Risk of glomerular diseases, proteinuria and hematuria following mRNA (BNT162b2) and inactivated (CoronaVac) SARS-CoV-2 vaccines

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ABSTRACT

Background. With accruing case reports on de novo or relapsing glomerular diseases (GD) following different SARS-CoV-2 vaccines, we evaluated the risk of GD following BNT162b2 and CoronaVac vaccines.

Methods. A modified self-controlled case series analysis was conducted using anonymized, territory-wide SARS-CoV-2 vaccination records in Hong Kong. All Hong Kong residents aged 18 years or above with outcomes of interest were included. Outcomes of interest were GD, proteinuria, or hematuria within 42 days following each dose of SARS-CoV-2 vaccines. Incidence per 100,000 doses of SARS-CoV-2 vaccines administered was calculated, and incidence rate ratios (IRRs) were estimated using conditional Poisson regression with seasonality adjustment.

Results. Between 23rd February 2021 and 31st March 2022, 4,062 patients had an incident diagnosis of GD, proteinuria, or hematuria with 2,873 of them being vaccinated during the observation period. The incidence of the composite events 1-41 days after vaccination were 3.7 (95% CI: 3.1-4.4) per 100,000 doses of BNT162b2 administered, and 6.5 (95% CI: 5.7-7.5) per 100,000 doses CoronaVac administered. There was no significant increase in the risks of composite events following the first (BNT162b2: IRR = 0.76, 95% CI: 0.56-1.03; CoronaVac: IRR = 0.92, 95% CI 0.72-1.19), second (BNT162b2: IRR = 0.92, 95% CI 0.72-1.17; CoronaVac: IRR = 0.88, 95% CI 0.68-1.14) or third (BNT162b2: IRR = 0.39, 95% CI 0.15-1.03; CoronaVac: IRR = 1.18, 95% CI 0.53-2.63) dose of SARS-CoV-2 vaccines.

Conclusions. There was no evidence of increased risks of de novo or relapsing GD with either BNT162b2 or CoronaVac vaccines.

Keywords: COVID-19, glomerular diseases, hematuria, proteinuria
KEY LEARNING POINTS

What is already known about this subject?
- Since the widespread rollout of SARS-CoV-2 vaccination programs, there is an increasing number of case reports published for de novo or relapse of different glomerular diseases.
- To date, the association between COVID-19 vaccines and glomerular diseases remained unclear.

What this study adds?
- Current population-based pharmacovigilance study revealed no increased risks of de novo or relapsing glomerular diseases after BNT162b2 or CoronaVac vaccines.

What impact this may have on practice or policy?
- Real-world pharmacovigilance studies should be continued to provide more robust evidence on the association between glomerular diseases and COVID-19 vaccines.
INTRODUCTION
Since the coronavirus disease (COVID-19) outbreak due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in early 2020, tremendous efforts have been placed on preventive vaccination. Several types of vaccines are approved for emergency use for immunization against the SARS-CoV-2 virus, and population-based vaccination campaigns have been promoted across the globe within a short period since the World Health Organization's declaration of the pandemic. A nationwide safety analysis of BNT162b2 in Israel demonstrated a reduced risk of acute kidney injury (AKI) after vaccination, plausibly due to protection against undiagnosed COVID-19. On the contrary, there is an increasing number of case reports published for de novo or relapse of different glomerular diseases (GD) since the widespread rollout of SARS-CoV-2 vaccination programs across the globe. These case reports include antineutrophil cytoplasmic antibodies associated with vasculitis and nephritis, crescentic glomerulonephritis, membranous nephropathy, anti-glomerular basement membrane nephritis, IgA vasculitis and nephritis, minimal change disease (MCD), IgG4 related nephritis, and lupus nephritis. Furthermore, 14% of patients with urologic side effects reported hematuria post-SARS-CoV-2 mRNA vaccines in the US Vaccine Adverse Event Reporting System (VAERS). Among the published cases, BNT162b2 appeared to be the most frequent vaccine preceding GD.

In Hong Kong Special Administrative Region, China, a territory-wide vaccination program with BNT162b2 (Comirnaty, BioNTech/Pfizer/Fosun) and CoronaVac (Sinovac Life Sciences) commenced on 6th March and 23rd February 2021, respectively. BNT162b2 vaccine was the first SARS-CoV-2 mRNA vaccine approved by the US Food and Drug Administration (FDA), while CoronaVac is an inactivated whole-virion SARS-CoV-2 vaccine using the adjuvant aluminium hydroxide. The Department of Health of Hong Kong received spontaneous reports of nephropathy following SARS-CoV-2 vaccination. Hence, the regulatory-initiated pharmacovigilance programme (The COVID-19 Vaccines Adverse Events Response and Evaluation (CARE)) conducted this population-based, retrospective study to evaluate and compare the incidences of GD, proteinuria and hematuria following SARS-CoV-2 vaccines.

MATERIALS AND METHODS
Data Source
Anonymised, territory-wide SARS-CoV-2 vaccination records obtained from the Department of Health (the Government agency responsible for overseeing the implementation of mass vaccination in Hong Kong) and electronic medical records retrieved from the Hong Kong Hospital Authority (HA) were linked using a unique de-identified mapping key. HA is a statutory body serving as a major publicly funded healthcare provider and sole publicly funded acute care provider. It manages all publicly-funded hospitals, specialist out-patient clinics, general out-patient clinics and emergency rooms in Hong Kong with hospitalization coverage of more than 70%. All Hong Kong residents are eligible to have publicly subsidized healthcare services provided by the HA. The centralized electronic medical records from HA included patient demographics, date of registered death, drug dispensing records, diagnoses, procedures, and laboratory tests and have previously been used to evaluate drug safety and epidemiological studies. The two linked data sources have also been extensively used for SARS-CoV-2 vaccine safety research including Bell's palsy, myocarditis, thromboembolic events, herpes zoster and safety in vulnerable groups of subjects.
**Study design**

A modified self-controlled case series (SCCS) design was used to investigate the risk of GD, proteinuria or hematuria following BNT162b2 and CoronaVac from 23rd February 2021 to 31st March 2022 (i.e. from the first day of CoronaVac available to the public to the end of the study period).

SCCS is a within-individual study design that was developed specifically for assessing vaccine safety and has been widely used in vaccine safety monitoring for outcomes such as thromboembolic events, hematological disorders and herpes zoster-related hospitalization. The SCCS compares the incidence of outcomes in the exposure period to the non-exposure period within an individual and the time-invariant covariates (e.g. socioeconomic and genetic) are therefore inherently controlled and the time-varying covariates can be adjusted (age and seasonal effect).

Since the outcome event that occurred before vaccination could affect the subsequent exposures, we applied a modified SCCS extension, developed for event-dependent exposure. This inclusion in the modified SCCS is essential because the lack of vaccination records may indicate cancellation of vaccination appointments, and may tend to occur more often for earlier events (before they had the opportunity to be vaccinated). Thus, the absence of vaccination will be informative regarding the timing of the event, and it is important to note that these unvaccinated patients did not act as controls. A comprehensive discussion on the modified SCCS for SARS-CoV-2 vaccine research can be found in a recent publication.

**Cohort identification**

All Hong Kong residents aged 18 years or above with outcomes of interest who had used any HA services between 1st January 2018 and 31st March 2022 were identified. We used the first event in the study period and excluded patients with outcomes of interest before the 23rd February 2021. Patients who received heterologous SARS-CoV-2 vaccines or who were diagnosed with COVID-19 infection before 31st March 2022 were also excluded from the analysis. In order to evaluate the risk of relapsing GD, a secondary analysis was conducted by limiting patients with a diagnosis of GD before 23rd February 2021.

**Exposure**

Unlike standard SCCS, the modified SCCS model includes non-vaccinated people with the outcomes of interest during the observation period to inform the timing of the events by adjusting for the monthly seasonal effects. Three risk periods, which were 1-41 days after the first, second and third dose, respectively, were evaluated in the SCCS analysis. The duration of the risk period was chosen because a systematic review reported that the onset of acute kidney complications ranged from 1 to 37 days after vaccination. Day 0 was considered as a separate risk period to ensure it is not included in the baseline and to avoid event misclassifications. The rest of the period from 23rd February 2021 to 31st March 2022 was defined as baseline periods. A schematic presentation of the SCCS design is shown in Figure 1.

**Outcomes**

The outcome of interest was a composite of GD using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) (447.6, 580.x, 581.x, 582.x, 583.x), proteinuria (ICD-9-CM: 791.0) and hematuria (ICD-9-CM: 599.7). The ICD-9-CM codes chosen include both proliferative (such as AAV or IgAN) and non-proliferative (such as MCD membranous nephropathy) forms of GD. Proteinuria and hematuria were also
chosen as surrogate markers as they are prevalent for various kidney histopathology. We used principal inpatient diagnoses and the earliest date of hospital admission as the event date. Patients with diagnoses other than GD, proteinuria or hematuria on the same day were excluded to minimize the bias due to misclassification.

**Sample size**
As there was no trial conducted to examine the risk of GD post-SARS-CoV-2 vaccination, a relative risk of 1.1-3.0 was assumed, 48-9,824 events were required to achieve 80% power at a 0.05 significance level for SCCS analysis with an observation period of 402 days and vaccination coverage of 90%. A detailed sample size calculation for SCCS analysis is provided in Supplementary Figure 1.

**Statistical analysis**
The incidence of outcomes following SARS-CoV-2 vaccination (cases per 100,000 doses of vaccine) were estimated. Conditional Poisson regression was used to estimate the incidence rate ratio (IRR) and its corresponding 95% confidence interval by comparing the incidence rates of outcomes of interest in different risk periods versus the baseline period. We applied the modified SCCS for event-dependent exposure analysis using the function "eventdepenexp" in the R-package "SCCS" which is designed for the situation where the assumption that the occurrence of an event does not influence subsequent exposures might be violated.

Separate analyses were conducted for each outcome of interest. Subgroup analyses were also conducted for age <65 and age ≥ 65, sex and diabetes status. Two sensitivity analyses were performed to assess the robustness of this study by 1) varying the duration of risk periods from 14 to 98 days after vaccination and; 2) including day 0 in the primary analysis.

All statistical tests were two-sided and p-values of less than 0.05 were considered significant. Statistical analysis was considered using R version 4.1.2 and SAS version 9.4 for Windows (SAS Institute, Inc, Cary, NC). At least two investigators (FWTC, XWQ or CHA) independently performed the statistical analyses for quality assurance.

**Ethics approval**
Ethical approval for this study was granted by the Institutional Review Board of the University of HK/HA HK West Cluster (UW21-149 and UW21-138) and the Department of Health Ethics Committee (LM 21/2021).

**RESULTS**
A total of 3,465,434 people were identified from the electronic medical database after excluding people who never used HA services, were aged below 18 years, were infected with COVID-19 or received heterologous vaccines. Among them, 1,635,257 and 1,289,081 individuals received the first dose of BNT162b2 and CoronaVac, respectively. 1,557,974 (95.3%) and 1,133,547 (87.9%) individuals completed the two doses of BNT162b2 and CoronaVac respectively. 751,538 (46.0%) received BNT162b2 as booster while 509,577 (39.5%) received CoronaVac as booster.

There were a total of 6,304 composite events between 23rd February 2021 and 31st March 2022. Among them, 4,062 events were incident diagnoses without any other diagnoses and 2,873 cases were vaccinated during the observation period. 147 (3.6%, out of 4,062) and 192 (4.7%) of the incident events occurred within 1-41 days after BNT162b2 and CoronaVac
vaccination, respectively. The crude incidence was 3.7 events (95% CI: 3.1-4.4) per 100,000 doses administered for BNT162b2 recipients, and 6.5 (95% CI: 5.7-7.5) events per 100,000 doses administered for CoronaVac recipients within 1-41 days. The median time to events following vaccination was 19.5 days (IQR: 7.75-33.25) for BNT162b2 and 19 days (IQR:11-28.5) for CoronaVac. Figure 2 summarizes the selection flow in the analysis, and the baseline characteristics of these patients are summarized in Table 1.

Table 2 shows the IRRs of the composite events following the SARS-CoV-2 vaccination. Compared to the baseline period, no increased risk of GD, proteinuria or hematuria was observed in any risk period for both BNT162b2 (IRR: 1st dose: 0.76 (0.56-1.03); 2nd dose: 0.92 (0.72-1.17); 3rd dose:0.39 (0.15-1.03)) and CoronaVac (IRR: 1st dose: 0.92 (0.72-1.19); 2nd dose: 0.88 (0.68-1.14; 3rd dose: 1.18 (0.53-2.63)). Subgroup analyses by age, sex and diabetes status were similar to the primary analysis. Concerning the risk of relapsing GD, no increased risk was observed after SARS-CoV-2 vaccination and the results are summarized in Table 4.

Sensitivity analyses with various risk periods demonstrated consistent findings (Supplementary Table 1) in both vaccines. The results were also consistent after taking day 0 into the risk period (Supplementary Table 2).

**DISCUSSION**

To the best of our knowledge, this is the first population-based study using the SCCS method to examine the risk of GD, proteinuria and hematuria after SARS-CoV-2 vaccinations. The current study did not identify any increased risk of de novo or relapsing GD, proteinuria or hematuria after BNT162b2 or CoronaVac vaccination. Our findings suggested that the absolute risk of GD, proteinuria and hematuria is low following SARS-CoV-2 vaccination and lower than the risk of AKI reported in the literature, a known complication, following COVID-19 infection. 

Despite plenty of case reports of GD after SARS-CoV-2 vaccines, the causal association between them remains to be confirmed. The pathophysiology of GD following the SARS-CoV-2 vaccine has been speculated to be dysregulated T-cell-mediated immunity in MCD and enhanced antibody production in IgA nephropathy. Other mechanisms, including autoimmunity due to molecular mimicry or bystander activation, have also been proposed in various kidney injuries. It should however be noted that other than vaccines, medications, infections, autoimmune diseases, malignancies, and allergens have been reported to be associated with various types of GD.

Our finding is consistent with the observation from Caza et al. They identified 29 patients with biopsy-proven GD who were recently vaccinated. It appeared that there was no overall increase in the incidence of GD when compared to the historical data in their practice. On the contrary, our result is different from the nationwide analysis of BNT162b2 vaccination in Israel, which only reported 20 AKI events out of 912,019 vaccinated individuals. In the Israel study, ICD-9-CM codes for acute renal failure (584.5, 584.6, 584.7, 584.8 and 584.9) were used to monitor the potential adverse events following vaccination. However, a prior study has shown that the sensitivity for AKI is low for these ICD-9-CM codes and may therefore underestimate the incidence of AKI.

Apart from using the ICD-9-CM code for GD, proteinuria and hematuria were also included as surrogate markers of GD. Wu et al. summarized that proteinuria and hematuria were
prevalent for various kidney histopathology. Urine protein ≥ 1g/day was present in 58.0% of reported cases with MCD, 35.7% with IgA nephropathy and 40% with vasculitis. Similarly, hematuria was found in 21.1% of patients diagnosed with MCD, 85.7% with IgA nephropathy and 70% with vasculitis. Hence, including these two parameters can minimize the potential under-reporting of GD by diagnostic codes alone. The results from sensitivity analyses were consistent with the primary findings, indicating that the risk of GD is minimal from a clinical perspective.

Precise information about the timing of event onset is critical in SCCS as cases with delayed diagnosis may be mapped to the baseline period by mistake. As a result, we conducted a sensitivity analysis by varying the duration of the risk period from 14 days to 98 days to examine the effects of delayed diagnosis and did not reveal an increased risk during this period of time. As for the time lag due to diagnostic workup, the date of hospitalization was used as the event date instead of the date of diagnosis. Thus, the delay due to diagnostic workup would be minimal in our study.

There are several limitations in the current study. Firstly, similar to other large database pharmacovigilance studies, the detailed results of kidney biopsy and the aetiology of kidney complications were not available in our data source. Some of the acute nephropathies were not coded in ICD-9-CM, which might introduce misclassification bias due to under-captured events. With proteinuria and hematuria as surrogate markers, the potential misclassification bias could be minimized. Nevertheless, the misclassification bias due to under-reporting should not affect our interpretation of the results because only patients with diagnosis codes of interest are included in SCCS. Secondly, our current sample size may not be sufficient to detect an incidence rate ratio of 1.2 or less. However, given the small absolute risk of the outcomes, based on current published information on the safety and effectiveness of vaccination, the benefit of vaccination outweighs the risk of GD, proteinuria or hematuria. Thirdly, despite the global interest in heterologous vaccination, our current analysis could not elucidate its effect on GD, proteinuria or hematuria because of the limited sample size. Further analysis would be conducted with the increasing uptake of heterologous vaccines as booster doses.

In conclusion, the current study found no evidence of increased risks of de novo or relapsing GD after BNT162b2 or CoronaVac vaccination for individuals without COVID-19 infection. Being the first SCCS study evaluating the impact of SARS-CoV-2 vaccines on the risk of GD, further studies are warranted to confirm our findings.

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CONFLICT OF INTEREST STATEMENT
FWTC, SXQ and CHA declare that there is no conflict of interest. CKHW reports the receipt of General Research Fund, Research Grant Council, Government of Hong Kong SAR; EuroQol Research Foundation, all outside the submitted work. CSLC has received grants from the Food and Health Bureau of the Hong Kong Government, Hong Kong Research Grant Council, Hong Kong Innovation and Technology Commission, Pfizer, IQVIA, and Amgen; personal fees from Primevigilance Ltd.; outside the submitted work. FTTL has been supported by the RGC Postdoctoral Fellowship under the Hong Kong Research Grants
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AUTHORS’ CONTRIBUTIONS
FWTC, SXQ, CKHW, SCWT 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. FWTC, SXQ and CHA undertook the statistical analysis. FWTC, SXQ and CKHW wrote the first draft of the manuscript. ICKW is the principal investigator and provided oversight for all aspects of this project. CSLC, FTTL, XL, EYFW, EWYC and SCWT 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. FWTC, SXQ, CKHW and ICKW have accessed and verified the data used in the study. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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DATA AVAILABILITY STATEMENT
Data will not be available for others as the data custodians have not given permission.
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Figure 1 Observation timeline of a hypothetical patient in the modified self-controlled case series

- Risk period – day of vaccination
- Risk period – 1 to 41 days of vaccination
- Baseline period
Figure 2 Inclusion and exclusion criteria for modified self-controlled case series analysis of people from 23rd February 2021 to 31st March 2022 in Hong Kong SAR, China.

- Unvaccinated patients during the observation period were included to inform the timing of events by adjusting for the monthly seasonal effects. These unvaccinated patients did not act as controls.
Table 1 Characteristics of patients with nephritis receiving BNT162b2 or CoronaVac vaccination during the observation period in the self-controlled case series studies

|                          | BNT162b2 | CoronaVac |
|--------------------------|----------|-----------|
| N                        | 1133     | 1740      |
| Sex, male (%)            | 721 (63.6) | 1105 (63.5) |
| Age, years (mean (SD))   | 61.50 (16.83) | 70.57 (14.50) |
| Asthma (%)                | 7 (0.6) | 19 (1.1) |
| Chronic pain (%)         | 35 (3.1) | 48 (2.8) |
| Chronic pulmonary disease (%) | 17 (1.5) | 58 (3.3) |
| Cirrhosis (%)             | 2 (0.2) | 7 (0.4) |
| Dementia (%)              | 9 (0.8) | 47 (2.7) |
| Depression (%)            | 24 (2.1) | 25 (1.4) |
| Type 2 diabetes (%)       | 161 (14.2) | 311 (17.9) |
| Hypertension (%)          | 350 (30.9) | 730 (42.0) |
| Hypothyroidism (%)        | 13 (1.1) | 30 (1.7) |
| Inflammatory bowel disease (%) | 0 (0.0) | 0 (0.0) |
| Irritable bowel syndrome (%) | 2 (0.2) | 4 (0.2) |
| Parkinson's disease (%)   | 2 (0.2) | 20 (1.1) |
| Peptic ulcer disease (%)  | 9 (0.8) | 20 (1.1) |
| Peripheral vascular disease (%) | 2 (0.2) | 0 (0.0) |
| Psoriasis (%)             | 1 (0.1) | 1 (0.1) |
| Rheumatoid arthritis (%)  | 10 (0.9) | 3 (0.2) |
| Schizophrenia (%)         | 1 (0.1) | 12 (0.7) |
| Malignancy (%)            | 27 (2.4) | 62 (3.6) |
| Medication use in previous 90 days |           |           |
| **Renin-angiotensin system agents** | 231 (20.4) | 451 (25.9) |
| **Beta blockers**         | 147 (13.0) | 275 (15.8) |
| **Calcium channel blockers** | 252 (22.2) | 553 (31.8) |
| **Diuretics**             | 63 (5.6) | 153 (8.8) |
| **Lipid-lowering agents** | 288 (25.4) | 567 (32.6) |
| **Insulins**              | 30 (2.6) | 69 (4.0) |
| **Antidiabetic medications** | 237 (20.9) | 417 (24.0) |
| **Glucocorticoids**       | 45 (4.0) | 59 (3.4) |
| **Immunosuppressants**    | 47 (4.1) | 36 (2.1) |
Table 2 Risks of glomerular diseases, proteinuria or hematuria following the first, second and doses of BNT162b2 or CoronaVac vaccination using the modified self-controlled case series

|                      | BNT162b2 |               |               |               | CoronaVac |               |               |               |               |               |               |               |
|----------------------|----------|---------------|---------------|---------------|-----------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|
|                      | Number   | person-year   | Event / person-year | IRR (95% CI) | p-value   | Number | person-year | Event / person-year | IRR (95% CI) | p-value   |
| Baseline             | 2,172    | 2341.75       | 0.93          | -             | -         | 2,735  | 2927.41     | 0.93          | -             | -         |
| Day 1-41 after 1st dose | 50       | 70.19         | 0.71          | 0.76 (0.56-1.03) | 0.073   | 85     | 133.53      | 0.64          | 0.92 (0.72-1.19) | 0.528   |
| Day 1-41 after 2nd dose | 89       | 104.03        | 0.86          | 0.92 (0.72-1.17) | 0.487   | 88     | 117.81      | 0.75          | 0.88 (0.68-1.14) | 0.324   |
| Day 1-41 after 3rd dose | 8        | 32.62         | 0.25          | 0.39 (0.15-1.03) | 0.058   | 19     | 35.40       | 0.54          | 1.18 (0.53-2.63) | 0.681   |

Note: CI = Confidence Interval, IRR = incidence rate ratio
## Table 3 Subgroup analysis of modified self-controlled case series

|                         | BNT162b2 |                      | CoronaVac |                      |
|-------------------------|----------|----------------------|----------|----------------------|
|                         | After 1<sup>st</sup> dose | After 2<sup>nd</sup> dose | After 1<sup>st</sup> dose | After 2<sup>nd</sup> dose |
|                         | Number of events | person-year | IRR (95% CI) | Number of events | person-year | IRR (95% CI) | Number of events | person-year | IRR (95% CI) | Number of events | person-year | IRR (95% CI) |
| **Overall**             | 0.76     | (0.56-1.03)         | 0.92     | (0.72-1.17)         | 0.39     | (0.15-1.03)         | 0.92     | (0.72-1.17)         | 0.39     | (0.15-1.03)         |
| Glomerular diseases     | 3        | 9.86                | -        | 14                   | 1.09     | (0.60-2.01)         | 1        | 3.25                | -        |                      |
| Proteinuria             | 1        | 4.27                | -        | 2                    | 1.18     | (0.32-3.76)         | -        |                      | -        |                      |
| Hematuria               | 46       | 56.12               | 0.88     | (0.64-1.21)          | 0.85     | (0.57-1.27)         | 6        | 28.18               | 0.32     | (0.10-1.04)         |
|                         |          |                     |          |                      |          |                      |          |                      |          |                      |
| **Age**                 |          |                     |          |                      |          |                      |          |                      |          |                      |
| Age ≥ 65                | 25       | 33.33               | 0.79     | (0.51-1.22)          | 44       | 46.14               | 1.05     | (0.74-1.49)         | 3        | 14.57               | 0.25     | (0.07-0.92)         |
| Age < 65                | 25       | 36.87               | 0.71     | (0.46-1.11)          | 45       | 57.90               | 0.80     | (0.56-1.44)         | 5        | 18.05               | 1.38     | (0.11-17.67)        |
|                         |          |                     |          |                      |          |                      |          |                      |          |                      |
| **Sex**                 |          |                     |          |                      |          |                      |          |                      |          |                      |
| Male                    | 35       | 44.71               | 0.76     | (0.53-1.10)          | 55       | 67.01               | 0.83     | (0.61-1.25)         | 7        | 23.20               | 0.37     | (0.13-1.04)         |
| Female                  | 15       | 25.48               | 0.74     | (0.42-1.31)          | 34       | 37.02               | 1.09     | (0.71-1.66)         | 1        | 9.41                | -        |                      |
|                         |          |                     |          |                      |          |                      |          |                      |          |                      |
| **Diabetes status**     |          |                     |          |                      |          |                      |          |                      |          |                      |
| Yes                     | 8        | 7.66                | 1.35     | (0.58-3.11)          | 15       | 13.95               | 1.44     | (0.78-2.66)         | 0        | 4.42                | -        |                      |
| No                      | 42       | 60.53               | 0.70     | (0.51-0.98)          | 74       | 90.08               | 0.86     | (0.66-1.13)         | 8        | 27.99               | 0.38     | (0.14-1.01)         |
|                         |          |                     |          |                      |          |                      |          |                      |          |                      |
| **Note:** CI = Confidence Interval, IRR = incidence rate ratio
Table 4 Risks of relapse of glomerular diseases following the first, second and third doses of BNT162b2 or CoronaVac vaccination using the modified self-controlled case series

|                  | BNT162b2 | CoronaVac |
|------------------|----------|-----------|
|                  | Number of events | person-year | Event / person-year | IRR (95% CI) | p-value | Number of events | person-year | Event / person-year | IRR (95% CI) | p-value |
| Baseline         | 753      | 806.88    | 0.93         | -               | -        | 991          | 1050.51     | 0.94         | -               | -        |
| Day 1-41 after 1st dose | 7      | 15.70     | 0.45         | 0.43 (0.21-0.88) | 0.020    | 17           | 39.20       | 0.43         | 0.72 (0.39-1.32) | 0.289   |
| Day 1-41 after 2nd dose | 9      | 22.73     | 0.40         | 0.60 (0.29-1.25) | 0.175    | 14           | 29.31       | 0.48         | 0.70 (0.36-1.35) | 0.286   |
| Day 1-41 after 3rd dose | 6      | 6.11      | 0.98         | 1.09 (0.35-3.39) | 0.885    | 3            | 6.50        | 0.46         | 1.53 (0.32-7.36) | 0.596   |

Note: CI = Confidence Interval, IRR = incidence rate ratio