

# THE LANCET

## Healthy Longevity

### Supplementary appendix 2

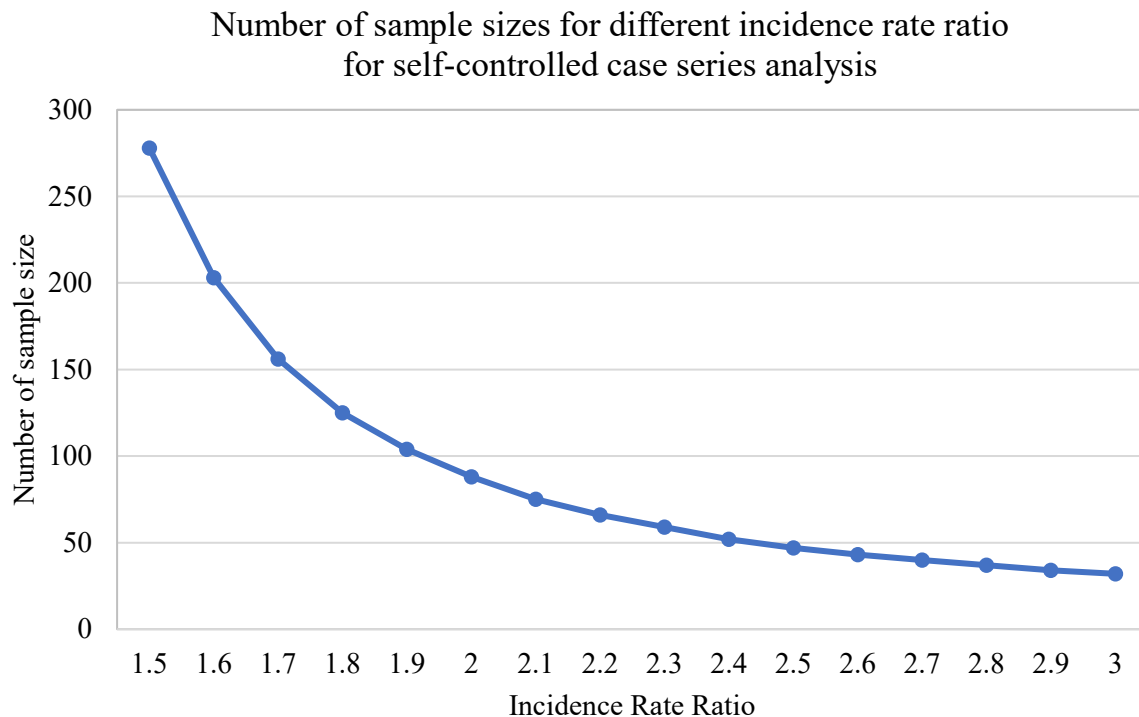
This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Wan EYF, Wang Y, Chui CSL, et al. Safety of an inactivated, whole-virion COVID-19 vaccine (CoronaVac) in people aged 60 years or older in Hong Kong: a modified self-controlled case series. *Lancet Healthy Longev* 2022; **3**: e491–500.

### **Supplementary information. The assumptions of SCCS analysis**

Theoretically, three assumptions have to be fulfilled when adopting the SCCS model<sup>1</sup>. The first assumption is that the outcome events occur and recur independently so that the likelihood of an event happening would not be affected by previous episodes. This assumption might have been violated in this study because some of the outcome events tend to recur or increase the likelihood of future episodes. To tackle this problem, only the first incidence of a specific AESI during the observation period was taken into consideration, and subsequent episodes in the same person during the study period were omitted<sup>1</sup>. The second assumption in the SCCS model is that the incidence of an outcome event does not affect the exposure. In this study evaluating vaccine safety, those with a history of any of the outcome events were less likely to get vaccinated. Hence, the inventors of SCCS strongly proposed to use a modified SCCS model to assess the COVID-19 vaccine safety<sup>2</sup>. The modified SCCS model was adopted to take into consideration that outcomes of interest would affect exposure<sup>2,3</sup>. Those who did not receive vaccination but experienced an outcome event were included in the modified SCCS model such that the probability of getting vaccinated in people with outcome events could be estimated<sup>2</sup>. This probability could be applied to adjust the association between vaccination and AESI. This modified SCCS model has been applied to evaluate COVID-19 vaccine safety<sup>2</sup>. The last assumption is that no outcome event is censored during the entire observation period. Therefore, we did not conduct censoring in the modified SCCS analysis, which means all patients included in the analysis would have an observation period from February 23, 2021 to January 31, 2022. Even death cases would not affect their observation period according to the design of modified SCCS analysis. Using the modified SCCS model, patients who died during the observation period could also be taken into account<sup>2</sup>.

## Supplementary Figure 1. Sample size calculation for self-controlled case series analysis



Remark: Previous studies showed that the risk ratio was 2.43 for lymphadenopathy; 1.40 for appendicitis; 3.24 for myocarditis;<sup>4</sup> the odds ratio was 2.39 for Bell's palsy<sup>5</sup>; 3.57 for carditis<sup>6</sup>; the incidence rate ratio was 1.93 for cardiac arrhythmia<sup>7</sup>; and the adjusted rate ratio was 1.48 for haemorrhagic disease<sup>8</sup>. We assumed the relative risk of all AESI from 1.5 to 3.0 in the exposure period of 21 days after first or second dose. According to the vaccination program in Hong Kong, the maximum observation periods is 342 days from Feb 23, 2021 to Jan 31, 2022 and the predefined risk period is 21 days in first or second dose. To achieve 80% power and detect the incidence rate ratio from 1.5 to 3.0 at 0.05 significant level, the required sample sizes for self-control case series ranging from 32 to 278. The blue points were sample sizes according to different risk ratio from 1.5 to 3.0 by 0.1. To the best of our knowledge, there is no published article on the approach of sample size estimation for modified SCCS. Therefore, we applied the standard SCCS sample size calculation as reference. The sample size calculation was conducted by R version 4.1.0 (R Foundation for Statistical Computing, Vienna, Austria)<sup>3,9,10</sup>.

### Reference

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**Supplementary Table 1. List of the definition of Adverse Events of Special Interest using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code**

| AESI                                       | ICD-9 codes  |
|--|--|
| Auto-immune diseases                       |  |
| Guillain-Barré Syndrome                    | 357.0  |
| Acute disseminated encephalomyelitis       | 323.6x, 323.8x   |
| Narcolepsy                                 | 347.xx, 89.17, 89.18, 307.4, 780.5   |
| Acute aseptic arthritis                    | 274.0x, 696.0x, 716.5x, 716.6x, 716.9x, 712.xx, 711.5x   |
| Type 1 Diabetes                            | 250.x1, 250.x3   |
| (Idiopathic) Thrombocytopenia              | 287.3x, 287.4x, 287.5, 279.12, 283.11, 284.1x, 446.6x, 776.1x  |
| Subacute thyroiditis                       | 245.1x   |
| Cardiovascular system diseases             |  |
| Microangiopathy                            | 446.6x   |
| Heart failure                              | 428.xx, 398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93   |
| Stress cardiomyopathy                      | 429.83   |
| Coronary artery disease                    | 410.xx-414.xx, V45.81, 36.0x, 36.1x  |
| Arrhythmia                                 | 427.xx, 426.xx, 624.x, 794.3x, 785.0x  |
| Myocarditis                                | 422.xx, 429.0x, 420.9x, 423.9x   |
| Circulatory system diseases                |  |
| Thromboembolism                            | 410.xx, 415.1x, 453.xx, 443.xx, 444.xx, 445.xx, 433.xx, 434.xx, 435.xx, 436.xx, 437.0x, 437.1x, 437.6x, 437.8x, 437.9x, 451.x, 452.x, 325.xx, 286.6x, 459.9x, 434.01, 557.0x, 557.9x, 453.40, 453.41, 453.42, 36.0x, 36.1x, 36.2x, 36.3x |
| Hemorrhagic disease                        | 286.5x, 286.7, 287.xx, 430.xx, 431.xx, 432.0x, 432.9x, 99.06   |
| Single Organ Cutaneous Vasculitis          | 709.1x, 446.2x, 287.0x   |
| Hepato-renal system diseases               |  |
| Acute liver injury                         | 570.xx, 573.3x   |
| Acute kidney injury                        | 584.xx, 586.xx   |
| Acute pancreatitis                         | 577.0x   |
| Nerves and central nervous system diseases |  |
| Generalized convulsion                     | 345.xx, 780.3x, 779.0x   |
| Meningoencephalitis                        | 322.9x, 323.0x, 323.4x, 323.5x, 323.6x, 323.8x, 323.9x, 323.7x, 330.8x, 337.73, 046.3x, 049.8x, 036.1x, 056.01, 136.2x, 130.xx, 054.3x, 049.0x, 094.1x, 072.2x, 013.0x, 062.4x, 049.9x, 045.0x, 062.xx                                   |
| Transverse myelitis                        | 323.0x, 323.4x, 323.5x, 323.6x, 323.8x, 341.2x   |
| Bell's Palsy                               | 351.0x, 351.8x, 351.9x   |
| Respiratory system disease                 |  |
| Acute respiratory distress syndrome        | 518.8x, 518.5x, 96.7x  |
| Skin, bone, and joints system diseases     |  |
| Erythema multiforme                        | 695.1x   |
| Chilblain – like lesions                   | 991.5x   |
| Other system diseases                      |  |
| Anaphylaxis                                | 995.0, 995.1, 995.3, 995.4, 999.4x 708.9, 519.11, 786.1, 458.9   |
| Anosmia, ageusia                           | 781.1x   |
| Kawasaki disease                           | 446.1x   |
| Rhabdomyolysis                             | 728.88, 728.89, 791.3  |

**Supplementary Table 2. Pre-existing comorbidities and medication use of the patients receiving CoronaVac vaccination**

|   | <b>Overall</b> | <b>CoronaVac recipients with 1 dose</b> | <b>CoronaVac recipients with 2 doses</b> | <b>CoronaVac recipients with 3 doses</b> |
|---|----------------|---|--|--|
| Number  | 622317         | 126736                                  | 384056                                   | 111525                                   |
| <b><i>Pre-existing comorbidities</i></b>                          |                |   |  |  |
| Hypertension (%)  | 244739 (39.3)  | 59230 (46.7)                            | 149596 (39.0)                            | 35913 (32.2)                             |
| Diabetes (%)  | 118514 (19.0)  | 30405 (24.0)                            | 72166 (18.8)                             | 15943 (14.3)                             |
| Myocardial infarction (%)   | 2931 (0.5)     | 951 (0.8)                               | 1695 (0.4)                               | 285 (0.3)                                |
| Congestive Heart Failure (%)                                      | 4889 (0.8)     | 1929 (1.5)                              | 2573 (0.7)                               | 387 (0.3)                                |
| Vascular disease (%)  | 29654 (4.8)    | 8138 (6.4)                              | 17166 (4.5)                              | 4350 (3.9)                               |
| Peripheral vascular disease (%)                                   | 1317 (0.2)     | 437 (0.3)                               | 727 (0.2)                                | 153 (0.1)                                |
| Cerebrovascular disease (%)                                       | 27900 (4.5)    | 8597 (6.8)                              | 16248 (4.2)                              | 3055 (2.7)                               |
| Asthma (%)  | 6336 (1.0)     | 1647 (1.3)                              | 3713 (1.0)                               | 976 (0.9)                                |
| Chronic obstructive pulmonary disease (%)                         | 13934 (2.2)    | 3983 (3.1)                              | 8123 (2.1)                               | 1828 (1.6)                               |
| Dementia (%)  | 1786 (0.3)     | 612 (0.5)                               | 1116 (0.3)                               | 58 (0.1)                                 |
| Paralysis (%)   | 838 (0.1)      | 277 (0.2)                               | 506 (0.1)                                | 55 (0.0)                                 |
| Chronic renal failure (%)   | 7905 (1.3)     | 2709 (2.1)                              | 4314 (1.1)                               | 882 (0.8)                                |
| Mild liver disease (%)  | 753 (0.1)      | 193 (0.2)                               | 473 (0.1)                                | 87 (0.1)                                 |
| Moderate-severe liver disease (%)                                 | 453 (0.1)      | 112 (0.1)                               | 291 (0.1)                                | 50 (0.0)                                 |
| Ulcers (%)  | 6206 (1.0)     | 1644 (1.3)                              | 3702 (1.0)                               | 860 (0.8)                                |
| Rheumatoid arthritis and other inflammatory polyarthropathies (%) | 1733 (0.3)     | 466 (0.4)                               | 1028 (0.3)                               | 239 (0.2)                                |
| Malignancy (%)  | 14644 (2.4)    | 4353 (3.4)                              | 8387 (2.2)                               | 1904 (1.7)                               |
| Metastatic solid tumour (%)                                       | 1633 (0.3)     | 553 (0.4)                               | 925 (0.2)                                | 155 (0.1)                                |
| Acute respiratory infections (%)                                  | 16299 (2.6)    | 4901 (3.9)                              | 9685 (2.5)                               | 1713 (1.5)                               |
| Viral infections (%)  | 1116 (0.2)     | 345 (0.3)                               | 638 (0.2)                                | 133 (0.1)                                |
| <b><i>Medication use within 90 days</i></b>                       |                |   |  |  |
| Renin-angiotensin-system agents (%)                               | 146908 (23.6)  | 39025 (30.8)                            | 87177 (22.7)                             | 20706 (18.6)                             |
| Beta blockers (%)   | 92180 (14.8)   | 26019 (20.5)                            | 54206 (14.1)                             | 11955 (10.7)                             |
| Calcium channel blockers (%)                                      | 222807 (35.8)  | 55633 (43.9)                            | 134965 (35.1)                            | 32209 (28.9)                             |
| Diuretics (%)   | 27791 (4.5)    | 8736 (6.9)                              | 16015 (4.2)                              | 3040 (2.7)                               |
| Nitrates (%)  | 20663 (3.3)    | 6341 (5.0)                              | 11762 (3.1)                              | 2560 (2.3)                               |
| Lipid lowering agents (%)   | 219447 (35.3)  | 55120 (43.5)                            | 131070 (34.1)                            | 33257 (29.8)                             |
| Insulins (%)  | 14591 (2.3)    | 4532 (3.6)                              | 8490 (2.2)                               | 1569 (1.4)                               |
| Antidiabetic drugs (%)  | 118342 (19.0)  | 31004 (24.5)                            | 71540 (18.6)                             | 15798 (14.2)                             |
| Antiarrhythmic drugs (%)  | 1240 (0.2)     | 396 (0.3)                               | 666 (0.2)                                | 178 (0.2)                                |
| Cardiac glycosides (%)  | 2724 (0.4)     | 973 (0.8)                               | 1487 (0.4)                               | 264 (0.2)                                |
| Oral anticoagulants (%)   | 9375 (1.5)     | 3406 (2.7)                              | 4960 (1.3)                               | 1009 (0.9)                               |
| Parenteral anticoagulants (%)                                     | 891 (0.1)      | 390 (0.3)                               | 450 (0.1)                                | 51 (0.0)                                 |
| Antiplatelets (%)   | 82114 (13.2)   | 23374 (18.4)                            | 47714 (12.4)                             | 11026 (9.9)                              |
| Antifibrinolytics and hemostatics (%)                             | 1371 (0.2)     | 409 (0.3)                               | 805 (0.2)                                | 157 (0.1)                                |
| Hormonal agents (contraceptives, HRT, SERM) (%)                   | 5168 (0.8)     | 1549 (1.2)                              | 2917 (0.8)                               | 702 (0.6)                                |
| Glucocorticoids (%)   | 5768 (0.9)     | 1751 (1.4)                              | 3316 (0.9)                               | 701 (0.6)                                |
| Antidepressants (%)   | 27779 (4.5)    | 7380 (5.8)                              | 16495 (4.3)                              | 3904 (3.5)                               |
| Bevacizumab (%)   | 54 (0.0)       | 27 (0.0)                                | 24 (0.0)                                 | 3 (0.0)                                  |
| Tranexamic acid (%)   | 1346 (0.2)     | 396 (0.3)                               | 794 (0.2)                                | 156 (0.1)                                |
| Antiepileptic drugs (%)   | 10964 (1.8)    | 3147 (2.5)                              | 6498 (1.7)                               | 1319 (1.2)                               |

**Supplementary Table 3. Adjusted incidence rate ratio and risk difference of adverse event of special interest after vaccination of CoronaVac**

|   | Reference |       | First dose            |   | Second dose |                       |   | Third dose |                       |   |
|---|-----------|-------|-----------------------|---|-------------|-----------------------|---|------------|-----------------------|---|
|   | Event     | Event | Adjusted IRR (95% CI) | Risk difference (95% CI), incidence per 100,000 persons | Event       | Adjusted IRR (95% CI) | Risk difference (95% CI), incidence per 100,000 persons | Event      | Adjusted IRR (95% CI) | Risk difference (95% CI), incidence per 100,000 persons |
| <b>Any adverse event of special interest</b>                    | 17610     | 324   | 0.85 (0.75,0.96)      | -25.53 (-51.80,-5.23)                                   | 290         | 0.96 (0.85,1.09)      | -5.64 (-27.93,13.17)                                    | 54         | 1.18 (0.83,1.69)      | 22.54 (-32.83,64.25)                                    |
| <b>Autoimmune disease</b>                                       | 2166      | 46    | 0.85 (0.62,1.17)      | -3.07 (-13.19,3.21)                                     | 53          | 1.09 (0.82,1.47)      | 1.56 (-4.91,6.95)                                       | 9          | 1.44 (0.53,3.88)      | 5.51 (-19.00,16.18)                                     |
| Narcolepsy  | 1212      | 30    | 0.78 (0.53,1.14)      | -3.71 (-14.42,2.07)                                     | 42          | 1.18 (0.84,1.65)      | 2.01 (-3.05,6.48)                                       | 8          | 1.82 (0.57,5.86)      | 5.97 (-12.51,13.63)                                     |
| Acute aseptic arthritis   | 776       | 16    | 1.42 (0.78,2.58)      | 1.25 (-1.71,3.78)                                       | 10          | 1.12 (0.58,2.16)      | 0.44 (-4.52,3.32)                                       | 0          | NA                    | NA  |
| <b>Cardiovascular diseases</b>                                  | 11091     | 163   | 0.83 (0.69,0.99)      | -12.93 (-30.59,-0.67)                                   | 145         | 0.95 (0.80,1.14)      | -3.07 (-17.43,8.32)                                     | 27         | 1.05 (0.64,1.71)      | 2.78 (-38.09,28.37)                                     |
| Heart failure   | 4258      | 39    | 0.74 (0.50,1.09)      | -3.90 (-14.11,1.20)                                     | 26          | 0.74 (0.49,1.13)      | -3.76 (-14.56,1.64)                                     | 2          | 0.59 (0.13,2.61)      | -7.69 (-91.48,8.59)                                     |
| Coronary artery disease   | 5732      | 74    | 0.73 (0.56,0.95)      | -10.39 (-25.37,-1.39)                                   | 69          | 0.83 (0.64,1.07)      | -5.92 (-18.46,2.04)                                     | 18         | 1.11 (0.59,2.10)      | 2.85 (-22.63,17.12)                                     |
| Arrhythmia  | 5399      | 88    | 0.91 (0.71,1.18)      | -2.64 (-13.48,4.99)                                     | 66          | 0.96 (0.73,1.25)      | -1.26 (-11.86,6.49)                                     | 12         | 1.37 (0.67,2.80)      | 7.57 (-16.18,21.02)                                     |
| Myocarditis   | 187       | 4     | 1.96 (0.70,5.53)      | 0.55 (-1.02,1.91)                                       | 3           | 1.78 (0.50,6.28)      | 0.49 (-2.31,1.96)                                       | 0          | NA                    | NA  |
| <b>Circulatory system</b>                                       | 11452     | 174   | 0.77 (0.65,0.92)      | -18.56 (-37.74,-4.99)                                   | 152         | 0.89 (0.75,1.05)      | -8.04 (-23.86,3.65)                                     | 26         | 1.17 (0.69,1.99)      | 9.47 (-31.36,35.24)                                     |
| Thromboembolism   | 10312     | 156   | 0.76 (0.64,0.92)      | -17.79 (-36.55,-4.74)                                   | 140         | 0.91 (0.76,1.09)      | -5.71 (-20.21,5.20)                                     | 24         | 1.15 (0.67,1.97)      | 7.32 (-32.24,31.63)                                     |
| Haemorrhagic disease  | 1791      | 21    | 0.70 (0.42,1.15)      | -2.86 (-12.40,1.20)                                     | 16          | 0.59 (0.34,1.05)      | -4.50 (-17.79,0.42)                                     | 2          | 1.77 (0.21,14.98)     | 2.85 (-34.06,8.38)                                      |
| <b>Hepato-renal system</b>                                      | 2089      | 23    | 0.94 (0.60,1.48)      | -0.43 (-6.23,3.01)                                      | 17          | 0.85 (0.51,1.41)      | -1.24 (-9.03,2.70)                                      | 0          | NA                    | NA  |
| Acute liver injury  | 217       | 4     | 0.68 (0.22,2.06)      | -0.39 (-6.69,0.99)                                      | 1           | 0.28 (0.04,2.10)      | -2.13 (-5.02,1.01)                                      | 0          | NA                    | NA  |
| Acute kidney injury   | 1420      | 13    | 1.10 (0.58,2.07)      | 0.28 (-3.51,2.54)                                       | 6           | 0.63 (0.26,1.55)      | -1.85 (-14.26,1.74)                                     | 0          | NA                    | NA  |
| Acute pancreatitis  | 594       | 6     | 0.68 (0.29,1.61)      | -1.36 (-11.33,1.74)                                     | 12          | 1.36 (0.72,2.57)      | 0.77 (-1.82,2.81)                                       | 0          | NA                    | NA  |
| <b>Nerves and central nervous system</b>                        | 1451      | 33    | 1.18 (0.79,1.76)      | 1.62 (-3.55,5.83)                                       | 28          | 1.16 (0.76,1.76)      | 1.45 (-4.21,5.84)                                       | 4          | 0.96 (0.27,3.34)      | -0.46 (-35.63,9.47)                                     |
| Generalized convulsion  | 860       | 11    | 1.20 (0.63,2.27)      | 0.45 (-2.59,2.46)                                       | 5           | 0.68 (0.26,1.76)      | -1.28 (-12.22,1.90)                                     | 1          | 0.60 (0.12,3.07)      | -1.85 (-33.40,2.97)                                     |
| Bell's Palsy  | 538       | 22    | 1.34 (0.81,2.23)      | 1.89 (-2.39,5.47)                                       | 21          | 1.41 (0.85,2.33)      | 2.17 (-1.69,5.67)                                       | 3          | 1.24 (0.25,6.03)      | 1.44 (-29.07,8.29)                                      |
| <b>Respiratory system (Acute respiratory distress syndrome)</b> | 3629      | 18    | 0.31 (0.19,0.51)      | -19.96 (-50.02,-6.52)                                   | 29          | 0.59 (0.40,0.87)      | -6.35 (-17.81,-1.03)                                    | 9          | 1.25 (0.51,3.07)      | 1.81 (-11.52,7.98)                                      |
| <b>Others</b>   | 211       | 4     | 2.62 (0.66,10.38)     | 0.80 (-1.29,2.30)                                       | 4           | 3.37 (0.79,14.45)     | 0.91 (-0.69,2.37)                                       | 0          | NA                    | NA  |
| Rhabdomyolysis  | 207       | 3     | 2.44 (0.48,12.36)     | 0.66 (-2.51,2.13)                                       | 4           | 4.16 (0.96,18.09)     | 0.86 (-0.11,2.19)                                       | 0          | NA                    | NA  |
| Anaphylaxis <sup>1</sup>  | 1484      | 1     | 0.42 (0.06,2.86)      | -1.38 (-33.00,1.40)                                     | 5           | 2.61 (1.08,6.31)      | 0.61 (0.03,1.81)  | 0          | NA                    | NA  |

Notes: IRR = Incidence rate ratio; CI = confidence interval. Adjusted IRR was obtained from conditional Poisson regression adjusted for seasonal effect from self-controlled case series analysis.

1. The follow-up period of the incidence of anaphylaxis is 2 days (i.e. 0-1 day post-vaccination), and the anaphylaxis was not included in the calculation of the incidence of the overall adverse event of special interest.

**Supplementary Table 4. Mean and variance of the incidence of adverse event of special interest**

|   | Mean   | Variance |
|---|--------|----------|
| <b>Any adverse event of special interest</b>                    | 145.45 | 145.24   |
| <b>Autoimmune disease</b>                                       | 18.07  | 18.06    |
| Guillain-Barré Syndrome   | 0.16   | 0.16     |
| Acute disseminated encephalomyelitis                            | 0.16   | 0.16     |
| Narcolepsy  | 13.20  | 13.20    |
| Acute aseptic arthritis   | 4.21   | 4.21     |
| Type 1 Diabetes   | 0.00   | 0.00     |
| (Idiopathic) Thrombocytopenia                                   | 0.16   | 0.16     |
| Subacute thyroiditis  | 0.00   | 0.00     |
| <b>Cardiovascular diseases</b>                                  | 61.60  | 61.56    |
| Microangiopathy   | 0.00   | 0.00     |
| Heart failure   | 10.96  | 10.96    |
| Stress cardiomyopathy   | 0.00   | 0.00     |
| Coronary artery disease   | 28.05  | 28.04    |
| Arrhythmia  | 28.08  | 28.07    |
| Myocarditis   | 1.13   | 1.13     |
| Circulatory system  | 63.85  | 63.81    |
| Thromboembolism   | 57.49  | 57.46    |
| Haemorrhagic disease  | 6.57   | 6.57     |
| Single Organ Cutaneous Vasculitis                               | 0.00   | 0.00     |
| <b>Hepato-renal system</b>                                      | 6.82   | 6.82     |
| Acute liver injury  | 0.83   | 0.83     |
| Acute kidney injury   | 3.14   | 3.14     |
| Acute pancreatitis  | 2.91   | 2.91     |
| <b>Nerves and central nervous system</b>                        | 10.60  | 10.60    |
| Generalized convulsion  | 2.75   | 2.75     |
| Meningoencephalitis   | 0.32   | 0.32     |
| Transverse myelitis   | 0.16   | 0.16     |
| Bell's Palsy  | 7.45   | 7.45     |
| <b>Respiratory system (Acute respiratory distress syndrome)</b> | 9.12   | 9.12     |
| <b>Skin and mucous membrane, Joints system</b>                  | 0.16   | 0.16     |
| Erythema multiforme   | 0.16   | 0.16     |
| Chilblain - like lesions  | 0.00   | 0.00     |
| <b>Others</b>   | 1.29   | 1.29     |
| Anosmia, ageusia  | 0.16   | 0.16     |
| Kawasaki Disease  | 0.00   | 0.00     |
| Rhabdomyolysis  | 1.13   | 1.13     |
| <b>Anaphylaxis</b>  | 0.99   | 0.99     |

Notes: Individuals with adverse event of special interest (AESI) within 21 days (2 days for anaphylaxis) after CoronaVac vaccination were coded as 1 while others were coded as 0. The mean and variance were presented in the unit of 0.00001.



**Supplementary Table 5. Adjusted incidence rate ratio and risk difference of adverse event of special interest after vaccination of CoronaVac in different age groups**

|   | Reference |       | First dose            |   | Second dose |                       |   | Third dose |                       |   |
|---|-----------|-------|-----------------------|---|-------------|-----------------------|---|------------|-----------------------|---|
|   | Event     | Event | Adjusted IRR (95% CI) | Risk difference (95% CI), incidence per 100,000 persons | Event       | Adjusted IRR (95% CI) | Risk difference (95% CI), incidence per 100,000 persons | Event      | Adjusted IRR (95% CI) | Risk difference (95% CI), incidence per 100,000 persons |
| <b>Age &lt;80 (n=983,531)<sup>1</sup></b>                       |           |       |                       |   |             |                       |   |            |                       |   |
| <b>Any adverse event of special interest</b>                    | 11670     | 248   | 0.81 (0.71,0.93)      | -31.28 (-60.84,-9.02)                                   | 250         | 0.99 (0.86,1.13)      | -1.57 (-23.08,16.95)                                    | 48         | 1.16 (0.80,1.70)      | 18.70 (-37.12,59.70)                                    |
| <b>Autoimmune disease</b>                                       | 1603      | 38    | 0.82 (0.58,1.16)      | -4.13 (-16.49,3.08)                                     | 50          | 1.14 (0.84,1.54)      | 2.27 (-4.37,8.04)                                       | 8          | 1.35 (0.46,3.90)      | 4.82 (-26.43,17.03)                                     |
| <b>Cardiovascular diseases</b>                                  | 6518      | 119   | 0.80 (0.65,0.98)      | -13.66 (-32.97,-0.86)                                   | 118         | 0.98 (0.81,1.20)      | -0.95 (-14.76,10.18)                                    | 25         | 1.07 (0.64,1.79)      | 3.55 (-35.31,27.47)                                     |
| <b>Circulatory system</b>                                       | 7114      | 127   | 0.75 (0.61,0.91)      | -19.52 (-40.90,-5.03)                                   | 127         | 0.93 (0.77,1.12)      | -4.45 (-19.43,6.97)                                     | 25         | 1.28 (0.76,2.17)      | 12.80 (-20.68,35.13)                                    |
| <b>Hepato-renal system</b>                                      | 992       | 12    | 0.66 (0.35,1.24)      | -2.52 (-13.42,1.44)                                     | 13          | 0.80 (0.45,1.44)      | -1.23 (-9.09,2.24)                                      | 0          | NA                    | NA  |
| <b>Nerves and central nervous system</b>                        | 974       | 29    | 1.22 (0.80,1.88)      | 2.05 (-3.73,6.79)                                       | 26          | 1.29 (0.84,1.99)      | 2.53 (-2.85,7.22)                                       | 4          | 1.13 (0.30,4.21)      | 1.30 (-33.29,11.06)                                     |
| <b>Respiratory system (Acute respiratory distress syndrome)</b> | 2167      | 15    | 0.35 (0.21,0.59)      | -16.31 (-45.23,-4.37)                                   | 25          | 0.67 (0.44,1.02)      | -4.38 (-15.07,0.20)                                     | 6          | 1.25 (0.45,3.47)      | 1.77 (-14.04,8.31)                                      |
| <b>Age ≥80 (n=325,730)<sup>1</sup></b>                          |           |       |                       |   |             |                       |   |            |                       |   |
| <b>Any adverse event of special interest</b>                    | 5940      | 76    | 1.03 (0.78,1.35)      | 6.83 (-79.09,74.55)                                     | 40          | 0.81 (0.58,1.13)      | -56.94 (-209.87,33.33)                                  | 6          | 1.41 (0.48,4.18)      | 69.95 (-313.18,217.61)                                  |
| <b>Autoimmune disease</b>                                       | 563       | 8     | 1.21 (0.52,2.83)      | 2.41 (-22.83,15.76)                                     | 3           | 0.68 (0.21,2.22)      | -6.54 (-92.36,13.39)                                    | 1          | 1.97 (0.12,31.55)     | 6.86 (-174.19,23.60)                                    |
| <b>Cardiovascular diseases</b>                                  | 4573      | 44    | 0.91 (0.62,1.32)      | -11.16 (-81.68,32.44)                                   | 27          | 0.81 (0.53,1.23)      | -25.21 (-118.93,25.49)                                  | 2          | 0.85 (0.20,3.54)      | -18.65 (-521.42,96.39)                                  |
| <b>Circulatory system</b>                                       | 4338      | 47    | 0.85 (0.59,1.21)      | -19.15 (-92.05,23.27)                                   | 25          | 0.69 (0.45,1.06)      | -47.40 (-161.95,7.11)                                   | 1          | 0.39 (0.01,15.31)     | -164.18 (-13150.24,123.24)                              |
| <b>Hepato-renal system</b>                                      | 1097      | 11    | 1.86 (0.90,3.82)      | 8.44 (-3.19,22.23)                                      | 4           | 1.03 (0.36,2.98)      | 0.52 (-54.55,20.00)                                     | 0          | NA                    | NA  |
| <b>Nerves and central nervous system</b>                        | 477       | 4     | 0.95 (0.31,2.93)      | -0.37 (-33.14,9.69)                                     | 2           | 0.49 (0.10,2.31)      | -6.99 (-125.99,8.35)                                    | 0          | NA                    | NA  |
| <b>Respiratory system (Acute respiratory distress syndrome)</b> | 1462      | 3     | 0.23 (0.06,0.80)      | -38.51 (-300.72,-1.38)                                  | 4           | 0.38 (0.14,1.05)      | -18.26 (-128.81,1.05)                                   | 3          | 1.39 (0.21,9.04)      | 3.18 (-76.74,18.54)                                     |

Notes: IRR = Incidence rate ratio; CI = confidence interval. Adjusted IRR was obtained from conditional Poisson regression adjusted for seasonal effect from self-controlled case series analysis.

1. Numbers in each subgroup were calculated as the total of CoronaVac recipients and unvaccinated individuals aged at least 60 years old.

**Supplementary Table 6. Adjusted incidence rate ratio and risk difference of adverse event of special interest after vaccination of CoronaVac in different Charlson Comorbidity Index groups**

| Reference   |       | First dose            |   |                       | Second dose           |   |                      | Third dose            |   |                        |
|---|-------|-----------------------|---|-----------------------|-----------------------|---|----------------------|-----------------------|---|------------------------|
| Event   | Event | Adjusted IRR (95% CI) | Risk difference (95% CI), incidence per 100,000 persons | Event                 | Adjusted IRR (95% CI) | Risk difference (95% CI), incidence per 100,000 persons | Event                | Adjusted IRR (95% CI) | Risk difference (95% CI), incidence per 100,000 persons |                        |
| <b>Charlson Comorbidity Index &lt;3 (n=427,729)<sup>1</sup></b> |       |                       |   |                       |                       |   |                      |                       |   |                        |
| <b>Any adverse event of special interest</b>                    | 4906  | 135                   | 0.89 (0.74,1.07)  | -17.15 (-53.87,9.62)  | 137                   | 1.04 (0.87,1.25)  | 5.31 (-22.97,30.07)  | 27                    | 1.20 (0.72,2.03)  | 23.05 (-59.95,76.84)   |
| Autoimmune disease  | 619   | 16                    | 0.70 (0.42,1.17)  | -7.92 (-34.05,3.58)   | 26                    | 1.29 (0.84,1.97)  | 4.17 (-4.57,12.17)   | 5                     | 1.43 (0.41,5.04)  | 5.61 (-36.27,19.87)    |
| Cardiovascular diseases   | 2414  | 57                    | 0.89 (0.67,1.18)  | -6.33 (-30.02,9.38)   | 52                    | 0.88 (0.66,1.18)  | -6.92 (-31.89,9.36)  | 15                    | 1.30 (0.63,2.67)  | 11.72 (-35.66,38.11)   |
| Circulatory system  | 2749  | 72                    | 0.88 (0.68,1.14)  | -8.11 (-33.03,8.69)   | 62                    | 0.92 (0.71,1.20)  | -5.13 (-29.41,11.93) | 17                    | 1.78 (0.89,3.58)  | 26.59 (-8.84,51.14)    |
| Hepato-renal system   | 239   | 3                     | 0.44 (0.14,1.42)  | -5.52 (-49.23,2.33)   | 8                     | 1.31 (0.62,2.75)  | 1.03 (-4.77,4.97)    | 0                     | NA  | NA                     |
| Nerves and central nervous system                               | 305   | 16                    | 1.47 (0.82,2.66)  | 3.37 (-3.45,9.53)     | 11                    | 1.27 (0.66,2.45)  | 2.23 (-7.89,9.03)    | 0                     | NA  | NA                     |
| Respiratory system (Acute respiratory distress syndrome)        | 601   | 7                     | 0.47 (0.22,1.01)  | -7.71 (-38.25,0.08)   | 10                    | 0.69 (0.35,1.36)  | -3.13 (-20.31,2.88)  | 1                     | 0.69 (0.10,4.51)  | -3.18 (-94.31,8.56)    |
| <b>Charlson Comorbidity Index ≥3 (n=881,532)<sup>1</sup></b>    |       |                       |   |                       |                       |   |                      |                       |   |                        |
| <b>Any adverse event of special interest</b>                    | 12704 | 189                   | 0.81 (0.69,0.96)  | -35.80 (-77.91,-5.89) | 153                   | 0.89 (0.75,1.06)  | -18.83 (-57.60,9.99) | 27                    | 1.20 (0.73,1.98)  | 26.17 (-62.32,84.59)   |
| Autoimmune disease  | 1547  | 30                    | 0.97 (0.65,1.46)  | -0.46 (-12.26,7.18)   | 27                    | 0.98 (0.65,1.48)  | -0.34 (-12.09,7.31)  | 4                     | 1.36 (0.27,6.84)  | 4.72 (-60.54,19.35)    |
| Cardiovascular diseases   | 8677  | 106                   | 0.77 (0.62,0.97)  | -20.40 (-50.02,-1.61) | 93                    | 0.99 (0.79,1.24)  | -0.53 (-20.90,15.60) | 12                    | 0.89 (0.46,1.72)  | -9.03 (-95.33,33.47)   |
| Circulatory system  | 8703  | 102                   | 0.70 (0.55,0.88)  | -28.85 (-61.55,-7.96) | 90                    | 0.85 (0.68,1.07)  | -11.59 (-36.00,4.82) | 9                     | 0.74 (0.32,1.70)  | -23.65 (-161.84,31.41) |
| Hepato-renal system   | 1850  | 20                    | 1.13 (0.67,1.91)  | 1.03 (-6.02,5.93)     | 9                     | 0.63 (0.31,1.29)  | -5.07 (-27.81,2.78)  | 0                     | NA  | NA                     |
| Nerves and central nervous system                               | 1146  | 17                    | 0.97 (0.56,1.69)  | -0.28 (-11.37,5.97)   | 17                    | 1.07 (0.62,1.85)  | 0.68 (-9.05,6.71)    | 4                     | 1.28 (0.33,5.01)  | 2.34 (-30.20,11.73)    |
| Respiratory system (Acute respiratory distress syndrome)        | 3028  | 11                    | 0.26 (0.13,0.49)  | -30.98 (-94.89,-7.82) | 19                    | 0.55 (0.34,0.89)  | -8.73 (-28.26,-0.96) | 8                     | 1.46 (0.51,4.17)  | 3.36 (-14.20,11.17)    |

Notes: IRR = Incidence rate ratio; CI = confidence interval. Adjusted IRR was obtained from conditional Poisson regression adjusted for seasonal effect from self-controlled case series analysis.

1. Numbers in each subgroup were calculated as the total of CoronaVac recipients and unvaccinated individuals aged at least 60 years old.

**Supplementary Table 7. Adjusted incidence rate ratio and risk difference of adverse event of special interest after vaccination of CoronaVac after excluding the patients infected by COVID-19 before or during the study period**

|   | Reference |       | First dose            |   | Second dose |                       |   | Third dose |                       |   |
|---|-----------|-------|-----------------------|---|-------------|-----------------------|---|------------|-----------------------|---|
|   | Event     | Event | Adjusted IRR (95% CI) | Risk difference (95% CI), incidence per 100,000 persons | Event       | Adjusted IRR (95% CI) | Risk difference (95% CI), incidence per 100,000 persons | Event      | Adjusted IRR (95% CI) | Risk difference (95% CI), incidence per 100,000 persons |
| <b>Any adverse event of special interest</b>                    | 17592     | 324   | 0.85 (0.75,0.96)      | -25.20 (-51.43,-4.93)                                   | 290         | 0.96 (0.85,1.09)      | -5.63 (-27.95,13.21)                                    | 54         | 1.18 (0.83,1.69)      | 22.56 (-32.92,64.34)                                    |
| <b>Autoimmune disease</b>                                       | 2165      | 46    | 0.85 (0.62,1.17)      | -3.09 (-13.23,3.20)                                     | 53          | 1.09 (0.82,1.47)      | 1.56 (-4.93,6.96)                                       | 9          | 1.44 (0.54,3.88)      | 5.54 (-18.98,16.22)                                     |
| Narcolepsy  | 1211      | 30    | 0.78 (0.53,1.14)      | -3.73 (-14.48,2.06)                                     | 42          | 1.18 (0.84,1.65)      | 2.01 (-3.08,6.48)                                       | 8          | 1.83 (0.57,5.88)      | 6.00 (-12.47,13.66)                                     |
| Acute aseptic arthritis   | 776       | 16    | 1.42 (0.78,2.58)      | 1.25 (-1.71,3.78)                                       | 10          | 1.12 (0.58,2.16)      | 0.44 (-4.52,3.32)                                       | 0          | NA                    | NA  |
| <b>Cardiovascular diseases</b>                                  | 11079     | 163   | 0.83 (0.69,0.99)      | -12.60 (-30.17,-0.41)                                   | 145         | 0.95 (0.80,1.14)      | -3.02 (-17.40,8.38)                                     | 27         | 1.05 (0.64,1.71)      | 2.81 (-38.12,28.44)                                     |
| Heart failure   | 4256      | 39    | 0.74 (0.50,1.11)      | -3.77 (-13.85,1.33)                                     | 26          | 0.74 (0.49,1.13)      | -3.79 (-14.62,1.63)                                     | 2          | 0.59 (0.13,2.60)      | -7.77 (-91.99,8.59)                                     |
| Coronary artery disease   | 5722      | 74    | 0.73 (0.57,0.95)      | -10.27 (-25.20,-1.29)                                   | 69          | 0.83 (0.64,1.07)      | -5.88 (-18.42,2.09)                                     | 18         | 1.12 (0.59,2.10)      | 2.92 (-22.55,17.19)                                     |
| Arrhythmia  | 5395      | 88    | 0.91 (0.71,1.18)      | -2.64 (-13.49,5.01)                                     | 66          | 0.96 (0.73,1.25)      | -1.27 (-11.89,6.50)                                     | 12         | 1.37 (0.67,2.80)      | 7.59 (-16.21,21.06)                                     |
| Myocarditis   | 187       | 4     | 1.96 (0.70,5.53)      | 0.55 (-1.02,1.91)                                       | 3           | 1.78 (0.50,6.28)      | 0.49 (-2.31,1.96)                                       | 0          | NA                    | NA  |
| <b>Circulatory system</b>                                       | 11440     | 174   | 0.78 (0.65,0.92)      | -18.49 (-37.68,-4.92)                                   | 152         | 0.89 (0.75,1.05)      | -8.03 (-23.88,3.68)                                     | 26         | 1.17 (0.69,1.99)      | 9.50 (-31.38,35.31)                                     |
| Thromboembolism   | 10302     | 156   | 0.76 (0.64,0.92)      | -17.80 (-36.58,-4.73)                                   | 140         | 0.91 (0.76,1.09)      | -5.70 (-20.22,5.23)                                     | 24         | 1.15 (0.67,1.97)      | 7.35 (-32.26,31.70)                                     |
| Haemorrhagic disease  | 1788      | 21    | 0.70 (0.42,1.16)      | -2.82 (-12.31,1.25)                                     | 16          | 0.59 (0.33,1.05)      | -4.52 (-17.85,0.42)                                     | 2          | 1.76 (0.21,14.94)     | 2.84 (-34.28,8.39)                                      |
| <b>Hepato-renal system</b>                                      | 2087      | 23    | 0.95 (0.60,1.49)      | -0.38 (-6.15,3.06)                                      | 17          | 0.85 (0.51,1.41)      | -1.24 (-9.04,2.71)                                      | 0          | NA                    | NA  |
| Acute liver injury  | 216       | 4     | 0.70 (0.23,2.11)      | -0.36 (-6.49,1.02)                                      | 1           | 0.28 (0.04,2.08)      | -2.17 (-50.69,1.00)                                     | 0          | NA                    | NA  |
| Acute kidney injury   | 1419      | 13    | 1.10 (0.58,2.07)      | 0.28 (-3.51,2.54)                                       | 6           | 0.63 (0.26,1.55)      | -1.84 (-14.26,1.74)                                     | 0          | NA                    | NA  |
| Acute pancreatitis  | 594       | 6     | 0.68 (0.29,1.61)      | -1.36 (-11.35,1.74)                                     | 12          | 1.36 (0.72,2.57)      | 0.77 (-1.82,2.81)                                       | 0          | NA                    | NA  |
| <b>Nerves and central nervous system</b>                        | 1448      | 33    | 1.18 (0.79,1.76)      | 1.65 (-3.52,5.86)                                       | 28          | 1.16 (0.76,1.76)      | 1.47 (-4.20,5.86)                                       | 4          | 0.96 (0.27,3.34)      | -0.46 (-35.69,9.48)                                     |
| Generalized convulsion  | 858       | 11    | 1.20 (0.63,2.28)      | 0.46 (-2.58,2.47)                                       | 5           | 0.68 (0.27,1.76)      | -1.27 (-12.21,1.91)                                     | 1          | 0.60 (0.12,3.07)      | -1.85 (-33.46,2.97)                                     |
| Bell's Palsy  | 537       | 22    | 1.34 (0.81,2.23)      | 1.91 (-2.36,5.50)                                       | 21          | 1.41 (0.85,2.33)      | 2.17 (-1.70,5.68)                                       | 3          | 1.24 (0.25,6.03)      | 1.44 (-29.12,8.30)                                      |
| <b>Respiratory system (Acute respiratory distress syndrome)</b> | 3625      | 18    | 0.31 (0.19,0.51)      | -19.99 (-50.10,-6.53)                                   | 29          | 0.59 (0.40,0.87)      | -6.37 (-17.85,-1.04)                                    | 9          | 1.25 (0.51,3.06)      | 1.80 (-11.57,7.99)                                      |
| <b>Others</b>   | 211       | 4     | 2.62 (0.66,10.38)     | 0.80 (-1.29,2.30)                                       | 4           | 3.37 (0.79,14.45)     | 0.91 (-0.69,2.37)                                       | 0          | NA                    | NA  |
| Rhabdomyolysis  | 207       | 3     | 2.44 (0.48,12.36)     | 0.67 (-2.51,2.14)                                       | 4           | 4.16 (0.96,18.09)     | 0.86 (-0.11,2.20)                                       | 0          | NA                    | NA  |
| Anaphylaxis <sup>1</sup>  | 1484      | 1     | 0.42 (0.06,2.86)      | -1.38 (-33.06,1.40)                                     | 5           | 2.61 (1.08,6.31)      | 0.61 (0.03,1.81)  | 0          | NA                    | NA  |

Notes: IRR = Incidence rate ratio; CI = confidence interval. Adjusted IRR was obtained from conditional Poisson regression adjusted for seasonal effect from self-controlled case series analysis. There were 2,057 individuals excluded from this sensitivity analysis due to infection of COVID-19 before or during the study period.

1. The follow-up period of the incidence of anaphylaxis is 2 days (i.e. 0-1 day post-vaccination), and the anaphylaxis was not included in the calculation of the incidence of the overall adverse event of special interest.

**Supplementary Table 8. Adjusted incidence rate ratio and risk difference of adverse event of special interest after vaccination of CoronaVac with exposure periods of 14 days**

|   | Reference |       | First dose            |   | Second dose |                       |   | Third dose |                       |   |
|---|-----------|-------|-----------------------|---|-------------|-----------------------|---|------------|-----------------------|---|
|   | Event     | Event | Adjusted IRR (95% CI) | Risk difference (95% CI), incidence per 100,000 persons | Event       | Adjusted IRR (95% CI) | Risk difference (95% CI), incidence per 100,000 persons | Event      | Adjusted IRR (95% CI) | Risk difference (95% CI), incidence per 100,000 persons |
| <b>Any adverse event of special interest</b>                    | 17853     | 210   | 0.81 (0.70,0.94)      | -21.44 (-43.50,-5.27)                                   | 183         | 0.90 (0.77,1.05)      | -10.09 (-29.73,4.90)                                    | 32         | 0.94 (0.63,1.41)      | -5.80 (-60.08,29.50)                                    |
| <b>Autoimmune disease</b>                                       | 2203      | 29    | 0.80 (0.55,1.17)      | -2.95 (-12.39,2.20)                                     | 37          | 1.14 (0.81,1.59)      | 1.43 (-3.51,5.58)                                       | 5          | 0.90 (0.31,2.55)      | -1.38 (-32.67,9.11)                                     |
| Narcolepsy  | 1241      | 19    | 0.74 (0.47,1.18)      | -2.90 (-12.58,1.70)                                     | 28          | 1.16 (0.78,1.71)      | 1.15 (-3.06,4.61)                                       | 4          | 0.84 (0.26,2.70)      | -1.64 (-31.56,6.97)                                     |
| Acute aseptic arthritis   | 784       | 10    | 1.24 (0.62,2.49)      | 0.56 (-2.85,2.76)                                       | 8           | 1.36 (0.65,2.84)      | 0.77 (-2.48,2.98)                                       | 0          | NA                    | NA  |
| <b>Cardiovascular diseases</b>                                  | 11210     | 109   | 0.81 (0.66,1.00)      | -9.16 (-23.52,0.10)                                     | 90          | 0.88 (0.70,1.09)      | -5.60 (-18.98,3.73)                                     | 17         | 0.93 (0.54,1.60)      | -2.82 (-37.95,17.00)                                    |
| Heart failure   | 4288      | 22    | 0.60 (0.37,0.97)      | -4.10 (-14.41,-0.13)                                    | 14          | 0.58 (0.33,1.02)      | -4.44 (-17.14,0.13)                                     | 1          | 0.45 (0.06,3.41)      | -7.31 (-130.26,5.89)                                    |
| Coronary artery disease   | 5787      | 51    | 0.77 (0.57,1.03)      | -5.61 (-16.72,0.63)                                     | 44          | 0.79 (0.58,1.08)      | -4.88 (-16.17,1.63)                                     | 11         | 0.91 (0.45,1.84)      | -1.81 (-27.20,10.19)                                    |
| Arrhythmia  | 5457      | 59    | 0.86 (0.63,1.18)      | -2.99 (-13.05,3.30)                                     | 42          | 0.91 (0.66,1.25)      | -1.91 (-11.56,4.40)                                     | 7          | 1.04 (0.48,2.28)      | 0.75 (-24.24,12.40)                                     |
| Myocarditis   | 190       | 2     | 1.32 (0.33,5.21)      | 0.16 (-3.30,1.33)                                       | 2           | 1.74 (0.39,7.70)      | 0.27 (-2.54,1.44)                                       | 0          | NA                    | NA  |
| <b>Circulatory system</b>                                       | 11570     | 121   | 0.81 (0.67,0.99)      | -9.84 (-24.06,-0.47)                                    | 97          | 0.85 (0.69,1.05)      | -7.61 (-21.91,2.11)                                     | 16         | 1.00 (0.56,1.81)      | 0.13 (-38.47,21.57)                                     |
| Thromboembolism   | 10419     | 110   | 0.81 (0.66,1.00)      | -8.82 (-22.35,-0.08)                                    | 88          | 0.86 (0.69,1.07)      | -6.44 (-19.91,2.71)                                     | 15         | 1.01 (0.55,1.85)      | 0.21 (-36.25,20.09)                                     |
| Haemorrhagic disease  | 1803      | 13    | 0.68 (0.37,1.24)      | -2.17 (-11.28,1.28)                                     | 13          | 0.76 (0.42,1.38)      | -1.43 (-9.15,1.82)                                      | 1          | 1.04 (0.10,10.55)     | 0.18 (-57.71,5.99)                                      |
| <b>Hepato-renal system</b>                                      | 2102      | 15    | 0.91 (0.51,1.61)      | -0.48 (-6.43,2.53)                                      | 12          | 0.91 (0.51,1.64)      | -0.44 (-6.53,2.62)                                      | 0          | NA                    | NA  |
| Acute liver injury  | 218       | 3     | 0.72 (0.19,2.76)      | -0.26 (-7.31,1.08)                                      | 1           | 0.46 (0.06,3.44)      | -0.78 (-26.07,1.20)                                     | 0          | NA                    | NA  |
| Acute kidney injury   | 1426      | 9     | 1.15 (0.53,2.52)      | 0.28 (-3.29,2.21)                                       | 4           | 0.66 (0.25,1.75)      | -1.13 (-11.27,1.57)                                     | 0          | NA                    | NA  |
| Acute pancreatitis  | 601       | 3     | 0.49 (0.15,1.62)      | -1.84 (-18.12,1.21)                                     | 8           | 1.29 (0.60,2.78)      | 0.40 (-2.09,2.03)                                       | 0          | NA                    | NA  |
| <b>Nerves and central nervous system</b>                        | 1473      | 21    | 1.08 (0.67,1.74)      | 0.55 (-4.56,4.03)                                       | 20          | 1.23 (0.75,2.00)      | 1.30 (-3.10,4.72)                                       | 2          | 0.67 (0.14,3.22)      | -3.53 (-59.18,6.51)                                     |
| Generalized convulsion  | 867       | 6     | 0.94 (0.40,2.26)      | -0.09 (-4.55,1.66)                                      | 4           | 0.85 (0.30,2.41)      | -0.28 (-6.86,1.74)                                      | 0          | NA                    | NA  |
| Bell's Palsy  | 552       | 15    | 1.30 (0.73,2.30)      | 1.19 (-2.65,4.13)                                       | 15          | 1.46 (0.82,2.60)      | 1.64 (-1.59,4.51)                                       | 2          | 1.23 (0.26,5.91)      | 0.99 (-21.03,6.08)                                      |
| <b>Respiratory system (Acute respiratory distress syndrome)</b> | 3647      | 15    | 0.44 (0.26,0.73)      | -8.03 (-24.34,-1.60)                                    | 16          | 0.50 (0.30,0.82)      | -6.18 (-19.37,-0.95)                                    | 7          | 1.50 (0.58,3.91)      | 2.07 (-6.21,6.33)                                       |
| <b>Others</b>   | 214       | 2     | 1.50 (0.28,8.11)      | 0.27 (-4.86,1.65)                                       | 3           | 3.18 (0.74,13.63)     | 0.55 (-0.66,1.74)                                       | 0          | NA                    | NA  |
| Rhabdomyolysis  | 209       | 2     | 2.03 (0.37,11.10)     | 0.41 (-3.16,1.71)                                       | 3           | 3.80 (0.86,16.68)     | 0.59 (-0.29,1.77)                                       | 0          | NA                    | NA  |
| Anaphylaxis <sup>1</sup>  | 1484      | 1     | 0.42 (0.06,2.86)      | -1.38 (-33.00,1.40)                                     | 5           | 2.61 (1.08,6.31)      | 0.61 (0.03,1.81)  | 0          | NA                    | NA  |

Notes: IRR = Incidence rate ratio; CI = confidence interval. Adjusted IRR was obtained from conditional Poisson regression adjusted for seasonal effect from self-controlled case series analysis.

1. The follow-up period of the incidence of anaphylaxis is 2 days (i.e. 0-1 day post-vaccination), and the anaphylaxis was not included in the calculation of the incidence of the overall adverse event of special interest.

**Supplementary Table 9. Adjusted incidence rate ratio and risk difference of adverse event of special interest after vaccination of CoronaVac with exposure periods of 28 days**

|   | Reference |       | First dose            |   | Second dose |                       |   | Third dose |                       |   |
|---|-----------|-------|-----------------------|---|-------------|-----------------------|---|------------|-----------------------|---|
|   | Event     | Event | Adjusted IRR (95% CI) | Risk difference (95% CI), incidence per 100,000 persons | Event       | Adjusted IRR (95% CI) | Risk difference (95% CI), incidence per 100,000 persons | Event      | Adjusted IRR (95% CI) | Risk difference (95% CI), incidence per 100,000 persons |
| <b>Any adverse event of special interest</b>                    | 17414     | 411   | 0.81 (0.72,0.91)      | -43.98 (-76.40,-18.12)                                  | 385         | 0.96 (0.86,1.07)      | -8.16 (-33.71,13.61)                                    | 68         | 1.13 (0.78,1.64)      | 22.17 (-55.45,78.42)                                    |
| <b>Autoimmune disease</b>                                       | 2141      | 54    | 0.72 (0.53,0.97)      | -8.62 (-22.96,-0.54)                                    | 69          | 1.08 (0.82,1.40)      | 1.56 (-5.61,7.57)                                       | 10         | 1.15 (0.41,3.19)      | 2.85 (-37.66,18.11)                                     |
| Narcolepsy  | 1192      | 37    | 0.70 (0.49,0.99)      | -7.21 (-21.07,-0.10)                                    | 54          | 1.14 (0.84,1.55)      | 2.07 (-3.76,7.13)                                       | 9          | 1.59 (0.47,5.35)      | 6.14 (-22.32,16.32)                                     |
| Acute aseptic arthritis   | 772       | 17    | 1.06 (0.59,1.91)      | 0.27 (-4.89,3.31)                                       | 13          | 1.10 (0.60,2.04)      | 0.45 (-4.72,3.54)                                       | 0          | NA                    | NA  |
| <b>Cardiovascular diseases</b>                                  | 10995     | 205   | 0.79 (0.67,0.93)      | -21.51 (-43.13,-5.83)                                   | 190         | 0.93 (0.79,1.09)      | -5.79 (-22.47,7.39)                                     | 36         | 1.11 (0.68,1.81)      | 7.69 (-41.65,39.05)                                     |
| Heart failure   | 4232      | 48    | 0.72 (0.49,1.05)      | -5.94 (-19.10,0.85)                                     | 41          | 0.96 (0.67,1.37)      | -0.65 (-9.13,5.03)                                      | 4          | 1.04 (0.29,3.74)      | 0.61 (-45.61,13.65)                                     |
| Coronary artery disease   | 5688      | 95    | 0.70 (0.55,0.88)      | -15.60 (-33.07,-4.41)                                   | 89          | 0.78 (0.62,0.98)      | -10.03 (-25.05,-0.55)                                   | 21         | 0.91 (0.49,1.69)      | -3.60 (-42.99,16.74)                                    |
| Arrhythmia  | 5347      | 112   | 0.92 (0.73,1.15)      | -3.42 (-15.92,5.62)                                     | 89          | 0.98 (0.78,1.24)      | -0.72 (-12.11,8.11)                                     | 17         | 1.90 (0.84,4.28)      | 17.46 (-7.91,32.28)                                     |
| Myocarditis   | 186       | 5     | 1.76 (0.71,4.35)      | 0.56 (-1.02,1.96)                                       | 3           | 1.19 (0.34,4.20)      | 0.21 (-4.97,1.94)                                       | 0          | NA                    | NA  |
| <b>Circulatory system</b>                                       | 11328     | 230   | 0.79 (0.68,0.92)      | -22.96 (-44.57,-6.99)                                   | 211         | 0.93 (0.80,1.08)      | -6.22 (-23.19,7.29)                                     | 35         | 1.30 (0.76,2.21)      | 19.90 (-29.14,51.72)                                    |
| Thromboembolism   | 10200     | 209   | 0.79 (0.67,0.93)      | -20.53 (-41.07,-5.58)                                   | 191         | 0.93 (0.80,1.09)      | -5.51 (-21.67,7.28)                                     | 32         | 1.23 (0.71,2.12)      | 14.36 (-34.78,45.05)                                    |
| Haemorrhagic disease  | 1775      | 26    | 0.66 (0.42,1.04)      | -4.82 (-16.93,0.47)                                     | 26          | 0.79 (0.50,1.23)      | -2.53 (-11.91,2.23)                                     | 3          | 3.28 (0.29,37.03)     | 6.43 (-29.48,11.73)                                     |
| <b>Hepato-renal system</b>                                      | 2077      | 29    | 0.89 (0.59,1.36)      | -1.08 (-8.21,3.05)                                      | 23          | 0.87 (0.55,1.37)      | -1.35 (-9.47,3.12)                                      | 0          | NA                    | NA  |
| Acute liver injury  | 216       | 5     | 0.63 (0.24,1.70)      | -0.58 (-7.03,0.89)                                      | 1           | 0.19 (0.03,1.47)      | -4.13 (-82.22,0.69)                                     | 0          | NA                    | NA  |
| Acute kidney injury   | 1413      | 17    | 1.13 (0.63,2.03)      | 0.51 (-3.62,3.18)                                       | 9           | 0.76 (0.36,1.57)      | -1.37 (-10.96,2.29)                                     | 0          | NA                    | NA  |
| Acute pancreatitis  | 590       | 7     | 0.57 (0.25,1.28)      | -2.72 (-16.11,1.18)                                     | 15          | 1.28 (0.70,2.34)      | 0.77 (-2.34,3.08)                                       | 0          | NA                    | NA  |
| <b>Nerves and central nervous system</b>                        | 1435      | 39    | 1.04 (0.72,1.51)      | 0.53 (-6.44,5.56)                                       | 37          | 1.17 (0.80,1.72)      | 1.93 (-4.10,6.84)                                       | 5          | 0.77 (0.21,2.86)      | -4.01 (-63.46,10.68)                                    |
| Generalized convulsion  | 856       | 13    | 0.56 (0.24,1.31)      | -2.70 (-16.78,1.23)                                     | 7           | 0.50 (0.21,1.21)      | -3.38 (-19.76,0.89)                                     | 1          | 0.01 (0.00,0.02)      | -633.01 (-3141.47,-119.70)                              |
| Bell's Palsy  | 528       | 25    | 1.13 (0.70,1.83)      | 1.06 (-5.04,5.34)                                       | 27          | 1.40 (0.88,2.22)      | 2.60 (-1.54,6.48)                                       | 4          | 1.24 (0.29,5.37)      | 1.77 (-29.17,9.58)                                      |
| <b>Respiratory system (Acute respiratory distress syndrome)</b> | 3607      | 26    | 0.32 (0.21,0.49)      | -26.79 (-59.30,-10.43)                                  | 42          | 0.63 (0.45,0.88)      | -7.44 (-19.36,-1.33)                                    | 10         | 0.93 (0.37,2.34)      | -1.02 (-27.43,9.08)                                     |
| <b>Others</b>   | 211       | 4     | 1.71 (0.42,7.00)      | 0.54 (-3.51,2.18)                                       | 4           | 2.26 (0.49,10.54)     | 0.72 (-2.69,2.30)                                       | 0          | NA                    | NA  |
| Rhabdomyolysis  | 207       | 3     | 1.60 (0.31,8.29)      | 0.42 (-5.18,2.04)                                       | 4           | 2.78 (0.59,13.14)     | 0.72 (-1.63,2.14)                                       | 0          | NA                    | NA  |
| Anaphylaxis <sup>1</sup>  | 1484      | 1     | 0.42 (0.06,2.86)      | -1.38 (-33.00,1.40)                                     | 5           | 2.61 (1.08,6.31)      | 0.61 (0.03,1.81)  | 0          | NA                    | NA  |

Notes: IRR = Incidence rate ratio; CI = confidence interval. Adjusted IRR was obtained from conditional Poisson regression adjusted for seasonal effect from self-controlled case series analysis.

1. The follow-up period of the incidence of anaphylaxis is 2 days (i.e. 0-1 day post-vaccination), and the anaphylaxis was not included in the calculation of the incidence of the overall adverse event of special interest.