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RESEARCH ARTICLE

Association between the risk of seizure and COVID-19 vaccinations: A self-controlled case-series study

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Abstract

Objective: The risk of seizure following BNT162b2 and CoronaVac vaccinations has been sparsely investigated. This study aimed to evaluate this association.

Method: Patients who had their first seizure-related hospitalization between February 23, 2021 and January 31, 2022, were identified in Hong Kong. All seizure episodes happening on the day of vaccination (day 0) were excluded, since clinicians validated that most of the cases on day 0 were syncopal episodes. Within-individual comparison using a modified self-controlled case series analysis was applied to estimate the incidence rate ratio (IRR) with 95% confidence intervals (CIs) of seizure using conditional Poisson regression.

Eric Yuk Fai Wan and Vanessa Wai Sei Ng contributed equally to this work.

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Results: We identified 1656 individuals who had their first seizure-related hospitalization (BNT162b2: 426; CoronaVac: 263; unvaccinated: 967) within the observation period. The incidence of seizure was 1.04 (95% CI .80–1.33) and 1.11 (95% CI .80–1.50) per 100 000 doses of BNT162b2 and CoronaVac administered, respectively. Sixteen and 17 individuals, respectively, received a second dose after having a first seizure within 28 days after the first dose of BNT162b2 and CoronaVac vaccinations. None had recurrent seizures after the second dose. There was no increased risk during day 1–6 after the first (BNT162b2: IRR = 1.39, 95% CI = .75–2.58; CoronaVac: IRR = 1.19, 95% CI = .50–2.83) and second doses (BNT162b2: IRR = 1.36, 95% CI = .72–2.57; CoronaVac: IRR = .71, 95% CI = .22–2.30) of vaccinations. During 7–13, 14–20, and 21–27 days post-vaccination, no association was observed for either vaccine.

Significance: The findings demonstrated no increased risk of seizure following BNT162b2 and CoronaVac vaccinations. Future studies will be warranted to evaluate the risk of seizure following COVID-19 vaccinations in different populations, with subsequent doses to ensure the generalizability.

KEYWORDS
COVID-19 vaccinations, modified self-controlled case series, seizure

1 | INTRODUCTION

The safety of the coronavirus disease 2019 (COVID-19) vaccines remains a major public health interest since their approval for emergency use. Seizures following vaccination has been considered as a possible complication and listed as one of the adverse events of special interest by the International Coalition of Medicines Regulatory Authorities (ICMRA) and World Health Organization (WHO).[1] Theoretically, seizures are caused by an abnormally excessive or disrupted neuronal activity in the brain, but the underlying causes of seizures remain unclear. New-onset seizures following administration of various types of non–COVID-19 vaccines have been reported, such as febrile seizures during childhood; some were nonfebrile seizures in adults.[2,3] Furthermore, some researchers proposed a mechanism by which severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may influence the central nervous system, directly or through the blood-brain barrier, triggering seizures in patients who contracted COVID-19 infection.[4,5] Currently, there is no evidence to show whether viral load or delivery platforms (e.g., messenger RNA [mRNA] liponanoparticles) in the COVID-19 vaccines could enter the brain and hence disrupt the neuronal activity. Therefore, COVID-19 vaccinations may also possibly trigger seizures like other non–COVID-19 vaccines.

The current COVID-19 vaccination program in Hong Kong provides two authorized vaccines: CoronaVac from Sinovac BioNTech (Hong Kong) Limited (equivalent to Sinovac Life Sciences Company Limited) and BNT162b2 from Fosun-BioNTech (equivalent to Pfizer-BioNTech). Phase 3 clinical trials of CoronaVac identified one case with fever and seizure after vaccination,[6] whereas seizures were not reported specifically in Phase 3 clinical trials of BNT162b2.[7] Despite some case reports on individuals with seizures after receiving mRNA COVID-19 vaccines,[8,9] a cohort study conducted in Israel showed no increased risk of seizure following BNT162b2 vaccination.[10] Nevertheless, the results may be limited to confounding and selection bias.[10]

Key points

- The false-positive rate of seizure was very high on the day of vaccination.
- The incidence rates of seizure following BNT162b2 and CoronaVac vaccinations in our study were very low.
- Among the individuals who had seizure within 28 days after the first dose of the vaccinations, none of them developed recurrent seizure after the second dose.
- Findings from this study showed no association between the risk of seizure and coronavirus disease 2019 (COVID-19) vaccinations.
- Our findings can reassure the public on the safety of COVID-19 vaccines, enhance their confidence in the vaccines, and consequently help achieve herd immunity against the virus.

Yet there is no study to evaluate the association of seizures after CoronaVac vaccination or other inactivated virus vaccines.[8,9] The individuals described in the case reports who had first seizure after vaccination have neither known neurological nor known psychiatric conditions, suggesting the possibility that the seizure was triggered by the vaccine itself. Although no conclusion on the causal relationship could be drawn, these reported cases merited further investigation, and WHO also recommends regulators to monitor for the occurrence of seizures after mRNA vaccination.[1] Given the wide use of BNT162b2 and CoronaVac in 195 countries and regions,[11] the uncertainty on the risk of adverse effects following vaccination is of utmost importance to address the ongoing public concern on vaccine safety. Hence, this study aims to evaluate the risk of seizures following CoronaVac and BNT162b2 vaccinations using population-based electronic health care records in Hong Kong.

2 | METHODS

2.1 | Data sources

We utilized the routine electronic health records from the clinical management system under the Hospital Authority (HA) with linkage to a population-based COVID-19 vaccination record from the Department of Health (DH), the Government of the Hong Kong Special Administrative Region (HKSAR). HA is a sole publicly-funded health care provider that manages public hospitals, general and specialist outpatient clinics, and emergency rooms, covering over 70% of hospitalizations in Hong Kong; more than 20 million attendances at these sites were recorded in the year 2018–2019.[12,13] Each resident in Hong Kong has a unique Hong Kong Identity Card Number, which allows the HA to create an electronic health record for each patient to link up with all hospitals and clinics. The clinical management system, including patients' information, diagnoses, prescriptions, and laboratory tests, provides real time data support and monitoring for clinical management. A data linkage between the clinical data from the HA and vaccination records from the DH is established using the Hong Kong Identity Card Number or passport number of each Hong Kong resident. This database has been used previously to conduct pharmacovigilance studies on the risk of adverse effects after COVID-19 vaccinations.[14–21]

2.2 | Study design

We undertook a within-individual comparison using a modified self-controlled case series (SCCS) method to evaluate the risk of seizures following COVID-19 vaccinations. The major advantages of this method is its ability to implicitly control all time-invariant confounding factors, such as family history, genetic factors, and socioeconomic status, which are uncommonly available in electronic health record databases.[22]

2.3 | SCCS assumptions

There are three assumptions to be fulfilled in order to produce valid and unbiased results.[22] First, because patients might be more likely to have another seizure after they had their first episode, this might violate the assumption of event independence. Therefore, only incident seizures were considered as the outcome of interest and individuals with previous history of seizures were excluded. Second, the event of interest should not affect the probability of subsequent exposure. It is possible that patients who had a seizure would delay or cancel the subsequent vaccination. Therefore, we adopted a SCCS model for event-dependent exposures (i.e., modified SCCS) as an extension of the standard SCCS, which was designed specifically to handle the situation when the subsequent exposure is affected following the occurrence of event.[23] Unlike the standard SCCS, this modified SCCS model requires all unvaccinated individuals with the outcome of interest to be included. Inclusion of unvaccinated individuals contributes to the estimation of the temporal effect and the probability of receiving vaccination among patients with seizure, but not directly to the effect of the vaccine on the risk of seizure.[23] Finally, the observation period should not be censored by the outcome of interest (e.g., death caused by seizure). The modified SCCS model could also address this issue and adjust for such bias.[23] This method has been used in evaluating the safety of COVID-19 vaccines and its validity has been guaranteed.[24–32]

2.4 | Study population

We identified all vaccinated and unvaccinated individuals who were hospitalized with a primary diagnosis of seizure (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes 333.2, 345, 649.4, 779, and 780.3) at least once between February 23, 2021 and January 31, 2022. Because the recent use of antiepileptic medications may alter the seizure threshold and indicates a higher possibility of previous seizure that might not be recorded in the database, individuals who had ever received antiepileptic drugs within 90 days before the start of observation were excluded.

2.5 | Exposures and outcome

Study exposures were defined as BNT162b2 or CoronaVac vaccinations among individuals who were diagnosed with an incident seizure in the inpatient setting. In Hong Kong, the Expert Committee on Clinical Events Assessment Following COVID-19 Immunization was established to provide independent clinical adjudication of potential causal links between adverse events following immunization and COVID-19 vaccines. Seizures are listed under intensive monitoring as an adverse event following immunization. Based on anecdotal observation from our investigators in this Expert Committee, in the current pandemic situation with the top emergency response level activated by the DH, health care professionals might be more inclined to report suspicious cases than in the pre-vaccination period, which might result in an increased number of reported cases that are suspicious of a seizure. Therefore, we conducted a case validation analysis on a preliminary data set of 107 vaccinated individuals with incident seizure-related hospitalization after COVID-19 vaccination between February 23, 2021 and January 31, 2022, in Hong Kong using the same data sources. The cases were identified using ICD-9-CM diagnosis code. Two local neurologists (K.K.L. and R.S.K.C.) reviewed the detailed discharge summaries, which document the clinical presentation, investigations (e.g., electroencephalography, brain imaging, and blood tests), and medication use for each case of suspected seizure independently, and classified the seizure diagnoses according to the diagnostic manual from the International League Against Epilepsy (ILAE).[33] The overall positive predictive value (PPV) for the seizure cases based on the ICD-9-CM code were 79.4% and the PPV on the day of first or second dose of vaccination was low (11.1%). Most of the misclassified cases on the day of vaccination were vasovagal syncopal episodes, with or without convulsion. After excluding the cases that happened on the day of each dose of vaccination, the PPV increased to 85.7%. Therefore, to obtain reliable evaluation on the association between COVID-19 vaccination and seizures, all cases coded with seizure that happened on the day of vaccination were excluded in this study. Details on the validation were shown in Appendix S1.

Starting from January 1, 2022, and onward, the new arrangement of the booster dose has been rolled out for adults who were already fully vaccinated with the second dose received at least 6 months before.[34] However, our vaccination records retrieved was only up to January 31, 2022, so the majority of the vaccine recipients have not yet received the booster dose. Therefore, individuals who received the booster dose before January 31, 2022, were excluded, as this study aims at the effect of the first two doses. The individual observation period started on February 23, 2021 and ended on January 31, 2022. The exposure risk periods were defined as 28 days following the first and second doses of vaccination. Each risk period was further sub-divided into four sub-intervals, namely (1) days 1–6; (2) days 7–13; (3) days 14–20; and (4) days 21–27, where day 0 was defined as the day of vaccination. Individuals who had a seizure-related hospitalization on day 0 were excluded because the PPV was low on day 0, and we eliminated the possibility that an individual who had a seizure-related hospitalization before the vaccination, although this is unlikely to happen. Any other periods that do not fall into the above risk periods, including the time before the first dose of vaccination, >28 days after the first and second doses, were considered as baseline period. For individuals who received only the first dose within the observation period, the remaining time post-vaccination (>28 days after first dose) was considered as baseline period. The corresponding admission date of the seizure-related hospitalization is considered as the event date. A graphical representation of the study design timeline of a hypothetical participant is illustrated in Figure 1.

2.6 | Statistical analysis

The incidence rates of seizure in both BNT162b2 and CoronaVac vaccine groups were estimated using Poisson regression. The modified SCCS was applied using the R function "eventdepenexp" in the R-package "SCCS."[35] Season of the year was adjusted in monthly categories. The adjusted incidence rate ratio (IRR) and its 95% confidence intervals (CIs) were estimated by comparing the incidence rates of seizure in different risk periods with that in the baseline period using conditional Poisson regression. If IRR was >1, it means there was an increased risk associated with the vaccine, and vice versa for IRR <1. If IRR = 1, no association is observed between the vaccines and risk of seizure.

To ensure the robustness of the findings, we conducted five sensitivity analyses. First, to observe any impact of including false-positive cases on day 0 after each dose on the risk of seizure, we included cases that happened on day 0. Second, based on our validation analysis, the PPV was 57% and 50% on the first and second day after each dose of vaccination, respectively (Appendix S1). To ensure the minimal effect on the results by the false-positive cases, we excluded the individuals who had seizure on the first and second day after each dose from the analysis. Third, it is possible that the assumption of SCCS might be violated that the observation might not be censored at random when observation ends before the booster dose. Therefore, we conducted three sensitivity analysis by including individuals who received booster dose and censoring the

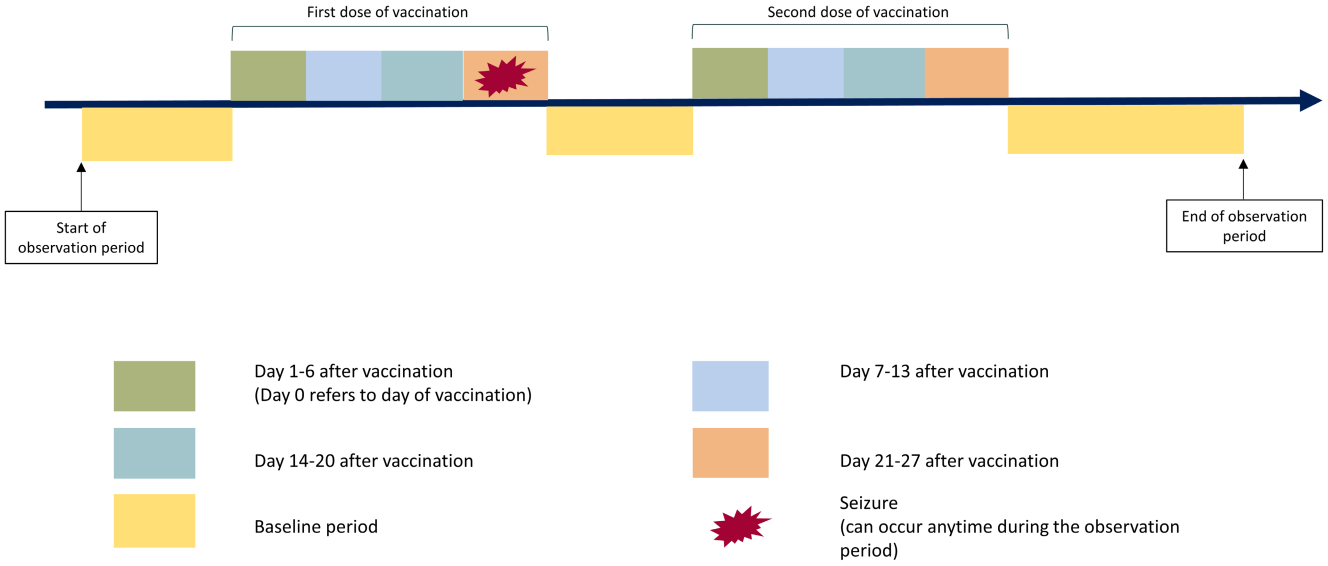

FIGURE 1 Graphical illustration of a single hypothetical patient in the self-controlled case-series analysis. This figure shows the study design and timeline for a single hypothetical participant.

observation at different times, namely, (1) on January 31, 2022 (regardless of if the patients received the booster dose), (2) 4 months after the latest dose, and (3) the day before the booster dose.

All statistical tests were two sided and p-values $< .05$ were considered significant. At least two investigators (EYFW, VWSN, and VKCY) conducted each of the statistical analyses independently for quality assurance using R version 4.0.3.

3 | RESULTS

After excluding (1) 137 people with different vaccine types between the first and second doses, (2) 32 868 people with second or booster dose record but without first dose record, and (3) 27 people with inconsistent duplicated records, a total of 3 275 244 individuals have been recorded to have received their first dose of BNT162b2 between March 6, 2021 and January 31, 2022, of which 3 006 037 (91.8%) individuals received both doses of BNT162b2, whereas 2 046 986 individuals have been recorded to have received their first dose of CoronaVac between February 23, 2021 and January 31, 2022, of which 1 779 573 (86.9%) individuals received both doses of CoronaVac. There were 6 311 083 doses of BNT162b2 and 3 855 953 doses of CoronaVac administered as first or second doses.

A total of 1656 patients who had their incident seizure in the inpatient setting were included in the analysis (Figure 2). Of these, 426 and 263 received at least one dose of BNT162b2 and CoronaVac, respectively. Three hundred forty-four of BNT162b2 recipients and 205 of CoronaVac recipients were vaccinated with two doses. The incidence of seizure was 1.04 (95% CI .80–1.33) and 1.11 (95% CI .80–1.50) per 100 000 doses of BNT162b2 and CoronaVac administered, respectively. The incidence rate of seizure was .042 (95% CI .032–.054) per 100 000 person-days for BNT162b2 and .041 (95% CI: .029–.055) per 100 000 person-days for CoronaVac. Patients who were vaccinated with BNT162b2 were younger than those receiving CoronaVac vaccinations (BNT162b2: 40.5 years; CoronaVac: 55.2 years). Figure 3 showed no pattern in the onset time of seizure after BNT162b2 and CoronaVac vaccinations. Among the patients who had seizure within 28 days after first dose of vaccination, 16 of 35 (45.7%) and 17 of 21 (81.0%) received a second dose of BNT162b2 and CoronaVac vaccinations, respectively. None of them had recurrent seizure within 28 days after receiving their second doses. Patients' demographics and baseline comorbidities were summarized in Table 1.

The main analysis indicated no association between both vaccines and the risk of seizures (Table 2). Compared to baseline periods, no increased risk was observed in any periods after each dose of BNT162b2 vaccinations. The magnitude of IRR gradually decreased after each dose. Similarly, no association was observed for CoronaVac and no specific pattern on the changes of IRR was identified. In our sensitivity analysis, an increased risk of seizure (IRR = 1.94, 95% CI 1.13–3.34) was observed during day 0–6 following the first dose of BNT162b2 vaccination after including the seizure cases that were recorded on day 0, whereas no association was detected for CoronaVac. Results of the sensitivity analyses remained robust and did not change the overall conclusion (Table S1).

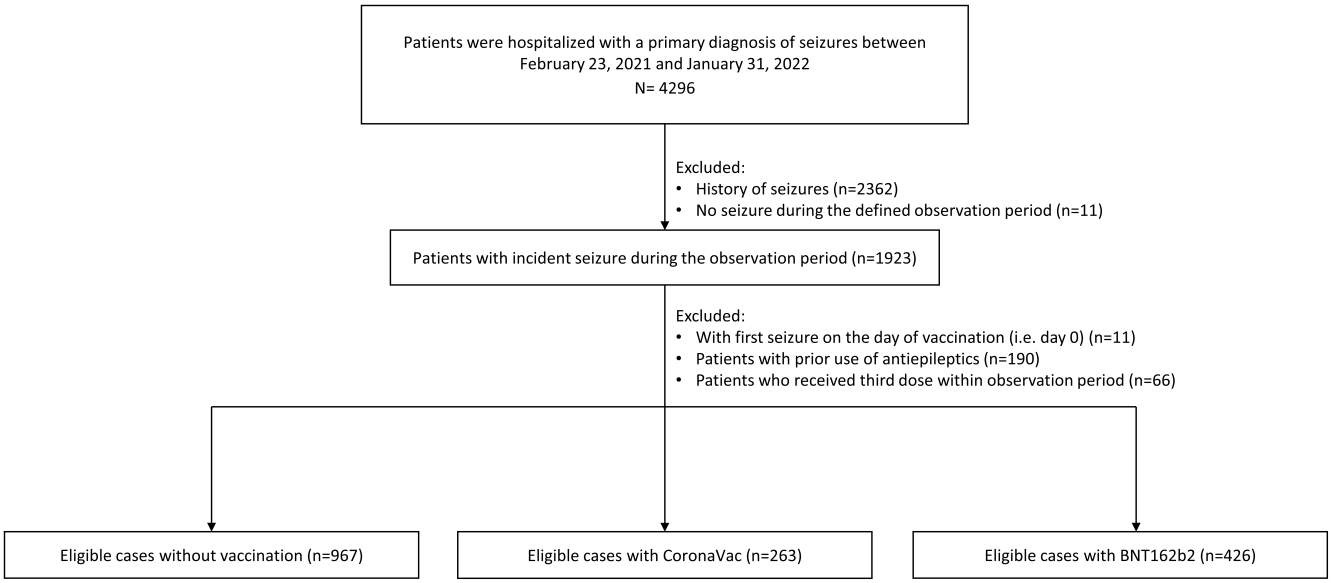

FIGURE 2 Flowchart of patient selection. This figure shows the selection process of individuals included in the self-controlled case-series analysis.

4 | DISCUSSION

In this population-based study, we did not observe an increased risk of seizures following COVID-19 vaccinations. A total of 45.7% of BNT162b2 recipients and 81.0% of CoronaVac recipients with an incident seizure within 28 days after their first dose of vaccination received their second doses. More important, none of them had another seizure within 28 days after the second dose. In addition to the low incidence rate of seizure in both vaccine groups, these descriptive statistics demonstrated the rarity of seizure among people after vaccination. Given the low absolute risk of seizure (~1 case per 100 000 doses) after vaccination, the increase in absolute risk should be very small, even if the relative risks were statistically significant. The incidence rates of seizure of both BNT162b2 and CoronaVac vaccines were similar and it is likely to be the background rate of having seizure among the general public, suggesting that COVID-19 vaccinations might not trigger seizures. Findings from this present study could provide real-world evidence of the safety of COVID-19 vaccines and improve the vaccination hesitancy, especially for individuals who are concerned about the adverse events of the vaccines. In the view of current situation of COVID-19 pandemic leading to far-reaching complications and deaths,[36] benefits of vaccination still outweigh its risks.

Neurological complications following COVID-19 vaccinations are rare. Most of the current evidence were limited to case reports.[8,9] Only one analytical study using the Israeli population examined the risk of seizure following BNT162b2 vaccination and showed no increased risk with the vaccination,[10] but the authors acknowledged that their results may be affected by confounding at baseline. Our findings strengthen the evidence by addressing this potential bias using within-individual comparison study design. The current evidence from the randomized clinical trials of CoronaVac vaccines cannot draw a concrete conclusion due to an insufficient number of events. An interim analysis of a randomized clinical trial in Turkey reported that only one person presented with a seizure 43 days after the second dose of CoronaVac vaccination, but confirmed that it was due to the recent diagnosis of brain cancer and probably unrelated to the vaccine.[6] Another randomized clinical trial in China did not report any occurrence of seizures in the participants who were vaccinated with CoronaVac.[37] Our study is the first analytical study adding to the existing evidence that no association between CoronaVac vaccination and the risk of seizure was detected. In terms of the biological mechanism, no biological pathway has yet been proposed on how the mRNA lipo-nanoparticle or the inactivated virus may provoke seizures. Our findings were consistent with the current literature from epidemiological and mechanistic perspectives. Some prior studies showed a positive association of febrile seizures following the administration of non–COVID-19 vaccines (e.g., inactivated or live attenuated virus vaccines) but the studies were limited to only toddlers and children.[2,3] Only seven children or adolescents had seizure within 28 days after COVID-19 vaccinations in our study. Such a small number of seizures could not shed light on the potential association between the risk of seizure and COVID-19 vaccines among children

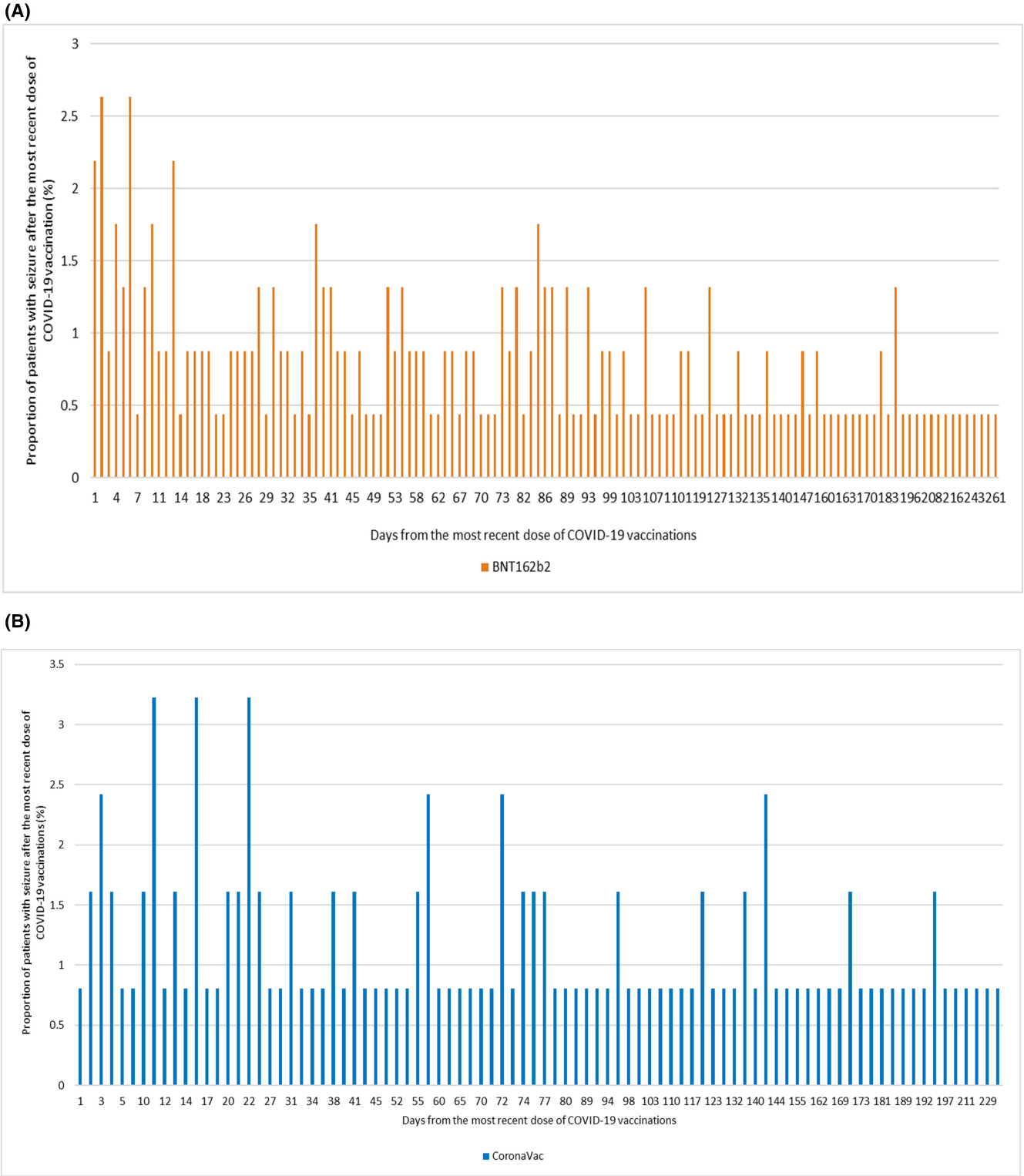

FIGURE 3 (A) Distribution of the onset time of seizure after BNT162b2 vaccination. This figure shows the pattern of the distribution of onset of seizure-related hospitalization after BNT162b2 vaccination. (B) Distribution of the onset time of seizure after CoronaVac vaccination. This figure shows the pattern of the distribution of onset of seizure-related hospitalization after CoronaVac vaccination.

and adolescents. At the time of the writing, the government of HKSAR has not yet approved vaccination for children younger than 3 years of age, so our findings could not be generalizable to younger populations. Further studies with larger sample sizes will be warranted to examine the risk of seizure in children and adolescents, as they might have a more active immune system than adults and are more prone to febrile seizures.

TABLE 1 Baseline characteristics of patients included

Characteristics	BNT162b2 (*N* = 426)	CoronaVac (*N* = 263)
Age, mean (SD)	40.5 (20.2)	55.2 (19.8)
Male, no. (%)	245 (57.5)	153 (58.2)
Comorbidities, n (%)		
Diabetes mellitus	18 (4.2)	29 (11.0)
Hypertension	42 (9.9)	54 (20.5)
Atrial fibrillation	18 (4.2)	13 (4.9)
Stroke or systemic embolism	14 (3.3)	14 (5.3)
Coronary artery disease	10 (2.4)	12 (4.6)
Asthma	5 (1.2)	1 (.4)
Chronic obstructive pulmonary disease	6 (1.4)	3 (1.1)
Dementia	0 (.0)	5 (1.9)
Mood disorder	37 (8.7)	44 (16.7)
Substance abuse	6 (1.4)	13 (4.9)
Brain infections	4 (.9)	0 (.0)
Concurrent medications, n (%)		
Antihypertensive drugs	52 (12.2)	78 (29.7)
Lipid modifying drugs	43 (10.1)	59 (22.4)
Diuretics	8 (1.9)	8 (3.0)
Antidiabetic drugs	18 (4.2)	28 (10.7)
Antidepressants	21 (4.9)	28 (10.7)
Antipsychotics	24 (5.6)	23 (8.8)
Hypnotics and anxiolytics	27 (6.3)	21 (8.0)

Abbreviation: SD, standard deviation.

TABLE 2 Results of self-controlled case series analysis

Risk periods	No. of events	Person-years	IRR[a] (95% CI)
BNT162b2 (n = 1393)			
After first dose			
1 to 6 days[b]	15	8.11	1.39 (.75–2.58)
7 to 13 days	14	7.89	1.29 (.62–2.67)
14 to 20 days	4	7.65	.32 (.10–1.03)
21 to 27 days	2	2.30	.89 (.22–3.67)
After second dose			
1 to 6 days[b]	11	6.56	1.36 (.72–2.57)
7 to 13 days	3	6.42	.36 (.11–1.16)
14 to 20 days	6	6.32	.72 (.31–1.69)
21 to 27 days	7	6.20	.83 (.39–1.77)
Baseline	1331	1256.70	
CoronaVac (n = 1230)			
After first dose			
1 to 6 days[b]	6	5.00	1.19 (.50–2.83)
7 to 13 days	4	4.79	.78 (.28–2.17)
14 to 20 days	7	4.59	1.38 (.61–3.09)
21 to 27 days	4	4.30	.90 (.32–2.55)
After second dose			
1 to 6 days[b]	3	3.90	.71 (.22–2.30)
7 to 13 days	6	3.86	1.43 (.61–3.34)
14 to 20 days	2	3.72	.48 (.11–1.99)
21 to 27 days	5	3.55	1.17 (.47–2.94)
Baseline	1193	1121.35	

Abbreviation: CI, confidence interval; IRR, incidence rate ratio.

[a]IRR was conducted by conditional Poisson regression and adjusted with seasonal effect.

[b]Day 0 was defined as the day of vaccination and excluded from the analysis.

In our validation analysis, the PPV of seizure cases was very low on day 0. It reported that the majority of the misclassified cases that happened rapidly (ranging from minutes to hours) after the COVID-19 vaccination were vasovagal syncopal episodes, with or without convulsion. Syncope is one of the manifestations of immunization-related stress response that occurs commonly in individuals who developed blood–injury–injection phobia or anxiety before vaccination as defined by WHO.[38] Patients with vasovagal reactions may present with tonic–clonic like movements that are often mistaken for epileptic seizures, potentially leading to vaccine hesitancy, especially when it occurs after the first dose.[39] Furthermore, there was a differential incidence of syncope between BNT162b2 recipients and CoronaVac recipients. This could be possibly due to the previous debate on the safety profile and the efficacy of the BNT162b2 vaccines using the new mRNA technology. We conducted a sensitivity analysis of including all cases with an ICD-9-CM code of seizure occurring on day 0. The results showed an increased risk during days 0–6 after the first dose of BNT162b2, whereas no association was observed with CoronaVac vaccination. Compared to the main analysis, where we excluded cases on day 0, the "increased" risk was no longer observed, suggesting that the inclusion of cases on day 0 artificially inflated the risk. Therefore, it is likely that the "increased risk" was driven mainly by syncope rather than seizure. Our main analysis also showed that the onset of seizure was unlikely to be related to the vaccine itself. Furthermore, caution should be taken in evaluating the validity of the seizure diagnosis, especially on day 0, to avoid overestimation when evaluating vaccine safety in the future.

There are some notable strengths in our study. First, we conducted a validation analysis of seizure cases following the COVID-19 vaccination in Hong Kong by local hospital specialists. The validity of the ICD-9-CM codes of seizure was low on day 0 and the PPV increased to more than 80% after excluding the cases that occurred on day 0. Therefore, the outcome misclassification is unlikely after excluding the cases on the day 0. Second, some of

the confounders that are underlying risk factors of seizure might not be available in the database and hence bias the results, such as genetic factors, family history of epilepsy, and socioeconomic status. With the use of modified SCCS, all measured and unmeasured time-invariant confounders were controlled implicitly and, therefore, prevent bias from the results.

Our study had some limitations. Although a considerable number of patients who had seizure-related hospitalization was included in the analysis, the observed negative findings might be due partially to limited sample leading to underpowered statistics. Our study population consists predominantly of Chinese so we could not eliminate the possibility of genetic differences leading to different responses to the vaccines. Furthermore, only incident seizure-related hospitalization was considered as the outcome of interest in our study. Therefore, those with mild forms of seizures (e.g. focal seizures) who were not hospitalized and sought medical consultation at outpatient clinics might not be captured. Further studies with a larger sample in different populations will be warranted to ensure the generalizability of our findings. Because the observation period of our study covered only up to the second dose at the time of writing, the possibility of subsequent booster doses affecting the risk of seizure could not be eliminated. Future studies on subsequent booster doses will also be warranted.

5 | CONCLUSION

We did not observe an increased risk of seizures observed following either BNT162b2 or CoronaVac vaccinations. Our study provides reassurance to the public and hopefully enhances their confidence in the vaccination program. Future studies are warranted in assessing the risk of seizure following COVID-19 vaccinations in different populations with subsequent doses, especially young people and different ethnicities.

AUTHOR CONTRIBUTIONS

EYFW, VWSN, and ICKW had the original idea for the study; contributed to the development of the study; extracted data from the source database; constructed the study design and the statistical model; reviewed the literature; and act as guarantors for the study. EYFW, VWSN, and VKCY conducted statistical analysis. EYFW, VWSN, and ICKW wrote the first draft of the manuscript. ICKW is the principal investigator and provided oversight for all aspects of this project. EYFW, VWSN, RSKC, VKCY, CSLC, CKHW, FTTL, XL, EWYC, IFNH, KKL, and ICKW provided critical input to the analyses, design, and discussion. All authors contributed to the interpretation of the analysis, critically reviewed and revised the manuscript, and approved the final manuscript as submitted.

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CONFLICT OF INTEREST

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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