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Invasive pneumococcal disease, pneumococcal pneumonia and all-cause pneumonia during COVID-19 in Hong Kong – a retrospective observational study

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3 1 **Title: Invasive pneumococcal disease, pneumococcal pneumonia and all-cause**
4 2 **pneumonia during COVID-19 in Hong Kong – a retrospective observational**
5 3 **study**
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3 26 **Abstract**

4
5 27 **Objectives:** To compare the incidence and severity of invasive pneumococcal
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7 28 diseases (IPD), pneumococcal pneumonia and pneumonia during COVID-19 period
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9 29 with widely practiced of universal masking and social distancing to that of previous 5
10
11 30 years.

12
13 31 **Design:** Retrospective observational study on incidence of invasive pneumococcal
14
15 32 diseases (IPD), pneumococcal pneumonia and all-cause pneumonia between Period
16
17 33 1 (January 2015-December 2019) and period 3 (March 2020-March 2021).

18
19 34 **Setting:** Episode-based data by retrieval of hospitalization records from the Hospital
20
21 35 Authority's territory-wide electronic medical record database.

22
23 36 **Participants:** Hospitalized patients with invasive pneumococcal diseases (IPD)
24
25 37 (n=742), pneumococcal pneumonia (n=2163) and all-cause pneumonia (n=453,999)
26
27 38 at age 18 or above. Control diagnoses were included to assess confounding from
28
29 39 health-seeking behaviors

30
31 40 **Interventions:** Period 3 with widely practiced of universal masking

32
33 41 **Primary and secondary outcome:** Primary outcome is the incidence of diseases
34
35 42 between two periods. Secondary outcomes include disease severity surrogated by
36
37 43 length of stay and mortality.

38
39 44 **Results:** Monthly average number of IPD, pneumococcal pneumonia and all-cause
40
41 45 pneumonia hospitalization significantly decreased by 88.9%, 72.5% and 17.5%
42
43 46 (p<0.0005). Change in trend from period 1 to period 3 was -70% (p=0.0025), -43%
44
45 47 (p=0.0014) and -11% (p<0.0005). LOS for IPD and pneumococcal pneumonia
46
47 48 episodes were insignificantly different in the two periods while that for all-cause
48
49 49 pneumonia had a slight decrease from 11.7 days to 10.8 days (p<0.005). No
50
51 50 reductions in control diagnoses were observed.

51
52 51 **Conclusions:** Incidence of IPD, pneumococcal pneumonia, and all-cause pneumonia
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54 52 decreased during COVID-19 pandemic. This was observed with universal masking
55
56 53 and social distancing. We proposed this is related to reduce transmission of respiratory
57
58 54 viruses and bacteria.

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3 56 **Strength and limitations of this study:**
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- 5 57 • A territory-wide study with near 100% practice of universal masking
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7 58 • Other factors including temperature and air quality were also included in
8
9 59 our analysis
10
11 60 • Disease severity of IPD, pneumococcal pneumonia, and all-cause
12
13 61 pneumonia were compared between the two periods
14
15 62 • Data from private sector (<10%) were not included in our study
16
17 63 • The causal relationship cannot be ascertained from this retrospective
18
19 64 study
20

21 66 This research received no specific grant from any funding agency in the public,
22
23 67 commercial or not-for-profit sectors.
24

25
26 69 There are no competing interests.
27
28 70

29 71 **Authors' contributions:**

30
31 72 **King-Pui Florence Chan and Ting-Fung Ma** were involved in study concept and
32
33 73 design; acquisition, analysis and interpretation of data; drafting the work and final
34
35 74 approval of the manuscript. **Mary Sau-Man Ip** were involved in critical revision of
36
37 75 manuscript for important intellectual content and final approval of the manuscript. **Pak-**
38
39 76 **Leung Ho** was involved in study concept and design; analysis and interpretation of
40
41 77 data; drafting of manuscript; critical revision of the manuscript for important intellectual
42
43 78 content; study supervision; and approval of the final version of the manuscript.
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49 81 **Keywords:** pneumococcal, COVID-19, masking, regression analysis
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51 82

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3 83 **Text**
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5
6 84 **Introduction**
7

8 85 Coronavirus disease 2019 (COVID-19) due to severe acute respiratory syndrome
9 86 coronavirus 2 (SARS-CoV-2) infections was first reported in late 2019 [1]. It became
10 87 a global pandemic and was declared as a public health emergency of international
11 88 concern on 30 January 2020 by the World Health Organization [2]. As of 21st June
12 89 2021, more than 178 million people were infected, causing more than 3.8 million
13 90 deaths globally.

14
15 91 Pneumococcal disease is caused by *Streptococcus pneumoniae* infection, with at
16 92 least 100 known serotypes of pneumococci [3]. Pneumococcal disease can be roughly
17 93 divided into non-invasive disease and invasive disease. Non-invasive disease
18 94 includes sinusitis, acute otitis media and pneumonia. Invasive pneumococcal disease
19 95 (IPD) is defined as isolation of *Streptococcus pneumoniae* from a normally sterile sites,
20 96 including blood and cerebrospinal fluid [4]. IPD is a notifiable disease in Hong Kong
21 97 since 9th January 2015. Pneumococcal infection is a major cause of morbidity and
22 98 mortality worldwide [5], with 1.6 million estimated deaths annually in 2005 [6].
23 99 Incidence of IPD and mortality of pneumococcal pneumonia are higher in extremes of
24 100 age [7-8].

25
26 101 The first pneumococcal conjugated vaccine (PCV), Prevnar 7 (PCV7) was
27 102 introduced to United States in 2000 and incorporated in Hong Kong Childhood
28 103 Immunisation Programme for children under 2 years old since September 2009. In
29 104 Hong Kong, PCV7 was replaced by the 10-valent and 13-valent pneumococcal
30 105 conjugate vaccines (PCV10 and PCV13) in 2010 and 2011 respectively [9-10].
31 106 PCV13 was effective in preventing vaccine-type pneumococcal pneumonia,
32 107 bacteraemia and nonbacteraemic community-acquired pneumonia [11]. Decline in
33 108 incidences of all-cause pneumonia in children and elderly was reported after
34 109 implementation of PCV in childhood vaccination program [12-13]. 23-valent
35 110 polysaccharide vaccine (PPSV23) was effective in preventing pneumococcal
36 111 pneumonia and reducing mortality from pneumococcal pneumonia in nursing home
37 112 residents [14]. Pneumonia is a common disease causing hospitalization, accounting
38 113 for 2.9% of all inpatient discharges and death in Hong Kong [15]. It is the second
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3 114 leading cause of death with age specific death rates increased markedly after age 65
4 [16].
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8 117 Whether patients with COVID-19 are more susceptible to pneumococcal
9
10 118 superinfection is still under debate. Superinfection of pneumococcal in COVID-19
11
12 119 patients was reported [17]. Yet, low frequency of bacterial coinfection in patients with
13
14 120 early COVID-19 was also observed [18-19]. There is limited evidence on the
15
16 121 incidence and severity of IPD, pneumococcal pneumonia, and all-cause pneumonia
17
18 122 during COVID-19 pandemic, especially in area where universal masking and social
19
20 123 distancing were widely practiced. Since January 2020, universal masking in public
21
22 124 area was voluntarily performed by Hong Kong citizens against infection by COVID-
23
24 125 19. Cross sectional telephone self-reported surveys by the Hong Kong Public
25
26 126 Opinion Research Institute (HKPORI). Percentage of wearing mask was 74.5% on
27
28 127 20th-23rd January 2020 (n=1,008), 97.6% on 5th-20th February (n=10,405) and
29
30 128 98.9% on 4th-19th March (n=15,739) [20]. On 23rd July 2020, masking was
31
32 129 mandatory in public area upon the introduction of Prevention and Control of Disease
33
34 130 (Wearing of Mask) Regulation (Cap. 599I). Social distancing measurements were
35
36 131 voluntarily practiced by public and implemented by government since 25th January
37
38 132 2020. These public health interventions were shown to associated with relatively low
39
40 133 rate of COVID-19 and early termination of influenza season in Hong Kong [21]. Our
41
42 134 previous studies suggested universal masking and social distancing were associated
43
44 135 with significant reduction in acute exacerbation of chronic obstructive pulmonary
45
46 136 disease and asthma in Hong Kong [22,23]. In the current study, we hypothesized
47
48 137 that the aforementioned COVID-19 related public health interventions and reduction
49
50 138 in respiratory virus activities would be associated with reduction in hospitalization
51
52 139 due to pneumococcal infections and pneumonia in general.
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141 **Materials and Methods**

142 A retrospective study assessing the numbers of IPD, pneumococcal pneumonia, and
143 all-cause pneumonia which required hospital hospitalization during the period of
144 COVID-19 in Hong Kong, comparing with that in the preceding five years as
145 baseline. The study period was 1st January 2015 to 31st March 2021 with exclusion
146 of 1st January 2020 to 28th February 2020 from analysis, when universal masking
147 was not yet completely executed.

149 **Data source**

150 Episode-based data was obtained by retrieval of hospitalization records from the
151 Hospital Authority's territory-wide electronic medical record database, Clinical Data
152 Analysis and Reporting System (CDARS), which provides 90% of in-patient hospital
153 care service in Hong Kong [22,23].

154
155 Diagnosis code of pneumococcal pneumonia (ICD-9 code 481) was searched on
156 CDARS. IPD is a notifiable disease since January 2015 with monthly number notified
157 cases and age obtained from the Department of Health, HKSAR. Monthly number of
158 influenza virus detection was collected from a territory-wide laboratory surveillance
159 for both in-patients and out-patients in both public and private medical sectors from
160 the Centre for Health Protection, HKSAR [15].

161
162 All-cause pneumonia including the following ICD-9 codes for viral, bacterial,
163 tuberculous, fungal and unspecified pneumonia, pneumonia due to inhalation of food
164 or vomitus and lung abscess were obtained from CDARS (ICD-9 code 003.22,
165 055.1, 0.1160-1.1166, 112.4, 115, 117.3, 480, 481, 482, 483.1, 483.8, 485, 486,
166 487, 507.0, 513).

168 **Patient and public involvement**

169 This observational study based on the practice of universal masking by Hong Kong
170 citizens to prevent COVID-19 infections and its relationship with hospital admissions
171 of various diseases, particularly on the infectious disease aided in the development
172 of the research question. Patients who were admitted with the diagnosis of IPD,
173 pneumococcal pneumonia, pneumonia, acute kidney injury fracture hip and

1
2
3 174 peritonitis due to peritoneal dialysis were included in the study. Demographics data
4
5 175 (including sex, age), clinical data (including hospitalization date, length of stay,
6
7 176 episode death, date of death) were collected. The results including admission
8
9 177 number of various diseases were available in the CHP website and the Hospital
10 178 Authority Statistics Report [16].
11

12 179

13 180 ***Inclusion/ exclusion criteria***

14
15 181 Patients with 1) age 18 or above 2) hospitalization for the listed diseases
16
17 182 (pneumococcal pneumonia, IPD and pneumonia) were included in the study.
18

19 183

20 184 Children at aged 0 to 17 years old were excluded in this study. Duplicated record of
21
22 185 single patient with different diagnoses in same hospital admission were removed.
23

24 186

25 187 ***Other diagnoses***

26
27 188 Number of hospitalization for other common medical and surgical conditions including
28
29 189 acute kidney injury (ICD-9 code 580, 584), fracture hip (ICD-9 code 820) and peritonitis
30
31 190 due to peritoneal dialysis (PD peritonitis) (ICD-9 code 996.68) were collected. These
32
33 191 were included to evaluate the possibility of decrease in hospital attendance due to
34
35 192 various reasons such as fear of COVID-19 infection in hospital.
36

37 193

38 194 ***Other variables***

39 195 Monthly mean ambient temperature was obtained from the Hong Kong Observatory
40
41 196 [24]. Air quality was measured by air quality health index (AQHI), which is calculated
42
43 197 based on the cumulative health risk attributable to a 3-hour moving average
44
45 198 concentrations of ozone, nitrogen dioxide, sulphur dioxide and particulate matter [25].
46
47 199 It was reported in scale of 1 to 10 and 10+ and grouped into five health risk categories,
48
49 200 namely low [1-3], moderate [4-6], high [7], very high [8-10] and serious [10+] with
50
51 201 different precautionary actions were advised. People with respiratory illness were
52
53 202 advised to minimize their outdoor stay when AQHI high to serious. The AQHI was
54
55 203 reported hourly in 13 stations located in different area of Hong Kong. The total number
56
57 204 of hours with AQHI recorded as high to serious grades were expressed as percentage
58
59 205 of total number of hours collected in a month.
60

206

207 ***Statistical method***

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3 208 Total number of hospitalizations due to IPD, pneumococcal pneumonia and all-cause
4 pneumonia were collected and analysed. Each disease was further divided into three
5 209 different age groups, including 18 to 49 years, 50 to 64 years, and 65 years or above
6 210 for analysis.
7 211
8 212

9 213 Analysis was done on the number of hospitalizations between January 2015 to
10 214 December 2019, the period prior COVID-19 (period 1) and March 2020 to March
11 215 2021 (period 3), while January to February 2020 (period 2) was treated as transition
12 216 period and excluded from the analysis. Wilcoxon rank sum test was first used to
13 217 analyse the statistical significance of number of hospitalizations between period 1
14 218 and period 3. Generalized linear models were then applied for statistical inference of
15 219 various types of responses. Log-linear model was used for studying the effect of
16 220 pandemic as intervention under segmented regression framework in term of the
17 221 change in trend (i.e. an increase or decrease in the level of the segment) between
18 222 period 1 (pre-intervention segment) and period 3 (post-intervention segment) on the
19 223 monthly hospitalization count [26]. Temporal effect was adjusted by covariates,
20 224 including AQHI, temperature and effect of masking.
21 225

22 226 Generalized linear model was used for comparing the mortality rate of individuals
23 227 between the two time periods [27]. Hospitalization length of stay (LOS) was
24 228 described in days using mean and standard deviation. Statistical inference of the
25 229 LOS in hospitalization of individuals was done by Wilcoxon rank sum test with odds
26 230 ratio and relative risks and confidence intervals calculated [26].
27 231

28 232 Monthly incidence rate for each disease was calculated using the total population
29 233 followed by age groups stratification (18 to 49 years, 50 to 64 years and ≥ 65 years)
30 234 and expressed as number per 100,000 person-year. Age-specific population data
31 235 was obtained from the Census and Statistics Department.
32 236

33 237 ***Ethics Approval***

34 238 The study was approved by the Institutional Review Board of the University of Hong
35 239 Kong/ Hospital Authority Hong Kong West Cluster (Reference Number UW-21-325).
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241 Results

242 *Invasive pneumococcal disease*

243 The total number of notified IPD episodes was 742 in the entire study, with 699
244 reported in period 1 and 17 reported in period 3. Pneumococcal serotypes for 684 of
245 the 699 episodes in period 1, and 13 of the 17 episodes in period 3m were
246 successfully determined. The proportions attributed to PCV13 serotypes was 66.5%
247 (465/699) and 29.4% (5/17) respectively for period 1 and period 3. Serotype 3 was
248 the commonest serotype in both periods, accounting for 41.3% (289/699) and 17.6%
249 (3/17) of total, respectively. From period 1 to period 3, the monthly number of IPD
250 caused by PCV13 serotypes declined by 95.1% (95%CI 93.4%-96.4%) while those
251 for non-PCV13 serotypes declined by 83.0% (95%CI 78.8%-86.5%).

252
253 Monthly number of IPD peaked in January-February each year except in 2016, with
254 the peak in April (Figure 1A). Monthly average number of notified IPD episodes was
255 11.7 ± 6.2 in period 1, with significant decrease to 1 ± 4.3 in period 3 ($p < 0.0005$). By
256 log-linear model segmented regression, relative risk of IPD in period 3 was 0.85
257 (95%CI 0.75-0.96, $p = 0.0089$) (Table S1). Further analysis on the relative risk of
258 different age groups showed significant decline in relative risk of IPD in aged ≥ 65
259 years (0.78, 95%CI 0.61-0.99, $p = 0.041$). Estimated change in trend in the mean
260 number of cases from period 1 to period 3 was -70% (95%CI -87% to -35%,
261 $p = 0.0025$) (Figure 1A, Table S1).

262
263 Incidence rate per 100,000 person-years was 2.2 in period 1 and 0.2 in period 3, with
264 an interval reduction of 88.9% (95%CI 79.8%-98.0%, $p < 0.0005$) (Table 1). IPD is
265 most prevalent in age ≥ 65 . The magnitude of reduction in incidence rate was similar
266 across different age groups, ranging from 81.3% to 93.5% ($p < 0.0005$ for all age
267 groups) (Table 1).

268
269 The overall LOS for IPD was 18.8 ± 48.4 days in period 1 and 31.6 ± 79.2 days in
270 period 3 (Table 2), but the difference was statistically insignificant ($p = 0.89$).
271 Statistically insignificant variations in LOS of different age groups were observed.

272

273

274 ***Pneumococcal pneumonia***

275 In the entire study period, there were 2,163 episodes of hospitalization for
276 pneumococcal pneumonia, with 1970 episodes in period 1 and 119 episodes in
277 period 3 (Table 1). Monthly number of pneumococcal pneumonia was peaked in
278 January-February each year except in 2016, with the peak in April (Figure 1B). The
279 average monthly hospitalizations was 32.8 ± 9.9 episodes in period 1, with significant
280 drop to 9.2 ± 3.9 episodes in period 3 ($p < 0.0005$). By log-linear model segmented
281 regression, relative risk of pneumococcal pneumonia was 0.90 (95%CI 0.86-0.95,
282 $p < 0.005$) in period 3. Trend analysis revealed a change of -43% (95%CI -59% to -
283 19%, $p = 0.0014$, Figure 1B, Table S1) from period 1 to period 3. Age groups analysis
284 showed similar change in trend for all age groups, with statistical significance in
285 aged ≥ 65 years (-41%, 95%CI -61% to -12%, $p = 0.010$) from period 1 to period 3
286 (Table S1, Figure S1).

287
288 Overall, the incidence rate of hospitalization for pneumococcal pneumonia
289 decreased significantly by 72.5% (95%CI 65.9%-79.1%, $p < 0.0005$), from 6.2 per
290 100,000 person-years in period 1 to 1.7 per 100,000 person-years in period 3 (Table
291 1). Incidence rate per 100,000 person year showed statistically significant reduction
292 in all age groups, ranging from 73.0% to 82.5%.

293
294 The overall LOS for pneumococcal pneumonia in period 1 and period 3 was
295 17.7 ± 27.5 days and 19.5 ± 26.3 days in all age group ($p = 0.051$) (Table 2). Age group
296 stratification showed insignificant decrease in length of stay in those aged 18-49
297 years ($p = 0.8051$) and aged ≥ 65 years ($p = 0.226$). Increase in length of stay from
298 18.8 ± 32.6 days to 31.7 ± 48.1 days was observed in age group 50-64 years, and was
299 statistically significant ($p = 0.019$). Mortality rate for all ages was 13.1 (95% CI 11.7%-
300 14.8%) in period 1 and 22.7 (95%CI 15.5%-31.3%) in period 3 ($p = 0.0187$). Mortality
301 rate was only statistically significant in aged 50-64 years ($p = 0.0007$) but not in aged
302 18-49 years ($p = 0.9917$) and aged ≥ 65 years ($p = 0.246$)(Table 2).

305 ***All-cause pneumonia***

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3 306 In the entire study period, total hospitalization episodes for all-cause pneumonia was
4
5 307 453,999, of which 372,660 episodes in period 1 and 67,474 episodes in period 3.
6
7 308 Monthly number of all-cause pneumonia peaked in January to March each year
8
9 309 (Figure 1C). Mean monthly number of hospitalizations for all-cause pneumonia
10
11 310 declined by 16.4% (95%CI 15.7%-17.1%, $p<0.0005$) from 6211 ± 845.0 episodes in
12
13 311 period 1 to 5190.3 ± 593.8 episodes in period 3 ($p<0.0005$) (Figure 1C). Estimated
14
15 312 change in trend in the mean number of cases in period 3 was -11% (95%CI -13% to
16
17 313 -10%, $p<0.0005$). By log-linear model segmented regression, relative risk of all-
18
19 314 cause pneumonia in period 3 compared with period 1 was 0.98 (95%CI 0.98-0.99,
20
21 315 $p<0.0005$) (Table S1).
22
23 316

24
25 317 Overall, the incidence rate per 100,000 person-years was 1,169.7 in period 1, with
26
27 318 17.5% (95%CI 16.8%-18.2%, $p<0.0005$) reduction in period 3 to 964.5 per 100,000
28
29 319 person-years in period 3 (Table 1). The incidence rate decrease in period 3
30
31 320 compared to period 1 in all age groups.

32
33 321 The overall LOS for all-cause pneumonia episodes was 11.7 ± 31.7 days in period 1
34
35 322 and 10.8 ± 15.0 days in period 3 ($p<0.005$) (Table 2). Different age groups showed
36
37 323 decrease in LOS but were only statistically significant in age 18-49 years and 50-64
38
39 324 years. The mortality rate increased from 20.5% (95% CI 20.4%-20.6%) in period 1 to
40
41 325 24.2% (95%CI 24.9%-25.6%) in period 3 ($p<0.005$) for all-cause pneumonia. The
42
43 326 increase in mortality rate was statistically significant in all age groups (Table 2).
44
45 327

46 328

47 329 **Influenza**

48
49 330 The total number of influenza A or B viruses detected from January 2015 to March
50
51 331 2021 in Hong Kong was 123,732. The monthly number of influenza detections
52
53 332 decreased drastically by 99.5% (95%CI 99.4%-99.5%, $p<0.0005$) from $1,966\pm 2179$ in
54
55 333 period 1 to 10 ± 18 in period 3 (Figure 1D). The monthly average number of respiratory
56
57 334 specimens tested was 4313 ± 1172 in period 1 and 3203 ± 1868 in period 3.

58
59 335 By log-linear model segmented regression, relative risk of influenza was 0.92 (95%CI
60
336 0.88-0.95, $p<0.0005$). Estimated change in trend in the mean number of detections in
337
338 337 period 3 was -99.0% (95%CI -99.3% to -98.7%, $p<0.0005$) of that in period 1 (Figure
1D)

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3 3394
5 3406
7 341 ***Other diagnosis: acute kidney injury, PD peritonitis and fracture hip***8
9 342 The monthly average number of hospitalization episodes for acute kidney injury in10
11 343 period 1 and period 3 was 807.8 ± 87.5 and 911.7 ± 62.6 , respectively ($p < 0.0005$)12
13 344 (Figure 2) The monthly average number of hospitalization episodes for PD peritonitis14
15 345 was 246.7 ± 27.7 in period 1 and 255.9 ± 31.9 in period 3 ($p = 0.23$). The monthly16
17 346 average number of hospitalization episodes for fracture hip was 432.9 ± 53.1 in period18
19 347 1 and 417.3 ± 51.6 in period 3 ($p = 0.37$)
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349 Discussion

350

351 Hong Kong is a city with population of 7.5 million where universal masking and social
352 distancing were widely practiced during the COVID-19 pandemic period. This study
353 showed a drastic decrease in numbers of hospitalization for IPD and pneumococcal
354 pneumonia and a lesser but still very significant decrease in all cause pneumonia
355 after anti-COVID-19 measures in March 2020 to March 2021.

356

357 During COVID-19 period, decrease in incidence of IPD were observed in Taiwan and
358 Singapore [28-29]. The decrease in IPD in Hong Kong was greater magnitude
359 compare to other countries [30]. Our study added new information on the incidence
360 and severity of IPD, pneumococcal pneumonia and all-cause pneumonia in terms of
361 age-stratification.

362

363 Introduction of the current pneumococcal conjugate vaccines has been highly
364 successful in reducing the incidence of pneumococcal diseases worldwide [31, 32].
365 Vaccine efficacy of PCV13 against vaccine type IPD in children aged ≤ 5 years was
366 86%-96% [33]. In adults aged ≥ 65 years, the vaccine efficacy against vaccine type
367 IPD was reported as 75% and against vaccine type community-acquired pneumonia
368 were reported as 45.6% and 72.8% respectively [11, 34]. In contrast, PPV23 only
369 has vaccine efficacy of 24% against vaccine type community acquired pneumonia in
370 aged ≥ 65 years [35]. In Hong Kong, a marked reduction in vaccine type IPD was
371 observed in children few years after implementation of PCV in 2009. However, the
372 indirect effect on adult IPD was not evident. Annual number of adult IPD
373 hospitalization remains static in period 1 (Figure 1A). Universal masking in Hong
374 Kong was shown to decrease the incidence of SARS-CoV2 [36-37] and influenza
375 [38] during the COVID-19 pandemic. Our study showed 88.9% reduction in incidence
376 of adult IPD. The drastic decrease in incidence of IPD included both vaccine and
377 non-vaccine types and was comparable and greater than the reported figure after
378 introduction of pneumococcal vaccines [11,32]. IPD can lead to significant mortality
379 and morbidity [39]. Our study showed decrease in incidence and trend of IPD and
380 were statistically significant. The decrease in mortality of IPD during the COVID-19
381 pandemics was statistically insignificant, which can be contributed by the relative
382 small sample size.

383

384 The incidence of all-cause pneumonia showed a much lower magnitude of decrease
385 with the lesser decrease observed in those aged ≥ 65 years (supplementary file,
386 Figure S1C). This can be explained by subgroup of pneumonia due to inhalation of
387 food or vomitus, i.e. aspiration pneumonia and is more prevalent in age group 65
388 years old or above. The population of Hong Kong has been seeing an aging trend
389 and the population of 65 years old or above was 1,114,600 in 2015, and increased to
390 1,371,800 in 2020. In our study, the lesser decrease in incidence of all-cause
391 pneumonia in 2019 – 2020 was observed in those aged 65 years or above,
392 suggesting that the magnitude of decrease in all-cause pneumonia may be limited by
393 any potential increase in aspiration pneumonia in the expanding number of elderly
394 people. Secondly, the risk of aspiration pneumonia would not be affected by
395 measures of universal masking or social distancing, thus reducing their protective
396 effect on all-cause pneumonia.

397

398 Pneumococcal pneumonia and IPD are debilitating diseases which have been
399 shown to require long length of hospital stay and high hospital cost [40-41]. The LOS
400 in pneumococcal pneumonia was slightly increased from 17.7 to 19.5 days but was
401 statistically insignificant. Looking into different age groups, only patients with age 50
402 to 64 years old showed statistically significant increase in LOS, while patients in age
403 group 18 to 49 years old and 65 years old or above showed slight decrease. The
404 severity of pneumococcal pneumonia can be comparable in the two periods.

405

406 Health seeking behaviour was also evaluated in our study. Admissions of non-
407 communicable diseases revealed either statistically insignificant decrease in hospital
408 attendance or statistically significant increase in hospital attendance. Our study
409 covered more than one year time for COVID-19 pandemics with a relatively stable
410 number of hospital attendance. Hence, the decrease in incidence of pneumococcal
411 pneumonia, IPD and all-cause pneumonia cannot be explained by health seeking
412 behaviour alone.

413

414 Collateral damages were observed during the COVID-19 pandemic [42-43], some of
415 which were contributed by the decrease in general medical services to concentrate
416 healthcare resources for the care of SARS-CoV-2 patients and the prevention of

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3 417 possible viral spread. However, due to the relatively small number of COVID-19
4 cases in Hong Kong, provision of acute medical services was minimally disrupted. In
5 418 our study, the data on admissions for fractures, acute kidney injury and PD peritonitis
6 419 showed no decrease during the Covid pandemic. Hence the observed decrease in
7 420 hospital admissions for pneumococcal pneumonia, IPD and all-cause pneumonia
8 421 should not be artefactual. Masking can be an effective yet low-cost preventive
9 422 measurement for citizens at high risk of pneumococcal infections.
10 423
11 424
12 425

13 426 **Limitations**

14 427 This study is a retrospective observational study and the direct effect of universal
15 428 masking on pneumococcal pneumonia, IPD and all-cause pneumonia cannot be
16 429 ascertained. However, our study covered a period of more than one year when
17 430 universal masking was practiced and a consistent observation of decrease in
18 431 hospitalization for these diseases were seen. Other factors, namely ambient
19 432 temperature and AQHI, that might have possible effect on the hospitalization
20 433 numbers were also included in our analysis.
21 434

22 435 Our study focused on hospital hospitalization numbers to Hospital Authority. For IPD,
23 436 the incidence was obtained from Central of Health Protection, HKSAR, which
24 437 included data from both public and private hospitals data. The LOS and mortality
25 438 data of IPD were retrieved from the database in Hospital Authority. Admissions to
26 439 private hospital due to pneumococcal pneumonia and all-cause pneumonia were not
27 440 included in our study. However, Hospital Authority is the largest healthcare provider
28 441 in Hong Kong which provides 90% of in-patient services in Hong Kong [44]. Data
29 442 from Hospital Authority is representable for the general epidemiology of Hong Kong.
30 443

31 444 **Conclusions**

32 445 The incidence of pneumococcal pneumonia, IPD and all-cause pneumonia
33 446 decreased during COVID-19 pandemics compare to the data in previous five years.
34 447 This was observed with widely practice of universal masking and social distancing.
35 448 We propose the decrease is attributed to universal masking and social distancing
36 449 which reduced the transmission of bacteria or virus and related bacterial
37 450 superinfection.

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Table 1. Incidence and number per 100,000 person year of pneumococcal pneumonia, invasive pneumococcal disease (IPD) and pneumonia

Disease ^a	All ages		18-49 years		50-64 years		≥65 years	
	No. of episodes	Incidence rate per 100,000 person-years	No. of episodes	Incidence rate per 100,000 person-years	No. of episodes	Incidence rate per 100,000 person-years	No. of cases	Incidence rate per 100,000 person-years
IPD								
Period 1	699	2.2	125	0.7	195	2.2	379	6.2
Period 2	26	2.4	5	0.9	6	2.0	15	6.6
Period 3	17	0.2	3	0.08	8	0.4	6	0.4
% reduction ^b		88.9% (79.8%-98.0%) ^{***}		88.6% (66.8%-110.4%) ^{***}		81.3% (62.1%-100.4%) ^{***}		93.5% (82.2%-104.8%) ^{***}
Pneumococcal pneumonia								
Period 1	1,970	6.2	217	1.3	435	4.9	1,318	21.7
Period 2	74	6.9	11	2.0	14	4.7	49	32.4
Period 3	119	1.7	8	0.2	24	1.2	87	5.9
% reduction		72.5% (65.9%-79.1%) ^{***}		82.5% (64.5%-100.5%) ^{***}		74.8% (61.0%-88.6%) ^{***}		73.0% (65.2%-80.8%) ^{***}
All-cause pneumonia								
Period 1	372,660	1169.7	19,502	115.3	38,360	432.4	314,798	5177.1
Period 2	13,865	1288.2	843	153.6	1,448	484.6	11,574	5062.3
Period 3	67,474	964.5	2,473	69.3	6,181	318.3	58,820	3958.0
% reduction		17.5% (16.8%-18.2%) ^{***}		39.9% (37.1%-42.7%) ^{***}		26.4% (24.3%-28.5%) ^{***}		23.5% (22.8%-24.3%) ^{***}

^aPeriod 1, January 2015 to December 2019 (before covid-19); period 2, January 2020 to February 2020 (transition period); period 3 March 2020 to March 2021 (post-COVID-19).

^b Percentage reduction in period 3 relative to period 1 as the baseline

*p < 0.05 to 0.01, **p < 0.01 to 0.005, ***p < 0.005

Table 2. Mean length of stay and mortality rate of pneumococcal pneumonia, invasive pneumococcal disease (IPD) and pneumonia in the periods

	Mean length of stay (days)				Mortality rate (%)			
	All ages	18-49 years	50-64 years	≥65 years	All ages	18-49 years	50-64 years	≥65 years
IPD								
Period 1	18.8 ± 48.4	27.9 ± 102.8	17.7 ± 19.1	15.9 ± 18.9	12.1(8.8-16.1)	9.1(3.4-18.7)	8.4(3.7-15.9)	15.3(10.3-21.4)
Period 3	31.6 ± 79.2	6.3 ± 5.2	76.4 ± 140.3	14.1 ± 9.9	6.3(1.6-30.2)	0.0	0.0	14.3(3.6-57.9)
Pneumococcal Pneumonia								
Period 1	17.7 ± 27.5	16.9 ± 28.0	18.8 ± 32.6*	17.5 ± 25.6	13.1(11.7-14.8)*	4.2(1.9-7.7)	7.5(5.3-10.5)**	16.3(13.6-18.7)
Period 3	19.5 ± 26.3	13.6 ± 15.6	31.7 ± 48.1*	16.8 ± 16.6	22.7(15.5-31.3)*	0.0	29.2(12.6-51.1)**	23.0(14.6-33.2)
All-cause pneumonia								
Period 1	11.7 ± 31.7***	10.3 ± 42.5***	13.4 ± 45.1**	11.7 ± 28.9	20.5(20.4-20.6)***	5.3(4.9-5.6)*	13.0(11.4-12.0)***	22.4(22.2-22.4)***
Period 3	10.8 ± 15.0***	9.4 ± 16.5***	11.9 ± 20.1**	10.7 ± 14.3	24.2(24.9-25.6)***	6.8(5.9-7.9)*	16.1(5.2-17.0)***	27.0(26.6-27.3)***

*p <0.05 to 0.01, **p <0.01 to 0.005, ***p<0.005

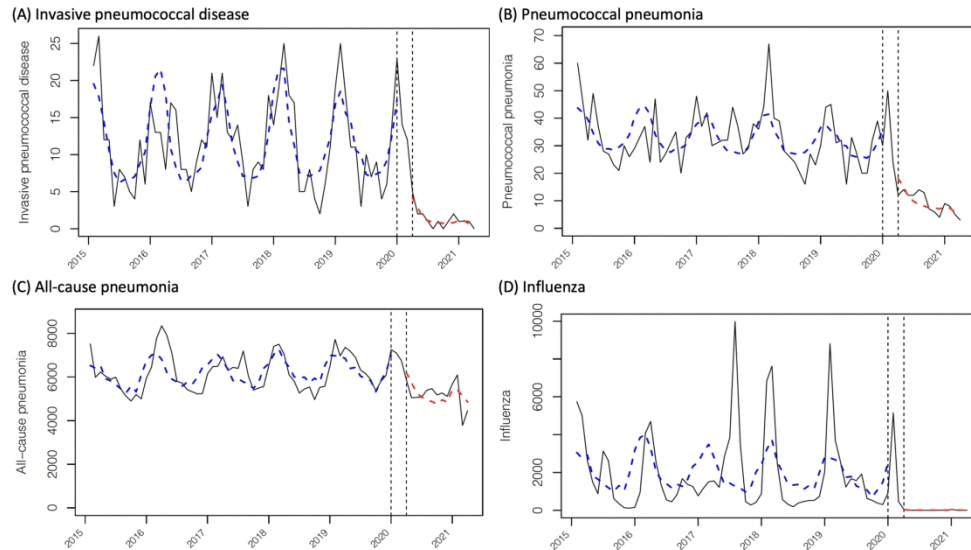


Figure 1. Trend analysis of monthly numbers of invasive pneumococcal disease (IPD), pneumococcal pneumonia, all-cause pneumonia, and influenza in Hong Kong, January 2015 to March 2021. Numbers of IPD were those obtained through mandatory notification. Numbers of pneumococcal pneumonia and all-cause pneumonia were territory-wide hospitalizations by discharge diagnoses. Numbers of influenza viruses were those detected in respiratory specimens in a territory-wide laboratory surveillance.

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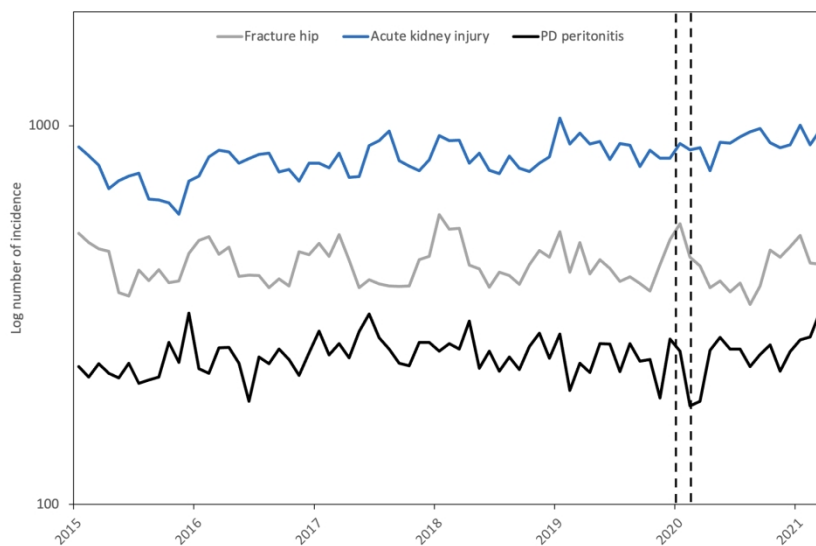


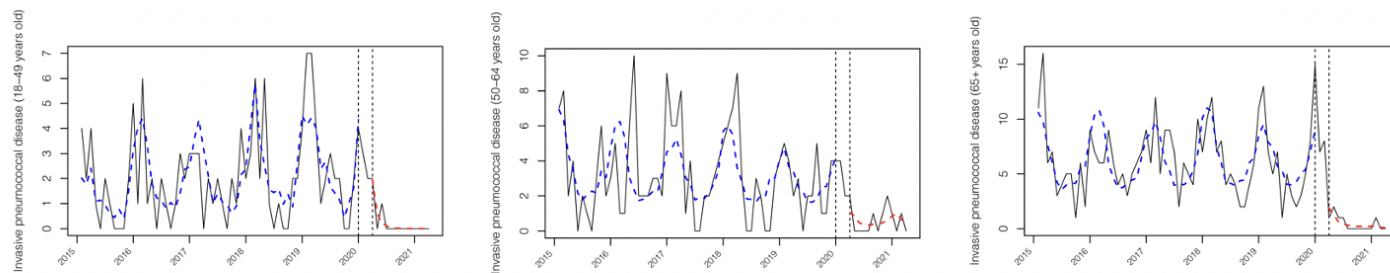
Figure 2. Admission numbers of fracture hip, acute kidney injury and PD peritonitis.

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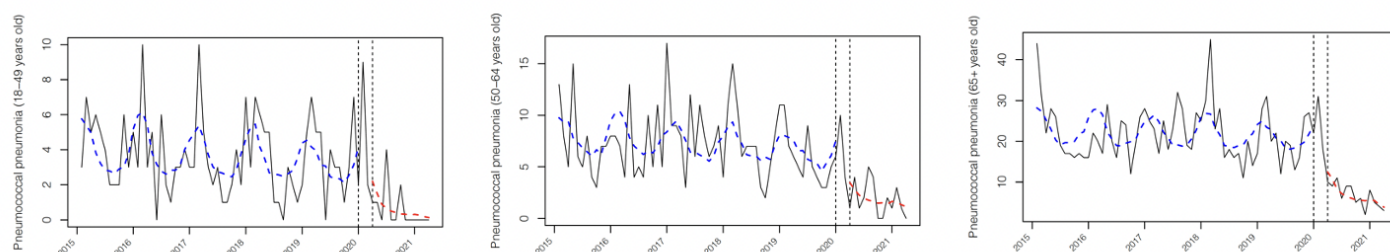
Supplementary file.

Figure S1. Trend analysis of monthly number of (A) age-stratified hospitalizations for invasive pneumococcal disease, (B) age-stratified hospitalizations for pneumococcal pneumonia, (C) age-stratified hospitalizations for and (D) monthly percentage of air quality health index (AQHI) high to serious and (E) monthly average ambient temperature.

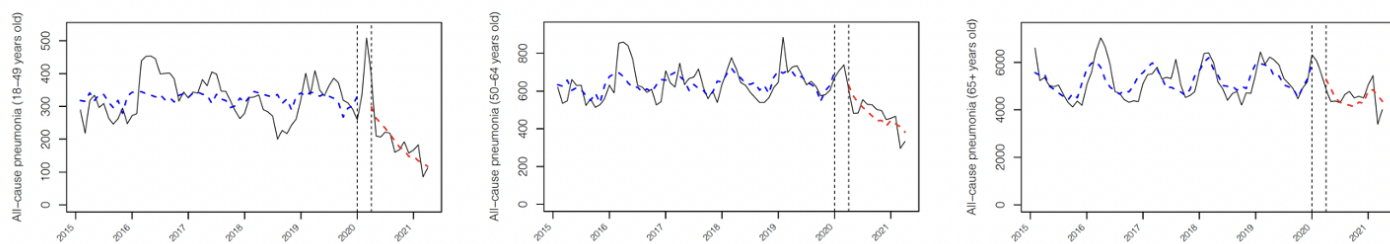
(A) Invasive pneumococcal disease



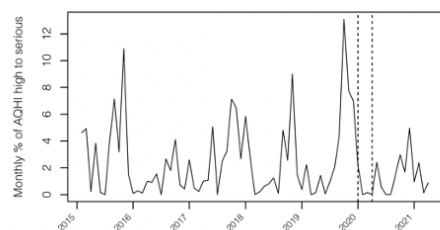
(B) Pneumococcal pneumonia



(C) All cause pneumonia



(D) Monthly % of AQHI high to serious



(E) Monthly average temperature

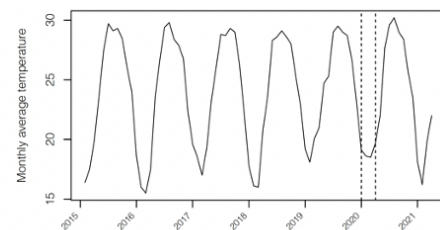


Table S1. Trend analysis of monthly number of hospitalization by age groups in periods before and after the COVID-19 pandemic

	Relative risk (95% CI)		Change in trend#
	Period 1 ^	Period 3^	
IPD			
All ages	1.0020 (0.9977-1.064)	0.8484 (0.7501-0.9597)**	-70.39% (-86.55% to -34.73%)**
18-49 years	1.0129 (1.0022-1.0238)	0.5272 (0.2176-1.2772)	-31.27% (-89.72% to 359.72%)
50-64 years	0.9969 (0.9888-1.0051)	0.9585 (0.8087-1.1362)	-70.43% (-92.80% to 21.42%)
65 years or above	1.0012 (0.9953-1.0071)	0.7777 (0.6111-0.9897)*	-70.83% (-91.59% to 1.12%)
Pneumococcal Pneumonia			
All ages	0.9978(0.9953-1.0004)	0.9042(0.8621-0.9483)***	-42.79% (-59.36% to -19.48%)*
18-49 years	0.9964(0.9887-1.0042)	0.6768(0.2171-2.1093)	-32.32% (-78.29% to 110.93%)
50-64 years	0.9962(0.9907-1.0017)	0.9174(0.8260-1.0189)	-50.21% (-76.93% to 7.48%)
65 years or above	0.9986(0.9954-1.0017)	0.9107(0.8612-0.9640)*	-41.19% (-60.82% to -11.73%)*
All-cause pneumonia			
All ages	1.0014(1.0012-1.0016)***	0.9835(0.9815-0.9855)***	-11.24% (-12.76% to -9.7%)***
18-49 years	1.0000(0.9992-1.0008)	0.9263(0.9164-0.9364)***	-6.05% (-13.41% to 1.94%)
50-64 years	1.0015(1.0009-1.0021)***	0.9620(0.9556-0.9684)***	-9.32% (-14.14% to -4.22%)***
65 years or above	1.0011(1.0009-1.0013)***	0.9879(0.9858-0.9901)***	-13.30% (-12.94% to -9.64%)***

^Trend in period 1 (January 2015 to December 2019) and 3 (March 2020 to March 2021), the (relative risk expressed the month-to-month change in hospitalization numbers

#Estimate the change in trend in the mean monthly number of cases in period 3, compare with the monthly trend in period 1

*p <0.05 to 0.01, **p <0.01 to 0.005, ***p<0.005

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6,7
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	6,7
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	6,7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6,7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6,7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7,8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7,8
		(b) Describe any methods used to examine subgroups and interactions	7,8
		(c) Explain how missing data were addressed	N/A
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	7,8

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9-12
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9-12
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	9-12
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-12
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-12
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	13,14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	3

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Invasive pneumococcal disease, pneumococcal pneumonia and all-cause pneumonia in Hong Kong during the COVID-19 pandemic compared with the preceding 5 years: a retrospective observational study

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2
3 1 **Title: Invasive pneumococcal disease, pneumococcal pneumonia and all-cause**
4 2 **pneumonia in Hong Kong during the COVID-19 pandemic compared with the**
5 3 **preceding 5 years: a retrospective observational study**
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26 **Abstract**

27 **Objectives:** To compare the incidence and severity of invasive pneumococcal
28 diseases (IPD), pneumococcal pneumonia and all-cause pneumonia during COVID-
29 19 period with widely practiced of universal masking and social distancing to that of
30 previous 5 years.

31 **Design:** Retrospective observational study on incidence of invasive pneumococcal
32 diseases (IPD), pneumococcal pneumonia and all-cause pneumonia between January
33 2015-December 2019 and March 2020-March 2021. January-February 2020 was
34 excluded from analysis as it was treated as transitional period between normal time
35 and pandemic, where universal masking was not completely executed.

36 **Setting:** Episode-based data by retrieval of hospitalization records from the Hospital
37 Authority's territory-wide electronic medical record database in Hong Kong.

38 **Participants:** Hospitalized patients with invasive pneumococcal diseases (IPD)
39 (n=742), pneumococcal pneumonia (n=2163) and all-cause pneumonia (including
40 COVID-19 pneumonia, n=453,999) at age 18 or above. Control diagnoses were
41 included to assess confounding from health-seeking behaviors.

42 **Primary and secondary outcome:** Primary outcome is the incidence of diseases
43 between two periods. Secondary outcomes include disease severity surrogated by
44 length of stay and mortality.

45 **Results:** Monthly average number of IPD, pneumococcal pneumonia and all-cause
46 pneumonia hospitalization significantly decreased by 88.9% (95%CI 79.8%-98.0%,
47 $p<0.0005$), 72.5% (95%CI 65.9%-79.1%, $p<0.0005$) and 17.5% (95%CI 16.8%-18.2%,
48 $p<0.0005$). Change in trend from January 2015-December 2019 to March 2020-March
49 2021 was -70% (95%CI -87% to -35%, $p=0.0025$), -43% (95%CI -59% to -19%,
50 $p=0.0014$) and -11% (95%CI -13% to -10%, $p<0.0005$). LOS for IPD and
51 pneumococcal pneumonia episodes were insignificantly different in the two periods.
52 No reductions in control diagnoses were observed.

53 **Conclusions:** Incidence of IPD, pneumococcal pneumonia, and all-cause pneumonia
54 decreased during COVID-19 pandemic. This was observed with universal masking
55 and social distancing. We proposed this is related to reduce transmission of respiratory
56 viruses and bacteria.

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57 **Strength and limitations of this study:**

- 58 • A territory-wide study with near 100% practice of universal masking
59 • Other factors including temperature and air quality were also included in
60 our analysis
61 • Disease severity of IPD, pneumococcal pneumonia, and all-cause
62 pneumonia were compared between the two periods
63 • Data from private sector (<10%) were not included in our study
64 • The causal relationship cannot be ascertained from this retrospective
65 study
66

67 **Funding:** This research received no specific grant from any funding agency in the
68 public, commercial or not-for-profit sectors.
69

70 **Competing interests:** There are no competing interests.
71

72 **Data availability statements:** No additional data is available.
73

74 **Authors' contributions:**

75 **King-Pui Florence Chan and Ting-Fung Ma** were involved in study concept and
76 design; acquisition, analysis and interpretation of data; drafting the work and final
77 approval of the manuscript. **Mary Sau-Man Ip** were involved in critical revision of
78 manuscript for important intellectual content and final approval of the manuscript. **Pak-**
79 **Leung Ho** was involved in study concept and design; analysis and interpretation of
80 data; drafting of manuscript; critical revision of the manuscript for important intellectual
81 content; study supervision; and approval of the final version of the manuscript.
82

83 **Word count:** 3991

84 **Keywords:** pneumococcal, COVID-19, masking, regression analysis
85

1
2
3 86 **Text**
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5
6 87 **Introduction**
7

8 88 Coronavirus disease 2019 (COVID-19) due to severe acute respiratory syndrome
9 coronavirus 2 (SARS-CoV-2) infections was first reported in late 2019 [1]. It became
10 89 a global pandemic and was declared as a public health emergency of international
11 90 concern on 30 January 2020 by the World Health Organization [2]. As of 21st June
12 91 2021, more than 178 million people were infected, causing more than 3.8 million
13 92 deaths globally.
14 93

15 94 Pneumococcal disease is caused by *Streptococcus pneumoniae* infection, with at
16 95 least 100 known serotypes of pneumococci [3]. Pneumococcal disease can be
17 96 roughly divided into non-invasive disease and invasive disease. Non-invasive
18 97 disease includes sinusitis, acute otitis media and pneumonia. Invasive
19 98 pneumococcal disease (IPD) is defined as isolation of *Streptococcus pneumoniae*
20 99 from a normally sterile sites, including blood and cerebrospinal fluid [4]. IPD is a
21 100 notifiable disease in Hong Kong since 9th January 2015. Pneumococcal infection is
22 101 a major cause of morbidity and mortality worldwide [5], with 1.6 million estimated
23 102 deaths annually in 2005 [6]. Incidence of IPD and mortality of pneumococcal
24 103 pneumonia are higher in extremes of age [7-8].
25 26 27 28 29

30 104 The first pneumococcal conjugated vaccine (PCV), Prevnar 7 (PCV7) was
31 105 introduced to United States in 2000 and incorporated in Hong Kong Childhood
32 106 Immunisation Programme for children under 2 years old since September 2009 [9-
33 107 10]. In Hong Kong, PCV7 was replaced by the 10-valent and 13-valent
34 108 pneumococcal conjugate vaccines (PCV10 and PCV13) in 2010 and 2011
35 109 respectively [11-12]. PCV13 was effective in preventing vaccine-type pneumococcal
36 110 pneumonia, bacteraemia and nonbacteraemic community-acquired pneumonia [13].
37 111 Decline in incidences of all-cause pneumonia in children and elderly was reported
38 112 after implementation of PCV in childhood vaccination program [14-15]. 23-valent
39 113 polysaccharide vaccine (PPSV23) was effective in preventing pneumococcal
40 114 pneumonia and reducing mortality from pneumococcal pneumonia in nursing home
41 115 residents [16]. In our locality, elderly at age 65 years and above without high risk
42 116 conditions, namely immunodeficiency or chronic cardiac, pulmonary, liver or renal
43 117 disease, or diabetes mellitus were recommended to receive either a single dose of
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3 118 PCV13 or a single dose of PPSV23. Number of PPSV23 vaccine recipients at age
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5 119 65 years or above increased from 35,000 in year 2015/2016 to 81,700 in 2019/2020,
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7 120 reaching accumulative 45.5% of population in the age group vaccinated in
8
9 121 2019/2020 [17]. Pneumonia is a common disease causing hospitalization,
10
11 122 accounting for 2.9% of all inpatient discharges and death in Hong Kong [18]. It is the
12
13 123 second leading cause of death with age specific death rates increased markedly
14
15 124 after age 65 [17].
16

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17 126 Whether patients with COVID-19 are more susceptible to pneumococcal
18
19 127 superinfection is still under debate. Superinfection of pneumococcal in COVID-19
20
21 128 patients was reported [19]. Yet, low frequency of bacterial coinfection in patients with
22
23 129 early COVID-19 was also observed [20-21]. There is limited evidence on the
24
25 130 incidence and severity of IPD, pneumococcal pneumonia, and all-cause pneumonia
26
27 131 during COVID-19 pandemic, especially in area where universal masking and social
28
29 132 distancing were widely practiced. Since January 2020, universal masking in public
30
31 133 area was voluntarily performed by Hong Kong citizens against infection by COVID-
32
33 134 19. Cross sectional telephone self-reported surveys by the Hong Kong Public
34
35 135 Opinion Research Institute (HKPORI) showed percentage of wearing mask was
36
37 136 74.5% on 20th-23rd January 2020 (n=1,008), 97.6% on 5th-20th February
38
39 137 (n=10,405) and 98.9% on 4th-19th March (n=15,739) [22]. On 23rd July 2020,
40
41 138 masking was mandatory in public area upon the introduction of Prevention and
42
43 139 Control of Disease (Wearing of Mask) Regulation (Cap. 599I). Social distancing
44
45 140 measurements were voluntarily practiced by public and implemented by government
46
47 141 since 25th January 2020. These public health interventions were shown to
48
49 142 associated with relatively low rate of COVID-19 and early termination of influenza
50
51 143 season in Hong Kong [23]. Our previous studies suggested universal masking and
52
53 144 social distancing were associated with significant reduction in acute exacerbation of
54
55 145 chronic obstructive pulmonary disease and asthma in Hong Kong [24,25]. In the
56
57 146 current study, we hypothesized that the aforementioned COVID-19 related public
58
59 147 health interventions and reduction in respiratory virus activities would be associated
60
148 with reduction in hospitalization due to pneumococcal infections and pneumonia in
149 general.

151 **Materials and Methods**

152 A retrospective study assessing the numbers of IPD, pneumococcal pneumonia, and
153 all-cause pneumonia which required hospital hospitalization during the period of
154 COVID-19 in Hong Kong, comparing with that in the preceding five years as
155 baseline. The study period was 1st January 2015 to 31st March 2021 with exclusion
156 of 1st January 2020 to 28th February 2020 from analysis, when universal masking
157 was not yet completely executed.

159 **Data source**

160 Episode-based data was obtained by retrieval of hospitalization records from the
161 Hospital Authority's territory-wide electronic medical record database, Clinical Data
162 Analysis and Reporting System (CDARS), which provides 90% of in-patient hospital
163 care service in Hong Kong [24,25].

164
165 Diagnosis code of pneumococcal pneumonia (ICD-9 code 481) was searched on
166 CDARS. IPD is a notifiable disease since January 2015 with monthly number notified
167 cases and age obtained from the Department of Health, Hong Kong Special
168 Administrative Region (HKSAR). Monthly number of influenza virus detection was
169 collected from a territory-wide laboratory surveillance for both in-patients and out-
170 patients in both public and private medical sectors from the Centre for Health
171 Protection (CHP), HKSAR [17].

172
173 All-cause pneumonia including the following ICD-9 codes for viral, bacterial,
174 tuberculous, fungal and unspecified pneumonia, pneumonia due to inhalation of food
175 or vomitus and lung abscess were obtained from CDARS (ICD-9 code 003.22,
176 055.1, 0.1160-1.1166, 112.4, 115, 117.3, 480, 481, 482, 483.1, 483.8, 485, 486,
177 487, 507.0, 513). Patient with COVID-19 associated pneumonia was included in the
178 all-cause pneumonia dataset. The contribution of COVID-19 within all-cause
179 pneumonia was queried using ICD codes for COVID-19 disease (ICD-9 code 079.89,
180 480.8, 519.8). Demographics data (including sex, age), clinical data (including
181 hospitalization date, length of stay, episode death, date of death) were collected. The
182 results including admission number of various diseases were available in the CHP
183 website and the Hospital Authority Statistics Report [17,26].

184

Inclusion/ exclusion criteria

186 Patients with 1) age 18 or above 2) hospitalization for the listed diseases
187 (pneumococcal pneumonia, IPD and pneumonia) were included in the study.

188

189 Children at aged 0 to 17 years old were excluded in this study. Duplicated record of
190 single patient with different diagnoses in same hospital admission were removed.

191

Other diagnoses

193 Number of hospitalization for other common medical and surgical conditions including
194 acute kidney injury (ICD-9 code 580, 584), fracture hip (ICD-9 code 820) and peritonitis
195 due to peritoneal dialysis (PD peritonitis) (ICD-9 code 996.68) were collected. These
196 were included to evaluate the possibility of decrease in hospital attendance due to
197 various reasons such as fear of COVID-19 infection in hospital. These diseases were
198 selected as are non-communicable diseases and have minimal interactions with
199 environmental factors including mean ambient temperature and air-pollution.

200

Other variables

202 Monthly mean ambient temperature was obtained from the Hong Kong Observatory
203 [27]. Air quality was measured by air quality health index (AQHI), which is calculated
204 based on the cumulative health risk attributable to a 3-hour moving average
205 concentrations of ozone, nitrogen dioxide, sulphur dioxide and particulate matter [28].
206 It was reported in scale of 1 to 10 and 10+ and grouped into five health risk categories,
207 namely low [1-3], moderate [4-6], high [7], very high [8-10] and serious [10+] with
208 different precautionary actions were advised. People with respiratory illness were
209 advised to minimize their outdoor stay when AQHI high to serious. The AQHI was
210 reported hourly in 13 stations located in different area of Hong Kong. The total number
211 of hours with AQHI recorded as high to serious grades were expressed as percentage
212 of total number of hours collected in a month.

213

Statistical method

215 Total number of hospitalizations due to IPD, pneumococcal pneumonia and all-cause
216 pneumonia were collected and analysed. Each disease was further divided into three

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3 217 different age groups, including 18 to 49 years, 50 to 64 years, and 65 years or above
4
5 218 for analysis.

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8 220 Analysis was done on the number of hospitalizations between January 2015 to
9
10 221 December 2019, the period prior COVID-19 (period 1) and March 2020 to March
11
12 222 2021 (period 3), while January to February 2020 (period 2) was treated as transition
13
14 223 period and excluded from the analysis. Wilcoxon rank sum test was first used to
15
16 224 analyse the statistical significance of number of hospitalizations between period 1
17
18 225 and period 3. Generalized linear models were then applied for statistical inference of
19
20 226 various types of responses. Log-linear model was used for studying the effect of
21
22 227 pandemic as intervention under segmented regression framework in term of the
23
24 228 change in trend (i.e. an increase or decrease in the level of the segment) between
25
26 229 period 1 (pre-intervention segment) and period 3 (post-intervention segment) on the
27
28 230 monthly hospitalization count. Regression coefficients of log-linear model can be
29
30 231 interpreted as the effect due to pandemic by log-linear model [29]. Temporal effect
31
32 232 was adjusted by covariates, including AQHI, temperature and effect of masking.

33
34 233

35 234 Generalized linear model was used for comparing the mortality rate of individuals
36
37 235 between the two time periods [30]. Hospitalization length of stay (LOS) was
38
39 236 described in days using median and standard deviation. Statistical inference of the
40
41 237 LOS in hospitalization of individuals was done by Wilcoxon rank sum test with odds
42
43 238 ratio and relative risks and confidence intervals calculated [29].

44
45 239

46 240 Monthly incidence rate for each disease was calculated using the total population
47
48 241 followed by age groups stratification (18 to 49 years, 50 to 64 years and ≥ 65 years)
49
50 242 and expressed as number per 100,000 person-year. Age-specific population data
51
52 243 was obtained from the Census and Statistics Department.

53
54 244

55 245 ***Ethics Approval***

56 246 The study was approved by the Institutional Review Board of the University of Hong
57
58 247 Kong/ Hospital Authority Hong Kong West Cluster (Reference Number UW-21-325).

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60 248

61 249 ***Patient and public involvement***

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3 250 Patients or the public were not involved in the design, or conduct, or reporting, or
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5 251 dissemination plans of our research.
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For peer review only

253 **Results**

254 ***Invasive pneumococcal disease***

255 The total number of notified IPD episodes was 742 in the entire study, with 699
256 reported in period 1 and 17 reported in period 3. Pneumococcal serotypes for 684 of
257 the 699 episodes in period 1, and 13 of the 17 episodes in period 3 were
258 successfully determined. The proportions attributed to PCV13 serotypes was 66.5%
259 (465/699) and 29.4% (5/17) respectively for period 1 and period 3. Serotype 3 was
260 the commonest serotype in both periods, accounting for 41.3% (289/699) and 17.6%
261 (3/17) of total, respectively. From period 1 to period 3, the monthly number of IPD
262 caused by PCV13 serotypes declined by 95.1% (95%CI 93.4%-96.4%) while those
263 for non-PCV13 serotypes declined by 83.0% (95%CI 78.8%-86.5%), and those for
264 PPSV23 serotypes declined by 94.1% (95% CI 92.3%-95.5%). The small difference
265 between declines in PCV13 and PPSV23 serotypes was mainly attributed to
266 serotype 6A which was included in PCV13 but not in PPSV23.

267

268 Monthly number of IPD peaked in January-February each year except in 2016, with
269 the peak in April (Figure 1A and Figure S2). Monthly average number of notified IPD
270 episodes was 11.7 ± 6.2 in period 1, with significant decrease to 1 ± 4.3 in period 3
271 ($p < 0.0005$). By log-linear model segmented regression, relative risk of IPD in period
272 3 was 0.85 (95%CI 0.75-0.96, $p = 0.0089$) (Table S1). Further analysis on the relative
273 risk of different age groups showed significant decline in relative risk of IPD in aged
274 ≥ 65 years (0.78, 95%CI 0.61-0.99, $p = 0.041$). Estimated change in trend in the mean
275 number of cases from period 1 to period 3 was -70% (95%CI -87% to -35%,
276 $p = 0.0025$) (Figure 1A, Table S1).

277

278 Incidence rate per 100,000 person-years was 2.2 in period 1 and 0.2 in period 3, with
279 an interval reduction of 88.9% (95%CI 79.8%-98.0%, $p < 0.0005$). Incidence rate ratio
280 between period 1 and period 3 was 0.11 (95%CI 0.07-0.18, $p < 0.0005$) (Table 1). IPD
281 is most prevalent in age ≥ 65 . The magnitude of reduction in incidence rate was
282 similar across different age groups, ranging from 81.3% to 93.5% ($p < 0.0005$ for all
283 age groups) (Table 1).

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3 285 The overall median LOS for IPD was 12 (Interquartile range, IQR 16) days in period
4 286 1 and 12 (IQR 11) days in period 3 (Table 2), with statistically insignificant difference
5 287 (p=0.89). Statistically insignificant variations in LOS of different age groups were
6 288 observed.
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10 289

11 290 ***Pneumococcal pneumonia***

12 291 In the entire study period, there were 2,163 episodes of hospitalization for
13 292 pneumococcal pneumonia, with 1970 episodes in period 1 and 119 episodes in
14 293 period 3 (Table 1). Monthly number of pneumococcal pneumonia was peaked in
15 294 January-February each year except in 2016, with the peak in April (Figure 1B and
16 295 Figure S2). The average monthly hospitalizations was 32.8 ± 9.9 episodes in period 1,
17 296 with significant drop to 9.2 ± 3.9 episodes in period 3 ($p < 0.0005$). By log-linear model
18 297 segmented regression, relative risk of pneumococcal pneumonia was 0.90 (95%CI
19 298 0.86-0.95, $p < 0.005$) in period 3. Trend analysis revealed a change of -43% (95%CI -
20 299 59% to -19%, $p = 0.0014$, Figure 1B, Table S1) from period 1 to period 3. Age groups
21 300 analysis showed similar change in trend for all age groups, with statistically
22 301 significance in aged ≥ 65 years (-41%, 95%CI -61% to -12%, $p = 0.010$) from period 1
23 302 to period 3 (Table S1, Figure S1).
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36 304 Overall, the incidence rate of hospitalization for pneumococcal pneumonia
37 305 decreased significantly by 72.5% (95%CI 65.9%-79.1%, $p < 0.0005$), from 6.2 per
38 306 100,000 person-years in period 1 to 1.7 per 100,000 person-years in period 3.
39 307 Incidence rate ratio between period 1 and period 3 was 0.28 (95%CI 0.23-0.33,
40 308 $p < 0.0005$) (Table 1). Incidence rate per 100,000 person year showed statistically
41 309 significant reduction in all age groups, ranging from 73.0% to 82.5%.
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48 311 The overall median LOS for pneumococcal pneumonia in period 1 and period 3 was
49 312 9 (IQR 14) days and 12 (IQR 17) days in all age group ($p = 0.051$) (Table 2). Age
50 313 group stratification showed insignificant changes in length of stay in those aged 18-
51 314 49 years ($p = 0.8051$) and aged ≥ 65 years ($p = 0.226$). Increase in length of stay from 9
52 315 (IQR 15) days to 13 (IQR 20) days was observed in age group 50-64 years, and was
53 316 statistically significant ($p = 0.019$). Mortality rate for all ages was 13.1% (95% CI
54 317 11.7%-14.8%) in period 1 and 22.7% (95%CI 15.5%-31.3%) in period 3 ($p = 0.0187$).
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3 318 Mortality rate was only statistically significant in aged 50-64 years ($p=0.0007$) but not
4
5 319 in aged 18-49 years ($p=0.9917$) and aged ≥ 65 years ($p=0.246$) (Table 2).
6
7 320
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10 322 **All-cause pneumonia**

11 323 In the entire study period, total hospitalization episodes for all-cause pneumonia was
12 324 453,999, of which 372,660 episodes in period 1 and 67,474 episodes in period 3.

13
14
15 325 Monthly number of all-cause pneumonia peaked in January to March each year
16
17 326 (Figure 1C and Figure S2). Mean monthly number of hospitalizations for all-cause
18
19 327 pneumonia declined by 16.4% (95%CI 15.7%-17.1%, $p<0.0005$) from 6211 ± 845.0
20
21 328 episodes in period 1 to 5190.3 ± 593.8 episodes in period 3 ($p<0.0005$) (Figure 1C).
22
23 329 Estimated change in trend in the mean number of cases in period 3 was -11%
24
25 330 (95%CI -13% to -10%, $p<0.0005$). By log-linear model segmented regression,
26
27 331 relative risk of all-cause pneumonia in period 3 compared with period 1 was 0.98
28
29 332 (95%CI 0.98-0.99, $p<0.0005$) (Table S1).
30

31 334 Overall, the incidence rate per 100,000 person-years was 1,169.7 in period 1, with
32
33 335 17.5% (95%CI 16.8%-18.2%, $p<0.0005$) reduction in period 3 to 964.5 per 100,000
34
35 336 person-years in period 3. Incidence rate ratio between period 1 and period 3 was
36
37 337 0.83 (95%CI 0.82-0.83, $p<0.0005$) (Table 1). The incidence rate decrease in period
38
39 338 3 compared to period 1 in all age groups.
40

41 340 The overall median LOS for all-cause pneumonia episodes was 6 (IQR 9) days in
42
43 341 period 1 and 6 (IQR 10) days in period 3 ($p<0.005$) (Table 2). Different age groups
44
45 342 showed decrease in LOS but were only statistically significant in age 18-49 years
46
47 343 and 50-64 years. The mortality rate increased from 20.5% (95% CI 20.4%-20.6%) in
48
49 344 period 1 to 24.2% (95%CI 24.9%-25.6%) in period 3 ($p<0.005$) for all-cause
50
51 345 pneumonia. The increase in mortality rate was statistically significant in all age
52
53 346 groups (Table 2).
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55 348 For subgroup of aspiration pneumonia, total number of hospitalization in the entire
56
57 349 study period was 21,183, with 17990 episodes in period 1 and 2684 episodes in
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3 350 period 3. Mean monthly number of aspiration pneumonia was 299.8 ± 31.3 in period 1
4
5 351 and 206.5 ± 30.5 in period 3 ($p < 0.0005$).
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10 354 **COVID-19**

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12 355 In period 3, the total reported cases of COVID-19 infection at age 18 or above was
13
14 356 10,348 [15]. Among these patients, 331 were diagnosed with pneumonia. Majority of
15
16 357 them were in the age group 65 years old or above ($n=175$). 58 of them were in age
17
18 358 group 18-49 while 98 patients in age group 50-64.
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20 359

21 360 22 361 **Influenza**

23
24 362 The total number of influenza A or B viruses detected from January 2015 to March
25
26 363 2021 in Hong Kong was 123,732. The monthly number of influenza detections
27
28 364 decreased drastically by 99.5% (95%CI 99.4%-99.5%, $p < 0.0005$) from $1,966 \pm 2179$ in
29
30 365 period 1 to 10 ± 18 in period 3 (Figure 1D and Figure S2). The monthly average number
31
32 366 of respiratory specimens tested was 4313 ± 1172 in period 1 and 3203 ± 1868 in period
33
34 367 3.

35
36 368 By log-linear model segmented regression, relative risk of influenza was 0.92 (95%CI
37
38 369 0.88-0.95, $p < 0.0005$). Estimated change in trend in the mean number of detections in
39
40 370 period 3 was -99.0% (95%CI -99.3% to -98.7%, $p < 0.0005$) of that in period 1 (Figure
41
42 371 1D)
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46 374 **Other diagnosis: acute kidney injury, PD peritonitis and fracture hip**

47
48 375 The monthly average number of hospitalization episodes for acute kidney injury in
49
50 376 period 1 and period 3 was 807.8 ± 87.5 and 911.7 ± 62.6 , respectively ($p < 0.0005$)
51
52 377 (Figure 2) The monthly average number of hospitalization episodes for PD peritonitis
53
54 378 was 246.7 ± 27.7 in period 1 and 255.9 ± 31.9 in period 3 ($p = 0.23$). The monthly
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56 379 average number of hospitalization episodes for fracture hip was 432.9 ± 53.1 in period
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58 380 1 and 417.3 ± 51.6 in period 3 ($p = 0.37$)
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Discussion

Hong Kong is a city with population of 7.5 million where universal masking and social distancing were widely practiced during the COVID-19 pandemic period. This study showed a drastic decrease in numbers of hospitalization for IPD and pneumococcal pneumonia and a lesser but still very significant decrease in all cause pneumonia after anti-COVID-19 measures in March 2020 to March 2021.

During COVID-19 period, decrease in incidence of IPD were observed in Taiwan and Singapore [31-32]. The decrease in IPD in Hong Kong was greater magnitude compare to other countries [33]. Our study added new information on the incidence and severity of IPD, pneumococcal pneumonia and all-cause pneumonia in terms of age-stratification.

Introduction of the current pneumococcal conjugate vaccines has been highly successful in reducing the incidence of pneumococcal diseases worldwide [34,35]. Vaccine efficacy of PCV13 against vaccine type IPD in children aged ≤ 5 years was 86%-96% [36]. In adults aged ≥ 65 years, the vaccine efficacy against vaccine type IPD was reported as 75% and against vaccine type community-acquired pneumonia were reported as 45.6% and 72.8% respectively [13,37]. In contrast, PPV23 only has vaccine efficacy of 24% against vaccine type community acquired pneumonia in aged ≥ 65 years [38]. In Hong Kong, a marked reduction in vaccine type IPD was observed in children few years after implementation of PCV in 2009 [10,12]. However, the indirect effect on adult IPD was not evident. Annual number of adult IPD hospitalization remains static in period 1 (Figure 1A). Universal masking in Hong Kong was shown to decrease the incidence of SARS-CoV2 [39,40] and influenza [41] during the COVID-19 pandemic. Our study showed 88.9% reduction in incidence of adult IPD. The drastic decrease in incidence of IPD included both vaccine and non-vaccine types and was comparable and greater than the reported figure after introduction of pneumococcal vaccines [13,35]. IPD can lead to significant mortality and morbidity [42]. Our study showed decrease in incidence and trend of IPD and were statistically significant. The decrease in mortality of IPD during the COVID-19 pandemics was statistically insignificant, which can be contributed by the relative small sample size.

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417 Incidence of all-cause pneumonia showed a much lower magnitude of decrease with
418 the lesser decrease observed in those aged ≥ 65 years (supplementary file, Figure
419 S1C). In our study, patients with diagnosis of pneumonia during the hospital stay
420 were included. On review of data, majority of pneumonia patients in age group 65
421 years or above had other comorbidities including dementia, diabetes mellitus and
422 malignancy included in the same admission. The prevalence of chronic disease is
423 higher in elderly. The population of Hong Kong has been seeing an aging trend and
424 the population of 65 years old or above was 1,114,600 in 2015, and increased to
425 1,371,800 in 2020. The incidence of chronic disease, for example, malignancy
426 increased for 38.1% from 2008 to 2018 [17]. Patients with chronic diseases are at
427 higher risk of acquiring infection including pneumonia. Moreover, chronic disease
428 can be the cause leading to hospital admission with subsequent development of
429 hospital acquired pneumonia.

430

431 Pneumococcal pneumonia and IPD are debilitating diseases which have been
432 shown to require long length of hospital stay and high hospital cost [43-44]. The LOS
433 in pneumococcal pneumonia was slightly increased from 17.7 to 19.5 days but was
434 statistically insignificant. Looking into different age groups, only patients with age 50
435 to 64 years old showed statistically significant increase in LOS, while patients in age
436 group 18 to 49 years old and 65 years old or above showed slight decrease. The
437 severity of pneumococcal pneumonia can be comparable in the two periods.

438

439 Health seeking behaviour was also evaluated in our study. Admissions of non-
440 communicable diseases revealed either statistically insignificant decrease in hospital
441 attendance or statistically significant increase in hospital attendance. The incidence
442 of AKI increased in our study from 807.8 ± 87.5 in period 1 to 911.7 ± 62.6 in period 3.
443 Drug induced AKI is an important cause in Asia [45]. Possible explanation can be
444 due to the health seeking behaviour of patients with intake of over-the counter
445 medication for mild diseases prior seeking help from the hospital. Yet the exact
446 cause of increase in incidence of AKI should be investigated. Our study covered
447 more than one year time for COVID-19 pandemics with a relatively stable number of
448 hospital attendance. Hence, the decrease in incidence of pneumococcal pneumonia,

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3 449 IPD and all-cause pneumonia cannot be explained by health seeking behaviour
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5 450 alone.

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8 452 Collateral damages were observed during the COVID-19 pandemic [46-47], some of
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10 453 which were contributed by the decrease in general medical services to concentrate
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12 454 healthcare resources for the care of SARS-CoV-2 patients and the prevention of
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14 455 possible viral spread. However, due to the relatively small number of COVID-19
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16 456 cases in Hong Kong, provision of acute medical services was minimally disrupted. In
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18 457 our study, the data on admissions for fractures, acute kidney injury and PD peritonitis
19
20 458 showed no decrease during the Covid pandemic. Hence the observed decrease in
21
22 459 hospital admissions for pneumococcal pneumonia, IPD and all-cause pneumonia
23
24 460 should not be artefactual. Masking can be an effective yet low-cost preventive
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26 461 measurement for citizens at high risk of pneumococcal infections.
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29 464 **Limitations**

30 465 This study is a retrospective observational study and the direct effect of universal
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32 466 masking on pneumococcal pneumonia, IPD and all-cause pneumonia cannot be
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34 467 ascertained. However, our study covered a period of more than one year when
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36 468 universal masking was practiced and a consistent observation of decrease in
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38 469 hospitalization for these diseases were seen. Other factors, namely ambient
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40 470 temperature and AQHI, that might have possible effect on the hospitalization
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42 471 numbers were also included in our analysis. However, the individual effects of
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44 472 universal masking, social distancing (e.g. closure of schools, bars and pubs) and
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46 473 other strategies cannot be evaluated separately. It is modelled by the effect of
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48 474 pandemic as a whole in our study.

49 475

50 476 Our study focused on hospital hospitalization numbers to Hospital Authority. For IPD,
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52 477 the incidence was obtained from Central of Health Protection, HKSAR, which
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54 478 included data from both public and private hospitals data. The LOS and mortality
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56 479 data of IPD were retrieved from the database in Hospital Authority. Admissions to
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58 480 private hospital or those received out-patient treatment for pneumococcal pneumonia
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60 481 and all-cause pneumonia were not included in our study. However, Hospital
482 Authority is the largest healthcare provider in Hong Kong which provides 90% of in-

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3 483 patient services in Hong Kong [26]. Data from Hospital Authority is representable for
4 the general epidemiology of Hong Kong.
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8 486 **Conclusions**

9
10 487 The incidence of pneumococcal pneumonia, IPD and all-cause pneumonia
11 decreased during COVID-19 pandemics compare to the data in previous five years.
12 488
13 489 This was observed with widely practice of universal masking and social distancing.
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15 490 We propose the decrease is attributed to universal masking and social distancing
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17 491 which reduced the transmission of bacteria or virus and related bacterial
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19 492 superinfection.
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3 494 **Figure caption**
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6 495 **Figure 1.** Trend analysis of monthly numbers of invasive pneumococcal disease
7 496 (IPD), pneumococcal pneumonia, all-cause pneumonia, and influenza in Hong Kong,
8 497 January 2015 to March 2021. Numbers of IPD were those obtained through
9 498 mandatory notification. Numbers of pneumococcal pneumonia and all-cause
10 499 pneumonia were territory-wide hospitalizations by discharge diagnoses. Numbers of
11 500 influenza viruses were those detected in respiratory specimens in a territory-wide
12 501 laboratory surveillance. The two vertical lines delineated the time intervals from
13 502 January 2015 to December 2019 (period 1, prior to COVID-19), January to February
14 503 2020 (period 2, excluded from analysis) and March 2020 to March 2021 (period 3,
15 504 COVID-19 pandemic).
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24 506 **Figure 2.** Admission numbers of fracture hip, acute kidney injury and PD peritonitis.
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Table 1. Incidence and number per 100,000 person year of pneumococcal pneumonia, invasive pneumococcal disease (IPD) and pneumonia

Disease ^a	All ages		18-49 years		50-64 years		≥65 years	
	No. of episodes	Incidence rate per 100,000 person-years	No. of episodes	Incidence rate per 100,000 person-years	No. of episodes	Incidence rate per 100,000 person-years	No. of cases	Incidence rate per 100,000 person-years
IPD								
Period 1	699	2.2	125	0.7	195	2.2	379	6.2
Period 2	26	2.4	5	0.9	6	2.0	15	6.6
Period 3	17	0.2	3	0.08	8	0.4	6	0.4
% reduction ^b		88.9% (79.8%-98.0%) ^{***}		88.6% (66.8%-110.4%) ^{***}		81.3% (62.1%-100.4%) ^{***}		93.5% (82.2%-104.8%) ^{***}
IRR ^c		0.11(0.07-0.18) ^{***}		0.11(0.04-0.36) ^{***}		0.19(0.09-0.38) ^{***}		0.07(0.03-0.15) ^{***}
Pneumococcal pneumonia								
Period 1	1,970	6.2	217	1.3	435	4.9	1,318	21.7
Period 2	74	6.9	11	2.0	14	4.7	49	32.4
Period 3	119	1.7	8	0.2	24	1.2	87	5.9
% reduction		72.5% (65.9%-79.1%) ^{***}		82.5% (64.5%-100.5%) ^{***}		74.8% (61.0%-88.6%) ^{***}		73.0% (65.2%-80.8%) ^{***}
IRR ^c		0.28(0.23-0.33) ^{***}		0.18(0.09-0.35) ^{***}		0.25(0.17-0.38) ^{***}		0.27(0.22-0.34) ^{***}
All-cause pneumonia								
Period 1	372,660	1169.7	19,502	115.3	38,360	432.4	314,798	5177.1
Period 2	13,865	1288.2	843	153.6	1,448	484.6	11,574	5062.3
Period 3	67,474	964.5	2,473	69.3	6,181	318.3	58,820	3958.0
% reduction		17.5% (16.8%-18.2%) ^{***}		39.9% (37.1%-42.7%) ^{***}		26.4% (24.3%-28.5%) ^{***}		23.5% (22.8%-24.3%) ^{***}
IRR ^c		0.83(0.82-0.83) ^{***}		0.60(0.58-0.63) ^{***}		0.74(0.72-0.76) ^{***}		0.77(0.76-0.77) ^{***}

^a Period 1, January 2015 to December 2019 (before covid-19); period 2, January 2020 to February 2020 (transition period); period 3 March 2020 to March 2021 (post-COVID-19).

^b Percentage reduction in period 3 relative to period 1 as the baseline

^c Incidence ratio between period 1 and period 3

*p < 0.05 to 0.01, **p < 0.01 to 0.005, ***p < 0.005

Table 2. Median length of stay and mortality rate of pneumococcal pneumonia, invasive pneumococcal disease (IPD) and pneumonia in the periods

	Median length of stay; days (IQR)#				Mortality rate; % (95%CI)			
	All ages	18-49 years	50-64 years	≥65 years	All ages	18-49 years	50-64 years	≥65 years
IPD								
Period 1	12 (16)	13 (19)	13 (17)	12 (13)	12.1 (8.8-16.1)	9.1 (3.4-18.7)	8.4 (3.7-15.9)	15.3 (10.3-21.4)
Period 3	12 (11)	4 (3)	16 (19)	12 (6)	6.3 (1.6-30.2)	0.0	0.0	14.3 (3.6-57.9)
Pneumococcal Pneumonia								
Period 1	9 (14)	7 (14)	9 (15)*	10 (14)	13.1 (11.7-14.8)*	4.2 (1.9-7.7)	7.5 (5.3-10.5)**	16.3 (13.6-18.7)
Period 3	12 (17)	7 (13)	13 (20)*	12 (16)	22.7 (15.5-31.3)*	0.0	29.2 (12.6-51.1)**	23.0 (14.6-33.2)
All-cause pneumonia								
Period 1	6 (9)***	4 (6)***	6 (9)**	6 (10)	20.5 (20.4-20.6)***	5.3 (4.9-5.6)*	13.0 (11.4-12.0)***	22.4 (22.2-22.4)***
Period 3	6 (10)***	4 (8)***	6 (10)**	6 (10)	24.2 (24.9-25.6)***	6.8 (5.9-7.9)*	16.1 (5.2-17.0)***	27.0 (26.6-27.3)***

*p <0.05 to 0.01, **p <0.01 to 0.005, ***p<0.005

IQR= interquartile range

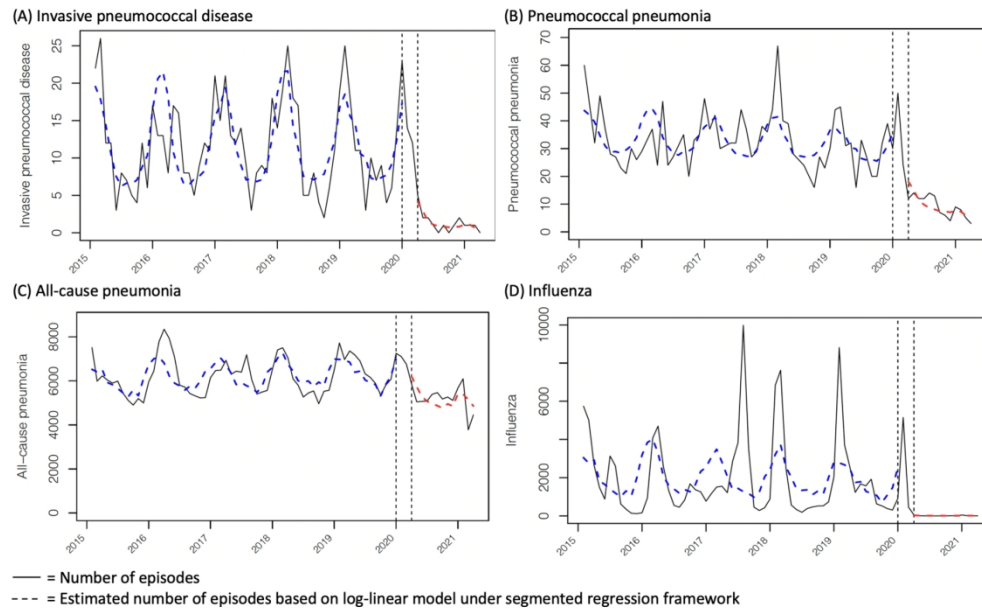


Figure 1. Trend analysis of monthly numbers of invasive pneumococcal disease (IPD), pneumococcal pneumonia, all-cause pneumonia, and influenza in Hong Kong, January 2015 to March 2021. Numbers of IPD were those obtained through mandatory notification. Numbers of pneumococcal pneumonia and all-cause pneumonia were territory-wide hospitalizations by discharge diagnoses. Numbers of influenza viruses were those detected in respiratory specimens in a territory-wide laboratory surveillance. The two vertical lines delineated the time intervals from January 2015 to December 2019 (period 1, prior to COVID-19), January to February 2020 (period 2, excluded from analysis) and March 2020 to March 2021 (period 3, COVID-19 pandemic).

352x218mm (144 x 144 DPI)

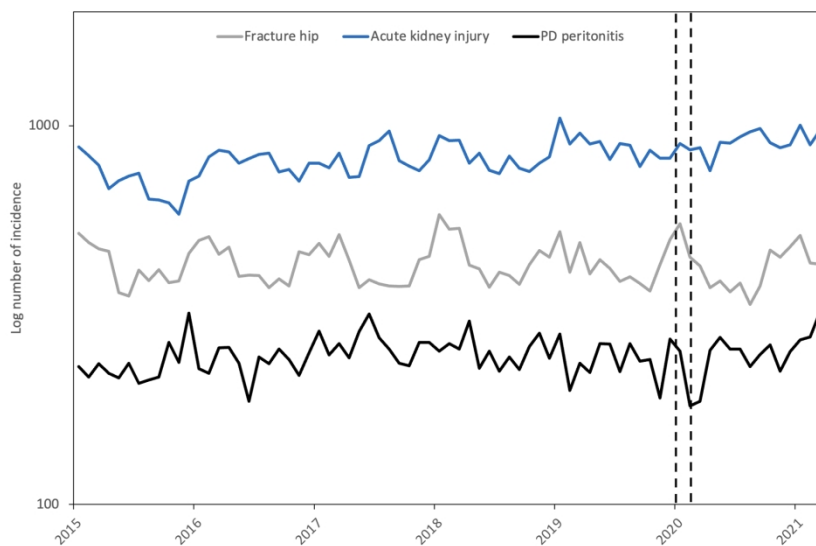


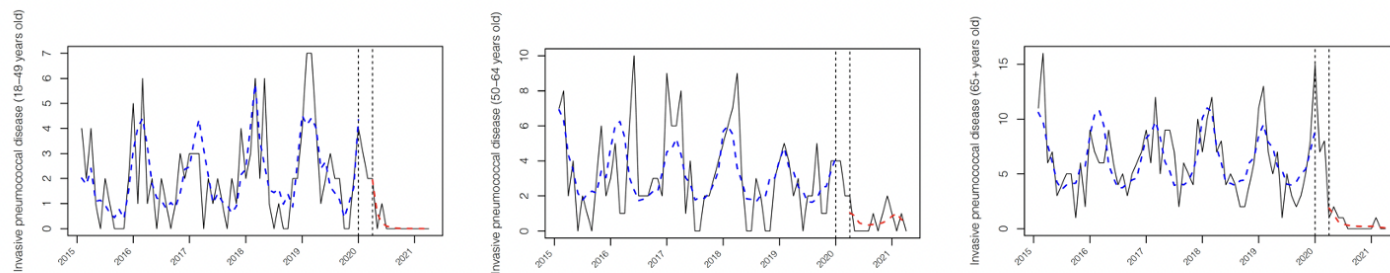
Figure 2. Admission numbers of fracture hip, acute kidney injury and PD peritonitis.

419x237mm (144 x 144 DPI)

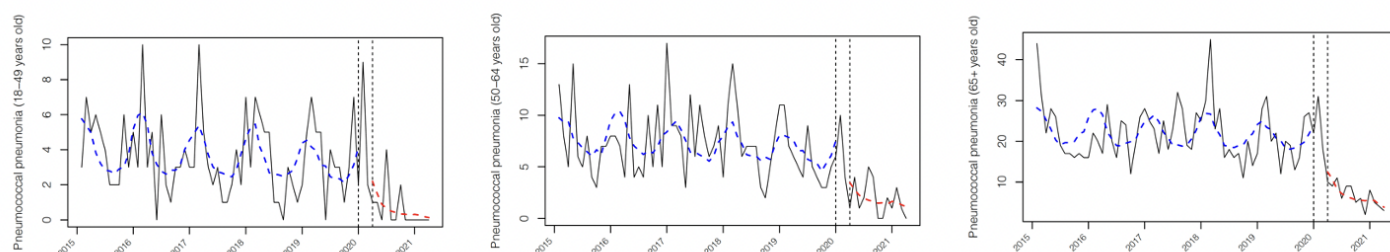
Supplementary file.

Figure S1. Trend analysis of monthly number of (A) age-stratified hospitalizations for invasive pneumococcal disease, (B) age-stratified hospitalizations for pneumococcal pneumonia, (C) age-stratified hospitalizations for and (D) monthly percentage of air quality health index (AQHI) high to serious and (E) monthly average ambient temperature.

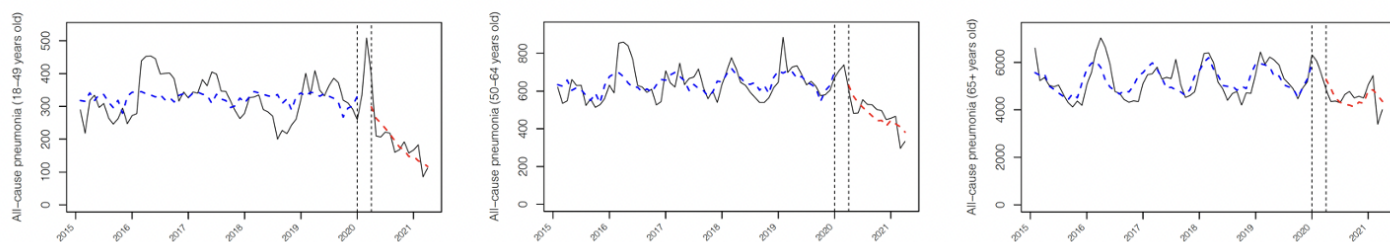
(A) Invasive pneumococcal disease



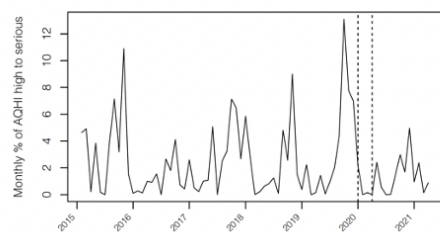
(B) Pneumococcal pneumonia



(C) All cause pneumonia



(D) Monthly % of AQHI high to serious



(E) Monthly average temperature

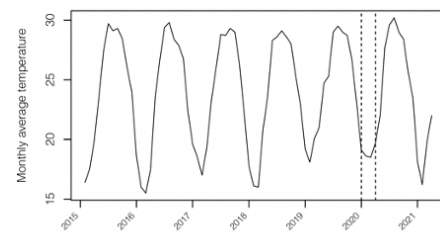
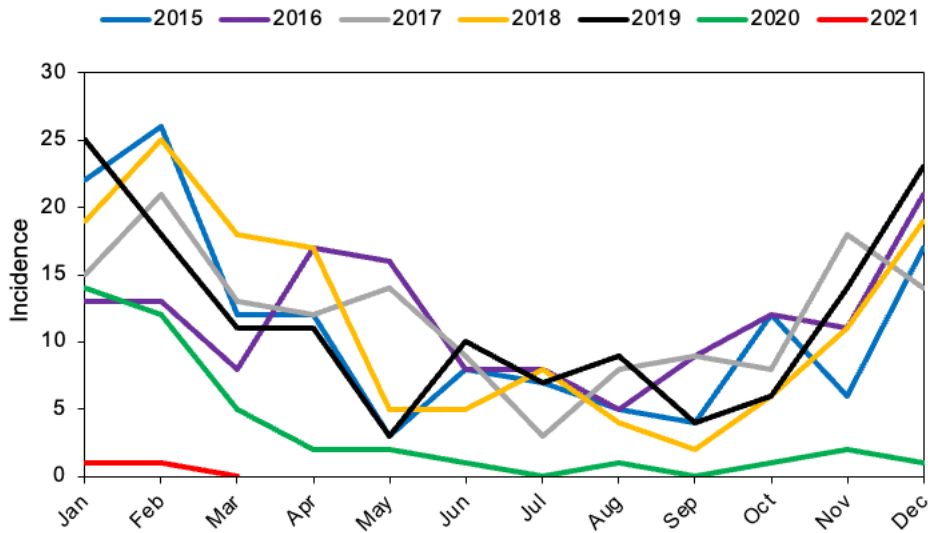
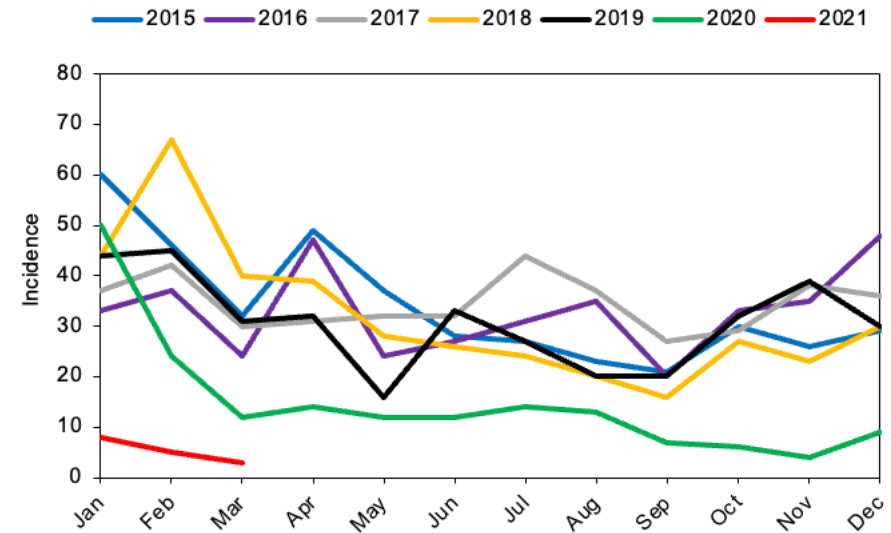


Figure S2. Monthly incidence of (A) Invasive pneumococcal disease (IPD), (B) Pneumococcal pneumonia, (C) All-cause pneumonia and (D) Influenza in January 2015 to March 2021.

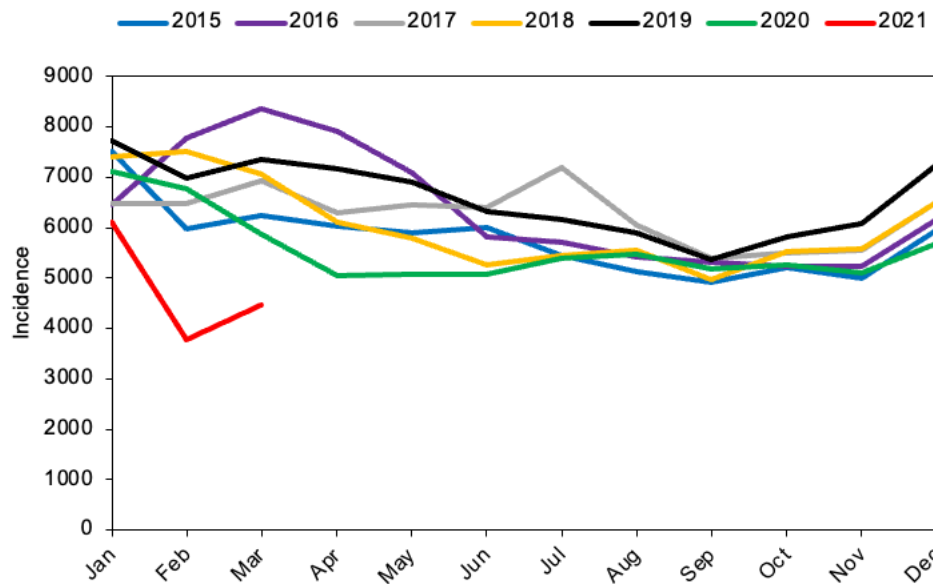
(A) Invasive pneumococcal disease



(B) Pneumococcal pneumonia



(C) All-cause pneumonia



(D) Influenza

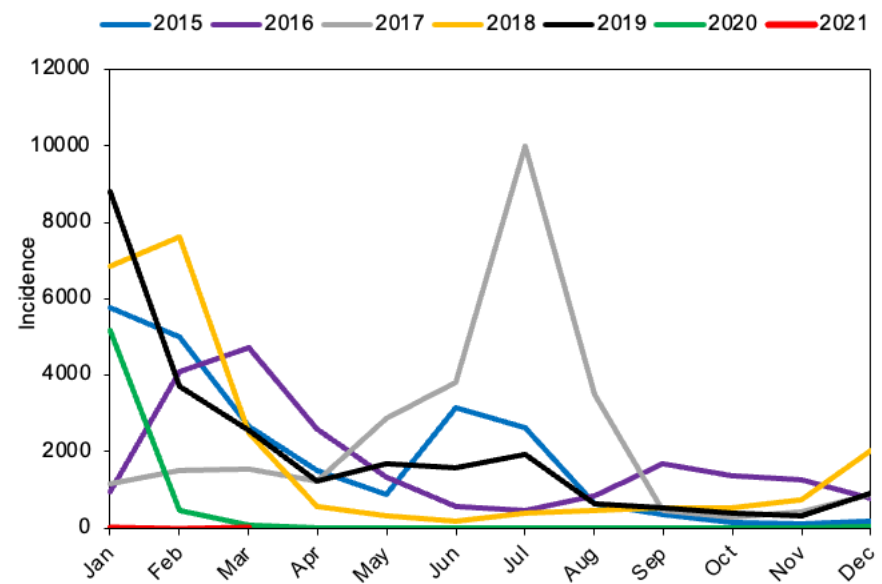


Table S1. Trend analysis of monthly number of hospitalization by age groups in periods before and after the COVID-19 pandemic

	Relative risk (95% CI)		Change in trend#
	Period 1 ^	Period 3^	
IPD			
All ages	1.0020 (0.9977-1.064)	0.8484 (0.7501-0.9597)**	-70.39% (-86.55% to -34.73%)**
18-49 years	1.0129 (1.0022-1.0238)	0.5272 (0.2176-1.2772)	-31.27% (-89.72% to 359.72%)
50-64 years	0.9969 (0.9888-1.0051)	0.9585 (0.8087-1.1362)	-70.43% (-92.80% to 21.42%)
65 years or above	1.0012 (0.9953-1.0071)	0.7777 (0.6111-0.9897)*	-70.83% (-91.59% to 1.12%)
Pneumococcal Pneumonia			
All ages	0.9978(0.9953-1.0004)	0.9042(0.8621-0.9483)***	-42.79% (-59.36% to -19.48%)*
18-49 years	0.9964(0.9887-1.0042)	0.6768(0.2171-2.1093)	-32.32% (-78.29% to 110.93%)
50-64 years	0.9962(0.9907-1.0017)	0.9174(0.8260-1.0189)	-50.21% (-76.93% to 7.48%)
65 years or above	0.9986(0.9954-1.0017)	0.9107(0.8612-0.9640)*	-41.19% (-60.82% to -11.73%)*
All-cause pneumonia			
All ages	1.0014(1.0012-1.0016)***	0.9835(0.9815-0.9855)***	-11.24% (-12.76% to -9.7%)***
18-49 years	1.0000(0.9992-1.0008)	0.9263(0.9164-0.9364)***	-6.05% (-13.41% to 1.94%)
50-64 years	1.0015(1.0009-1.0021)***	0.9620(0.9556-0.9684)***	-9.32% (-14.14% to -4.22%)***
65 years or above	1.0011(1.0009-1.0013)***	0.9879(0.9858-0.9901)***	-13.30% (-12.94% to -9.64%)***

^Trend in period 1 (January 2015 to December 2019) and 3 (March 2020 to March 2021), the (relative risk expressed the month-to-month change in hospitalization numbers

#Estimate the change in trend in the mean monthly number of cases in period 3, compare with the monthly trend in period 1

*p <0.05 to 0.01, **p <0.01 to 0.005, ***p<0.005

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6,7
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	6,7
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	6,7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6,7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6,7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	6,7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7,8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7,8
		(b) Describe any methods used to examine subgroups and interactions	7,8
		(c) Explain how missing data were addressed	N/A
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	7,8

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60**Results**

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10-13
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-13
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	10-13
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-13
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10-13

Discussion

Key results	18	Summarise key results with reference to study objectives	14-15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-15

Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	3
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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Invasive pneumococcal disease, pneumococcal pneumonia and all-cause pneumonia in Hong Kong during the COVID-19 pandemic compared with the preceding 5 years: a retrospective observational study

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Secondary Subject Heading:	Epidemiology, Public health, Respiratory medicine
Keywords:	COVID-19, Respiratory infections < THORACIC MEDICINE, Thoracic medicine < INTERNAL MEDICINE, Epidemiology < INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES

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2
3 1 **Title: Invasive pneumococcal disease, pneumococcal pneumonia and all-**
4 **cause pneumonia in Hong Kong during the COVID-19 pandemic compared**
5 **with the preceding 5 years: a retrospective observational study**
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11 5 King-Pui Florence Chan, MBBS¹, Ting-Fung Ma, MPhil², Mary Sau-Man Ip¹, MD,
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2
3 26 **Abstract**

4
5 27 **Objectives:** To compare the incidence and severity of invasive pneumococcal
6
7 28 diseases (IPD), pneumococcal pneumonia and all-cause pneumonia during COVID-
8
9 29 19 pandemic period with universal masking and social distancing to that of previous
10
11 30 5 years.

12
13 31 **Design:** Retrospective observational study on incidence of invasive pneumococcal
14
15 32 diseases (IPD), pneumococcal pneumonia and all-cause pneumonia between
16
17 33 January 2015-December 2019 and March 2020-March 2021. January-February 2020
18
19 34 was excluded from analysis as it was treated as transitional period between normal
20
21 35 time and pandemic.

22
23 36 **Setting:** Episode-based data by retrieval of hospitalization records from the Hospital
24
25 37 Authority's territory-wide electronic medical record database in Hong Kong.

26
27 38 **Participants:** Hospitalized patients with invasive pneumococcal diseases (IPD)
28
29 39 (n=742), pneumococcal pneumonia (n=2163) and all-cause pneumonia (including
30
31 40 COVID-19 pneumonia, n=453,999) at age 18 or above. Control diagnoses were
32
33 41 included to assess confounding from health-seeking behaviors.

34
35 42 **Primary and secondary outcome:** Primary outcome is the incidence of diseases
36
37 43 between two periods. Secondary outcomes include disease severity surrogated by
38
39 44 length of stay and mortality.

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41 45 **Results:** Monthly average number of IPD, pneumococcal pneumonia and all-cause
42
43 46 pneumonia hospitalization significantly decreased by 88.9% (95%CI 79.8%-98.0%,
44
45 47 $p<0.0005$), 72.5% (95%CI 65.9%-79.1%, $p<0.0005$) and 17.5% (95%CI 16.8%-
46
47 48 18.2%, $p<0.0005$), respectively. Change in trend from January 2015-December 2019
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49 49 to March 2020-March 2021 was -70% (95%CI -87% to -35%, $p=0.0025$), -43%
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51 50 (95%CI -59% to -19%, $p=0.0014$) and -11% (95%CI -13% to -10%, $p<0.0005$),
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53 51 respectively. Length of stay for IPD and pneumococcal pneumonia episodes were
54
55 52 insignificantly different in the two periods. No reductions in hospitalizations for control
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57 53 diagnoses were observed.

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57 54 **Conclusions:** Incidence of IPD, pneumococcal pneumonia, and all-cause
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59 55 pneumonia decreased during COVID-19 pandemic. This was observed with
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3 56 universal masking and social distancing. We postulated this is related to reduced
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5 57 transmission of respiratory viruses and bacteria.
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10 59 **Strength and limitations of this study:**

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12 60 • A territory-wide study with near 100% practice of universal masking and
13
14 61 wide practice of social distancing
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16 62 • Other factors including temperature and air quality were also included in
17
18 63 our analysis
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20 64 • Disease severity of IPD, pneumococcal pneumonia, and all-cause
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22 65 pneumonia were compared between the two periods
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24 66 • Data from private sector (<10%) were not included in our study
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26 67 • The causal relationship cannot be ascertained from this retrospective
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28 68 study
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30 70 **Funding:** This work is partly funded by a grant from the Health and Medical
31
32 71 Research Fund (reference number CID-HKU1-13), Food and Health Bureau, The
33
34 72 Government of the Hong Kong Special Administrative Region.
35

36 74 **Competing interests:** There are no competing interests.
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38 75

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40 76 **Data availability statements:** No additional data is available.
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42 77

43 78 **Authors' contributions:**

44
45 79 **King-Pui Florence Chan and Ting-Fung Ma** were involved in study concept and
46
47 80 design; acquisition, analysis and interpretation of data; drafting the work and final
48
49 81 approval of the manuscript. **Mary Sau-Man Ip** were involved in critical revision of
50
51 82 manuscript for important intellectual content and final approval of the manuscript.
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53 83 **Pak-Leung Ho** was involved in study concept and design; analysis and
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55 84 interpretation of data; drafting of manuscript; critical revision of the manuscript for
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57 85 important intellectual content; study supervision; and approval of the final version of
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59 86 the manuscript.
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88 **Word count:** 4174

89 **Keywords:** pneumococcal, COVID-19, masking, regression analysis

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For peer review only

91 Text

92 Introduction

93 Coronavirus disease 2019 (COVID-19) due to severe acute respiratory syndrome
94 coronavirus 2 (SARS-CoV-2) infections was first reported in late 2019 [1]. It became
95 a global pandemic and was declared as a public health emergency of international
96 concern on 30 January 2020 by the World Health Organization [2]. As of 22
97 September 2021, more than 229 million people were infected, causing more than 4.7
98 million deaths globally.

99 Pneumococcal disease is caused by *Streptococcus pneumoniae* infection, with at
100 least 100 known serotypes of pneumococci [3]. Pneumococcal disease can be
101 roughly divided into non-invasive disease and invasive disease. Non-invasive
102 disease includes sinusitis, acute otitis media and pneumonia. Invasive
103 pneumococcal disease (IPD) is defined as isolation of *Streptococcus pneumoniae*
104 from a normally sterile sites, including blood and cerebrospinal fluid [4]. IPD is a
105 notifiable disease in Hong Kong since 9th January 2015. Pneumococcal infection is
106 a major cause of morbidity and mortality worldwide [5], with 1.6 million estimated
107 deaths annually in 2005 [6]. Incidence of IPD and mortality of pneumococcal
108 pneumonia are higher at extremes of age [7-8].

109 The first pneumococcal conjugated vaccine (PCV), Prevnar 7 (PCV7) was
110 introduced to United States in 2000 and incorporated in Hong Kong Childhood
111 Immunisation Programme for children under 2 years old since September 2009 [9-
112 10]. In Hong Kong, PCV7 was replaced by the 10-valent and 13-valent
113 pneumococcal conjugate vaccines (PCV10 and PCV13) in 2010 and 2011
114 respectively [11-12]. PCV13 was effective in preventing vaccine-type pneumococcal
115 pneumonia, bacteraemia and nonbacteraemic community-acquired pneumonia [13].
116 Decline in incidences of all-cause pneumonia in children and elderly was reported
117 after implementation of PCV in childhood vaccination program [14-15]. 23-valent
118 polysaccharide vaccine (PPSV23) was effective in preventing pneumococcal
119 pneumonia and reducing mortality from pneumococcal pneumonia in nursing home
120 residents [16]. In our locality, elderly at age 65 years and above without high risk
121 conditions, namely immunodeficiency or chronic cardiac, pulmonary, liver or renal
122 disease, or diabetes mellitus were recommended to receive either a single dose of

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3 123 PCV13 or a single dose of PPSV23. Number of PPSV23 vaccine recipients at age
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5 124 65 years or above increased from 35,000 in year 2015/2016 to 81,700 in 2019/2020,
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7 125 with approximately 46% of population in the age group cumulatively vaccinated in
8
9 126 2020 [17]. Pneumonia is a common disease causing hospitalization, accounting for
10
11 127 2.9% of all inpatient discharges and death in Hong Kong [18]. It is the second
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13 128 leading cause of death with age specific death rates increased markedly after age 65
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15 129 [17].
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17 131 Whether patients with COVID-19 are more susceptible to pneumococcal
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19 132 superinfection is still under debate. Superinfection of pneumococcal in COVID-19
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21 133 patients was reported [19]. Yet, low frequency of bacterial coinfection in patients with
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23 134 early COVID-19 was also observed [20-21]. There is limited evidence on the
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25 135 incidence and severity of IPD, pneumococcal pneumonia, and all-cause pneumonia
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27 136 during COVID-19 pandemic, especially in area where universal masking and social
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29 137 distancing were widely practiced. Since January 2020, universal masking in public
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31 138 area was voluntarily performed by Hong Kong citizens against COVID-19. Cross
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33 139 sectional telephone self-reported surveys by the Hong Kong Public Opinion
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35 140 Research Institute (HKPORI) showed percentage of wearing mask was 74.5% on
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37 141 20th-23rd January 2020 (n=1,008), 97.6% on 5th-20th February (n=10,405) and
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39 142 98.9% on 4th-19th March (n=15,739) [22]. On 23rd July 2020, masking was
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41 143 mandatory in public area upon the introduction of Prevention and Control of Disease
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43 144 (Wearing of Mask) Regulation (Cap. 599I). Social distancing measurements were
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45 145 voluntarily practiced by public and implemented by government since 25th January
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47 146 2020. These public health interventions were shown to associate with relatively low
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49 147 rate of COVID-19 and early termination of influenza season in Hong Kong [23]. Our
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51 148 previous studies suggested universal masking and social distancing were associated
52
53 149 with significant reduction in acute exacerbation of chronic obstructive pulmonary
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55 150 disease and asthma in Hong Kong [24,25]. In the current study, we hypothesized
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57 151 that the aforementioned COVID-19 related public health interventions and reduction
58
59 152 in respiratory virus activities would be associated with reduction in hospitalization
60
153 due to pneumococcal infections and pneumonia in general.

155 **Materials and Methods**

156 A retrospective study assessing the numbers of IPD, pneumococcal pneumonia, and
157 all-cause pneumonia which required hospital hospitalization during the period of
158 COVID-19 in Hong Kong, comparing with that in the preceding five years as baseline
159 was conducted. The study period was 1st January 2015 to 31st March 2021 with
160 exclusion of 1st January 2020 to 28th February 2020 from analysis, when public
161 health practices such as mask wearing were not yet fully adopted.

163 **Data source**

164 Episode-based data was obtained by retrieval of hospitalization records from the
165 Hospital Authority's territory-wide electronic medical record database, Clinical Data
166 Analysis and Reporting System (CDARS), which provides 90% of in-patient hospital
167 care service in Hong Kong [24,25].

169 Diagnosis code of pneumococcal pneumonia (ICD-9 code 481) was searched on
170 CDARS. IPD is a notifiable disease since January 2015 with monthly number notified
171 cases and age obtained from the Department of Health, Hong Kong Special
172 Administrative Region (HKSAR). Monthly number of influenza virus detection was
173 collected from a territory-wide laboratory surveillance for both in-patients and out-
174 patients in both public and private medical sectors from the Centre for Health
175 Protection (CHP), HKSAR [17].

177 All-cause pneumonia including the following ICD-9 codes for viral, bacterial,
178 tuberculous, fungal and unspecified pneumonia, pneumonia due to inhalation of food
179 or vomitus and lung abscess were obtained from CDARS (ICD-9 code 003.22,
180 055.1, 0.1160-1.1166, 112.4, 115, 117.3, 480, 481, 482, 483.1, 483.8, 485, 486, 487,
181 507.0, 513). Patient with COVID-19 associated pneumonia was included in the all-
182 cause pneumonia dataset. The contribution of COVID-19 within all-cause pneumonia
183 was queried using ICD codes for COVID-19 disease (ICD-9 code 079.89, 480.8,
184 519.8). Demographics data (including sex, age), clinical data (including
185 hospitalization date, length of stay, episode death, date of death) were collected. The
186 results including admission number of various diseases were available in the CHP
187 website and the Hospital Authority Statistics Report [17,26].

188

Inclusion/ exclusion criteria

Patients with 1) age 18 or above 2) hospitalization for the listed diseases (pneumococcal pneumonia, IPD and pneumonia) were included in the study.

192

Children at aged 0 to 17 years old were excluded in this study. Duplicated record of single patient with different diagnoses in same hospital admission were removed.

195

Other diagnoses

Number of hospitalization for other common medical and surgical conditions including acute kidney injury (ICD-9 code 580, 584), fracture hip (ICD-9 code 820) and peritonitis due to peritoneal dialysis (PD peritonitis) (ICD-9 code 996.68) were collected. These were included to evaluate the possibility of decrease in hospital attendance due to various reasons such as fear of COVID-19 infection in hospital. These diseases were selected as are non-communicable diseases and have minimal interactions with environmental factors including mean ambient temperature and air-pollution.

205

Other variables

Monthly mean ambient temperature was obtained from the Hong Kong Observatory [27]. Air quality was measured by air quality health index (AQHI), which is calculated based on the cumulative health risk attributable to a 3-hour moving average concentrations of ozone, nitrogen dioxide, sulphur dioxide and particulate matter [28]. It was reported in scale of 1 to 10 and 10+ and grouped into five health risk categories, namely low [1-3], moderate [4-6], high [7], very high [8-10] and serious [10+] with different precautionary actions were advised. People with respiratory illness were advised to minimize their outdoor stay when AQHI high to serious. The AQHI was reported hourly in 13 stations located in different area of Hong Kong. The total number of hours with AQHI recorded as high to serious grades were expressed as percentage of total number of hours collected in a month.

218

Statistical method

Total number of hospitalizations due to IPD, pneumococcal pneumonia and all-cause pneumonia were collected and analysed. Each disease was further divided into three

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2
3 222 different age groups, including 18 to 49 years, 50 to 64 years, and 65 years or above
4
5 223 for analysis.
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8 225 Analysis was done on the number of hospitalizations between January 2015 to
9
10 226 December 2019, the period prior COVID-19 (period 1) and March 2020 to March
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12 227 2021 (period 3), while January to February 2020 (period 2) was treated as transition
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14 228 period and excluded from the analysis. Wilcoxon rank sum test was first used to
15
16 229 analyse the statistical significance of number of hospitalizations between period 1
17
18 230 and period 3. Generalized linear models were then applied for statistical inference of
19
20 231 various types of responses. Log-linear model was used for studying the effect of
21
22 232 pandemic as intervention under segmented regression framework in term of the
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24 233 change in trend (i.e. an increase or decrease in the level of the segment) between
25
26 234 period 1 (pre-intervention segment) and period 3 (post-intervention segment) on the
27
28 235 monthly hospitalization count. Regression coefficients of log-linear model can be
29
30 236 interpreted as the effect due to pandemic by log-linear model [29]. We assumed
31
32 237 temporal dependence can be adjusted by the effect of pandemic, including masking,
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34 238 social distancing and other behavioural changes, and climate related variables
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36 239 including temperature and AQHI.
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39 241 Generalized linear model was used for comparing the mortality rate of individuals
40
41 242 between the two time periods [30]. Hospitalization length of stay (LOS) was
42
43 243 described in days using median and standard deviation. Statistical inference of the
44
45 244 LOS in hospitalization of individuals was done by Wilcoxon rank sum test with odds
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47 245 ratio and relative risks and confidence intervals calculated [29].
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49 246

50 247 Monthly incidence rate for each disease was calculated using the total population
51
52 248 followed by age groups stratification (18 to 49 years, 50 to 64 years and ≥ 65 years)
53
54 249 and expressed as number per 100,000 person-year. Age-specific population data
55
56 250 was obtained from the Census and Statistics Department.
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59 252 ***Ethics Approval***

60 253 The study was approved by the Institutional Review Board of the University of Hong
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255 Kong/ Hospital Authority Hong Kong West Cluster (Reference Number UW-21-325).

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256 ***Patient and public involvement***

257 Patients or the public were not involved in the design, or conduct, or reporting, or
258 dissemination plans of our research.

For peer review only

260 **Results**

261 ***Invasive pneumococcal disease***

262 The total number of notified IPD episodes was 742 in the entire study, with 699
263 reported in period 1 and 17 reported in period 3. Pneumococcal serotypes for 684 of
264 the 699 episodes in period 1, and 13 of the 17 episodes in period 3 were
265 successfully determined. The proportions attributed to PCV13 serotypes was 66.5%
266 (465/699) and 29.4% (5/17) respectively for period 1 and period 3. Serotype 3 was
267 the commonest serotype in both periods, accounting for 41.3% (289/699) and 17.6%
268 (3/17) of total, respectively. From period 1 to period 3, the monthly number of IPD
269 caused by PCV13 serotypes declined by 95.1% (95%CI 93.4%-96.4%) while those
270 for non-PCV13 serotypes declined by 83.0% (95%CI 78.8%-86.5%), and those for
271 PPSV23 serotypes declined by 94.1% (95% CI 92.3%-95.5%). The small difference
272 between declines in PCV13 and PPSV23 serotypes was mainly attributed to
273 serotype 6A which was included in PCV13 but not in PPSV23.

274

275 Monthly number of IPD peaked in January-February each year except in 2016, with
276 the peak in April (Figure 1A and Figure S1). Monthly average number of notified IPD
277 episodes was 11.7 ± 6.2 in period 1, with significant decrease to 1 ± 4.3 in period 3
278 ($p < 0.0005$). By log-linear model segmented regression, relative risk of IPD in period
279 3 was 0.85 (95%CI 0.75-0.96, $p = 0.0089$) (Table S1). Further analysis on the relative
280 risk of different age groups showed significant decline in relative risk of IPD in aged
281 ≥ 65 years (0.78, 95%CI 0.61-0.99, $p = 0.041$). Estimated change in trend in the mean
282 number of cases from period 1 to period 3 was -70% (95%CI -87% to -35%,
283 $p = 0.0025$) (Figure 1A, Table S1).

284

285 Incidence rate per 100,000 person-years was 2.2 in period 1 and 0.2 in period 3, with
286 an interval reduction of 88.9% (95%CI 79.8%-98.0%, $p < 0.0005$). Incidence rate ratio
287 between period 1 and period 3 was 0.11 (95%CI 0.07-0.18, $p < 0.0005$) (Table 1). IPD
288 is most prevalent in age ≥ 65 . The magnitude of reduction in incidence rate was
289 similar across different age groups, ranging from 81.3% to 93.5% ($p < 0.0005$ for all
290 age groups) (Table 1).

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3 292 The overall median LOS for IPD was 12 (Interquartile range, IQR 16) days in period
4
5 293 1 and 12 (IQR 11) days in period 3 (Table 2), with statistically insignificant difference
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7 294 (p=0.89). Statistically insignificant variations in LOS of different age groups were
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9 295 observed.

10 296

11 297 ***Pneumococcal pneumonia***

12 298 In the entire study period, there were 2,163 episodes of hospitalization for
13
14 299 pneumococcal pneumonia, with 1970 episodes in period 1 and 119 episodes in
15
16 300 period 3 (Table 1). Monthly number of pneumococcal pneumonia was peaked in
17
18 301 January-February each year except in 2016, with the peak in April (Figure 1B and
19
20 302 Figure S1). The average monthly hospitalizations was 32.8 ± 9.9 episodes in period 1,
21
22 303 with significant drop to 9.2 ± 3.9 episodes in period 3 ($p < 0.0005$). By log-linear model
23
24 304 segmented regression, relative risk of pneumococcal pneumonia was 0.90 (95%CI
25
26 305 0.86-0.95, $p < 0.005$) in period 3. Trend analysis revealed a change of -43% (95%CI -
27
28 306 59% to -19%, $p = 0.0014$, Figure 1B, Table S1) from period 1 to period 3. Age groups
29
30 307 analysis showed similar change in trend for all age groups, with statistically
31
32 308 significance in aged ≥ 65 years (-41%, 95%CI -61% to -12%, $p = 0.010$) from period 1
33
34 309 to period 3 (Table S1, Figure S2).

35 310

36 311 Overall, the incidence rate of hospitalization for pneumococcal pneumonia
37
38 312 decreased significantly by 72.5% (95%CI 65.9%-79.1%, $p < 0.0005$), from 6.2 per
39
40 313 100,000 person-years in period 1 to 1.7 per 100,000 person-years in period 3.
41
42 314 Incidence rate ratio between period 1 and period 3 was 0.28 (95%CI 0.23-0.33,
43
44 315 $p < 0.0005$) (Table 1). Incidence rate per 100,000 person year showed statistically
45
46 316 significant reduction in all age groups, ranging from 73.0% to 82.5%.

47 317

48 318 Majority of the patients with pneumococcal pneumonia were treated with in-patient
49
50 319 care. The total number of patients treated as outpatients and discharged from
51
52 320 emergency department was 30 in period 1 and 0 in period 3.

53 321

54
55 322 The overall median LOS for pneumococcal pneumonia in period 1 and period 3 was
56
57 323 9 (IQR 14) days and 12 (IQR 17) days in all age group ($p = 0.051$) (Table 2). Age
58
59 324 group stratification showed insignificant changes in length of stay in those aged 18-

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2
3 325 49 years ($p=0.8051$) and aged ≥ 65 years ($p=0.226$). Increase in length of stay from 9
4 326 (IQR 15) days to 13 (IQR 20) days was observed in age group 50-64 years, and was
5 327 statistically significant ($p=0.019$). Mortality rate for all ages was 13.1% (95% CI
6 328 11.7%-14.8%) in period 1 and 22.7% (95%CI 15.5%-31.3%) in period 3 ($p=0.0187$).
7 329 Mortality rate was only statistically significant in aged 50-64 years ($p=0.0007$) but not
8 330 in aged 18-49 years ($p=0.9917$) and aged ≥ 65 years ($p=0.246$) (Table 2).
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332 **All-cause pneumonia**

15 333 In the entire study period, total hospitalization episodes for all-cause pneumonia was
16 334 453,999, of which 372,660 episodes in period 1 and 67,474 episodes in period 3.
17 335 Among the 67,474 patients in period 3, 331 were diagnosed with COVID-19 and
18 336 pneumonia. Monthly number of all-cause pneumonia peaked in January to March
19 337 each year (Figure 1C and Figure S1). Mean monthly number of hospitalizations for
20 338 all-cause pneumonia declined by 16.4% (95%CI 15.7%-17.1%, $p<0.0005$) from
21 339 6211 \pm 845.0 episodes in period 1 to 5190.3 \pm 593.8 episodes in period 3 ($p<0.0005$)
22 340 (Figure 1C). Estimated change in trend in the mean number of cases in period 3 was
23 341 -11% (95%CI -13% to -10%, $p<0.0005$). By log-linear model segmented regression,
24 342 relative risk of all-cause pneumonia in period 3 compared with period 1 was 0.98
25 343 (95%CI 0.98-0.99, $p<0.0005$) (Table S1).
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38 345 Overall, the incidence rate per 100,000 person-years was 1,169.7 in period 1, with
39 346 17.5% (95%CI 16.8%-18.2%, $p<0.0005$) reduction in period 3 to 964.5 per 100,000
40 347 person-years in period 3. Incidence rate ratio between period 1 and period 3 was
41 348 0.83 (95%CI 0.82-0.83, $p<0.0005$) (Table 1). The incidence rate decrease in period
42 349 3 compared to period 1 in all age groups.
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48 351 The overall median LOS for all-cause pneumonia episodes was 6 (IQR 9) days in
49 352 period 1 and 6 (IQR 10) days in period 3 ($p<0.005$) (Table 2). Different age groups
50 353 showed decrease in LOS but were only statistically significant in age 18-49 years
51 354 and 50-64 years. The mortality rate increased from 20.5% (95% CI 20.4%-20.6%) in
52 355 period 1 to 24.2% (95%CI 24.9%-25.6%) in period 3 ($p<0.005$) for all-cause
53 356 pneumonia. The increase in mortality rate was statistically significant in all age
54 357 groups (Table 2).
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5 359 For subgroup of aspiration pneumonia, total number of hospitalization in the entire
6
7 360 study period was 21,183, with 17990 episodes in period 1 and 2684 episodes in
8
9 361 period 3. Mean monthly number of aspiration pneumonia was 299.8 ± 31.3 in period 1
10
11 362 and 206.5 ± 30.5 in period 3 ($p < 0.0005$).

12 363

13 364

15 365 **COVID-19**

17 366 In period 3, the total reported cases of COVID-19 infection at age 18 or above was
18
19 367 10,348 [15]. Among these patients, 331 were diagnosed with pneumonia. Majority of
20
21 368 them were in the age group 65 years old or above ($n=175$). 58 of them were in age
22
23 369 group 18-49 while 98 patients in age group 50-64. None of the patients were
24
25 370 diagnosed with coinfection of COVID-19 and pneumococcal pneumonia.

26 371

27 372

29 373 **Influenza**

31 374 The total number of influenza A or B viruses detected from January 2015 to March
32
33 375 2021 in Hong Kong was 123,732. The monthly number of influenza detections
34
35 376 decreased drastically by 99.5% (95%CI 99.4%-99.5%, $p < 0.0005$) from $1,966 \pm 2179$
36
37 377 in period 1 to 10 ± 18 in period 3 (Figure 1D and Figure S1). The monthly average
38
39 378 number of respiratory specimens tested was 4313 ± 1172 in period 1 and 3203 ± 1868
40
41 379 in period 3.

42 380 By log-linear model segmented regression, relative risk of influenza was 0.92
43
44 381 (95%CI 0.88-0.95, $p < 0.0005$). Estimated change in trend in the mean number of
45
46 382 detections in period 3 was -99.0% (95%CI -99.3% to -98.7%, $p < 0.0005$) of that in
47
48 383 period 1 (Figure 1D)

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50 385

53 386 **Other diagnosis: acute kidney injury, PD peritonitis and fracture hip**

55 387 The monthly average number of hospitalization episodes for acute kidney injury in
56
57 388 period 1 and period 3 was 807.8 ± 87.5 and 911.7 ± 62.6 , respectively ($p < 0.0005$)

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59 389 (Figure 2) The monthly average number of hospitalization episodes for PD peritonitis

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3 390 was 246.7±27.7 in period 1 and 255.9±31.9 in period 3 (p=0.23). The monthly
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5 391 average number of hospitalization episodes for fracture hip was 432.9±53.1 in period
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7 392 1 and 417.3±51.6 in period 3 (p=0.37)
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394 Discussion

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396 Hong Kong is a city with population of 7.5 million where universal masking and social
397 distancing were widely practiced during COVID-19 pandemic period. This study
398 showed a drastic decrease in numbers of hospitalization for IPD and pneumococcal
399 pneumonia and a lesser but still very significant decrease in all cause pneumonia
400 after anti-COVID-19 measures in March 2020 to March 2021.

401

402 During COVID-19 period, decrease in incidence of IPD were observed in Taiwan and
403 Singapore [31,32]. The decrease in IPD in Hong Kong was greater magnitude
404 compare to other countries [33]. Our study added new information on the incidence
405 and severity of IPD, pneumococcal pneumonia and all-cause pneumonia in terms of
406 age-stratification.

407

408 In our COVID-19 patients, there was no pneumococcal co-infection. This may partly
409 be contributed by the infrequent investigation of pneumonia with pneumococcal
410 urinary tests and PCR assays. In an Italian study of 469 COVID-19 patients, 9% was
411 found to be positive for urinary pneumococcal antigen. However, the positive result
412 had no impact on clinical outcome [34]. In another study that investigated the
413 respiratory specimens of COVID-19 patients using PCR assays, 60% were found to
414 be positive for *Streptococcus pneumoniae* but it was unable to distinguish between
415 colonization and infection [35]

416

417 Introduction of the current pneumococcal conjugate vaccines has been highly
418 successful in reducing the incidence of pneumococcal diseases worldwide [36,37].
419 Vaccine efficacy of PCV13 against vaccine type IPD in children aged ≤ 5 years was
420 86%-96% [38]. In adults aged ≥ 65 years, the vaccine efficacy against vaccine type
421 IPD was reported as 75% and against vaccine type community-acquired pneumonia
422 were reported as 45.6% and 72.8% respectively [13,39]. In contrast, PPV23 only has
423 vaccine efficacy of 24% against vaccine type community acquired pneumonia in
424 aged ≥ 65 years [40]. In Hong Kong, a marked reduction in vaccine type IPD was
425 observed in children few years after implementation of PCV in 2009 [10,12].
426 However, the indirect effect on adult IPD was not evident. Annual number of adult
427 IPD hospitalization remains static in period 1 (Figure 1A). Universal masking and

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3 428 social distancing measures in Hong Kong was shown to have an association with
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5 429 decrease in the incidence of SARS-CoV2 [41,42] and influenza [43] during the
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7 430 COVID-19 pandemic. Our study showed 88.9% reduction in incidence of adult IPD.
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9 431 The drastic decrease in incidence of IPD included both vaccine and non-vaccine
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11 432 types and was comparable and greater than the reported figure after introduction of
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13 433 pneumococcal vaccines [13,37]. IPD can lead to significant mortality and morbidity
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15 434 [44]. Our study showed decrease in incidence and trend of IPD and were statistically
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17 435 significant. The decrease in mortality of IPD during the COVID-19 pandemics was
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19 436 statistically insignificant, which can be contributed by the relative small sample size.
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21 437
22 438 Incidence of all-cause pneumonia showed a much lower magnitude of decrease with
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24 439 the lesser decrease observed in those aged ≥ 65 years (supplementary file, Figure
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26 440 S2C). In our study, patients with diagnosis of pneumonia during the hospital stay
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28 441 were included. On review of data, majority of pneumonia patients in age group 65
29
30 442 years or above had other comorbidities including dementia, diabetes mellitus and
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32 443 malignancy included in the same admission. The prevalence of chronic disease is
33
34 444 higher in elderly. The population of Hong Kong has been seeing an aging trend and
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36 445 the population of 65 years old or above was 1,114,600 in 2015, and increased to
37
38 446 1,371,800 in 2020. The incidence of chronic disease, for example, malignancy
39
40 447 increased by 38.1% from 2008 to 2018 [17]. Patients with chronic diseases are at
41
42 448 higher risk of acquiring infection including pneumonia. Moreover, chronic disease
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44 449 can be the cause leading to hospital admission with subsequent development of
45
46 450 hospital acquired pneumonia.
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48 451
49 452 Pneumococcal pneumonia and IPD are debilitating diseases which have been
50
51 453 shown to require long length of hospital stay and high hospital cost [45,46]. The LOS
52
53 454 in pneumococcal pneumonia was slightly increased from 17.7 to 19.5 days but was
54
55 455 statistically insignificant. Looking into different age groups, only patients with age 50
56
57 456 to 64 years old showed statistically significant increase in LOS, while patients in age
58
59 457 group 18 to 49 years old and 65 years old or above showed slight decrease. The
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61 458 severity of pneumococcal pneumonia were comparable in the two periods.
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63 459
64 460 Health seeking behaviour was also evaluated in our study. Admissions of non-
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66 461 communicable diseases revealed either statistically insignificant decrease in hospital

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3 462 attendance or statistically significant increase in hospital attendance. The incidence
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5 463 of AKI increased in our study from 807.8 ± 87.5 in period 1 to 911.7 ± 62.6 in period 3.
6
7 464 Drug induced AKI is an important cause in Asia [47]. Possible explanation can be
8
9 465 due to the health seeking behaviour of patients with intake of over-the counter
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11 466 medication for mild diseases prior seeking help from the hospital. Yet the exact
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13 467 cause of increase in incidence of AKI should be investigated. Our study covered
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15 468 more than one year time for COVID-19 pandemics with a relatively stable number of
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17 469 hospital attendance. Hence, the decrease in incidence of pneumococcal pneumonia,
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19 470 IPD and all-cause pneumonia cannot be explained by health seeking behaviour
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21 471 alone.

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23 472
24 473 Collateral damages were observed during the COVID-19 pandemic [48-49], some of
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26 474 which were contributed by the decrease in general medical services to concentrate
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28 475 healthcare resources for the care of SARS-CoV-2 patients and the prevention of
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30 476 possible viral spread. However, due to the relatively small number of COVID-19
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32 477 cases in Hong Kong, provision of acute medical services was minimally disrupted. In
33
34 478 our study, the data on admissions for fractures, acute kidney injury and PD peritonitis
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36 479 showed no decrease during the COVID-19 pandemic. Hence the observed
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38 480 decrease in hospital admissions for pneumococcal pneumonia, IPD and all-cause
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40 481 pneumonia should not be artefactual.

41 482 42 483 43 484 **Limitations**

44 485 This is a retrospective observational study and the direct effect of universal masking,
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46 486 social distancing (e.g. closure of schools, bars and pubs) and other strategies on
47
48 487 pneumococcal pneumonia, IPD and all-cause pneumonia cannot be ascertained.
49
50 488 However, our study covered a period of more than one year when infection control
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52 489 related behavioral changes were made throughout, with a consistent observation of
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54 490 decrease in hospitalization for these diseases seen. Other factors, namely ambient
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56 491 temperature and AQHI, that might have possible effect on the hospitalization
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58 492 numbers were also included in our analysis. However, the individual effects of
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60 493 universal masking, social distancing and other strategies cannot be evaluated
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separately. It is modelled by the effect of pandemic as a whole in our study.

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4 496 Our study focused on hospital hospitalization numbers in the Hospital Authority. For
5 497 IPD, the incidence was obtained from Central of Health Protection, HKSAR, which
6 498 included data from both public and private hospitals data. The LOS and mortality
7 499 data of IPD were retrieved from the database in Hospital Authority. Admissions to
8 500 private hospital or those received out-patient treatment for pneumococcal pneumonia
9 501 and all-cause pneumonia were not included in our study. However, Hospital
10 502 Authority is the largest healthcare provider in Hong Kong which provides 90% of in-
11 503 patient services in Hong Kong [26]. Data from Hospital Authority is representable for
12 504 the general epidemiology of Hong Kong.
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23 506 **Conclusions**

24 507 The incidence of pneumococcal pneumonia, IPD and all-cause pneumonia
25 508 decreased during COVID-19 pandemics compare to the data in previous five years.
26 509 This was observed with widespread practice of universal masking and social
27 510 distancing. While causality cannot be shown from our data, it is likely that the
28 511 decrease could be attributed to universal masking and social distancing, which would
29 512 have reduced the transmission of bacteria and viruses and related bacterial
30 513 superinfection.
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3 515 **Figure caption**
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6 516 **Figure 1.** Trend analysis of monthly numbers of invasive pneumococcal disease
7 517 (IPD), pneumococcal pneumonia, all-cause pneumonia, and influenza in Hong Kong,
8 518 January 2015 to March 2021. Numbers of IPD were those obtained through
9 519 mandatory notification. Numbers of pneumococcal pneumonia and all-cause
10 520 pneumonia were territory-wide hospitalizations by discharge diagnoses. Numbers of
11 521 influenza viruses were those detected in respiratory specimens in a territory-wide
12 522 laboratory surveillance. The two vertical lines delineated the time intervals from
13 523 January 2015 to December 2019 (period 1, prior to COVID-19), January to February
14 524 2020 (period 2, excluded from analysis) and March 2020 to March 2021 (period 3,
15 525 COVID-19 pandemic).
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24 527 **Figure 2.** Admission numbers of fracture hip, acute kidney injury and PD peritonitis.
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Table 1. Incidence and number per 100,000 person year of pneumococcal pneumonia, invasive pneumococcal disease (IPD) and pneumonia

	All ages		18-49 years		50-64 years		≥65 years	
Disease ^a	No. of episodes	Incidence rate per 100,000 person-years	No. of episodes	Incidence rate per 100,000 person-years	No. of episodes	Incidence rate per 100,000 person-years	No. of cases	Incidence rate per 100,000 person-years
IPD								
Period 1	699	2.2	125	0.7	195	2.2	379	6.2
Period 2	26	2.4	5	0.9	6	2.0	15	6.6
Period 3	17	0.2	3	0.08	8	0.4	6	0.4
% reduction ^b		88.9% (79.8%-98.0%) ^{***}		88.6% (66.8%-110.4%) ^{***}		81.3% (62.1%-100.4%) ^{***}		93.5% (82.2%-104.8%) ^{***}
IRR ^c		0.11(0.07-0.18) ^{***}		0.11(0.04-0.36) ^{***}		0.19(0.09-0.38) ^{***}		0.07(0.03-0.15) ^{***}
Pneumococcal pneumonia								
Period 1	1,970	6.2	217	1.3	435	4.9	1,318	21.7
Period 2	74	6.9	11	2.0	14	4.7	49	32.4
Period 3	119	1.7	8	0.2	24	1.2	87	5.9
% reduction		72.5% (65.9%-79.1%) ^{***}		82.5% (64.5%-100.5%) ^{***}		74.8% (61.0%-88.6%) ^{***}		73.0% (65.2%-80.8%) ^{***}
IRR ^c		0.28(0.23-0.33) ^{***}		0.18(0.09-0.35) ^{***}		0.25(0.17-0.38) ^{***}		0.27(0.22-0.34) ^{***}
All-cause pneumonia								
Period 1	372,660	1169.7	19,502	115.3	38,360	432.4	314,798	5177.1
Period 2	13,865	1288.2	843	153.6	1,448	484.6	11,574	5062.3
Period 3	67,474	964.5	2,473	69.3	6,181	318.3	58,820	3958.0
% reduction		17.5% (16.8%-18.2%) ^{***}		39.9% (37.1%-42.7%) ^{***}		26.4% (24.3%-28.5%) ^{***}		23.5% (22.8%-24.3%) ^{***}
IRR ^c		0.83(0.82-0.83) ^{***}		0.60(0.58-0.63) ^{***}		0.74(0.72-0.76) ^{***}		0.77(0.76-0.77) ^{***}

^a Period 1, January 2015 to December 2019 (before covid-19); period 2, January 2020 to February 2020 (transition period); period 3 March 2020 to March 2021 (post-COVID-19).

^b Percentage reduction in period 3 relative to period 1 as the baseline

^c Incidence rate ratio between period 1 and period 3

*p <0.05 to 0.01, **p <0.01 to 0.005, ***p <0.005

Table 2. Median length of stay and mortality rate of pneumococcal pneumonia, invasive pneumococcal disease (IPD) and pneumonia in the periods

	Median length of stay; days (IQR)#				Mortality rate; % (95%CI)			
	All ages	18-49 years	50-64 years	≥65 years	All ages	18-49 years	50-64 years	≥65 years
IPD								
Period 1	12 (16)	13 (19)	13 (17)	12 (13)	12.1 (8.8-16.1)	9.1 (3.4-18.7)	8.4 (3.7-15.9)	15.3 (10.3-21.4)
Period 3	12 (11)	4 (3)	16 (19)	12 (6)	6.3 (1.6-30.2)	0.0	0.0	14.3 (3.6-57.9)
Pneumococcal Pneumonia								
Period 1	9 (14)	7 (14)	9 (15)*	10 (14)	13.1 (11.7-14.8)*	4.2 (1.9-7.7)	7.5 (5.3-10.5)**	16.3 (13.6-18.7)
Period 3	12 (17)	7 (13)	13 (20)*	12 (16)	22.7 (15.5-31.3)*	0.0	29.2 (12.6-51.1)**	23.0 (14.6-33.2)
All-cause pneumonia								
Period 1	6 (9)***	4 (6)***	6 (9)**	6 (10)	20.5 (20.4-20.6)***	5.3 (4.9-5.6)*	13.0 (11.4-12.0)***	22.4 (22.2-22.4)***
Period 3	6 (10)***	4 (8)***	6 (10)**	6 (10)	24.2 (24.9-25.6)***	6.8 (5.9-7.9)*	16.1 (5.2-17.0)***	27.0 (26.6-27.3)***

*p <0.05 to 0.01, **p <0.01 to 0.005, ***p<0.005

IQR= interquartile range

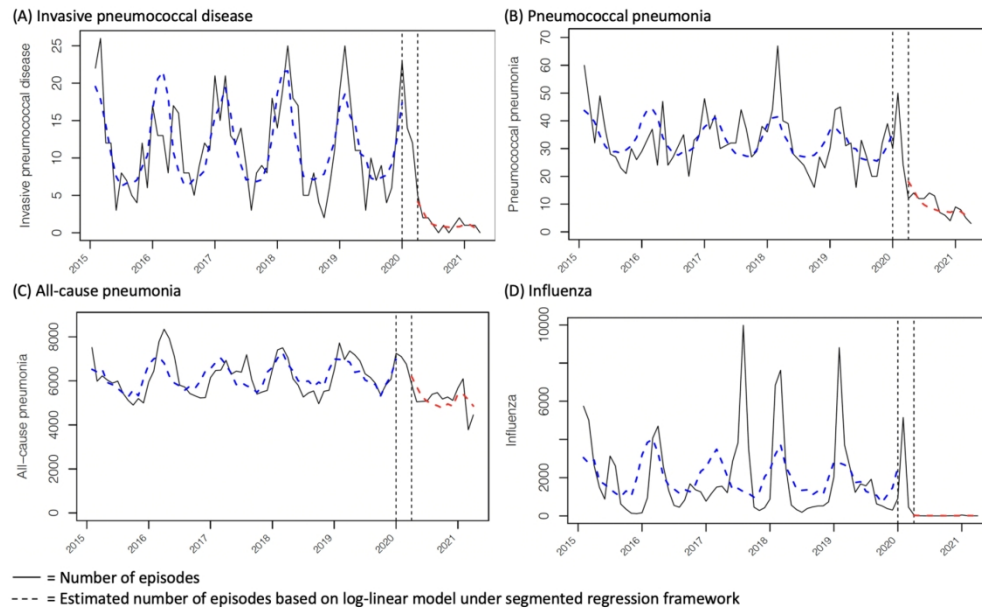


Figure 1. Trend analysis of monthly numbers of invasive pneumococcal disease (IPD), pneumococcal pneumonia, all-cause pneumonia, and influenza in Hong Kong, January 2015 to March 2021. Numbers of IPD were those obtained through mandatory notification. Numbers of pneumococcal pneumonia and all-cause pneumonia were territory-wide hospitalizations by discharge diagnoses. Numbers of influenza viruses were those detected in respiratory specimens in a territory-wide laboratory surveillance. The two vertical lines delineated the time intervals from January 2015 to December 2019 (period 1, prior to COVID-19), January to February 2020 (period 2, excluded from analysis) and March 2020 to March 2021 (period 3, COVID-19 pandemic).

352x218mm (144 x 144 DPI)

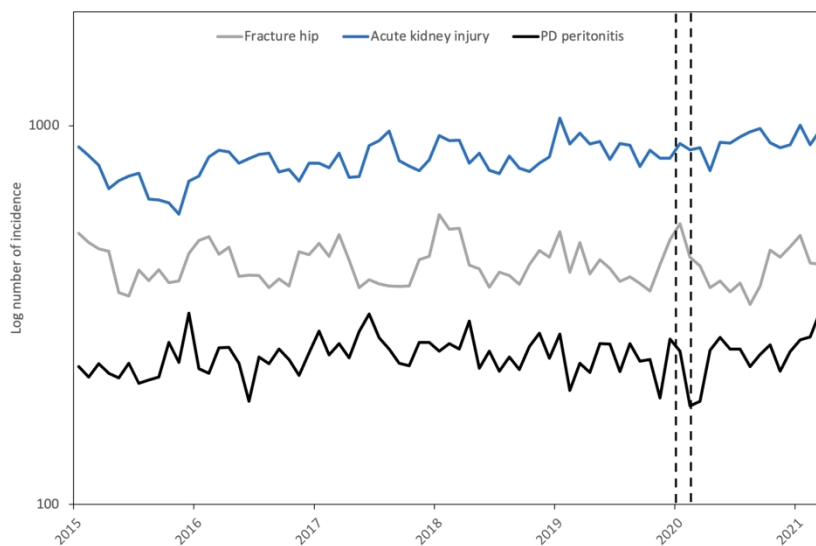


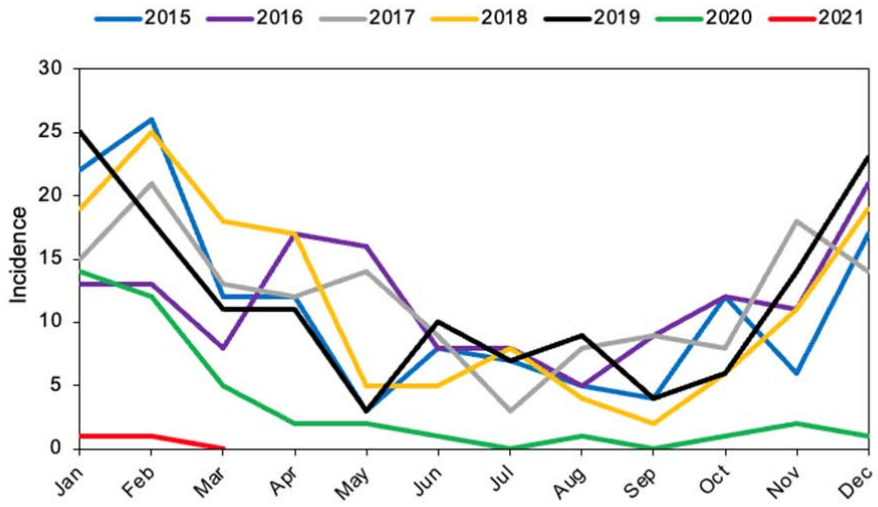
Figure 2. Admission numbers of fracture hip, acute kidney injury and PD peritonitis.

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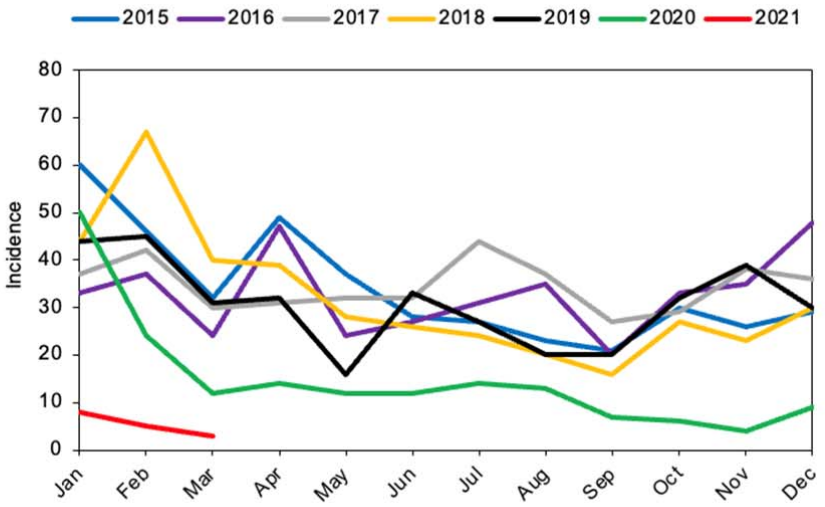
Supplementary file.

Figure S1. Monthly incidence of (A) Invasive pneumococcal disease (IPD), (B) Pneumococcal pneumonia, (C) All-cause pneumonia and (D) Influenza in January 2015 to March 2021.

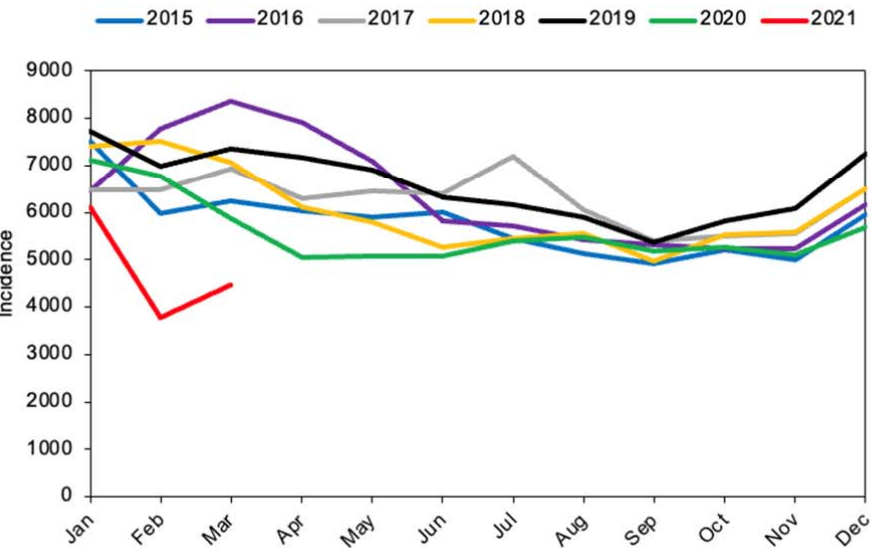
(A) Invasive pneumococcal disease



(B) Pneumococcal pneumonia



(C) All-cause pneumonia



(D) Influenza

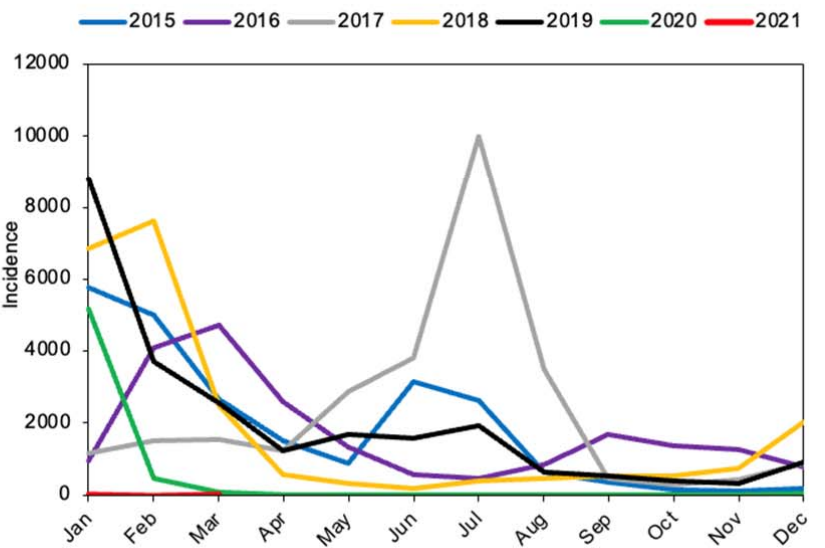
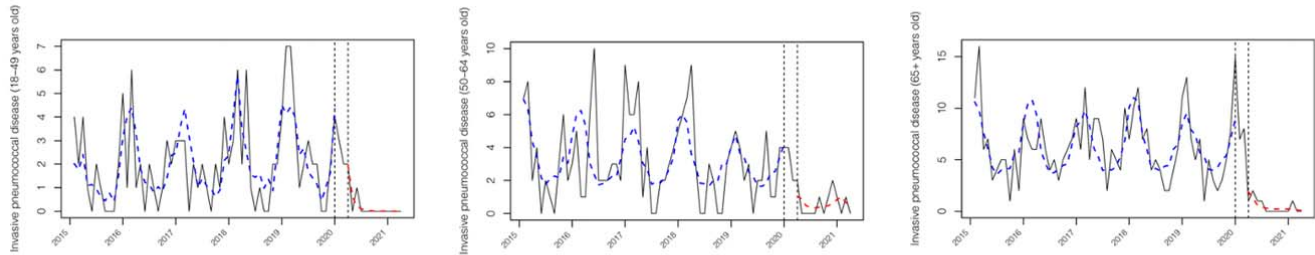
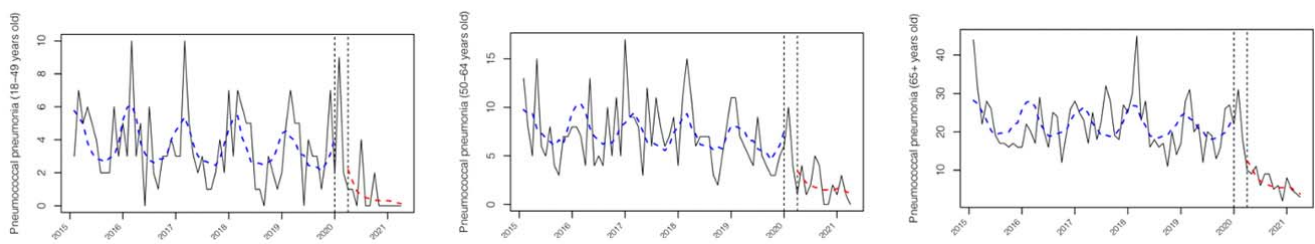


Figure S2. Trend analysis of monthly number of (A) age-stratified hospitalizations for invasive pneumococcal disease, (B) age-stratified hospitalizations for pneumococcal pneumonia, (C) age-stratified hospitalizations for and (D) monthly percentage of air quality health index (AQHI) high to serious and (E) monthly average ambient temperature.

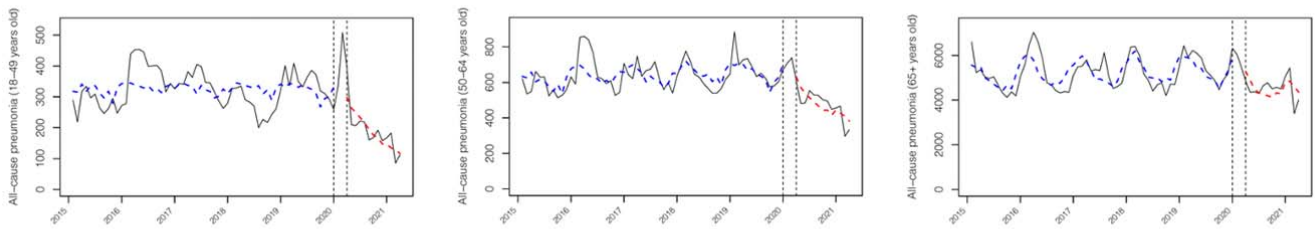
(A) Invasive pneumococcal disease



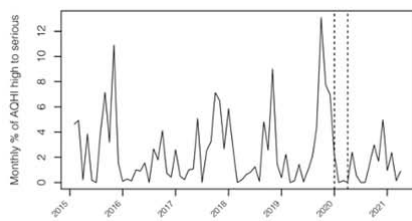
(B) Pneumococcal pneumonia



(C) All cause pneumonia



(D) Monthly % of AQHI high to serious



(E) Monthly average temperature

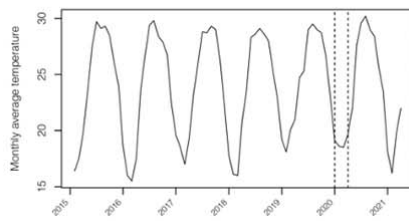


Table S1. Trend analysis of monthly number of hospitalization by age groups in periods before and after the COVID-19 pandemic

	Relative risk (95% CI)		Change in trend#
	Period 1 ^	Period 3^	
IPD			
All ages	1.0020 (0.9977-1.064)	0.8484 (0.7501-0.9597)**	-70.39% (-86.55% to -34.73%)**
18-49 years	1.0129 (1.0022-1.0238)	0.5272 (0.2176-1.2772)	-31.27% (-89.72% to 359.72%)
50-64 years	0.9969 (0.9888-1.0051)	0.9585 (0.8087-1.1362)	-70.43% (-92.80% to 21.42%)
65 years or above	1.0012 (0.9953-1.0071)	0.7777 (0.6111-0.9897)*	-70.83% (-91.59% to 1.12%)
Pneumococcal Pneumonia			
All ages	0.9978(0.9953-1.0004)	0.9042(0.8621-0.9483)***	-42.79% (-59.36% to -19.48%)*
18-49 years	0.9964(0.9887-1.0042)	0.6768(0.2171-2.1093)	-32.32% (-78.29% to 110.93%)
50-64 years	0.9962(0.9907-1.0017)	0.9174(0.8260-1.0189)	-50.21% (-76.93% to 7.48%)
65 years or above	0.9986(0.9954-1.0017)	0.9107(0.8612-0.9640)*	-41.19% (-60.82% to -11.73%)*
All-cause pneumonia			
All ages	1.0014(1.0012-1.0016)***	0.9835(0.9815-0.9855)***	-11.24% (-12.76% to -9.7%)***
18-49 years	1.0000(0.9992-1.0008)	0.9263(0.9164-0.9364)***	-6.05% (-13.41% to 1.94%)
50-64 years	1.0015(1.0009-1.0021)***	0.9620(0.9556-0.9684)***	-9.32% (-14.14% to -4.22%)***
65 years or above	1.0011(1.0009-1.0013)***	0.9879(0.9858-0.9901)***	-13.30% (-12.94% to -9.64%)***

^Trend in period 1 (January 2015 to December 2019) and 3 (March 2020 to March 2021), the relative risk expressed the month-to-month change in hospitalization numbers of period 3 compared to period 1

#Estimate the change in trend in the mean monthly number of cases in period 3, compare with the monthly trend in period 1

*p <0.05 to 0.01, **p <0.01 to 0.005, ***p<0.005

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	7-8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	7-8
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	7-8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	7-8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8-9
		(b) Describe any methods used to examine subgroups and interactions	8-9
		(c) Explain how missing data were addressed	N/A
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	8-9

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60**Results**

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11-15
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11-15
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	11-15
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11-15
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11-15

Discussion

Key results	18	Summarise key results with reference to study objectives	16-17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18-19
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16-19
Generalisability	21	Discuss the generalisability (external validity) of the study results	16-18

Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	3
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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.