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Risks of COVID-19-related hospitalisation and mortality among individuals with mental disorders following BNT162b2 and CoronaVac vaccinations: A case-control study

Hei Hang Edmund Yiu [a,1], Vincent K.C. Yan [a,1], Yue Wei [a], Xuxiao Ye [a], Caige Huang [a], David J. Castle [b,c], Celine S.L. Chui [d,e,f], Francisco T.T. Lai [a,d,g], Xue Li [a,d,h], Carlos K.H. Wong [a,d,g], Eric Y.F. Wan [a,d,g], Ian C.K. Wong [a,d,i,j,*], Esther W. Chan [a,d,k,l,*]

[a] Centre for Safe Medication Practice and Research, Department of Pharmacology and Pharmacy, LKS Faculty of Medicine, University of Hong Kong, Hong Kong SAR, China
[b] Department of Psychiatry, The University of Tasmania, Hobart, Tasmania, Australia
[c] Centre for Mental Health Service Innovation, Statewide Mental Health Services, Hobart, Tasmania, Australia
[d] Laboratory of Data Discovery for Health ($D^2$4H), Hong Kong Science and Technology Park, Hong Kong SAR, China
[e] School of Nursing, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China
[f] School of Public Health, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China
[g] Department of Family Medicine and Primary Care, School of Clinical Medicine, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China
[h] Department of Medicine, School of Clinical Medicine, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China
[i] Aston School of Pharmacy, Aston University, Birmingham, United Kingdom
[j] Expert Committee on Clinical Events Assessment Following COVID-19 Immunization, Department of Health, The Government of the Hong Kong SAR, Hong Kong SAR, China
[k] Department of Pharmacy, The University of Hong Kong-Shenzhen Hospital, Shenzhen, China
[l] The University of Hong Kong Shenzhen Institute of Research and Innovation, Shenzhen, China

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ABSTRACT

Concerns have been raised regarding potential weaker vaccine immunogenicity with higher immune suppression for individuals with pre-existing mental disorders. Yet, data on the effectiveness of COVID-19 vaccinations among this vulnerable population are limited. A case-control study was conducted to investigate the risks of COVID-19-related hospitalisation and mortality among individuals with mental disorders following one to three doses of BNT162b2 and CoronaVac vaccinations in Hong Kong. Data were extracted from electronic health records, vaccination and COVID-19 confirmed case records. Conditional logistic regression was applied with adjustment for comorbidities and medication history. Subgroup analyses were performed with stratification: by age (< 65 and ≥ 65) and mental disorders diagnosis (depression, schizophrenia, anxiety disorder, and bipolar disorder). Two doses of BNT162b2 and CoronaVac significantly reduced COVID-19-related hospitalisation and mortality. Further protection for both outcomes was provided after three doses of BNT162b2 and CoronaVac. The vaccine effectiveness magnitude of BNT162b2 was generally higher than CoronaVac, but the difference diminished after the third dose. Individuals with mental disorders should be prioritised in future mass vaccination programmes of booster doses or bivalent COVID-19 vaccines. Targeted strategies should be developed to resolve the reasons behind vaccine hesitancy among this population and increase their awareness on the benefits of vaccination.

* Corresponding authors at: Centre for Safe Medication Practice and Research, Department of Pharmacology and Pharmacy, General Office, L02-56 2/F, Laboratory Block LKS Faculty of Medicine, The University of Hong Kong, 21 Sassoon Road, Pokfulam, Hong Kong SAR, China.
E-mail addresses: wongick@hku.hk (I.C.K. Wong), ewchan@hku.hk (E.W. Chan).
[1] Co-first authors with equal contributions.

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1. Introduction

With the rapid emergence of novel Coronavirus disease (COVID-19) 'variants of concern' globally, countries are boosting their national vaccination rates for protecting citizens against COVID-19-related severe outcomes. In Hong Kong, a messenger RNA (mRNA) vaccine (BNT162b2) by Fosun Pharma/BioNTech Comirnaty and an inactivated vaccine (CoronaVac) by Sinovac Biotech Hong Kong Limited have been authorised for use since early 2021. Individuals aged 18 years or above are recommended to take the third dose as soon as 90 days after the second dose (The Government of the Hong Kong Special Administrative Region, 2022a). Between 24 February 2022 and 28 December 2022, vaccination was a prerequisite for entering a vast range of recreational and catering premises such as fitness centres, catering business premises, and residential care homes (The Government of the Hong Kong Special Administrative Region, 2022b). Omicron BA.2 was the predominant variant circulating locally in Hong Kong from January 2022 until May 2023 (Mefsin et al., 2022; Surveillance Division of the Communicable Disease Branch of the Centre for Health Protection, 2023). Post-marketing studies have shown that BNT162b2 and CoronaVac vaccinations are effective for this COVID-19 variant against COVID-19-related severe complications and mortality among the general adult population (McMenamin et al., 2022; Yan et al., 2022). However, there is a lack of research investigating vaccine effectiveness in vulnerable individuals, including those with pre-existing mental disorders.

Mental disorders are associated with impaired immune system, increased inflammation and dysregulated antiviral immunity (Leschak & Eisenberger, 2019; Mazereel et al., 2021). Studies revealed a significant association between pre-existing mental disorders or the use of psychopharmacological drugs, and increased risks of COVID-19-related hospitalisation and mortality (Bitan et al., 2021; Shinn & Viron, 2020; Toubasi et al., 2021; Vai et al., 2021; Wang et al., 2021). Severe mental illness (SMI) such as schizophrenia also carry an elevated risk of cognitive deficits (Sheffield et al., 2018), which may limit individuals' ability to follow health and social guidance during the pandemic. A lower rate of medication adherence among people with SMI after COVID-19 infection, has also been reported (Shinn & Viron, 2020). Moreover, substance use disorders such as tobacco use dependence also contribute significant infection risks, due to higher prevalence of angiotensin converting enzyme II (ACE-2) receptors in their airways (Leung et al., 2020). In light of these factors, the investigation of COVID-19 vaccine effectiveness was key to determining the level of protection offered to this at-risk population. Some studies related to vaccine immunogenicity suggested that individuals with mental disorders such as major depression, schizophrenia, and insomnia are susceptible to attenuated immune vaccine response following measles, influenza or Plain Pertussis vaccinations, compared to healthy individuals (Bonkat et al., 2022; Mazereel et al., 2021; Xiao et al., 2022). Also, compared to individuals without mental disorders, a US study found that individuals with mental disorders were at higher risk of COVID-19 breakthrough infection following full mRNA (Pfizer-Bio NTech and Moderna) or viral vector (Johnson & Johnson-Janssen) vaccinations (Nishimi et al., 2022). These raise uncertainty about potential differences in the vaccine effectiveness profile between individuals with and without mental disorders. With a view to examining COVID-19-related severe outcomes among individuals with mental disorders following COVID-19 vaccinations, this study aims to investigate the effectiveness of one to three doses of BNT162b2 and CoronaVac vaccinations on the risks of COVID-19-related hospitalisation and mortality among individuals with mental disorders during the Omicron dominant period in Hong Kong.

2. Methods

A case-control study was conducted to explore the relationship between vaccination status and COVID-19-related hospitalisation and mortality between 1 January 2022 and 15 August 2022 among individuals aged $\geq$ 18 with the diagnosis of mental disorder (International Classification of Diseases, Ninth Revision [ICD-9] code: 290.x–319.x). The data in this study were extracted from three sources: electronic health records in the clinical management system under the Hospital Authority (HA), vaccination records from the Department of Health (DH), and COVID-19 confirmed case records from the Centre for Health Protection (CHP) in Hong Kong. The HA manages all public hospitals and institutions, specialist out-patient clinics and general out-patient clinics in Hong Kong. The DH is a statutory health adviser and agency of the government responsible for upholding community public health. The CHP commits to the protection of community health, promotion of healthy living, and partnership with stakeholders for preventing communicable and non-communicable diseases. Anonymous unique identifiers were used for linkage between the databases. These databases have been used for previous COVID-19 vaccine studies (Wan et al., 2022a; Wan et al., 2022b; Yan et al., 2022).

In Hong Kong, individuals were assigned to the same vaccine brand for their first two doses. They were allowed to switch to another vaccine brand for their third dose. Vaccination status was therefore categorised into eight groups based on the combinations of vaccine dose: (1) one-dose BNT162b2, (2) one-dose CoronaVac, (3) two-doses BNT162b2, (4) two-doses CoronaVac, (5) three-doses BNT162b2, (6) three-doses CoronaVac, (7) two-doses BNT162b2 followed by one-dose CoronaVac (BBC), and (8) two-doses CoronaVac followed by one-dose BNT162b2 (CCB). COVID-19 related hospitalisation and mortality were defined as hospitalisation and all-cause mortality within 28 days of COVID-19 infection confirmed by polymerase chain reaction (PCR) tests. Individuals admitted to hospitals were restricted to those with severe COVID-19 symptoms (e.g. shortness of breath, chest pain or confusion) since February 2022. Individuals with milder COVID-19 symptoms were instead isolated at home or community quarantine centres operated by the government. Cases for this study were defined as patients with COVID-19-related hospitalisation or mortality during the study period. Controls were individuals who attended HA services during the study period but did not have COVID-19-related hospitalisation or mortality. Patients with a history of COVID-19, a fourth-dose vaccination, and without pre-existing mental health disorder were excluded in this study. Each case was matched up to 10 controls by age, gender, index date, and Charlson Comorbidity Index. The study observes guidelines from the Strengthening the reporting of observational studies in epidemiology (STROBE) statement for reporting case-control studies.

2.1. Statistics analyses

Conditional logistic regression adjusted for comorbidities (cancer, chronic kidney disease, respiratory disease, diabetes mellitus, cardiovascular disease, dementia), and medication use within the past 90 days (renin-angiotensin-system agents, beta blockers, calcium channel blockers, diuretics, nitrates, lipid-lowering agents, insulins, antidiabetic drugs, oral anticoagulants, antiplatelets, immunosuppressants, antipsychotic drugs, anxiolytics, and antidepressants) was used to explore the association between vaccination status and risks of COVID-19-related outcomes. Crude and adjusted odds ratios (ORs) and their 95 % confidence intervals are reported. Vaccine effectiveness was calculated by (1-adjusted OR) x100 %. Two subgroup analyses with stratification for age groups ($<$ 65 and $\geq$ 65) and four mental disorder diagnoses (depression [ICD-9 296.2, 296.3, 300.4, 311.x], schizophrenia [ICD-9 295.x], anxiety disorder [ICD-9 300.0], and bipolar disorder [ICD-9 296.0, 296.1,

296.4–296.8]) were performed. Three sensitivity analyses were conducted. Firstly, in addition to patients with COVID-19 infection confirmed by PCR tests, those confirmed by Rapid Antigen Test (RAT) were also included. Secondly, patients with vaccination status within 14 days of the latest dose were excluded in consideration of the time required for vaccines to develop sufficient immunity (Baraniuk, 2021). Thirdly, in view of a significant reduction in vaccine effectiveness 6 months after vaccination, patients with vaccination status beyond 180 days since the latest dose were excluded (Feikin et al., 2022). Statistical analyses were performed independently by three investigators (VKCY, YW, HHEY) using RStudio version 4.2.1.

This study was approved by the Central Institutional Review Board of the Hospital Authority of Hong Kong (CIRB-2021-005-4) and the DH Ethics Committee (LM171/2021).

3. Results

In total, 10,633 and 3,216 cases were matched to 98,334 and 29,459 controls for COVID-19-related hospitalisation and COVID-19-related mortality, respectively (Fig. 1). Baseline characteristics of matched cases and controls for both outcomes are shown in Table 1. In general, individuals with COVID-19-related mortality were older than those with COVID-19-related hospitalisation. When stratifying individuals by specific mental disorder diagnosis, there was a higher proportion of individuals with depression, compared to those with schizophrenia, anxiety disorder and bipolar disorder.

For the risks of COVID-19-related hospitalisation and mortality under different vaccination status (Fig. 2 and Table 2), the magnitudes of vaccine effectiveness for both BNT162b2 and CoronaVac vaccinations were higher with more vaccine doses received. Also, vaccine effectiveness magnitude against COVID-19-related hospitalisation and mortality for BNT162b2 was generally higher than that for CoronaVac. Compared to unvaccinated individuals, vaccine effectiveness for COVID-19-related hospitalisation outcomes increased from 50.0 % (95 % CI, 42.0–56.9 %) to 72.5 % (95 % CI, 69.6–75.1 %) for BNT162b2 and from 15.2 % (95 % CI, 10.3–19.8 %) to 51.6 % (95 % CI, 48.6–54.4 %) for CoronaVac when vaccine administration increased from one to two. Similarly, vaccine effectiveness for COVID-19-related mortality increased from 70.8 % (95 % CI, 57.6–80.0 %) to 88.1 % (95 % CI, 83.3–91.6 %) for BNT162b2 and from 40.9 % (95 % CI, 34.5–46.8 %) to 68.5 % (95 % CI, 64.2–72.4 %) for CoronaVac with one vs two doses.

Notably, a third dose offered extra protection against both outcomes. Vaccine effectiveness against COVID-19-related hospitalisation outcomes following three doses of BNT162b2 and CoronaVac was 84.0 % (95 % CI, 81.2–86.4 %) and 68.3 % (95 % CI, 64.4–71.7 %), respectively. Vaccine effectiveness against COVID-19-related mortality following three doses of BNT162b2 and CoronaVac was 98.3 % (95 % CI, 94.4–99.5 %) and 88.1 % (95 % CI, 82.0–92.2 %), respectively. Vaccine effectiveness against COVID-19-related hospitalisation (79.8 % [95 % CI, 73.1–84.8 %]) and mortality (89.7 % [95 % CI, 73.3–96.0 %]) was also high for CCB vaccination status. However, the association between BBC vaccination status and the risks of COVID-19-related hospitalisation and mortality was not statistically significant.

Vaccine effectiveness by age group (< 65 and ≥ 65) are reported in Supplementary Tables 1 and 2. The risk reduction pattern of COVID-19-related hospitalisation across both age groups was similar between the two types of vaccines. For COVID-19-related mortality, compared to individuals aged < 65 (BNT162b2: 84.7 % [95 % CI, 31.3–96.6 %]; CoronaVac: 46.9 % [95 % CI, 0.3–71.7 %]), a slightly lower vaccine effectiveness magnitude was observed for those aged ≥ 65 (BNT162b2: 69.1 % [95 % CI, 54.5–79.0 %]); CoronaVac: 40.7 % [95 % CI, 34.1–46.7 %]) following the first dose. However, the difference diminished when individuals received second and third doses. A third dose vaccination provided the highest protection against COVID-19-related hospitalisation and mortality for both age groups.

Baseline characteristics of cases and controls for COVID-19-related hospitalisation and mortality among mental disorder subgroups (depression, schizophrenia, anxiety disorder, and bipolar disorder) and vaccine effectiveness results for these subgroups are documented in Supplementary Tables 3–8. The cases and controls for individuals with bipolar disorder were on average younger than individuals with depression, schizophrenia, and anxiety disorder. Compared to individuals with depression and schizophrenia, the magnitude of vaccine effectiveness against COVID-19-related hospitalisation was generally greater among those with anxiety disorder. The magnitude of vaccine effectiveness difference was greatest after receipt of third dose, in which BNT162b2 and CoronaVac offered 94.0 % (95 % CI, 84.0–97.8 %) and 86.9 % (95 % CI, 70.4–94.2 %) protection to individuals with anxiety disorder, compared to those with depression (81.3 % [95 % CI, 73.3–86.9 %] and 70.4 % [95 % CI, 59.9–78.1 %]) and schizophrenia (79.6 % [95 % CI, 66.0–87.8 %] and 67.3 % [95 % CI, 49.2–78.9 %]). The magnitude of vaccine effectiveness against COVID-19-related mortality was higher among individuals with depression, relative to those with schizophrenia after the first and second doses. Vaccine effectiveness against COVID-19-related mortality among those with anxiety disorder and bipolar disorder are not reported in this study, due to insufficient identified cases and controls. The results of the sensitivity analyses were consistent to the main analyses (Supplementary Tables 9–11).

4. Discussion

This is the first study of which we are aware, that investigated the risks of COVID-19-related hospitalisation and mortality among individuals with various types of pre-existing mental disorders under different vaccination status, during the Omicron dominant period. Consistent significant risk reduction against COVID-19-related hospitalisation and mortality were observed with increasing number of vaccine doses. BNT162b2 was generally more effective than CoronaVac regardless of the number of doses received. Notably, effectiveness of both vaccines against hospitalisation and mortality risks surpassed 50 % after receiving two doses. Comparable to the vaccine effectiveness results for the general population aged ≥ 65 (Yan et al., 2022), a third dose vaccination offered significant extra protection to recipients, especially against COVID-19-related mortality. This suggests the importance of a booster dose for lowering the risks of COVID-19-related severe outcomes, thus reducing overload on medical services and exhaustion of available resources in hospitals.

Individuals with mental disorders tend to be differentially prone to immune suppression and inflammation (Leschak & Eisenberger, 2019; Mazereel et al., 2021), and thus are at increased risks of COVID-19 infection, hospitalisation and mortality (Bitan et al., 2021; Shinn & Viron, 2020; Toubasi et al., 2021; Vai et al., 2021; Wang et al., 2021). Also, studies have found that mental disorders correlate with other physical comorbidities such as diabetes, cancer, and hypertension, worsening COVID-19-related outcomes (Gold et al., 2020; Jeppesen & Benros, 2019). Moreover, lifestyle behaviours including substance use disorders, which are prevalent in individuals with schizophrenia, bipolar disorder and other SMI, increase the exposure risk to COVID-19 infection and severe outcomes (Leung et al., 2020). Executive dysfunction and lower education level or literacy are other crucial risk factors impacting people with SMI in terms of their ability to process COVID-19 health advice accurately (Sheffield et al., 2018; Tempelaar et al., 2017). All these factors increased the vulnerability of individuals with mental disorders during the COVID-19 pandemic. The pandemic has also increased the chance of developing mental disorders and worsening the

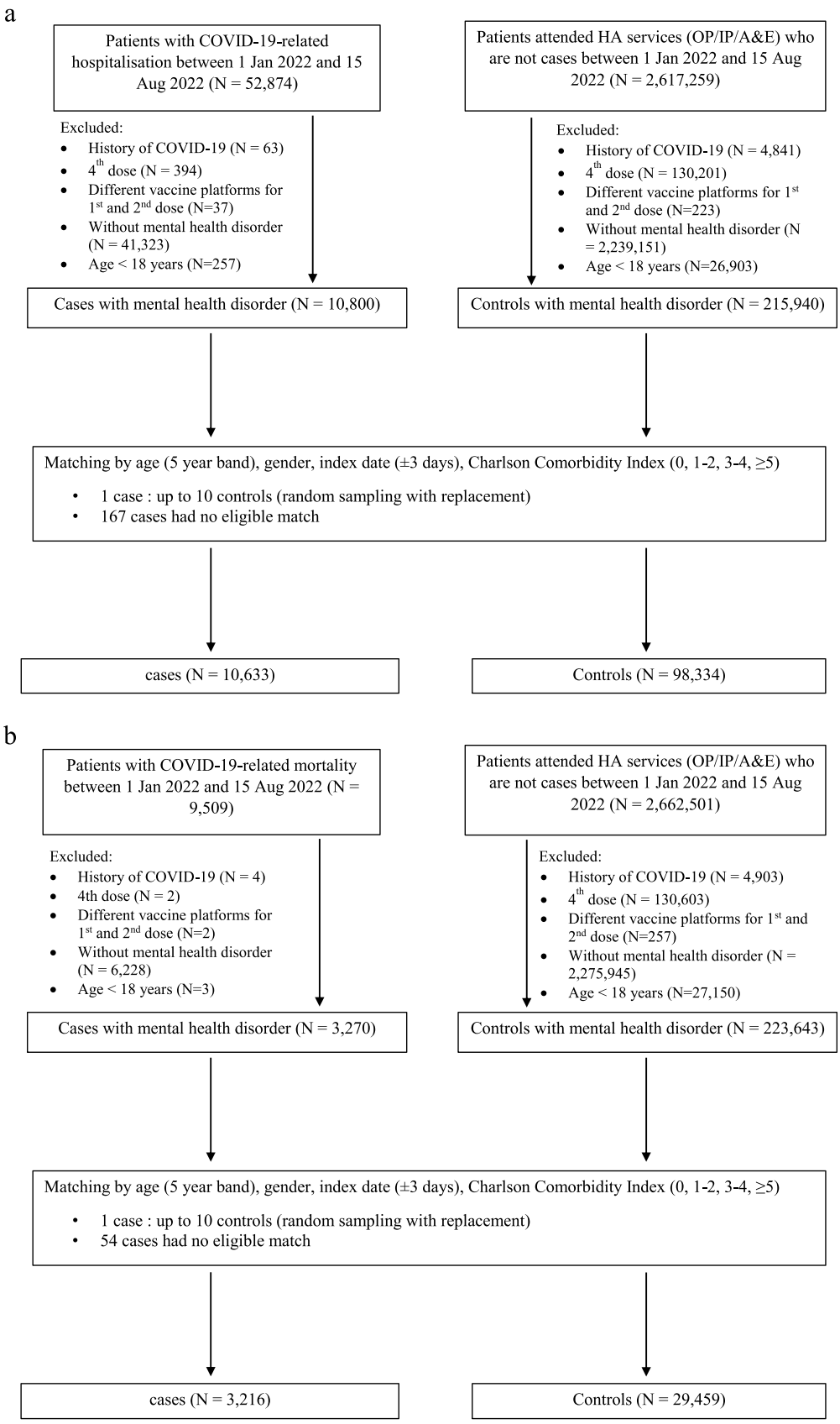

Fig. 1. Cases and controls for COVID-19-related hospitalisation and mortality.
a: COVID-19-related hospitalisation.
A&E: accident and emergency; HA: Hospital Authority of Hong Kong; IP: inpatient; OP: outpatient.
b: COVID-19-related mortality.
A&E: accident and emergency; HA: Hospital Authority of Hong Kong; IP: inpatient; OP: outpatient.

Table 1
Characteristics of cases and controls for COVID-19-related hospitalisation and mortality.

	Hospitalisation		Mortality	
	Cases N = 10,633	Controls N = 98,334	Cases N = 3,216	Controls N = 29,459
Age, years (mean (SD))	77.36 (17.06)	77.12 (16.97)	85.03 (10.77)	84.75 (10.50)
Sex, male (%)	5,190 (48.8)	47,300 (48.1)	1,689 (52.5)	15,303 (51.9)
Charlson Comorbidity Index (mean (SD))	1.57 (1.68)	1.31 (1.32)	1.98 (1.79)	1.67 (1.44)
Time since recent dose (mean (SD))	64.71 (67.31)	64.15 (71.14)	57.22 (63.27)	49.19 (59.53)
Mental disorder subgroups (%)				
Depression	1,394 (13.1)	16,809 (17.1)	266 (8.3)	3,693 (12.5)
Schizophrenia	1,004 (9.4)	4,942 (5.0)	209 (6.5)	957 (3.2)
Anxiety disorder	333 (3.1)	5,752 (5.8)	49 (1.5)	1,208 (4.1)
Bipolar disorder	170 (1.6)	986 (1.0)	24 (0.7)	130 (0.4)
Pre-existing comorbidities (%)				
Cancer	671 (6.3)	4,562 (4.6)	222 (6.9)	1,595 (5.4)
Chronic Kidney Disease	873 (8.2)	6,185 (6.3)	394 (12.3)	2,726 (9.3)
Respiratory disease	1,174 (11.0)	9,283 (9.4)	373 (11.6)	3,685 (12.5)
Diabetes	3,115 (29.3)	34,002 (34.6)	988 (30.7)	10,932 (37.1)
Cardiovascular disease	7,039 (66.2)	67,647 (68.8)	2,400 (74.6)	22,847 (77.6)
Medication use within 90 days (%)				
Renin-angiotensin-system agents	3,169 (29.8)	33,139 (33.7)	946 (29.4)	10,768 (36.6)
Beta blockers	2,431 (22.9)	19,571 (19.9)	829 (25.8)	6,237 (21.2)
Calcium channel blockers	4,728 (44.5)	47,437 (48.2)	1,605 (49.9)	15,728 (53.4)
Diuretics	1,750 (16.5)	8,952 (9.1)	860 (26.7)	3,402 (11.5)
Nitrates	993 (9.3)	6,425 (6.5)	372 (11.6)	2,360 (8.0)
Lipid lowering agents	4,480 (42.1)	49,427 (50.3)	1,290 (40.1)	15,942 (54.1)
Insulins	995 (9.4)	4,550 (4.6)	752 (23.4)	1,635 (5.6)
Antidiabetic drugs	2,326 (21.9)	26,672 (27.1)	675 (21.0)	8,034 (27.3)
Oral anticoagulants	657 (6.2)	4,672 (4.8)	222 (6.9)	1,751 (5.9)
Antiplatelets	4,016 (37.8)	31,597 (32.1)	1,498 (46.6)	11,792 (40.0)
Immunosuppressants	100 (0.9)	222 (0.2)	192 (6.0)	52 (0.2)
Antipsychotic drugs	3,683 (34.6)	19,798 (20.1)	1,071 (33.3)	6,239 (21.2)
Anxiolytics	1,802 (16.9)	10,103 (10.3)	494 (15.4)	2,829 (9.6)
Antidepressants	3,286 (30.9)	28,711 (29.2)	929 (28.9)	7,923 (26.9)

SD: standard deviation.

situation for those with pre-existing mental disorders, due to stress and loneliness following COVID-19 guidelines, along with a heightened fear of infection (Clemente-Suárez et al., 2021). Accumulation of these psychological risk factors creates a vicious circle among individuals with mental disorders, contributing to reduced antibody level responses and negatively impacting vaccine immune response (Madison et al., 2021).

This study explores the effectiveness of an mRNA (BNT162b2) and an inactivated (CoronaVac) COVID-19 vaccine in Hong Kong. mRNA vaccines serve as both pathogen-specific immunogen and adjuvant for stimulating adaptive immunity (Teijaro & Farber, 2021), whilst inactivated vaccines disable viral replication by bonding to the genes of beta-propiolactone (Kandeil et al., 2021). The T cells and B cells respond to the surface proteins of the virus and the binding antibodies prevent entrance of the virus into host cells. Previous studies show that individuals with mental disorders have an increased risk of impaired vaccine immunogenicity, most marked in the elderly (Bonkat et al., 2022; Glaser & Kiecolt-Glaser, 2005; Mazereel et al., 2021; Xiao et al., 2022). For example, individuals with depression have been shown to have impaired lymphocyte function and attenuated natural killer cell activity (Kronfol, 2002). Individuals with schizophrenia have altered immune and inflammatory responses, indicated by an increased C-reactive protein and altered cytokine levels (Fernandes et al., 2016). Although concerns have been raised regarding the potential weaker COVID-19 vaccine response among individuals with mental disorders, no substantial vaccine effectiveness differences were identified in this study, relative to the general population in Hong Kong (Yan et al., 2022). COVID-19 vaccination is still the most effective preventive strategy for protecting this at-risk population.

Vaccine hesitancy, which is defined as a delay in acceptance or refusal of safe vaccines despite availability of vaccine services, was prevalent among individuals with mental disorders due to the lack of vaccination motivation and awareness, information mistrust, and fear of needles, etc (MacDonald, 2015; Payberah et al., 2022). A study from a psychiatric care centre in the US found that the vaccine acceptance rate for the first dose of Moderna vaccine was less than 50 %, which was around 13 % lower than in the general community population (Shahani et al., 2021). Another study from Israel found a significantly longer time to reach vaccination amongst individuals with schizophrenia (Bitan et al., 2022). Understanding uptake barriers among this at-risk population is essential to help correct misconceptions about COVID-19 vaccine (Sheffield et al., 2018). Previous studies found that the ability for Omicron neutralization was highly limited without the third booster dose vaccination. The effectiveness of vaccines could be reduced by the Omicron variant, as more than 30 mutations were observed in the spike protein when compared to other variants (Alpha, Beta, Delta and Gamma) (Burki, 2022), lowering the antibodies produced by the vaccines (Sohan et al., 2022). A booster dose increases the breadth of humoral immunity and cross-reactivity of neutralizing antibody response (Garcia-Beltran et al., 2022). As individuals with SMI are susceptible to higher immune dysregulation when compared to those with milder mental disorders, COVID-19 vaccines are particularly necessary for those with long-term SMI. Clinical decision makers should communicate the importance of promoting vaccination amongst these high-risk groups. Specific attention should be paid to the elderly, given that our study found that the vaccine effectiveness magnitude of one-dose-only vaccine against COVID-19-related mortality was lower for those aged $>$ 65 years. The cases and controls for COVID-19-related mortality identified in this study were also generally older than those for COVID-19-related hospitalisation, emphasising the need of a booster dose for the elderly with mental disorders against serious COVID-19 outcomes.

This is the first study to investigate both mRNA (BNT162b2) and inactivated (CoronaVac) vaccine effectiveness across a broad coverage of all common mental disorders in a Chinese setting. The results can help to raise vaccination awareness for individuals with mental disorders, given that both BNT162b2 and CoronaVac were effective against severe

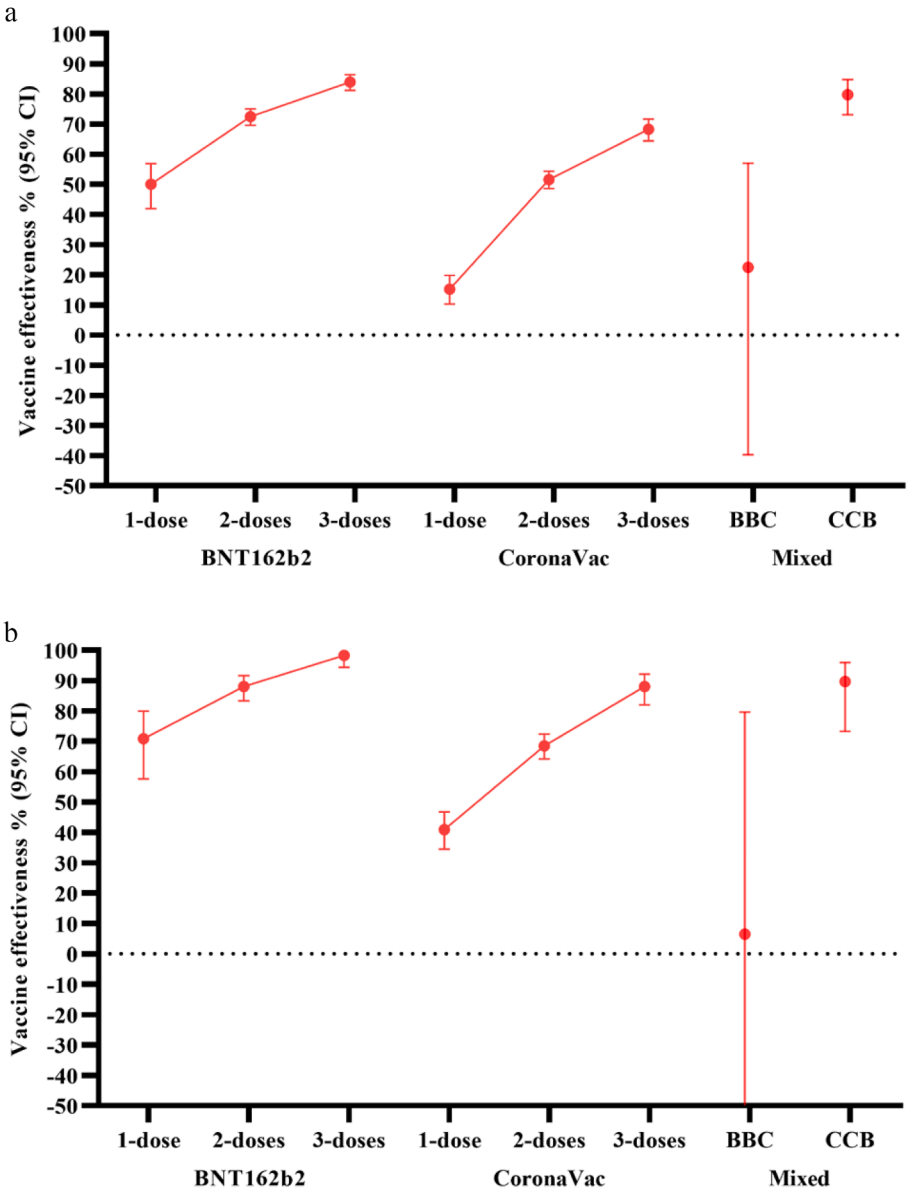

Fig. 2. Visual representation of vaccine effectiveness against COVID-19-related hospitalisation and mortality among individuals with mental disorders.
a: COVID-19-related hospitalisation.
b: COVID-19-related mortality.
BBC: two doses of BNT162b2 followed by one CoronaVac booster dose; CCB: two doses of CoronaVac followed by one BNT162b2 booster dose; CI: confidence interval.

Table 2
Main analysis for the risk of COVID-19-related hospitalisation and mortality among individuals with mental disorders under different vaccination status.

Vaccination status	Case	Control	Crude OR (95 % CI)	Adjusted OR (95 % CI)	VE % (95 % CI)
			Hospitalisation		
Unvaccinated	5,227	32,436	Reference	Reference	Reference
1 dose					
BNT162b2	212	2,617	0.441 (0.381 - 0.511)	0.500 (0.431 - 0.580)	50.0 (42.0 - 56.9)
CoronaVac	2,138	16,314	0.805 (0.762 - 0.850)	0.848 (0.802 - 0.897)	15.2 (10.3 - 19.8)
2 doses					
All BNT162b2	508	10,303	0.236 (0.213 - 0.260)	0.275 (0.249 - 0.304)	72.5 (69.6 - 75.1)
All CoronaVac	1,887	23,599	0.422 (0.398 - 0.447)	0.484 (0.456 - 0.514)	51.6 (48.6 - 54.4)
3 doses					
All BNT162b2	172	5,212	0.133 (0.113 - 0.156)	0.160 (0.136 - 0.188)	84.0 (81.2 - 86.4)
All CoronaVac	424	6,406	0.266 (0.238 - 0.297)	0.317 (0.283 - 0.356)	68.3 (64.4 - 71.7)
BBC	14	92	0.622 (0.347 - 1.114)	0.775 (0.430 - 1.397)	22.5 (-39.7 - 57.0)
CCB	51	1,355	0.159 (0.120 - 0.212)	0.202 (0.152 - 0.269)	79.8 (73.1 - 84.8)
			Mortality		
Unvaccinated	2110	11,722	Reference	Reference	Reference
1 dose					
BNT162b2	34	711	0.242 (0.170 - 0.344)	0.292 (0.200 - 0.424)	70.8 (57.6 - 80.0)
CoronaVac	635	6,221	0.548 (0.498 - 0.603)	0.591 (0.532 - 0.655)	40.9 (34.5 - 46.8)
2 doses					
All BNT162b2	40	1,905	0.091 (0.066 - 0.126)	0.119 (0.084 - 0.167)	88.1 (83.3 - 91.6)
All CoronaVac	356	6,778	0.251 (0.222 - 0.284)	0.315 (0.276 - 0.358)	68.5 (64.2 - 72.4)
3 doses					
All BNT162b2	3	749	0.015 (0.005 - 0.047)	0.017 (0.005 - 0.056)	98.3 (94.4 - 99.5)
All CoronaVac	31	1,113	0.088 (0.060 - 0.131)	0.119 (0.078 - 0.180)	88.1 (82.0 - 92.2)
BBC	2	16	0.567 (0.129 - 2.487)	0.935 (0.203 - 4.313)	6.5 (-331.3 - 79.7)
CCB	5	244	0.077 (0.032 - 0.189)	0.103 (0.040 - 0.267)	89.7 (73.3 - 96.0)

BBC: two doses of BNT162b2 followed by one CoronaVac booster dose; CCB: two doses of CoronaVac followed by one BNT162b2 booster dose; CI: confidence interval; OR: odds ratio; VE: vaccine effectiveness.

COVID-19-related-outcomes among this at-risk population. There are several limitations for this study. Similar to other observational studies using data from electronic health records, only healthcare service utilisation from public hospitals is available within the dataset. Hospitalisation and mortality records of private clinics and hospitals were not captured in our analysis. Although our study provides a general vaccine effectiveness profile of individuals with all forms of mental disorders, we did not individually explore the vaccine effectiveness of other types of mental disorders (e.g. attention deficit hyperactivity disorder, autism, and eating disorder) in addition to the four mental disorders in the subgroup analyses. Furthermore, due to the small number of cases, there was limited statistical power to evaluate effectiveness of the vaccine combination BBC, and the COVID-19-related mortality risk following vaccinations for individuals with anxiety and bipolar disorders. Lastly, the effectiveness of a fourth dose vaccination was not investigated in this study. In November 2022, a second generation COVID-19 vaccine by Fosun Pharma/BioNTech Comirnaty was authorised in Hong Kong for fourth dose use for individuals aged 50 years and above or immunocompromised persons aged 12 years or above (The Government of the Hong Kong Special Administrative Region, 2022c). Future research could explore the safety and effectiveness of this vaccine adapted for Omicron subvariants among individuals with pre-existing mental disorders.

5. Conclusion

This study reveals a lower risk of COVID-19-related hospitalisation and mortality associated with an increased number of vaccine doses among individuals with pre-existing mental disorders. Consistent with the general population, a high third-dose vaccination effectiveness for this vulnerable population supports the essential role of booster vaccination in providing sufficient immunity against COVID-19-related severe outcomes.

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The funder had no role in design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

CRediT authorship contribution statement

Hei Hang Edmund Yiu: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing – original draft. **Vincent K.C. Yan:** Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing – original draft. **Yue Wei:** Conceptualization, Formal analysis, Investigation, Data curation, Writing – review & editing. **Xuxiao Ye:** Conceptualization, Writing – review & editing. **Caige Huang:** Conceptualization, Writing – review & editing. **David J. Castle:** Conceptualization, Writing – review & editing. **Celine S.L. Chui:** Conceptualization, Writing – review & editing. **Francisco T.T. Lai:** Conceptualization, Writing – review & editing. **Xue Li:** Conceptualization, Writing – review & editing. **Carlos K.H. Wong:** Conceptualization, Writing – review & editing. **Eric Y.F. Wan:** Conceptualization, Writing – review & editing. **Ian C.K. Wong:** Writing – review & editing, Supervision, Project administration, Funding acquisition. **Esther W. Chan:** Writing – review & editing, Supervision, Project administration, Funding acquisition.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2023.115515.

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