





# Respiratory admissions before and during the COVID-19 pandemic with mediation analysis of air pollutants, mask-wearing and influenza rates

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## Abstract

**Background and objective:** Decline in hospitalizations for various respiratory diseases has been reported during the COVID-19 pandemic, but what led to such an observation is uncertain.

**Methods:** This was a territory-wide, retrospective cohort study involving all public hospital admissions in Hong Kong from 1 January 2017 to 31 December 2020. Hospital admissions for respiratory diseases, including asthma, COPD and non-COVID pneumonia, were assessed. COVID-related admissions were excluded from this study. The time of commencement of the pandemic was taken from the fourth week of January 2020. The associations between air pollutant levels, influenza and mask-wearing rates with hospital admissions were assessed by mediation analyses.

**Results:** There were altogether 19,485, 78,693 and 238,781 admissions for asthma, COPD and non-COVID pneumonia from January 2017 to December 2020. There was a marked reduction in hospital admissions of asthma, COPD and non-COVID pneumonia (37%, 36% and 12% decrease in average daily admissions, respectively) during the COVID-19 pandemic compared to before. Air pollutant levels and influenza rate were decreased while mask-wearing rate was increased. Collinearity of mask-wearing rates and pandemic year was observed. For COPD, NO<sub>2</sub>, SO<sub>2</sub>, PM10 and influenza rates (4%, 11%, 4% and 4% of the total effect, respectively), while for non-COVID pneumonia, PM10 and influenza rates (11% and 52%, respectively) had significant mediation effect on changes in hospital admissions before and during the COVID-19 pandemic.

**Conclusion:** During the COVID-19 pandemic, a decrease in air pollutant levels and influenza rate had mediation effect on the reduction in hospitalizations of COPD and non-COVID pneumonia.

## KEYWORDS

asthma, COPD, coronavirus disease, COVID-19, pneumonia

## INTRODUCTION

The COVID-19 pandemic has changed the healthcare landscape. These changes include not just a large number of patients with COVID-19 requiring medical care, but also the care being delivered or the way patients seek attention for medical illnesses during the COVID-19 pandemic. There were reports about the decline in hospitalizations for acute coronary syndrome, stroke, gastrointestinal and liver

disease<sup>1–4</sup> as medical resources shifted to manage infected patients.

The airway and lungs are the primary organs affected during viral respiratory infection, and patients with respiratory diseases would be at risk of serious complications from COVID-19 infection. A study suggested that chronic obstructive pulmonary disease (COPD) patients had greater severity of COVID-19 infection and increased mortality.<sup>5</sup> In contrast, other studies have found that asthma, COPD and

non-COVID pneumonia admissions decreased during the pandemic compared to before. Some studies have suggested better hygiene and wearing face masks would decrease viral respiratory infections and subsequent exacerbations of airway diseases.<sup>6–9</sup> Reduction in air pollution secondary to lockdown of cities might contribute to fewer hospital admissions.<sup>10</sup> However, many of these studies have not assessed the mediating effects of the factors associated with exacerbations of airway diseases and pneumonia, such as the effect of air pollutant levels, influenza rate and mask-wearing rate, etc.

This territory-wide study aimed to assess the mediation effects of air pollutant levels, influenza rate and community mask-wearing rate on the change of respiratory hospitalization (asthma, COPD and non-COVID pneumonia) of adults before (from January 2017 to the third week of January 2020) and during (from the fourth week of January 2020 to last week of December 2020) the COVID-19 pandemic. This study would enhance our understanding of the reasons behind the decrease in respiratory admissions during the COVID-19 pandemic.

## METHODS

This was a territory-wide, retrospective cohort study involving all public hospital admissions in Hong Kong (HK) from 1 January 2017 to 31 December 2020. Hospital admissions for respiratory diseases, including asthma, COPD and non-COVID pneumonia, were assessed. COVID-related admissions were excluded from this study. The time of the onset of the pandemic was taken from the fourth week of January 2020, when our city started to have confirmed COVID-19 cases.<sup>11</sup>

Data were retrieved from the Clinical Data Analysis and Reporting System (CDARS), an electronic healthcare database, of the Hospital Authority in HK.<sup>12</sup> This system captured the health data of patients attending public hospitals in HK. The public hospital system in HK looks after approximately 90% of the 7.5 million population.

Episode-based data for hospital admissions were retrieved using ICD-9 codes. Cases aged  $\geq 18$  with a principal diagnosis of asthma (493), COPD (491–492) and pneumonia (480–488) were identified. Exclusion criteria included age  $< 18$  years and patients with COVID-19 infection (identified by ICD-9 code 480.8 or ICD-10 code J12.8). We focused on adults only in this study as young children admitted with wheezing were difficult to differentiate from having viral illness or asthma. In addition, COPD does not occur in children. Furthermore, the causes and thresholds for hospitalization for childhood asthma and pneumonia might be very different from those of adults. Demographic data, including age, gender, admission date, hospital length of stay and episode mortality (post-discharge mortality not included), were recorded.

## SUMMARY AT A GLANCE

The reason behind the observation of decline in respiratory hospitalizations during the COVID-19 pandemic was uncertain. This study found that air pollutants levels and influenza rate had mediation effects on the decrease in hospitalizations for COPD and non-COVID pneumonia, but not for asthma during the COVID-19 pandemic.

These data were collected in the study period: ambient temperature, humidity, air pollutants including ozone (O<sub>3</sub>), nitrogen dioxide (NO<sub>2</sub>), sulphur dioxide (SO<sub>2</sub>), particulate matter (PM<sub>10</sub>), rate of face mask-wearing and rate of influenza A/B infection. Mean weekly ambient temperature in degree Celsius and humidity data in percentage were obtained from the Hong Kong Observatory.<sup>13</sup> Mean weekly levels of O<sub>3</sub>, NO<sub>2</sub>, SO<sub>2</sub> and PM<sub>10</sub> at general monitoring stations were obtained from the Hong Kong Environmental Protection Department (HKEPD).<sup>14</sup> Influenza rates were obtained from the Center for Health Protection.<sup>15</sup> The face mask-wearing data were collected by cross-sectional telephone surveys among the general population of HK in February, March and April 2020.<sup>11</sup> Subjects were asked whether they would wear a face mask on leaving their homes. The face mask-wearing rate was estimated to be 1% from 2017 to 2019. Based on the survey, face mask-wearing rates were 74.5% in January, 97.5% in February and 98.8% from March 2020 onwards.<sup>11</sup>

The effect of air pollutant levels, influenza virus rate and community mask-wearing rate on admission counts of the respiratory diseases between the COVID (January Week 4 2020–December Week 4 2020) and non-COVID (January Week 1 2017–January Week 3 2020) periods were assessed by mediation analyses (see Appendix S1 in the Supporting Information for more details) in separate models with adjustment by meteorological variables.<sup>16</sup> Admission numbers, air pollutants, influenza virus rate and meteorological parameters were represented as average daily values in a week. Changes in admissions during the COVID-19 pandemic compared to before were assessed by Poisson regression model. Continuous variables were presented as mean (standard deviation) or median (interquartile-range [IQR]), as appropriate, while categorical variables were expressed as *n* (%). For comparisons of admissions, age, gender, length of hospitalization and mortality between the COVID and non-COVID periods, Student *t*-test, Mann–Whitney *U* test and Fisher exact test were used as appropriate. All tests were two-tailed, and *p* values  $< 0.05$  were considered statistically significant. Statistical analyses were performed using R packages V.4.0.3, including mediation, readxl, car, dplyr and haven (R Foundation for Statistical Computing, Vienna, Austria) and IBM SPSS Statistics 26 (IBM Corporation, Armonk, NY).

**TABLE 1** Admission and mortality data for asthma, COPD and non-COVID pneumonia

		January 2020 Week 4–December 2020 Week 4 (a)	January 2017 Week 1–January 2020 Week 3 (b)	<i>p</i> -value, Difference between (a) and (b)
Asthma	Number of admissions	2792	16,693	
	Median [IQR] of daily number of admissions	8 [7–9]	14 [13–16]	<0.001 <sup>a</sup>
	Length of hospitalization, mean (SD) (median [IQR]) (days)	3.77 (5.49) (2 [1–4])	3.97 (6.37) (2 [1–4])	0.082 <sup>a</sup>
	Mortality <i>n</i> (%)	13 (0.47%)	77 (0.46%)	1.000 <sup>b</sup>
	Age (mean, SD)	60.90 (19.86)	62.08 (20.71)	0.004 <sup>c</sup>
	Gender (M:F) (% male)	1069:1723 (38.3%)	5903:10,790 (35.4%)	0.003 <sup>b</sup>
COPD	Number of admissions	11,065	67,628	
	Median [IQR] of daily number of admissions	32 [29–33.5]	60 [53–68]	<0.001 <sup>a</sup>
	Length of hospitalization, mean (SD) (median [IQR]) (days)	6.61 (9.52) (4 [2–7])	6.69 (10.68) (4 [2–7])	0.203 <sup>a</sup>
	Mortality <i>n</i> (%)	305 (2.76%)	1469 (2.17%)	<0.001 <sup>b</sup>
	Age (mean, SD)	77.51 (10.16)	77.72 (10.00)	0.037 <sup>c</sup>
	Gender (M:F) (% male)	9978:1087 (90.3%)	59,463:8165 (87.9%)	<0.001 <sup>b</sup>
Non-COVID pneumonia	Number of admissions	44,815	193,966	
	Median [IQR] of daily number of admissions	120 [115–129.5]	165 [138–192]	<0.001 <sup>a</sup>
	Length of hospitalization, mean (SD) (median [IQR]) (days)	9.11 (12.97) (5 [3–11])	9.00 (21.17) (5 [2–10])	0.513 <sup>a</sup>
	Mortality <i>n</i> (%)	10,401 (23.21%)	31,345 (16.16%)	<0.001 <sup>b</sup>
	Age (mean, SD)	79.38 (15.38)	77.44 (16.63)	<0.001 <sup>c</sup>
	Gender (M:F) (% male)	25,365:19,450 (56.6%)	102,774:91,192 (52.9%)	<0.001 <sup>b</sup>

<sup>a</sup>Mann–Whitney *U* test.<sup>b</sup>Fisher's Exact test.<sup>c</sup>Student *t*-test.

## RESULTS

There were altogether 19,485, 78,693 and 238,781 admissions for asthma, COPD and non-COVID pneumonia respectively from January 2017 to December 2020. The number of admissions, age, gender, length of hospitalization and mortality for patients with the principal diagnosis of asthma, COPD and non-COVID pneumonia are shown in Table 1.

The median daily number of admissions from the fourth week of January 2020 to December 2020 were significantly lower for asthma, COPD and non-COVID-pneumonia compared to January 2017 to the third week of January 2020. The length of hospitalization for asthma, COPD and non-COVID pneumonia, however, showed no differences between the two periods. The mortality rates for hospitalized patients were higher for COPD and non-COVID chest infection when comparing the COVID period to the pre-COVID period (2.76% vs. 2.17%,  $p \leq 0.001$  for COPD; 23.21 vs. 16.16%,  $p \leq 0.001$  for non-COVID pneumonia), but there was no significant difference noted for asthma.

The characteristics of the meteorological parameters, air pollutant levels, influenza activity and mask-wearing rate are

listed in Table 2. Decreased air pollutant levels of NO<sub>2</sub>, SO<sub>2</sub> and PM10 were observed in the pandemic compared to the pre-pandemic period. The rate of influenza detection was markedly reduced. On the other hand, the mask-wearing rate was increased (mean [SD] 2.5 [10.4] vs. 98.1 [3.6]%,  $p < 0.001$ ).

There was a marked decrease in hospitalizations for asthma, COPD and non-COVID pneumonia (37%, 36% and 12% decrease in average admissions per day, respectively) compared with the data in the past 3 years before the pandemic. Relationships of the weekly admission number of asthma, COPD, non-COVID pneumonia with air pollutant levels are shown in Figure 1 while data with influenza and mask-wearing rate are shown in Figure 2. There were variations in the levels of air pollutants and respiratory admissions over time, and respiratory admissions appeared to follow the trend of the level of air pollutants and influenza rates.

Since mask-wearing rates started to increase markedly during the COVID-19 pandemic and remained at a high level during the whole pandemic period, we assessed if there was collinearity on the indicator of 'pre-COVID vs. COVID period' in modelling with different respiratory diseases, with

**TABLE 2** Data on the temperature, humidity, air pollutants, influenza activity and mask-wearing

	January 2020 Week 4–December 2020 Week 4	January 2017 Week 1–January 2020 Week 3	<i>p</i> -value
Ambient temperature (weekly average) (°C)	24.7 (4.6)	24.0 (4.7)	0.362 <sup>a</sup>
Ambient temperature (range, min–max) (°C)	15.4–30.4	10.8–30.6	
Humidity (weekly average) (%)	77.7 (6.6)	78.0 (7.3)	0.793 <sup>a</sup>
Humidity (range, min–max) (%)	63.0–88.6	48.7–90.5	
Air pollutant levels (weekly average [SD])			
Nitrogen dioxide (µg/m <sup>3</sup> )	32.0 (7.5)	39.2 (8.8)	<0.001 <sup>a</sup>
Ozone (µg/m <sup>3</sup> )	51.3 (21.3)	54.0 (21.2)	0.464 <sup>a</sup>
Sulphur dioxide (µg/m <sup>3</sup> )	4.4 (0.7)	6.4 (1.6)	<0.001 <sup>a</sup>
Respirable suspended particulates (PM10) (µg/m <sup>3</sup> )	25.5 (12.2)	33.3 (12.5)	<0.001 <sup>a</sup>
Mask-wearing %, (weekly average % of the population) (median [IQR])	98.1 (3.6) (98.8 [98.8–98.8])	2.5 (10.4) (1 [1–1])	<0.001 <sup>b</sup>
Influenza A/B virus detected (average daily incidents in a week) (median [IQR])	5.4 (24.3) (0 [0–0])	70.7 (83.2) (43 [16–84])	<0.001 <sup>b</sup>

<sup>a</sup>Student *t*-test.<sup>b</sup>Mann–Whitney *U* test.

mask-wearing rate added in those models. The variance inflation factors (VIF)<sup>17</sup> of the indicator for ‘before and during the COVID pandemic’ corresponding to the respiratory diseases are presented in Table 3. VIFs of the indicator for ‘before and during the COVID pandemic’ for asthma, COPD and non-COVID pneumonia admissions were >5 when ‘mask-wearing rate’ was added, indicating the presence of collinearity of mask-wearing rates and time periods.<sup>18</sup>

Mediation analyses were performed for each factor of air pollutants and influenza rate and the results are shown in Table 4 (mask-wearing rate was not assessed due to collinearity with the pandemic period). For asthma, air pollutants and influenza rate were not mediators for changes in hospital admissions before and during the COVID-19 pandemic. For COPD, NO<sub>2</sub>, SO<sub>2</sub>, PM10 and influenza rates (4%, 11%, 3.8% and 3.8% of the total effect, respectively) and non-COVID pneumonia, PM10 and influenza rates (with 11% and 52% of the total effect, respectively) had significant mediation effect on changes in hospital admissions before and during the COVID-19 pandemic. As the COVID-19 pandemic started after the first 3 weeks of 2020, we have also performed a sensitivity analysis by taking away all the data in the first 3 weeks of 2017–2020. The results were similar and are shown in Table S1 in the Supporting Information.

## DISCUSSION

This study has demonstrated a marked reduction in hospitalizations for asthma, COPD and non-COVID pneumonia (37%, 36% and 12% average daily admissions, respectively) during the COVID-19 pandemic compared with the data in the past 3 years. Moreover, we observed significantly higher mortality rates of COPD and non-COVID pneumonia

(0.59% and 7.05% increments, respectively). Air pollutant levels were also significantly lower during the pandemic presumably due to lockdown in the Pearl Delta region resulting in reduction in traffic and pollutant emissions by industries. For asthma, air pollutants and influenza rates were not mediators for changes in hospital admissions before and during the COVID-19 pandemic. For COPD, NO<sub>2</sub>, SO<sub>2</sub>, PM10 and influenza rates, while for non-COVID pneumonia, PM10 and influenza rates had significant mediation effect on changes in hospital admissions before and during the COVID-19 pandemic.

The reduction of asthma admissions during the period of the COVID-19 pandemic was similar to the lockdown period in the first 18 weeks of 2020 in Scotland and Wales (36%)<sup>19</sup> but less than that from February to July 2020 in Korea (52%).<sup>6</sup> Most studies did not examine the interactions of potential mediation/association factors with acute admissions. Some studies reported a decrease in influenza rate, increase in mask-wearing rate and social distancing measures such as lockdown, but the association or contribution of these factors with acute admissions was unclear.<sup>6,19</sup>

Our study found no increase in the mortality rate of hospitalized patients during the pandemic for asthma admissions, which was similar to the observation in meta-analyses.<sup>20–22</sup> Previous studies did not observe asthma patients having a higher risk of being infected, hospitalized or having worse clinical outcomes from COVID-19.<sup>23</sup> A meta-analysis even reported asthma was significantly related to a reduced risk for COVID-19 mortality.<sup>22</sup> However, our study was different from previous studies, as we excluded all COVID-19 cases and found that non-COVID related asthma attacks requiring hospitalization did not increase mortality during the pandemic.

For COPD admissions, a study found that lockdown in the first 30 weeks of 2020 in Scotland and Wales was associated with a 48% overall reduction in emergency admissions

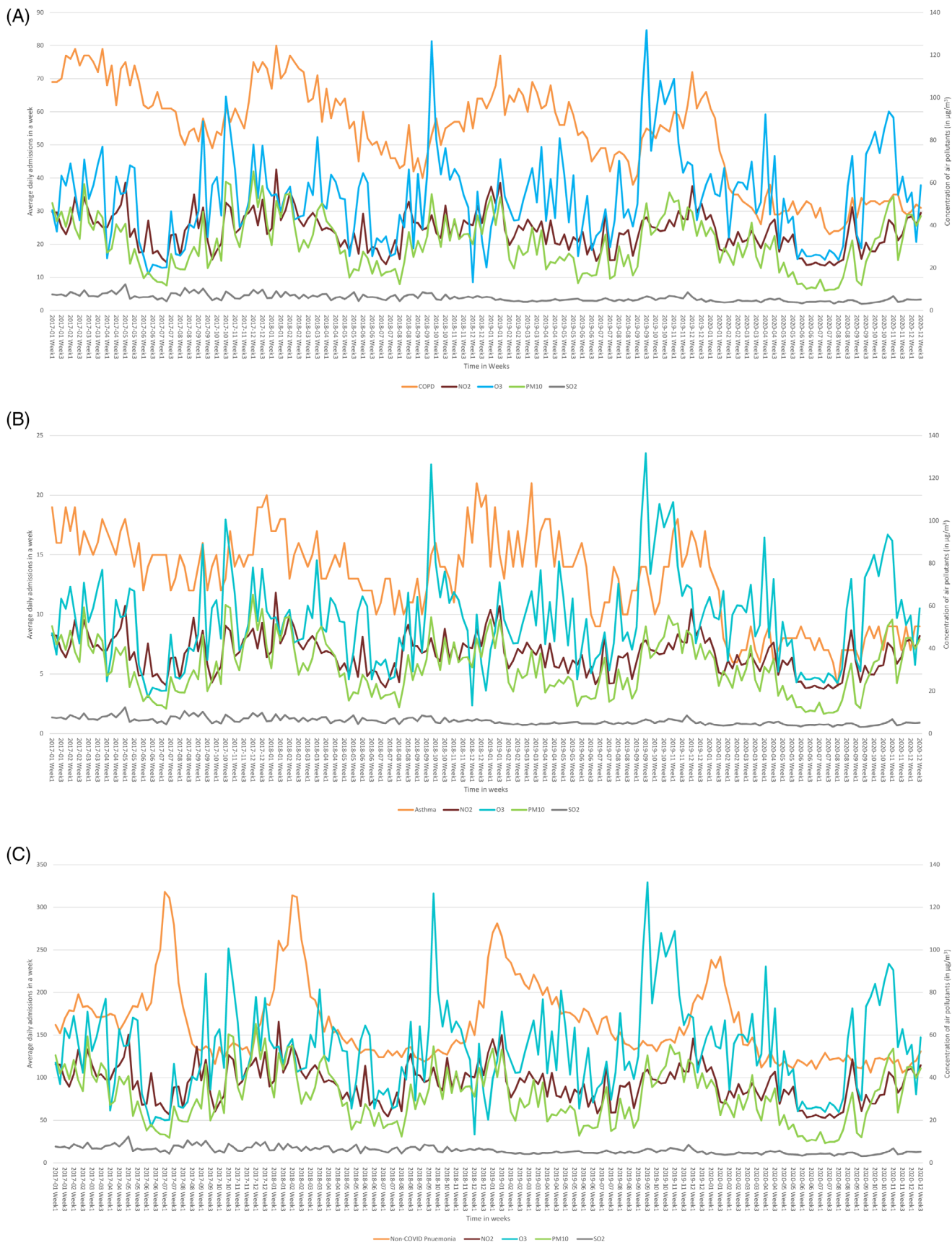


FIGURE 1 Average daily admissions for (A) asthma, (B) COPD and (C) non-COVID pneumonia and air pollutant levels

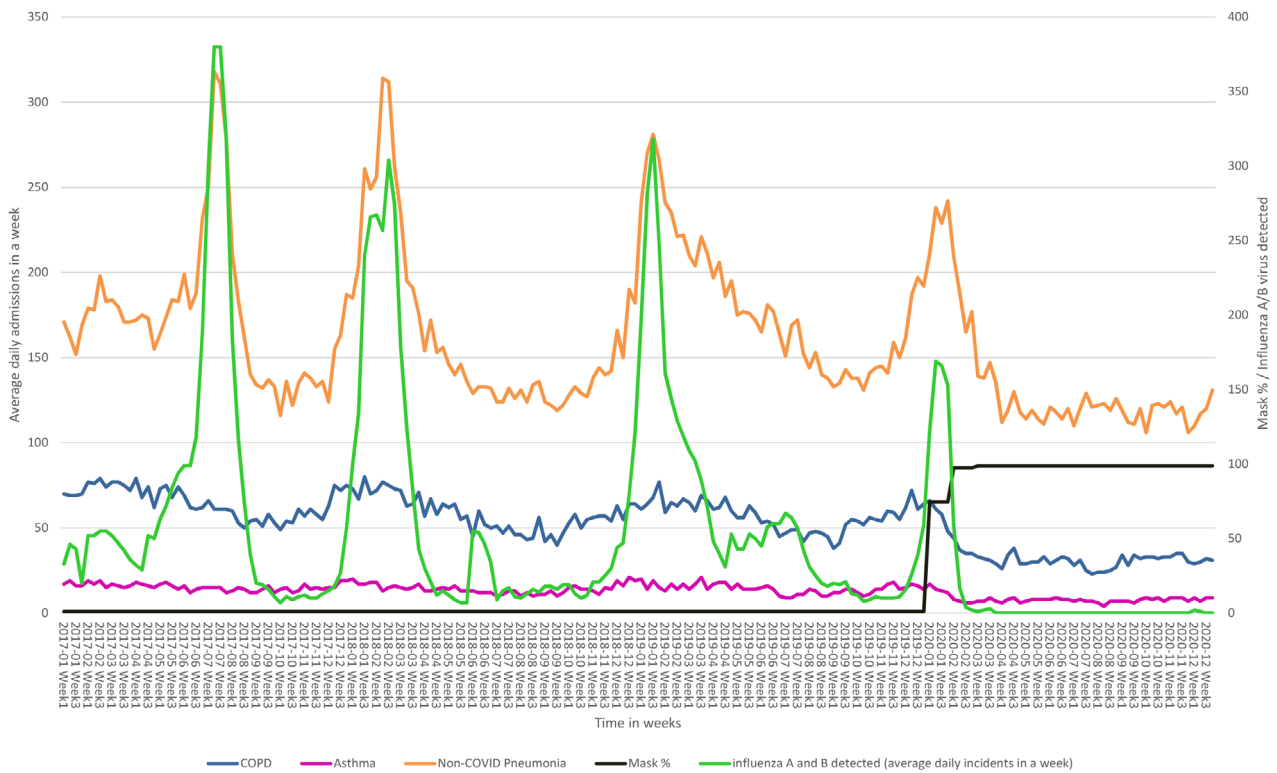


FIGURE 2 Average daily admissions for asthma, COPD and non-COVID pneumonia and the influenza and mask-wearing rate

TABLE 3 Variance inflation factor of the indicator of 'pre-COVID versus COVID period' on the respiratory diseases admissions

	All data		Without data of the first 3 weeks of 2017–2020	
	VIF without mask-wearing rate	VIF with mask-wearing rate	VIF without mask-wearing rate	VIF with mask-wearing rate
Asthma	1.00	12.73	1.00	424.01
COPD	1.00	12.51	1.00	420.59
Non-COVID pneumonia	1.01	13.54	1.00	318.72

Abbreviation: VIF, variance inflation factor.

for COPD without significant change in deaths due to COPD.<sup>24</sup> In Singapore, COPD admissions decreased by 58% from February to July 2020 compared to the pre-pandemic period but mortality was not assessed.<sup>25</sup> Our study period covered the first three waves of COVID-19 in HK where there were tight social distancing measures and gathering ban. There were reduced attendance rates at the public hospital respiratory clinics while general practitioners were seeing fewer patients than usual as many people with chronic illness would stay more at home for fear of being infected by SARS-CoV2 in the community. Lack of prompt and proper medical attention with delayed admissions and milder exacerbations being treated at home rather than admitted might have contributed to the higher in-hospital mortality due to acute exacerbations of COPD.

In this study, we found that for COPD, air pollutant levels and influenza rate had mediation effect on the reduction in hospitalizations during the pandemic. Our previous

study found that ambient air pollutants had an adverse effect on hospital admissions for COPD, particularly in winter.<sup>26</sup> With the lower air pollutant levels during the pandemic, air pollutants probably would lead to fewer admissions than the pre-pandemic period. A study in Singapore found a lower rate of PCR-positive respiratory viruses in the patients admitted with COPD (the pandemic vs. the pre-pandemic rates were 10.8% vs. 48.8%) but the proportion of various viruses was not reported.<sup>25</sup> A study in the Netherlands found human metapneumovirus rate remained stable during the COVID-19 pandemic compared to before.<sup>27</sup> During the outbreak of SARS-CoV1 in HK in 2003, community hygienic measures such as mask-wearing and hand hygiene significantly reduced the incidence of various respiratory viral infections.<sup>28</sup> Since February 2020, there has been almost no influenza activity in HK presumably related to universal mask-wearing, hand hygiene and other stringent social distancing measures.<sup>29</sup>

**T A B L E 4** Mediation analyses of the effect of air pollutants, mask-wearing rate and influenza rate on the average daily admissions of respiratory diseases in the pre-COVID and COVID periods (all data)

Mediators	Asthma				COPD				Non-COVID pneumonia						
	ACME	ADE	Total effect	Proportion mediated	p	ACME	ADE	Total effect	Proportion mediated	p	ACME	ADE	Total effect	Proportion mediated	p
NO <sub>2</sub>	-0.173	-12.692	-12.865	0.013	0.46	-2.247	-50.176	-52.423	0.043	<0.001	0.44	-54.966	-54.527	-0.008	0.88
O <sub>3</sub>	-0.0337	-12.806	-12.84	0.003	0.58	-0.22	-52.212	-52.432	0.004	0.44	1.532	-55.953	-54.421	-0.028	0.35
SO <sub>2</sub>	-0.577	-12.231	-12.808	0.045	0.092	-6.075	-46.296	-52.372	0.116	<0.001	4.289	-59.008	-54.72	-0.078	0.35
PM10	-0.25	-12.509	-12.759	0.020	0.18	-1.991	-50.325	-52.316	0.038	0.004	6.09	-60.923	-54.834	-0.111	0.048
Influenza rate	-0.194	-12.659	-12.853	0.015	0.26	-2.002	-50.199	-52.2	0.038	<0.001	-26.229	-24.049	-50.279	0.522	<0.001

Note: ACME, average causal mediation effect (indirect effect of the pre-COVID vs. COVID period on the admission numbers for individual mediators, controlled for meteorological parameters); ADE, average direct effect (direct effect of the pre-COVID vs. COVID period on admission numbers, controlled for meteorological parameters). Total effect, sum of ACME and ADE. Proportion mediated, ACME/total effect. p = p-value on ACME was based on quasi-Bayesian CI. The unit of ADE, ACME, and total effect is "average daily admissions". An example of the interpretation of the values of the Table can be found in the footnote of Table S1 in the Supporting Information.

During the COVID-19 pandemic, many places, such as Denmark, New York, Korea and Taiwan reported a reduction in hospitalization for non-COVID pneumonia.<sup>6,30-32</sup> A study in Denmark observed an increase in mortality of non-COVID pneumonia.<sup>30</sup> However, these reports did not assess the factors that would contribute to this observation. While a decline in air pollutant levels and influenza infection rate might have contributed (as shown by the mediation effect of these factors on hospital admission in this study), people's behaviour of attending hospital service during the pandemic would possibly have an effect, and this was not assessed in our study. A study in Italy noted an overall reduction in emergency department non-COVID admissions in 2020 by 39.5% compared to 2019.<sup>33</sup> There was an increase in triage urgency levels for the emergency admissions.<sup>34</sup> It is possible that milder patients with community-acquired pneumonia were treated by general practitioners as out-patients. Admission of patients with more severe rather than milder pneumonia probably contributed to higher in-hospital mortality.

The strength of this study was that the mediation effect of the related factors for hospitalizations of respiratory diseases was assessed. This study examined a longer duration of the pandemic when compared to earlier publications. This study was limited by the retrospective design based on diagnosis coding, and thus individual patient characteristics were not assessed. Also, only the rate of influenza, but not for other respiratory viruses, was evaluated in this study. Due to the collinearity in modelling the hospitalization with mask-wearing rate and the indicator of pre- and COVID-19 pandemic, we cannot conclude whether mask-wearing rates mediate the change in admissions. Factors such as behavioural changes of patients during the pandemic, including related changes in self-management and smoking cessation, hesitance to visit the emergency department and so on, were not assessed in this study.

In conclusion, during the COVID-19 pandemic, there was a decrease in hospitalization for asthma, COPD and non-COVID pneumonia, while the mortality rates of patients hospitalized for COPD and non-COVID pneumonia were increased. Reduction in air pollutants levels and influenza rate had mediation effect on the decrease in hospitalizations for COPD and non-COVID pneumonia during the COVID-19 pandemic compared to before, but this was not observed for asthma.

**AUTHOR CONTRIBUTION**

**Fanny Wai San Ko:** Conceptualization (lead); data curation (equal); formal analysis (equal); methodology (equal); project administration (lead); writing – original draft (lead); writing – review and editing (equal). **Louis Ho Shing Lau:** Conceptualization (equal); data curation (equal); methodology (equal); writing – review and editing (equal). **So Shan Ng:** Data curation (equal); writing – review and editing (equal). **Terry Cheuk Fung Yip:** Conceptualization (equal); data curation (equal); formal analysis (equal); writing – review and editing (equal). **Grace Lai Hung Wong:** Conceptualization (equal); data curation (equal); methodology

(equal); writing – review and editing (equal). **Ka Pang Chan:** Data curation (equal); writing – review and editing (equal). **Tat On Chan:** Formal analysis (equal); writing – review and editing (equal). **David Shu Cheong Hui:** Conceptualization (equal); methodology (equal); project administration (equal); writing – original draft (equal); writing – review and editing (equal).

## CONFLICT OF INTEREST

None declared.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## HUMAN ETHICS APPROVAL DECLARATION


This study received approval by the Joint Chinese University of Hong Kong–New Territories East Cluster Clinical Research Ethics Committee (CREC reference no. 2020.276). No individual patient consent was required for this study as data were obtained from health databases without the identifications of individual patients.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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