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Further investigation is needed to determine whether the decrease in IgG positivity after vaccination with CoronaVac parallels decreasing protection against severe disease. Effectiveness against intensive care unit (ICU) admission was 91.6% (95% CI 90.5–92.5) in Chile during the vaccine scaling-up campaign.<sup>9</sup> Decisions made by policy makers about the need for a third dose will benefit from seroepidemiology studies, but the most relevant information to assess vaccine effectiveness should be protection in terms of reduction of deaths and ICU admissions, especially considering new emerging variants. Equitable access to robust vaccines is the ideal scenario, but in reality the universal provision of any COVID-19 vaccine presents a challenge.

We declare no competing interests.

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## The association between COVID-19 vaccination and Bell’s palsy

In the past 100 days, more than 3 billion doses of SARS-CoV-2 vaccines have been administered globally.<sup>1</sup> With 20 vaccines currently authorised in at least one country and 108 under clinical development as of July 20, 2021,<sup>2</sup> there is ongoing public concern regarding the possible adverse effects of SARS-CoV-2 immunisation. An adverse event reported in the product information of two vaccines developed with a novel mRNA technology is Bell’s palsy, a form of acute facial nerve paralysis.<sup>3</sup> So far there has been no clear evidence of association between COVID-19 vaccination and facial paralysis. However, the findings from Eric Wan and colleagues’ study<sup>4</sup> in *The Lancet Infectious Diseases* showed an overall increased risk of Bell’s palsy after immunisation with CoronaVac (Sinovac Biotech), a vaccine that uses the inactivated virus.

Despite the numerical imbalance of Bell’s palsy cases observed in trials of the two mRNA vaccines,<sup>5,6</sup> but not in those of other vaccine platforms,<sup>7</sup> the relevant regulatory bodies, including the US Food and Drug Administration and the UK Medicines and Healthcare

products Regulatory Agency among others, have argued that the observed frequency in vaccinated individuals was no higher than the expected background rate. A closer look at these figures and analysis of crude real-world data from pharmacovigilance agencies estimated that Bell’s palsy occurred more often in the mRNA vaccine groups than would be expected in the general population.<sup>8</sup> Two research letters later provided indirect evidence for the safety of mRNA vaccines from a Bell’s palsy standpoint. In one letter, the WHO pharmacovigilance database was used to show that mRNA COVID-19 vaccines did not confer an increased risk of facial paralysis when compared with other viral vaccines.<sup>9</sup> In the other letter, the authors concluded that patients with COVID-19 have a greater risk of acquiring Bell’s palsy than those who were vaccinated against the disease.<sup>10</sup>

The controversy was again addressed by the findings from a relatively small case-control study from Israel,<sup>11</sup> in which 37 patients with Bell’s palsy were matched to 74 controls and no association with mRNA-based



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SARS-CoV-2 vaccination was found (adjusted odds ratio [OR] for exposure 0.84 [95% CI 0.37–1.90;  $p=0.67$ ]). Of note, hospital admissions due to facial nerve palsy in January and February, 2020, and January and February, 2021, were 29–112% greater than in the same period in the 5 preceding years, but this was not deemed significant.<sup>11</sup>

Wan and colleagues used different population-based approaches to evaluate the possible association between Bell's palsy and mRNA (BNT162b2; Fosun-BioNTech) and inactivated virus (CoronaVac) vaccines in Hong Kong.<sup>4</sup> Using a voluntary surveillance reporting system and electronic health records, the authors found a substantial increase in the age-standardised incidence of Bell's palsy during the vaccination programme compared with the same period in previous years. For example, after accounting for confounding variables, the incidence difference with the same observation period in 2020 was 41.5 cases per 100 000 person-years (95% CI 11.7 to 71.4) for CoronaVac and 17.0 (–6.6 to 40.6) for BNT162b2. In the nested case-control study, 298 patients with clinically confirmed Bell's palsy were selected. 1181 control individuals were randomly matched (4:1) to each case according to sex, age, date of hospital attendance (to control for seasonality of the disease), and setting (to reduce selection bias). The results suggested a significantly increased risk of Bell's palsy associated with receiving CoronaVac (adjusted OR 2.385 [95% CI 1.415–4.022];  $p=0.0011$ ) for CoronaVac, but no significant difference in risk associated with receiving BNT162b2 (1.755 [0.886–3.77];  $p=0.11$ ). Owing to the timing of vaccine rollout in Hong Kong, vaccination was notably less common in this population compared with in the study done in Israel. For example, in Wan and colleagues' study, only 84 (7.1%) individuals in the control population had been vaccinated,<sup>4</sup> compared with 59.5% in the previous study,<sup>11</sup> which might have influenced the strength of the association. On the other hand, data collected during the early stages of vaccination in Hong Kong might have introduced selection bias because only people in specific categories of workers and age groups were vaccinated. These caveats are not trivial because the background incidence of Bell's palsy varies greatly with age<sup>12</sup> and the vaccines

are likely to have different safety profiles in different age groups.

From a clinical, patient-oriented perspective, none of the studies published so far provide definitive evidence to inform the choice of a specific vaccine in individuals worldwide with a history of Bell's palsy. However, the data published by Wan and colleagues do offer valuable information for a rational and informed choice of COVID-19 vaccines for patients in Hong Kong, and for those in countries where both BNT162b2 and CoronaVac are available. While waiting for conclusive evidence on vaccine-associated facial paralysis, one certainty remains: the benefit of getting vaccinated outweighs any possible risk.

We declare no competing interests.

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