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Background

COVID-19 vaccines and oral antivirals (molnupiravir and nirmatrelvir-ritonavir) reduce the health impact of SARS-CoV-2 infections through modifying the host immunity and suppressing viral replications. Population-level clinical and virological outcomes may reflect individual immune responses to the virus among patients with COVID-19 who received these pharmaceutics in comparison with those not receiving such interventions, and may inform optimal implementation of control measures especially for high-risk populations during the post-pandemic era.

Clinical and virological assessment on effects of COVID-19 vaccination and oral antivirals among elderly patients during omicron waves in Hong Kong Y Lin¹, J Blais¹, B Yang¹, TK Tsang¹, BJ Cowling^{1,2}, P Wu^{1,2}

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Results

Vaccination was found to be associated with a lower mortality risk, and the risk for individuals that were fully vaccinated was prominently lower than that for those who were partially vaccinated (Figure 1). Treatment with either molnupiravir or nirmatrelvir-ritonavir demonstrated significant effects in reducing in-hospital mortality (OR: 0.56, 95% CI: 0.49-0.64 for treatment with molnupiravir and 0.23 (0.17-0.32) for nirmatrelvir-ritonavir respectively; Figure 1), and insignificant interactive effects were found between vaccination and oral antiviral treatments.

Objectives

This study aimed to evaluate the clinical and virological outcomes in relation to patients' demographic and clinical characteristics including vaccination and use of antivirals, aiming to highlight the possible protective effects of both oral interventions in different aspects.

Methods

We analyzed healthcare data for inpatients with COVID-19 admitted into public hospitals over omicron waves in Hong Kong during February 25 - December 31, 2023, to evaluate occurrence of in-hospital mortality and temporal patterns of viral shedding in relation to patients' vaccination status and antiviral treatments considering the demographic and other clinical factors.

Majority of individuals included in the analyses for clinical severity were tested with Ct values from RT-qPCR during admission, and around 30-40% of individuals with Ct values were tested more than twice, providing sufficient longitudinal Ct values for the construction of individual viral shedding patterns over time. It was shown that vaccination and treatment with nirmatrelvir-ritonavir were associated with pronouncedly faster viral clearance particularly in the unvaccinated patients compared with the vaccinated counterparts (Figures 2-3). Only a marginal relationship with the change of viral burden was observed in patients treated with molnupiravir (Figure 3).

(molnupiravir)				B (nirmatrelvir-ritonavir)			
(moniupitatit)	β (95% CI), days			β (95% CI), days			
Vaccination status	1			Vaccination status		!	
Unvaccinated			Ref	Unvaccinated			Ref
Partially vaccinated	+		-2.40 (-2.67,-2.13)	Partially vaccinated	+		-2.62 (-2.90,-2.34)
Fully vaccinated	-		-3.14 (-3.57,-2.72)	Fully vaccinated	-	1	-3.14 (-3.58,-2.69)
Antiviral treatment	i			Antiviral treatment		l	
No	1		Ref	No		1	Ref
Yes	+		-0.70 (-1.07,-0.34)	Yes			-4.30 (-5.03,-3.57)
Age group				Age group			
60-79yrs			Ref	60-79yrs			Ref
≥80yrs		٠	1.49 (1.28,1.71)	≥80yrs		+	1.34 (1.11,1.57)
Sex	1			Sex			
Female	1		Ref	Female		1	Ref
Male		•	0.89 (0.68,1.09)	Male		+	1.04 (0.81,1.26)
Charlson Comorbidity Index				Charlson Comorbidity Index	(Ì	
0			Ref	0			Ref
1-2		+	1.28 (1.06,1.50)	1-2		+	1.20 (0.95,1.45)
3-14	1	+	2.60 (2.27,2.94)	3-14		- 1	 3.08 (2.69,3.48)
Epidemic period	 			Epidemic period			
Off peak	1		Ref	Off peak			Ref
Peak		+	1.33 (1.00,1.66)	Peak		•	1.58 (1.19,1.96)
Partially vaccinated x treated	1		0.90 (0.33,1.47)	Partially vaccinated x treate	ed		2.12 (1.21,3.03)
Fully vaccinated x treated	1		0.96 (0.35,1.57)	Fully vaccinated x treated			- 3.01 (2.18,3.84)
-5	-3 -1	1 3			-5 -3 -1		3

A (molnupiravir)						
	OR (95% CI)					
Vaccination status						
Unvaccinated		Ref				
Partially vaccinated	•	0.57 (0.51,0.63)				
Fully vaccinated	•	0.30 (0.24,0.37)				
Antiviral treatment						
No		Ref				
Yes	•	0.56 (0.49,0.64)				
Age group						
60-79yrs		Ref				
≥80yrs	-	2.45 (2.21,2.73)				
Sex						
Female		Ref				
Male	+	1.33 (1.21,1.47)				
Charlson Comorbidity Index						
0	1	Ref				
1-2	-	1.49 (1.35,1.65)				
3-14		2.29 (2.00,2.63)				
Epidemic period						
Off peak		Ref				
Peak		1.52 (1.27,1.82)				
0.0 1.0 2.0 3.0						

B (nirmatrelvir-ritonavir)	OR (95% CI)	
Vaccination status		
Unvaccinated	R	ef
Partially vaccinated	• 0.53 (0.4	7,0.60)
Fully vaccinated	• 0.27 (0.2	1,0.35)
Antiviral treatment		
No	R	ef
Yes	• 0.23 (0.1	7,0.32)
Age group		
60-79yrs	R	ef
≥80yrs	 2.46 (2.1	8,2.77)
Sex		
Female	R	ef
Male		1,1.51)
Charlson Comorbidity Index		
0	R	ef
1-2	→ 1.46 (1.3	0,1.64)
3-14	 2.35 (1.9	9,2.77)
Epidemic period		
Off peak	R	ef
Peak	— 1.35 (1.08	8,1.69)
	0.0 1.0 2.0 3.0	

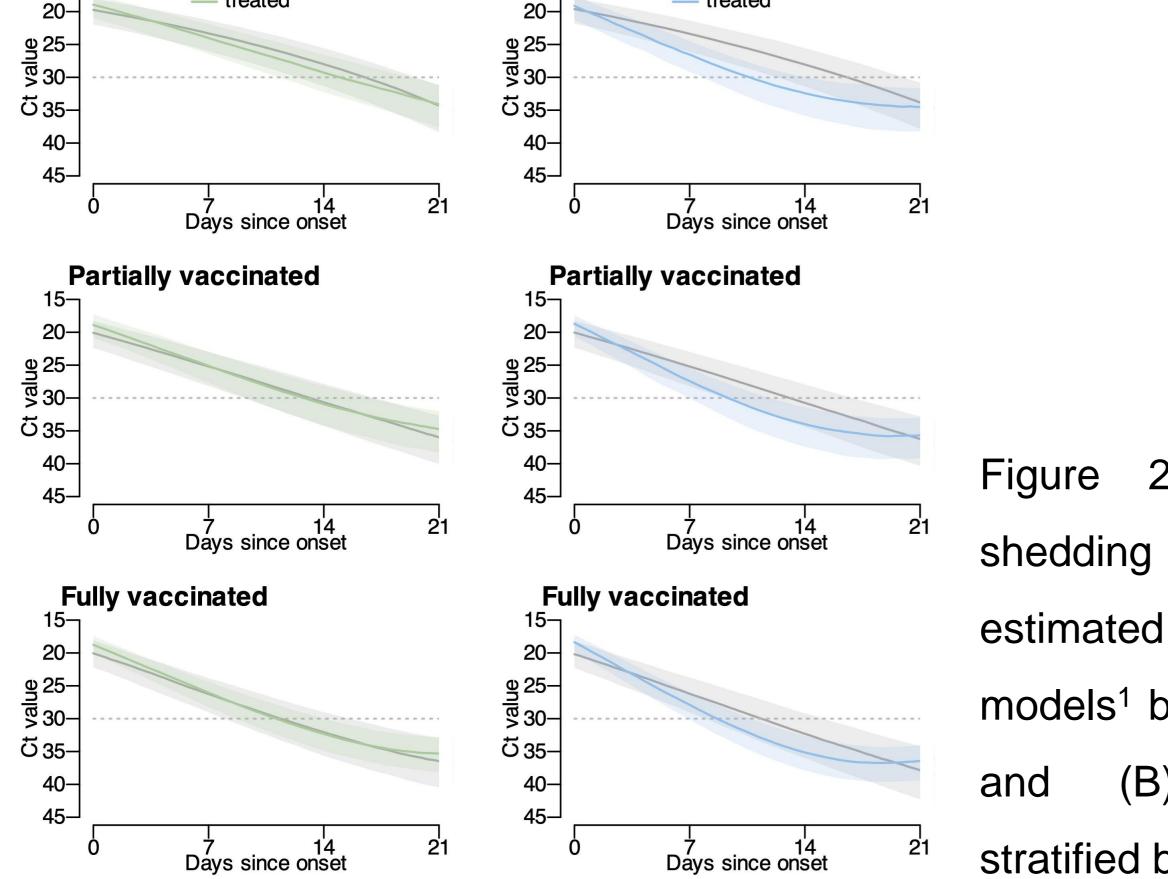
Figure 1. Associations estimated from the logistic regression model between (A) molnupiravir and (B) nirmatrelvir-ritonavir and the risk of in-hospital mortality adjusting for vaccination status and other potential confounders.

В Unvaccinated Unvaccinated - non-treated non-treated Figure 3. Associations estimated from the linear regression model between (A) molnupiravir and (B) nirmatrelvir-ritonavir and the duration of effective viral shedding (based on the trajectory of daily viral burden since onset estimated from random-effects models¹), adjusting for vaccination status and other potential confounders.

Conclusion

Our study demonstrates that both COVID-19 vaccines and oral antivirals were

independently associated with a better clinical outcome and faster viral clearance,



2. Trajectory viral OŤ

since symptom onset

random-effects estimated from

models¹ between (A) molnupiravir

nirmatrelvir-ritonavir, **(B)**

stratified by vaccination status.

especially nirmatrelvir-ritonavir. Further studies may be needed to investigate the

interactive effect between vaccination and nirmatrelvir-ritonavir on viral kinetics to

explore underlying mechanisms of immune responses to the viral infection.

References

[1] Lin Y, Wu P, Tsang TK, et al. Viral kinetics of SARS-CoV-2 following onset of COVID-19 in symptomatic patients infected with the ancestral strain and omicron BA.2 in Hong Kong: a retrospective observational study. Lancet Microbe 2023; 4(9): e722-e31.

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