Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

database when reporting is incomplete. Therefore, we urge all countries to report all suspected cases of severe and unexpected adverse drug reactions to international pharmacovigilance systems in a transparent and timely manner to improve the collective knowledge on the safety of these vaccines.

We declare no competing interests.

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Although the incidence of Bell's palsy in the general population is low (15–30 cases per 100 000 person-years),[1] Bell's palsy following exposure to SARS-CoV-2 vaccines has attracted attention. In line with clinical trial data that suggested a substantial but non-significant risk of Bell's palsy following exposure to mRNA SARS-CoV-2 vaccines (rate ratio 7·0, p=0·07),[1] a case series and nested case-control study reported a non-significantly increased risk of Bell's palsy following BNT162b2 vaccination. However, this population-based study found a significantly increased risk of Bell's palsy following use of an inactivated (CoronaVac) SARS-CoV-2 vaccine (odds ratio 2·385, 95% CI 1·415–4·022).[2] Although a number of limitations have been considered, Eric Yuk Fai Wan and colleagues[2] might have overlooked possible selection bias, which was partly due to their method of selecting study participants and partly due to substantially different COVID-19 vaccination rates between different age groups (appendix). The very low vaccination rate among those aged 70 years or older was attributable to widespread concerns about adverse events following vaccination.[3]

Although a nested case-control study is an efficient method for conducting a cohort study, selection bias can occur when people in the cohort do not have equal chance of being selected for case-control analysis. In the nested case-control study by Wan and colleagues,[2] cases and controls were selected from patients admitted to emergency rooms or hospital wards rather than all the people who were eligible for vaccination, probably because of the robustness of clinical data.[2] Using published local statistics,[4,5] it can be shown that the proportion of people aged 65 years and older attending emergency rooms from 2020 to 2021 was significantly higher than that of the counterpart in the rest of the general population (35·0% *vs* 14·4%).

We show how selection bias can overestimate Bell's palsy risk in cohort analyses (table). Assuming that (1) Bell's palsy occurs at equal rates among vaccinated and unvaccinated people, (2) there is a higher proportion of older people (≥65 years) with a lower overall vaccination rate among eligible people who are attending emergency rooms or hospitals wards, and (3) all cases of Bell's palsy are captured in emergency rooms or hospital wards owing to its acute and disabling symptoms, selecting cases and controls from emergency rooms and hospital wards rather than all people who are eligible for vaccination would overestimate the risk of Bell's palsy. The bigger the difference in vaccination rates between selected and non-selected people, the more severe the bias.

See Online for appendix

	People with Bell's palsy	People without Bell's palsy	Subtotal	Bell's palsy rate	Rate ratio
All people eligible for vaccination (n=200000)					
Subgroup A* (n=100000)					
Vaccinated	9	29991	30000	0·03%	1·00
Unvaccinated	21	69979	70000	0·03%	..
Subgroup B† (n=100000)					
Vaccinated	21	69979	70000	0·03%	1·00
Unvaccinated	9	29991	30000	0·03%	..
Subgroups A and B combined (n=200000)					
Vaccinated	30	99970	100000	0·03%	1·00
Unvaccinated	30	99970	100000	0·03%	..
Subgroup A (all patients with Bell's palsy captured)					
Vaccinated	30	29991	30021	0·10%	2·33
Unvaccinated	30	69979	70009	0·04%	..

*Subgroup A: patients who presented to emergency rooms or hospital wards, comprising a higher proportion of older people (≥65 years) with a lower overall vaccination rate of 30%. †Subgroup B: other eligible people, who are relatively younger, with a higher overall vaccination rate of 70%.

Table: **Cohort analyses with hypothetical figures to show the effect of selection bias**

We hope our views regarding possible selection bias in observational studies of Bell's palsy following COVID-19 vaccination could put things in perspective and ease concerns.

We declare no competing interests.

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Authors' reply

Kwok-Chiu Chang and Fuk-Yip Kong suggest that possible selection bias in our nested case-control study could be due to the control participants (ie, patients admitted to emergency rooms or hospital wards) being older than all participants eligible for vaccination in the general population. 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 and Kong does not apply to our study.

We acknowledge that the health of participants eligible for vaccination might be relatively better than the health of our control participants. 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 study.[2] We addressed this issue in our analysis by adjusting baseline characteristics, including comorbidities and concurrent medication use. Therefore, such characteristics should not have had a significant effect on our results or conclusions.

To further address Chang and Kong's concern on the difference in baseline characteristics between cases and controls,[1] we conducted further post-hoc sensitivity analysis by excluding control participants with neoplasms or exposure to antibacterial drugs because there were substantial differences between cases and controls (neoplasm 5% *vs* 13%; antibacterial drugs 7% *vs* 13%).[1] The results were similar to the main findings (table), which further supports the robustness of our study.

As is the case for all observational studies, the effect of unmeasured confounding in our nested case-control study cannot be completely ruled out. The self-controlled case series method has become a popular alternative study design for drug safety studies.[2] It was specifically developed to evaluate vaccine safety with the advantage of reducing unmeasured confounding through the comparisons within individuals.[3,4] Because of the small number of events and a short follow-up period in our study, we were unable to apply such a method. We appreciate Chang and Kong's interest in our study and, as stated in our paper, further study is warranted to confirm our findings.

	Number of patients (n=295)*	Number of control participants (n=908)	Crude odds ratio (95% CI)	p value	Adjusted odds ratio (95% CI)	p value
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 (ie, diabetes, hypertension, asthma, rheumatoid arthritis, stroke, and migraine), infections in the past 90 days (acute respiratory infections), and medication use in the past 90 days (antiviral drugs, systemic corticosteroids, immunosuppressants). *Three patients were excluded as the corresponding control participants were excluded because of neoplasms or the antibacterial drugs used.

Table: **Sensitivity analysis excluding control participants with neoplasms or antibacterial drugs used in the nested case-control study**

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