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Self-reported reactogenicity of CoronaVac (Sinovac) compared with Comirnaty (Pfizer-BioNTech): A prospective cohort study with intensive monitoring



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ABSTRACT

Objective: CoronaVac (Sinovac) Covid-19 vaccine has recently been approved for emergency use by the World Health Organization. However, data on its reactogenicity in real-world settings is scant. This study aimed to compare self-reported post-vaccination adverse reactions between CoronaVac and Comirnaty (Pfizer-BioNTech).

Methods: We adopted a prospective cohort study design using online surveys from the day of first-dose vaccination with intensive follow-up through two weeks after the second dose (11 time points). The primary outcome was adverse reactions (any versus none) and secondary outcomes were the sub-categories of adverse reactions (local, systemic, and severe allergic reactions). Potential effect modification across multimorbidity status, older age, and sex was examined.

Results: In total, 2,098 participants who were scheduled to complete the 14th-day survey were included, with 46.2% receiving Comirnaty. Retention rate two weeks after the second dose was 81.0% for the CoronaVac group and 83.6% for the Comirnaty group. Throughout the follow-up period, 801 (82.7%) of those receiving Comirnaty and 543 (48.1%) of those receiving CoronaVac reported adverse reactions. Adjusted analysis suggested that compared with Comirnaty, CoronaVac was associated with 83%-reduced odds of any adverse reactions [adjusted odds ratio (AOR) = 0.17, 95% confidence interval (CI) 0.15–0.20], 92%-reduced odds of local adverse reactions (AOR = 0.08, 95% CI 0.06–0.09), and 76%-reduced odds of systemic adverse reactions (AOR = 0.24, 95% CI 0.16–0.28). No significant effect modification was identified.

Conclusion: This post-marketing study comparing the reactogenicity of Covid-19 vaccines suggests a lower risk of self-reported adverse reactions following vaccination with CoronaVac compared with Comirnaty.

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1. Introduction

CoronaVac (Sinovac) Covid-19 vaccine, an inactivated virus vaccine, has been approved for emergency use by the World Health

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Organization (WHO) [1]. Phase I/II [2] and phase III clinical trials [3] as well as preliminary post-marketing research [4] have presented reassuring data on the safety profile, indicated by the absence or rare incidence of adverse events of interest, and a satisfactory level of efficacy in the protection against Covid-19. Nevertheless, little research has examined its reactogenicity, i.e. a vaccine property with regard to the production of expected adverse reactions, particularly through active self-report data collection about typically mild to moderate and self-limiting reactions requiring minimal to no medical interventions [5]. The occurrence of adverse reactions is not directly correlated to efficacy level. No research has compared CoronaVac's reactogenicity with messenger RNA (mRNA) vaccines [6], which are developed on a different technological platform and typically more widely used in Western countries [7]. A prolonged absence of this important information may worsen the problem of vaccine hesitancy [8] and hamper our efforts in the fight against the pandemic.

Comirnaty (Pfizer-BioNTech) Covid-19 vaccine utilises mRNA for immunization against Covid-19 [9,10] As of July 2021, >100 countries have approved it for emergency use and rolled out massive vaccination programs. From published clinical data [11,12], it is observed that a relatively high proportion of vaccinated individuals reported discomfort or adverse reactions following vaccination [10,13]. In a large randomized controlled trial [10], approximately 80% of vaccinated adults aged 16-55 reported at post-vaccination adverse reactions following both doses (first dose: 83%; second dose: 78%) such as pain at the injection site, fatigue, dizziness, etc. This proportion is seemingly lower among those who received CoronaVac in clinical trials conducted in Turkey [14] and China [2], in which only 18.9 to 35.0% of vaccinated individuals reported adverse reactions within 28 days post-vaccination (second dose). The phase III clinical trial of BBIBP-CorV, another inactivated virus vaccine, also showed that only less than half of the vaccinated individuals had any adverse reactions (both doses combined) [15]. To our knowledge, the comparative reactogenicity of CoronaVac and Comirnaty is yet to be explored in the same population.

Hong Kong is among jurisdictions that has approved the emergency use of both vaccines and implemented publicly funded mass vaccination programs for residents' immunization against Covid-19 since February 2021 [16]. This study aims to describe and compare post-marketing, self-reported reactogenicity of CoronaVac and Comirnaty after both the first and second doses in this predominantly Chinese population, which represents highly important information especially in countries where the infection rate is low and the side effects of vaccines are of public concern. We hypothesized a milder reactogenicity of CoronaVac compared with Comirnaty. Potential effect modification of age, sex, and multimorbidity status on this difference was also examined.

2. Methods

2.1. Study design

Under the Covid-19 vaccines adverse events response and evaluation programme commissioned by the Hong Kong Government, we adopted a prospective cohort design with self-reported data collected on the first-dose vaccination day, as well as the first, second, third, seventh, and the fourteenth day following both doses of vaccination (11 time points). A 14-day follow-up period is consistent with the common existing literature and enhances the comparability of this research [12]. Baseline demographic and health status information were collected on the day of the first-dose and self-reports of adverse reactions of various types were collected throughout the observation period, i.e. all time points.

2.2. Participants

We recruited participants aged 16 or above receiving the first dose of either CoronaVac and Comirnaty at community vaccination centers run by the Government or at private clinics (only for CoronaVac) starting from 27th February 2021. We supplemented the active in-person recruitment with flyers including a quick-response (QR) link to the online survey distributed at healthcare facilities. The link to follow-up surveys was sent to participants via instant text messages and surveys were conducted online using Qualtrics, an online data collection platform. Only those participants who were scheduled to complete the 14th-day follow-up survey for the second dose according to the recommended dosing interval, i.e. number of days, between the two doses were included in the analysis. Participants could withdraw from the study anytime.

This study was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (UW-21-090) and the Department of Health Ethics Committee (LM 21/2021). Upon recruitment, written informed consent from the participants were obtained. The consent form, patient information leaflet, paper questionnaires can be downloaded from our website (https://www.hkcare.hku.hk/).

2.3. Outcomes

The primary outcome of this study was self-reported adverse reactions (any versus none). Secondary outcomes were dichotomous indicators of the three sub-categories of self-reported adverse reactions, including local (numbness, soreness, pain, swelling, redness, and itch), systemic (sore throat, tiredness, fever, chills, sweating, cough, headache, muscle pain, joint pain, pain in limbs, abdominal pain, diarrhea, nausea, vomiting, poor appetite, insomnia, feeling unwell, enlarged lymph nodes, rash, and temporary one-sided facial drooping), and severe allergic reactions (hypotension, dizziness, itchy skin rash, swelling of face or tongue, and wheezing/shortness of breath).

2.4. Exposure

Vaccine type (CoronaVac versus Comirnaty) was the primary exposure of the analysis because they were the only available vaccine options in Hong Kong. As a secondary exposure, we also compared the second dose of vaccination against the first dose.

2.5. Effect modifier

Multimorbidity, defined as the presence of two or more listed chronic conditions [17] (ankylosing spondylitis, asthma, psoriasis, rheumatoid arthritis, systemic lupus erythematosus, cancer remission, cancer under treatment, hypertension, hypercholesterolemia, heart disease, diabetes, stroke, neurological disorders, mental health disorders, liver problems, and kidney problems), was examined as an effect modifier in the association of vaccine type and adverse reactions. This list considered the prevalence and relevance of the conditions as well as the comparability of the findings with the existing literature [18]. We also examined sex (men versus women) and older age (60 or more versus 59 or less) as potential effect modifiers.

2.6. Multivariable adjustment

At the person-level, covariates including age, sex (men versus women), educational attainment (primary or below, secondary, post-secondary, and university or above), history of allergy to medications and to food (any versus none), smoking status (non-

smoker, former smoker, and current smoker), alcohol use (non-drinker, former drinker, occasional drinker, and regular drinker), number of chronic medications (none, 1–2, 3–4, 5–9, and 10 or more), and a range of chronic conditions (binary indicators, as listed above) were included for multivariable adjustment.

At the measurement level (each follow-up survey), specific follow-up days (vaccination day, first-, second-, third-, seventh-, and fourteenth-day post-vaccination) and second-dose (versus the first) were also adjusted for.

2.7. Statistical analysis

A random-intercept logistic regression model was implemented to examine the association between vaccine type (CoronaVac versus Comirnaty) and adverse reactions with multivariable adjustment where only the intercept was specified as random and the other factors as fixed. Individual participants were treated as a random factor. Listwise deletion was applied for missing data. We conducted sensitivity analyses with one-to-one propensity score matching (nearest-neighbor approach, caliper = 0.01) and inverse probability of treatment weighting based on the same personlevel covariates respectively, was used as alternative approaches to multivariable adjustment to test the robustness of the results. We investigated the potential effect modification on this association by testing for the interaction between potential modifiers and vaccine type in extended models.

Stratified by vaccine type, a secondary analysis was conducted to compare the first and second dose of vaccination in terms of the association with adverse reactions. In the analyses, it was assumed that the assumption for the model, normal distribution of the random intercept, was true.

2.8. Sample size consideration

According to the widely adopted events-per-variable rule of thumb of 50 [19], we estimated we required 1,500 participants for a list of 30 covariates. We took a prudent approach and recruited over one-third more than this number to maximize the power of this study.

3. Results

As of 5th July 2021, 1,129 participants receiving CoronaVac and 969 receiving Comirnaty were recruited and were scheduled to complete the 14th-day follow-up survey for the second dose. For the 14th-day follow-up survey following the second dose, the retention rate was 81.0% for the CoronaVac group and 83.6% for the Comirnaty group. Response rates by follow-up day and vaccine type are tabulated as **eTable 1**. Chi-square tests showed that for Day 2, 3, and 7 for both doses, the Comirnaty group had a higher response rate (P < 0.05) although both groups had response rates exceeding 80% throughout the follow-up period.

3.1. Cohort characteristics

As shown in Table 1, the 46.7% of the CoronaVac group and 51.7% of the Comirnaty group were men. Mean age was 46.5 years for CoronaVac compared with 43.1 for Comirnaty. In total, 49.6% (CoronaVac) and 63.0% of the participants attained university education level. Current smokers constituted 10.1% (CoronaVac) and 5.9% (Comirnaty) of the groups, and 8.3% (CoronaVac) and 11.5% (Comirnaty) were regular drinkers. Around one-fifth of the participants were on at least one chronic medication at the time of vaccination for both vaccine groups. There were 7.3% (CoronaVac) and 5.8% (Comirnaty) of the participants who had a history of allergy to

medications and 6.2% (CoronaVac) and 6.7% (Comirnaty) to food and other substances. For both groups, hypertension was the most prevalent chronic condition among participants (9.0% for CoronaVac; 10.3% for Comirnaty), followed by hypercholesterolemia (7.2% for CoronaVac; 7.6% for Comirnaty) and diabetes (2.8% for CoronaVac; 3.6% for Comirnaty).

3.2. Adverse reactions

Throughout the follow-up period, 801 (82.7%) of those receiving Comirnaty and 543 (48.1%) of those receiving CoronaVac reported adverse reactions of any type. Among those reporting any adverse reactions at any time point following the first dose (n = 1,082), 65.6% reported adverse reactions at some point following the second, but among those who did not have adverse reactions at any time point following the first dose (n = 1,016), only 25.8% reported adverse reactions at some point following the second dose.

Fig. 1 shows the proportion [with 95% confidence interval (CI)] of participants reporting any type of adverse reactions at each time point throughout the observation period. For both vaccines, this proportion peaked on the first day post-vaccination and gradually declined. In general, more participants reported adverse reactions following the second rather than the first dose. **eFigure 1**, **eFigure 2** and **eFigure 3** show the proportion of participants reporting local, systemic, and severe allergic reactions throughout the follow-up period respectively, with largely similar patterns observed.

Fig. 2 are bar charts showing the five most commonly reported adverse reactions by vaccine type and dose (first versus second) two weeks post-vaccination. For both doses, pain at injection site, tiredness, muscle pain, headache, and swelling at the injection site were the five most frequently reported adverse reactions.

3.3. Multivariable adjusted analysis

As shown in Table 2, our random-intercept logistic regression model suggested that compared with Comirnaty, receiving Corona-Vac was associated with 83%-reduced odds of any adverse reactions [adjusted odds ratio (AOR) = 0.17, 95% CI 0.15–0.20], 92%-reduced odds of local adverse reactions (AOR = 0.08, 95% CI 0.06–0.09), and 76%-reduced odds of systemic adverse reactions (AOR = 0.24, 95% CI 0.16–0.28). Sensitivity analysis using propensity score matching and inverse probability of treatment weighting suggested highly consistent results (see **eTable 2 and eTable 3**). Extended models testing for the interaction between potential effect modifiers yielded no statistically significant results (P > 0.05).

Table 3 shows the adjusted odds ratios of adverse reactions following the second dose compared with the first. For adverse reactions of any type, there were 18%-increased odds (AOR = 1.18, 95% CI 1.01–1.37) for the second dose compared with the first among those receiving CoronaVac. Among those receiving Comirnaty, there were 106% increased odds (AOR = 2.06, 95% CI 1.81–2.35). For all three sub-types of adverse reactions, significantly increased odds were observed in the Comirnaty group. Among those receiving CoronaVac, significantly increased odds were only observed for local adverse reactions.

4. Discussion

The results confirmed our hypothesis that CoronaVac had milder reactogenicity compared with Comirnaty. We found that the risk of adverse reactions (overall, local, and systemic) two weeks post-vaccination is significantly lower among those receiving CoronaVac compared with Comirnaty. This risk difference does not vary significantly between those living with multimorbidity

Table 1 Cohort characteristics.

	CoronaVac	Comirnaty		
n	1129	969	Standardized mean difference	
Age (mean (SD))	46.49 (14.42)	43.13 (16.54)	0.217	***
Sex = Male (%)	527 (46.7)	498 (51.7)	0.101	*
Educational attainment (%)	227 (1017)	100 (0111)	0.301	***
Primary and below	20 (1.8)	27 (2.8)	-1	
Secondary	373 (33)	215 (22.2)		
Post-secondary	176 (15.6)	116 (12)		
University or above	560 (49.6)	610 (63)		
Smoking status (%)	,	,	0.172	**
Non-smoker	974 (86.3)	888 (91.6)		
Former smoker	40 (3.5)	24 (2.5)		
Current smoker	114 (10.1)	57 (5.9)		
Alcohol use (%)	111 (1011)	57 (515)	0.144	*
Non-drinker	807 (71.5)	632 (65.4)		
Occasional drinker	223 (19.8)	221 (22.9)		
Former drinker	5 (0.4)	3 (0.3)		
Regular drinker	94 (8.3)	111 (11.5)		
Number of chronic medications (%)	- (- (-) -)	()	0.147	*
None	917 (81.2)	761 (78.5)		
1-2	155 (13.7)	155 (16)		
3-4	40 (3.5)	39 (4)		
5–9	13 (1.2)	14 (1.4)		
10 or more	4 (0.4)	0 (0)		
History of allergy to medications (%)	82 (7.3)	56 (5.8)	0.059	
History of allergy to food and other substances (%)	70 (6.2)	65 (6.7)	0.022	
Chronic conditions (%)	()	()		
Asthma	10 (0.9)	18 (1.9)	0.084	
Psoriasis	0 (0)	1 (0.1)	0.045	
Rheumatoid arthritis	0 (0)	3 (0.3)	0.079	
Systemic lupus erythematosus	1 (0.1)	0 (0)	0.042	
Cancer remission	8 (0.7)	4 (0.4)	0.040	
Cancer under treatment	1 (0.1)	4 (0.4)	0.065	
Hypertension	102 (9)	100 (10.3)	0.043	
Hypercholesterolemia	81 (7.2)	74 (7.6)	0.018	
Heart disease	18 (1.6)	16 (1.7)	0.004	
Diabetes	32 (2.8)	35 (3.6)	0.044	
Stroke	2 (0.2)	3 (0.3)	0.027	
Neurological disorder	1 (0.1)	2 (0.2)	0.031	
Mental health disorder	10 (0.9)	8 (0.8)	0.007	
Liver problems	6 (0.5)	10 (1)	0.057	
Kidney problems	3 (0.3)	5 (0.5)	0.040	
Morbidity status (%)	• •	, ,	0.076	
No chronic conditions	935 (82.8)	778 (80.3)		
One	132 (11.7)	124 (12.8)		
Two	46 (4.1)	47 (4.9)		
Three	12 (1.1)	16 (1.7)		
Four or more	4 (0.4)	4 (0.4)		

^{***} P < 0.05. ** P < 0.01. * P < 0.001

and those without, between men and women, and between older and non-older adults in our cohort. We also observed a higher risk of adverse reactions following the second dose compared with the first, with larger differences among those receiving Comirnaty. Our findings may further inform individual and public choices of vaccines.

Post-marketing research on Covid-19 vaccines in real-world settings is still accruing, with most studies focusing on serious adverse events which typically require medical interventions or even tertiary care.[20] While this line of research is highly important to establish the safety profile, the reactogenicity of vaccines, represented by adverse reactions that are mild and oftentimes fully self-resolves, also has a considerable impact on individual and public decisions with regard to vaccine uptake [21]. To the best of our knowledge, this current post-marketing study is the first to compare the reactogenicity of CoronaVac with Comirnaty in the same population. Our findings are in line with previous clinical trial data [10,14]. For instance, the recently published phase III clinical trial results suggested that approximately one-fifth of the volunteers receiving CoronaVac experienced any type of adverse

reactions [14] and approximately 80% of individuals receiving Comirnaty reported adverse reactions after both doses, such as pain at the injection site, in the first seven days [10].

Recently published data obtained from vaccinated healthcare workers in Hong Kong suggested that, compared with Comirnaty, the quantity of antibodies induced in adults receiving CoronaVac is substantially lower [22]. Also, it has been suggested in a *meta*-analysis that, across different vaccine platforms, there are obvious trade-offs between various qualities of the vaccines including mild reactogenicity and the strength of the triggered immune response [11]. It is possible that the general immune response induced by vaccination was weaker among those receiving CoronaVac, compared with those receiving Comirnaty, and thus potentially a lower risk of adverse reactions followed the vaccination of the participants; further immunoepidemiologic studies are needed to test this hypothesis because there is no direct relationship between side effects and protection.

Given the real-world observational design, randomization was not feasible to further eliminate any residual confounding effects beyond the multivariable adjustment made in the models. Specif-

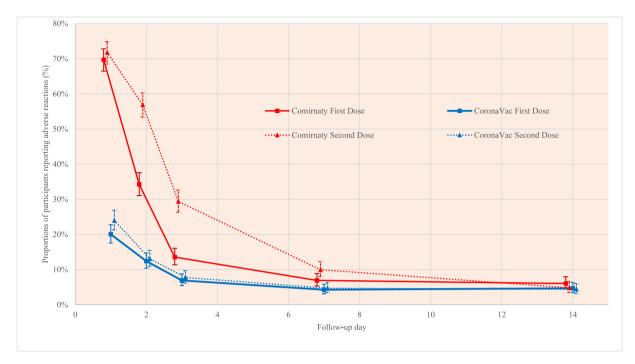


Fig. 1. Proportions (with 95% confidence intervals) of self-reported adverse reactions by vaccine type and dose (first versus second). Sample size varies across timepoints with different retention rate on different follow-up days.

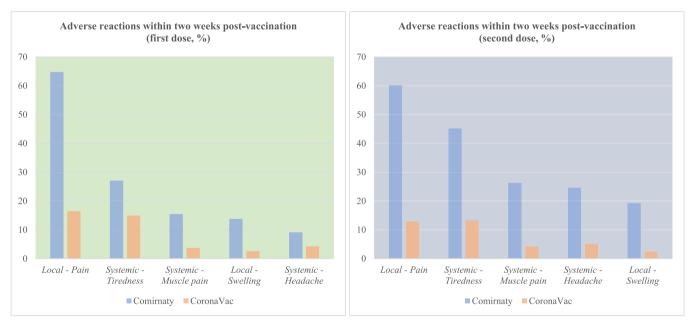


Fig. 2. Proportions of participants reporting specific adverse reactions two weeks post-vaccination.

ically, there could be unobserved characteristics of individuals that were associated with the choice of vaccine type and, simultaneously, with self-reports of adverse reactions, such that the results were biased towards the rejection of the null hypothesis. Nonetheless, based on our literature search and clinical reasoning we did not identify any further potential confounders to consider and include in the analysis. Besides residual confounding, other limitations that need to be taken into consideration while interpreting the results include the design of serial self-report online survey, which entails a risk of omitting the follow-up survey of individuals (from the missing follow-up data) who had more serious adverse reactions and required medical interventions or were even hospi-

talized. However, both vaccine groups had a response rate of > 80% throughout the follow-up period and any bias should not affect the results and conclusions substantially. Also, more serious adverse reactions, if any, would most likely be captured in the routine medical databases which are closely monitored and reported. In addition, this study lacked the clinical confirmation of the adverse reactions and the causality assessment which would have strengthened the causal inferences from the observed associations.

Previous research on vaccine hesitancy suggested that reactogenicity is among the multitude of factors considered while making the decision to receive a vaccine or not [23]. A clearer outline

Table 2Adjusted odds ratios ^a of self-reported adverse reactions for those who received CoronaVac compared with those receiving Comirnaty.

	Odds ratio (95% confidence interval)
Adverse reactions	
Any	0.17 (0.15-0.20) ***
Local ^b	0.08 (0.06-0.09) ***
Systemic ^c	0.24 (0.16-0.28) ***
Severe allergic reactions d	0.62 (0.36-1.06)

^{***} P < 0.05, ** P < 0.01, * P < 0.001

- b Including numbness, soreness, pain, swelling, redness, and itch
- ^c Including sore throat, tiredness, fever, chills, sweating, cough, headache, muscle pain, joint pain, pain in limbs, abdominal pain, diarrhea, nausea, vomiting, poor appetite, insomnia, feeling unwell, enlarged lymph nodes, rash, and temporary one-sided facial drooping
- ^d Including hypotension, dizziness, itchy skin rash, swelling of face or tongue, and wheezing/shortness of breath

Table 3Adjusted odds ratios ^a of self-reported adverse reactions arising from the second dose compared with the first dose of CoronaVac and Comirnaty.

	Odds ratio (95% confidence interval)		
	CoronaVac	Comirnaty	
Adverse reactions			
Any	1.18 (1.01-1.37) *	2.06 (1.81-2.35) ***	
Local ^b	1.39 (1.11-1.75) **	2.04 (1.77-2.36) ***	
Systemic ^c	1.12 (0.92-1.38)	3.09 (2.65-3.61) ***	
Severe allergic reactions d	1.15 (0.62-2.15)	2.01 (1.21-3.33) **	

^{***} P < 0.05, ** P < 0.01, * P < 0.001

- ^b Including numbness, soreness, pain, swelling, redness, and itch
- ^c Including sore throat, tiredness, fever, chills, sweating, cough, headache, muscle pain, joint pain, pain in limbs, abdominal pain, diarrhea, nausea, vomiting, poor appetite, insomnia, feeling unwell, enlarged lymph nodes, rash, and temporary one-sided facial drooping
- ^d Including hypotension, dizziness, itchy skin rash, swelling of face or tongue, and wheezing/shortness of breath

of the types of anticipated adverse reactions following vaccination should enable more informed decisions for both individuals and governments. Specifically, our study findings should help shape the public's expectation of the reactogenicity of CoronaVac, as compared with the more widely investigated Comirnaty [24]. Vaccination or medical leave policies could be formulated on the basis of our findings. Nevertheless, further research in other populations is warranted to verify our results and test for generalizability. The Government of Hong Kong continues to monitor all serious adverse events following immunization (AEFI). To date, there have not been major safety signals on serious AEFI. However, successful infection control and risk mitigation strategies against Covid-19 [25] has led to a very low COVID-19 infection rate in Hong Kong (<12,000 cases in a population of over seven million people as of July 2021). In this context, the self-reported adverse reactions of vaccines become an important factor in the decision of vaccine uptake.

In conclusion, this first post-marketing study comparing the reactogenicity of CoronaVac and Comirnaty in the same population

suggests a lower risk of self-reported adverse reactions following vaccination with CoronaVac compared with Comirnaty.

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Data availability statement

Authorization to access the data may be considered by the authors upon reasonable requests. Requests to access these datasets should be directed to the corresponding author, ewchan@hku.hk.

6. Ethics approval

This study was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (UW-21–090) and the Department of Health Ethics Committee (LM 21/2021).

Informed consent

Upon recruitment, written informed consent from the participants were obtained. The consent form, patient information leaflet, paper questionnaires can be downloaded from our website (https://www.hkcare.hku.hk/).

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: [Ian Chi Kei Wong reports financial support was provided by Food and Health Bureau of the Hong Kong Special Administration Region Government. Esther Wai Yin Chan reports a relationship with Hospital Authority that includes: consulting or advisory and speaking and lecture fees. Esther Wai Yin Chan reports a relationship with Research Grants Council (RGC, Hong Kong) that includes: funding grants. Esther Wai Yin Chan reports a relationship with Research Fund Secretariat of the Food and Health Bureau that includes: funding grants. Esther Wai Yin Chan reports a relationship with National Natural Science Fund of China that includes: funding grants. Esther Wai Yin Chan reports a relationship with Wellcome Trust that includes: funding grants. Esther Wai Yin Chan reports a relationship with Bayer that includes: funding grants. Esther Wai Yin Chan reports a relationship with Bristol-Myers Squibb that includes: funding grants. Esther Wai Yin Chan reports a relationship with Pfizer that includes: funding grants. Esther Wai Yin Chan reports a relationship with Janssen that includes: funding grants. Esther Wai Yin Chan reports a relationship with Amgen that includes: funding grants. Esther Wai Yin Chan reports a relationship with Takeda that includes: funding grants. Esther Wai Yin Chan reports a relationship with Narcotics Division of the Security Bureau of HKSAR that includes: funding grants. Francisco Tsz Tsun Lai reports a relationship with RGC Postdoctoral Fellowship, Hong Kong Research Grants Council that includes: funding grants. Xue Li reports a relationship with Food and Health Bureau of the Government of the Hong Kong SAR that includes: funding grants. Xue Li reports a relationship with Janssen that includes: funding grants. Xue Li reports a relationship with Pfizer that includes: funding grants. Xue Li reports a relationship with The University of Hong Kong that includes: funding grants. Xue Li reports a relationship with Merck Sharp & Dohme that includes: consulting or advisory. Celine Sze Ling Chui reports a relationship with Food and Health

a Odds ratios adjusted for dose (1st versus 2nd), follow-up day, age, sex, educational attainment, allergy to medications, allergy to food and other substances, smoking status, alcohol use, number of chronic medications, ankylosing spondylitis, asthma, psoriasis, rheumatoid arthritis, systemic lupus erythematosus, cancer remission, cancer under treatment, hypertension, hypercholesterolemia, heart disease, diabetes, stroke, neurological disorders, mental health disorders, liver problems, and kidney problems

a Odds ratios adjusted for follow-up day, age, sex, educational attainment, allergy to medications, allergy to food and other substances, smoking status, alcohol use, number of chronic medications, ankylosing spondylitis (only for CoronaVac), asthma, psoriasis (only for Comirnaty), rheumatoid arthritis (only for Comirnaty), systemic lupus erythematosus (only for CoronaVac), cancer remission, cancer under treatment, hypertension, hypercholesterolemia, heart disease, diabetes, stroke, neurological disorders, mental health disorders, liver problems, and kidney problems

Bureau of the Hong Kong Government that includes: funding grants. Celine Sze Ling Chui reports a relationship with Hong Kong Research Grant Council that includes: funding grants. Celine Sze Ling Chui reports a relationship with Hong Kong Innovation and Technology Commission that includes: funding grants. Celine Sze Ling Chui reports a relationship with Pfizer that includes: funding grants. Celine Sze Ling Chui reports a relationship with IQVIA that includes: funding grants. Celine Sze Ling Chui reports a relationship with Amgen that includes: funding grants. Celine Sze Ling Chui reports a relationship with PrimeVigilance Ltd that includes: consulting or advisory. Eric Yuk Fai Wan reports a relationship with Food and Health Bureau of the Government of the Hong Kong SAR that includes: funding grants. Eric Yuk Fai Wan reports a relationship with Hong Kong Research Grants Council that includes: funding grants. Ian Chi Kei Wong reports a relationship with Amgen that includes: funding grants, Ian Chi Kei Wong reports a relationship with Bristol-Myers Squibb that includes: funding grants. Ian Chi Kei Wong reports a relationship with Pfizer that includes: funding grants. Ian Chi Kei Wong reports a relationship with Janssen that includes: funding grants. Ian Chi Kei Wong reports a relationship with Bayer that includes: funding grants. Ian Chi Kei Wong reports a relationship with GSK that includes: funding grants. Ian Chi Kei Wong reports a relationship with Novartis that includes: funding grants. Ian Chi Kei Wong reports a relationship with Hong Kong RGC that includes: funding grants. Ian Chi Kei Wong reports a relationship with Hong Kong Health and Medical Research Fund that includes: funding grants. Ian Chi Kei Wong reports a relationship with National Institute for Health Research in England that includes: funding grants. Ian Chi Kei Wong reports a relationship with European Commission that includes: funding grants. Ian Chi Kei Wong reports a relationship with National Health and Medical Research Council in Australia that includes: funding grants. Ian Chi Kei Wong reports a relationship with Janssen that includes: speaking and lecture fees. Ian Chi Kei Wong reports a relationship with Medice that includes: speaking and lecture fees.].

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2022.01.062.

References

- World Health Organization. Interim recommendations for use of the inactivated COVID-19 vaccine, CoronaVac, developed by Sinovac [Internet].
 2021 [cited 2021 Jul 18]. Available from: https://apps.who.int/iris/rest/ bitstreams/1348680/retrieve
- [2] Zhang Y, Zeng G, Pan H, Li C, Hu Y, Chu K, et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18–59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. Lancet Infect Dis. 2021;21(2):181–92.
- [3] Tanriover MD, Doğanay HL, Akova M, Güner HR, Azap A, Akhan S, et al. Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey. The Lancet 2021;398(10296):213–22.
- [4] Jara A, Undurraga EA, González C, Paredes F, Fontecilla T, Jara G, et al. Effectiveness of an Inactivated SARS-CoV-2 Vaccine in Chile. N Engl J Med 2021;385(10):875-84.
- [5] Mathioudakis AG, Ghrew M, Ustianowski A, Ahmad S, Borrow R, Papavasileiou LP, et al. Self-Reported Real-World Safety and Reactogenicity of COVID-19 Vaccines: A Vaccine Recipient Survey. Life (Basel, Switzerland). 2021;11.

- [6] McDonald I, Murray SM, Reynolds CJ, Altmann DM, Boyton RJ. Comparative systematic review and meta-analysis of reactogenicity. immunogenicity and efficacy of vaccines against SARS-CoV-2 npj Vaccines 2021;6(1). https://doi. org/10.1038/s41541-021-00336-1.
- [7] Chodick G, Tene L, Rotem RS, Patalon T, Gazit S, Ben-Tov A, et al. The Effectiveness of the Two-Dose BNT162b2 Vaccine: Analysis of Real-World Data. Clin Infect Dis 2021. https://doi.org/10.1093/cid/ciab438.
- [8] Robertson E, Reeve KS, Niedzwiedz CL, Moore J, Blake M, Green M, et al. Predictors of COVID-19 vaccine hesitancy in the UK household longitudinal study. Brain Behav Immun [Internet]. 2021;94:41–50.
- [9] Walsh EE, Frenck RW, Falsey AR, Kitchin N, Absalon J, Gurtman A, et al. Safety and Immunogenicity of Two RNA-Based Covid-19 Vaccine Candidates. N Engl J Med 2020;383(25):2439–50.
- [10] Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med. 2020;383 (27):2603–15.
- [11] Gringeri M, Mosini G, Battini V, Cammarata G, Guarnieri G, Carnovale C, et al. Preliminary evidence on the safety profile of BNT162b2 (Comirnaty): new insights from data analysis in EudraVigilance and adverse reaction reports from an Italian health facility. Human Vaccines & Immunotherapeutics 2021;17(9):2969-71.
- [12] Borobia AM, Carcas AJ, Pérez-Olmeda M, Castaño L, Bertran MJ, García-Pérez J, et al. Immunogenicity and reactogenicity of BNT162b2 booster in ChAdOx1-S-primed participants (CombiVacS): a multicentre, open-label, randomised, controlled, phase 2 trial. Lancet [Internet]. 2021;398:121–30. Available from https://www.sciencedirect.com/science/article/pii/S0140673621014203.
- [13] Krantz MS, Kwah JH, Stone CA, Phillips EJ, Ortega G, Banerji A, et al. Safety Evaluation of the Second Dose of Messenger RNA COVID-19 Vaccines in Patients With Immediate Reactions to the First Dose. JAMA Intern Med 2021;181(11):1530. https://doi.org/10.1001/jamainternmed.2021.3779.
- [14] Tanriover MD, Doğanay HL, Akova M, Güner HR, Azap A, Akhan S, et al. Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey. Lancet. Elsevier 2021;398:213–22.
- [15] Al Kaabi N, Zhang Y, Xia S, Yang Y, Al Qahtani MM, Abdulrazzaq N, et al. Effect of 2 Inactivated SARS-CoV-2 Vaccines on Symptomatic COVID-19 Infection in Adults: A Randomized Clinical Trial. JAMA 2021;326(1):35. https://doi.org/10.1001/jama.2021.8565.
- [16] Yu Y, Lau JTF, Lau MMC, Wong MCS, Chan PKS. Understanding the Prevalence and Associated Factors of Behavioral Intention of COVID-19 Vaccination Under Specific Scenarios Combining Effectiveness, Safety, and Cost in the Hong Kong Chinese General Population. Int J Health Policy Manag 2021. https://doi.org/10.34172/jihpm.2021.02.
- [17] Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study 2012;380:37–43.
- [18] Huntley AL, Johnson R, Purdy S, Valderas JM, Salisbury C. Measures of multimorbidity and morbidity burden for use in primary care and community settings: A systematic review and guide. Ann. Fam. Med. 2012;10(2):134–41.
- [19] van Smeden M, Moons KGM, de Groot JAH, Collins GS, Altman DG, Eijkemans MJC, et al. Sample size for binary logistic prediction models: Beyond events per variable criteria. Stat Methods Med Res 2019;28(8):2455–74.
- [20] Dagan N, Barda N, Kepten E, Miron O, Perchik S, Katz MA, et al. BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting. N Engl J Med 2021;384(15):1412-23.
- [21] Finney Rutten LJ, Zhu X, Leppin AL, Ridgeway JL, Swift MD, Griffin JM, et al. Evidence-Based Strategies for Clinical Organizations to Address COVID-19 Vaccine Hesitancy. Mayo Clin Proc [Internet]. 2021;96(3):699–707.
- [22] Lim WW, Mak L, Leung GM, Cowling BJ, Peiris M. Comparative immunogenicity of mRNA and inactivated vaccines against COVID-19. The Lancet Microbe 2021;2(9):e423. https://doi.org/10.1016/S2666-5247(21) 00177-4
- [23] Rief W. Fear of Adverse Effects and COVID-19 Vaccine Hesitancy: Recommendations of the Treatment Expectation Expert Group. JAMA Health Forum 2021;2(4):e210804. https://doi.org/10.1001/jamahealthforum.2021.0804.
- [24] Fabiani M, Ramigni M, Gobbetto V, Mateo-Urdiales A, Pezzotti P, Piovesan C. to 24 March 2021. Eurosurveillance [Internet]. 2021;26(17). https://doi.org/10.2807/1560-7917.ES.2021.26.17.2100420.
- [25] Wong SYS, Kwok KO, Chan FKL. What can countries learn from Hong Kong's response to the COVID-19 pandemic? CMAJ [Internet]. CMAJ 2020;192: E511-5. Available from https://www.cmaj.ca/content/192/19/E511.