations of seizure and SE with COVID-19 infection in both previously unaffected individuals and those with a prior epilepsy diagnosis.^{26,27} This further emphasizes the consequences of COVID-19 infection in medically vulnerable individuals and the urgent need to avoid COVID-19 infection.

4.1 | Limitations

This survey only reports on the vaccination experiences of individuals with DS aged 12 years and older, as younger children were not eligible to receive the vaccine when this survey was performed. The single 11-year-old child who received the COVID-19 vaccine (outside United States/Canada) was included in the 12 years and older group. Although this study provides an initial assessment of the experiences of a large cohort of individuals with DS who received multiple doses of the COVID-19 vaccine, it lacks information on how younger individuals with DS might react to the vaccine. It is usual for seizure types and triggers to change with age in DS, and seizures often become less frequent and less prolonged with a decreased incidence of SE in adults with DS.²⁸ Given the nature of this study (retrospective survey), participation bias and recall bias are possible confounders. However, the large number of responders in both vaccinated and unvaccinated groups in a rare disease like DS should help mitigate this limitation.

4.2 | Conclusions

In conclusion, this study provides valuable information for families, caregivers, those patients who might have a better cognitive function, and health care providers navigating decisions regarding COVID-19 vaccination for individuals with DS. Vaccination against the SARS-CoV-2 virus is the most promising tool to avoid COVID-19 severe infection. The high percentage of caregivers still indicating hesitancy to have their loved ones with DS vaccinated against COVID-19 speaks to the huge need to provide real-world experience and highlight the minimal risks reported with COVID-19 vaccine in this group. This allows parents and providers to weigh the minimal risks of

receiving the vaccination compared to the potential for severe illness and death caused by COVID-19 infection as well as the unknowns surrounding the long-term impacts of COVID-19 illness in this medically complex population of individuals with DS.

ACKNOWLEDGMENT

We want to acknowledge the families of patients with Dravet Syndrome who participated in this study.

CONFLICT OF INTEREST


None of the authors has any relevant conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

ORCID

Veronica Hood  <https://orcid.org/0000-0002-1988-4980>

Anne T. Berg  <https://orcid.org/0000-0002-0298-5523>

Kelly G. Knupp  <https://orcid.org/0000-0002-1967-0827>

Quratulain Zulfiqar-Ali  <https://orcid.org/0000-0002-3984-5276>

M. Scott Perry  <https://orcid.org/0000-0002-1825-846X>

Ingrid E. Scheffer  <https://orcid.org/0000-0002-2311-2174>

Elaine Wirrell  <https://orcid.org/0000-0003-3015-8282>

Danielle M. Andrade  <https://orcid.org/0000-0003-0953-2698>

<https://orcid.org/0000-0003-0953-2698>

REFERENCES

1. World Health Organization. WHO coronavirus (COVID-19) dashboard [Internet]. Updated 2021 Nov 8 [cited 2021 Nov 9]. Available from: <https://covid19.who.int>
2. Baden LR, Sahly HME, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med*. 2020;384:403–16.
3. Sadoff J, Gray G, Vandebosch A, Cárdenas V, Shukarev G, Grinsztejn B, et al. Safety and efficacy of single-dose Ad26.COV2.S vaccine against Covid-19. *N Engl J Med*. 2021;384:2187–201.
4. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med*. 2020;383:2603–15.
5. Centers for Disease Control and Prevention. Science brief: COVID-19 vaccines and vaccination [Internet]. Updated 2021 Sep 15 [cited 2021 Oct 8]. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html>
6. Centers for Disease Control and Prevention. Household pulse survey (HPS): COVID-19 vaccination among people with disabilities [Internet]. Updated 2021 Oct 11 [cited 2021 Nov 9]. Available from: https://covid.cdc.gov/covid-data-tracker/#-vaccinations-disability-status_
7. Centers for Disease Control and Prevention. COVID-19 vaccines for people with disabilities [Internet]. Updated 2021 May 14 [cited 2021 Sep 15]. Available from: <https://www.cdc.gov/>

- [coronavirus/2019-ncov/vaccines/recommendations/disabilities.html](https://doi.org/10.1111/epi.17250)
8. LaRovere KL, Riggs BJ, Poussaint TY, Young CC, Newhams MM, Maamari M, et al. Neurologic involvement in children and adolescents hospitalized in the United States for COVID-19 or multisystem inflammatory syndrome. *JAMA Neurol.* 2021;78:536–47.
 9. Wu YW, Sullivan J, McDaniel SS, Meisler MH, Walsh EM, Li SX, et al. Incidence of Dravet syndrome in a US population. *Pediatrics.* 2015;136:e1310–5.
 10. Dravet C. Dravet syndrome history. *Dev Med Child Neurol.* 2011;53:1–6.
 11. Li W, Schneider AL, Scheffer IE. Defining Dravet syndrome: an essential pre-requisite for precision medicine trials. *Epilepsia.* 2021;62(9):2205–17.
 12. McIntosh AM, McMahon J, Dibbens LM, Iona X, Mulley JC, Scheffer IE, et al. Effects of vaccination on onset and outcome of Dravet syndrome: a retrospective study. *Lancet Neurol.* 2010;9:592–8.
 13. Barrera MN, Lillo MM, Collado CR, Fernández-Mensaque RC, Charro AAC. Epilepsia mioclónica severa de la infancia. Estudio epidemiológico analítico. *Rev Neurol.* 2000;30:620.
 14. Berkovic SF, Harkin L, McMahon JM, Pelekanos JT, Zuberi SM, Wirrell EC, et al. De-novo mutations of the sodium channel gene SCN1A in alleged vaccine encephalopathy: a retrospective study. *Lancet Neurol.* 2006;5:488–92.
 15. Caraballo RH, Fejerman N. Dravet syndrome: a study of 53 patients. *Epilepsy Res.* 2006;70:231–8.
 16. Tro-Baumann B, von Spiczak S, Lotte J, Bast T, Haberlandt E, Sassen R, et al. A retrospective study of the relation between vaccination and occurrence of seizures in Dravet syndrome. *Epilepsia.* 2011;52:175–8.
 17. Wong PTY, Wong VC-N. Prevalence and characteristics of vaccination triggered seizures in Dravet syndrome in Hong Kong: a retrospective study. *Pediatr Neurol.* 2016;58:41–7.
 18. Damiano JA, Deng L, Li W, Burgess R, Schneider AL, Crawford NW, et al. SCN1A variants in vaccine-related febrile seizures: a prospective study. *Ann Neurol.* 2020;87:281–8.
 19. Verbeek NE, Wassenaar M, van Campen JS, Sonsma A, Gunning B, Knoers N, et al. Seizure precipitants in Dravet syndrome: what events and activities are specifically provocative compared with other epilepsies? *Epilepsy Behav.* 2015;47:39–44.
 20. Wirrell EC, Laux L, Donner E, Jette N, Knupp K, Meskis MA, et al. Optimizing the diagnosis and management of Dravet syndrome: recommendations from a North American consensus panel. *Pediatr Neurol.* 2017;68:18–34.e3.
 21. Andrade DM, Berg AT, Hood V, Knupp KG, Koh S, Laux L, et al. Dravet syndrome: a quick transition guide for the adult neurologist. *Epilepsy Res.* 2021;177:106743.
 22. Balestrini S, Wilson G, Eldred C, Evans H, Sisodiya SM. The impact of COVID-19 in Dravet syndrome: a UK survey. *Acta Neurol Scand.* 2021;143:389–95.
 23. Clayton LM, Balestrini S, Cross JH, Wilson G, Eldred C, Evans H, et al. The impact of SARS-CoV-2 vaccination in Dravet syndrome: a UK survey. *Epilepsy Behav.* 2021;124:108258.
 24. Shao S, Wang C, Chang K, Hung M, Chen H, Liao S. Guillain-Barré syndrome associated with COVID-19 vaccination. *Emerg Infect Dis.* 2021;27:3175–8.
 25. Centers for Disease Control and Prevention. Selected adverse events reported after COVID-19 vaccination [Internet]. Updated 2022 Mar 1 [cited 2021 Mar 2]. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html>
 26. Kurd M, Hashavya S, Benenson S, Gilboa T. Seizures as the main presenting manifestation of acute SARS-CoV-2 infection in children. *Seizure.* 2021;92:89–93.
 27. Dono F, Nucera B, Lanzone J, Evangelista G, Rinaldi F, Speranza R, et al. Status epilepticus and COVID-19: a systematic review. *Epilepsy Behav.* 2021;118:107887.
 28. Selvarajah A, Zulfiqar-Ali Q, Marques P, Rong M, Andrade DM. A systematic review of adults with Dravet syndrome. *Seizure.* 2021;87:39–45.

How to cite this article: Hood V, Berg AT, Knupp KG, Koh S, Laux L, Meskis MA, et al. COVID-19 vaccine in patients with Dravet syndrome: Observations and real-world experiences. *Epilepsia.* 2022;63:1778–1786. <https://doi.org/10.1111/epi.17250>