

Adverse event reporting and Bell's palsy risk after COVID-19 vaccination – Authors' Reply

Author: Ian Chi Kei Wong, PhD^{1,2,3,4*}, Eric Yuk Fai Wan, PhD^{1,2,5}, Celine Sze Ling Chui, PhD^{2,6,7}, Xue Li, PhD^{1,2,8}, Esther Wai Yin Chan, PhD^{1,2}

*Corresponding author

1 Centre for Safe Medication Practice and Research, Department of Pharmacology and Pharmacy, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong, China.

2 Laboratory of Data Discovery for Health (D²4H), Hong Kong Science and Technology Park, Sha Tin, Hong Kong SAR, China.

3 Expert Committee on Clinical Events Assessment Following COVID-19 Immunization, Department of Health, The Government of the Hong Kong Special Administrative Region, Hong Kong SAR, China.

4 Research Department of Practice and Policy, School of Pharmacy, University College London, United Kingdom.

5 Department of Family Medicine and Primary Care, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China.

6 School of Nursing, Li Ka Shing Faculty of Medicine, The University of Hong Kong SAR, Hong Kong, China.

7 School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China.

8 Department of Medicine, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China.

Full professor: Ian Chi Kei Wong.

Address for correspondence:

Professor Ian Chi Kei Wong

Postal Address: L2-57, Laboratory Block, 21 Sassoon Road, Pokfulam, Hong Kong

Email: wongick@hku.hk

Tel: +852 3917 9441

Selection bias may overestimate the risk of Bell's palsy following COVID-19 vaccination – Reply

Chang et al. suggested that the possibility of selection bias in our nested case-control study could be due to potential control subjects (i.e., patients admitted to emergency rooms or hospital wards) being older than all subjects eligible for vaccination in the general population¹. However, as we used a matched case-control study design, this concern is irrelevant. As stated in our methods, we matched each case with a control using the exact year of age in our analysis. Hence, the hypothetical example for potential selection bias referred to by Chang et al. does not apply to our study.

We acknowledge that the health condition of subjects eligible for vaccination may be relatively healthier compared to our control subjects. A possible reason is that relatively healthy individuals with high-risk occupations were given priority for vaccination in the rollout schedule of the vaccination programme in Hong Kong, which is included in our article². We addressed this in our analysis by adjusting baseline characteristics including comorbidities and concurrent medications use. Therefore, such characteristics should not have had a significant effect on our results or conclusions. To further address Chang et al.'s concern on the difference in baseline characteristics between cases and controls¹, we conducted further post-hoc sensitivity analysis by excluding control subjects with neoplasms or exposure to antibacterial drugs, where there were substantial differences between cases and controls (neoplasm: 5% vs 13%; antibacterial drugs: 7% vs 13% in Table 2 in our published study²). Table 1 showed that the results were similar with the main findings, which further supports the robustness of our study.

As in the case for all observational study, the effect of unmeasured confounding in our nested case-control study cannot be completely ruled out. In recent years, the self-controlled case series (SCCS) method has become a popular alternative study design for drug safety studies³. It was specifically developed to evaluate vaccine safety with the advantage of reduced unmeasured confounding through the comparisons within individuals^{4,5}. Due to the small number of events and a short follow-up period in our previous study, we were unable to apply such a method. We appreciate Chang et al.'s interest in our study, and as stated in our paper, further study should be warranted to confirm our findings.

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Table 1. Sensitivity analysis excluding control subjects with neoplasms or antibacterial drugs used in the nested case-control study.

	Number of case patients (N=295[†])	Number of controls (N=908)	Crude odds ratio (95% CI)	P-value	Adjusted odds ratio (95% CI)	P-value
Total						
Not vaccinated	253 (86%)	828 (91%)	(Ref)		(Ref)	
CoronaVac	28 (9%)	50 (6%)	2.049 (1.221 - 3.438)	0.0066	2.196 (1.293 - 3.728)	0.0036
BNT162b2	14 (5%)	30 (3%)	1.636 (0.842 - 3.178)	0.15	1.745 (0.888 - 3.430)	0.11

Cases and controls were matched according to age, sex, setting, and admission date. Odds ratios for Bell's palsy were estimated by conditional logistic regression adjusted for smoking status, pre-existing comorbidities (diabetes mellitus, hypertension, asthma, rheumatoid arthritis, stroke, migraine, infections in the past 90 days (acute respiratory infections), and medication use in the past 90 days (antiviral drugs, systemic corticosteroids, immunosuppressants).

[†]Three cases were excluded as the corresponding controls were excluded due to neoplasms or antibacterial drugs used.