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.

be insufficient power to detect publication bias, but by using a conservative approach we were able to take this into account.[1]

We highlight that there are limitations in our study, and clearly state that effect sizes might be overestimated due to a lack of adjustment of potential confounders. The unadjusted results are correctly reported and adjustment for potential confounders can be made by readers in light of the number of comparisons they wish to consider.

Monitoring AST, ALT, and serum albumin during the early phases of dengue disease will provide the opportunity to better understand how these parameters might detect the early onset of severe dengue, which in turn can help optimise and innovate patient care across transmission settings.

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See Online for appendix

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

The comparison of the risk–benefit balance of COVID-19 vaccines in real-world populations has presented new challenges over the past few months. For instance, the detection of rare adverse events is unresolved by clinical trials but mandatory to better inform clinical decision-making in countries where several vaccines are available.[1] However, heterogeneity in the distribution of different COVID-19 vaccines among countries and populations makes such comparisons difficult.

We read with interest the Article by Eric Yuk Fai Wan and colleagues,[2] which explored the association between Bell's palsy, the mRNA-based BNT162b2 vaccine, and the inactivated CoronaVac vaccine in Hong Kong.[2] Hong Kong is one of the rare places where both types of vaccines are available, allowing direct comparison of their efficacy and safety from a unique database. The results of this study suggest a higher risk of developing Bell's palsy in individuals who received CoronaVac than in those who were unvaccinated, and also in those who received the BNT162b2 vaccine. Surprisingly, this safety signal has not been detected by global pharmacovigilance systems.

Since 1968, the WHO pharmacovigilance database has collected and aggregated suspected adverse drug reactions that are spontaneously reported by patients and health professionals from more than 150 countries. This system allows early detection of rare adverse drug reactions by identifying unexpectedly increased proportions of adverse drug reactions reported with a particular drug compared with other drugs in the database (ie, disproportionality signals).[3] Comparison of signals between drugs is challenging in global pharmacovigilance databases because of the heterogeneity in pharmacovigilance systems, unmeasured confounding, change in the rate of adverse events reported to pharmacovigilance systems with drug time on the market, and media coverage of drugs or adverse events, or both. However, COVID-19 vaccines are a rare case for which comparison of signals could be relevant because of similar therapeutic indication, use, and time on the market.[4]

As of Aug 31, 2021, the WHO pharmacovigilance database contained 770 343 reports of adverse events with the BNT162b2 vaccine, of which 7892 were reports of facial paralysis (the method for case identification has been described elsewhere).[5] However, only 30 091 reports of adverse events had been made for CoronaVacc, of which 38 were reports of facial paralyses. Therefore, the disproportionality signals of facial paralysis are lower for Coronavac than for BNT162b2, which differs from the findings of Wan and colleagues' study.

This discrepancy could be due to several reasons. First, the broad media coverage of this potential adverse event might have stimulated its reporting with mRNA vaccines. Second, the low number of adverse events reported with CoronaVac vaccines does not allow for an accurate estimate of the proportion of rare adverse drug reactions. Several large countries that used CoronaVac did not report any adverse events as part of the WHO Program for International Drug Monitoring (appendix pp 1–2).

The results of Wan and colleagues' study highlight the risk of false conclusions being drawn from comparison of disproportionality signals in an international pharmacovigilance

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.

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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**