

**A SELECTION OF TEN READINGS ON TOPICS RELATED TO
COVID-19 AND RESPIRATORY VIRUS VACCINATION STRATEGIES FOR FAMILY PHYSICIANS
(2025 UPDATE)**

FPSCI 30 – SATURDAY, 18 OCT 2025: 2.00pm – 5.00pm
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Selection of readings made by A/Prof Goh Lee Gan

**READING 1 – LONG-TERM MULTISYSTEMIC SYSTEMIC SEQUELAE—COVID-19 AND
INFLUENZA COMPARED: RETROSPECTIVE COHORT STUDY**

Wee LE,¹ Ho RWL,² Lim JT,³ Chiew CJ,⁴ Lye DCB,⁵ Tan KB.⁶ Long-term multisystemic sequelae post-hospitalisation for Omicron COVID-19 vs influenza: A retrospective cohort study. *Int J Infect Dis.* 2025 Sep;158:107946. PMID: 40499677.

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ABSTRACT

OBJECTIVES: To contrast long-term sequelae post-COVID-19 hospitalisations attributed to Omicron, vs seasonal influenza; stratified by vaccination.

METHODS: Retrospective population-based cohort study in Singapore, including all adult COVID-19 hospitalisations post-Omicron emergence (1 January 2022 – 3 September 2023), and historical influenza hospitalisations (1 January 2017 – 3 September 2023). Risks of post-acute diagnoses/symptoms 31-300 days post-COVID-19 hospitalisation, vs influenza, were estimated using overlap-weighted competing-risks-regression, with death as a competing risk.

RESULTS: 70,628 COVID-19 hospitalisations and 10,454 influenza hospitalisations were included. Lower overall risk of post-acute cardiac symptoms (adjusted-hazards-ratio, aHR=0.77 [95% CI=0.64-0.92]; P<0.001) was observed following any COVID-19 hospitalisation vs influenza. Similarly, lower risk of any post-acute cardiac diagnosis/symptoms (aHR=0.80 [95% CI=0.68-0.94]; P<0.001) was observed following unboosted COVID-19 hospitalisations vs unvaccinated influenza, and lower risk of other cardiac disorders (e.g., heart failure) was observed following boosted COVID-19 hospitalisations vs vaccinated influenza (aHR=0.58 [95% CI=0.39-0.86]; P<0.001). However, risks of post-acute cognitive impairment and fatigue/malaise were significantly higher post-COVID-19 vs influenza (cognition: aHR=1.34 [95% CI=1.08-1.68]; P<0.001; fatigue/malaise: aHR=1.75 [95% CI=1.23-2.50]; P<0.001) and when unboosted COVID-19 was compared against unvaccinated influenza (memory/cognition: aHR=1.67 [95% CI=1.27-2.19]; P<0.001; fatigue/malaise: aHR=1.77 [95% CI=1.18-2.64]; P<0.001).

CONCLUSION: Risks of cognitive impairment/fatigue were increased while risk of cardiac sequelae was significantly lower post-COVID-19 vs influenza in unboosted/unvaccinated individuals. Vaccination for COVID-19/influenza remains important during endemicity.

READING 2 – RISK FACTORS FOR SEVERE COVID-19 OUTCOMES IN ASIA PACIFIC REGION: A LITERATURE REVIEW

Thompson M,^{1,#} Buttery AK,^{1,#} Clarke C,¹ Oh SX,² Chan M,³ Lee BH,⁴ Iino T,⁵ Wang YA.⁶ Risk factors for severe COVID-19 outcomes in the Asia-Pacific region: a literature review. *Front Public Health*. 2025 Jun 9;13:1562179. PMID: 40612551.

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ABSTRACT

This comprehensive synthesis of severe COVID-19 risk factors specific to the Asia-Pacific (APAC) region addresses gaps in previous global studies, which often overlook regional demographic, epidemiological, and healthcare system variations.

Three databases (PubMed, Ovid MedLine, Scopus) and two preprint platforms (BioRxiv, MedRxiv) were searched between 1 December 2019, and 31 March 2023. English-language publications from 11 APAC countries/regions (Australia, Hong Kong, Japan, Macau, New Zealand, Philippines, Singapore, South Korea, Taiwan, Thailand, and Vietnam) reporting conditions associated with severe COVID-19 outcomes in adults (aged ≥ 16 years) were included.

Of 295 publications screened, 123 met inclusion criteria, mostly from South Korea (n=68) and Japan (n=23). Common risk factors included older age, male sex, obesity, diabetes, heart failure, renal disease, and dementia. Less commonly, hypertension, chronic obstructive pulmonary disease, cardio-and cerebrovascular disease, immunocompromise, autoimmune disorders, and mental illness were reported.

To date, no prior region-specific synthesis of risk factors for severe COVID-19 outcomes across the APAC region has been identified. The findings support the development of tailored vaccination strategies and public health interventions at both national and regional levels, helping ensure high-risk populations are prioritised in ongoing COVID-19 prevention and management efforts.

READING 3 – SEVERITY OF RSV VERSUS SARS-COV-2 OMICRON INFECTION AND INFLUENZA INFECTION AMONGST HOSPITALISED SINGAPOREAN ADULTS: A NATIONAL COHORT STUDY

Wee LE,¹⁻⁴ Ho RWL,¹ Tan KB,^{1,2,5,6,12} Lim JT,^{1,5} Young B,^{1,5,7} Boon Lye DC,^{1,5,7} Chiew CJ,^{1,6} Yung CF,^{2,5,11} Venkatachalam ^{1,3,4} Sim JXY,^{3,4} Cheong HY,⁸ Ng TY.^{9,10} Severity of respiratory syncytial virus versus SARS-CoV-2 Omicron and influenza infection amongst hospitalised Singaporean adults: a national cohort study. *Lancet Reg Health West Pac*. 2025 Feb 20;55:101494. PMID: 40060306.

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ABSTRACT

BACKGROUND: More data is required to contextualise respiratory-syncytial-virus (RSV) disease burden, versus other vaccine-preventable respiratory-viral-infections (RVIs) in older adults. We aimed to compare severity of RSV in hospitalised adults versus influenza/boosted COVID-19.

METHODS: Retrospective population-based cohort study, including all adult RSV hospitalisations (2021 – 2023) in Singapore. Disease severity (28-day mortality/intensive-care-unit [ICU] admission) and healthcare utilisation in RSV hospitalisations were compared with contemporaneous influenza hospitalisations and COVID-19 hospitalisations in 2023. Outcomes for COVID-19 were stratified by type/receipt of boosters. Comparative severity of RSV versus COVID-19/influenza was evaluated using multivariate logistic regression, adjusted for confounders. Generalised linear models were utilised to estimate excess length-of-stay/costs of RSV hospitalisation versus COVID-19/influenza as a rate-ratio.

FINDINGS: 12,811 hospitalised adults were included (RSV: N=1,332; influenza: N=3,999; COVID-19: N=7,480). Amongst RSV hospitalisations, 5.4% (72/1,332) died within 28 days; 3.8% (51/1,332) required ICU. Median length-of-stay (RSV) was 5.0 days (IQR=3.0-8.0). Older age/diabetes were associated with greater odds of 28-day mortality in RSV hospitalisations. Higher odds of 28-day mortality/ICU admission and higher healthcare utilisation was observed in RSV hospitalisations versus influenza. Conversely, RSV was less severe than unboosted COVID-19, with lower odds of 28-day mortality (adjusted-odds-ratio, aOR=0.56 [95% CI=0.40-0.79]) and rate-ratio for length-of-stay/costs significantly <1. However, higher odds of ICU (aOR=1.80 [95% CI=1.07-3.00]) were observed in RSV hospitalisations, versus COVID-19 hospitalisations boosted <1 year prior with updated vaccines.

INTERPRETATION: Hospitalisations attributed to RSV were more severe than influenza. RSV disease was less severe versus COVID-19 in unboosted patients but severity was not significantly different from COVID-19 in boosted individuals.

FUNDING: National Medical Research Council, Singapore.

READING 4 – PROTECTION AND WANING OF VACCINE-INDUCED, NATURAL, AND HYBRID IMMUNITY TO SARS-COV-2 IN HONG KONG

Jiang J,¹ Yin G,¹ Lam KF,^{1,2} Lau EHY,³ Lin Y,³ Cowling BJ.^{3,4} Protection and waning of vaccine-induced, natural and hybrid immunity to SARS-CoV-2 in Hong Kong. *Expert Rev Vaccines*. 2025 Dec;24(1):252-260. PMID: 40137440.

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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 emphasise booster campaigns and hybrid immunity pathways to enhance population-level immunity and guide future COVID-19 management in Hong Kong.

READING 5 – PREFERENCES FOR NONPHARMACEUTICAL INTERVENTIONS DURING ENDEMIC PHASE OF COVID-19

Wang Y,¹ Har CE,¹ Tan SHX,¹ Cheng HS,¹ Ang IYH.¹ Preferences for Nonpharmaceutical Interventions During the Endemic Phase of COVID-19: Discrete Choice Experiment. *JMIR Public Health Surveill.* 2025 Jun 4;11:e67725. PMID: 40470547.

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ABSTRACT

BACKGROUND: Nonpharmaceutical interventions (NPIs) are effective tools for pandemic containment but often impose significant socioeconomic consequences that intensify over time. Public support and compliance to NPIs are crucial to ensure their effectiveness.

OBJECTIVES: This study aimed to elicit preferences of a Singaporean population for the reintroduction of NPIs in response to the emergence of a new SARS-CoV-2 variant during the COVID-19 endemic phase.

METHODS: A web-based discrete choice experiment (DCE) was conducted. DCE attributes reflected key NPIs implemented in Singapore during the COVID-19 pandemic from 2020 to 2022, including mask wearing, dining restrictions, suspension of vocalisation activities and large-scale events, quarantine after international travel, and mandatory vaccine boosters. Participants were recruited from a demographically representative online panel. Statistical analysis was performed using a mixed-logit model and mixed-mixed multinomial logit model.

RESULTS: A total of 1,552 participants were included in the analysis. Overall preferences from the mixed-logit model showed that mask wearing was valued, both in public and indoors. Dining restrictions allowing groups of up to five people were preferred, but stricter dining restrictions allowing up to two people or no dining out were not favoured. Prohibiting large-scale events was not preferred. Participants accepted quarantine at home but opposed quarantine in government facilities. Two classes emerged from the mixed-mixed logit model: class 1 ("Prefer NPIs") and class 2 ("Prefer No NPIs"). While class 1 (39%) was only opposed to a complete prohibition on dining in at food and beverage establishments, no NPIs were preferred by class 2 (61%). Both classes were not opposed to mandatory mask wearing, dining restrictions allowing groups of up to five people, and mandatory vaccine boosters. Sex, age, education, employment status, the number of COVID-19 vaccine shots received, and risk attitude were associated with individuals' likelihood of belonging to a specific preference group.

CONCLUSIONS: Following the emergence of a new SARS-CoV-2 variant after a prolonged period of restrictions, less disruptive NPIs such as mask wearing indoors were valued by the public and should be swiftly reinstated. Adaptive strategies should be adopted for more contentious NPIs, such as strict dining restrictions and quarantine policies. Public preferences should be considered in the design and selection of NPIs for future pandemic containment strategies to enhance compliance and effectiveness.

READING 6 – ESTIMATION OF TRAJECTORY OF COVID-19 VACCINES EFFECTIVENESS AGAINST INFECTION

Jiang J,¹ Yin G,¹ Lam KF,² Lau EHY,³ Lin Y,³ Cowling BJ.⁴ Estimation of trajectory of COVID-19 vaccines effectiveness against infection. *Vaccine*. 2025 May 10;55:127067. PMID: 40158307.

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ABSTRACT

This large-scale cohort study conducted in Hong Kong examined the time-varying protective effects of various COVID-19 vaccines and dosing regimens against the Omicron BA.1/BA.2 variants.

An innovative pharmacokinetic/pharmacodynamic model was employed to estimate the trajectory of vaccine effectiveness over time.

Results indicated that the maximum protection for a single dose reached 0.120 for CoronaVac and 0.171 for Comirnaty. The peak protective effectiveness for the second and third doses were observed at 0.348 and 0.522, respectively. In a 4-dose regimen, CoronaVac demonstrated a maximum protective effectiveness of 0.548, stabilising at 0.487, while Comirnaty achieved a maximum effectiveness of 0.784, stabilising at 0.714 six months after the administration of the last dose. The vaccine effectiveness exhibited a rising and then declining pattern, peaking approximately 1-2 months post-vaccination. Understanding waning immunity is crucial for optimising vaccination strategies and policies as viral evolution continues. This real-world study captured changing dynamics that may differ from clinical trials with limited follow-up, providing essential evidence to guide the optimisation of vaccination efforts. Ongoing monitoring of vaccine effectiveness remains critical as the viral landscape evolves.

OBJECTIVES: This study aims to investigate the time-varying protective effects of various COVID-19 vaccines and dosing regimens against infections caused by the Omicron BA.1/BA.2 in Hong Kong.

METHODS: This territory-wide cohort study from Hong Kong combined vaccination records, confirmed COVID-19 cases, and census data from January 2022 to May 2022 to comprehensively analyse the time-varying protective effects of different COVID-19 vaccines and dosing regimens against Omicron BA.1 and BA.2 infections. A 4-parameter pharmacokinetic/pharmacodynamic model was used to estimate the trajectory of vaccine effectiveness over time.

RESULTS: Among 6.2 million adults, the maximum protective effectiveness for a single vaccine dose reached 0.120 for CoronaVac and 0.171 for Comirnaty. For the second and third doses, peak effectiveness were observed at 0.348 for CoronaVac and 0.522 for Comirnaty. Notably, a 4-dose regimen resulted in maximum protections of 0.548 for CoronaVac and 0.785 for Comirnaty, which stabilised at 0.487 and 0.714, respectively, six months following the last doses. The vaccine effectiveness exhibited a rising then declining pattern, peaking around 1-2 months post-vaccination, underscoring the importance of ongoing vaccination strategies.

CONCLUSIONS: Understanding the waning of vaccine protection over time is critical for informing optimal vaccination strategies, booster schedules, and public health policies. This real-world study can capture changing dynamics that might differ from clinical trials, which have more limited follow-up periods, and can provide crucial evidence to guide optimisation of vaccination strategies. Ongoing monitoring of vaccine effectiveness remains crucial as the viral evolution continues.

READING 7 –OMICRON SARS-COV-2 OUTCOMES IN VACCINATED INDIVIDUALS WITH HEART FAILURE AND ISCHAEMIC HEART DISEASE

Wee LE,^{1-3,#} Loy EX,^{1,#} Tan KB,^{1,2,4,13,14} Lye DCB,^{1,4,6,12} Hausenloy DJ,^{2,6,10,11} Yap J,^{2,9} Yeo KK,^{2,9} Lim JT,^{4,#} Chia YW,⁴⁻⁶ Chan MYY,^{6,7} Lim SL.⁶⁻⁸ Omicron SARS-CoV-2 outcomes in vaccinated individuals with heart failure and ischaemic heart disease. *Ann Acad Med Singap.* 2025 Apr 30;54(5):270-282. PMID: 40471109.

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ABSTRACT

INTRODUCTION: Outcomes after SARS-CoV-2 Omicron infection in patients with heart failure (HF) and ischaemic heart disease (IHD) remain poorly defined.

METHOD: In a highly vaccinated cohort of adult Singapore citizens and permanent residents, we used Cox proportional hazards models (adjusted for sociodemographic variables and comorbidities) to compare the risks of Omicron infection, COVID-19-related hospitalisation, and severe COVID-19 between individuals with HF or IHD and matched controls without these conditions.

RESULTS: From national databases, we identified 15,426 HF patients matched 1:-3 to 41,221 controls, and 110,442 IHD patients matched 1:-2 to 223,843 controls. Over 80% of HF and IHD patients had received at least three vaccine doses. During the Omicron-predominant period, both HF and IHD cohorts demonstrated higher adjusted risks of COVID-19 hospitalisation compared with matched controls (HF: adjusted hazard ratio [aHR] 1.77, 95% confidence interval [CI] 1.65-1.90; IHD: aHR 1.21, 95% CI 1.17-1.26). Among those with at least 1 HF-or IHD-related admission in the prior year, hospitalisation risk was further elevated (HF: aHR 1.27, 95% CI 1.13-1.42; IHD: aHR 1.11, 95% CI 1.01-1.23). Receipt of ≥ 3 vaccine doses was associated with substantially lower risk of severe COVID-19 versus only 2 doses (HF: aHR 0.35, 95% CI 0.28-0.43; IHD: aHR 0.27, 95% CI 0.23-0.32). A fourth dose conferred additional reductions in infection and adverse outcomes, though CIs for infection overlapped with those for three doses.

CONCLUSION: During Omicron predominance, HF and IHD patients experienced greater risk of COVID-19 hospitalisation and severe COVID-19 versus matched controls. Booster vaccinations attenuated these risks. Individuals with recent HF/IHD admissions should be prioritised for receipt of booster vaccine doses.

READING 8 – DISCRIMINATION OF A SINGLE-ITEM SCALE TO MEASURE INTENTION TO HAVE A COVID-19 VACCINE

Sim J,¹ Smith LE,² Amlôt R,^{2,3} Rubin GJ,^{3,4} Sevdalis N,⁵ Sherman SM.⁶ Discrimination of a single-item scale to measure intention to have a COVID-19 vaccine. *PLoS One*. 2025 May 5;20(5):e0322503. PMID: 40323983.

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ABSTRACT

AIM: When developing public health measures in a pandemic, it is important to examine attitudes and beliefs relating to vaccination uptake. We report the discrimination of a single-item vaccination intention scale and derive cutpoints in terms of sensitivity (true positives) and specificity (true negatives) in relation to subsequent vaccination status.

SUBJECT AND METHODS: In a sample of UK adults (n=1,119) recruited through an online survey platform, vaccination intention was measured on a 0-10 numerical rating scale (0=very unlikely, 10=very likely) at the beginning of the UK COVID-19 vaccination rollout (January 2021), and self-reported vaccination status was gathered after vaccination had been offered to all adults (October 2021). Discrimination of the scale was measured by the area under the receiver operating characteristic (ROC) curve.

RESULTS: The responders reporting being vaccinated or unvaccinated were 1,034 (92.4%) and 85 (7.6%), respectively. The area under the ROC curve was 0.956 (95% CI.943, 0.967), indicating a high degree of discrimination. The combined value of sensitivity and specificity was greatest at a cutpoint of 8 on the scale (sensitivity=0.821, specificity=0.988). If, however, the individual values of sensitivity and specificity are required to be simultaneously optimised, this occurs at point 6 (sensitivity=0.886, specificity=0.871).

CONCLUSION: We recommend a 0-10 intention scale as a validated, practical measure of vaccination intention in public health practice, with a cutpoint of 8 on the scale as optimal, unless sensitivity and specificity are to be simultaneously optimised, when 6 is the optimal cutpoint.

READING 9 - COMPARATIVE ANALYSIS OF THE ROLE OF HEALTHCARE BELIEFS ON CHILDHOOD VACCINATION UPTAKE AMONG PARENTS IN MALAYSIA AND SINGAPORE DURING THE COVID-19 PANDEMIC

Jiang J,¹ Yin G,¹ Lam KF,² Lau EHY,³ Lin Y,³ Cowling BJ.⁴ Estimation of trajectory of COVID-19 vaccines effectiveness against infection. *Vaccine*. 2025 May 10;55:127067. PMID: 40158307.

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