



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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

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.

\**Kwok-Chiu Chang, Fuk-Yip Kong*  
 kcchang.hk@gmail.com

Hong Kong Special Administrative Region, China

- Ozonoff A, Nanishi E, Levy O. Bell's palsy and SARS-CoV-2 vaccines. *Lancet Infect Dis* 2021; **21**: 450–52.
- Wan EYF, Chui CSL, Lai FTT, et al. Bell's palsy following vaccination with mRNA (BNT162b2) and inactivated (CoronaVac) SARS-CoV-2 vaccines: a case series and nested case-control study. *Lancet Infect Dis* 2021; published online Aug 16. [https://doi.org/10.1016/S1473-3099\(21\)00451-5](https://doi.org/10.1016/S1473-3099(21)00451-5).
- Tsang E. Why has Hong Kong's vaccine drive stumbled, and should side effects concern? March 11, 2021. <https://www.scmp.com/news/hong-kong/health-environment/article/3124961/why-has-hong-kongs-coronavirus-vaccination-drive> (accessed Aug 18, 2021).
- Census and Statistics Department. Table 1B: population by sex and age. 2021. [https://www.censtat.gov.hk/en/web\\_table.html?id=1B#](https://www.censtat.gov.hk/en/web_table.html?id=1B#) (accessed Aug 19, 2021).
- Hospital Authority Data Sharing Portal. Major statistics. 2021. <https://www3.ha.org.hk/Data/HASStatistics/MajorReport> (accessed Aug 25, 2021).
- Drug Office, Department of Health. Safety monitoring of COVID-19 vaccines in Hong Kong. June 30, 2021. [https://www.drugoffice.gov.hk/eps/do/en/doc/Safety\\_Monitoring\\_of\\_COVID-19\\_Vaccines\\_in\\_Hong\\_Kong.pdf.20210806](https://www.drugoffice.gov.hk/eps/do/en/doc/Safety_Monitoring_of_COVID-19_Vaccines_in_Hong_Kong.pdf.20210806) (accessed Aug 25, 2021).

### 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

	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**

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.<sup>2</sup> 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,<sup>1</sup> 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%).<sup>1</sup> 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.<sup>2</sup> It was specifically developed to evaluate vaccine safety with the advantage of reducing unmeasured confounding through the comparisons within individuals.<sup>3,4</sup> 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.

ICKW reports research funding from Amgen, Bristol Myers Squibb, Pfizer, Janssen, Bayer, GlaxoSmithKline, Novartis, the Hong Kong Research Grants Council, the Hong Kong Health and Medical Research Fund, the National Institute for Health Research in England, European Commission, and the National Health and Medical Research Council in Australia. ICKW also reports receiving speakers fees from Janssen and Medice, outside the submitted work. ICKW is also an independent non-executive director of Jacobson Medical in Hong Kong. EYFW has received research grants from the Food and Health Bureau of the Government of the Hong Kong Special Administrative Region (SAR), and the Hong Kong Research Grants Council, 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, and personal fees from Primevigilance, outside the submitted work. XL has received research grants from the Food and Health Bureau of the Government of the Hong Kong SAR, research and educational grants from Janssen and Pfizer, internal funding from the University of Hong Kong, and consultancy fees from Merck Sharp & Dohme, outside the submitted work.

EWYC reports honorarium from Hospital Authority, grants from the Hong Kong Research Grants Council, Research Fund Secretariat of the Food and Health Bureau, grants from National Natural Science Fund of China, Wellcome Trust, Bayer, Bristol Myers Squibb, Pfizer, Janssen, Amgen, Takeda, and the Narcotics Division of the Security Bureau of the Hong Kong SAR, outside the submitted work.

\*Ian Chi Kei Wong, Eric Yuk Fai Wan, Celine Sze Ling Chui, Xue Li, Esther Wai Yin Chan  
wongjick@hku.hk

Centre for Safe Medication Practice and Research, Department of Pharmacology and Pharmacy (ICKW, EYFW, XL, EWYC), Department of Family Medicine and Primary Care (EYFW), School of Nursing (CSLC), School of Public Health (CSLC), and Department of Medicine (XL), Li Ka Shing Faculty of Medicine, University of Hong Kong, Hong Kong SAR, China; Laboratory of Data Discovery for Health (D24H), Hong Kong Science and Technology Park, Sha Tin, Hong Kong SAR, China (ICKW, EYFW, CSLC, XL, EWYC); Expert Committee on Clinical Events Assessment Following COVID-19 Immunization, Department of Health, Government of the Hong Kong SAR, Hong Kong SAR, China (ICKW); Research Department of Practice and Policy, School of Pharmacy, University College London, London, UK (ICKW)

- 1 Wan EYF, Chui CSL, Lai FTT, et al. Bell's palsy following vaccination with mRNA (BNT162b2) and inactivated (CoronaVac) SARS-CoV-2 vaccines: a case series and nested case-control study. *Lancet Infect Dis* 2021; published on Aug 16. [https://doi.org/10.1016/S1473-3099\(21\)00451-5](https://doi.org/10.1016/S1473-3099(21)00451-5).
- 2 Man KK, Lau WC, Coghill D, et al. Association between methylphenidate treatment and risk of seizure: a population-based, self-controlled case-series study. *Lancet Child Adolesc Health* 2020; 4: 435-43.
- 3 Whitaker HJ, Paddy Farrington C, Spiessens B, Musonda P. Tutorial in biostatistics: the self-controlled case series method. *Stat Med* 2006; 25: 1768-97.
- 4 Weldelessie YG, Whitaker HJ, Farrington CP. Use of the self-controlled case-series method in vaccine safety studies: review and recommendations for best practice. *Epidemiol Infect* 2011; 139: 1805-17.

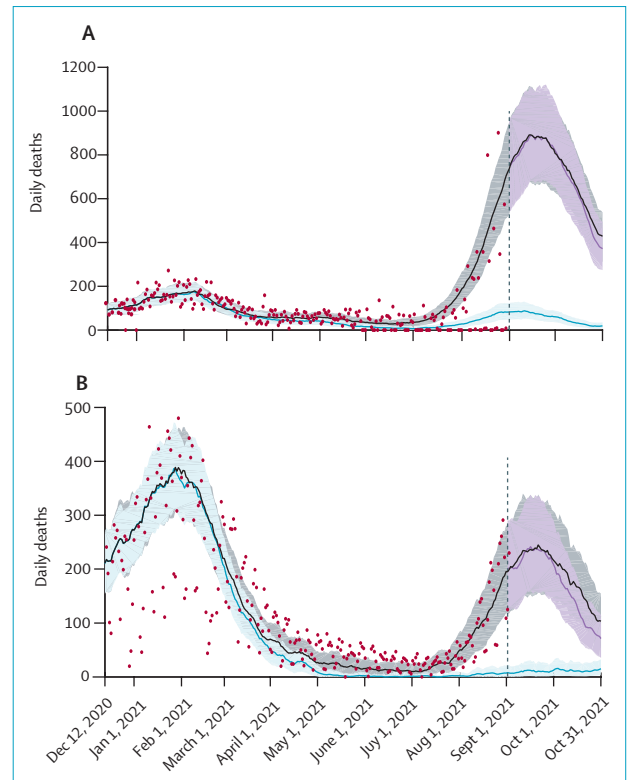
## Implications of suboptimal COVID-19 vaccination coverage in Florida and Texas

In July, 2021, another wave of COVID-19 began in the USA as the highly infectious delta (B.1.617.2) SARS-CoV-2 variant drove outbreaks predominantly affecting states with relatively low

vaccination coverage. Some US states have shown the feasibility of rapidly achieving high vaccination coverage. Specifically, an average of 74.0% of adults had been fully vaccinated in Vermont, Connecticut, Massachusetts, Maine, and Rhode Island by July 31. By contrast, two states facing substantial delta-driven surges, Florida and Texas, had fully vaccinated only 59.5% and 55.8% of their adult residents, respectively.<sup>1</sup> Here, we estimate the deaths, hospital admissions, and infections that could have been averted if Florida and Texas had matched the average vaccination pace of the top-performing states and vaccinated 74.0% of their adult populations by the end of July.

We adapted our agent-based model of SARS-CoV-2 transmission<sup>2,3</sup> to the demography, contact patterns, and age-stratified vaccination trajectories of Florida and Texas. We further accounted for the emergence and spread of the alpha (B.1.1.7), gamma (P.1), iota (B.1.526), and delta variants, in addition to the original strain.<sup>2,3</sup> Vaccine efficacies against infection and symptomatic and severe disease for different vaccine types, each variant, and by vaccine dosage were parameterised from clinical studies (appendix pp 4-5). The model was calibrated to the reported incidence in each state between Oct 1, 2020, and Aug 31, 2021 (appendix p 6). Using the calibrated model, we evaluated the impact of enhanced vaccination rollout by scaling the daily vaccine doses distributed to achieve 74.0% coverage of fully vaccinated adults by July 31, 2021, and continued with the associated daily rates of vaccine rollout. We then simulated the epidemiological trajectories of outbreaks in Florida and Texas and compared them with the observed cases, hospital admissions, and deaths in these two states from Dec 12, 2020, to Aug 31, 2021.

We found that enhanced vaccination would have markedly blunted the increase in cases, hospital admissions, and deaths in Florida and Texas



**Figure:** Model projections of daily deaths in (A) Florida and (B) Texas. Black lines show mean estimates, with uncertainty bounds of simulations shown in grey shaded areas. Red dots are reported data. Blue lines and shaded areas show the model projections for mean estimates and uncertainty bounds under the counterfactual scenario of enhanced vaccination with 74.0% coverage of adults by July 31, 2021. The purple lines and shaded areas show the model projections for mean estimates and uncertainty bounds under the scenario of a 50% increase in daily vaccination rate starting from Sept 1, 2021. All uncertainty bounds are 95% credible intervals.

(figure; appendix p 6). From the start of vaccination on Dec 12, 2020, until Aug 31, 2021, Florida had reported 2 221 520 COVID-19 cases and Texas had reported 2 142 833. Achieving 74.0% vaccination coverage by July 31 and continuing with the associated daily rate would have averted 664 007 additional cases (95% credible interval [CrI] 419 219-848 020) in Florida and 647 906 additional cases (507 298-789 885) in Texas (appendix p 7). By Aug 31, the enhanced vaccination in Florida would have reduced hospital admissions by 61 327 (95% CrI 49 723-73 501) and deaths by 16 235 (13 243-19 473). The reduction in hospital admissions in Texas during the same period would have been 37 587 (95% CrI 31 575-44 659) and the reduction in deaths would have

See Online for appendix



Published Online  
October 7, 2021  
[https://doi.org/10.1016/S1473-3099\(21\)00620-4](https://doi.org/10.1016/S1473-3099(21)00620-4)