Meteorological Factors Facilitated Increased Legionnaires' Disease Notifications and Mortality Pre-COVID-19 and COVID-19 in Hong Kong

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Article

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Abstract

Annual notification number of Legionnaires' disease (LD) increased from 66 cases in 2015 to 104 cases in 2020 in Hong Kong, with a case fatality rate (CFR) of 17.3% in 2020. This study investigated possible meteorological factors associated with confirmed LD cases and deaths. The negative binomial regression model was used for monthly LD confirmed cases and the Poisson regression model was used for monthly LD mortality cases. A decision tree model was adopted to identify the thresholds of meteorological factors if any. The confirmed LD cases were highest in July while the LD mortality were highest in August. A negative binomial regression model confirmed that maximum air temperature (P=0.081, RR=1.3, 95% CI=0.97-1.75) and rainfall (P=0.009, RR=1.02, 95% CI=1.0004-1.003) were positively correlated with the increase in confirmed LD cases. A Poisson regression model confirmed that maximum air temperature (P=0.034, RR=1.71, 95%CI=1.04-2.80) was positively correlated with the surge in LD mortality. When rainfall exceeds 78.8 mm, the public should be alerted of the increased risk of contracting LD. Temperature and rainfall were positively associated with the confirmed LD cases in Hong Kong.

Introduction

Legionnaires' disease (LD) ranked fourth (17.3%) in terms of case fatality rate (CFR) among the 13 notifiable diseases with all other causes (AOC) in Hong Kong in 2020 (Supplementary: Table S1). The associations of environmental factors with confirmed Legionnaires' Disease (LD) cases have been reported in the literature; Tanimoto et al[1] found apparent evidence of Legionella spp. bacteria being transmitted via water mist in hot-spring spas among the ageing populations in Japan. Lam et al[2] found that Legionella spp. bacteria widely colonized in cooling towers in Singapore, which has abundant high-rise buildings. With the COVID-19 lockdown and subsequent reopening, Rhoads et al[3] expressed concern that extended water stagnation in buildings would increase the number of confirmed LD cases, and Palazzolo et al[4] reported that an Italian male aged 40 years who worked as a restaurant dishwasher contracted LD 3 days after the COVID-19 lockdown restriction was eased in Rome. O'Connor et al[5] developed a PCR test kit to detect bacteria in the Legionella genus in water with a single test. Hozalski et al6[6] suggested that flushing of stagnant water after the COVID-19 shutdown could reduce the Legionella infection risk, and Lancaster et al[7] encouraged building management personnel to monitor water stagnancy before reopening to reduce morbidity and mortality.

The literature reports clinical epidemiological evidence of LD and COVID-19 pneumonia coinfection, with Legionella spp. being the main species isolated in Europe[8,9,10], the United States (US)[11], and Canada[12]. Dey et al1[13] reported LD and COVID-19 coinfection in patients, similar to that of "1918 Spanish flu" bacterial coinfection. Lai et al1[14] warned that up to 50% of patients with LD and COVID-19 coinfection do not survive.

Other works in the literature identified climatic variables and seasons associated with the number of confirmed LD cases. Ricketts et al[15] explored quarterly and annual data and found some evidence suggesting that the effect of the interaction of relative humidity and temperature on the increased number of confirmed LD cases in England was highly significant. Precipitation increased the confirmed LD cases in Taiwan[16]. Brandsema et al[17] found an association of warm and wet weather with an increased number of confirmed LD cases in the summer of 2010 in the Netherlands. Oda et al[18] reported a male aged 62 years contracting LD after the Heavy Rain Event of July 2018 in Japan. Temperature, rainfall, and atmospheric pressure have been associated with the numbers of confirmed LD cases in Denmark, Germany, Italy and the Netherlands[19]. The average temperature was significantly associated with the number of confirmed LD cases in South Korea[20]. Simmering et al[21] analyzed LD cases in the middle Atlantic region and confirmed that LD cases were more common in summer in the US. Falconi et al[22] observed a seasonal pattern from mid-September to mid-August in the number of confirmed LD cases after 2003 in the US. Ozeki et al[23] found two seasonal peaks of confirmed LD cases between June and November 2005–2009 in both Tokyo and Saitama, Japan.

Previous literature focused on the association of the number of confirmed LD cases with environmental factors, epidemiological factors, or meteorological factors in Asia, Europe, or North America. Accordingly, our research aims to fill the knowledge gap and analyze the number of confirmed LD cases and deaths in association with potential meteorological factors in HK.

Methods

Data

We obtained (a) daily death micro-data sets from the Census and Statistical Department of HK from 2015–2020, (b) monthly meteorological variables from the HK Observatory Department from 2015-2021[24] and (c) monthly number of confirmed LD cases from the Department of Health from January 2015 to November 2021[25]. We retrieved LD deaths by using the International Classification of Disease, 10th revision (ICD-10) A48.1 in the death registry data from the Census and Statistics Department of Hong Kong. All methods were performed in accordance with the relevant guidelines and regulations.

Statistical analysis

We employed negative binomial regression to model our raw monthly confirmed LD case as the dependent variable considering raw meteorological factors as independent variables since we found that the raw monthly confirmed LD cases are over-dispersed counts variables where the mean of the confirmed LD cases does not equal the variance confirmed LD cases. While, we used Poisson regression to model raw monthly LD deaths with raw meteorological variables, because the mean and variance of the LD deaths are almost the same. Finally, we constructed a decision tree to identify possible weather thresholds for public policy decision making regarding LD.

Results

Confirmed cases mortality

LD ranked the fourth (17.3%) in terms of CFR among the 13 notifiable diseases with all other cause (AOC) mortality data in HK in 2020. The CFR of LD more than doubled (101.9%) in HK from 2019–2020 (Fig. 1), when the COVID-19 outbreak began.

A total of 591 confirmed LD cases were reported in HK from January 2015-November 2021. We found that the confirmed LD cases increased in HK during this time (Fig. 2).

June to August had the largest number of confirmed LD cases (40%), and the summer month of July accounted for the largest number of accumulated confirmed LD cases (15%) (Fig. 3).

The annual rate of confirmed LD cases increased from 0.88 to 1.4 per 100,000 standard population from 2015 to 2018 and remain 1.4 PTSP in 2018, 2019 and 2020, respectively. An abnormal surge in the number of monthly confirmed LD cases (21 cases) in February 2020 is shown in Supplementary: Figure S1. This was the month immediately after the first case of COVID-19 case was reported in HK in January 2020.

Fifty-three LD deaths (case fatality rate 10.1%) were identified in HK from 2015 to 2020. We found that the annual increase in LD CFR doubled from 2019 to 2020 in HK after the COVID-19 outbreak. Leung et al[26] found a more than 4-fold increase in the number of confirmed LD cases from 2005 to 2015. August had the largest number of accumulated LD deaths in our study period (Fig. 3).

Descriptive analysis of confirmed LD cases and mortality with monthly weather variables

We now examined the associations of confirmed LD cases and mortality in HK with the city's meteorological variables, described below. Supplementary: Table S2 shows the monthly number of confirmed LD cases with meteorological variables covering 83 months in HK from 2015–2021. Supplementary: Table S3 shows monthly LD mortality with meteorological variables covering 72 months in HK from 2015–2020. Since the LD mortality data we retrieved were daily data, we stratified the LD-related mortality into months per year. We aimed to determine whether the number of confirmed LD confirmed cases and related deaths in HK were associated with monthly meteorological variables, including maximum air temperature (in °C), average air temperature (in °C), relative humidity and rainfall (in mm).

Negative binomial regression for LD confirmed cases

Previous studies[22,27] used Poisson regression to model confirmed LD cases. On the basis of their approach, we conducted the goodness of fit and Wald's statistics tests, which rejected the null hypothesis (Supplementary: Appendix D and Table S6). Then, we constructed a negative binomial regression model[28], and the results were confirmed by the t test, log-likelihood ratio test, and $\chi 2$ tests(Supplementary: Appendix E and Table S7).

Using the number of confirmed LD cases in the 83-month dataset from January 2015 to November 2021, we constructed a negative binomial regression model (Supplementary: Appendix G) to study the marginal effects of air temperature, relative humidity, and rainfall on confirmed numbers. Table 1 shows that the maximum air temperature and rainfall amount were statistically associated, but the relative humidity and average air temperature were not.

Table 1
Negative binomial model results for the number of confirmed LD cases associated with monthly weather variables. CI, confidence interval; RR, relative risk; S.E., standard error; 95% CI, 95% confidence interval of relative risk. *$p < 0.1$, **$p < 0.05$, ***$p < 0.01$. N = 591 number of confirmed LD cases.

Variable	Coefficient	S.E.	Pr(> z)	RR	95% CI
Intercept	0.478	1.625	0.769	1.61	0.07-39
Maximum air temperature	0.264	0.151	0.081*	1.3	0.97–1.75
Average air temperature	-0.231	0.154	0.135	0.79	0.60-1.075
Relative humidity	0.493	1.871	0.792	0.61	0.02-23
Rainfall	0.002	0.001	0.009***	1.02	1.0004–1.003

The relative risk associated with the maximum air was 1.3 while the relative risk associated with the rainfall amount was 1.02. This confirmed that monthly maximum air temperature was the most important factor positively correlated to the number of monthly confirmed LD cases, followed by rainfall. To examine the effect of the month of July, we defined the month of July of every year as a categorical variable (true/false, true if the confirmed case occurred in July, false if otherwise). The July effect was statistically significant (P = 0.025), as shown in Supplementary: Table S4. This quantitatively confirmed our visual finding that July had the largest number of accumulated monthly confirmed LD cases, as shown in Fig. 3. Furthermore, to examine the February 2020 spike in confirmed LD cases, we defined February 2020 as a categorical variable (true/false, true if the confirmed case occurred in February 2020, false if otherwise). Similarly, the February 2020 spike was statistically significant (P = 0.016) (Supplementary: Table S5). The relative risk associated with the February 2020 spike was 3.27 (95% CI 1.24–8.58). This further confirmed the abnormally large number of confirmed LD cases in February 2020 amid the COVID-19 pandemic, as shown in Supplementary: Figure S1.

Poisson regression for LD mortality

The 72-month monthly LD-related mortality data had a Poisson distribution because the mean (0.74) almost equalled the variance (0.79). We also confirmed the hypothesis by the goodness of fit test(Supplementary: Appendix F). Poisson regression (Supplementary: Appendix G) was applied to study the marginal effects of air temperatures, relative humidity, and rainfall on mortality numbers. Table 2 shows that the factors of maximum air temperature, average air temperature, and rainfall amount were statistically significant, but relative humidity was not. The relative risk associated with the maximum air temperature equalled 1.71. This confirmed that monthly maximum air temperature was the most important factor positively related to the number of monthly LD deaths.

Table 2

Poisson model results for the number of LD-related deaths associated with monthly weather variables. CI, confidence interval; RR, relative risk; S.E., standard error; 95% CI, 95% confidence interval of relative risk. *$p < 0.1$, **$p < 0.05$, ***$p < 0.01$. $N = 53$ number of LD-related deaths

Variable	Coefficient	S.E.	Pr(> z)	RR	95% CI
Intercept	-6.585	2.622	0.012**	0.001	8×10^{-6}-0.24
Maximum air temperature	0.536	0.252	0.034*	1.71	1.04–2.80
Average air temperature	-0.424	0.253	0.093*	0.65	0.40–1.07
Relative humidity	3.14	2.397	0.190	23.11	0.21–2537
Rainfall	-0.002	0.001	0.035**	0.997	0.9957–0.9998

Decision management for LD

Considering that maximum monthly air temperature and rainfall amount were important factors that were positively associated with the number of monthly confirmed LD cases, we built a decision tree model[29] (Supplementary: Appendix G). When rainfall reaches the “danger” zone, i.e., when the amount of rainfall is above 78.8 (in mm) and the Gini impurity of rainfall equals 3.4%, public messaging should alert the general public and healthcare providers to the risk of new-onset LD (Supplementary: Figure S2). We found that a large number of confirmed LD cases occurred when rainfall was higher than or equal to 334.8 (in mm) on the right side of the tree in Supplementary: Figure S3.

Discussion

Our retrospective study analyzed a total of 591 confirmed LD cases in HK from 2015–2021 and 53 LD-related deaths in HK from 2015–2020. The LD case fatality rate remained high, at over 10%. An abnormal increase in the number of confirmed LD cases occurred in February 2020, which was the month immediately following that of the first reported COVID-19 case in HK (January 2020). An increase in the LD notification number was observed from 2015 to 2020 (157%), and the annual increase of CFR of LD doubled (101.9%), from 2019 to 2020, after the COVID-19 outbreak. Overall, June to August had the largest number of confirmed LD cases (40%), which is in accordance with that of Ricketts et al,15 and the summer month of July accounted for the largest number of accumulated confirmed LD cases (15%) from 1 January 2015 to 30 November 2021. In addition to HK, North America, Europe, and Australia also experienced increases in the number of confirmed LD cases amid the COVID-19 pandemic.[30] We also found that the number of confirmed LD cases and related deaths had a lag of approximately one month, from July to August, which is in accordance with Riddell et al who stated that the incubation period of Legionella spp. is 2–10 days.[31] We also found that the LD-related death characteristics by gender and age are highly consistent with that of the confirmed LD cases in Leung et al.[26]

As reported in the previous study[17], warm weather is an important factor in LD development (Falconi et al[22] found July to be the most significant month). Regarding the number of monthly confirmed LD cases in HK from January 2015-November 2021, our study data quantitatively supplements that of Leung et al[26] in terms of the number of confirmed LD cases in HK(Supplementary: Table S4). Furthermore, we are the first to report that the February 2020 spike was positively correlated with an abnormally large number of confirmed LD cases in HK in 2020; February 2020 was the month immediately following that of the first reported case of COVID-19 in HK (January 2020). In recent years, there has been increasing interest in studying the meteorological factors potentially associated with the increase in the number of confirmed LD cases. Unexpectedly, our study found that in HK, relative humidity ($P > 0.05$) was not significantly associated with the number of confirmed LD cases or related deaths; these results are in contrast with those of Ricketts et al, who found a significant association with humidity in England and Wales,[15] but in accordance with those of Chen et al in Taiwan.[16] Temperature and amount of rainfall, on the other hand, are related to the confirmed LD cases in HK, which is in accordance with studies in Scotland[16], Netherlands[17], Taiwan[19], Denmark[20], and Seoul Korea[27].

Strong seasonal patterns were observed in the monthly data for maximum air temperature, average air temperature, relative humidity, and rainfall, though the two air temperature variables were highly correlated visually, which is in accordance with Ozeki et al.23 Our initial simple analysis using 83-month-average (83 MA) and relative risk found that the probability of contracting LD was inconclusive; for example, the relative risks associated with the monthly maximum air temperature above the 83 MA (26.9ºC, RR = 0.98, 95% CI = 0.88–1.07), the monthly average air temperature above the 83 MA (24.2ºC, RR = 1.03, 95% CI = 0.93–1.13), relative humidity and rainfall were inconclusive. Likewise, we found that the probabilities of dying from LD were increased by 72% and 62% when exposed to a monthly maximum air temperature above the 72 MA (26.7ºC, RR = 1.72, 95% CI = 1.06–2.79) and a monthly average air temperature above the 72 MA (24.05ºC, RR = 1.62, 95% CI = 1.014–2.595); however, the results of relative humidity and rainfall were inconclusive (RR = 0.65, 95% CI = 0.416–1.018; RR = 1.03, 95% CI = 0.658–1.620), respectively(Supplementary: Appendix H). Therefore, we further used more appropriate statistical models to analyze the raw number of confirmed LD cases (instead of transformed variable) as the response variable and raw weather variables (instead of transformed variables) as the explanatory variables to achieve conclusive results.[32] Our study is the first to use negative binomial regression to model the number of confirmed LD cases and confirm that maximum air temperature is a robust risk factor positively related to the number of monthly confirmed LD cases (P = 0.081, RR = 1.3, 95% CI = 0.71–1.75). Rainfall was also positively related to the number of monthly confirmed LD cases with a relative risk marginally higher than one (P = 0.009, RR = 1.02, 95% CI = 1.0004–1.003). Furthermore, our Poisson regression model confirmed that maximum air temperature was positively related to the number of LD-related deaths (P = 0.034, RR = 1.71, 95% CI = 1.04–2.80).

From a public healthcare management policy perspective, our retrospective study suggests that the local government should inform the general public more about LD risk in HK. Frequent disinfection of water pipes in buildings during COVID-19 lockdowns should be implemented before reopening to prevent LD. Testing for LD and COVID-19 coinfection are also suggested to avoid missing a potential LD case in a COVID-19 patient. These are ongoing public health concerns. Rainfall exceeding 78.8 (in mm) is likely to increase the likelihood of contracting LD in HK, which is in accordance with Oda et al.[18] We hypothesized that during the hot summer months (June-August)[29] and rainy days in Hong Kong, more people tend to stay indoors longer with the air-conditioning turned on in the office or at home in a typical summer month. This could potentially result in people inhaling contaminated water aerosols released from the air-conditioning.[33] As such, this could potentially increase the risk of contracting and dying from LD during the hot summer months. However, this hypothesis should be tested by future study. Weather related risk alerts should be disseminated from the HK Observatory Department to the general public and healthcare professionals when the weather risk threshold identified in our study is reached to prevent LD in HK; government should also educate people on regular air-conditioning maintenance during hot summers to minimize confirmed LD cases and deaths in HK.

Conclusion

The annual case fatality rate of LD doubled from 2019 to 2020 in HK after the COVID-19 outbreak. The risk of contracting LD in July (P = 0.025, RR = 1.81) was 81% higher than the risk in any other month. Negative binomial regression confirmed that maximum air temperature (P = 0.081, RR = 1.3) and rainfall (P = 0.009, RR = 1.02) were positively related to the number of confirmed LD cases. Poisson regression found that maximum air temperature (P = 0.034, RR = 1.71) was positively correlated to the number of LD-related deaths. From a public policy perspective, the general public and healthcare professionals should be alerted when the amount of rainfall increases above 78.8 (in mm), which will increase the likelihood of contracting LD in HK because people would be highly likely or likely to stay indoors longer during rainy days and hot summers with air-conditioning on for potential inhalation of contaminated air aerosols.

Declarations

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Author contributions statement

Y.Z. conceived and designed the analysis; contributed analysis tools; conducted the analysis; drafted the paper and revised the paper. F.C. conceived and designed the analysis; reviewed and revised the paper; and managed the project. G.T. conceived and designed the analysis; collected data; reviewed and revised the paper. L.Y. reviewed and revised the paper; checked compliance. All authors reviewed the manuscript.

Declaration of competing interest

The authors declare that there are no competing interests.

Data Availability Declaration

Some examples of data availability statements are given below: The data that support the findings of this study are available:

1) From [the Census and Statistical Department, Hong Kong, SAR, China]: Daily mortality per person micro data sets from the Census and Statistical department in HK 2015-2020,. Restrictions apply to the availability of these data, which were used under licence for this study. Such data can be obtained via a direct request to the Census Department (with a certain fee).

2) From the HK Observatory Department 2015-2021 for monthly meteorological data:

[Online]. Available: https://www.hko.gov.hk/en/wxinfo/pastwx/mws/mws.htm 3)

From the Department of Health: Monthly legionaries' disease numbers from January 2015 to November 2021 are available. The number of notifiable infectious diseases by month are available from the Department of Health, The Government of the Hong Kong Special Administrative Region. January 2015 - December 2021. [Online]. Available: https://www.chp.gov.hk/en/static/24012.html

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Figures

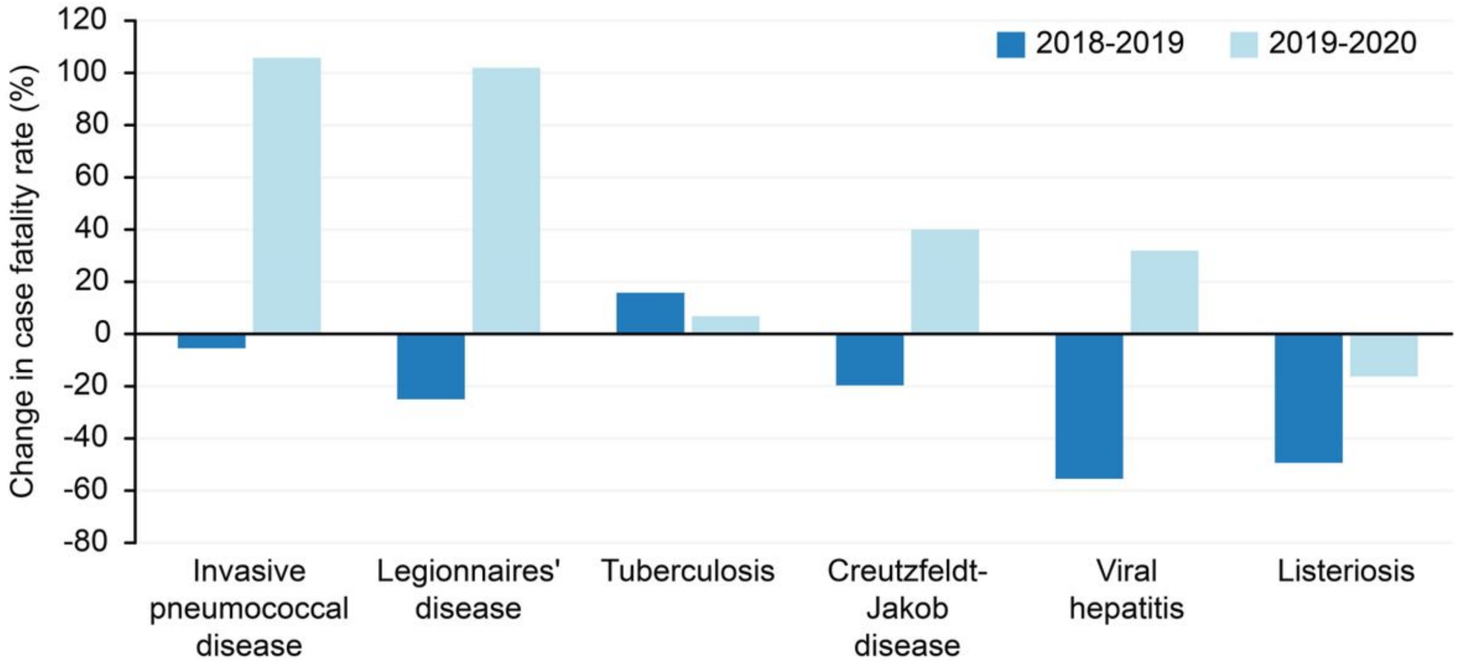

Figure 1

Annual change in the case fatality rate of the six leading causes of death from 2018 to 2020 in Hong Kong.

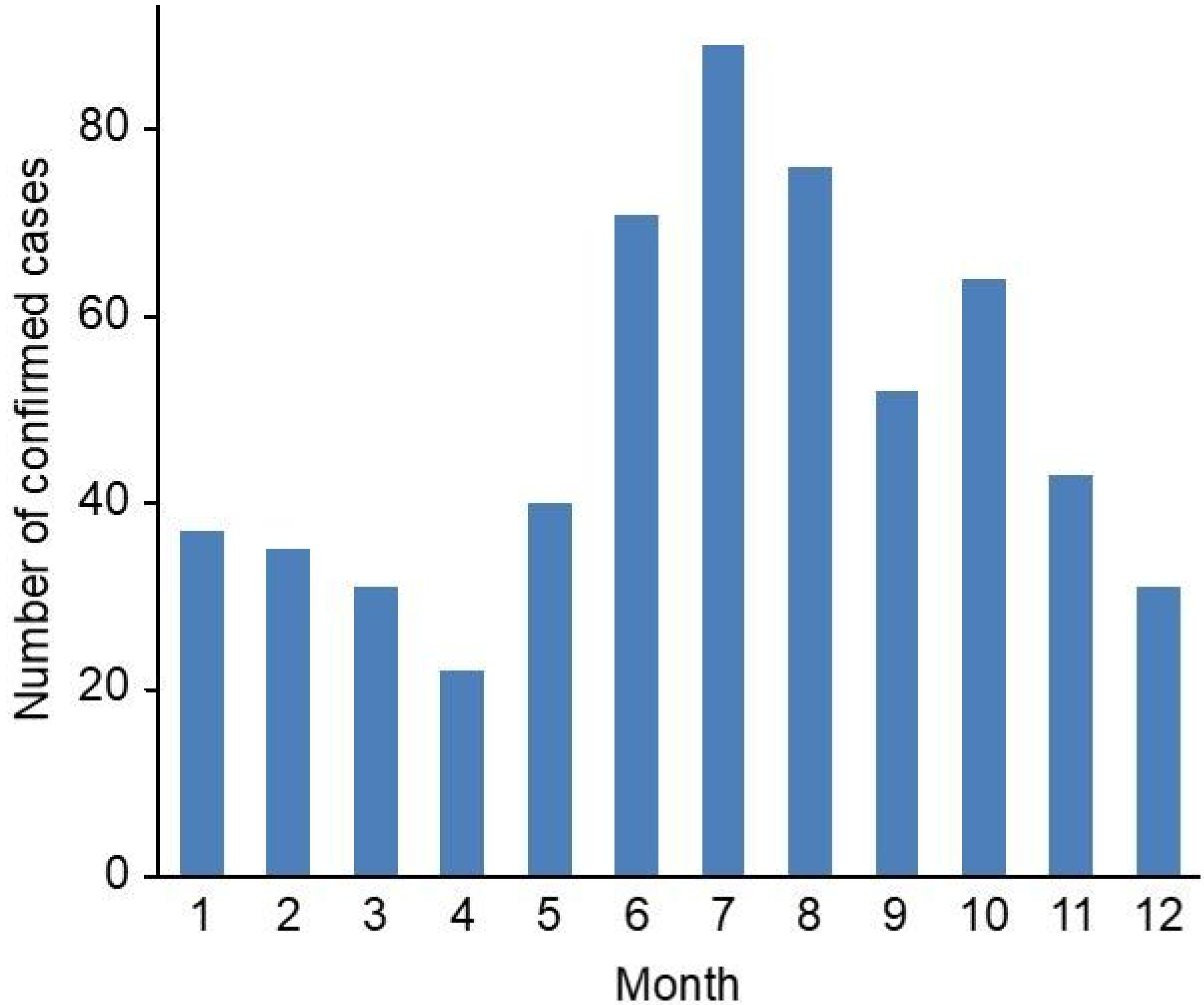

Figure 2

The bar chart shows the accumulated monthly number of confirmed LD cases. We can see that July had the largest accumulated number of confirmed LD cases in HK, 2015-2020.

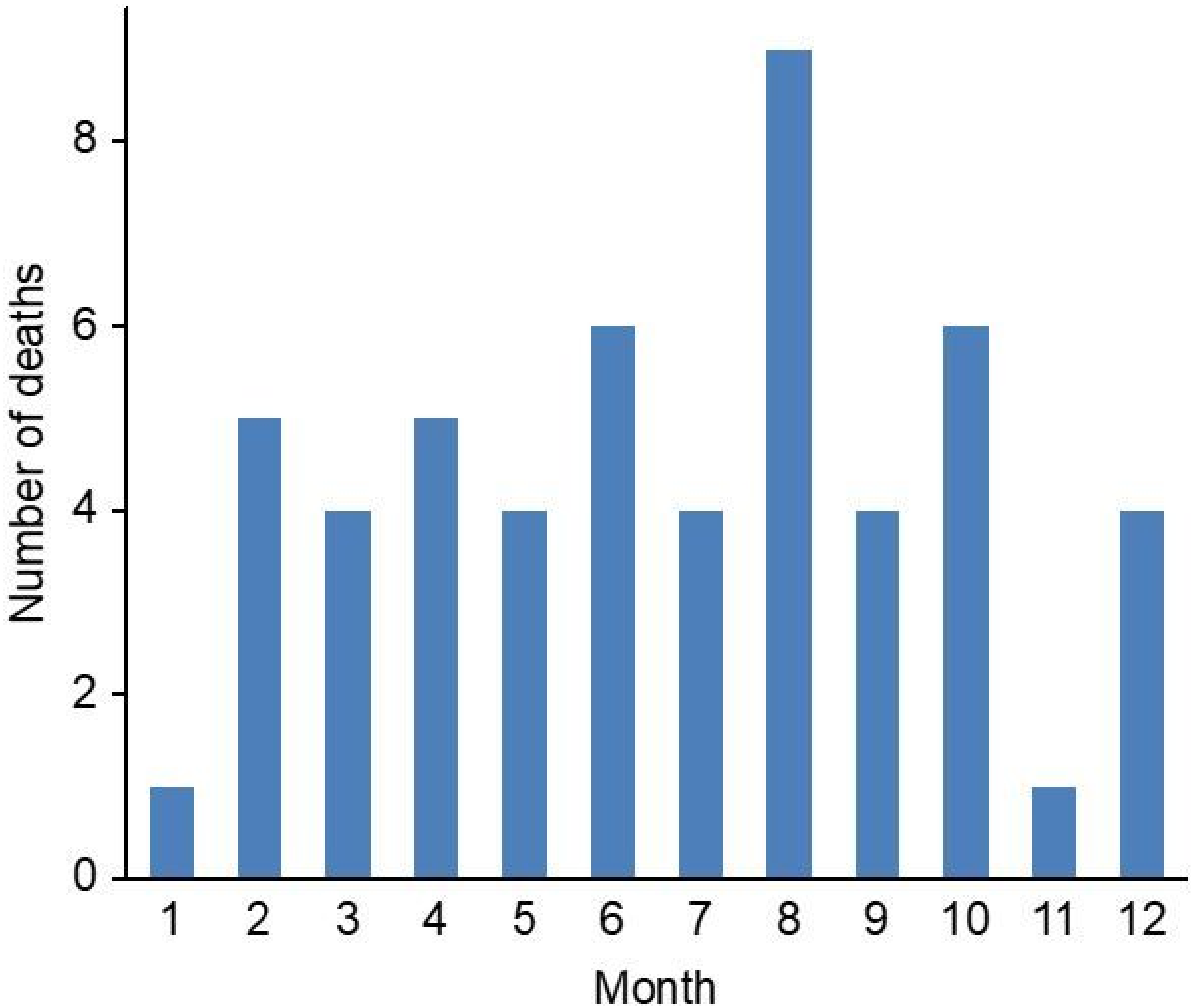

Figure 3

The bar chart shows the accumulated monthly number of LD-related death cases. We can see that August had the largest number of accumulated LD-related deaths in HK, 2015-2020.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementsHKLDv8.3.docx