# Indoor environmental factors and acute respiratory illness in a prospective cohort of community-dwelling older adults

Lefei Han[a], Jinjun Ran[b], Kwok-Hung Chan[c], Yim-Wah Mak[a], Lorna Suen[a], Benjamin John. Cowling[b], Lin Yang[a]*

[a] School of Nursing, the Hong Kong Polytechnic University, Hong Kong Special Administrative Region, People's Republic of China.

[b] School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong Special Administrative Region, People's Republic of China.

[c] Department of Microbiology, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong Special Administrative Region, People's Republic of China.

Running titles: Indoor environments and ARI

*Correspondence to Dr Lin Yang, GH515, School of Nursing, The Hong Kong Polytechnic University, Hung Hom, Hong Kong Special Administrative Region, China. Tel: +852 2766 6398, Fax: +852 2364 9663x

Email: l.yang@polyu.edu.hk

**Key words**: Indoor, temperature, humidity, acute respiratory illness, influenza.

Word count: 3489

This is a pre-copyedited, author-produced version of an article accepted for publication in Journal of Infectious Diseases following peer review. The version of record Lefei Han, Jinjun Ran, Kwok-Hung Chan, Yim-Wah Mak, Lorna Suen, Benjamin John Cowling, Lin Yang, Indoor Environmental Factors and Acute Respiratory Illness in a Prospective Cohort of Community-Dwelling Older Adults, The Journal of Infectious Diseases, Volume 222, Issue 6, 15 September 2020, Pages 967–978 is available online at https://doi.org/10.1093/infdis/jiaa188.

## Abstract

**Background**: Ambient environmental factors have been associated with respiratory infections in ecological studies, but few studies have explored the impact of indoor environmental factors in detail. This study aimed to investigate the impact of indoor environment on the risk of acute respiratory illness (ARI) in a subtropical city.

**Method**: A prospective cohort study was conducted in 285 community-dwelling older adults from December 2016 through to May 2019. Individual household indoor environment data and ARI incidence were continuously collected. A time-stratified case-crossover analysis was conducted to estimate the excess risk (ER) of ARI associated with per unit increase of daily mean indoor temperature, relative humidity (RH) and absolute humidity (AH).

**Result**: In total, 168 episodes of ARI were reported with an average risk of 36.8% per year. We observed a negative association of ARI with indoor AH up to five lag days in cool season, with a 6-day cumulative ER estimate of -9.0% (95% confidence interval: -15.9%, -1.5%). Negative associations between household temperature or RH and ARI were less consistent across warm and cool seasons.

**Discussion**: Lower indoor AH in household was associated with a higher risk of ARI in the community dwelling older adults in Hong Kong during cold season.


Word count: 3489

## Introduction

Ambient temperature and humidity have been associated with the incidence of acute respiratory illness (ARI) 1-3. Most ARI episodes in older populations are caused by respiratory viruses, such as influenza, respiratory syncytial virus (RSV), rhinovirus and others 4, 5. Previous studies have showed that in temperate regions, the activities of respiratory pathogens such as influenza tend to peak when both ambient temperature and humidity are low 6-8. However, in tropical and subtropical regions, the role of ambient environmental factors on respiratory pathogen epidemics, such as influenza and RSV is less consistent and inconclusive 9-11.

One possible reason could be the lack of assessment to indoor environments where 80% of daily time is spent 12. Previous studies have suggested indoor environment may not associate with outdoor environment, especially in extremely hot and cold days 13-17. It could probably explain the inconsistent findings of the effects of ambient environmental factors on influenza seasonal surges. However, few studies evaluated the impacts of indoor environments on respiratory infections 18-20 and none have been conducted in the community settings of tropical and subtropical regions.

We conducted a prospective cohort study in the subtropical city of Hong Kong by recruiting 285 community dwelling people aged 65+ years, with the aim to explore the impact of household environmental factors, including temperature, relative humidity (RH) and absolute humidity (AH), on ARI incidence. We choose older adults as our target population, because they face a higher disease burden associated with respiratory infections and tend to spend more time inside their households than younger populations 21.

## Methods

### Study population

Participants were recruited from the elderly community centers located in Hong Kong Island (HKI) with one million population. Convenience sampling and snowball sampling were adopted to recruit people by following inclusion criteria: 1) aged 65 years or above, 2) living in HKI alone or with family. Participants were excluded if 1) having mental disorder, memory loss, chronic respiratory diseases; and 2) planning to move to another house or travelling for longer than one month, 3) having a scheduled hospitalization during the study period. If there were more than one eligible persons from a household, only one of them was recruited.

### Baseline data collection

A flow chart of data collection is shown in Figure 1. The first round of participant recruitment was conducted from December 2016 to April 2017 and the second round was from January to May 2018. We scheduled the first home visits to collect the individual data of sociodemographic characteristics and lifestyle, including age, sex, education, smoking, outside daily activity, influenza and pneumococcal vaccination history, and diagnosed medical conditions. We also collected the household information, including type of house, floor level, years of living, number of rooms, room size, usage of air-conditioner and (de)humidifier. Supermarket vouchers of HK$ 300 (≈ US$ 38) were given to each participant as token of appreciation.

### Indoor and outdoor environment data

A digital data logger (HOBO Temp/RH 3.5% Data Logger UX100-003, Onset Corporation; Bourne, Massachusetts) was installed on the wall or furniture of the living room to continuously collect indoor temperature and RH at 1-hr intervals during the entire follow-up period. The loggers were fixed at 1.0 - 1.8m height, away from any window, air-conditioners, ventilation systems or heat sources. All the data loggers were calibrated by the manufacturer, to detect temperature from 0°C to 50°C with accuracy of ± 0.21°C, and RH from 25% to 95% with accuracy of ± 5%. The batteries of data loggers could last for at least one year and were replaced at the end of the first-year follow-up. Research assistants made monthly phone calls to participants to ensure the proper functioning of data loggers.

Daily mean outdoor temperature, total amount of precipitation, concentrations of ambient fine particulate matters ($PM_{2.5}$) and ozone ($O_3$) were retrieved from the weather stations and air monitoring stations that geographically closest to each household address. Daily mean outdoor RH was retrieved only from Wong Chuk Hang station due to data availability. Daily mean of indoor and outdoor absolute humidity was converted from temperature and RH using the Clausius-Clayeron equation 22.

**Outcome measurement**

All participants were asked to immediately report acute respiratory symptoms during the follow-up period via either an online report platform or phone calls to research assistants. The dates of symptom onset, over-the-counter medication, outpatient visits or hospitalization for respiratory symptoms (if any) were also collected. To increase the report rate, research assistants reminded them or collected these data via monthly phone calls.

Respiratory virus shedding in the upper respiratory tract normally peak at 1-2 days after illness onset and decrease to undetectable level by 6-7 days 23. When participants reported their symptoms within seven days of disease onset, research assistants collected the nasopharyngeal and throat specimens at their home, following standardized method 24. Specimens were transported at 4°C to the microbiology laboratory of Queen Mary Hospital and cryopreserved at -80°C before testing. Reverse transcription polymerase chain reaction (RT-PCR) tests of influenza virus (type A and B) were conducted by following the laboratory protocol 25. A supermarket coupon of HK$20 (~US$2.6) was given to participants upon each home visit for specimen collection to appreciate their time.

We defined an ARI episode as the onset of at least two of the following acute respiratory symptoms: feverishness, cough, headache, sore throat and myalgia 26. We excluded episodes if participants reported: 1) travel history within 7 days prior to the symptom onset; and 2) the second episode if the interval of two episodes within the same participants were shorter than two weeks. To compare with local ARI activity, weekly influenza-like illness (ILI) consultation rates reported by sentinel general outpatient clinics (GOPC) and laboratory surveillance of respiratory viruses were retrieved from Hong Kong Centers for Health Protection (CHP) [27] and were converted to monthly scale by date weighted calculation.

## Statistical analysis

We used a case-crossover design to evaluate the association between indoor and outdoor environments and ARI incidence. This design has been widely used to assess the short-term effects of environment exposures [28], in which each case serves as their own control. Environmental exposure was compared between the periods prior to the ARI episodes (case) and the periods without ARI episodes (referent). We used a time-stratified approach to select referent period by matching the same days of week within the same month of each ARI episode. This approach was less likely to give biased effect estimates and confounded by temporal trends [29,30].

We used conditional logistic regression models to estimate the odds ratios (ORs) between daily mean temperature, RH, AH and ARI incidence. Spearman correlation coefficients between indoor, outdoor environmental factors and time-varying covariates during case and referent periods were calculated to assess the collinearity between explanatory factors. Highly correlated covariates (r>0.7 or <-0.7) would be entered separately into regression models. According to the criteria, indoor and outdoor environmental variables were analyzed separately (Supplementary Table S1). Under indoor or outdoor models, daily average temperature and RH were entered in models together, whereas daily average AH was analyzed solely (Supplementary Table S2).

We first added only environmental factors into the models to estimate their associations with ARI incidence. Other time-varying variables were subsequently added to calculate the adjusted ORs. Model 2 added precipitation to Model 1. Model 3 further added the variables of outdoor $PM_{2.5}$ and $O_3$ concentrations. The typical models were as follows:

$$\begin{cases} logit(P) = \beta_0 + \beta_{temp} x_{temp,t} + \beta_{RH} x_{RH,t} + \beta_i x_{i,t} & (1.1) \\ logit(P) = \beta_0 + \beta_{AH} x_{AH,t} + \beta_i x_{i,t} & (1.2) \end{cases}$$

where $t$ is the onset date or a referent date; $x_i$ is the time-varying variables, including precipitation, $PM_{2.5}$ and $O_3$; $\beta$ is vectors of coefficients of variables.

We estimated single-lag day effects of environmental factors by adding daily data from the onset date of the ARI episode to the six-preceding day (termed $lag_0$ - $lag_6$), respectively. The cumulative effects up to six lag days ($lag_{01}$ - $lag_{06}$) were accessed by adding a moving average of daily data. Considering Hong Kong normally experiences two peaks of respiratory infections in a year, we stratified the analysis by warm (May - October) and cool seasons (November - April) to investigate the seasonal variation in effect estimates. We choose Model 3 as our final model given precipitation, $PM_{2.5}$ and $O_3$ may modify the effect estimates between environmental factors and ARI [10, 31-33].

We presented the results by using excess risk (ER%) of ARI incidence and their respective 95% confidence intervals (CIs) associated with per unit increase of environmental factors, which were calculated as ER% = (OR – 1) ×100%. We conducted several sensitivity analysis by changing the referent and the daily environment measures to evaluate the robustness of our effect estimates. (Supplement materials)

All analyses were conducted using the package 'survival' in R software (version 3.5.3).

### Ethical consideration

Written consent forms were obtained for all participants at recruitment. The ethics approval was obtained from the Institutional Review Board of Hong Kong Polytechnic University.

## Results

### Descriptive statistics

We recruited 231 participants during December 2016 to April 2017, 60 dropped out by the end of the first-year follow-up. 54 participants were recruited during January to May 2018 and a total of 225 participants were followed up in the second year (Figure 1). Five participants died from non-respiratory diseases during the follow-up period. The average follow-up period was 608 days and the phone call frequency were 10.8 times per year. The median age at recruitment was 77.0 years, ranging from 65.1 to 95.2 years (Table 1). Among the total 285 participants, 81.8% were female, 73.3% with at least one chronic disease, and 36.8% living in public estates. 94.4% of households owned at least one air-conditioners, 26.3% owned one dehumidifier, and none owned a humidifier. All participants were living in apartments of high-rise buildings, with a median living area of 36.2 square meters per household. One-third of the participants were living alone, and the household size ranged from 1 to 6 people. The geographic locations of participated households were showed in Figure 2.

## Seasonal patterns

Both indoor and outdoor environmental factors showed clear seasonal variations during the study period (Figure 3A-C). Daily average indoor temperature was higher than outdoor temperature in cool season, and similar with outdoor temperature in warm season. Daily average indoor RH was lower than outdoor RH. Indoor AH was similar with outdoor AH in cool seasons, while in warm seasons, indoor AH was lower than outdoor AH. We observed variations of daily average indoor temperature, RH and AH across different households. The variations of each indoor parameters were larger in warm seasons as compared to those in cool season (Figure 4). The mean and standard deviation of indoor and outdoor environmental factors during case and referent periods of ARI episodes were shown in Table S3.

## ARI incidence

A total of 168 ARI episodes were reported from 112 participants, including 75 episodes in warm seasons and 93 in cool seasons. There was no difference between the participants with and without ARI at baseline, except that the ARI group were slightly younger (Table 1). Of 68 specimen samples collected, six were positive for influenza A. Monthly numbers of ARI episodes in the elderly cohort and ILI consultation rates of Hong Kong are plotted in Figure 3D. The ARI episodes in the cohort peaked ahead of the ILI consultation rate in 2017-18 but slightly lagged behind in 2019.

### Temperature

Model 1-3 gave similar effect estimates. The effect estimates from model 3 are present from hereafter. During the whole study period, we observed negative associations of indoor temperature with ARI in the single-day lag model, but not in outdoor temperature. The negative associations of indoor temperature were greatest at lag 2 day and were marginally found in cool season rather than warm season (Figure 5A). In the cumulative-lag models, there is no association of outdoor temperature with ARI in cool season, but weakly negative associations of indoor temperature across different lag days were found. In warm season, the indoor and outdoor temperature had negative point estimates but with wide confidence intervals (Figure 6A).

### Relative humidity

The single- and cumulative-lag effect estimates of indoor and outdoor RH on ARI incidence are shown in Figure 5B and 6B. For the whole study period, most point estimates were negative, but none were statistically significant. In cool season, the ERs of indoor and outdoor RH had similar estimates, and both peaked at lag 3 day and the cumulative effects were only observed for outdoor RH at lag 0-5 days (ER: -3.9%, 95%CI: -7.4%, -0.2%). In warm season, the effects diverged at lag 3, with a positive point estimate for indoor RH and null for outdoor RH. The cumulative effects tended to be null beyond lag 0-2 days for indoor RH, but the outdoor estimates were consistently negative across different lag days.

### Absolute humidity

Negative associations between indoor and outdoor AH and ARI incidence were found from lag 2 to lag 5 day in all seasons (Figure 5C). Similar patterns were observed in cool season and the estimates of indoor and outdoor AH both peaked at lag 3 day. In warm season, the point estimates of indoor AH were positive at lag 3 day and the rest were close to null, whereas all the estimates of outdoor AH remained negative. The cumulative effects of indoor and outdoor AH were similar (Figure 6C). In cool season, both two effect estimates were peaked at lag 0-5 days. Indoor AH (ER: -9.0%, 95%CI: -

15.9%, -1.5%) had a larger estimate than outdoor AH (ER: -6.8%, 95%CI: -13.5%, 0.4%). In warm season, the cumulative effects of indoor AH tended to be null beyond lag 0-2 days, but the effect estimates of outdoor AH were consistently negative.

## Discussion

Most previous studies on environmental factors and respiratory infections adopted an ecological study design, which suffered from an unavoidable ecological fallacy. Nearly all of them were focused on outdoor climate factors. However, most people spent more time indoors and the lack of evidence from indoor environments made the previous findings less conclusive. To our knowledge, our study is the first prospective cohort study to investigate indoor and outdoor environment exposure and the risk of ARI at individual level. In our study, participants spent on average 80% of their daily time in their apartments, which was consistent with an early investigation in the US [12]. By using the case-crossover design, we were able to adjust for time independent factors, including time trends, season, demographics, health status, household size *etc*. We found significantly negative associations between indoor AH and ARI, particularly in cool season. Although the associations between indoor temperature/RH and ARI seldom reached significance, the negative effect estimates were consistently observed across different single- and cumulative-lag days models. Our findings fill in an important research gap on the impact of indoor environmental factors on ARI risks in community and household settings.

It remains a great challenge to elucidate the impacts of environmental factors on survival and transmission of respiratory viruses given their multiple transmission routes and nonspecific symptoms [34, 35]. Since lower virus titers in older people make diagnosis challenging [36], we adopted ARI as our case definition. Previous studies reported influenza (21%) and rhinovirus/enteroviruses (21%) were most frequently detected among ARI outpatients [35]. The seasonal pattern of ARI was found consistent with those of influenza activities in community worldwide [37, 38]. There are other definitions available, such as ILI adopted in clinical surveillance, but it showed low sensitivity in older people 5.

We observed large differences in indoor environments across households particular in warm season, which were likely due to the usage of air-conditioners or (de)humidifiers. It may lead to a stable environment and the impact of short-term environmental factors was less likely observed. The findings were consistent with another indoor study about influenza transmission in a tropical region in summer season 18. In contrast, during mild winter in Hong Kong, indoor heating devices are uncommon used. We found indoor AH had small variance across households and was highly correlated with outdoor AH (r=0.96). The correlations between indoor and outdoor environments in cool seasons was higher than theirs in warm seasons. It was different from temperate regions d ue to the wide use of indoor heating devices in winter 17.

We observed negative associations between indoor AH and ARI, which significant from lag 2 to lag 5 days in cool season and peaked on the lag 3 day. These findings coincided with the incubation periods of many acute respiratory virus infections 39. The negative associations of indoor AH were comparable to those of outdoor AH in cool season, but only the associations of indoor AH were statistically significant. The findings were in line with previous studies that suggested ambient AH could be an optimal predictor of influenza incidence if indoor data was absent 7, 9, 20.

We found a weak association between indoor temperature and ARI. The effect estimates were comparable to other studies in tropical and subtropical regions, which reported marginally negative associations between outdoor temperature and laboratory-confirmed influenza 40, 41. Regional heterogeneity in the impacts of outdoor climates on respiratory virus activities have long been noticed. In high latitude regions, temperature had greater effects on respiratory virus compared to low latitude regions 10. In our study, indoor temperature (mean: 25.4°C) was warmer than other studies in tropical regions with outdoor temperature (mean: 22.8 - 25.0°C), and studies in temperate regions (mean: 9.2 – 14.3°C) 42, 43.

The impact of indoor RH was less evident in our study. RH is a relative measurement of humidity that considering the association between temperature and water vapor, inadequate adjustment of temperature may exist. Some study suggested an interactive effect of influenza incidence between temperature and RH [9]. Due to our small sample size, we did not observe such interactive effect (data not shown). We stratified the analysis in cool and warm seasons to explore any potential seasonal difference on the associations of environmental factors. The results showed non-significantly negative association between indoor RH and ARI in cool seasons and less consistent pattern in warm seasons. We noted great intra- and inter-day variations of indoor RH, which may have potential impact on the effect estimations. Future studies may consider the variability of RH on the association with influenza activities.

The negative associations between indoor environments and ARI incidence echo the findings of previous experimental studies. Studies in animals and *in vitro* culture systems found the survival of lipid enveloped virus, such as influenza, RSV, parainfluenza and coronaviruses were greatest in dry environment (i.e. RH 20% or 30%) [6,34,44]. Lower humidity could also exacerbate the progress of droplet evaporation, thereby facilitating the airborne transmission of pathogen-laden droplet nuclei [45]. Temperature can affect the state of pathogens protein and genome (RNA or DNA). Pathogens can live longer at low temperature (i.e. 5°C) [6,34]. In addition, dry and cold environment could slow down mucociliary clearance impair innate antiviral defence and delay repair of respiratory epithelial tissues [46]. However, environmental conditions tested in these experimental studies barely represent the variation of true environmental condition in subtropical and tropical regions. Future studies shall consider a wider range of environmental factors to elucidate the optimal ranges of pathogens survival and transmission.

Some limitations of our study shall be noted. First, linearity assumption in our models may not hold for all environmental factors. Some studies reported a U-shape relationship between temperature (or AH) and laboratory-confirmed influenza in temperate regions [10,47], while others found linear associations in tropical and subtropical regions [2,7]. Nevertheless, we investigated seasonal variation of the effects, and negative associations were consistently observed across seasons. Second, ARI incidences might be underreported, and it remains challenges to obtain specimens at the right timing. We only found six laboratory-confirmed influenza cases (annual rate: 1.3% and test positive rate: 8.8%), which were comparable to other studies in community. Studies in British and Peru reported the rates of laboratory-confirmed influenza were 1.4%-2.9% per-season and influenza positive rates were 6%-9% [48,49]. Third, despite the case-crossover design being able to control time-independent confounding factors, other time varying confounders remain uncontrolled, such as household ventilation and daily activities patterns of participants. These unmeasured factors shall not vary too much between the onset and referent periods. Last, our findings may not be generalizable to younger people or other higher risk groups of ARI because they spend substantial time in working environments and have different contact patterns.

## Conclusions

Our study is among the first to explore the effects of indoor environmental factors on ARI incidence. Lower indoor AH was found associated with ARI incidence, particularly in cool season. The findings could provide important evidence on the mechanism of influenza or other respiratory infections seasonal outbreaks in tropical and subtropical regions. Large-scale studies are warranted to comprehensively understand the impacts of indoor combined with outdoor environments on the risk of influenza infections and may lead to novel interventions to minimize the transmission of respiratory pathogens.

## Notes

**Funding**

This study was supported by RGC Early Career Scheme [F-PP2W] from the University Grants Committee and Departmental General Research Fund from the Hong Kong Polytechnic University [G-YBFW], the Hong Kong Special Administrative Region.

**Acknowledgements**

The authors would like to thank Ka-Long Chan, Nick. P. Lau and Shi Zhao for their assistance in data collection and management. We also thank Dr Xiangqian Lao, Prof Hai Guo, Dr. Kwok-Wai Mui, Dr Lim-Tim Wong and Dr John Yuen for providing technical and lab support. We thank Dr Wan Yang for helpful discussion on manuscript.

**Conflicts of interest**

BJC reports receipt of honoraria from Sanofi Pasteur and Roche. Other authors report no potential conflicts of interest.

**Disclaimer**

The study has been presented in part on the OPTIONS X 2019. 28 Aug – 1 Sep 2019, Singapore. (Poster)

**Contact information**

Correspondence to Dr Lin Yang, GH515, School of Nursing, The Hong Kong Polytechnic University, Hung Hom, Hong Kong Special Administrative Region, China. Tel: +852 2766 6398, Fax: +852 2364 9663x, Email: l.yang@polyu.edu.hk

## References

1. Lowen AC, et al. Roles of humidity and temperature in shaping influenza seasonality. J Virol. 2014;88(14):7692-5.

2. Kamigaki T, et al. Seasonality of Influenza and Respiratory Syncytial Viruses and the Effect of Climate Factors in Subtropical-Tropical Asia Using Influenza-Like Illness Surveillance Data, 2010 - 2012. PLoS One. 2016;11(12):e0167712.

3. Ikaheimo TM, et al. A Decrease in Temperature and Humidity Precedes Human Rhinovirus Infections in a Cold Climate. Viruses. 2016;8(9).

4. Chasqueira MJ, et al. Respiratory infections in elderly people: Viral role in a resident population of elderly care centers in Lisbon, winter 2013-2014. Int J Infect Dis. 2018;69:1-7.

5. Falsey AR, et al. Respiratory syncytial virus and other respiratory viral infections in older adults with moderate to severe influenza-like illness. J Infect Dis. 2014;209(12):1873-81.

6. Lowen AC, et al. Influenza virus transmission is dependent on relative humidity and temperature. PLoS Pathog. 2007;3(10):1470-6.

7. Shaman J, et al. Absolute humidity modulates influenza survival, transmission, and seasonality. Proc Natl Acad Sci U S A. 2009;106(9):3243-8.

8. Shaman J, et al. Absolute humidity and the seasonal onset of influenza in the continental United States. PLoS Biol. 2010;8(2):e1000316.

9. Deyle ER, et al. Global environmental drivers of influenza. Proc Natl Acad Sci U S A. 2016;113(46):13081-6.

10. Tamerius J, et al. Environmental predictors of seasonal influenza epidemics across temperate and tropical climates. PLoS Pathog. 2013;9(3):e1003194.

11. Tang JW, et al. Correlations between climate factors and incidence -- a contributor to RSV seasonality. Rev Med Virol. 2014;24(1):15-34.

12. Graham SE, et al. Developing meaningful cohorts for human exposure models. J Expo Anal Environ Epidemiol. 2004;14(1):23-43.

13. White-Newsome JL, et al. Climate change and health: indoor heat exposure in vulnerable populations. Environ Res. 2012;112:20-7.

14. Quinn A, et al. Indoor temperature and humidity in New York City apartments during winter. Sci Total Environ. 2017;583:29-35.

15. Nguyen JL, et al. The relationship between indoor and outdoor temperature, apparent temperature, relative humidity, and absolute humidity. Indoor Air. 2014;24(1):103-12.

16. Hanley BP, et al. Aerosol influenza transmission risk contours: a study of humid tropics versus winter temperate zone. Virol J. 2010;7:98.

17. Tamerius J, et al. Socioeconomic and Outdoor Meteorological Determinants of Indoor Temperature and Humidity in New York City Dwellings. Weather Clim Soc. 2013;5(2):168-79.

18. Tamerius J, et al. Influenza transmission during extreme indoor conditions in a low-resource tropical setting. Int J Biometeorol. 2017;61(4):613-22.

19. Xie C, et al. Detection of influenza and other respiratory viruses in air sampled from a university campus: a longitudinal study. Clin Infect Dis. 2019.

20. Marr LC, et al. Mechanistic insights into the effect of humidity on airborne influenza virus survival, transmission and incidence. J R Soc Interface. 2019;16(150):20180298.

21. Iuliano AD, et al. Estimates of global seasonal influenza-associated respiratory mortality: a modelling study. Lancet. 2018;391(10127):1285-300.

22. Wallace JM, et al. Atomospheric Science, An Introduction Survey. 2nd Edition ed. Academic, New York2006.

23. Ip DKM, et al. The Dynamic Relationship Between Clinical Symptomatology and Viral Shedding in Naturally Acquired Seasonal and Pandemic Influenza Virus Infections. Clin Infect Dis. 2016;62(4):431-7.

24. CDC. Influenza specimen collection Centers for Disease Control and Prevention, U.S Department of Health and Human Services2007. Available from: https://www.cdc.gov/flu/pdf/freeresources/healthcare/flu-specimen-collection-guide.pdf.

25. Chan KH, et al. Comparison of nasopharyngeal flocked swabs and aspirates for rapid diagnosis of respiratory viruses in children. J Clin Virol. 2008;42(1):65-9.

26. Monto AS, et al. Zanamivir prophylaxis: an effective strategy for the prevention of influenza types A and B within households. J Infect Dis. 2002;186(11):1582-8.

27. The Centre for Health Protection (CHP) of the Department of Health Hong Kong2020 [cited 2020 11 Feb]. Available from: https://www.chp.gov.hk/en/index.html.

28. Maclure M. The case-crossover design: a method for studying transient effects on the risk of acute events. Am J Epidemiol. 1991;133(2):144-53.

29. Janes H, et al. Case-crossover analyses of air pollution exposure data: referent selection strategies and their implications for bias. Epidemiology. 2005;16(6):717-26.

30. Carracedo-Martinez E, et al. Case-crossover analysis of air pollution health effects: a systematic review of methodology and application. Environ Health Perspect. 2010;118(8):1173-82.

31. Wong CM, et al. Modification by influenza on health effects of air pollution in Hong Kong. Environ Health Perspect. 2009;117(2):248-53.

32. Horne BD, et al. Short-Term Elevation of Fine Particulate Matter Air Pollution and Acute Lower Respiratory Infection. Am J Respir Crit Care Med. 2018;198(6):759-66.

33. Ali ST, et al. Ambient ozone and influenza transmissibility in Hong Kong. Eur Respir J. 2018;51(5).

34. Tang JW. The effect of environmental parameters on the survival of airborne infectious agents. Journal of the Royal Society Interface. 2009;6:S737-S46.

35. Fowlkes A, et al. Viruses associated with acute respiratory infections and influenza-like illness among outpatients from the Influenza Incidence Surveillance Project, 2010-2011. J Infect Dis. 2014;209(11):1715-25.

36. Talbot HK, et al. The diagnosis of viral respiratory disease in older adults. Clin Infect Dis. 2010;50(5):747-51.

37. Koul PA, et al. Pandemic and seasonal influenza viruses among patients with acute respiratory illness in Kashmir (India). Influenza Other Respir Viruses. 2011;5(6):e521-7.

38. Bayer C, et al. Internet-based syndromic monitoring of acute respiratory illness in the general population of Germany, weeks 35/2011 to 34/2012. Euro Surveill. 2014;19(4).

39. Lessler J, et al. Incubation periods of acute respiratory viral infections: a systematic review. Lancet Infect Dis. 2009;9(5):291-300.

40. Soebiyanto RP, et al. The role of temperature and humidity on seasonal influenza in tropical areas: Guatemala, El Salvador and Panama, 2008-2013. PLoS One. 2014;9(6):e100659.

41. Yang W, et al. Dynamics of influenza in tropical Africa: Temperature, humidity, and co-circulating (sub)types. Influenza Other Respir Viruses. 2018.

42. Price RHM, et al. Association between viral seasonality and meteorological factors. Sci Rep. 2019;9(1):929.

43. Barreca AI, et al. Absolute humidity, temperature, and influenza mortality: 30 years of county-level evidence from the United States. Am J Epidemiol. 2012;176 Suppl 7:S114-22.

44. Noti JD, et al. High humidity leads to loss of infectious influenza virus from simulated coughs. PLoS One. 2013;8(2):e57485.

45. Wei J, et al. Airborne spread of infectious agents in the indoor environment. Am J Infect Control. 2016;44(9):S102-S8.

46. Kudo E, et al. Low ambient humidity impairs barrier function and innate resistance against influenza infection. Proc Natl Acad Sci U S A. 2019.

47. Azziz BE, et al. Seasonality, timing, and climate drivers of influenza activity worldwide. J Infect Dis. 2012;206(5):838-46.

48. Hayward AC, et al. Comparative community burden and severity of seasonal and pandemic influenza: results of the Flu Watch cohort study. Lancet Respir Med. 2014;2(6):445-54.

49. Tinoco YO, et al. Burden of Influenza in 4 Ecologically Distinct Regions of Peru: Household Active Surveillance of a Community Cohort, 2009-2015. Clin Infect Dis. 2017;65(9):1532-41.

**Table 1. Descriptive characteristics of participating households at the first home visit.**

| Variables | Total (n=285)<br>Median (IQR) or N (%) | Non-ARI (n=173)<br>Median (IQR) or N (%) | ARI (n=112)<br>Median (IQR) or N (%) | ARI vs non-ARI<br>*P* values | Laboratory confirmed influenza (n=6)<br>Median (IQR) or N (%) |
|---|---|---|---|---|---|
| Age, years | 77.0 (71.7, 82.5) | 78.5 (72.3, 83.3) | 75.9 (70.4, 80.5) | 0.002 * | 75.2 (72.6, 76.8) |
| Female | 233 (81.8%) | 144 (83.2%) | 89 (79.5%) | 0.517 | 5 (83.3%) |
| BMI | | | | 0.771 | |
| < 23 | 129 (45.3%) | 77 (44.5%) | 52 (46.4%) | | 3 (50.0%) |
| 23 - 25 | 60 (21.1% | 35 (20.2%) | 25 (22.3%) | | 1 (16.7%) |
| > 25 | 96 (33.7%) | 61 (35.3%) | 35 (31.3%) | | 2 (33.3%) |
| Education | | | | 0.257 | |
| No Education received/Kindergarten | 67 (23.5%) | 47 (27.2%) | 20 (17.9%) | | 1 (16.7%) |
| Primary School | 103 (36.1%) | 62 (35.8%) | 41 (36.6%) | | 1 (16.7%) |
| Secondary School | 47 (16.5%) | 23 (13.3%) | 24 (21.4%) | | 1 (16.7%) |
| High School | 34 (11.9%) | 20 (11.6%) | 14 (12.5%) | | 2 (33.3%) |
| Tertiary Education | 34 (11.9%) | 21 (12.1%) | 13 (11.6%) | | 1 (16.7%) |
| District | | | | 0.834 | |
| Central and Western | 66 (23.2%) | 39 (22.5%) | 27 (24.1%) | | 2 (33.3%) |
| Southern | 71 (24.9%) | 45 (26.0%) | 26 (23.2%) | | 0 (0.0%) |
| Eastern | 132 (46.3%) | 78 (45.1%) | 54 (48.2%) | | 3 (50.0%) |
| Wan Chai | 16 (5.6%) | 11 (6.4%) | 5 (4.5%) | | 1 (16.7%) |
| Family Income ($HKD per month) | | | | 0.807 | |
| Low (<5000) | 158 (55.4%) | 99 (57.2%) | 59 (52.7%) | | 3 (50.0%) |
| Medium (5000-14999) | 85 (29.8%) | 48 (27.7%) | 37 (33.0%) | | 1 (16.7%) |
| High (>15000) | 22 (7.7%) | 14 (8.1%) | 8 (7.1%) | | 2 (33.3%) |
| Unknown | 20 (7.0%) | 12 (6.9%) | 8 (7.1%) | | 0 (0.0%) |
| Type of Housing | | | | 0.695 | |
| Public Estate | 105 (36.8%) | 66 (38.2%) | 39 (34.8%) | | 1 (16.7%) |
| Home Ownership Scheme Flats | 31 (10.9%) | 20 (11.6%) | 11 (9.8%) | | 2 (33.3%) |

| | | | | | |
|---|---|---|---|---|---|
| Private flat or renting house | 149 (52.3%) | 87 (50.3%) | 62 (55.4%) | | 3 (50.0%) |
| Medical condition (at least one) | 209 (73.3%) | 126 (72.8%) | 83 (74.1%) | 0.823 | 6 (100.0%) |
| Smoking history | 29 (10.2%) | 18 (10.4%) | 11 (9.8%) | 1.000 | 2 (33.3%) |
| Influenza vaccination for current season | 199 (69.8%) | 125 (72.3%) | 74 (66.1%) | 0.373 | 2 (33.3%) |
| Pneumonia vaccination [a] | 132 (46.3%) | 83 (47.9%) | 49 (43.8%) | 0.564 | 2 (33.3%) |
| Owning of air-conditioners in home | 269 (94.4%) | 161 (93.1%) | 108 (96.4%) | 0.346 | 6 (100.0%) |
| Owning of dehumidifier in home | 75 (26.3%) | 43 (24.9%) | 32 (28.6%) | 0.624 | 2 (33.3%) |
| Owning of humidifier in home | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1.000 | 0 (0.0%) |
| Household size | | | | 0.773 | |
| 1 | 99 (34.7%) | 58 (33.5%) | 41 (36.6%) | | 1 (16.7%) |
| 2-3 | 170 (59.6%) | 106 (61.3%) | 64 (57.1%) | | 5 (83.3%) |
| 4-7 | 16 (5.6%) | 9 (5.2%) | 7 (6.3%) | | 0 (0.0%) |
| Years of living in house | 25.0 (14.0, 34.0) | 24.5 (15.0, 32.3) | 25.0 (13.0, 35.0) | 0.765 | 23.5 (20.5, 28.8) |
| Total house area ($m^2$) | 36.2 (27.9, 50.2) | 36.5 (27.9, 50.4) | 36.2 (27.9, 48.8) | 0.708 | 47.6 (33.7, 61.4) |
| Area of living room + dining room ($m^2$) | 15.9 (12.8, 18.6) | 17.2 (13.0, 20.4) | 15.9 (12.8, 18.6) | 0.260 | 18.6 (17.5, 18.6) |
| Area of master bedroom ($m^2$) | 7.4 (5.6, 11.1) | 7.4 (5.6, 10.3) | 7.6 (6.0, 11.1) | 0.623 | 9.8 (6.4, 12.8) |
| Daily average hours in home in the past 7 days (h) | 20.0 (18.0, 21.0) | 20.0 (18.0, 21.0) | 20.0 (18.0, 21.0) | 0.447 | 21.2 (19.5, 21.9) |

Abbreviations: ARI, acute respiratory illness; IQR, interquartile range; BMI, body mass index.

* Denotes statistically significant ($p<0.05$) difference between ARI cases and no-ARI cases in two sample Mann–Whitney *U* test or *Chi-square* tests.

[a] Acceptance pneumonia vaccination in the past 10 years at baseline.

## Figure titles and legends

**Figure 1.** Flow chart of data collection and outcomes.

**Figure 2**. Geographic distribution of participating households, weather monitoring stations and air pollution monitoring stations. Weather monitoring stations: Happy Valley (HV), Hong Kong Park (HKP), Shau Kei Wan (SKW) and Wong Chuk Hang (HKS); Weather monitoring stations for precipitation: Happy Valley (HV), Quarry Bay (QB) and Shau Kei Wan (SKW); Air pollution monitoring stations: Central/Western (CW), Central (CN), Causeway Bay (CB), Eastern(EN). The map is the composite of imageries from ArcGIS 10.4.

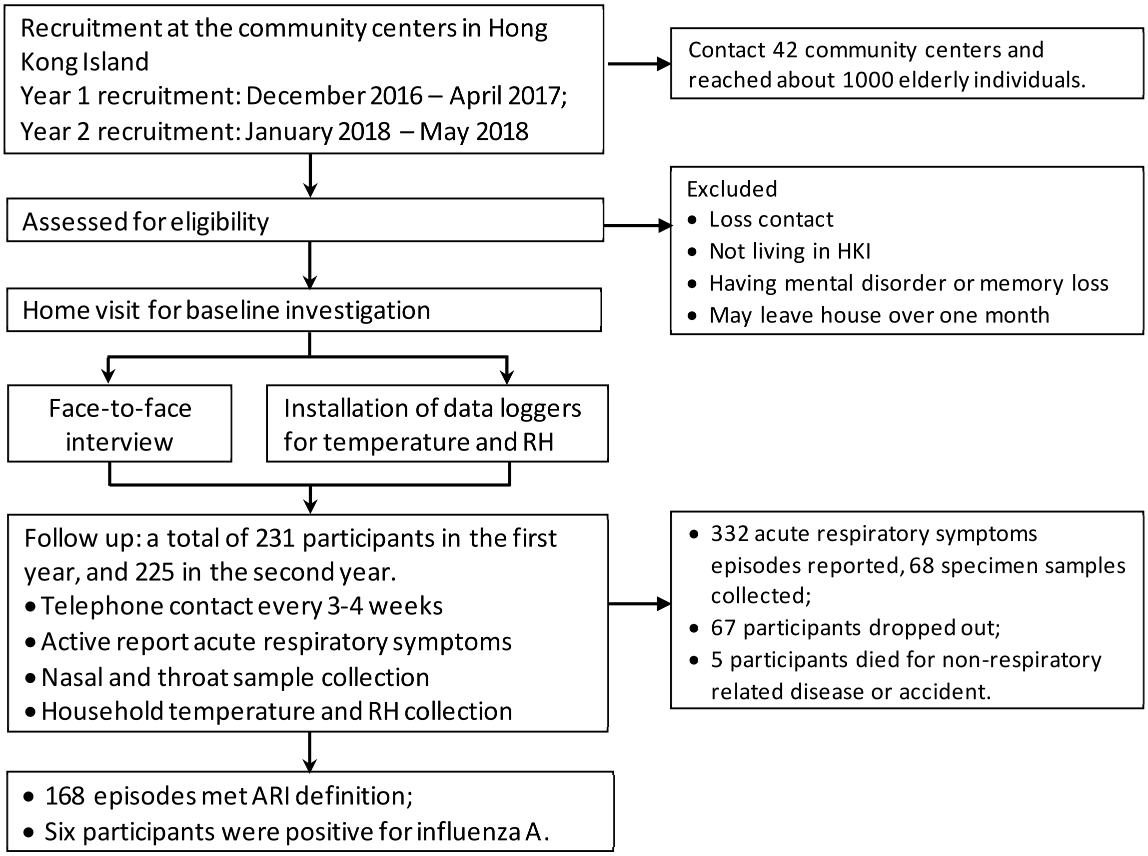
**Figure 3.** Daily average indoor and outdoor (A) temperature, (B) relative humidity, (C) absolute humidity, (D) monthly ARI counts of ARI of the cohort (bar) and ILI consultation rate (per 1,000 consultations) reported by sentinel general outpatient clinics in Hong Kong (line), January 2017 - May 2019.

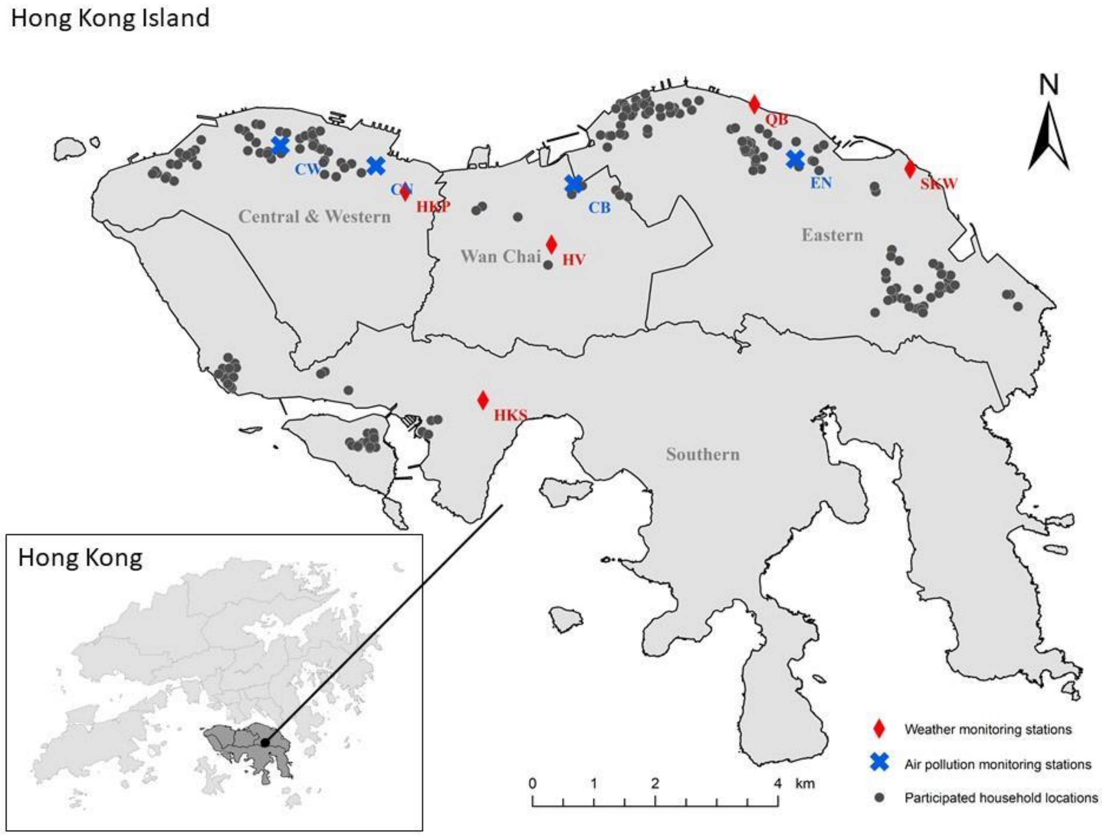
**Figure 4.** The distribution of daily average indoor (A) temperature, (B) relative humidity and (C) absolute humidity across households. The filled contours indicate the 0.5th – 99.5th (light blue), 10th – 90th (blue) and 25th – 75th (dark blue) percentiles of daily indoor mean value among the participated households in each day. Warm seasons are highlighted in grey.

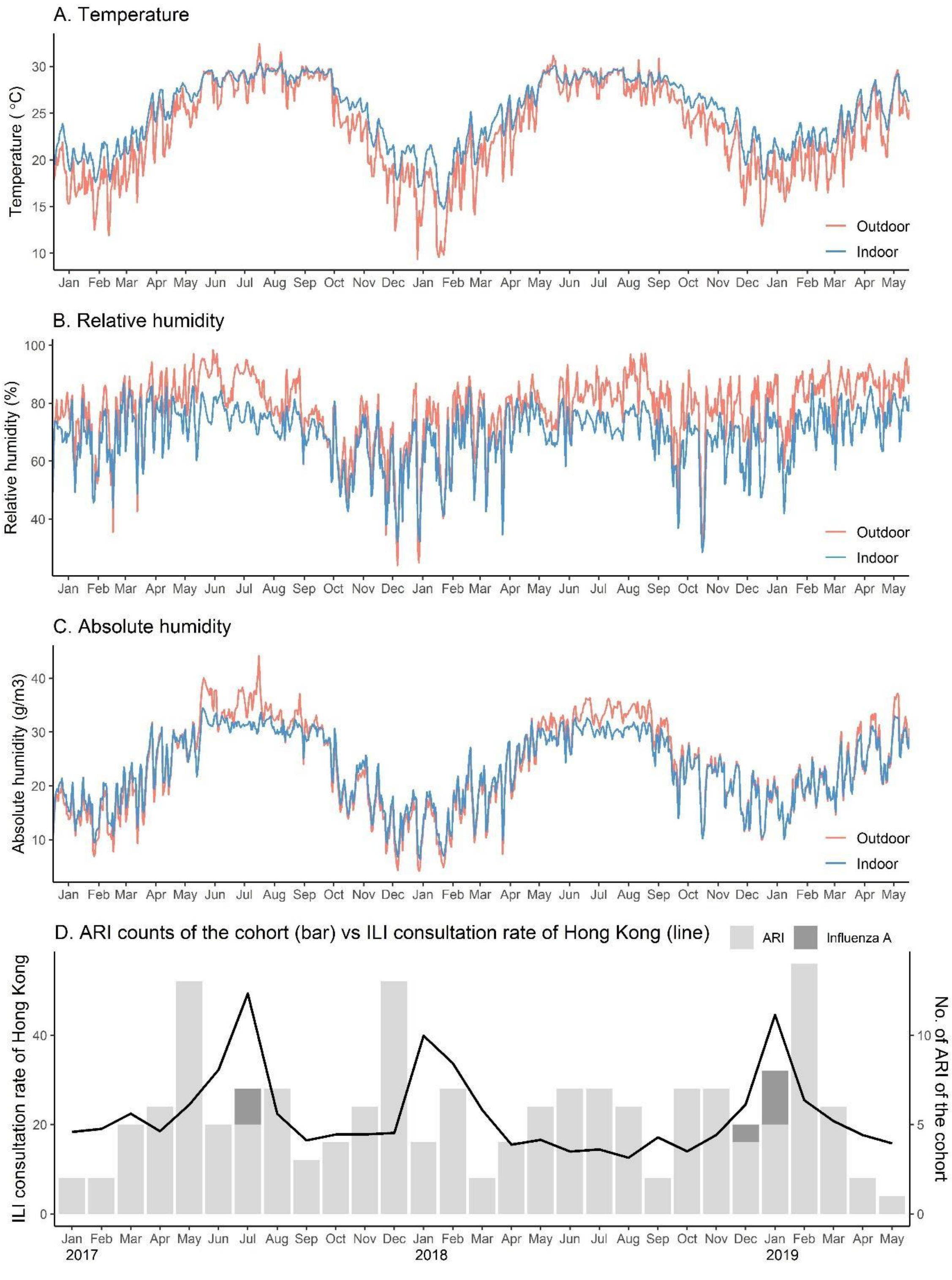
**Figure 5**. Plots of single-lag day effect estimates. Excess risks (95% confidence interval) of ARI incidences associated with per unit increase up to lag six day (0 to 6) are compared for indoor and outdoor (A) temperature, (B) relative humidity and (C) absolute humidity. * Denotes statistically significant ($p<0.05$) difference of the environment exposure between case and referent periods in conditional logistic regression.

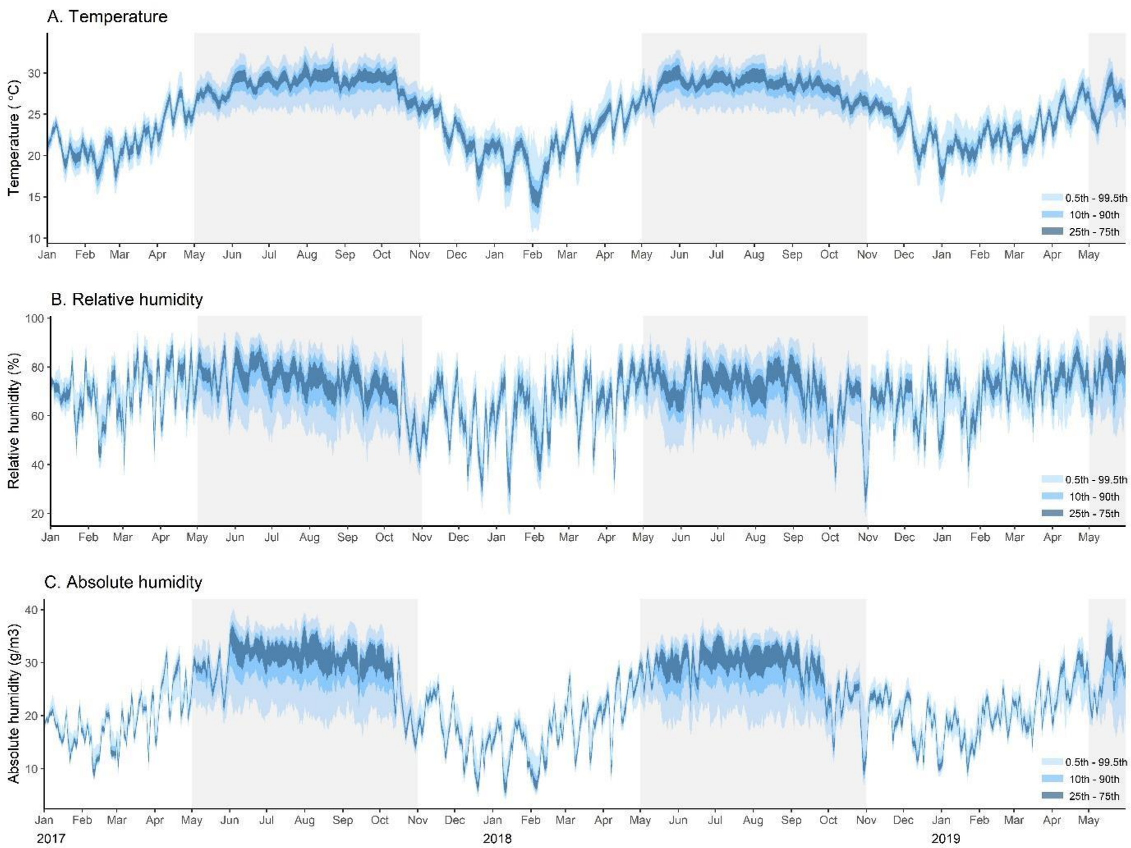
**Figure 6**. Plots of cumulative-lag day effect estimates. Excess risks (95% confidence interval) of ARI incidences associated with per unit increase up to six preceding days (lag01 – lag06), for indoor and outdoor (A) temperature, (B) relative humidity and (C) absolute humidity. * Denotes statistically

significant ($p<0.05$) difference of the environment exposure between case and referent periods in conditional logistic regression.

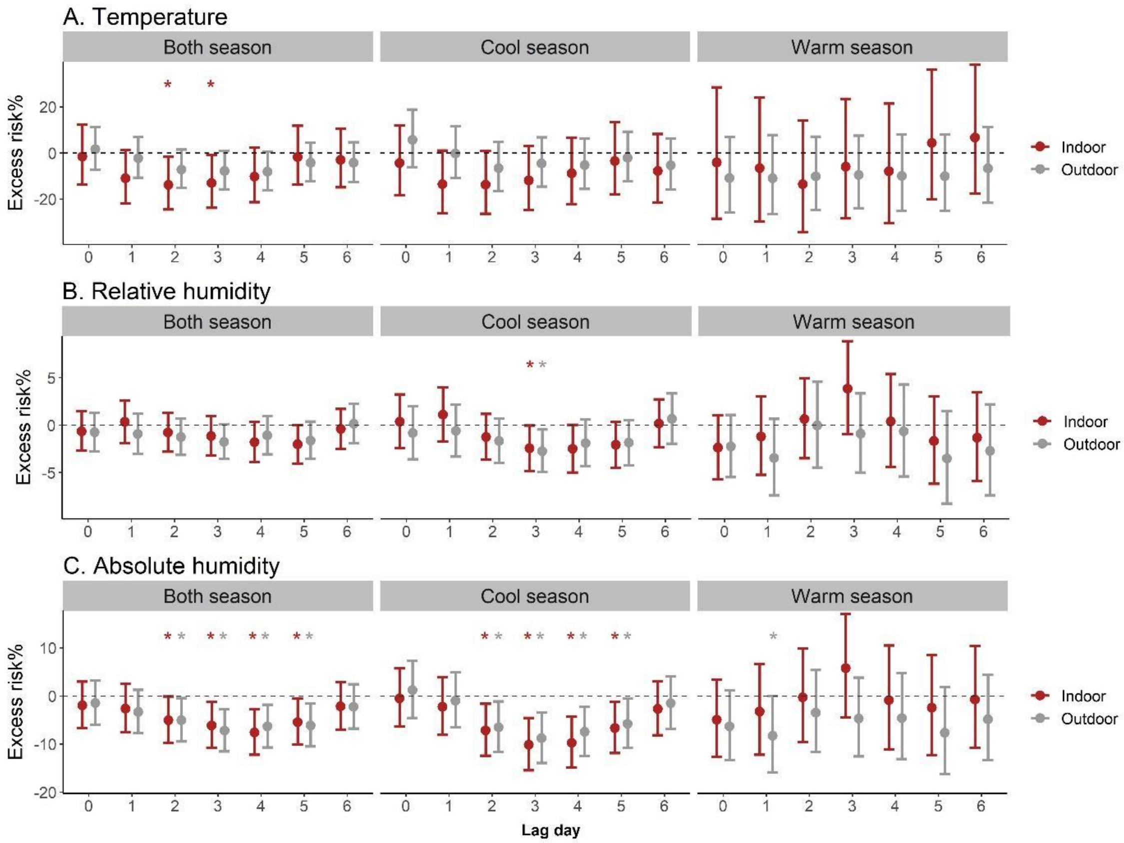

Recruitment at the community centers in Hong Kong Island
Year 1 recruitment: December 2016 – April 2017;
Year 2 recruitment: January 2018 – May 2018
Contact 42 community centers and reached about 1000 elderly individuals.
Assessed for eligibility
Excluded
Loss contact
Not living in HKI
Having mental disorder or memory loss
May leave house over one month
Home visit for baseline investigation
Face-to-face interview
Installation of data loggers for temperature and RH
Follow up: a total of 231 participants in the first year, and 225 in the second year.
Telephone contact every 3-4 weeks
Active report acute respiratory symptoms
Nasal and throat sample collection
Household temperature and RH collection
332 acute respiratory symptoms episodes reported, 68 specimen samples collected;
67 participants dropped out;
5 participants died for non-respiratory related disease or accident.
168 episodes met ARI definition;
Six participants were positive for influenza A.


Hong Kong Island
N
CW
CB
QB
EN
SKW
HV
HKS
Central & Western
Wan Chai
Eastern
Southern
Hong Kong
Weather monitoring stations
Air pollution monitoring stations
Participated household locations
0 1 2 4 km


A. Temperature
Temperature ( °C)
30
25
20
15
10
Outdoor
Indoor
Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar Apr May
B. Relative humidity
Relative humidity (%)
100
80
60
40
Outdoor
Indoor
Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar Apr May
C. Absolute humidity
Absolute humidity (g/m3)
40
30
20
10
Outdoor
Indoor
Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar Apr May
D. ARI counts of the cohort (bar) vs ILI consultation rate of Hong Kong (line)
ARI
Influenza A
ILI consultation rate of Hong Kong
40
20
0
No. of ARI of the cohort
10
5
0
Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar Apr May
2017
2018
2019

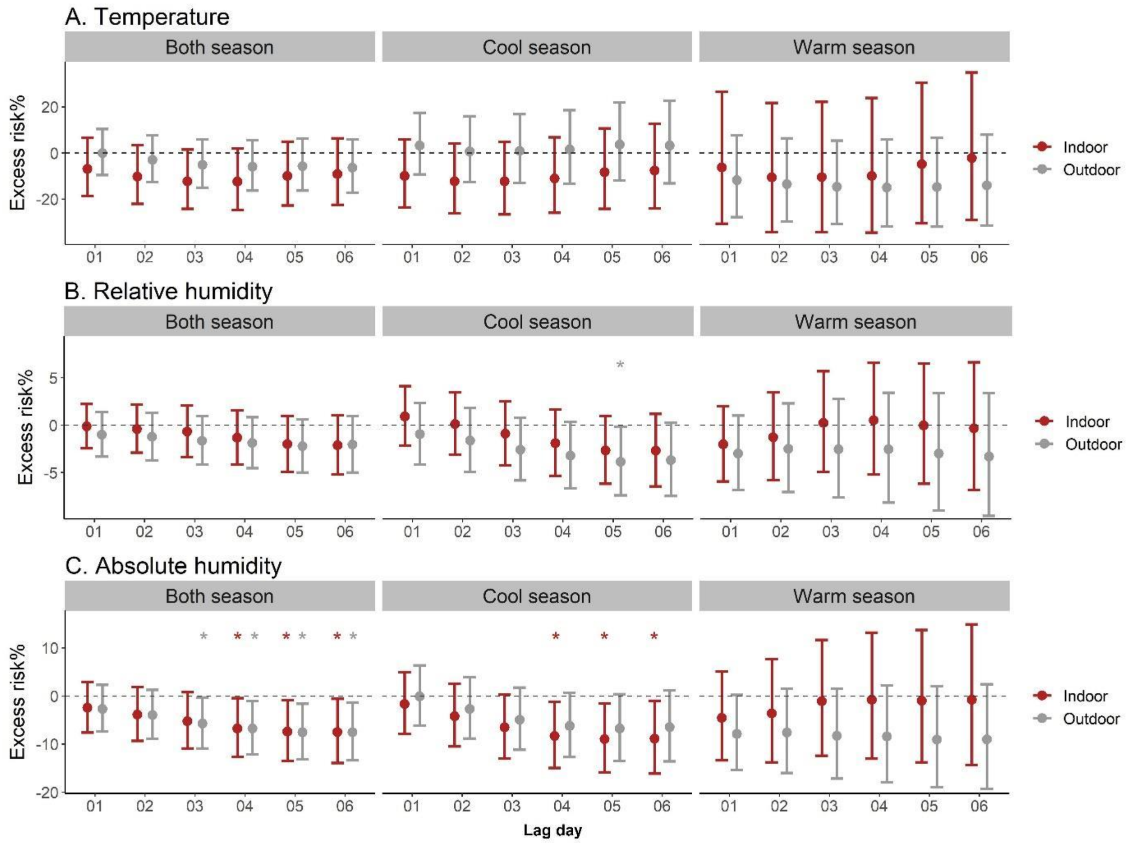

A. Temperature
Temperature (°C)
B. Relative humidity
Relative humidity (%)
C. Absolute humidity
Absolute humidity (g/m3)
0.5th - 99.5th
10th - 90th
25th - 75th
Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar Apr May
2017
2018
2019

470


A. Temperature
Both season
Cool season
Warm season
Excess risk%
20
0
-20
0 1 2 3 4 5 6
B. Relative humidity
Both season
Cool season
Warm season
Excess risk%
5
0
-5
0 1 2 3 4 5 6
C. Absolute humidity
Both season
Cool season
Warm season
Excess risk%
10
0
-10
-20
0 1 2 3 4 5 6
Lag day
Indoor
Outdoor

471

472



A. Temperature
Both season
Cool season
Warm season
Excess risk%
20
0
-20
01
02
03
04
05
06
Indoor
Outdoor
B. Relative humidity
Both season
Cool season
Warm season
Excess risk%
5
0
-5
C. Absolute humidity
Both season
Cool season
Warm season
Excess risk%
10
0
-10
-20
Lag day