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Protection and waning of vaccine-induced, natural and hybrid immunity to SARS-CoV-2 in Hong Kong

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ABSTRACT

Background: As the COVID-19 pandemic transitions into its fourth year, understanding the dynamics of immunity is critical for implementing effective public health measures. This study examines vaccine-induced, natural, and hybrid immunity to SARS-CoV-2 in Hong Kong, focusing on their protective effectiveness and waning characteristics against infection during the Omicron BA.1/2 dominant period.
Research Design and Methods: We conducted a territory-wide retrospective cohort study using vaccination and infection records from the Hong Kong Department of Health. The analysis included over 6.5 million adults, applying the Andersen-Gill model to estimate protective effectiveness while addressing selection bias through inverse probability weighting.
Results: Vaccine-induced immunity peaked one month after the first dose but waned rapidly, while boosters significantly prolonged protection. Infection-induced immunity showed higher initial effectiveness but declined faster than vaccine-induced immunity. Hybrid immunity provided the most durable protection. mRNA vaccines (Comirnaty) demonstrated greater effectiveness and slower waning compared to inactivated vaccines (CoronaVac).
Conclusions: Hybrid immunity represents the most effective strategy for sustained protection against SARS-CoV-2. Public health policies should emphasize booster campaigns and hybrid immunity pathways to enhance population-level immunity and guide future COVID-19 management in Hong Kong.

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1. Introduction

As the coronavirus disease 2019 (COVID-19) pandemic enters its fourth year, we find ourselves in an era marked by 'long COVID,' transitioning from the acute phase of the pandemic. Although COVID-19 was declared no longer a public health emergency of international concern as of 5 December 2024 [1], there have been over 776 million reported infections and an estimated 7 million fatalities attributed to the virus worldwide [2]. This underscores its significant impact, particularly in regions like Hong Kong [3,4]. Therefore, understanding the dynamics of SARS-CoV-2 immunity is critical for implementing effective public health measures in Hong Kong and beyond.

Immunity to SARS-CoV-2 can be acquired through three distinct pathways: vaccine-induced, natural, and hybrid immunity. Each pathway offers unique protective advantages, characterized by varying degrees of persistence and effectiveness over time. Vaccine-induced immunity, developed through vaccination, has been instrumental in reducing the severity of COVID-19 infections and preventing hospitalizations [3–7]. The development and distribution of COVID-19 vaccines have been marked by significant advancements and challenges. The unprecedented speed of vaccine development, from genome sequencing to emergency use authorization, was a major achievement [8]. However, concerns persist about the duration of vaccine-conferred protection and the need for booster doses [9]. Natural immunity, acquired following infection with SARS-CoV-2, also plays a significant role in shaping the overall immune response. Research indicates that individuals who have recovered from COVID-19 May exhibit a distinct immune profile, combining both humoral and cellular responses [10]. However, the strength and durability of this immunity can be influenced by factors such as the severity of the initial infection and the emergence of new variants [11]. Comparative studies have shown that the protective effectiveness of vaccine-induced and natural immunity is approximately equivalent [12], though these studies do not account for the effects of different types and numbers of vaccine doses. Hybrid immunity, resulting from a combination of vaccination and natural infection, has been shown to offer enhanced protection [13,14]. This form of immunity may provide enhanced protection against SARS-CoV-2 infection by leveraging the strengths of both immune responses. However, as immunity wanes, the effectiveness of both infection-induced and vaccine-induced protection may diminish, increasing the risk of reinfection, complications, or fatalities [9–14].

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Comprehending the dynamics of vaccine-induced, natural, and hybrid immunity, particularly concerning their waning effectiveness over time, is vital for optimizing vaccination strategies and public health responses. This paper aims to provide a comprehensive examination of the protection conferred by different types of immunity and their waning characteristics within the context of Hong Kong, thereby contributing to the ongoing discourse on effective COVID-19 management and prevention strategies.

2. Methods

2.1. Study design

In this territory-wide study, we conducted a comprehensive analysis using the vaccination records obtained from the Hong Kong Department of Health. These records included demographic information on individuals, such as sex, types of vaccines administered and vaccination dates. Additionally, we gathered confirmed COVID-19 case records from the Hong Kong Centre for Health Protection. We combined these datasets using unique pseudo-identifiers in order to explore the relationship between vaccination and infection with SARS-CoV-2. Individuals without vaccination and infection records are excluded from the combined dataset, which may introduce potential biases in estimating vaccine effectiveness. To enhance the robustness of our analysis, we augment the vaccination-infection dataset with data from the 2021 hong Kong Demographic Population Census, ensuring alignment based on age and gender [15,16].

Given the rapid evolution of the COVID-19 virus, single and multiple dominant variants can occur simultaneously during the pandemic. Therefore, we designated the study period from 1 January 2022, to 31 May 2022, when the BA.1/2 subvariant of Omicron was predominant in Hong Kong [17]. The COVID-19 Vaccination Program in Hong Kong was launched on 23 February 2021. As part of this initiative, the Vaccine Pass was introduced as a regulatory measure requiring individuals to present proof of COVID-19 vaccination for entry to or stay in designated venues. This initiative aimed to enhance Hong Kong's efforts in epidemic control and reinforce social distancing practices [18]. During the study period, two types of vaccines were administered, namely, Comirnaty (BNT162b2), an mRNA-based vaccine, and CoronaVac (Sinovac), an inactivated virus vaccine.

2.2. Study population

Most individuals received between zero and three doses, focusing specifically on adults who were either unvaccinated or had received one to three doses of a single vaccine type. For individuals with hybrid immunity resulting from both vaccination and infection, our analysis was limited to those who experienced breakthrough infections, excluding those who received vaccinations after their infection. The study was conducted in accordance with the Declaration of Helsinki. The need to obtain informed consent for this retrospective study was waived by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (HKU/HA HKW IRB) (Reference No.: UW 20–341 and date of approval: 17/2/2022).

2.3. Outcome and follow-up period

The objective of this study was to estimate the trajectory of protective effectiveness of vaccine-induced and infection-induced immunity against infection among the adult population during the Omicron BA.1/2 dominant period. Individuals were followed from 1 January 2022, until the end of the study period on 31 May 2022, the occurrence of the event of interest, or death. We assumed that individuals would not be reinfected within one month of their last infection.

2.4. Explanatory variables

To avoid immortal time bias [19], which can distort treatment effect conclusions by artificially inflating survival times for participants who are not at risk, we organized the risk set by calendar days. We accounted for time-dependent variables, including the duration since vaccination and the duration since infection. Our analysis considered a maximum of three vaccine doses and examined two vaccine types: Comirnaty and CoronaVac. Additionally, we included age and gender as predictors in our analysis.

2.5. Statistical analysis

To capture the time-dependent dynamics of vaccination and infection, we organized and analyzed the risk set according to calendar days and employed the Andersen-Gill (AG) model, a statistical approach designed to handle repeated events – such as multiple infections or vaccinations occurring in the same individual over time. This method builds on the widely used Cox proportional hazards model, which examines the time until a single event occurs, but extends it to account for situations where events can recur and risks may change over time [3–6]. We define day 1 as 1 January 2022, continuing through day 151, which corresponds to 31 May 2022. The hazard function of the outcome event for subject i on day t is then defined as follows:

$$\lambda_i(t) = \lambda_0(t)\exp\left[\boldsymbol{\alpha}^T\boldsymbol{x}_i(t) + z_i(t)V_i(t) - m_i(t)I_i(t)\right] \text{for } t = 1, 2, \ldots, 151,$$

where $\lambda_0(t) \geq 0$ is an unspecified baseline hazard function, $\boldsymbol{x}_i(t)$ is a vector of covariates that includes age and gender with the corresponding vector of regression coefficients $\boldsymbol{\alpha}$, $z_i(t)$ is the vaccination status with $z_i(t) = 0$ if the subject had not received any vaccination before day t and $z_i(t) = 1$ otherwise, $V_i(t)$ characterizes the time-varying effect of vaccination, $m_i(t)$ is the breakthrough infection status with $m_i(t) = 0$ if the subject had not been infected before day t and $m_i(t) = 1$ otherwise, $I_i(t)$ characterizes the time-varying effect of the infection.

To address the confounding of selection bias in observational study, inverse probability weighting (IPW) was applied to the Breslow partial likelihood [3,20]:

$$\frac{\prod_{i\in E(t)}\exp\left\{\boldsymbol{\alpha}^T x_i(t)+z_i(t)V_i(t)-m_i(t)I_i(t)\right\}^{\hat{w}_i(t)}}{\left\{\sum_{j\in R(t)}\hat{w}_j(t)\exp[\boldsymbol{\alpha}^T x_i(t)+z_i(t)V_i(t)-m_i(t)I_i(t)]\right\}^{\sum_{i\in E(t)}\hat{w}_i(t)}},$$

where $\hat{w}_i(t)$, $R(t)$ and $E(t)$ are the estimated inverse probability weight for subject i, the risk set, and the set of all subjects who experienced the event on day t, respectively.

Since vaccine-induced immunity was observed to wane and then stabilize at a certain level [12], the time-varying vaccination effect $V(t)$ will be estimated for different number of doses received on day t using a 4-parameter pharmacokinetic/pharmacodynamic (PK/PD) function [21]. Let $h_j(d)$ be the PK/PD function for the vaccine effect on the d-th day since administration of the j-th dose:

$$h_j(d)=\gamma_j\ln(C_j)-\ln\left\{C_j^{\gamma}+\left[\frac{\kappa_j}{\kappa_j-1}\left(e^{-d}-e^{-\kappa_j d}\right)\right]^{\gamma_j}\right\}+\delta_j\left(1-e^{-\kappa_j d}\right),$$

where $\kappa_j>0, \gamma_j>0, C_j>0$ and $\kappa_j\neq 1$. The time-varying vaccine effects are assumed to be additive, with the PK/PD functions considered identical for the second and third doses, but distinct for the first dose. Suppose that an individual received 3 doses of vaccine at day S_1, S_2 and S_3 with $S_1<S_2<S_3$, then the time-varying vaccination effect can be expressed as:

$$V(t)=\sum_{j=1}^{3}h_j(t-S_j).$$

The time-varying protective effectiveness of vaccine can be expressed as follows:

$$PE_V(t)=1-\exp[V(t)].$$

For the infection-induced immunity, we treat it as a 'special vaccine.' Suppose that an individual first gets infected on day U_1, then the time-varying infection-induced effect $I(t)$ on day t will be estimated using a modified exponential decay function [22], expressed as follows:

$$I(t)=Ae^{-B(t-U_1-28)^C}+D,\ \text{for}\ A,B,C\geq 0\ \text{and}\ -\infty<D<\infty,$$

where $(t-U_1-28)$ is based on the assumption that it takes 28 days for the protective effects of the infection-induced immunity to reach its peak, and that individuals will not be re-infected within 28 days following their initial infection. The protective effectiveness can be expressed as:

$$PE_I(t)=1-\exp[-I(t)].$$

3. Results

Our augmented dataset comprised approximately 7.4 million individuals from the Hong Kong population, of which around 6.5 million were adults. Figure 1 illustrates the trends in cohort sizes from January to June 2022. Adults were categorized into three age groups: 18–59 (reference group), 60–79, and 80 and above. Appendix Table A1 presents the number of events based on the cohorts and demographic characteristics, as well as the distribution of person-days at risk categorized by sex and age group across the 14 cohorts. The augmented dataset was divided into 16 equal-sized sub-datasets, and statistical models were conducted separately for each. The aggregate results were obtained using the divide-and-conquer (DAC) method [23,24].

Compared to the reference group of individuals aged 18–59, those aged 60–79 and 80 and above had relatively lower risks, with hazard ratios of 0.840 (95% CI: 0.832 to 0.848, $p<0.001$) and 0.955 (95% CI: 0.951 to 0.959, $p<0.001$), respectively. This may be attributed to younger individuals having a higher probability of exposure to the virus due to their greater level of social activities, including commuting to work. Additionally, females exhibited a relatively lower risk compared to males, with a hazard ratio of 0.918 (95% CI: 0.913 to 0.959, $p<0.001$) [25].

For the time-varying effect of vaccines, we assume that the first dose provides unique protection, while the second and third doses of the same vaccine share the same level of protection. Furthermore, we assume that the protective effectiveness of each dose is additive for a single vaccine type. Regarding infection-induced immunity, we treat infection as another way of stimulating the immune response and assume its corresponding protective effectiveness is also additive for cohorts with no prior vaccination. Figure 2 illustrates the time-varying protective effectiveness of vaccine-induced immunity (for Comirnaty and CoronaVac doses) and natural immunity against infection. From the trajectory estimation shown in Figure 2, we observe that the protective effectiveness of the first dose peaks at 0.89 and 1.03 months after vaccination, providing maximum protective effectiveness of 21.4% and 26.8% against infection for CoronaVac and Comirnaty, respectively. After this peak, the protective effectiveness decreases and stabilizes at −10.8% and 0.0% for CoronaVac and Comirnaty, respectively, over time, which aligns with findings from a previous cohort study. For the second and third doses, peak protection is reached slightly later than for the first dose, at around 1.53 and 1.52 months after vaccination, providing maximum protective effectiveness of 34.2% and 49.0% against infection for CoronaVac and Comirnaty, respectively. Following the peak, the protective effectiveness decreases and stabilizes at 20.0% and 33.4% for CoronaVac and Comirnaty, respectively.

For infection-induced immunity, peak protective effectiveness reaches 73.5% against infection, followed by a rapid waning effect, stabilizing at 19.8%, similar to the second or third dose of CoronaVac. This allows for a direct comparison between natural immunity and vaccine-induced immunity following the vaccination schedule (second dose: one month after the first; third dose: six months after the second) [18]. The cumulative protective effectiveness against infection for individuals receiving three doses and the protective effectiveness from infection are illustrated in Figure 3. For the three-dose regimen, Comirnaty provides maximum protection of 66.6%, stabilizing at 58.2% against infection after the third dose, while CoronaVac offers maximum protection of 42.2%, stabilizing at 32.1%. If individuals adhere to the official vaccination guidance, they can achieve maximum protective effectiveness against infection approximately 34 weeks after the first dose. Although infection-induced immunity may initially provide higher protection than vaccines, over time, and with continued vaccination, vaccine-

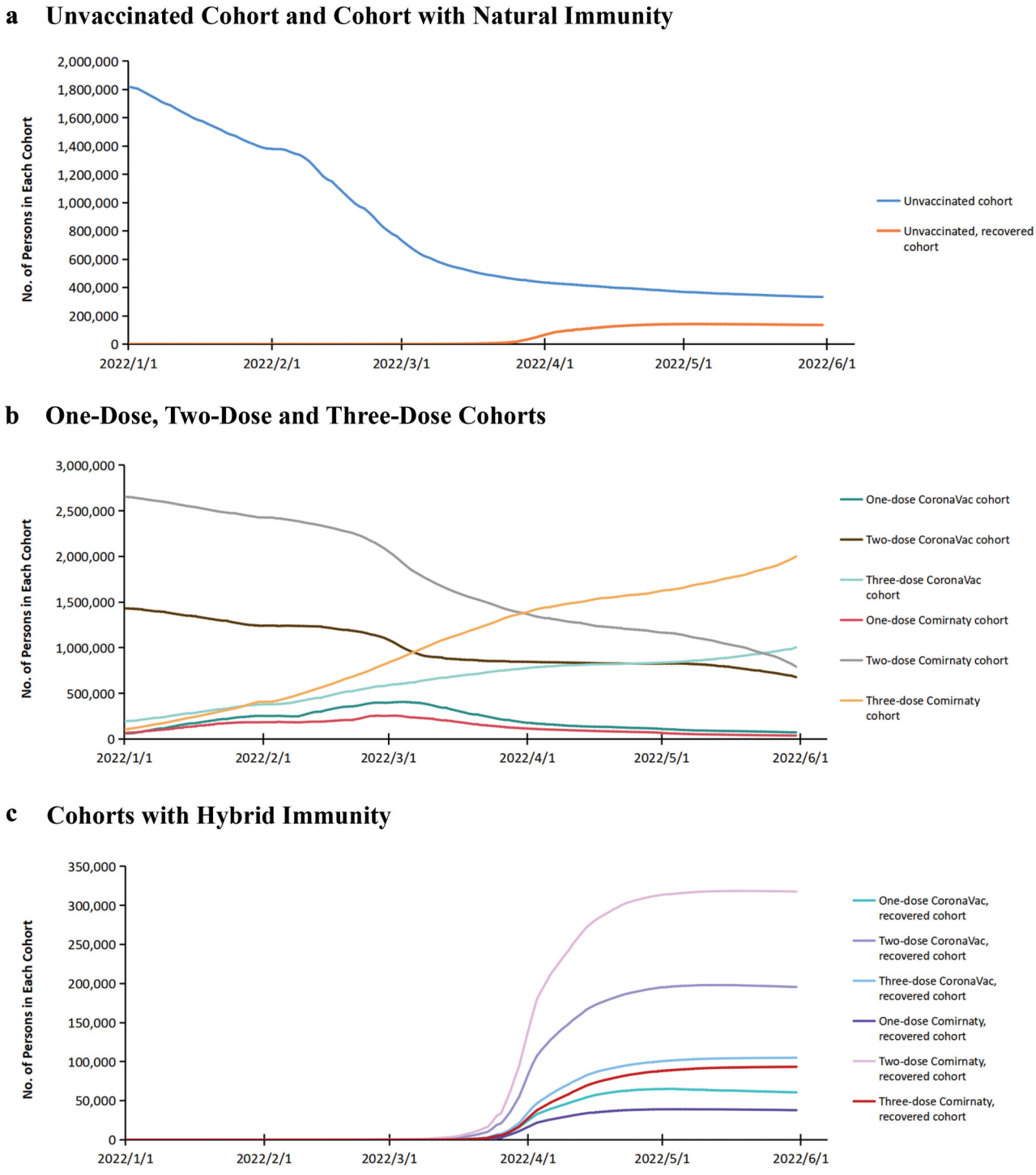

Figure 1. Daily number of persons in the study cohorts. (a) Unvaccinated cohort and cohort with natural immunity. (b) One-dose, two-dose and three-dose cohorts. (c) Cohorts with hybrid immunity.

induced protection will surpass that of infection-induced immunity. Figure 4 depicts the time-varying effects of a three-dose vaccination scheme, comparing scenarios with and without breakthrough infections. If an individual follows the previously mentioned three-dose vaccination scheme [18] and becomes infected at their most vulnerable point (six months after the last dose), the maximum protective effectiveness against reinfection will be 81.3% for CoronaVac (brown line) and 88.4% for Comirnaty (gray line) after 28 days since the last dose. The red and green lines in Figure 4 represent the protective effectiveness of the CoronaVac and Comirnaty cohorts, respectively, without breakthrough infections.

4. Discussion

This comprehensive study provides critical insights into the dynamics of vaccine-induced, natural, and hybrid immunity against SARS-CoV-2 during the Omicron BA.1/2 dominant

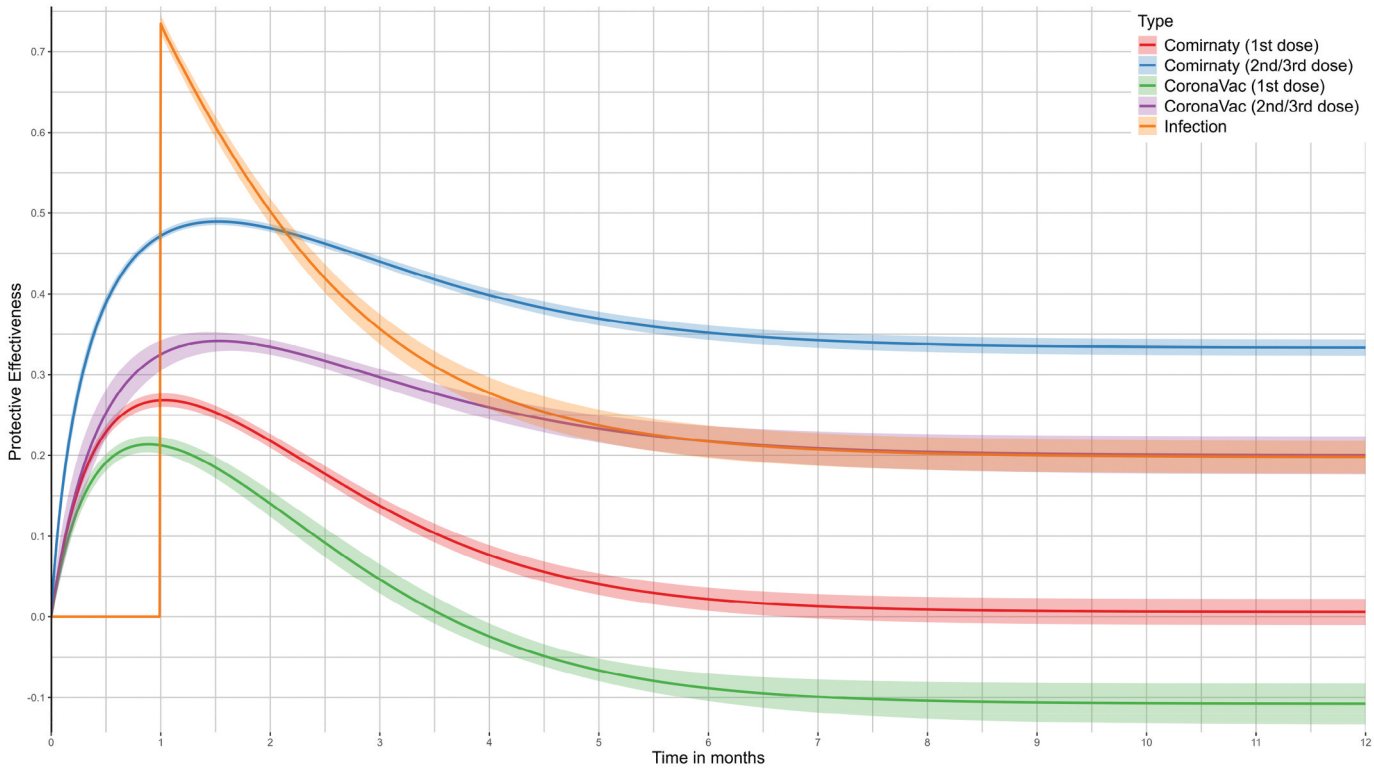

Figure 2. Time-varying effects of vaccine-induced and natural immunity against infection (Shaded bars indicate pointwise 95% CIs based on the fitted model).

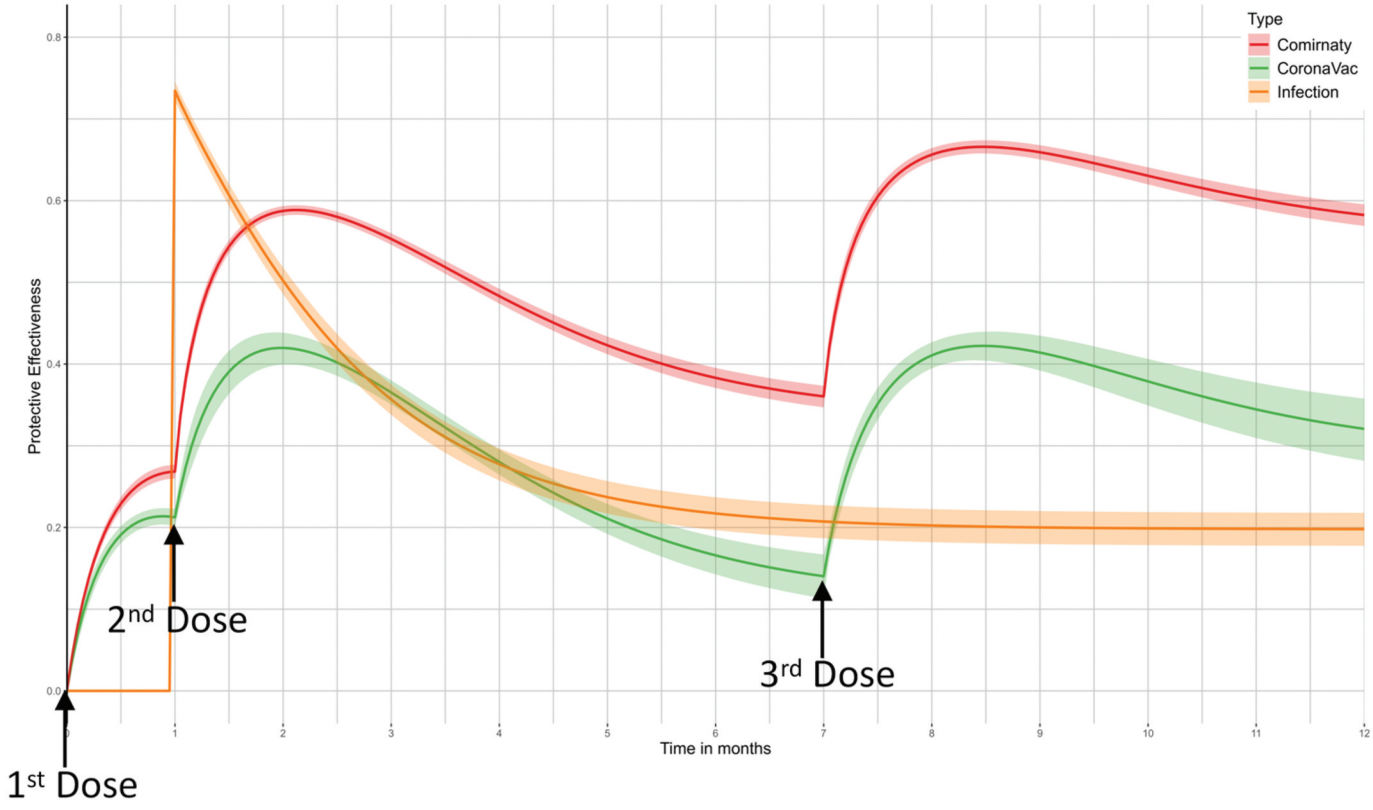

Figure 3. Time-varying effects of three-dose vaccination scheme and natural immunity against infection (Shaded bars indicate pointwise 95% CIs based on the fitted model).

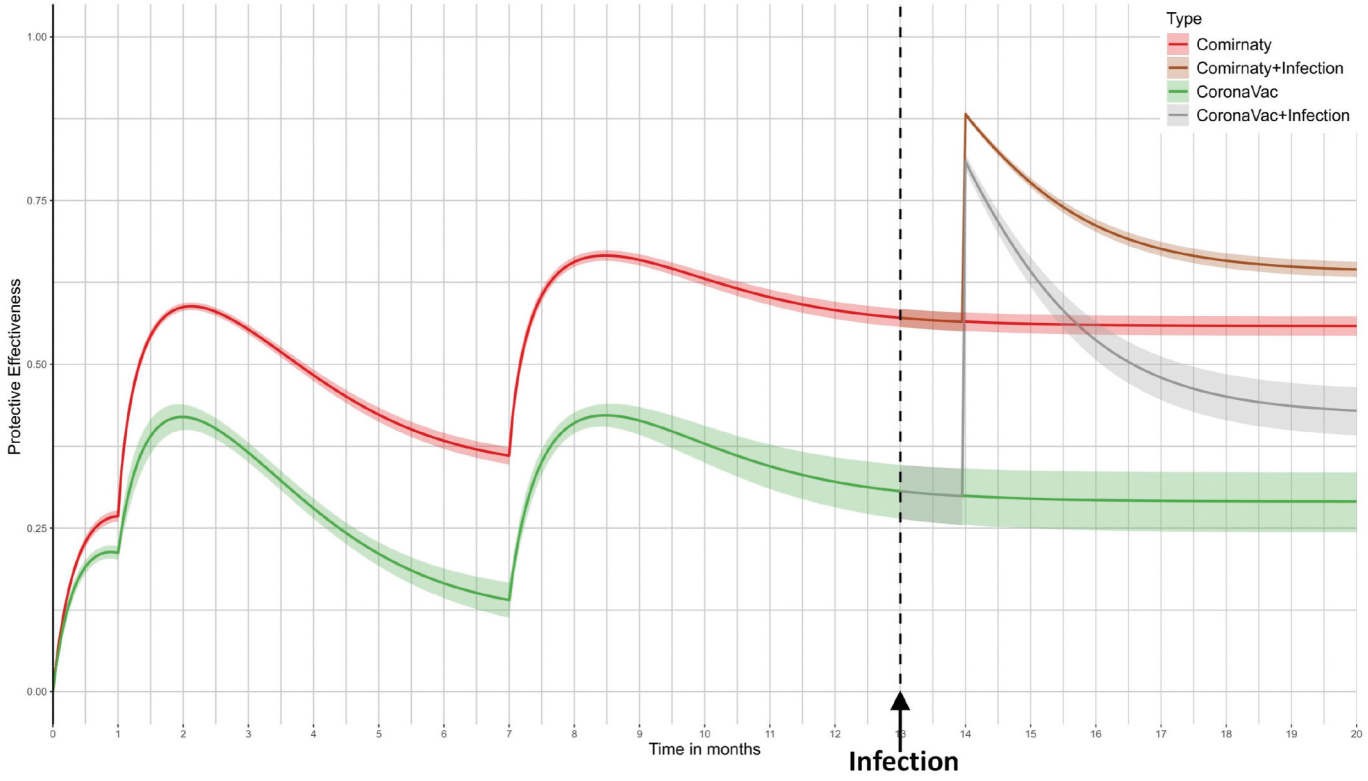

Figure 4. Time-varying effects of three-dose vaccination scheme with and without breakthrough infection (Shaded bars indicate pointwise 95% CIs based on the fitted model).

period in Hong Kong. By leveraging territory-wide data, including vaccination records, infection data, and demographic information, we estimated the time-varying protective effectiveness of immunity pathways and analyzed the waning effects over time. Our findings underscore several significant points that are essential for public health planning and vaccination strategies.

While retrospective cohort studies offer valuable insights, their reliance on preexisting data can introduce selection bias, as the study population may not be fully representative of the broader population. To address this limitation, we employed IPW, a robust statistical method that adjusts for potential imbalances in covariates between the study sample and the target population. By assigning weights based on the probability of inclusion, IPW effectively reduces bias and enhances the generalizability of our findings. Prior to the current study, some observational studies applied inverse probability weighting to assess the effectiveness of antiviral drugs or vaccines against hospitalization, severe complications, or death [3,26–28]. However, this approach has rarely been used to study their effects against infection. By using inverse probability weighting, this study confirms that vaccine-induced immunity plays a vital role in reducing the risk of infection, although its protective effectiveness wanes over time. The protective effectiveness of the first dose peaks around one month but diminishes rapidly, stabilizing at lower levels [14]. Notably, the second and third doses provide enhanced and more durable protection, with stabilization levels significantly higher than the first dose. This highlights the importance of completing multi-dose vaccination schedules to achieve optimal and sustained immunity. The findings align with previous studies that emphasize the added benefits of booster doses in combating emerging variants of concern [29].

Unlike previous study [12], infection-induced immunity demonstrates a higher peak protective effectiveness compared to vaccine-induced immunity [30,31]. However, this protection declines more rapidly over time and stabilizes at levels comparable to those of vaccine-induced immunity after multiple doses. This suggests that while natural immunity may offer robust early protection, it is not sufficient as a standalone strategy for long-term defense, especially in regions with high exposure risks like Hong Kong. Hybrid immunity, resulting from a combination of vaccination and natural infection, emerges as the most effective pathway for achieving durable and enhanced protection. Our analysis reveals that individuals with hybrid immunity exhibit the highest levels of immunity over time, with protection exceeding that of vaccine-induced or infection-induced immunity alone. This finding supports previous studies suggesting that hybrid immunity leverages the complementary strengths of humoral and cellular immune responses [13,14].

The study demonstrates that the type of vaccine administered significantly influences the trajectory of protective effectiveness. While both CoronaVac and Comirnaty provide substantial protection, mRNA vaccines (Comirnaty) outperform inactivated vaccines (CoronaVac) in terms of peak and stabilized effectiveness. Notably, Comirnaty exhibits a slower waning rate of protective effectiveness compared to CoronaVac, which is consistent with studies on the waning rates of

antibody levels over time [32]. This observation aligns with global evidence favoring mRNA vaccines for their ability to elicit stronger and more sustained immune responses [7,29]. However, it is important to note that the duration of observation in our study is rather brief, and further waning of immunity can be expected over longer periods. With the emergence of changing Omicron variants, some studies have even found negative efficacy over time, highlighting the need for ongoing monitoring and potential booster doses to maintain effective immunity [33]. This shortcoming has been alleviated by the use of time-dependent variable in the Andersen-Gill model that some individuals had their vaccinations long before the start of the follow-up period. Our findings underscore the importance of vaccine choice in tailoring vaccination strategies to maximize population-level immunity.

This study highlights the waning nature of immunity, regardless of its source, and the need for timely booster doses to sustain protective effectiveness. Our findings emphasize that adherence to official vaccination schedules is critical for maintaining optimal protection, particularly in the face of emerging variants. Public health policies must prioritize booster campaigns and consider hybrid immunity pathways to enhance overall population resilience against SARS-CoV-2 [34].

5. Limitations

Despite the strengths of this study, several limitations should be noted. First, the study period focuses on the Omicron BA.1/2 dominant phase, and the findings may not fully generalize to other variants. Second, the analysis assumes additive effects of vaccine doses and infection-induced immunity, potentially oversimplifying the complex interactions between immune responses. Third, different orders of vaccine and infection combinations, as well as mixed vaccine types [35], were not considered. Future research should address these factors and extend the analysis to other variants and longer follow-up periods to provide a more comprehensive understanding of immunity dynamics. Fourth, this study relies on reported COVID-19 cases. However, underreporting and insufficient testing in real-world settings may have impacted the results, potentially leading to an underestimation of infection rates [36,37]. Additionally, the study did not examine adverse reactions, which are an important aspect of vaccine policy development. Efficacy considerations alone are not sufficient to guide public health recommendations.

6. Conclusions

This study underscores the importance of understanding the dynamics of vaccine-induced, natural, and hybrid immunity to optimize public health strategies. Vaccine-induced immunity, particularly with mRNA vaccines, provides substantial protection, though booster doses are necessary to sustain effectiveness. Infection-induced immunity offers robust but transient protection, while hybrid immunity emerges as the most effective pathway for long-term defense. These findings advocate for continued vaccination efforts, timely booster campaigns, and leveraging hybrid immunity in high-risk populations to mitigate the risks of SARS-CoV-2 reinfection and complications. The insights from this study contribute to the ongoing discourse on COVID-19 management and inform evidence-based policies for achieving resilient population immunity.

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Declaration of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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Author contributions

Conceptualization, J Jiang, BJ Cowling and KF Lam; methodology, J Jiang and KF Lam; software, J Jiang; validation, J Jiang; formal analysis, J Jiang and KF Lam; investigation, J Jiang; resources, BJ Cowling and KF Lam; data curation, J Jiang, Y Lin and EHY Lau; writing – original draft preparation, J Jiang; writing – review and editing, J Jiang, EHY Lau, G Yin, BJ Cowling and KF Lam; visualization, J Jiang; supervision, EHY Lau, G Yin, BJ Cowling and KF Lam; project administration, BJ Cowling and KF Lam; funding acquisition, BJ Cowling. All authors have read and agreed to the published version of the manuscript.

Data sharing statement

The data that support the findings of this study are available from the Hospital Authority and the Department of Health of the Government of the Hong Kong Special Administrative Region but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the corresponding authors upon reasonable request and with permission of the Hospital Authority and the Department of Health of the Government of the Hong Kong Special Administrative Region.

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Appendix

Table A1. Demographic and clinical characteristics of the study cohorts.

	Sex		Age Group		
Cohort	Female	Male	18–59 yr	60–79 yr	≥80 yr
Unvaccinated cohort					
Person-days at risk – no.	67,350,132	52,828,137	61,418,053	38,341,379	20,418,837
SARS-CoV-2 infections/1,000,000 person-days at risk – no.	1400	1349	1727	979	1075
Daily infection rate — ‰	18.080	17.394	22.502	13.461	12.386
Unvaccinated, recovered cohort					
Person-days at risk – no.	4,739,981	3,432,771	5,765,443	1,752,299	655,010
SARS-CoV-2 infections/1,000,000 person-days at risk – no.	6	9	4	7	41
Daily infection rate — ‰	0.055	0.258	0.126	0.057	0.427
CoronaVac					
One-dose cohort					
Person-days at risk – no.	17,759,697	12,588,591	12,922,310	12,553,641	4,872,337
SARS-CoV-2 infections/1,000,000 person-days at risk – no.	2361	2648	2290	2603	2669
Daily infection rate — ‰	14.557	15.972	13.683	15.572	17.365
Two-dose cohort					
Person-days at risk – no.	87,233,931	65,204,819	89,313,389	52,362,671	10,762,690
SARS-CoV-2 infections/1,000,000 person-days at risk – no.	1321	1448	1387	1401	1153
Daily infection rate — ‰	13.619	14.937	14.204	14.325	11.778
Three-dose cohort					
Person-days at risk – no.	51,552,186	44,088,312	59,960,898	32,531,142	3,148,458
SARS-CoV-2 infections/1,000,000 person-days at risk – no.	1062	1170	1156	1069	711
Daily infection rate — ‰	10.573	11.574	11.486	10.412	7.711
One-dose, recovered cohort					
Person-days at risk – no.	2,054,033	1,552,125	1,544,267	1,592,432	469,459
SARS-CoV-2 infections/1,000,000 person-days at risk – no.	3	5	1	3	15
Daily infection rate — ‰	0.023	0.022	0.003	0.018	0.127
Two-dose, recovered cohort					
Person-days at risk – no.	6,232,450	5,025,776	6,899,364	3,837,028	521,834
SARS-CoV-2 infections/1,000,000 person-days at risk – no.	1	4	2	3	10
Daily infection rate — ‰	0.014	0.022	0.014	0.021	0.041
Three-dose, recovered cohort					
Person-days at risk – no.	2,933,958	2,776,910	3,796,121	1,813,005	101,742
SARS-CoV-2 infections/1,000,000 person-days at risk – no.	0	0	0	1	0
Daily infection rate — ‰	0.001	0.001	0.001	0.002	0.000
Comirnaty					
One-dose cohort					
Person-days at risk – no.	10,748,246	9,099,555	14,939,425	4,144,539	763,837
SARS-CoV-2 infections/1,000,000 person-days at risk – no.	2079	2156	2156	2036	1724
Daily infection rate — ‰	13.131	13.333	13.438	12.848	11.780
Two-dose cohort					
Person-days at risk – no.	147,005,994	116,971,283	220,818,607	39,361,533	3,797,137
SARS-CoV-2 infections/1,000,000 person-days at risk – no.	1180	1312	1261	1148	856
Daily infection rate — ‰	11.193	12.541	11.967	11.092	8.167
Three-dose cohort					
Person-days at risk – no.	88,146,349	71,146,269	126,354,282	30,980,144	1,958,192
SARS-CoV-2 infections/1,000,000 person-days at risk – no.	527	680	598	598	405
Daily infection rate — ‰	5.642	7.194	6.493	5.955	4.150
One-dose, recovered cohort					
Person-days at risk – no.	1,207,498	1,025,370	1,740,133	435,368	57,367
SARS-CoV-2 infections/1,000,000 person-days at risk – no.	1	3	0	7	17
Daily infection rate — ‰	0.003	0.342	0.000	0.490	2.284
Two-dose, recovered cohort					
Person-days at risk – no.	9,717,547	8,548,205	15,657,202	2,452,731	155,819
SARS-CoV-2 infections/1,000,000 person-days at risk – no.	0	1	1	1	13
Daily infection rate — ‰	0.001	0.066	0.032	0.004	0.049
Three-dose, recovered cohort					
Person-days at risk – no.	2,401,190	2,554,327	3,965,705	953,816	35,996
SARS-CoV-2 infections/1,000,000 person-days at risk – no.	0	1	0	2	0
Daily infection rate — ‰	0.000	0.004	0.001	0.007	0.000